Poster Session 2

Cell signalling and cell growth control 2

MP001 INDOXYL SULFATE ACCELERATES APOPTOSIS INDUCED BY SERUM WITHDRAWAL IN RAT AORTIC SMOOTH MUSCLE CELLS

Yoji Inishi[1], Yuri Tanaka[1], Hiroyasu Ishikawa[1], Yoshitsugu Iwakura[1], Haruka Masuda[1], Yasunori Takahashi[1], Nobuhiko Joki[1], Sonoo Mizuiri[2], Hiroki Hase[1]. *[1]Division of Nephrology, Department of Internal Medicine, Toho University Ohashi Medical Center, Tokyo, Japan; [2]Department of Nephrology, Toho University Omori Medical Center, Tokyo, Japan*

Introduction and Aims: Chronic kidney disease (CKD) is a major risk factor for atherosclerotic cardiovascular diseases. Recently it has been reported that apoptosis of aortic smooth muscle cells (AoSMCs) may relate to the atherosclerosis with plaque formation or calcification. Therefore, in the present study, we examined the effect of indoxyl sulfate (IS), which is thought to be one of uremic toxin, for apoptosis in cultured rat AoSMCs.
Methods: The induction of apoptosis was quantitated by assay of the caspase CPP32, which plays a direct role in the execution of cell death. And the activity of SAPK/JNK and P38 MAP kinase, which is known as apoptosis-inducing signal transduction, was assessed by standard immunoblot using phospho-specific antibodies.
Results: Twenty five μg/ml of IS, which is compatible with the concentration of IS in the serum of end-stage renal failure patients, induced 3.9±2.7 -fold increase in the caspase CPP32 activity responding to serum withdrawal for 12 hours. The blockade of organic anion transporter (OAT) by 0.5mM probenecid (Pb) abolished the effect of IS on the apoptosis in AoSMCs (relative increase in the caspase CPP32: Pb-, IS-; 1±0.1, Pb-, IS+; 2.4±0.2, Pb+, IS-; 0.9±0.1, Pb+, IS+; 1.2±0.1). Indoxyl sulfate activated SAPK/JNK in AoSMCs that was significantly elevated by 30 minutes and sustained for over 2 hours, although it did not affect the activation of P38 MAP kinase.
Conclusions: These results indicate that IS accelerates apoptosis induced by serum withdrawal in rat AoSMCs, which is mediated by cellular transport of IS via the OAT and may also be related to the activation of SAPK/JNK pathway. The induction of apoptosis by the accumulation of IS in blood due to CKD may play an important role in atherosclerotic lesion formation.

MP002 THE ROLE OF DYNAMIN-RELATED PROTEIN 1, A MEDIATOR OF MITOCHONDRIAL FISSION, IN THE TOXICITY INDUCED BY CYCLOSPORIN A IN LLC-PK1 CELLS

Gabriel de Arriba[1], Sara Ramirez-Rubio[2], Selma Benito-Martinez[2], Miryam Calvino-Fernandez[2], Maria Maiques-Camarero[2], Claudia Rodriguez-Pacho[2], Trinidad Parra-Cid[2]. *[1]Nefrología., H. Universitario Guadalajara, Dpto Medicina. UAH, Guadalajara, Spain; [2]Unidad de Investigación, H. Universitario de Guadalajara, Guadalajara, Spain*

Introduction and Aims: Mitochondria are implicated in apoptotic processes observed in several pathological alterations and in drug treatments. Mitochondrial changes occurring are both structural (lipid peroxidation, inner membrane permeabilization, tubular network fragmentation) and functional (electronic transport chain disruption, loss of membrane potential) which leads to releasing of proapoptotic molecules to cytosol. One of the triggering factors of these alterations is oxidative stress, being toxic effects of Cyclosporine A (CsA) related to ROS production and apoptosis.
In healthy cells, fusion and fission regulates mitochondrial morphology. Drp1 is a dynamin-related protein that mediates outer mitochondrial membrane fission. Upon induction of apoptosis, Drp1 translocates from the cytosol to mitochondria and can contribute to mitochondrial membrane fission.
Our aim was to analyze the mechanisms involved in cellular apoptosis induced by CsA in renal epithelial tubular cells (LLC-PK1) and evaluate the role Drp1 in this process.
Methods: LLC-PK1 cells were treated with CsA (10^{-6}M 24h) with and without VitE pre-addition (10^{-4}M 30'). We analyzed the permeability transition mitochondrial pore opening (PTP, calcein-AM labelling), cytochrome c release (anti-citochrome c IgG), cellular apoptosis (Alexa fluor-488-Annexin V and propidium iodide) and mitochondrial fission by confocal microscopy. We also studied the expression of Bax, Caspase 3 and Drp-1 protein (western blot).
Results: CsA caused the opening of PTP, release of mitochondrial cytochrome c and increase the rate of apoptotic/viable cells. Furthermore, CsA disrupted mitochondrial network rendering a fragmented phenotype. All these effects were inhibited when cells were preincubated with the antioxidant Vit E.
CsA also increased the expression of Bax and Caspase 3. Vit E inhibited the Bax increase but not modified the Caspase 3.
Finally, CsA increased the expression of Drp-1 and this increase was inhibited in cells pretreated with Vit E.
Conclusions: CsA caused apoptosis in LLC-PK1 cells. Our results suggest that in this effect are involved several proteins like Bax and Drp1, that can modify mitochondrial structure and function. CsA induced PTP formation and release of cytocrhome c from mitochondria. This event can trigger Caspase activation and apoptosis.
As Vit E pretreatment of cells can avoid apoptosis and inhibit the increase of Bax and Drp1 expression, we suggest that reactive oxygen species are implicated in apoptosis induced by CsA.

MP003 ★ THE AQUARETIC AGENT SATAVAPTAN (SR121463) EXERTS AN ANTI-PROLIFERATIVE EFFECT ON RENAL CANCER: ROLE OF VASOPRESSIN RECEPTOR-2 (V2r)

Davide Bolignano, Giuseppe Coppolino, Maria Antonietta Medici, Maria Teresa Sciortino, Michele Buemi. *Department of Internal Medicine, University of Messina, Messina, Italy*

Introduction and Aims: Vasopressin (AVP) is a hormone with anti-diuretic properties that also acts as a vasoconstrictor and neurotransmitter. Recent evidences suggest that AVP is also involved in cell growth of several neoplasias. Vasopressin V2 receptors (V2r) have been found to be over-expressed on the cell surface of pulmonary, pancreatic and mammary cancers. Through the activation of these receptors, AVP exercises a strong proliferative effect which, therefore, can be prevented by the administration of selective V2r antagonists, the so-called "aquaretic agents". Until now, any study have analyzed if AVP could have these effects on renal cancer too, considering that the kidney is physiologically an important target of this hormone. After all, AVP plays a fundamental role, through the activation of V2r, in the development and progression of ADPKD, a condition sharing several features with neoplasia. For these reasons, using a culture model, our study explored the question of whether human renal carcinoma cells express V2r and whether receptor activation modulates their proliferation.
Methods: Two human renal carcinoma cell lines, Caki-2 and A498, were examined. Hek-293 and CHO were used respectively as positive and negative control cells for V2r expression. The presence of V2r and its localization on cell surface was investigated by immunofluorescence techniques using specific anti-V2r antibodies. A RT-PCR was further employed to confirm the cellular expression of specific V2r mRNA. Desmopressin (dDAVP), an AVP-derived peptide with high V2r agonist activity, was added to cellular medium alone (1 nM) and in combination with the aquaretic agent Satavaptan (*SR121463B*, selective V2r antagonist; 1 nM). Cell proliferation was then assessed at 24, 48 and 72 hours respectively, using a hemacytometer.
Results: Immunofluorescence showed that CAKI-2 and A498 cells notably express the V2r on their surface: this presence was further confirmed by RT-PCR which have detected the synthesis of specific V2r mRNA. Administration of dDAVP induced an evident growth in both CAKI-2 (+18%, +24% and +28% from starting count at 24, 48 and 72 h respectively; $p<0.03$) and A498 (+14%, +18% and +23% from starting values at 24, 48 and 72 h respectively; $p<0.05$) cell lines. However, this proliferative effect was completely prevented by the simultaneous addition of the V2r antagonist Satavaptan to the medium.
Conclusions: Our study shows for the first time that renal cancer may

effectively synthesize and express the V2r, as previously observed for other extra-renal tumours. Furthermore, AVP exerts *in vitro* a strong proliferative effect by acting on this receptor, as the V2r blockage by Satavaptan is able to completely prevent the cellular growth. A validation of our findings with *in vivo* models is required to ascertain if the eventual presence of V2r could influence the clinical malignance of this neoplasia. In this point of view, it could also be proposed a new therapeutical application of aquaretic agents in the treatment of renal cancer, similarly to what successfully described in the therapy of ADPKD.

MP004 SOS1 DOWN-REGULATES EXTRACELLULAR MATRIX SYNTHESIS AND PROLIFERATION IN EMBRIONARY FIBROBLASTS THROUGH ERK AND AKT ACTIVATION

Fuentes-Calvo Isabel[1], Ana M. Blazquez-Medela[3], Esteller Alejandro[1], Santos Eugenio[2], Lopez-Novoa Jose Miguel[1], Martinez-Salagado Carlos[3]. *[1]Fisiologia y Farmacologia, Universidad de Salamanca, Salamanca, Spain; [2]Centro de Investigación del Cancer, Universidad de Salamanca, Salamanca, Spain; [3]Unidad de Investigación, Hospital Universitario de Salamanca, Salamanca, Spain*

Introduction and Aims: Fibrotic diseases are characterized by excessive production and deposition of extracellular matrix and an increase in cell proliferation. Transforming growth factor beta 1 (TGF-beta 1) is a profibrotic protein closely related with Ras signalling pathways. Ras proteins are small GTPases activated in response to growth factors stimulation which control different pathways in cell signalling cascades. The activity of Ras proteins is tightly controlled by switching between the GDP- and GTP-bound states. Sos1 is the main guanine nucleotide exchange factor that activates Ras. Studies from our laboratory have demonstrated a marked increase in renal Ras activation and in the expression of the phosphorylated forms of both Ras effectors, Erk1/2 and Akt, in a mouse model of tubulointerstitial fibrosis. We have also shown that there is a higher expression of extracellular matrix proteins as well as an increased expression of phospho-Erk and phospho-Akt in H- and N-Ras knockout (KO) fibroblasts. Thus, we have studied the role of Sos1 and the participation of phospho-Erk and phospho-Akt in TGF-beta 1-induced ECM synthesis and proliferation.
Methods: We have performed *in vitro* studies with embrionary fibroblasts from KO mice for Sos1 (*sos1*$^{-/-}$), and wild type fibroblasts (wt). ECM synthesis was analyzed by evaluating the expression of fibronectin and collagen type I by western blot. Fibroblast proliferation was measured by nuclei staining with crystal violet. Erk and Akt expression were also evaluated by western blot. Ras activation was determined by Ras pull-down assay with Raf.
Results: Ras activation is notably increased in *sos1*$^{-/-}$ fibroblast. Fibronectin and collagen type I expression are much bigger in *sos1*$^{-/-}$ fibroblasts than in wt fibroblasts, both in basal conditions and after TGF-beta 1 treatment. The absence of Sos1 do not induce significant differences in TGF-beta 1-induced proliferation. Both phospho-Erk and phospho-Akt expression are increased in *sos1*$^{-/-}$ fibroblasts in basal conditions; TGF-beta 1 increases phospho-Akt expression, but reduces phospho-Erk expression in *sos1*$^{-/-}$; phospho-Akt inhibition with LY294002 reduces ECM proteins expression and proliferation in *sos1*$^{-/-}$ fibroblasts; phospho-Erk inhibition with U0126 also reduces TGF-beta 1-induced fibronectin expression and proliferation, but it shows no effect on collagen type I expression in *sos1*$^{-/-}$ fibroblast.
Conclusions: These studies with Sos1 KO fibroblasts show that Ras may down-regulate TGF-beta 1-induced ECM synthesis and proliferation, and that both Akt and Erk signalling pathways participate in these increases.

MP005 PPARα, PPARγ AND COX-2 ARE MODULATED BY FATTY ACIDS IN HUMAN MESANGIAL CELLS

Giovanna Priante[1], Estella Musacchio[2], Bruno Baggio[1]. *[1]Nephrology Unit, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy; [2]Clinca Medica I, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy*

Introduction and Aims: Several evidence suggest a close relationship between polyunsaturated fatty acids (PUFAs) and renal inflammation and fibrosis, which are crucial stages in chronic kidney disease. Recent studies conducted in our laboratory indicate that the exposition of cultured HMC to different PUFAs had specific, chemical structure-related, effects on the gene expression of some pro-fibrotic factors such as TGFb, FN, CTGF and COLIV. *In vivo* and *in vitro* studies suggest that *n*-3 fatty acids could exert their anti-inflammatory action by reducing the generation of prostaglandins derived from Arachidonic Acid (AA) or directly through specific nuclear hormone receptors and ligand activated transcription factors that regulate target gene expression enzyme such as the peroxisomal proliferator-activated receptors (PPARs). It has been in fact demonstrated that activation of PPARs inhibits the production of pro-inflammatory factors. Moreover, in response to injury, inflammation, and/or cellular activation many tissues or cells including mesangial cells express the highly inducible gene COX-2.
Methods: To investigate the actual mechanisms by which PUFA can interfere with some stages in the development of renal fibrosis, we studied the effects of the n-3 fatty acid eicosapentaenoic acid (EPA) and the n-6 fatty acid AA on PPARα, PPARγ and ciclo-oxigenase 2 (COX-2) gene expression in primary cultures of non tumoral human mesangial cells (HMC). Fatty acids were used at a concentration of 50 μM for 1, 3, 6, 12, 24, 48 hours. The RNA expression was assayed by kinetic comparative RT-PCR using 18S RNA as the standard reference.
Results: Both AA and EPA stimulated PPARα and PPARγ expression. The treatment with EPA was more effective than that with AA (1.9 vs 1.6 fold stimulation over basal for PPARγ; 1.8 vs 1.5 for PPARα). The peak was reached after 6 hrs of treatment and expression levels returned to basal after 48 hrs. The simultaneous exposure of HMC to AA and EPA resulted in a further increase in the expression of both PPARs (2.3 fold stimulation over basal for PPARγ; 1.9 for PPARα) at the same time point. AA up-regulated COX-2 gene expression (1.5 fold stimulation over basal) while on the contrary EPA had no effect on this gene.
Conclusions: These preliminary results are in agreement with the hypothesis that n-3 fatty acids act directly on PPARs while the action of AA is mediated by COX-2 activation and the consequent PGJ2 production. These data thus represent a further insight in the mechanism of action of fatty acids at renal cell level. The opposite effects of EPA and AA on COX-2, considered as a pro-inflammatory enzyme and a chief target for the treatment of inflammatory diseases activation, confirm the possible beneficial influence of n-3 in the inflammation process.

MP006 INFLUENCE OF RAPAMYCIN ON PODOCYTE FUNCTION

Beate Vollenbroeker, Britta George, Hermann Pavenstaedt, Thomas Weide. *Department of Internal Medicine D, University Hospital Muenster, Muenster, Germany*

Introduction and Aims: The administration of the immunosuppressive drug rapamycin (Sirolimus, Rapa) after organ transplantation causes proteinuria in several patients. The molecular details of these medical intricacies are still poorly understood, although there are some hints supporting the hypothesis that rapamycin administration influences the biological function of glomerular podocytes. Rapamycin acts as an inhibitor of the Serin/Threonin kinase mTOR (mammalian target of rapamycin) which is involved in several signal transduction pathways. Therefore mTOR inhibition results in decreased cell proliferation and translational activity primarily avoiding the proliferation of rapidly splitting cells. Within this work we investigated the function of mTOR in postmitotic and terminally differentiated cells such as podocytes and how rapamycin might decrease podocytes function.
Methods: In order to get deeper insight how mTOR acts in podocytes we established an in vitro cell culture model system using human immortalized podocytes. We treated these cells with rapamycin or vehicle und used this approach to study differential gene expression on mRNA level using real-time PCR techniques via TaqMan array and on protein level using western blot and immunofluorescence techniques.
Results: Rapa treatment influences the expression and phosphorylation levels of mTOR associated proteins in podocytes. As expected, the phosphorylation of proteins downstream like p70s6k and 4E-BP1 is inhibited. Interestingly Rapa also has an influence on the phosphorylation of mTOR itself and the expression of raptor and rictor as well as proteins playing a key role in podocyte function. Furthermore Rapa causes a changes of the actin cytoskeleton in podocytes.
Conclusions: Rapa treatment has consequences on the function of postmitotic and terminally differentiated podocytes. The changes of the actin

cytoskeleton might be a first hint for an effacement of the podocyte foot processes, which would directly explain development of proteinuria. In a next step we will further analyze possible links between mTOR pathway and actin organization.

MP007 HYPERGLYCEMIA CAUSES ACCELERATED SENESCENCE AND TELOMERE SHORTENING IN PRIMARY HUMAN PROXIMAL TUBULAR CELLS (PTECs) STIMULATED TO DIVIDE IN VITRO

Daniela Verzola[1], Vanessa Procopio[1], M.Teresa Gandolfo[1], G.F. Gaetani[2], Annamaria Ferraris[2], Rosa Mangerini[2], Barbara Villaggio[1], Paolo Traverso[3], Annamaria Famà[1], Giacomo Deferrari[1], Giacomo Garibotto[1]. *[1]Department of Internal Medicine-Nephrology Division, University of Genoa, Genoa, Italy; [2]Dipartimento di Oncologia, Biologia e Genetica, University of Genoa and Istituto per la Ricerca sul Cancro, Genoa, Italy; [3]Urology Division, Ospedale S. Martino, Genoa, Italy*

Introduction and Aims: Cell senescence is characterized by an irreversible growth arrest and functional and morphologic changes, including enhanced expression of senescence markers, such as SA galactosidase (SA-β-gal), and different sets of genes, including negative regulators of the cell cycle. It has been theorized that the high frequency of end-stage renal disease in the elderly results from an interaction between cell senescence and age-associated diseases, such as hypertension and type 2 diabetes mellitus, that could hinder the limited ability of aged kidney to repair, and maintain epithelial functions.
In this study, we tested the effects of high ambient glucose on cellular senescence and telomere lenght in PTECs.
Methods: PTECs were cultured for 5,10 and 15 days in normal-glucose (NG 5.5 mM), high-glucose (HG 30 mM) or 24.5 mM mannitol (osmotic control). Proliferative capacity was measured by nuclear incorporation of 5-bromo-2-deoxy-uridine (BrdU). SA-b-gal activity was detected as a senescence marker. To investigate the role of the cell cycle check points regulators in controlling the HG-induced senescence, we evaluated by Western Blot the activation of the two pathways potentially implicated in senescence: the p53/p21 pathway and the $p16^{INK4a}$/ retinoblastoma pathway. Telomere length was assessed by Southern Blot.
Results: Passaged PTECs under HG presented a limited life span (or replicative senescence), with 8-fold decrease in BrdU incorporation ($p<0.001$) and growth-arrest ($p<0.001$ vs NG) after 15 days.Replicative senescence was associated with a marked increase in the SA b-Gal (+ 91% $p<0.03$). Early passage PTECs contained barely detectable levels of $p16^{INK4A}$ protein. HG treatment elicited an up regulation of $p16^{INK4A\ and\ Rb}$, while p53 and p21 were not expressed. Mean telomere (TRF) lengths decreased from 11.25 to 8.92 as an effect of replicative senescence ($p<0.05$ vs basal); in addition mean TRF decreased further to 4.39 kb in cells under HG ($p<0.05$ vs NG).
Conclusions: In conclusion, prolonged incubation of PTECs with HG resulted in a duration-dependent induction of a variety of senescent phenotypes, such as changes in cell morphology, decreases in proliferative rate, increased SA-b-Gal and $p16^{INK4A}$ and Rb protein up-regulation. In addition, HG induced senescence was associated with telomere shortening and activation of both the p16 telomere-dependent pathway and the p16/pRB-senescent pathway lending support to the novel finding of telomere-dependent tubule cell senescence in type 2 diabetic nephropathy. These data show that hyperglycaemia boosts common pathways involving somatic cell senescence in tubule cells and suggest that diabetic nephropathy can be regarded as a premature aging syndrome.

MP008 ANGIOGENIC POTENTIAL DIFFERS BETWEEN EPOETIN DELTA AND DARBEPOETIN ALFA

Carmel McVicar, Tom A. Gardiner, Alan W. Stitt. *Centre for Vision Science, Queen's University, Belfast, Northern Ireland, United Kingdom*

Introduction and Aims: Erythropoietin (EPO) has been shown to promote angiogenesis in experimental systems. This physiological response may be linked to activation of the EPO-receptor and/or CD 131 (β-common chain) expressed on microvascular endothelial cells. Erythropoiesis-stimulating agents (ESA) might therefore also be able to modulate angiogenesis. In the clinical setting, increased angiogenesis could be beneficial in situations such as wound repair and microvascular remodelling following infarction or ischaemia. Conversely, ESAs could be detrimental in clinical situations in which enhanced capillary formation is not beneficial, such as tumour neovascularization, rheumatoid arthritis and proliferative retinopathy.
Methods: We investigated the angiogenic activity of human-cell-derived epoetin delta (Dynepo®, Shire plc) and hyperglycosylated darbepoetin alfa at similar, broad concentration ranges (epoetin delta: 0.1–100 IU/mL; darbepoetin alfa: 0.0005–0.5 μg/mL; based on the conversion factor: 1 μg darbepoetin alfa = 200 IU epoetin delta). Angiogenic potential was assessed in primary isolates of human dermal microvascular endothelial cells (HDMECs) and the HMEC-1 endothelial cell line. In addition to assessing DNA replication and tube formation, angiogenesis was investigated in a unique *in vitro* 3-dimensional model which allows quantification of new vessels sprouting from a preformed vascular network.
Results: There was a 1.5–2-fold increase in angiogenesis with a low concentration (0.0005 μg/mL) of darbepoetin alfa in the HDMEC and HMEC-1, no change with an intermediate concentration (0.025 μg/mL) and an approximately 5-fold increase at a higher concentration (0.1 μg/mL) in HMEC-1 and 1.5-fold increase with HDMEC. Epoetin delta caused a significant reduction in angiogenic activity when compared with vehicle-only controls ($P < 0.01$–0.001) in HMEC-1. It also showed a reduction at 1.0 IU/mL in HDMEC. At concentrations $\geq$ 20 IU/mL or equivalent (i.e. greater than the therapeutic range), both ESAs produced a significant increase in angiogenesis ($P < 0.001$) although this increase was consistently less with epoetin delta than with darbepoetin alfa in both cells.
Conclusions: Using both primary endothelial cells and HMEC-1 cells, we demonstrated that epoetin delta and darbepoetin alfa differentially modulate angiogenic activity *in vitro*. Epoetin delta showed significantly less angiogenic potential than darbepoetin alfa at concentrations not exceeding the therapeutic range. These ESAs differ in both cell derivation and protein glycosylation, and this may account for the differences in angiogenic potential at similar pharmacokinetic concentrations. In clinical practice, reduced angiogenic potential of an ESA could have benefits in situations in which elevated angiogenesis contributes to pathology, such as tumour growth and metastasis.
Disclosure: This study was supported by a research grant from Shire plc.

MP009 BASAL SYNTHESIS OF REACTIVE OXYGEN SPECIES (ROS) REGULATE CONSTITUTIVE GENE EXPRESION THROUGH ACTIVATOR PROTEIN-1 (AP-1) ACTIVATION

Marta Gonzalez-Ramos, Mercedes Griera, Aranzazu Chamorro-Jorganes, Beatriz Herranz, Alicia Luengo, Marta Saura. *Department of Physiology, School of Medicine, University of Alcala, Alcala de Henares, Madrid, Spain*

Introduction and Aims: Constitutive genes, generally, encode housekeeping functions and are continuously expressed, at low levels, in all cells. Under physiological conditions, cells show a fine balance between the continuous ROS production and its removal by endogenous and exogenous antioxidants. Oxygen derivates have been shown to modify gene expression through the activation of transcription factors, such as nuclear factor κB (NF-κB) and activator protein-1 (AP-1). Transforming growth factor-β1 (TGF-β1) is a constitutive gene which contains, at least, two AP-1 binding sites in its promoter. We hypothesize that the basal ROS levels generated inside the cell contribute to maintain the constitutive expression of some of these genes through AP-1 activation. The aim of this study was analyzed the effect of the basal ROS production on the activation of the TGF-β1 promoter.
Methods: Cultured Human Mesangials Cells (HMC) were used between passages 3 and 10. Cells were transfected with a plasmid containing the whole human TGF-β1 promoter, the serial deletion mutants or the 3TP-Lux plasmid linked to luciferase reporter gene, using lipofectamine. Luciferase activity was measured in a luminometer. After transfection, HMC were incubated with catalase (80U/ml to 640 U/ml) during 16h. The intracellular catalase activity was measured by colorimetric techniques. ROS production was determined by flow cytometry using di-chloro-di-hidro-fluorescin diacetate probe after viability quantification with propide iodide. AP-1 activation was measured with electrophoretic mobility shift assays (EMSA).

Results: Exogenous catalase addition produced an increased in intracellular catalase activity and a decreased production of intracellular ROS in a dose-dependent way. Catalase reduces the basal activity of the whole TGF-β1 promoter. Transfection with deletion mutants of TGF-β1 promoter showed that the effect of catalase on the promoter activity, disappear when the fragment containing the AP-1 site was removed. Moreover, the result was confirmed by using transfection with 3TP-lux plasmid, which contains 3 AP-1 sites. 3TP-Lux activity was reduced after catalase incubation. Finally, AP-1 complex formation was inhibited by catalase, indicating that a basal level of ROS generation was necessary for its activation.
Conclusions: Taken together, the results suggest that incubation with catalase, which removes intracellular ROS, decreases the human TGF-β1 promoter basal activity, through the inhibition of AP-1 complex formation. Low levels of ROS production could be essential for the basal activation of some constitutive genes.

MP010 SNAIL MEDIATES TGF-beta1-INDUCED COX-2 IN HUMAN MESANGIAL CELLS

Soraya Velasco, Fernando Dorado, Jose M. López-Novoa, Alicia Rodríguez-Barbero. *Fisiología y Farmacología. Instituto Reina Sofía de Investigación Nefrológica. REDinREN, Universidad de Salamanca, Salamanca, Spain*

Introduction and Aims: Fibrosis is involved in the progressive loss of kidney func-tion that occurs in many conditions including glomerulonephritis, diabetes, urinary tract obstruction and chronic rejection of transplanted kidneys. Recently it has been shown that activation of the transcription factor Snail results in large scale epithe-lial to mesenchymal transitions (EMT) in the kidney, reproducing all the features of renal fibrosis. Extensive studies have demonstrated that transforming growth factor-beta (TGF-beta) plays an important role in the progression of renal diseases. TGF-beta has been linked mainly to fibrogenesis in experimental models of glomerulonephritis and diabetic nephropathy, diseases with an important inflammatory component. Interestingly, one of the remarkable effects of TGF-beta1 is the induction of COX-2 expression. Recently, we have demonstrated that TGF-beta1 regulates COX-2 expression in human mesangial cells. In addition, TGF-beta is a potent inducer of Snail and interestingly, the expression of Snail is observed in UUO-induced renal fibrosis. However, there are no data on the role of Snail in human mesangial cells. Thus, a major purpose of this study has been to assess the role of Snail on TGF-beta-induced COX-2 in human mesangial cells. We also investigated the involvement of the MAPK signalling pathway in this process.
Methods: Snail mRNA expression was analyze by PCR. Activation of p38 and ERK1/2 MAPK was assesed by Western blot. We also investigated the effect of Snail on COX-2 expression. For that purpose the expression vector pZeo-Snail was co-transfected in human mesangial cells together with a COX-2 promoter bound to luciferase. We inhibited the Snail expression in human mesangial cells by interference mRNA.
Results: In the present study, we demonstrate that exogenous TGF-beta1 induces an increase in Snail mRNA expression. In addition, TGF-beta1 activated p38 and ERK1/2 MAPK signalling pathways. To asses the possible implication of these signalling pathways on the TGF-beta-induced Snail expression we used specific inhibitors of these intracellular pathways. The p38 MAPK inhibitor SB203580 reduced a 40% the TGF-beta-induced Snail mRNA expression whereas the MEK-1 inhibitor U0126 a 26%. We also investigated the effect of Snail on COX-2 expression in human mesangial cells. The COX-2 promoter activity increased significantly with Snail expression. Snail inhibition significantly reduced the COX-2 promoter activity in basal conditions and in response to TGF-beta1.
Conclusions: Our results demonstrated that TGF-beta1 increased Snail mRNA expression, this process is mediated by p38 and ERK1/2 MAPK pathways. In addition, the TGF-beta-induced COX-2 expression is mediated by the transcription factor Snail. These results suggest that Snail could have a role on the development of renal mesangial pathology. Taking into account that TGF-beta triggers complex signalling cascades, some of which may be beneficial, inhibiting Snail may be a more specific way to treat renal disease than inhibiting the TGF-beta pathways.

MP011 Cdc42, A POTENT REGULATOR OF MYOCARDIN-RELATED TRANSCRIPTION FACTOR (MRTF) NUCLEAR TRANSLOCATION, IS INVOLVED IN THE REGULATION OF ALPHA-SMOOTH MUSCLE ACTIN (SMA) GENE EXPRESSION DURING EMT IN TUBULAR CELLS

Attila Sebe[1,2], Zsuzsa Erdei[1], Istvan Mucsi[3], Andras Kapus[2], Laszlo Rosivall[1]. *[1]Dept. of Pathophysiology, Pediatrics and Nephrology Research Group, Semmelweis University, Budapest, Hungary; [2]Dept. of Surgery, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada; [3]1st Dept. of Internal Medicine, Semmelweis University, Budapest, Hungary*

Introduction and Aims: Epithelial-mesenchymal transition (EMT) of tubular cells into α-smooth muscle actin (SMA)-expressing myofibroblasts is a central mechanism in tubulointerstitial fibrosis. Previously we described a "two-hit" model for EMT wherein an initial injury of the intercellular contacts and TGFβ1 are both required for SMA protein expression in LLC-PK1 kidney tubular cells. We found the Rho-ROK-MLC-MRTF-SRF pathway as being an important mediator of the cell contact disruption induced effects in LLC-PK1 cells. Further, the contribution of Rac1, PAK and p38 was described, as important regulators of myocardin-related transcription factor (MRTF) localization and SMA expression. Cdc42, an important cytoskeletal modulator, is another small G protein situated upstream of PAK and p38. Here we investigated its potential role as MRTF and SMA regulator.
Methods: Western blot, immunofluorescent microscopy and transient transfection/luciferase assay were performed on LLC-PK1 porcine tubular epithelial cells.
Results: Cell contact disassembly activated Cdc42. Transfection of a CA Cdc42 construct alone induced the activation of the SMA promoter. The DN Cdc42 construct prevented the activation of the promoter induced by cell contact disassembly, and reduced the effects of the combined, cell contact disrupting and TGF, treatment in confluent monolayers. Further, SRF showed a marked nuclear accumulation in CA Cdc42 transfected cells. Cdc42 induced the nuclear translocation of MRTF, while DN Cdc42 inhibited the LCM-provoked nuclear translocation of MRTF.
Conclusions: These results suggest the possible involvement of Cdc42 in the complex mechanisms regulating SMA expression. Cdc42 is involved in the regulation of MRTF cellular localization.

MP012 CHONDRO/OSTEOBLASTIC AND CARDIOVASCULAR DISEASE-ASSOCIATED GENES ARE MODULATED IN HUMAN CORONARY ARTERY SMOOTH MUSCLE CELLS CALCIFYING IN THE PRESENCE OF PHOSPHATE AND VITAMIN D STEROLS

V. Shalhoub[1], E.M. Shatzen[1], S.C. Ward[1], M. Boedigheimer[2], L. Twehues[2], J. McNinch[3], S. Scully[3], B. Twomey[4], M.A. Damore[4], P. Kiaei[4], D. Fitzpatrick[4], Z Pan[5], D. Martin[1]. *[1]Depts of Metabolic Disorders; [2]Computational Biology; [3]Pathology; [4]Molecular Sciences; [5]Lead Discovery, Amgen, Inc, Thousands Oaks, CA, USA*

Introduction and Aims: Vitamin D sterol administration, although a traditional treatment for secondary hyperparathyroidism (HPT), increases serum calcium (Ca) and phosphorus (P), and may be associated with increased vascular calcification. In vitro studies suggest that the vitamin D sterols regulate expression of genes associated with trans-differentiation of smooth muscle cells (SMC) to a chondro/osteoblastic cell type. The current study examined the effects of vitamin D sterols on human coronary artery SMC (CASMC) calcification and gene expression.
Methods: CASMCs were exposed in vitro to differentiation medium [beta-glycerophosphate (10 mM), ascorbic acid (50 mg/mL), and dexamethasone (10^{-9} M)] with and without calcitriol or paricalcitol (10^{-8} M) or the calcimimetic R-568 (10^{-8} M) for 7 days. Calcification was determined using a colorimetric assay after extraction of cell layers with HCl. Total RNA was isolated and examined by microarray.
Results: Exposure of CASMC to vitamin D sterols, but not the calcimimetic R-568, significantly increased calcification by 1.6 to 1.9-fold. Vitamin D exposure resulted in statistically significant induction (+) or repression (-) of genes involved in several pathways. The fold changes for calcitriol and paricalcitol, respectively, were: CYP24A1 [+10.1 and 3.87], mineralization pathway (ENPP1 [-1.32 and -1.21], apoptosis pathway (NLRP1 [+1.35 and

+1.15], GIP3 [-1.82 and -1.65], osteo/chondrogenesis pathway (OPG [+1.27 and +1.22], COL22A1 [1.45 and 1.24], HHIP [+1.34 and +1.23], CILP [+1.5 and +1.16], Dkk1 [+1.39 and +1.35], DLX2 [+1.22 and +1.1], BMP4 [+1.33 and +1.11], BMP6 [+1.26 and +1.11],TGFB2 [+1.8 and +1.45]), cardiovascular pathway (TGFBR2 [-1.2 and -1.10], HGF [-1.77 and -1.44], CORIN [-1.25 and -1.18], POSTN [-1.15 and -1.17], DSP1 [+1.33 and +1.21], TNC [-1.32 and -1.13]), cell cycle/differentiation pathway (MAPK13 [+1.34 and +1.13], PTPRF [+1.22 and +1.11]), and channels (SLC22A3 [+2.14 and +1.77] and KCNK3 [+1.47 and +1.14], compared with differentiation medium. R-568 had no observed effect on CASMC gene expression.

Conclusions: Although the fold change for nearly all genes is not greater than 2, it is likely the totality of these (and other) gene expression changes with vitamin D sterol treatment reflect the calcification phenotype. These data suggest that the SMC calcification observed with vitamin D sterols may be partially mediated through targeting genes that influence mineralization, apoptotic, osteo/chondrocytic, and cardiovascular pathways. Further studies to determine the precise roles of these events in the development of vascular calcification and cardiovascular disease are required.

Disclosure: All authors were employed by Amgen, Inc when the study was done.

MP013 PROTEASOME INHIBITOR MG-132 INDUCES APOPTOSIS IN RAT RENAL INTERSTITIAL FIBROBLASTS THROUGH JNK,p38 MAPK AND CASPASE-3 PATHWAY

Bingbing Zhu, Yuanmeng Jin, Lin Han, Hui Chen, Weiming Wang, Nan Chen. *Department of Nephrology, Ruijin Hospital, Shanghai Jiao Tong University, Shanghai, China*

Introduction and Aims: The proteasome inhibitor plays a pivotal role in controlling cell proliferation, apoptosis and differentiation in a variety of normal and tumor cells. The imbalance of proliferation and apoptosis of renal interstitial fibroblasts is one of the key events in the processing to the renal fibrosis. The aim of this study is to investigate the role and mechanism of MG-132, a specific dipeptide proteasomal inhibitor that inhibits 26S proteasome activity, on apoptosis in rat renal interstitial fibroblasts.

Methods: Renal interstitial fibroblasts (NRK-49F) were stimulated by TGF-β1 (5ng/ml) and pre-treated with MG-132 (0∼5μM).The cell proliferation was measured by MTT method. The cell cytotoxicity was tested by LDH method. The apoptosis was analyzed by flow cytometry, Hoechst 33258 staining and DNA ladder. The c-Jun-N-terminal kinase 1/2/3 (JNK1/2/3), c-jun1/2, p38 MAPK (mitogen-activated protein kinase), extracellular signal-regulating kinase 1/2 (ERK1/2), p-JNK1/2/3, p-p38, p-ERK1/2, caspase-3, bcl-2 and bax protein expression were examined by Western blot.

Results: TGF-β1 (5ng/ml) could stimulate the proliferation of NRK-49F (0.661±0.04 vs 0.495±0.06). MG-132 (0.1∼5umol/l) can inhibit the effect caused by TGF-β1. TGF-β1 could not induced the apoptosis (3.8%±0.4% vs 4.7%±1.6%). But MG-132 can significantly increase the percentage of early apoptotic NRK-49F in a dose-dependent manner with or without TGF-β1. Hoechst staining showed condensed or fragmented nuclei, apoptotic body after being incubated with 2.5μM MG-132 with or without 5ng/ml TGF-β1. The typical DNA fragmentation was also observed in these two groups. Western blot showed that 5ng/ml TGF-β1 with 2.5μM MG-132 resulted in phosphorylation of JNK and p38 protein expression in a time dependent manner, while ERK1/2 expression didn't change,which contributes to the followed activation of anti-apoptotic (caspase-3 and bax) and inactivation of pro-apoptotic (bcl-2) protein expression in a dose-dependent manner.

Conclusions: Proteasom inhibitor MG-132 could induce renal interstitial fibroblasts apoptosis stimulated by TGF-β1.The phosphorylation of JNK, p38 and the subsequent change of the activity of capase-3, bcl-2 and bax may take part in the MG132 induced apoptosis of renal interstitial fibroblasts by TGF-β1.

MP014 NITRIC OXIDE REGULATES INTEGRIN-LINKED KINASE IN VASCULAR ENDOTHELIUM

Beatriz Herranz-Sanchez, Carlos Zaragoza, Aranzazu Chamorro, Marta Gonzalez-Ramos, Maria Luisa Diez-Marques, Manuel Rodriguez-Puyol, Marta Saura. *Physiology, Alcala University, Alcala de Henares, Madrid, Spain; Fundacion Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Tres Cantos, Madrid, Spain; Physiology, Alcala University, Alcala de Henares, Madrid, Spain*

Introduction and Aims: Extracellular matrix (ECM) remodeling is a key feature of chronic cardiovascular diseases. In the kidney, impaired remodeling is a major cause of perivascular, interstitial, and glomerular fibrosis but also a common complication of chronic hypertension. Integrin linked kinase (ILK) is a protein serine/threonine kinase implicated in the regulation of endothelial cell survival, migration and differentiation of endothelial cells during angiogenesis and ECM remodeling. NO is critical for maintenance of cardiovascular homeostasis and a deficient NO synthesis o bioavailability is involved in many cardiovascular diseases. We hypothesized that NO could modulate ILK activity in vascular endothelial cells.

Methods: We used bovine aortic endothelial cells (BAEC) as cellular model and NOS-3 Knock-out and wild -type mice as *in vivo* model.

Results: We observed that ILK activity was increased after stimulation with stimuli that increased endothelial NO synthesis. BAEC were treated with VEGF (50 ng/ml for 2,5 minutes) and calcium ionophore A23187 (10^{-6} for 15 minutes) increasing NO production above basal level by 2-3 fold. Addition an NO donnor, DEA-NO, ($2{,}5\times10^{-5}$ M, 18 hours) increased ILK activity, measured by GSK phosphorylation. This increase was abolished by preincubation of endothelial cells with L-NAME (10^{-4} M) suggesting that NO could be regulating ILK activity. The increase in ILK activity was observed only after 18 hour incubation with the NO donnor, which suggest a change in ILK content. For that reason, we performed inmunohistochemistry in aortic sections of NOS-3 Knock-out and wild -type mice. NOS-3 KO mice showed a marked decrease in ILK content in the endothelial layer on the aorta compared to wild type mice. Phosphorylation of ILK targets, GSK and Akt was also assayed by immunohistochemistry, observing a parallel decrease.

Conclusions: Taken toghether these results indicate that NO is involved in ILK regulation and may play a role in the transduction of EC-integrin signals.

MP015 ★ INHIBITION OF THE ACIDOSIS-SENSING L-GLN TRANSPORTER SNAT2 IMPAIRS PROLIFERATION OF LBRM-TG6 T-LYMPHOCYTES

George Kosmadakis, Emma Clapp, Jeremy Brown, Kate Evans, Alan Bevington. *John Walls Renal Unit, Department of Infection, Immunity & Inflammation, University of Leicester, Leicester, United Kingdom*

Introduction and Aims: Impaired immune function leading to life-threatening infections is a major contributor to mortality in end-stage renal disease. Uraemic metabolic acidosis is known to impair growth in skeletal muscle by inhibiting SNAT2 L-Glutamine (L-Gln) transporters, leading to impaired growth signals through Phosphatidylinositol-3-kinase (PI3K) (Franch *et al* AJP 287, F700-6, 2004) and mammalian target of Rapamycin (mTOR) (Evans *et al* JASN 18, 1426-36, 2007). Such a mechanism might also impair the strongly L-Gln dependent cell proliferation involved in cellular immunity. The aim of this study was to determine whether acidosis and SNAT2 inhibition slow cell proliferation in the mouse T-lymphocyte model LBRM-TG6.

Methods: Cell division rate in LBRM-TG6 cells in Iscove's Medium with 2% serum was assessed from ^{3}H-Thymidine incorporation into DNA. Intracellular L-Gln was assayed by high performance liquid chromatography in neutralised deproteinised perchloric acid extracts. PI3K activity immunoprecipitated from cell lysates was assayed by a lipid kinase assay with ^{32}P-ATP, followed by separation of the ^{32}P-labelled product by thin layer chromatography and quantification by autoradiography and densitometry. Data presented are pooled from at least 3 independent experiments and are expressed as mean ± SEM.

Results: Analysis by RT-PCR confirmed that, as in muscle, SNAT2 is the predominant member of the SNAT/slc38 amino acid transporter family expressed in LBRM-TG6 cells. Lowering pH from 7.4 to 7.1 reduced

^{3}H-Thymidine incorporation from 65±3 to 44±3 dpm × 10^3/ug DNA in 16h (P=0.000012). Competitive inhibition of SNAT2 with its selective substrate MeAIB (10mM) also reduced incorporation from 98±7 to 61±8 dpm × 10^3/ug DNA (P=0.0017) but with slower onset (72h). In only 2h MeAIB reduced intracellular L-Gln from 4.5±0.7 to 2.9±0.7 nmol/mg protein (P=0.011). Blockade of growth signals through PI3K for 16h with the selective PI3K inhibitor LY294002 (12.5μM) strongly inhibited ^{3}H-Thymidine incorporation (86±3% decrease, P<0.00001). Similarly blockade of SNAT2 for 16h with MeAIB decreased PI3K activity to 46±15% of the control value, P=0.012).

Conclusions: In this T-lymphocyte model, as in skeletal muscle, the SNAT2 L-Gln transporter is an important mediator of the pH-dependence of cell growth, suggesting that previously reported detrimental effects of metabolic acidosis in muscle and the immune system occur, at least partly, through a common pathway involving SNAT2 and PI3K signalling.

MP016 ROLE OF ENDOPLASMIC RETICULUM STRESS IN URIC ACID-INDUCED ALTERATIONS IN APOPTOSIS AND SENESCENCE OF RENAL TUBULAR CELLS

Duk-Hee Kang, Mina Yu. *Division of Nephrology, Ewha University College of Medicine, Seoul, Korea*

Introduction and Aims: Endoplasmic reticulum (ER) stress is a cellular stress pathway induced by the accumulation of unfolded proteins in the ER which is initially a defense mechanism of cells against various stressful environments, but prolonged or severe ER stress can lead cell death. Recently, there is an accumulating evidence of the involvement of ER stress in renal cell survival and the progression of renal disease. Since we found that hyperuricemia was associated with an alteration of survival of renal tubular cells and renal disease progression, we investigated the role of ER stress on uric acid (UA)-induced apoptosis and senescence of rat proximal renal tubular cells (NRK) in in-vitro and in-vivo experiments.

Methods: Cellular ER stress was evaluated by measurement of the expression of glucose-regulated protein 78 (Grp78)/Grp94 and the phosphorylation of eukaryotic initiation factor (eIF2-α) by Western blotting and immunohistochemistry, and X box-binding protein (XBP-1) splicing by RT-PCR in cultured NRK cells and the kidney of hyperuricemic rats fed with 3% oxonic acid and low salt diet for 8 weeks. Senescence and apoptosis of NRK cells assessed by senescence-associated (SA) β-gal staining and FACScan analysis at 48 hours of stimulation. To investigate the effect of ER stress preconditioning, NRK cells were pretreated with ER stress-inducer, tunicamycin (1.5 μg/ml) for 12 hours or transfected with Grp78 with the recombinant adenoviral vector containing rat Grp78.

Results: The expression of ER stress-related molecules in cultured NRK cells was increased by UA (6-12 mg/dL) at 3 and 24 hours (p<0.01). Tubular expression of Grp78 (p=0.012) and eIF2-α (p=0.028) in renal cortex was also significantly increased in hyperuricemic rats (serum UA 2.2±0.7 mg/dL) compared to control rats (UA 0.92±0.24 mg/dL). Uric acid induced an increase in senescence and apoptosis of NRK cells, which was significantly decreased with pre-treatment of tunicamycin or Grp 78 transfection of NRK cells.

Conclusions: Our study suggests that UA induces the ER stress in renal tubules associated with cell senescence and apoptosis. However, UA-induced senescence and apoptosis were protected by ER stress pre-conditioning. Induction of ER stress markers by UA as well as cytoprotection of renal tubular cells by induction of ER chaperones support the hypothesis that ER stress plays an important role in UA-induced renal disease.

MP017 ACTIVATION OF SURVIVAL KINASES AND ROS CORRECTION IN PROTECTIVE EFFECT OF LEU-ENKEPHALINE POSTCONDITIONING IN HEK-293 CELLS

Yevgen Blagodarenko. *Medical Chemistry Department, Lugansk State Medical University, Lugansk, Ukraine*

Introduction and Aims: DOR stimulation is considered to play a significant role in the preconditioning and postconditioning diminishing of ischimia-reperfusion injury. Last works showed nearly the same efficiensy of postconditioning procedure compare to preconditioning. As postconditioning can be more effectivly used for clinical purpose we used DADLE treatment for the modeling of postconditioning effects in our cell model experiments to study the mechanism of the protective effect.

Methods: HEK-293 (human embryonic kidney) cells were grown in normal DMEM medium. Cells were stably transfected by the lipofection method with plasmid pcDNA 3.1 containing full-length cDNAs of the DOR HA tagged. Cell viability was evaluated by trypan blue staining and MTT assay. Activation of protein kinases was characterized by Western Blotting method using phosphospecific antibodies. ROS production was measured with the help of MitoTracker Red reagent (Invitrogen). Fluorescence was taken using an inverted confocal microscope Olympus IX-70.

Results: Phosphorylation of ERK and AKT kinases after the leu-enkephaline treatment showed time course dynamics. The maximum ERK activation after the DADLE treatment was observed after 15 minute, persisted after 1 hour and went down after 2 hours of incubation. The maximum phosphorylation was seen after 15 min with DADLE. After 1 hour of incubation AKT activity went down. In the concentration 0,1 μM DADLE 15 min treatment provide 1,55 fold JNK activation.

Survival effect of DADLE was also checked in the experiments with Staurosporin (STS) intoxication. STS intoxication during 12 hours decreased cell viability nearly to the half from control. Cells incubated with DADLE in parallel to STS intoxication showed more high viability. The same result of increased cells viability due to the 0,1 μM DADLE treatment in the conditions of STS intoxication was obtained in MTT assay.

STS intoxication of HEK-293-HA-DOR cells was followed by significant ERK activation. DADLE treatment diminished this effect of STS. ERK phosphorylation was nearly half less under the treatment of 0,1 μM DADLE than in the just STS treated probes. MitoTracker Red ROS assay showed that 0,1 μM DADLE treatment significantly decreased ROS production caused by the STS intoxication during 12 hours. The same effect of DADLE was observed and after 30 minutes of incubation. According to this effect of DADLE treatment we used this leu-enkephalin in another survival experiment model - hypoxia-reoxygenation. DOR stimulation is considered to play a significant role in the preconditioning and postconditioning diminishing of ischimia-reperfusion injury. 0,1 μM DADLE treatment in the moment of reoxygenation after the 3 hours of hypoxia increased viability of HEK-293-HA-DOR cells during 24 hours of incubation. ROS assay carried out after 1 hour of reoxygenation showed that DADLE treatment diminished ROS production wich was increased in non-treated cells, which underwent hypoxia-reoxygenation.

Conclusions: Thus, mechanism of protective effects of leu-enkephaline postconditioning involves regulation of MAP kinases and AKT activity and diminishing of increased ROS production.

Disclosure: This abstract was possible thanks to a grant given by INTAS YS Fellowship, Ref. Nr 05-109-5466.

MP018 MOLECULAR CHARACTERISTICS OF UPPER UROTHELIAL CARCINOMA FROM ENDEMIC REGIONS, ASSOCIATED WITH OR WITHOUT BALKAN ENDEMIC NEPHROPATHY

Marina Savin[1], Vladimir Bumbasirevic[2]. [1]*Clinic of Nephrology, Clinical Center of Serbia;* [2]*Institute of Histology and Human Embryology, Belgrade School of Medicine*

Introduction and Aims: By previous investigation, low proliferation level in relation to pronounced apoptosis in the upper urothelial carcinoma (UUTT) from endemic regions (ER) with Balkan nephropathy (BEN) was notified. Nearly third of patients may suffer from both BEN and associated UUTT, and the possible difference in the molecular characteristics between UUTT from ER associated with BEN and without BEN has been studied at present.

Methods: Out of 83 pts with UUTT, 33 patients from ER had BEN and UUTT (ERBEN), by histological diagnosis and positive family history for at least one those diseases. Two control groups of UUTT were included, 19 patients with UUTT from ER and without BEN (ERnoBEN) and 31 patients with UUTT coming outside ER (outside ER). The levels of proliferation marker protein PCNA, apoptosis type I marker protein PARP p89, and protein p53 expression were detected by immunohistochemistry on the tumor tissue obtained by nephrectomy, and it was compared with the incidence of tumor TUNEL + cells.

Results: In groups outside ER and ERnoBEN (aged 63.0±11.9 and 60.7±10.1 yrs) male patients were prevailed, and both genders had equal rates in ERBEN patients aged 66.7±7.8 yrs. The distributions of tumor grades 1 to 3 and pTa stages 1 to 4 did not significantly differ between three groups. Outside ER UUTT grade and PCNA+cells (r=0.53; p=0.003), ERnoBEN UUTT grade and p53 overexpression (r=0.46; p=0.048) correlated each other, and ERBEN tumor grade and stage were in relation to TUNEL+ cells (r=0.54; p=0.001 and r=0.45; p=0.008).
In UUTT outside ER the p53 overexpression were correlated linearly with increase in rates of PCNA (p=0.005) and TUNEL + cells (p=0.013), whereas PCNA and TUNEL rates did not significantly change with p53 overexpression in both groups from ER. Ix PARP p89 + cells were noticeably increased with moderate p53 overexpression in ERBEN tumors (p=0.001), and decreased in tumors outside ER (p=0.001) or in ERnoBEN tumors (p=ns). In addition, in tumors from ER greater indices of cumulative apoptosis (TUNEL + cell and PARP p89 + cells) may indicate the development of BEN (RR=1.64; 95%CI=1.04-2.59; p=0.032) presumably in older patients (RR=1.08; 95%CI=1.00-1.13; p=0.041), by multivariate analysis.
Conclusions: Markers p53 and TUNEL are important for estimation of UUTT malignancy in endemic regions, which is in favor to the toxic etiology of those tumors. Different patterns of molecular biomarkers for tumor apoptosis and p53 in UUTT from ER associated with and without BEN may suggest the diversity and multifactorial etiology or these tumors or represent different phases of the same disease.

MP019 INVOLVEMENT OF ENDOPLASMIC RETICULUM STRESS PROTEINS IN THE PROLIFERATION OF RENAL INTERSTITIAL FIBROSIS

Hassan Dihazi, Nitin K. Agarwal, Gerhard A. Müller. *Nephrology and Rheumatology, Medical Center Goettingen, Georg-August University Goettingen, Goettingen, Germany*

Introduction and Aims: Fibrosis is a process that is characterized by excessive accumulation of extra cellular matrix compromising organ function by replacing normal organ tissue. Tissue fibrosis can affect almost any parenchymal organ in particular tissues with common inflammations, such as the kidney. Renal fibrosis often leads to end-stage renal failure. Renal fibroblasts are thought to play a major role in the development of renal interstitial fibrosis. This is the final stage of a relatively uniform response of the kidney to sustained inflammation. The mechanisms leading to renal fibrosis remain poorly understood. Proteomics provide a new perspective to highlight the changes in protein expression associated with fibrosis and so lead to a better understanding of fibrosis.
Methods: We performed differential proteomics analysis with two established model cell lines to identify proteins and pathways involved in the development of cystic fibrosis. Differential two dimensional gel electrophoresis combined with mass spectrometry, Western blot and Immunofluorescence staining were performed.
Results: The proteomics analysis reveal that more than 40 proteins were altered in their expression in fibrotic cells compared to normal renal fibroblast. Among these proteins the endoplasmic reticulum proteins especially GRP78, GRP94, Erp57, Erp72, and Calreticulin were highly upregulated in fibrotic cells. Treatment of normal renal fibroblasts with human TGF-β 1 leads to a progressive upregulation of the ER-proteins in parallel to an increase in fibrosis markers e.g. alpha smooth muscle actin.
Conclusions: Our results highlight the role of ER stress proteins in the development of renal fibrosis.

Genetic diseases and molecular genetics

MP020 GLOMERULAR FILTRATION RATE IS OVERESTIMATED BY MDRD-DERIVED ESTIMATED GFR IN MALE BUT NOT IN FEMALE FABRY PATIENTS

Kristin Moberg Aakre[1], Atle Brun[1,2], Einar Svarstad[2,3]. [1]*Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway;* [2]*Institute of Medicine, University of Bergen, Bergen, Norway;* [3]*Medical Department, Haukeland University Hospital, Bergen, Norway*

Introduction and Aims: Estimated GFR (eGFR) usually underestimates GFR in the normal range. In Fabry disease recent reports emphasize the importance of timely initiation of enzyme replacement therapy (ERT) before GFR is reduced. The aim of the present study was to evaluate the performance of the estimated MDRD formula compared to gold standard GFR assessment in Fabry patients.
Methods: From April 2004 until September 2007 all Fabry patients ≥ 18 years (7 male and 12 female) who underwent iohexol GFR (mGFR, two-point method, baseline and after 4 hours, HPLC analysis) with simultaneously serum creatinine measurements were included in the study. The simplified MDRD formula (Isotope dilution mass spectrometry traceable serum creatinine assessments) was used for calculating the corresponding eGFR values. The difference between GFR methods was calculated as mGFR minus eGFR (ml/min/1.73m^2). The study group was compared with a matched (age, gender, mGFR and BMI) control group.
Results: Male, but not female patients showed a significant difference between GFR methods in the normal or near normal mGFR level (mean mGFR for all Fabry patients were 92, range 55-123 ml/min/1.73m^2). Cases and controls were similar in age, iohexol clearance and BMI values. The mean S-Creatinine values were lower, and the corresponding eGFR values higher in male Fabry patients compared to controls with similar mGFR, but these differences between groups were not significant, probably due to low numbers. There were significant correlation between mGFR and eGFR in female, but not in male Fabry patients.
Conclusions: Our findings indicate that the MDRD formula overestimates kidney function in male Fabry patients with normal or slightly reduced mGFR, and eGFR results should be interpreted with great care to avoid delay of medical treatment in this group.

MP021 ★ POLYMORPHISM IN THE METHYLENE TETRAHYDROFOLATE REDUCTASE GENE (MTHFR) IN THE NORMAL INDIAN POPULATION & IN PATIENTS OF END STAGE RENAL DISEASE ON MAINTAINENCE DIALYSIS

Debabrata Mukherjee, Kamal Sud, Madhu Khullar, Vinay Sakhuja. *Nephrology, Post Graduate Institute of Medical Education and Research, Chandigarh, India*

Introduction and Aims: Cardiovascular disease accounts for more than fifty percent of end stage renal disease deaths. Accelerated atherosclerosis seen in these patients has been linked to a number of factors including polymorphisms in MTHFR gene. The C667T polymorphism of the MTHFR gene has been reported to be associated with higher common carotid artery IMT and increased risk of coronary artery disease in patients on hemodialysis. The C677T, MTHFR mutation has a significantly heterogeneous distribution among different ethnic groups, a fact that may contribute to explain geographical or racial differences in the risk for vascular disease. There are very few studies evaluating polymorphism of the MTHFR gene in Indian pop-

Abstract MP020 – Table 1

	Men			Women		
	Fabry (N=7)	Control (N=7)	P-value	Fabry (N=12)	Control (N=12)	P-value
Age	29 (16, 41)	29 (18, 41)	0.94	45 (34, 56)	45 (35, 54)	1.00
BMI	22 (18, 25)	25 (21, 30)	0.17	27 (24, 30)	26 (23, 29)	0.79
S-Creatinine	75 (60, 89)	89 (73, 104)	0.13	65 (60, 71)	69 (60, 77)	0.49
eGFR (MDRD)	115 (86, 146)	93 (72, 115)	0.16	89 (78, 100)	84 (73, 96)	0.55
mGFR	92 (67, 116)	94 (68, 120)	0.87	92 (80, 105)	90 (76, 104)	0.78
Difference mGFR-eGFR	-24 (-41, -7)	1 (-9, 10)	0.01	3 (-5, 11)	5 (-5, 15)	0.73

Data are given as mean values with confidence intervals in brackets.

ulation and none evaluating the effect on this gene on Indian patients with CRF/ESRD on hemodialysis. This assumes greater importance since Asian Indians who have settled overseas and those in urban India have increased risk of coronary events. The study aimed at investigating the polymorphism of the MTHFR gene in the ESRD population vis a vie the normal population.
Methods: Established cases of ESRD on dialysis & normal healthy individuals were studied. A non-enzymatic method of DNA extraction from peripheral blood lymphocytes as described by Lahiri et al (1991) was used. The quality of DNA was checked by Agarose Gel Electrophoresis by the method of Maniatis et al. PCR was performed to amplify the desired region of exon 4 of MTHFR gene. It was carried out using the primers as reported by Frosst et al.
Results: Overall, 206 subjects (103 patients & 103 control) were investigated for MTHFR gene polymorphism. Eighty-seven (42.2%) were female and 119 (57.8%) were male. CC genotype was present in 85 controls (82.5%) and, CT genotype in 18 controls (17.5 %). TT genotype was not detected in any of the subjects. In females, 80% had the CC genotype & 20% had CT genotype, while 89% of males had CC genotype and 11% the CT genotype. The allele frequencies were 0.55 and 0.17 for the C allele and T allele respectively. Amongst the patients CC genotype was present in 76 pts (73.8%) and, CT genotype in 27 pts (26.2 %). TT genotype was not detected in any of the patients. Although the CT genotype was more prevalent in the patients than controls (26.2% vs 16.5%) the difference was not statistically significant, (p= 0.177). In females, 83.3% had the CC genotype & 16.7% had CT genotype, while 72.5% of males had CC genotype and 27.5% the CT genotype. The above differences were not statistically significant (p= 0.727). The allele frequencies were 0.57 and 0.26 for the C allele and T allele respectively. The mean arterial pressure and diastolic BP was higher in patients with CT genotype.
Conclusions: In Indians, the mutant T allele of MTHFR gene is extremely rare. TT genotype was not detected in any of the population studied. The frequency of the CT genotype is higher in patients of ESRD on dialysis than in the general population. Diastolic blood pressure and mean arterial pressures are higher in dialysis patients with the CT genotype.

MP022 FAMILIAL JUVENILE HYPERURICEMIC NEPHROPATHY: A NEW UROMODULIN MUTATION AND REPORT OF A PREGNANCY

Karl Lhotta[1], Anke Gehringer[2], Paul Jennings[3], Florian Kronenberg[2], Vladimirs Strazdins[4]. *[1]Clinical Nephrology Division, [2]Division of Genetic Epidemiology, [3]Division of Physiology, Innsbruck Medical University, Innsbruck, Austria; [4]Department of Nephrology, University Hospital for Children, Riga, Latvia*

Introduction and Aims: Familial juvenile hyperuricemic nephropathy (FJHN) is a rare autosomal disease caused by mutations in the uromodulin gene (*UMOD*) located on chromosome 16 and leading to gout, tubulointerstitial nephropathy and end-stage renal disease in adulthood.
Methods: A Latvian family suffering from autosomal dominant kidney disease and gout is described. Genetic analysis was performed by sequencing all exons of the UMOD gene.
Results: The father of the family developed ESRD at age 36. His daughter (2) was diagnosed with gout and chronic kidney disease at age 14. A renal biopsy revealed tubulointerstitial disease. Two sons (3 and 4) were diagnosed at age 9 and 4 with elevated uric acid levels and reduced fractional uric acid excretion. Patient 3 also suffered from recurrent macrohematuria. Patient 4 had normal urinary uromodulin, whereas it was reduced in patients 2 and 3 (see Table 1)

Table 1

	Patient 2	Patient 3	Patient 4
Gender	female	male	male
Age	23 y	13 y	5 y
Blood pressure	110/70	118/82	104/61
Gout	yes	no	no
Uric acid	6.55 mg/dl	5.2 mg/dl	3.7 mg/dl
Creatinine	2.05 mg/dl	1.36 mg/dl	0.54 mg/dl
eGFR	30 ml/min	52 ml/min	89 ml/min
FEUA	3.6%	1.6%	5.1%
Urinary umod/cr	0.02 mg/g	0.14 mg/g	9.43 mg/g

Screening of all 11 exons of the *UMOD* gene revealed a previously undescribed D196Y mutation.
Patient 2 became pregnant at age 23. During pregnancy serum creatinine decreased from 2.0 to 1.5 mg/dl and blood pressure remained in the low normal range. Except for hyperemesis pregnancy was uneventful and the baby was delivered at term. Analysis of umbilical cord blood and a mouth swab showed that the child also carried the D196Y mutation.
Conclusions: A novel *UMOD* mutation causing FJHN is described. The uromodulin excretion pattern observed in that family suggests that in FJHN urinary uromodulin decreases from normal values at childhood to extremely low levels in early adulthood. In addition, the first report of a pregnancy in a patient with FJHN shows normal adaption despite markedly reduced renal function.

MP023 ANTIBIOTIC-RESISTANT CYST INFECTION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Tatsuya Suwabe[1], Yoshifumi Ubara[1], Yasushi Higa[1], Shohei Nakanishi[1], Yuhji Marui[1], Jyunichi Hishino[1], Naoki Sawa[1], Hideyuki Katori[1], Fumi Takemoto[1], Michio Nakamura[1], Shinji Tomikawa[1], Shigeko Hara[2], Kenmei Takaichi[1]. *[1]Nephrology Center, Toranomon Hospital, Tokyo, Japan; [2]Health Care Unit, Toranomon Hospital, Tokyo, Japan*

Introduction and Aims: We have reported that renal transarterial embolization (TAE) or hepatic TAE is effective for patients with enlarged kidneys or livers. Although cyst infection is another serious complication in patients with ADPKD, the treatment of patients with antibiotic-resistant cyst infection is controversial. We evaluated 50 patients who were referred to our institution with severe antibiotic-resistant cyst infection from January 2004 to December 2006.
Methods: Cyst infection occurred in the both kidneys and liver. We grouped the patients as having liver cyst infection, renal cyst infection without prior renal TAE (pre-TAE), and renal cyst infection with prior renal TAE (post-TAE). Antibiotic-resistant liver cyst infection was found in 26 patients (9 males and 17 females) with an average age of 61.8 years (postdialysis:21; predialysis:5). Their mean serum albumin was 2.5 g/dL. Antibiotic-resistant renal cyst infection (pre-TAE) occurred in 15 patients (12 males and 3 females) with an average age of 60.0 years (postdialysis:13; predialysis:2) and a mean serum albumin of 2.7 g/dL. Antibiotic-resistant renal cyst infection (post-TAE) was detected in 9 postdialysis patients (6 males and 3 females) with an average age of 56.7 years and a mean serum albumin of 2.6 g/dL. The total hospitalization and systemic antibiotic administration for cyst infection between January 2004 and June 2007 was determined for each patient.
Results: There were 26 patients with refractory liver cyst infection. Liver cyst drainage was performed in all patients and 18 patients improved (including 1 patient after partial resection of the liver), but 3 patients relapsed and 5 patients died. The mean hospitalization period was 80.2 days. The mean duration of antibiotic administration was 101.0 days. Out of 15 pre-TAE patients with refractory renal cyst infection, renal cyst aspiration was performed in 4 patients and renal TAE was performed in 11. No patient developed recurrence. The mean hospitalization period was 44.6 days and the mean duration of antibiotic administration was 58.3 days. Out of 9 post-TAE renal cyst patients, aspiration was performed in 8 and nephrectomy was performed in 1. No patient developed recurrence. The mean hospitalization period was 48.4 days and the mean duration of antibiotic administration was 134.1 days.
Conclusions: Cyst infection was more serious in patients with hypoalbuminemia after the initiation of dialysis. In patients with renal cyst infection, renal TAE or cyst aspiration was effective. Although the mechanism by which renal TAE improves cyst infection is unclear, reducing cyst volume and kidney size may be important for the control of infection. Although drainage was effective for most patients with liver cyst infection, the prognosis was poor for infections resistance to drainage.

MP024 TGF β1 GENE POLYMORPHISMS AND PRIMARY VESICOURETERAL REFLUX IN CHILDHOOD

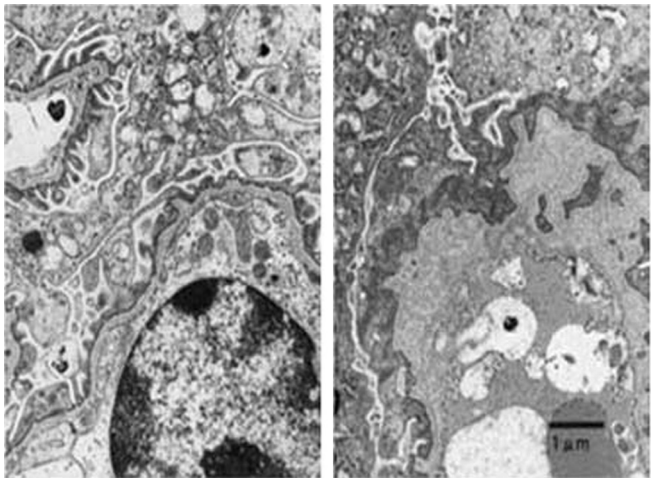
Magdalena Kowalewska-Pietrzak, Izabela Klich, Wojciech Mlynarski.
Department of Pediatrics, Medical University of Lodz, Lodz, Poland

Introduction and Aims: Transforming growth factor beta-1 (TGF β-1) is a cytokine, that plays a crucial role in normal cellular processes and tissue repair after injury. It has been recently found, that *TGF β-1* gene polymorphisms may contribute to increased susceptibility to renal parenchymal fibrosis.
The aim of this study was to evaluate an association of the *TGF β-1* gene polymorphisms (T-509C in the promoter region and Leu10Pro) with primary vesicoureteral reflux (VUR) and renal scarring.
Methods: Using case-control approach, we examined 121 children with primary VUR graded I° to V° (95 girls and 26 boys in age ranged from 1 mth to 13.7 yrs, median 3.3 yrs) and 169 healthy blood donors serving as controls. Among the controls Hardy-Weinberg equilibrium was confirmed for both polymorphic sites. Additionally, to prove a random sampling of controls, genetic distribution of analyzed *TGF β1* gene polymorphisms between control group and Caucasian population from the HAPMAP Project was compared, and no statistically significant differences were found. The genotyping of the *TGF β1* gene polymorphisms was performed by restriction fragment length polymorphism (RFLP) of genomic DNA. The ^{99m}Tc-DMSA or ^{99m}Tc-unitiol SPECT method was used to evaluate renal cortical scars in 84 out of 121 children with primary VUR.
Results: Statistical analysis of C-509T *TGF β1* gene polymorphism revealed significant differences in CC, CT, TT genotypes distribution between children with VUR and controls (29.7%, 43.0%, 27.3% and 44.6%, 43.3%, 12.1%, respectively) (p=0.0021). There were also higher frequency of T allele in VUR patients (48.8% vs. 33.7%; p=0.0005). Moreover, our data demonstrated that the carriers of the TT homozygous genotype are at increased risk of primary VUR, OR (*95%CI*) = 2.7 (1.46-5.08), which suggests a recessive mode of inheritance. *TGF β1* Leu10Pro CC, CT, TT genotypes distribution was similar in both (VUR and control) groups (17.4%, 38.0%, 44.6% and 12.8%, 33.5%, 53.7%, respectively). According to the evidence of renal scarring, 84 patients with VUR were stratified into two subgroups: 1A – absence of cortical scars (n=27) and 1B – presence of scars (n=57) with median age at presentation: 7.3 yrs in group 1A and 8.4 yrs in 1B (p=0.38) and median length of follow-up 3.1 yrs and 5.1 yrs in groups, respectively (p=0.06). There were no significant differences in genetic distribution of C-509T and Leu10Pro *TGF β-1*gene polymorphisms between subgroups of VUR patients.
Conclusions: Since some of previous reports have shown that the TT genotype of the C-509T *TGF β*1 gene polymorphism is a risk factor of renal scarring in primary VUR and the present study suggests an association of this polymorphism and the occurrence of primary VUR, further extensive approach on the larger sample size is needed to verify this inconsistency.
Disclosure: Supported by Polish State Committee for Scientific Research grant # 2P05E 01830.

MP025 THE FUNCTION OF GLOMERULI, FILTRATION IS INVOLEVED WITH DAMAGE TO THE GBM ITSELF

Tomohiro Murata[1], Michiyo Kiyohara[1], Kan Katayama[1], Kazuki Oosugi[1], Eiji Ishikawa[1], Toshihide Obe[1], Ichiro Naito[2], Masaaki Ito[1], Shinsuke Nomura[1]. *[1]Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan; [2]Department of Human Morphology, Okayama University Graduate School of Medicine, Okayama, Japan*

Introduction and Aims: Irregular thinning, thickening and lamellation of the glomerular basement membrane (GBM) is a specific finding of Alport syndrome and is diagnostically very valuable. The mechanism how defects of alpha chains of type IV collagen, which is the cause of this syndrome, leads this GBM change is not fully elucidated. While GBM is not the only basal membrane lacking type IV collagen alpha chain, the kidney is the only organ exhibiting morphological changes and function loss, and functions specific to glomeruli can thus be hypothesized to bring about damage to the GBM itself. Therefore it was examined whether reduction of glomerular filtration by the unilateral uretheral obstruction (UUO) method affects GBM change or not.
Methods: 6 week old alport mice underwent UUO or sham operation. At 6 weeks old, all mice exhibited broad GBM damage. Three weeks later (9 week old) all mice were sacrified and bilateral kidneys were removed to compare the UUO kidney, the contralateral unobstructed kidney and sham operated kidney.
Results: Light microscopy showed that, as expected, the left kidney with the ligated urinary tract exhibited marked hydronephrosis and interstitial changes. However, glomerular proliferation and sclerosis were basically not evident. In the right kidney, glomerular damage was more severe compared to the control group. Electron microscopy basically did not show GBM thinning, thickening or lamellation for the left kidney (left).
But in unobstructed kidney, GBM was more injured compared to sham operated kidney (right).



Conclusions: The unique function of glomeruli, filtration, is in fact involved with damage to the GBM itself. This GBM damage was shown to be reversible.

MP026 FUNCTIONALLY IMPORTANT RET GENE HAPLOTYPES AND GDNF GENE VARIANTS IN MEDULLARY SPONGE KIDNEY DISEASE

Rossella Torregrossa[1], Alessia Gozzini[2], Francesca Del Monte[2], Antonia Fabris[3], Lorenzo Citron[1], Antonio Lupo[3], Annalisa Tanini[2], Angela D'Angelo[1], Giovanni Gambaro[3], Franca Anglani[1]. *[1]Department of Medical and Surgical Sciences, Laboratory of Histomorphology and Molecular Biology of the Kidney, Division of Nephrology, University of Padova, Padova, Italy; [2]Department of Internal Medicine, University of Firenze, Firenze, Italy; [3]Division of Nephrology, University of Verona, Verona, Italy*

Introduction and Aims: Medullary sponge kidney (MSK) is a rare renal disorder characterized by cystic anomalies of precalyceal ducts, nephrocalcinosis, renal stones and nephronic tubule dysfunctions. Its pathogenesis has yet to be elucidated, but its association with different malformative conditions supports the idea of a developmental disorder and its involvement in familial cases shows the role of genetic factors. To date, no genetic study has been conducted. We hypothesize that genes regulating renal embryogenesis are good candidates to play a role in the pathogenesis of the disease. Particularly, GDNF and RET genes are necessary for the developing nephro-urological system and their expression is finely regulated. In this study, we investigated whether they may be considered disease-causing or susceptibility genes in MSK patients.
Methods: We collected 50 Venetian nephrolitiasic unrelated patients with MSK diagnosed by urography. All the cases were sporadic. We performed a mutation analysis of GDNF and RET genes using direct DNA sequencing and RFLP approaches.
Results: Seven patients had GDNF mutations in heterozygosity: a complex allele, constituted by the -45G>C and IVS2+18G>A nucleotide substitutions in the 5' UTR, an allele with the intronic mutation alone and the R93W mutation, described as a susceptibility allele in other disorders. Four of these cases were discovered to be familial and the sequence variants were

found to cosegregate with the disease in the pedigrees, except for the R93W. GDNF gene expression was evaluated by comparative RT/PCR in the renal tissue of one MSK patient with the intronic variant resulting, however, not significantly different from control samples. No mutations were found in the RET gene. We focused on functionally important polymorphisms of the promoter as well as the coding region. One SNP was found with an allele frequency different from the control sample: the G allele of SNP c2307 in exon 13 (p=0.002). We also observed a particular haplotype, never found in controls, at the -5 and -1 RET promoter SNP loci (AA) in one patient. The A/A genotype of SNP-5 was represented only in controls (p=0.009), while the G/A genotype showed a statistically significant overrepresentation in MSK patients (p=0.039). No AC/AC genotype at the RET promoter SNP loci was identified in MSK patients. Moreover, the AG haplotype composed by alleles at two SNPs (c2071 G>A and c2712 C>G) was found in homozygosity in three patients (p=0.026). Reconstructing RET haplotypes using the most significant SNPs in the pedigrees, one was identified recurrent and often associated with MSK and GDNF mutations.

Conclusions: We conclude that GDNF gene variants and specific RET haplotypes, alone or in association, may be highly associated with MSK phenotype.

MP027 EFFECTS OF ENZYME REPLACEMENT THERAPY ON THE PHYSICAL CAPACITY IN PATIENTS WITH FABRY DISEASE

Michael Alexander Zirbs[1], Frank Weidemann[2], Irina Davydenko[1], Andrea Emmert[1], Christoph Wanner[1], Frank Breunig[1]. *[1]Department of Medicine, University Hospital Wuerzburg, Nephrology, Wuerzburg, Germany; [2]Department of Medicine, University Hospital Wuerzburg, Cardiology, Wuerzburg, Germany*

Introduction and Aims: Fabry disease (FD) is an X-linked lysosomal storage disorder caused by deficiency of the enzyme α-galactosidase A. Patients exhibit decreased exercise tolerance, mainly as a cause of cardiac involvement with left ventricular hypertrophy and heart insufficiency, as well as muscular pain on exertion and heat intolerance.

We investigated the effect of enzyme replacement therapy (ERT) on the physical capacity in correlation to the plasma N-terminal pro brain natriuretic peptide (NT-proBNP) levels as a measure of left ventricular failure.

Methods: 64 patients (32 women) with FD (median age 41 years) were evaluated.

The stress test was performed on a bicycle ergometer starting at 25 Watts with stepwise increase by 25 Watts every two minutes, according to the German Society of Cardiology guidelines.

25 patients commenced ERT (Fabrazyme® 1 mg/kg body weight every two weeks) and were followed up to 5 years (mean follow up 2 years).

The reference value of maximal load (Pmax in Watts) was calculated for each patient by a standard formula: Pmax [W] = body weight [kg] x 3 for males and body weight [kg] x 2.5 for females minus 10% for every decade from the age of 30 years on.

The maximum heart rate was determined by using the formula: 220 - age of each patient in years, the NT-proBNP was measured using an electrochemiluminescence immunoassay.

Results: Overall physical capacity was significantly reduced with a mean of 72,2±28,8% ($p < 0.05$) compared to the estimated target value (100%). On average patients accomplished 70% of the calculated maximum heart rate.

On follow up in patients treated with ERT (n=25) ergometric values and maximum heart rate remained stable.

There was a significant increase of NT-proBNP (p=0.0059) and an inverse correlation of high NT-proBNP-values with low ergometric capacity (p=0.012) and low maximum heart rate (p=0.00078).

Conclusions: Patients with Fabry disease show a significantly reduced physical capacity. Despite an increase of the NT-proBNP (p=0.0059) as a marker of heart insufficiency, a stabilizing effect of the ERT has been found during follow up investigations over a 5 year period.

MP028 THE PREVALENCE OF PODOCIN (NPHS2) MUTATIONS IN PATIENTS WITH FSGS

Oktawia Mazanowska[1], Katarzyna Kasprzak-Koscielska[1], Dorota Kaminska[1], Magdalena Krajewska[1], Katarzyna Madziarska[1], Krzysztof Kazimierczak[1], Jozef Penar[1], Dominika Drulis-Fajdasz[1], Irena Wikiera[2], Danuta Zwolinska[2], Marian Klinger[1]. *[1]Dept. of Nephrology and Transplantation Medicine, Wroclaw Medical University, Wroclaw, Poland; [2]Department of Paediatric Nephrology, Wroclaw Medical University, Wroclaw, Poland*

Introduction and Aims: Focal segmental glomerulosclerosis (FSGS) is caused by alterations in podocytes induced by a circulating vascular permeability factor or by an intrinsic podocyte cellular defect. Mutations of the NPHS2 gene, which encodes podocin, cause a steroid-resistant nephrotic syndrome (NS) in children and sporadic FSGS in adults. Identification of homozygous mutation will enable us to avoid ineffective treatment and anticipate the low risk of recurrence after kidney transplantation. The objective of this report is to compare the clinical features in FSGS patients, who carried the molecular defect of podocin (carriers) with patients with no NPHS2 mutation (non-carriers).

Methods: The study included 34 caucasian patients (16F/19M) with biopsy proven FSGS, without known familial history of renal and systemic diseases. All of them presented proteinuria, from moderate to severe at presentation, at the mean age of 21.8 years (from 1.5 to 57 yr.). The therapy consisted of long course of prednisone, with temporary cyclophosphamide in few cases, and with prolonged use of CyA in some other. Molecular analysis of podocin Mutational analysis for NPHS2 (5'UTR, coding sequences and flanking region) was performed. All 8 exons of the NPHS2 gene were amplified by PCR using flanking intronic primers, subjected to automatic sequence analysis by dye-terminator reaction and compared to gene bank sequences for NPHS2 (NC_000001.9 reg. 177786299-177811691).

Results: The NPHS2 mutation was revealed in 6 out of 34 patients (17.6%), aged 18.4±14 at the onset of NS; all but one were females, and two of them progressed to ESRD. The homozygous mutation in 7th exon (290Met) was detected in one patient with aggressive course of FSGS (F; 30 year old at onset) and the necessity of renal replacement therapy within 12 months, and in 5th exon (229Gln) in second one (M; 12 year old at onset) with no progression of renal failure within nearly 30 yr. of observation. Three other patients presented heterozygous mutation (229Arg/Gln) in 5th exon, and one patient heterozygous mutation (290Val/Met) in 7th exon. The clinical course in the herozygous mutations carriers was not different comparing with non-carriers. In 3 patients partial remission was obtained (proteinuria decreased from 3.5±0.33 g/day at onset to 1.0±0.8 g/day at follow up) and 1 patient progressed to ESRD after 6.5y., whereas in the non-carrier group (10F, 18M) reduction of proteinuria from 6.3±4.5 g/day at onset to 2.43±2.2 g/day at follow up was observed in 24 patients (with complete remission in 12, and partial in 4), and progression to ESRD in 4 of them (14.3%) after 3.5 y (21-96 months).

Conclusions: The appearance of the heterozygous podocin (NSPHS2) mutation does not affect the clinical course of FSGS.

MP029 CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT: A CLINICAL AND EPIDEMIOLOGICAL STUDY IN THE ADULT POPULATION

D. Somenzi[1], C. Murtas[1], V. Corbani[1], L. Melfa[2], B. Bianco[1], S. Sanna-Cherchi[1,3], L. Allegri[1]. *[1]Dep. of Clinical Medicine, Nephrology and Health Science, University of Parma, Italy; [2]Dep. of Clinical Medicine, Nephrology and Health Science, Transplant Ward, University of Parma, Italy; [3]Division of Nephrology, Columbia University College of Physicians and Surgeons, New York, USA*

Introduction and Aims: Congenital anomalies of the kidney and urinary tract (CAKUT) account for a significant percentage of kidney disease in children and young adults. The bulk of epidemiological data comes from birth defects registries and pediatric centers but much less information is available from adult populations. Because several conditions can be clinically silent and progression to end-stage renal failure (ESRF) can take several decades, it is likely that a considerable percentage of patients are diagnosed in adulthood. Moreover, estimates of the relative proportion of familial cases still remain elusive. Our goal was to organize a clinical and

epidemiological database of every type of CAKUT of our adult nephrology and internal medicine Department.

Methods: We conducted an extensive screening through chart review of all prevalent and incident patients followed in our Department between March 2005 and September 2007. Data regarding clinical phenotype, demographics, age, age at diagnosis, imaging studies, family history, treatment and evolution to ESRF were collected.

Results: We systematically reviewed 2084 charts of adult outpatients and inpatients from a nephrologic ward, outpatient and inpatients from a kidney transplant unit and patients attending dialysis. We identified 147 patients (7%) with different types of CAKUT: 24% with solitary kidney, 19% with vesicoureteral reflux (VUR), 16% with renal hypodysplasia, 7% with uretero-pelvic junction obstruction (UPJO), 6% with duplicated collecting system, 4% with ectopic kidney, 4% with posterior urethral valves, 1% with multicystic dysplastic kidney, 1% with megaurether.

Overall, 19 (13%) patients presented multiple kidney and urinary tract anomalies.Seven among all affected individuals (5%) had extra-renal anomalies: mainly genital and osteo-chondral ones. Family history for nephropathy was positive in 14% of patients, while 7% had phenotypes included in the CAKUT spectrum: 16% among renal hypodysplasia, 7% among VUR, 0% in solitary kidney group. 37% of patients in our cohort developed ESRF by the age of 50: 100% in posterior-uretral valves category, 71% in VUR category, 33% in solitary kidney category, 29% in kidney hypodysplasia, 27% in UPJO.

Conclusions: Our results demonstrate that CAKUT represents a significant cause of renal disease in the adult population with a significant impact on renal survival. Altogether, solitary kidney and renal hypodysplasia represent 40% of all CAKUT in the adult population, a significantly higher percentage compared to the pediatric population, where posterior urethral valves and VUR are more common. This confirms our hypothesis of a late diagnosis of clinically silent conditions. The presence of positive family history in a fairly high percentage of cases suggests that screening of relatives could facilitate an early diagnosis and modify treatment strategies.

MP030 A RAPID TESTING PROCEDURE FOR FABRY DISEASE: MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION (MLPA)

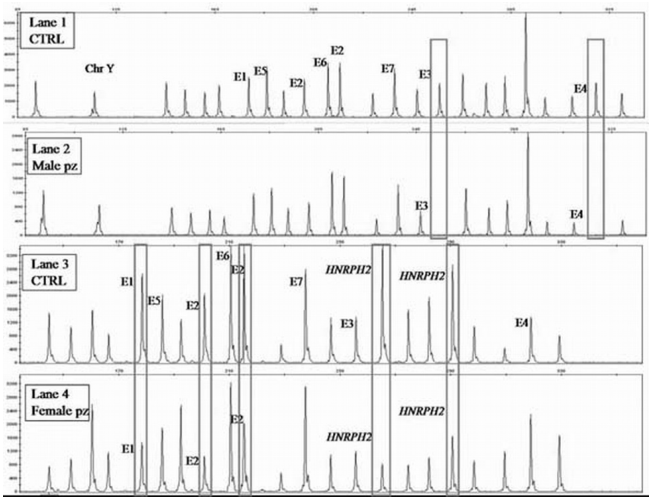
Annalisa Schirinzi[1], M. Centra[1], C. Prattichizzo[1], M. Gigante[2], V. Giancaspro[3], F. Petrarulo[3], M. De Fabritiis[2], R. Santacroce[4], M. Margaglione[4], L. Gesualdo[2], E. Ranieri[1]. *[1]Clinical Pathology, Univ. of Foggia, Italy; [2]Nephrology, Univ. of Foggia, Italy; [3]Nephrology, Osp Di Venere, Bari, Italy; [4]Medical Genetics, Univ of Foggia, Italy*

Introduction and Aims: Fabry Disease (FD) is an X-linked lysosomal storage disorder resulting from deficiency of α-Galactosidase A. This deficiency, due to *GLA* gene mutations, produces the accumulation of 2 neutral glycosphingolipids, in the kidney. Clinical features include also proteinuria in the 3rd or 4th decade of life, and progressive renal impairment. The FD diagnosis in the laboratory is widely defined in male patients by the enzymatic activity detection, whereas often fails to identify female carriers. In fact, normal levels of enzyme are probably due to a skewed X chromosome inactivation, even in presence of a severe phenotype. Therefore, mutation analysis is a valuable tool for the FD diagnosis. No single protocol is to date capable to detect all *GLA* mutations, due to the extreme variability in the germline mutations.

The aim of the present study was to evaluate the potential role in the FD genetic screening of a new method detecting *GLA* deletions, namely Multiplex Ligation-Dependent Probe Amplification (MLPA).

Methods: Two brothers and one unrelated female, clinically supposed Fabry patients, with renal failure, were analyzed. In all 3 subjects were performed a fluorimetric assay to determine the leukocytes enzyme activity and a sequencing of all exons. Subsequently, the MLPA analysis was carried out to detect the relative copy number of all *GLA* exon, as deletions and duplications.

Results: In both brothers, the clinical evidence (encompassing high proteinuria and renal failure, respectively) and the low activity of a-gal A (2 and 4 nmol/mg/h, respectively) were sufficient to confirm the Fabry diagnosis. MLPA analysis allowed us to identify a deletion of exons 3 and 4 as decreased height of peaks corresponding with these specific *GLA* exons, if compared to control sample (Fig. 1, Lanes 1 and 2). In the female subject, the enzymatic activity was normal (30 nmol/mg/h, normal range 20-64 nmol/mg/h), whereas the MLPA analysis revealed a deletion encompassing *GLA* exons 1 and 2, and the flanking gene, *HNRPH2* (Fig.1, Lane 4).



Conclusions: In conclusion, to perform an accurate diagnosis in a family with FD proband, the molecular analysis is necessary, and we show for the first time that MLPA assay is able to evidence deletions not detectable by standard screening methods. This aspect has implications for diagnosis and genetic counseling, especially regarding the availability of specific treatment or the prenatal diagnosis. Our data suggest that this screening should be systematically included in genetic testing of FD patients and that MLPA represents an easy, low cost and reliable system in the molecular diagnostics.

MP031 FAMILIAL C4B DEFICIENCY AND GLOMERULONEPHRITIS

Karina Soto[1], Yee Ling Wu[2], Henrique Martins[1], Chack-Yung Yu[2]. *[1]Nephrology and Medicine, Hospital Amadora Sintra, Lisbon, Portugal; [2]The Research Institute at Nationwide Children's Hospital and the Ohio State University, Columbus, OH, USA*

Introduction and Aims: Complement component C4 plays a central role in classical and lectin pathways. There are two isotypic forms of C4, C4A and C4B. Very few cases of membranoproliferative glomerulonephritis (MPGN) with homozygous C4B deficiency have been described. We report the case of a family with C4B deficiency with two members suffering from proliferative glomerulonephritis.

A 28 year old female was admitted with nephrotic syndrome, microhematuria, hypertension, and normal renal function. There was a family history of nephropathy (brother). Immunological analysis showed only low C4 and IgG levels without autoantibodies or cryoglobulins. Renal biopsy revealed MPGN type III. Immunossupresion treatment reduced proteinuria but remission was never achieved. A second renal biopsy at the fourth year of follow-up confirming MPGN type III with lesser immune deposits.

The clinical records of the patient's brother showed he had been diagnosed with Henoch Schonlein purpura and proliferative glomerulonephritis at the age of 14. He died in CAPD treatment. We hypothesize he was likely to suffer from hypocomplementemia.

Through clinical and laboratory family testing of all direct relatives, we found that her father and her sister's daughter had low C4 levels without disease. A phenotypic and genotypic study was conducted.

Methods: Genomic DNA samples were isolated from peripheral blood mononuclear cells from the patient, her father and her niece. A TaqMan-based realtime PCR (RT-PCR) strategy was applied to determine the copy numbers of total C4, C4A and C4B in each subject. Genomic Southern blot analysis was performed using DNA samples digested by TaqI restriction enzyme and probed for genes of the RP-C4-CYP21-TNX (RCCX) modules. Such TaqI RFLP allowed us to decipher the presence of the long and short C4 genes and their haplotypes.

Results: The RT-PCR results showed that the patient has a total of two C4 genes, which both code for C4A but no C4B. The father and the niece

each have three copies of C4 genes, by which two genes code for C4A and one gene codes for C4B. Genomic Southern blot analysis revealed the presence of homozygous, monomodular-long (L/L) RCCX structures for the patient. The father has heterozygous, bimodular LL, and monomodular L (LL/L). The niece has bimodular LS and monomodular L (LS/L). These observations allow us to make the following interpretation:
Patient: C4A (L)/C4A (L); homozygous C4B deficiency
Father: C4A (L) - C4B (L)/C4A (L); heterozygous C4B deficiency
Niece: C4A (L) - C4B (S)/C4A (L); heterozygous C4B deficiency.
Conclusions: Our data suggest that C4B deficiency may be the principal factor contributing to the development of MPGN in our patient and probably in the glomerulonephritis of her brother. Deficiencies of C4B have not been well-documented in MPGN III. The usual measurements of C4 levels are not adequate to detect a C4A or C4B deficiency. A C4 protein allotyping, and C4A and C4B genotyping would be beneficial.
Further investigations are necessary to determine the relationship between C4B deficiency and susceptibility to MPGN.

MP032 TWELVE NOVEL CLCN5 MUTATIONS AND A COMPLEX ALLELE IN DENT'S DISEASE PATIENTS

Enrica Tosetto[1], Monica Ceol[1], Federica Mezzabotta[1], Anita Ammenti[2], Licia Peruzzi[3], Maria Rosa Caruso[4], Giancarlo Barbano[5], Giuseppe Vezzoli[6], Giacomo Colussi[7], Mario Giordano[8], John Sayer[9], Angela D'Angelo[1], Franca Anglani[1]. *[1]Dept. of Medical and Surgical Sciences, Clinical Nephrology, University of Padua, Padova, Italy; [2]Pediatric Institute, University of Parma, Parma, Italy; [3]Div. of Nephrology, Dialysis and Transplantation, Regina Margherita Hospital, Torino, Italy; [4]Unit of Nephrology, Bergamo Hospital, Bergamo, Italy; [5]Div. of Nephrology, Dialysis and Kidney Transplantation, Pediatric Institute G. Gaslini, Genova, Italy; [6]Div. of Nephrology, Dialysis and Hypertension, IRCCS San Raffaele Hospital, Milano, Italy; [7]Unit of Nephrology, Varese Hospital, Varese, Italy; [8]Unit of Nephrology and Pediatric Dialysis, Pediatric Hospital, Bari, Italy; [9]Inst. of Human Genetics, Newcastle University, Newcastle, United Kingdom*

Introduction and Aims: Dent's disease 1 (DD) is an X-linked disorder of renal tubular epithelial function, associated with mutations in the *ClC-5* Cl^-/H^+ antiporter. Defects in the OCRL1 gene encoding a phosphatidyl-inositol 4,5 bisphosphate 5-phosphatase, usually mutated in patients (pt) with Lowe syndrome, have been demonstrated to lead to a Dent-like phenotype referred to as Dent 2 disease. Characteristic abnormalities include low-molecular-weight proteinuria and other features of Fanconi syndrome, such as glycosuria, aminoaciduria, and phosphaturia, but typically do not include proximal renal tubular acidosis. Progressive renal failure is common, as are hypercalciuria, nephrocalcinosis and kidney stones. No extrarenal manifestations have been recognized except for rickets, in a minority of patients. Mutations in the *CLCN5* gene have been reported consistently in pt with DD and a total of 107 different mutations have been so far reported.
Methods: Twenty nine pt with symptoms of DD were screened by SSCP analysis and by direct sequencing for the presence of mutations in the coding sequence and the exon-intron boundaries of the CLCN5 gene as well as in the 5' untranslated exons of the gene.
Results: We found 12 new mutations and one recurrent mutation (S244L) of the CLCN5 gene. Among these novel mutations, two are short in-frame deletion or insertion (261delG, T277_L278 ins S), two are frameshift mutations (L192fsX206, R589fsX592), three are donor splice-site mutations (IVS4 +4 A>G, IVS8 +1 G>T, IVS11 +1G>T) and five are missense mutations (W58L, G261R, G512D, W547R, P621L). The missense mutations involved amino acids highly conserved among different species and were predicted to affect protein function by both the web program SIFT and Polyphen. Taken together these results indicate that these missense mutations are pathogenic. We identified also a complex allele that consist of two mutations (S386F and S388fsX434) in one pt, inherited from his mother and grandmother.
Conclusions: Our study expands the number of CLCN5 mutations to 121 and for the first time identifies a complex allele as a disease causing mutation. It indicates that exons 8 and 10 are more frequently mutated: forty two percent of total mutations affect loop H and ClC-5 elices I to M, O to R and the C-terminal domain. Moreover the protein codons 58, 261, 512 and 547 are probably hot spots for mutations.

MP033 VARIATIONS OF NPHS2, ACTN4 AND TRPC6 IN CHINESE PATIENTS WITH ADULT ONSET FAMILIAL FOCAL SEGMENTAL GLOMERULAR SCLEROSIS

Bin Zhu[1], Chaohui Wang[1], Xiaoxia Pan[1], Hong Ren[1], Wen Zhang[1], Yaowen Xu[1], Cuilan Hao[1], Chunmin Pan[2], Yan Sheng[2], Huaidong Song[2], Nan Chen[1]. *[1]Nephrology, Jiao Tong University Ruijin Hospital, Shanghai, China; [2]Jiao Tong University Ruijin Hospital, Shanghai, China*

Introduction and Aims: NPHS2, ACTN4 and TRPC6 are the major components of podocyte in familial focal segmental glomerular sclerosis (FFSGS). The role of these molecules in Chinese patients with FFSGS remains unclear. The objective of this research is to investigate Variations of NPHS2, ACTN4 and TRPC6 in Chinese patients with adult onset familial focal segmental glomerular sclerosis (FSGS).
Methods: We screened 32 pedigrees gathered from July 1997 to May 2007 in our department with adult onset FFSGS. The diagnose criteria of FFSGS are one or more individuals had a kidney biopsy proven FSGS and at least one other individual with renal failure or proteinuria without clear cause. And the onset age is more than 15 years old. Genomic DNA extracted from peripheral blood cells were PCR-amplified to sequence for analysis of variations of NPHS2,ACTN4 and TRPC6. Sixty unrelated health persons were screened as control group.
Results: We identified a new heterozygotic missense mutation L316P of ACTN4 in a pedigree. The proband presented with 24h proteinuria of 931mg with hypertension and was diagnosed with FSGS by renal biopsy in 47 years old. His serum creatinine was 105 umol/L now. His mother had serum creatinine of 127umol/L and was also proven to have FSGS with renal biopsy in 57 yeas old for proteinuria and microscopic hematuria. His brother of the proband have 24h proteinuria with 910mg and remained remission after immunorepressive therapy. Renal function of individual in this pedigree progress slowly. The 3 members affected all have this heterozygotic mutation. We also found a new missense mutation Q899K of TRPC6 in another pedigree. The proband was diagnosed by renal biopsy with FSGS at the age of 35 with 24h proteinuria of 129mg. His serum creatinine was 70umol/L. His little sister was also confirmed to have FSGS by renal biopsy with 24h proteinuria of 2200mg. Her proteinuria remained abnormal with oral prednisone. Her serum creatinine was 172umol/L now (2 years from the time of diagnose). Their father has proteinuria (+) by urine dipsticks with normal renal functions at the age of 65. These 3 members all have this heterozygote missense mutation. The older sister of the proband without renal disease have no this mutation. We also identify a quiescent mutation G467G of TRPC6. We cannot find any mutations of NPHS to induce FFSGS 2 in these pedigrees.
Conclusions: We identified a new mutation L316P of ACTN4 and a new mutation Q899K of TRPC6 in 2 Chinese pedigrees with late onset familial FSGS respectively. There were no NPHS2 mutation found to induce FSGS in these pedigrees.

MP034 THE B ALLELE OF THE BSMI VITAMIN D RECEPTOR (VDR) GENE POLYMORPHISM IS INDEPENDENTLY ASSOCIATED TO LVH AND TO HIGHER PROGRESSION RATE OF LVH IN END STAGE RENAL DISEASE (ESRD) PATIENTS

Alessandra Testa, Francesca Mallamaci, Francesco A. Benedetto, Giovanni Tripepi, Carmine Zoccali. *CNR-IBIM, Clin. Epidemiology and Physiopath. of Renal Dis. and Hypertens., Reggio Calabria, Italy*

Introduction and Aims: Left ventricular hypertrophy (LVH) is a strong risk marker for death and cardiovascular complications in ESRD patients. Experimental evidence indicates that vitamin D deficiency and/or disturbed vitamin D signalling may be implicated in the high risk of ESRD because Vitamin D Receptor (VDR) knock-out mouse displays marked cardiac hypertrophy.
Methods: Because the BsmI VDR gene polymorphism may alter the VDR function, we performed a study contemplating cross-sectional and longitudinal observations aimed at establishing 1) the relationship between BsmI VDR gene polymorphism (high-throughput TaqMan allelic discrimination assay) and LV mass index (LVMI) measured by echocardiography 2) The predictive power of this polymorphism for progression in LV hypertrophy (LVH). One hundred eighty-two dialysis patients (age 59±15 yrs; 104

M and 78 F, all Caucasians) participated into the study and each patient underwent echocardiography twice, 18±2 months apart.
Results: The distribution of BsmI genotypes did not significantly deviate from Hardy-Weinberg equilibrium either in patients or in an age and sex matched group of healthy subjects. The frequency of the B allele (40.4%) in dialysis patients was similar that of healthy control subjects (38.6%). The number of B-alleles of BsmI polymorphism were directly and significantly related to LVMI (r=0.20, P=0.007). This relationship was quite robust because it remained unmodified (β=0.20, P=0.005) in a multivariate analysis adjusting for traditional risk factors (age, sex, smoking, systolic pressure, diabetes, cholesterol and previous CV events), factors peculiar to ESRD (haemoglobin, albumin, calcium*phosphate, KTV and duration of RDT), emerging risk factors (CRP, homocysteine and ADMA) and anti-hypertensive and calcitriol treatment. In the longitudinal study LVMI rose from 60.1±17.9 g/m$^{2.7}$ to 64.2±19.3 g/m$^{2.7}$ (P<0.001). Interestingly, patients carrying the B allele showed a higher progression rate of LVMI (Δ LVMI: +0.30±0.53 g/m$^{2.7}$/month) when compared to patients without the B allele (Δ LVMI: +0.08±0.49 g/m$^{2.7}$/month) (P=0.019) and this difference remained significant (P=0.03) also after data adjustment for all potential confounders including LVMI at baseline.
Conclusions: In dialysis patients, the B allele of the BsmI VDR gene polymorphism is strongly and independently related to LVH and it is associated to higher progression rate of LVH in these patients. Since genes are randomly transmitted (Mendelian randomization), our cross-sectional and longitudinal observations consistently support the hypothesis that altered Vitamin D signalling in vivo, in ESRD patients is implicated in LVH in ESRD patients.

MP035 METHYLARGININE ENZYMATIC MACHINERY AND LEPTIN IN ADIPOSE TISSUE IN CKD PATIENTS

Belinda Spoto, Leonardis Daniela, Francesca Mallamaci, Rosa M. Parlongo, Patrizia Pizzini, Giovanni Tripepi, Carmine Zoccali.
CNR-IBIM, Clin. Epid. and Physiopath. of Renal Dis. and Hypert., Reggio Calabria, Italy

Introduction and Aims: The enzymatic system that generates and degrades the endogenous inhibitor of the NO synthase, asymmetric dimethylarginine (ADMA), is expressed in human adipocytes (*Spoto B et al., J Nephrol 2007; 20: 554-559*). This finding appears of potential relevance because ADMA is involved in endothelial dysfunction, inflammation and insulin resistance. Since a major fat cell cytokine, Leptin, impinges upon the same processes we investigated in the adipose tissue the relationship between the gene expression of Leptin and genes that code for ADMA biosynthesis [protein-arginine methyltransferase: PRMT1, PRMT2, PRMT3] and degradation [dimethylarginine dimethylaminohydrolase: DDAH1, DDAH2].
Methods: Subcutaneous adipose tissue was harvested in 22 chronic kidney disease (CKD) patients and in 21 healthy subjects (HS) matched for age (53±13 vs 53±14 yrs), sex and BMI (26±4 vs 26±3 kg/m^2).
Results: Both in CKD (r=0.84, P<0.001) and in HS (r=0.57, P=0.007) plasma Leptin and gene expression levels of Leptin were strongly inter-related. Plasma levels of ADMA and Leptin were higher in CKD than in HS (p<0.01) whereas the gene expression of Leptin was by 41% lower in CKD than in HS pointing to reduced renal clearance as a relevant factor for the accumulation of this adipokine. Moreover, CKD patients showed higher PRMT1 (+33%, P=0.07), PRMT2 (+29%, P=0.006) and PRMT3 (+33%, P=0.003) gene expression as compared to HS. DDAH1-2 gene expression levels were also higher in CKD patients (+30% and +18%) than in HS. Interestingly, in CKD patients the gene expression of main enzymes that regulate ADMA metabolism (PRMT1-3 and DDAH1-2) was strongly and directly related with Leptin gene expression (r ranging from 0.52 to 0.68, p≤0.01) whereas no such an association existed in HS.
Conclusions: Enzymes that regulate ADMA synthesis are over-expressed in adipocytes of CKD patients. The gene expression of enzymes which control ADMA metabolism is tightly associated with that of Leptin in CKD patients. The links between the ADMA machinery with Leptin in CKD suggest that deranged methylarginine metabolism may be implicated in the altered regulation of this adipokine in ESRD.

MP036 SCREENING OF THE PKD1 GENE IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Jitka Stekrova[1], Stanislava Svobodova[1], Jana Reiterova[2], Miroslav Merta[2], Vera Kebrdlova[1], Milada Kohoutova[1]. [1]*Institute of Biology and Medical Genetics, First Faculty of Medicine and General Teaching Hospital, Prague, Czech Republic;* [2]*Nephrology Department, First Faculty of Medicine and General Teaching Hospital, Prague, Czech Republic*

Introduction and Aims: Autosomal dominant polycystic kidney disease (ADPKD), one of the commonest monogenic diseases of humans, is a systematic disorder with frequent hepatic and cardiovascular manifestations in addition to the progressive enlargement and destruction of the normal renal architecture by multiple fluid-filled cysts. This disease is incurred by mutations in the PKD1 and PKD2 genes. The PKD1 gene is located on the short arm of chromosome 16 and is responsible for 85-90% of all cases. Mutations in the PKD2 gene on the long arm of chromosome 4 cause this disease in 15% families. The phenotypes associated with PKD1 and PKD2 mutations are remarkably similar, except that the former often has a more severe disease course (average age at onset of end-stage renal failure of 53 compared to 69 years for PKD2). Protein products of these two genes polycystin-1 and polycystin-2 may interact with each other forming a large membrane-associated complex which has a crucial role in the regulation of cell proliferation, differentiation and normal renal tubulogenesis. However, mutation screening of the major ADPKD locus, PKD1, has proved to be difficult because of 1) the large transcript, 2) complex reiterated gene region, 3) no clear hot spots and 4) because most mutations are unique to a single family.
Methods: 14 patients with severe clinical course of ADPKD were tested for mutations in the PKD1 gene. 46 exons of the PKD1 gene were amplified by long range polymerase chain reaction (PCR) followed by nested PCR. Three different mutation detection techniques were used- direct sequencing, heteroduplex analysis (HA) and high-resolution melting (HRM). Suspected samples from HA and HRM were then sequenced.
Results: We have detected 3 short deletions, 2 nonsense mutations, 23 missense mutations and 27 polymorphisms. Missense mutations segregate with affected members in the families and are not present in 100 healthy control subjects. One deletion and one nonsense mutations have not been reported yet. Two deletions were present in introns and we will analyze their effect on the splicing on RNA level. Both these novel mutations were associated with severe manifestation of the disease. Renal insufficiency is already present in patients younger than 40 years.
Conclusions: Mutation detection of the PKD1 and PKD2 genes and the correlation of the mutations with clinical course is important as it might bring insights into the pathogenesis of the disease.
Supported by the grant projects IGA MZ CR NR/9427-3, VZ MSMT 0021620806

MP037 IDENTIFICATION OF NINETEEN MUTATIONS IN SLC12A3 GENE OF CHINESE PATIENTS WITH GITELMAN'S SYNDROME

Ling Qin[1], Hong Ren[1], Weiming Wang[1], Wen Zhang[1], Bin Han[2], Qi Feng[2], Nan Chen[1]. [1]*Nephrology, Jiao Tong University Ruijin Hospital, Shanghai, China;* [2]*National Center for Gene Research, Chinese Academy of Sciences, Shanghai, China*

Introduction and Aims: Gitelman's syndrome is a recessively inherited renal tubular disorder characterized by hypokalemic metabolic alkalosis, significant hypomagnesemia, low urinary calcium, secondary aldosteronism and normal blood pressure. The SLC12A3 gene encodes the thiazide sensitive Na-Cl co-transporter (NCCT) expressed in the apical membrane of the distal convoluted tubule. Inactivating mutations of this gene are responsible for Gitelman's syndrome (GS).
Methods: We searched for SLC12A3 gene mutations in 27 Chinese patients (16 males and 11 females, age 32±14 yrs)from 22 unrelated families with the clinical features of GS (hypokalemia, hypomagnesemia, metabolic alkalosis, hypocalciuria, and normal blood pressure). All 26 exons of SLC12A3 gene were analyzed using PCR followed by direct sequencing analysis. When heterozygous deletion or insertion mutations were found by direct sequencing, the PCR products were subcloned into PGEM-T Easy vector, followed sequencing using T7/SP6 sequencing primers.

Results: We identified nineteen mutations distributed throughout SLC12A3 gene. Twelve are novel mutations, including 7 missense mutations: G196V, T339I, N359K, Y386C C430G, G439V and L571P; two deletions: 1384delG(460Frameshift) and 346-353delACTGATGG (114Frameshift); one in-frame insertion: 997insC; one complex deletion-insertion: 492-496delTACGGinsA(162Frameshift) and one splice mutation combined with deletion, IVS7-1G>A & g.7427_7438del>CCGAAAATTTT. Seven were described previously, including six missense: T60M, C421F, D486N, R655H, R913Q, R928C and one deletion: 2883-2884delAG(959Frameshift). Surprisingly, we detected homozygous or heterozygous mutation T60M in 13 patients.
Conclusions: We reported the identification of nineteen mutations in the SLC12A3 gene, including 12 novel mutations in 27 Chinese patients with Gitelman's syndrome. T60M may be the most common mutation in Chinese patients with GS.

MP038 DOES TRANSFORMING GROWTH FACTOR-BETA1 (TGF-β1) GENE SINGLE NUCLEOTIDE POLYMORPHISMS (SNP) IN CODON 10 AND 25 INFLUENCE THE SERUM LEVEL OF TGF-β1 IN PATIENTS WITH PRIMARY GLOMERULONEPHRITIS (GN) AND LUPUS NEPHRITIS (LN)?

Pawel Olejniczak, Magdalena Polcyn-Adamczak, Zofia Niemir.
Department of Nephrology, Transplantology and Internal Diseases, University of Medical Sciences, Poznan, Poland

Introduction and Aims: Recently, the association between the TGF-β1 gene SNPs and susceptibility to the progression of chronic inflammatory kidney diseases has been suggested. The 868T/C (codon 10) and 913G/C (codon 25) SNPs of TGF-β1 are thought to influence the TGF-β1 production. However, the genotype, TGF-β1 serum level and the form of kidney disease differ dependent of the population studied, and thus this relationship remains unclear. The purpose of this study was to look for any association between the genetic background (868T/C and 913G/C TGF-β1 gene SNPs) and the serum level of TGF-β1 in Polish population of patients with GN and LN.
Methods: DNA was isolated from blood samples of 162 patients (132 with GN and 30 with LN) and 168 age-matched healthy controls (C). The SNP analysis was performed using the polymerase chain reaction – single strand conformation polymorphism (PCR-SSCP). The specificity of the fragments studied by PCR-SSCP was confirmed by sequencing. The serum level of TGF-β1 was measured using the specific enzyme immunoassay.
Results: No significant differences in the genotype distribution in TGF-β1 gene codon 10 were detected between C and patients with GN or LN (TT: 34.5% vs. 28.8% vs. 30% $p>0.05$; TC: 48.2% vs.56.1% vs. 56.7% $p>0.05$; CC: 17.3% vs.15.1% vs. 13.3% $p>0.05$). There were also no differences in the codon 25-genotype distribution (GG: 87.5% vs. 84% vs. 90% $p>0.05$; GC: 12.5% vs. 15.2% vs. 10% $p>0.05$). The serum levels of TGF-β1 were comparable in C and LN groups (41.8±13.9ng/mL vs. 44.9±21.8ng/mL). In contrast, the values obtained in patients with GN were lower (33.9±18.1ng/mL) and the difference between C and this group did reach almost significance ($p=0.07$). Interestingly, this was supported by a nearly significant difference between the distributions of TT genotype in codon 10 in C compared with CC genotype in the GN group ($p=0.06$). Other genotype constellations did not show any differences between the analyzed groups in terms of the serum level of TGF-β1.
Conclusions: Our results showed that none of the TGF-β1 SNPs analyzed was associated with the occurrence of GN or LN in the Polish population. Although the codon-10 CC genotype seems to influence the serum level of TGF-β1 in GN, it must be taken into consideration that other genetic, epigenetic or additional factors exist that affect TGF-β1 production and serum concentration of this cytokine.

Acute renal failure – Basic research 2

MP039 THE INFLUENCE OF LOW-PROTEIN SOY-BEAN DIET ON THE LEVEL OF BLOOD PRESSURE AND BLOOD SERUM INORGANIC ANIONS CONCENTRATIONS IN SPONTANEOUS-HYPERTENSIVE RATS (SHR) WITH EXPERIMENTAL CHRONIC RENAL FAILURE

Anatoliy Kucher[1], Marina Parastayeva[1], Irina Zubina[1], Olga Beresneva[1], Galina Ivanova[2], Ivan Kayukov[1]. *[1]Institute of Nephrology, State Medical University Named after I.P. Pavlov, Saint Petersburg, Russian Federation; [2]Pavlov Institute of Physiology, Saint Petersburg, Russian Federation*

Introduction and Aims: The aim of the study was to determine the effect of the standard and the low-protein soy-bean diet (LPD) on the blood pressure (BP) level, the left ventricular hypertrophy (LVH) and nitrate and sulfate concentrations in serum of spontaneous-hypertensive rats (SHR).
Methods: The following groups of male SHR rats have been examined: 1) control group – sham-operated rats receiving the standard diet containing 20% of animal protein (n=8); 2) rats after 5/6 nephrectomy (5/6 NE) on standard diet (n=8); 3) sham-operated rats receiving LPD (containing 10% soybean protein - SUPRO 760) (n=10); 4) 5/6 NE rats on LPD (n=9). The 5/6 NE was carried out in two-stage manner with the one week interval between the stages. The animals were slaughtered two months after the NE. The mean BP was measured just before the slaughter of animals by cuff method. The concentrations of nitrate and sulfate anions were evaluated in serum by the capillary electrophoresis using the "Kapel-103P" device (manufactured by "LUMEX", Saint Petersburg, Russia). LVH was estimated as the ratio of the myocardial mass to the mass of the body (mg/g).
Results: The value of BP in 5/6 NE rats on standard diet was greater than in control group (220±10 and 165±5 mm Hg, correspondingly, $p<0.001$). LPD prevented the increase of the BP: BP in group 3 was 170±5 mm Hg which was statistically lower than the values of BP in group 2 ($p<0.001$). There was no difference in BP in rats on LPD independently of decrease of renal function. LPD prevented the development of the LVH in rats with NE: LVH was equal to 3.26±0.03 in group 4 as compared to 4.23±0.25 in group 2, $p<0.001$. The level of NO^{3-} was the same in groups 3 (0.39+0.03 mmol/l), group 4 (0.34±0.03 mmol/l) and in controls (0.39±0.02 mmol/l). The concentration of SO_4^{2-} in rats on LPD (both NE and sham-operated) was higher than in rats on standard diet: in group 3 – 2.79±0.09 mmol/l, in group 4 – 2.66±0.10 mmol/l in comparison with group 1 – 2.05±0.05 mmol/l and group 2 – 2.21±0.08 mmol/l ($p<0.02$ in all cases).
Conclusions: Thus the low protein soybean diet revealed antihypertensive and cardioprotective effect in SHR rats with chronic renal failure. However the mechanism of the soybean protein impact on BP and the level of serum sulfates is unclear and needs further investigation.

MP040 THE EFFECT OF AMIFOSTINE ON RENAL INJURY DUE TO TOTAL BODY IRRADIATION

Diclehan Unsal[1], Galip Guz[2], Mustafa Kavutcu[3], Muge Akmansu[1], Suna Omeroglu[4]. *[1]Radiation Oncology, Gazi University Faculty of Medicine, Ankara, Turkey; [2]Nephrology, Gazi University Faculty of Medicine, Ankara; [3]Biochemistry, Gazi University Faculty of Medicine, Ankara, Turkey; [4]Histology, Gazi University Faculty of Medicine, Ankara, Turkey*

Introduction and Aims: Total-body irradiation (TBI) is an important part of the conditioning regimen for different malignancies, however, has a toxic effect on healthy tissues. Amifostine is a thiophosphate prodrug approved by the FDA for the prevention of toxicities associated with therapeutic radiation. The aim of the randomized experimental study was to investigate the effect of amifostine on renal injury due to TBI.
Methods: Forty male, Wistar-Albino rats were divided into the following four groups: 1. control, 2. amifostine, 3. Radiotherapy (RT), and 4. RT+amifostine. Cobalt 60 teletherapy instrument was used for a single peak whole body dose of 6.5 Gy RT. Amifostine (200 mg/kg) was applied i.p. to the rats in groups 2 and 4 30 minutes before irradiation. On week 12 postirradiation, 24-h urinary protein and creatinine excretion were measured. Blood hematocrit, serum BUN, and creatinine were assessed in the intracardiac blood taken at the time of sacrification. Nephrectomy was performed for

lipid peroxidation and enzymes (catalase, superoxide dismutase, glutathione peroxidase) determination, and histological assessment.
Results: Irradiation caused a statistically significant increase in serum BUN levels at 12 weeks (p=0.001), whereas amifostine-administered irradiated group show a difference in favor of drug administration (p=0.028). Twelve weeks after TBI, urinary protein level of the irradiated animals was 7 times higher than that of the nonirradiated control groups ($p<0.0001$). By the administration of amifostine, it was found to be decreased (p=0.001). Creatinine clearance decreased secondary to RT, but this decrease was weaker with amifostine administration. By the administration of amifostine in the irradiated groups, catalase activity and glutathione peroxidase activity were restored (p=0.001). Amifostine before RT significantly blunted the increase in mean histologic scores following TBI (p=0.002).
Conclusions: In conclusion, the study showed that a single dose amifostine (200mg/kg) ameliorated the renal injury following TBI.

MP041 BLOCKING OF TGF-β SIGNALING AMELIORATES EXPERIMENTAL MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

M.C. Banas[1], K.L. Hudkins[2], T.A. Wietecha[2], S. Alexandrescu[2], S. Ledbetter[3], B. Stoelcker[1], B. Banas[1], C.E. Alpers[2]. *[1]Department of Nephrology, University of Regensburg, Regensburg, Germany; [2]Department of Pathology, University of Washington, Seattle, WA, USA; [3]Genzyme Corporation, Framingham, MA, USA*

Introduction and Aims: TGF-β, in respect to matrix synthesis in the kidney, regulates the production of proteoglycans, fibronectin, and collagens in glomerular mesangial, epithelial, and endothelial cells. Its profibrotic potential is well known. We assessed the effectiveness of a murine monoclonal TGF-β neutralizing antibody (ID11, Genzyme Corporation, Framingham, MA) in thymic stromal lymphopoetin (TSLP) transgenic mice, a mouse model of cryoglobulinemic membranoproliferative glomerulonephritis (MPGN).
Methods: Wild type (WT) and TSLP transgenic mice were treated for 4 weeks with 0.5 mg/kg, 2.5 mg/kg, or 5 mg/kg ID11, respectively intraperitoneally 3 times per week. An isotype-matched irrelevant antibody, 13C4, was used as control. Serum TGF-β levels were analyzed by ELISA. Kidney morphology was evaluated by light microscopy (H&E, PAS and silver stain), and immunohistochemistry for macrophages (Mac2), cellular proliferation (Ki67) and collagen IV.
Results: Serum TGF-β levels in TSLP mice were decreased in a dose dependent manner. Mice treated with 0.5 mg/kg ID11 showed no differences (mean 1092.9 pg/ml) compared to control animals (1104.9 pg/ml), but treatment with 2.5 mg/kg reduced TGF-β levels (724.1 pg/ml) and at a dose of 5 mg/kg we observed a significant reduction of serum TGF-β levels (403.7 pg/ml) in TSLP mice. Both by light microscopy and morphometry we could detect a decrease in matrix deposition (mean collagen IV stain per glomerular area in WT control 12,4%, in TSLP control 22.48±0.019%, in TSLP ID11 5 mg/kg 15.36±0.039%). Glomerular hypertrophy in TSLP mice was reduced upon treatment (mean glomerular size WT control 2680 μm, TSLP control 3792 μm, TSLP ID11 5 mg/kg 3225 μm). Morphometry revealed less glomerular macrophage influx (Mac2 staining leukocytes) (mean macrophage number: WT control 0,88, TSLP 3,16, TSLP ID11 1,83 per glomerular cross section). In contrast, quantitation of Ki67+ proliferating cells and the cell number per glomerular cross-section revealed no differences between the groups. Since TSLP mice show a systemic disease, including splenomegaly, other organs were also evaluated. Remarkably spleen weight was reduced to 1.6% of total mouse weight after treatment with ID11 5mg/kg compared to 2.1% in control injected TSLP mice.
Conclusions: These results emphasize the important role of TGF-β in regulating fibrotic immune diseases and suggest that anti-TGF-β based strategies may be a useful therapeutic approach for treating glomerular diseases.

MP042 OVER-EXPRESSION OF HGF TO MODULATE THE POST-ANOXIC INFLAMMATORY RESPONSE IN TUBULAR EPITHELIAL CELLS

Marcella Franquesa[1], Anna Sola[2], Joan Torras[1], Gina Hotter[2], Nuria Lloberas[1], Inés Rama[1], Josep M. Grinyó[1], Immaculada Herrero-Fresneda[1]. *[1]Experimental Nephrology, IDIBELL-Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain; [2]Experimental Pathology, IIBB-CSIC, Barcelona, Spain*

Introduction and Aims: Hepatocyte growth factor (HGF) acts on renal tubular epithelial cells stimulating regeneration. In addition to its mitogenic, anti-apoptotic and proliferative effects, HGF also has anti-inflammatory and anti-fibrogenic effects.
Our group has demonstrated the anti-apoptotic, anti-fibrotic, pro-regenerative and anti-inflammatory effects of in vivo HGF electrotransfer in warm-ischemic and renal transplant models.
To elucidate the mechanisms underlying the beneficial in vivo effects of HGF in response to ischemia/reperfusion we focused on the tubular cell as the efector cell and main target of gene therapy in vivo, moving towards an in vitro system.
Methods: With a hypoxic chamber we induced oxygen deprivation followed by different reperfusion times to a tubular epithelial cell line stably transfected with HGF.
Inflammatory cytokine expression was analyzed by real time PCR and protein levels in the medium by Flow Cytometry. Phosphorylated STATs levels were analyzed with specific ELISA assay for DNA binding proteins. The balance of cell death-apoptosis was also established determined by LDH analysis and caspase 3 activity and cytocrom C release from mitochondria.
Results: Analyzing inflammatory cytokines we observed that HGF can inhibit MCP-1, Rantes, RelA and TGFbeta expression, while VEGF increases after long oxygen deprivations in the transfected cells. These cytokines expression levels were correlated with activated STAT1 and STAT5a levels. After long oxigen deprivation in tubular epthelial cells show increased levels of apoptosis that become higher after reoxygenation. HGF protects tubular epithelial cells from hypoxic cell death.
Conclusions: The over-expression of HGF in the tubular cell offers protection against the inflammatory disease initiated in the same cell. Moreover the down-regulation of these inflammatory cytokines can be key in impairing cell infiltrating in vivo and progression of fibrotic stages. The knowledge of this pathway is of great interest due to its possible use as a therapeutic target.

MP043 ANTIOXIDANT AND PROTECTIVE EFFECTS OF SILYMARIN ON ISCHEMIA AND REPERFUSION INJURY IN THE KIDNEY TISSUES OF RATS

Faruk Turgut[1], Omer Bayrak[2], Ferhat Catal[3], Reyhan Bayrak[4], Ali Fuat Atmaca[5], Akif Koc[2], Ali Akbas[6], Ali Akcay[1], Dogan Unal[2]. *[1]Department of Nephrology, Fatih University, [2]Department of Urology, [3]Department of Pediatry, [4]Department of Pathology, Fatih University, School of Medicine, Ankara, Turkey; [5]First Urological Clinic, Ataturk Training and Research Hospital, Ankara, Turkey; [6]Department of Biochemistry, Gaziosmanpasa University, Medical Faculty, Tokat, Turkey*

Introduction and Aims: Renal ischemia/reperfusion (I/R) injury is a major cause of acute renal failure. Silymarin is extracted from *Silybum marianum* and *Cynara cardunculus* seeds and fruits. The aim of this study is to investigate whether silymarin administration prevents the damage induced by I/R in rat kidneys.
Methods: Thirty male Wistar rats were randomly divided into 5 experimental groups (n=6, each) as follows; Control group, Sham-operated group, I/R group, Silymarin group, and I/R+silymarin group. In the I/R and I/R+silymarin groups, both renal arteries were occluded using nontraumatic microvascular clamps for 45 min. Then, at the end of 24 h of reperfusion, the animals were killed. Kidney function tests, serum oxidants and antioxidants were determined. Kidneys were used for histopathological analysis.
Results: Animals that subjected to I/R, exhibited significant increase in serum urea, creatinine and cystatin C levels compared to the rats treated with silymarin prior to the I/R process ($p<0.001$). Serum superoxide dismutase and glutathione peroxidase significantly higher, whereas nitric oxide, malondialdehyde and protein carbonyl significantly lower in I/R+silymarine

group compared to I/R group (Table 1). Semiquantitative assessment of the histological changes was graded and I/R group had significantly higher score compared to I/R+silymarin group (Figure 1).

Table 1. Serum malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), nitric oxide (NO) and protein carbonyl (PC) levels of groups

Groups (n=6)	Control	Sham	I/R	Silymarin	I/R+silymarin
MDA	0.24±0.02	0.30±0.12	0.49±0.08*	0.33±0.01	0.31±0.04
SOD	4.16±0.2	2.84±0.5	2.03±0.2*	3.01±0.3	3.1±0.1
GSH-Px	2108±100	2059±135	1630±124$^{\alpha}$	1929±231	1834±72
NO	47.1±5.1	56.3±5.9	84.1±7.5*	55.5±5.3	59.5±8.6
PC	669±51	837±63	981±98*	667±88	741±78

I/R; Ischemia/reperfusion, *p<0.001 compared to I/R + Silymarin, $^{\alpha}$p<0.05 compared to I/R + Silymarin.

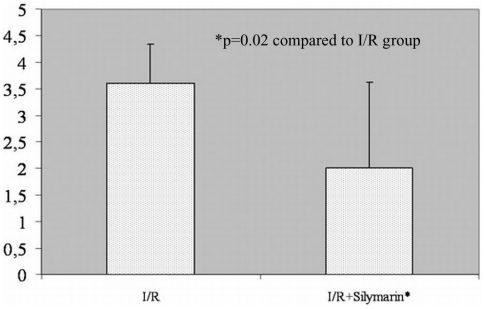


Figure 1. Semiquantitative assessment of the histological changes

Conclusions: Based on our findings, silymarin protects the kidneys against I/R injury. This finding may provide a basis for the development of novel therapeutic strategies for protection against the damages caused by I/R.

MP044 IMBALANCE BETWEEN VASCULAR ENDOTHELIAL GROWTH FACTOR AND ENDOSTATIN EXPRESSION IN THE MURINE MODEL OF ISCHEMIA/REPERFUSION-INDUCED ACUTE RENAL FAILURE

Enia Lucia Coutinho[1], Nestor Schor[1], Maria Helena Bellini[2]. [1]*Medicine Department/Nephrology Discipline, Federal University of São Paulo, São Paulo, Brazil;* [2]*Centro de Química e Meio Ambiente/IPEN-CNEN, University São Paulo, São Paulo, Brazil*

Introduction and Aims: Angiogenesis has recently attracted considerable attention as a component of remodeling after ischemic injury and renal ischemia-hypoxia is a leading cause of acute renal failure. Endostatin is the C-terminal fragment of collagen XVIII generated by proteolytic cleavage and it is well known as being an inhibitor of angiogenesis. Vascular endothelial growth factor (VEGF) stimulates endothelial cell proliferation, and endostatin directly antagonizes the biological effects of VEGF. The maintenance of microvessel renal cells is also thought to depend upon the local balance of VEGF and endostatin in the kidney. Therefore, this study was designed to determine whether there is a balance between VEGF and endostatin levels after ischemic injury.
Methods: Ischemic renal failure was induced via 45 min of bilateral occlusion of the renal artery and vein, followed by 12 h or 24 h of reperfusion. Whole kidney homogenate was examined by Western blot and ELISA and total RNA were extracted for analysis by quantitative PCR. Sections of renal tissue from ischemic/reperfused mice were immunostained for Endostatin, VEGF and the endothelial-specific marker CD31.
Results: Endostatin mRNA and protein expression increased during ischemia and at 12 h of reperfusion while VEGF were significantly higher after 24h of reperfusion than in control group *($p<0.01$)*. The ratio between VEGF and endostatin mRNA showed an increased VEGF in 6.16-fold after 24h of reperfusion *($p<0.001$)*, according to ELISA assay. In addition, the VEGF/endostatin protein levels ratio was significantly increased after 24 h of reperfusion. In ELISA assay to endostatin, the levels in renal tissue was remarkably increased during ischemia (*9.2-fold, $p<0.001$*), what was not found in serum, where the levels was not significantly changed (*$p=0.23$*). There was a significant correlation between VEGF and endostatin levels in both control mice *($r=1.03$, $p<0.01$)*. The immunohistological examination revealed glomerular and tubulointerstitial expression of endostatin and a difused staining to VEGF in epithelial cells and glomeruli. CD-31 staining showed a decreased staining during ischemia/reperfusion agreeing to endostatin expression.
Conclusions: Microvasculature remodeling is a *sine qua non* condition to tissue repair after ischemia/reperfusion-induced acute renal failure. Our data suggest that both molecules with opposite effect play a role in this process. Both specialized and non-specialized renal microvasculature are a target to VEGF and endostatin. Although, the endostatin expression is more prominent during ischemia and VEGF is more evident after reperfusion. These data suggest an imbalance between VEGF and endostatin in ischemia/reperfusion-induced acute renal failure. This imbalance might play a role in the pathogenesis of acute renal failure through its effect on angiogenesis during tissue repair.

MP045 ENDOSTATIN EXPRESSION IN EXPERIMENTAL ENDOTOXEMIC ACUTE RENAL FAILURE

Milena Cristina Cichy[1], Flavia Gomes Goes Rocha[1], Vivian Regina Tristão[1], Enia Lucia Coutinho[1], Angelo Cesar Almeida[1], Rodolfo Nürmberger Jr[3], Nestor Schor[1], Maria Helena Bellini[1,2]. [1]*Disciplina Nefrologia, Departamento de Medicina, Universidade Federal de São Paulo, UNIFESP-EPM, São Paulo, Brazil;* [2]*Departamento de Química e Meio Ambiente, Instituto de Pesquisas Energéticas e Nucleares - IPEN-CNEN-SP, São Paulo, Brazil;* [3]*Departamento de Patologia da Faculdade de Medicina Veterinária, Universidade de São Paulo, São Paulo, Brazil*

Introduction and Aims: Acute renal failure (ARF) is a frequent complication of gram-negative sepsis and augers a high risk of mortality. LPS-induced ARF is associated with hemodynamic changes that are strongly influenced by the overproduction of nitric oxide (NO) through the cytokine-mediated upregulation of inducible NO synthase (iNOS). LPS-induced reductions in systemic vascular resistance paradoxically culminate in renal vasoconstriction. Collagen XVIII is an important component of the extracellular matrix and is expressed in basement membranes. Its degradation, by matrix metalloproteases, cathepsins, and elastases, results in the generation of endostatin (ES) claimed to possess antiangiogenic activity and a prominent vasorelaxing agent. The aim of this study was to evaluate the endostatin expression in a model of endotoxemic ARF.
Methods: Male C57BL/6 mice were given 10 mg/kg *Escherichia coli* LPS as an intraperitoneal injection. At 4 or 12 h after LPS inoculation the animals were anesthetized and blood was collected via orbital sinus. This was followed immediately by cervical dislocation. One kidney was snap-frozen in liquid nitrogen and used for protein extraction and other was fixed in 10% phosphate buffered formalin for histology. Kidney proteins were extracted with 0.1M Tris-HCl, 0.01M EDTA, 0.1M DTT and SDS 1% and quantified by Bradford assay. The immunoreactivity of endostatin to purified polyclonal was analyzed by western blotting.
Results: Intraperitoneal LPS administration leaded to severe intrarenal ARF. A more than three-fold creatinina and two-fold urea indicated severe renal dysfunction. Compared with normal kidneys renal histology in LPS-induced ARF developed extent of tubular injury dilatation and flattening. Western blotting analysis revealed immunoreactive 20 KDa and 30kDa endostatin expression at 4 and 12 hours after LPS inoculation.
Conclusions: These data suggest the local synthesis of 20KDa and a 30-kDa endostatin-related fragment following LPS-induced ARF and suggest their role in the modulation of renal capillary density.

MP046 EFFECT OF LEFLUNOMIDE ON WILMS' TUMOR SUPPRESSOR-1 EXPRESSION IN RATS WITH PASSIVE HEYMANN NEPHRITIS

Changying Xing, Xueqing He, Xiufen Zhao, Jun Qian. *Dept. of Nephrology, First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China*

Introduction and Aims: To study the effect of leflunomide on Wilms' tumor suppressor-1 expression of renal tissues and on proteinuria in rats with passive Heymann nephritis.

Methods: Forty-five male Wistar rats were randomly assigned into three groups: a passive Heymann nephritis group (PHN group), a leflunomide-treated passive Heymann nephritis group (leflunomide group) and a control group. The PHN model was induced by injection of anti-FX1A serum through the tail vein. The leflunomide group was administered leflunomide daily by gavages. The PHN group and the control group were adminstered normal saline by the same approach. At the end of the 4th, 8th and 12th week after injection, specimens of the urine of five rats in each group were collected for 24 hours in order to detect 24-hr urinary protein. Then the rats were sacrificed and the kidneys were acquired for histological study under light microscope and electronic microscope. Western blot was used to detect the WT1 expression of renal tissues.
Results: At the end of the 4th week, the 24-hr urinary protein of the PHN group was higher than that of the control group ($P<0.01$), and that of the leflunomide group at the end of the 8th week ($P<0.01$). Both of them gradually increased. The 24-hr urinary protein of the leflunomide group was always lower than that of the PHN group ($P<0.01$) (Table 1). Histological study under light microscope and electronic microscope demonstrated leflunomide reduced glomerular lesions of the rat with PHN. At the end of the 4th week, the WT1 expressions of the PHN group and the leflunomide group were lower than that of the control group ($P<0.01$). The WT1 expression of the leflunomide group gradually increased. At the end of the 12th week, the WT1 expression of the leflunomide group was higher than that of the PHN group ($P<0.01$), but still lower than that of the control group.

Table 1. Changes of Protienuria at Different Weeks

Groups	N	At 4th Week	At 8th Week	At 12th Week
PHN	5	47.2±32.4*	288.0±141.6*	485.5±189.9*
Leflunomide	5	13.7±5.3$^{\Delta}$	141.0±57.9*$^{\Delta}$	301.2±117.0*$^{\Delta}$
Control	5	4.7±1.1	4.0±1.4	4.2±1.3

PNH, Passive Heymann Nephritis; *vs control group $p<0.01$; $^{\Delta}$vs PHN group $p<0.01$.

Conclusions: Leflunomide reduces proteinuria and immune deposits in glomeruli and may possesses role in PHN possibily through the up-regulation of WT1 in the podocyte.

MP047 REDUCED CORTICAL PERFUSION BUT PRESERVED GLOMERULAR PERFUSION IN UNILATERAL URETERAL OBSTRUCTION (UUO)-INDUCED RENAL INJURY IN MICE

Hitomi Watanabe, Rahul Das, Emma Hamilton, Antony Wheatley.
Department of Physiology, Otago School of Medical Science, Otago University, Dunedin, New Zealand

Introduction and Aims: Obstruction of the ureter leads to the death of renal cells and fibrosis of the kidney in humans. In the current investigation, we tested the hypothesis that reduced perfusion of the renal cortex is an early feature in UUO-induced renal injury in the mouse.
Methods: UUO was induced in C57BL6 mice (20-25g, 8-10 weeks old) under halothane anesthesia. At days 3 and 7 post-UUO, the cortical perfusion was investigated using intravital fluorescence microscopy (IVFM) to assess microcirculatory perfusion (FITC-dextran), leukocyte recruitment (Rhodamine 6G [Rh6G]) and cell viability (Hoescht33342 [Ho342]). A group of control mice was also included. Video-recorded images were digitised and exported to a G5 Mac computer for off-line analysis. Statistical analysis was performed using Instat 3.0.
Results: In the control kidney, perfusion of the peritubular capillaries (FITC-dextran) approached 100% and tubular cells were clearly visible (Ho342). Rh6G was clearly absorbed by healthy tubular cells. Glomeruli were not visible. Following UUO, cortical perfusion fell with time, to reach 40% by day 7. In the 7day UUO group, the incidence of hyperfluorescent-Ho342 nuclei was high, possibly indicating the presence of apoptotic cells. In the 7day- but not 3-day UUO kidney, glomeruli were clearly visible and glomerular flow was maintained, despite the destruction of the peritubular capillary network.
Conclusions: Our results indicate that a reduction in cortical perfusion precedes significant tubular injury in the UUO mouse. Interestingly, glomerular perfusion is still preserved at 7 days after UUO.
These studies were approved by the University of Otago Animal Ethics Committee. Study supported by New Zealand Lottery Health.

MP048 ERK1/2 ACTIVATION MEDIATES RENAL ISCHEMIC INJURY REPAIR

David Saenz-Morales[1], Belen Ponte[2], Elisa Conde[1], Ignacio Blanco-Sanchez[1], Maria Garcia-Martos[1], Laura Alegre[1], Fernando Liano[2], Maria Laura Garcia-Bermejo[1]. *[1]Pathology, Univ. Hospital Ramon y Cajal, Madrid, Spain; [2]Nephrology, Univ. Hospital Ramon y Cajal, Madrid, Spain*

Introduction and Aims: Renal ischemia/reperfusion (I/R) induces proximal tubule epithelium damage leading to kidney dysfunction. Several mechanisms have been involved in renal ischemic injury. However, data on mechanisms which promote proximal tubule regeneration after I/R are scarce.
Methods: Using an *in vivo* model of I/R in Sprague Dawley rats (SD), we have performed protein expression studies with antibody arrays. After 24h of reperfusion, when ischemic injury is maximum in this model, we have identified several over-expressed proteins, many of them involved in cell survival or tissue regeneration pathways.
Results: We have focused on ERK1/2 proteins which evidenced a significant expression. By immunohistochemistry in renal tissue paraffin-embebbed sections, we have studied the expression of the active form of ERK1/2, pERK1/2, and determined that pERK1/2 were significantly expressed in proximal tubules after 24h of reperfusion. Moreover immunoblots performed in renal lysates from Brown Norway rats, which exhibited better kidney regeneration than SD rats, revealed that p-ERK1/2 was markedly induced at 24h of reperfusion. Using an *in vitro* hypoxia/reoxygenation (H/R) model in rat proximal tubular epithelial cells (NRK-52E), which closely reproduces the tubular injury and recovery observed after I/R *in vivo*, we have determined that p-ERK1/2 were also induced at 24h of reoxygenation, correlating with cell proliferation and complete restoration of epithelial cell injury which was elicited by cytoskeleton alterations and intercellular adhesion disruption and also involved earlier ERK1/2 activation. ERK1/2 in rat kidneys at 24h of reperfusion could be induced by reparative growth factors activation since receptors for them such as EGFR and FGFR appeared significantly up-regulated in the antibody array. On the other hand, ERK1/2 might promote proliferation *in vivo* trough AP-1 activation, among other transcription factors, since c-Jun and c-Fos proteins were also markedly up-regulated at 24 post-ischemia.
Conclusions: In summary, using *in vivo* and *in vitro* models to study mechanisms responsible for kidney reparation after I/R, we have determined that these mechanisms overlapped with those of ischemic damage and identified the ERK1/2 expression and activation as factors contributing to proximal tubule regeneration.

MP049 THE EFFECT OF DIETARY GINGER (*ZINGIBER OFFICINALES* ROSC) ON RENAL ISCHEMIA/REPERFUSION INJURY IN RAT KIDNEYS

Ebru Uz[1], Omer Faruk[2], Ferhat Catal[3], Reyhan Bayrak[4], Omer Bayrak[2], Ali Atmaca[5], Omer Atis[6], Erol Yildirim[2], Ali Akcay[1]. *[1]Nephrology, Fatih University, School of Medicine, Ankara, Turkey; [2]Urology, Fatih University, School of Medicine, Ankara, Turkey; [3]Pediatri, Fatih University, School of Medicine, Ankara, Turkey; [4]Pathology, Fatih University, School of Medicine, Ankara, Turkey; [5]Urology, Fatih University, School of Medicine, Ankara, Turkey; [6]Urology, Ataturk Training and Research Hospital, Ankara, Turkey; [7]Biochemistry, Gaziosmanpasa University, Tokat, Turkey; [8]Urology, Fatih University, School of Medicine, Ankara, Turkey; [9]Nephrology, Fatih University, School of Medicine, Ankara, Turkey*

Introduction and Aims: Oxidative stress has been considered as one of the possible mechanisms of ischemia/reperfusion (I/R) injury in the kidney. The aim of this study was to analyze the possible protective effect of dietary ginger (*Zingiber officinales* Rosc), a free radical scavenger, on renal I/R injury in rats. The protective effect of ginger against the damage inflicted by reactive oxygen species (ROS) during renal I/R was investigated in Wistar albino rats using histopathological and biochemical parameters.
Methods: Thirty rats were randomly divided into 5 experimental groups (control, sham operated, ginger, I/R and I/R+ ginger groups, n=6 each). The ginger and I/R+ginger groups were fed on the test diet containing 5% ginger. The rats were subjected to bilateral renal ischemia followed by reperfusion in I/R and I/R+ ginger groups. At the end of the reperfusion period, rats

were sacrificed and kidney function tests, serum and tissue oxidants and antioxidants, renal morphology were evaluated.
Results: Serum urea, creatinin and cystatin C (CYC) levels were significantly elevated in the ischemia group but these levels remained unchanged in ginger+I/R group compared to I/R group. Reduction of glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) enzyme activity was significantly improved in the serum by the treatment with ginger compared to I/R group ($P<0.05$). Administration of ginger resulted in significant reduction levels of tissue malondialdehyde (MDA), NO, protein carbonyl contents (PCC) in the ginger+I/R group compared with the I/R group ($P<0.001$). Ginger supplementation in the diet before I/R injury resulted in higher total antioxidant capacity (TAC) and lower total oxidant status (TOS) levels than I/R group ($p<0.001$). The ginger supplemented diet prior to I/R process demonstrated marked reduction of the histological features of renal
Conclusions: The findings imply that ROS play a causal role in I/R induced renal injury and and ginger exert renoprotective effects probably by the radical scavenging and antioxidant activities.

MP050 ★ PROTECTIVE ROLE OF ERDOSTEINE ON RADIO-CONTRAST NEPHROPATHY IN RATS

Omer Bayrak[1], Arif Kaya[2], Burak Uz[2], Efkan Uz[3], Reyhan Bayrak[4], Ebru Uz[5], Faruk Turgut[5], Ozlem Alici[6], Cemile Koca[7], Atilla Ilhan[8]. *[1]Department of Urology, Fatih University, School of Medicine, Ankara, Turkey; [2]Department of Internal Medicine, Fatih University, School of Medicine, Ankara, Turkey; [3]Department of Biochemistry, Suleyman Demirel University, Faculty of Medicine, Isparta, Turkey; [4]Department of Pathology, Fatih University, School of Medicine, Ankara, Turkey; [5]Department of Nephrology, Fatih University, School of Medicine, Ankara, Turkey; [6]Department of Infection Diseases, Fatih University, School of Medicine, Ankara, Turkey; [7]Department of Biochemistry, Fatih University, School of Medicine, Ankara, Turkey; [8]Department of Neurology, Fatih University, School of Medicine, Ankara, Turkey*

Introduction and Aims: Radio-contrast nephropathy (RCN) is associated with increased morbidity and mortality. Erdosteine contains two blocked sulfhydryl groups. The reducing potential of these sulfhydryl groups accounts for free radical scavenging and antioxidant activity of erdosteine. The aim of the present study is to evaluate a possible protective role of erdosteine against RCN, besides the effect of erdosteine on malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT) and nitric oxide (NO) levels in the kidney tissue.
Methods: Twenty-four Wistar rats were randomized into four groups; Controls; only erdosteine (ERDO), only radio-contrast medium (RCM) and RCM+ERDO. Erdosteine was given 24 h prior to RCM injection and then given twice a day. After 4 days, rats were sacrificed. Kidney tissue MDA, SOD, CAT and NO were quantified and histopathological examinations of tissue sections were performed.
Results: After RCM, serum levels of urea and creatinine significantly increased. Erdosteine significantly decreased serum creatinine levels in RCM+ERDO group compared to RCM group (0.27 ± 0.05 mg/dl vs 0.37 ± 0.05 mg/dl, $p<0.05$). After RCM, renal MDA, NO and SOD activity increased, but CAT activity decreased in RCM group. Erdosteine administration decreased significantly MDA, NO and SOD activity in RCM+ERDO group compared to RCM group (Table 1). In histopathological examination, renal sections obtained from the rats treated with erdosteine demonstrated marked reduction of the histological features of renal injury, consisting of more focal and mild tubular necrosis.

Table 1. Kidney tissue antioxidant enzyme level and oxidant products for all groups

Groups (n=6)	SOD (U/mg protein)	CAT (k/g protein)	MDA (nmol/g wet tissue)	NO (μmol/g wet tissue)
Control	0.075±0.008	1.043±0.112	45.72±3.14	1.193±0.082
ERDO	0.076±0.008	0.952±0.110	46.20±3.13	1.032±0.110
RCM	0.093±0.007*	0.834±0.027	59.27±1.87*	1.690±0.066*
RCM+ERDO	0.075±0.003	0.927±0.074	48.11±4.08	1.122±0.123

ERDO; Erdostein, RCM; Radio-contrast media, SOD; Superoxide dismutase, CAT; Catalase, MDA; Malondialdehyde, NO; Nitric oxide, *$p<0.05$ compared to RCM+ERDO group.

Conclusions: Based on the present data, we conclude that erdosteine protects the kidneys against RCM.

MP051 TREATMENT WITH SILDENAFIL AMELIORATES PROGRESSION OF RENAL DAMAGE IN STREPTOZOTOCIN (STZ) INDUCED DIABETIC RAT

Chun Gyoo Ihm, Kyung Hwan Jeong, Ju Young Moon, Sang Ho Lee, Tae Won Lee. *Internal Medicine, Nephrology, Kyung-Hee Medical Center, Seoul, Korea*

Introduction and Aims: Diabetic nephropathy is associated with oxidative stress and reduced nitric oxide availability which, in turn, promotes hypertension and further progression of renal damage. Many of the biologic actions of nitric oxide (NO) are mediated by cyclic 3', 5' guanosine monophosphate (cGMP), which is rapidly degraded by type-5 phosphodiesterases (PDE-5). Therefore, I investigated if inhibition of PDE-5 by sildenafil (Viagra®) would retard the progression of diabetic nephropathy.
Methods: After streptozotocin induced diabetes, rats received either no treatment or therapy with sildenafil (50 mg/L in the drinking water) for 8 weeks. Cortical endothelial NO synthase (eNOS) and inducible NOS (iNOS) expressions were determined by the methods of RT-PCR and immunohistochemistry at 8 weeks. Renal expression and distribution of nitrotyrosine and ED-1 positive cell infiltration were also analyzed by immunohistochemistry. Cortical mRNA expression of MCP-1 was assessed by RT-PCR.
Results: In these studies, sildenafil treatment prevented deterioration of renal function, delayed the onset of albuminuria. Sildenafil significantly ameliorated albuminuria at 8 weeks without significant change of systolic blood pressure. Sildenafil administration significantly attenuated the increase of iNOS and MCP-1 expressions in RT-PCR. In immunohistochemistry, both eNOS and iNOS expression were significantly increased at 8 weeks of diabetic rats in renal tubules and glomeruli, as compared with that of control rats, whereas they were significantly decreased by sildenafil administration. Sildenafil administration also significantly attenuated the increase of nitrotyrosine expression in immunohistochemistry.
Conclusions: These observations suggest that currently available PDE-5 inhibitors have potential clinical value in the treatment of diabetic nephropathy.

MP052 EXPRESSION AND REGULATION OF PROLYL HYDROXYLASES (PHD) IN THE RAT KIDNEY AND IN ACUTE KIDNEY INJURY

Johannes Schoedel[1], Bernd Klanke[1], Bjoern Buchholz[1], Christina Warnecke[1], Wanja Bernhardt[1], Armin Kurtz[2], Kai-Uwe Eckardt[1], Carsten Willam[1]. *[1]Dept. of Nephrology & Hypertension, University of Erlangen-Nuremberg, Erlangen, Germany; [2]Dept. of Physiology, University of Regensburg, Regensburg, Germany*

Introduction and Aims: In the inner medullary regions of the kidney oxygen tensions are physiologically low because of the particular renal vascularity and the oxygen countercurrant mechanism. Therefore, differentiated and marked induction of the hypoxia inducible transcription factors (HIF) 1 and 2 has been demonstrated to be important for the tolerance of the kidney to regional or systemic hypoxia. HIF-1 and -2 are regulated by specific HIF-Prolyl Hydroxylases 1-3. However, expression and regulation of the PHDs in the kidney are poorly understood. We thus investigated occurrence and pathophysiological regulation of the 3 PHDs in the kidney.
Methods: In vivo protein and mRNA expression of the 3 PHDs in rat kidneys and models of acute renal failure were examined by immunohistochemistry, immunoblot analyses and ribonuclease protection assay. PHD mRNA levels in microdissected nephron segments were investigated by real-time PCR. In vitro murine proximal and distal tubular cells were used to determine regulation of PHD expression by hypoxia.
Results: All three PHD mRNA isoforms were detected in isolated tubular cells and in rat kidney extracts. Immunohistochemistry revealed PHD expression primarily in glomerula, distal tubules and interstitial cells. In microdissected nephron segments mRNA levels of all PHDs increased in distal nephron segments, where oxygen tensions are physiologically low. Systemic hypoxia led to upregulation of PHD3 mRNA predominantly in tubules involving the proximal tubule as well. Regions of high PHD expression were concordant to regions of HIF induction, implicating a regulative feed back loop. In the cisplatin model of toxic renal failure PHD1 and 3 expression were reduced, whereas in ischemia reperfusion injury

and contrast media nephropathy PHD3 mRNA and protein levels were induced.
Conclusions: HIF-1 and -2 play a key role in oxygen regulated gene expression. Preconditional stabilization of HIF by hypoxia or PHD inhibitors ameliorates the course of kidney failure in rat models of cisplatin induced nephropathy or ischemia reperfusion injury, respectively. Therefore, besides implications for oxygen sensing, knowledge of the distribution and regulation of the PHDs in the kidney may be important for potential drug interventions in the future.

MP053 REGULATION OF STRESS INDUCED PROTEINS IN ISCHEMIC ACUTE RENAL FAILURE IN A MODEL OF SUPEROXIDDISMUTASE-DEFICIENT MICE

Reinhard Schneider[1], Jens Wilhelm[1], Jan Galle[2], Christoph Wanner[1], Michael Gekle[3], Christoph Sauvant[4]. *[1]Dept. Medicine I, Div. Nephrology, Julius-Maximilians-University, Wuerzburg; [2]Dept. Nephrology, Klinikum Luedenscheid, Luedenscheid; [3]Julius-Bernstein-Institute of Physiology, Martin-Luther-University, Halle-Wittenberg; [4]Institute of Physiology, Julius-Maximilians-University, Wuerzburg, Germany*

Introduction and Aims: Generation of reactive oxygen species is an important detrimental factor after ischemic acute renal failure (iARF). Superoxid radicals (O_2^{-*}) cause inactivation of nitric oxide (NO^*) and generatation of toxic metabolites. Superoxid dismutase (SOD) is responsible for the initial step of O_2^{-*}-detoxification. Here we analysed the in-vivo influence of extracellular SOD (ecSOD) on kidney function after iARF, focusing on the regulation of stress induced proteins with potentially protective features in an ecSOD deficient mouse model.
Methods: Bilateral clamping of renal arteries for 45 min induced iARF in ecSOD deficient and wildtyp (wt) mice. 24h and 72h after iARF inulin (C_{IN}) and para-aminohippuric acid (C_{PAH}) clearance reflecting hemodynamic parameters, as well as PAH netsecretion (NS_{PAH}) reflecting secretory transport processes of the proximal tubule, were measured. Furthermore, protein expression of cyclooxygenases (COX1/COX2), hemeoxygenases (HO1/HO2) and heat shock protein 70 (HSP70) were analysed.
Results: Following iARF, ecSOD deficiency was associated with stronger deterioration of renal function in comparison to wt, followed by a gradual recovery 72 h after iARF, demonstrated for C_{IN}, C_{PAH} and NS_{PAH}. HO1 and HSP70 were characterized by a basal overexpression in ecSOD-/-. After iARF, HO1 and HSP70 were strongly induced with a significant larger change in ecSOD-/-. Basal increased COX1 expression in ecSOD deficiency was downregulated after iARF, while wt was characterized by an early COX1 induction. iARF lead to decreased COX2 expression in both ecSOD-/- and wt, but recovery was more pronounced in ecSOD deficient mice.
Conclusions: When comparing ecSOD deficient and wt mice the functional time course after iARF is significantly deteriorated in ecSOD-/-, demonstrating the important pathogenic impact of O_2^{-*} after ARF. ecSOD deficiency, reflecting increased O_2^{-*} toxicity, already leads to basally increased expression of stress proteins (HO1 und HSP70) and is characterized by accelerated overexpression after iARF. Significant COX2 downregulation after iARF in ecSOD deficient mice might be an explanation of the impaired tubular function.

MP054 TUBULOGLOMERULAR FEEDBACK RESPONSE AFTER RENAL ISCHEMIC PRECONDITIONING: STUDY IN THE ECTO-5ʹ-NUCLEOTIDASE (CD73) KNOCKOUT MICEv

Dan Yang Huang[1], Almut Grenz[1], Hartmut Osswald[1], Volker Vallon[2], Holger K. Eltzschig[3]. *[1]Institute of Pharmacology and Toxicology, University of Tuebingen, Tuebingen, Baden-Wuerttemberg, Germany; [2]Departments of Medicine and Pharmacology, UC San Diego & VASDHCS, San Diego, CA, USA; [3]Department of Anesthesiology and Perioperative Medicine, Denver, CO, USA*

Introduction and Aims: Ischemic preconditioning (IP) of the kidneys has been shown to induce protective effect against acute renal failure after renal ischemia. We reported before that ecto-5'-nucleotidase (CD73) gene deleted animals lost renal protection induced by IP and tubuloglomerular feedback response (TGF) was attenuated in CD73 knockout mice. To study the possible role of TGF in renal IP, we analyzed TGF responses using micropuncture technique in anesthetized CD73 wildtype (CD73+/+) and knockout (CD73-/-) mice with and without IP application.
Methods: Animals were prepared for standard micropuncture (Huang et al 2006) and thereafter IP (four cycles of 4 minutes of ischemia and 4 minutes of reperfusion) was introduced using hanging-weight system for left renal artery intermittent occlusion as described before (Grenz et al 2006). This preconditioning procedure was followed by 30 minutes of renal artery occlusion. Besides measuring glomerular filtration rate (GFR) by renal clearance of ^{3}H-inulin, TGF activity was assessed as change of single nephron glomerular filtration rate (SNGFR) determined from late proximal tubule (PT) and early distal tubule (DT) of the same nephron ($SNGFR_{PT}$-$SNGFR_{DT}$).
Results: Consistent with our previous finding, IP significantly improved urinary flow rate and GFR only in CD73+/+ but not in CD73-/- mice. Without IP treatment, $SNGFR_{PT}$-$SNGFR_{DT}$ was significantly higher in CD73+/+ compared with CD73-/- mice (1.9±0.3 vs. 1.0±0.1 nl/min, $p<0.05$). After IP application followed by 30 minutes of ischemia, the $SNGFR_{PT}$-$SNGFR_{DT}$ was significantly greater in CD73+/+ than in CD73-/- mice (3.3±0.4 vs. 1.0±0.2 nl/min, $p<0.05$), indicating enhanced TGF activity only in CD73+/+ mice.
Conclusions: Our data suggest that increased sensitivity of TGF after IP may limit tubular load to downstream medullary nephron segments, which have limited oxygen and blood supply, thereby contributing to preserve the integrity of the renal medulla and thus protects kidney functions.

MP055 AMBERCHROM CLASS RESIN ADSORPTION PROTECTS TUBULAR EPITHELIAL CELLS FROM APOPTOSIS AND LOSS OF FUNCTIONAL INTEGRITY INDUCED BY SEPTIC PLASMA

Vincenzo Cantaluppi[1], Carola Lauritano[1], Viktoria Weber[2], Giovanni Camussi[1], Ciro Tetta[3]. *[1]Nephrology, Dialysis and Renal Transplantation Unit, University of Torino, Torino, Italy; [2]University of Krems, Austria; [3]Fresenius Medical Care, Bad Homburg, Germany*

Introduction and Aims: The pathogenetic mechanisms of sepsis-associated AKI are complex and seem to be related not only to hypoperfusion, but also to a direct pro-apoptotic effect of circulating mediators on kidney resident cells. Adsorption-based extracorporeal therapies by using Amberchrom class of poly(styrene/benzene) resins have been previously shown to bind high amounts of pro- and anti-inflammatory cytokines potentially involved in the pathogenesis of AKI. The aim of this study was to evaluate whether plasma derived from septic patients induced loss of functional integrity and apoptosis of tubular cells, and the possible protective effects derived from unselective removal of soluble factors by Amberchrom class resin adsorption.
Methods: We collected plasma from 8 critically ill patients with sepsis-related AKI (inclusion into ADQI-RIFLE and American Cllege of Chest Physicians/Society of Critical Care criteria). Plasma were adsorbed by Amberchrom class resin for 120 minutes at 37° C in condition of slight agitation. ELISA test for different cytokines was performed on patient plasma. Human proximal tubular epithelial cells were incubated with plasma collected before and after absorption. The following in vitro test were done: cytotoxicity (MTT assay), apoptosis (TUNEL assay, caspase-3, -8 and -9 activities), trans-epithelial electrical resistance (TER), internalization of FITC-labeled albumin and immunofluorescence/FACS analysis of tight junction, endocytic receptor and adhesion molecules.
Results: Amberchrom resin adsorption induced a significant decrease of plasma TNF-alpha, IL-1beta, IL-8, IL-10, Fas-Ligand and CD40-Ligand. After resin adsorption, septic plasma lost their pro-apoptotic effect on tubular cells with a significant decrease ($p<0.05$) of caspase-3, 8 and 9 activities and the down-regulation of Fas signalling pathway. A significant decrease of adhesion of inflammatory cells on tubular cells was observed in presence of resin-treated plasma. This anti-inflammatory property was associated to the down-regulation of the adhesion receptor ICAM-1 and of the costimulatory molecule CD40 on tubular cell surface. Septic plasmas altered normal tubular trans-epithelial electrical resistance, a marker of cell polarity. This effect was concomitant to the down-regulation of the tight junction molecule ZO-1 and of the endocytic receptor megalin. By contrast, in presence of resin-adsorbed plasma, tubular cells maintained polarity, ZO-1/megalin expression and the ability to internalize albumin.

Conclusions: Amberchrom resin adsorption reduced the injurious effects exerted by plasma of critically ill septic patients on cultured tubular cells, thus contributing to the inhibition of apoptosis and the preservation of viability, polarity and correct tubular remodelling. These effects may be ascribed to the removal of inflammatory mediators involved in tissue injury, suggesting a protective effect of this plasma adsorption technique in the prevention and treatment of sepsis-related AKI.

MP056 SEVERITY OF ACUTE KIDNEY INJURY (AKI) IN RATS WITH UNLIMITED OR DEPRIVED OF FOOD ACCESS

Antoni Wystrychowski[1], Wojciech Wystrychowski[2], Ewa Obuchowicz[3], Lech Cierpka[2], Andrzej Wiecek[1]. *[1]Dept. of Nephrology, Endocrinology and Metabolic Diseases; [2]Dept. of General, Vascular and Transplant Surgery; [3]Dept. of Pharmacology, Medical University of Silesia, Katowice, Poland*

Introduction and Aims: Numerous experimental studies and clinical observations indicate that enteral nutrition may influence inflammatory reactions and determine the course of many diseases.
The aim of this study was to compare the course of acute ischemic and ischemic-endotoxemic in rats with unlimited access to food or starved for 24 hours preceding acute kidney injury (AKI).
Methods: Fourteen days after right nephrectomy ischemia/reperfusion was induced by 45' clamping of the renal vascular pedicle in 36 male Sprague-Dawley rats continuously fed (Gr II and IV) or starved for 24h before clamping (Gr I and III). 1 min. after clamping 1ml 0.9% NaCl (Gr I and II) or 2 mg/kg bw lipopolysaccharide (LPS; E. coli) (Gr III and IV) was given iv. Creatinine clearance (Cr_{Cl}; μl/min/100g b.w.), fractional sodium excretion (FE_{Na};%), and urine protein excretion (U_{prot}; mg/day) were estimated 48h after ischemia/reperfusion.
Results: As shown in table, ischemia of the sole kidney caused a more severe AKI in the fed animals, than in those deprived of food for 24h prior to ischemia (lower Cr_{Cl}, higher FE_{Na} and U_{prot} in Gr II vs. Gr I). Moreover, LPS aggravated the course of AKI in rats with unlimited food access, causing 50% mortality in the first 2 days following ischemia, whereas in fasted animals LPS did not exacerbate ischemic AKI.

	Groups			
	I	II	III	IV
Starvation	+	–	+	–
LPS	–	–	+	+
Initial number	8	8	10	10
Final number	8	8	10	5
Cr_{Cl} [μl/min/100g bw]	54.8±28.4	14.7±12.0*	39.8±33.8	24.1±19.9
FE_{Na} [%]	4.4±2.9	21.9±10.6*	10.9±11.8	7.5±7.0
U_{prot} [mg/day]	16.1±3.4	34.7±16.2*	14.6±5.6	15.0±6.6

Means ± SD; Mann-Whitney U test: *P<0.001; II vs. I.

Conclusions: Food deprivation before ischemia or ischemia plus endotoxemia reduces renal injury and prevents mortality of rats.

MP057 NOVEL HYPOXIA INDUCED TUBULAR CELL DEATH MODEL ASSOCIATED WITH INCREASED PERMEABILITYOF THE CELL MONOLAYER AND APOPTOSIS

Domokos Gero, Petra Szoleczky, Nora Nagy, Csaba Szabo. *CellScreen Applied Research Center, Semmelweis University, Budapest, Hungary*

Introduction and Aims: Acute renal failure is a common clinical problem and is associated with high mortality rate. The lack of specific treatment, which accounts for the little improvement in the outcome, necessitates novel therapeutic approaches. Renal tubular epithelial cell injury from ischemia has been long regarded as a result of necrotic cell death, however, apoptosis was recently identified as an important contributor to acute tubular cell death. Various other cell death programs (eg. necroptosis, parthanatos) have been identified in other tissues, though their relative contribution to ischemic tubular cell injury has not been evaluated.
We aimed to establish a cellular model of acute tubular necrosis that bears common features with ischemic renal injury and we investigated the role of various cell death processes using pharmacological inhibitors. We aimed to find transient oxygen and glucose deprivation conditions that preferentially induce cell death during the following normoxic-normoglycemic period.
Methods: Three renal cell lines (LLC-PK1, NRK, HK-2) and various oxygen-glucose deprivation protocols were evaluated. Cell viability was measured by the MTT and neutral red uptake assays. Caspase activation (active-caspase-3) was also measured by Western blotting. Pharmacological inhibitors of necrosis, apoptosis and necroptosis were added before or after the hypoxic challenge, and cell viability was measured after a 24-hour normoxic-normoglycemic period.
Results: Transient oxygen-glucose deprivation resulted in extensive cell death of the LLC-PK1 proximal tubular cells during the following normoxic-normoglycemic period. Such late-phase cell death was not observed in the other two cell lines. Caspase inhibitors (Z-VAD.FMK, CHO, Ac-DEVD-CHO) significantly increased cell viability after the onset of the 24-hour normoxic period. Poly(ADP-ribose) polymerase (PARP) inhibitor PJ34, necroptosis inhibitor necrostatin-1 showed no similar protective effect. Caspase-3 activation was also observed by Western blotting during the normoxic period. Reversible morphologic changes and an increase in the permeability of the tubular cell monolayer were also detected after oxygen-glucose deprivation.
Conclusions: In conclusion, a novel in vitro tubular cell death model of ischemic origin was established, in which the major cell death process is characterized by its late onset and caspase activation and is related to the proximal tubular origin of these cells. Necrosis and necroptosis are of lesser importance during this late phase cell death program. We propose that the associated changes in the permeability of the tubular cell monolayer also serves as a contributing factor to cellular dysfunction and the following cell death. The current experimental model is also amenable for cell-based high throughput screening of experimental compound libraries.

MP058 EFFECTS OF THE EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY ON ARTERIAL PRESSURE AND RENAL FUNCTION OF SPONTANEOUS HYPERTENSIVE RATS

Carlos Eduardo Carvalho de Matos, Andreia Silva de Oliveira, Clara Versolato Ravisckas, Ita Pferferman Heilberg, Nestor Schor, Vicente de Paulo Castro Teixeira, Valdemar Ortiz. *Medicine, University Federal of Sao Paulo, Sao Paulo, Brazil*

Introduction and Aims: Extracorporeal shock wave lithotripsy is currently the non invasive treatment of choice for superior urinary tract stones. However its safety is not completely established. There are clinical and experimental reports on renal function impairment and arterial hipertension after shock wave use. Furthermore there is controversy about shock wave induced arterial hypertension.
To evaluate the effects of the shock waves on arterial pressure and renal function in SHR (spontaneous hypertensive rats) and Wistar rats.
Methods: SHR and Wistar rats were submitted to right nefrectomy. Seven days later the rats had their left kidney submitted to 2000 shock wave (17 Kv) and divided into 4 groups.
Group I (Wistar rats) and Group II (SHR) were evaluated 24 hours after the shock waves.
Group III (Wistar rats) and Group IV (SHR Experiment) were evaluated 8 weeks after the shock waves. Additionally, there were a group of Wystar and a group of SHR right-sided nefrectomized rats with no application of shock waves serving as control groups.
The biochemical evaluation consisted Inuline (IN) clearance and Paraamino-hippurate (PAH).
The arterial pressure was measured through tail plestismography twice in week before right side nefrectomy, and before and after the shock waves.
Results: Our results are demonstrate below:

Glomerular Filtration (FG)/Renal Plasmatic Flow (FRP)

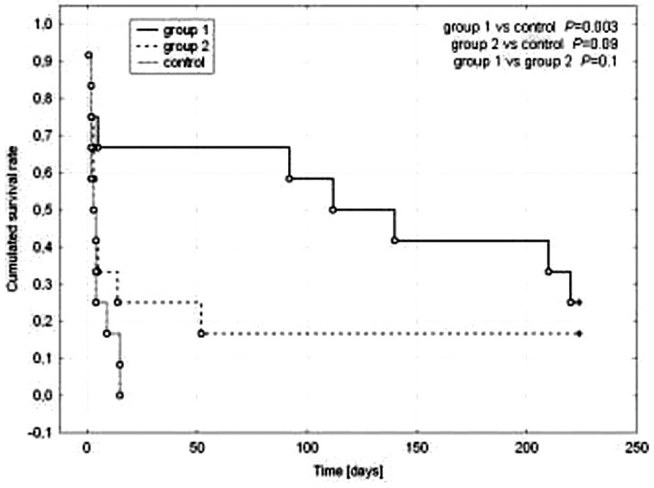
Groups	FG (ml/minute)	FRP (ml/minute)
Control Wistar	1,42±0,16	2,72±0,11
Control SHR	1,07±0,06	1,80±0,04
Wistar follow up 24 hs	0,37±0,08	0,60±0,12
SHR 24 hs	0,73±0,04	2,04±0,08
Wistar follow up 2 month	0,23±0,02	0,34±0,04
SHR follow up 2 month	0,30±0,03	0,43±0,09

Conclusions: Ours result demonstrate that the normotense animals did not manifest alterations in arterial pressure in neither 24 hours nor in 8 weeks after shock waves. On the other hand, SHR animals presented gradual worsening of the arterial pressure in 24 hours and 8 weeks after shock waves.
Shock waves can cause renal function impairrment in Wistar and SHR animals, and worsens the hypertensive condition in SHR animals.

MP059 EFFECT OF PENTOXIFYLLINE (PTX) ON SURVIVAL OF RATS WITH SOLITARY KIDNEY SUBJECTED TO 180 MIN ISCHEMIA

Antoni Wystrychowski[1], Wojciech Wystrychowski[2], Ewa Obuchowicz[3], Lech Cierpka[2], Andrzej Wiecek[1]. [1]*Dept. of Nephrology, Endocrinology and Metabolic Diseases;* [2]*Dept. of General, Vascular and Transplant Surgery;* [3]*Dept. of Pharmacology, Medical University of Silesia, Katowice, Poland*

Introduction and Aims: Ischemia-reperfusion injury results in acute renal failure, as well as progressive nephropathy that may lead to renal insufficiency over the long-term observation period. In the rat model of acute ischemic renal failure, PTX given prior to 45-min ischemia alleviates acute renal failure. We aimed to assess whether PTX inhibits also progression of chronic nephropathy and thus prolongs survival when given prior to or during long renal ischemia in rats.
Methods: Three groups of 12 male Sprague-Dawley rats each were subject to induction of chronic nephropathy by 180 min ischemia of one kidney and contralateral nephrectomy after 14 days. 90 min. before and 90 min. after start of clamping of renal pedicle animals were given respectively: PTX 100 mg/kg bw s.c. and 0.9% NaCl 1ml s.c. (group 1), or 0.9% NaCl 1ml s.c. and PTX 100 mg/kg bw s.c. (group 2), or 0.9% NaCl 1ml s.c. at both times (control). Surgical procedures were carried out in light ether anesthesia. Observation period was 224 days following nephrectomy. Survival was compared between the studied groups with Kaplan-Meier method, Coxs F test. Renal cause of death was verified by autopsy.
Results: Three rats from group 1, two from group 2, and none from the control group survived the entire observation period. The mean survival time in groups 1, 2 and the control group was 121.3±98.6, 44.8±84.9, and 5.3±5.0 days, respectively. Kaplan-Meier method revealed significantly longer survival time of rats from group 1, as compared to controls (figure).



Conclusions: PTX given prior to, but not during long kidney ischemia prolongs survival of rats with solitary kidney. This finding may have significant implications for clinical transplantology.

Acute renal failure – Clinical studies 2

MP060 TREATMENT OF CHRONIC HCV INFECTION IN HAEMODIALYSIS PATIENTS: SINGLE CENTER EXPERIENCE

Khalid Al- Saraan, Alaa Sabry, Mamdouh Abdulghafour, Naila Sherief. *Nephrology, Prince Sakman Center for Kidney Disease, Riyadh, Saudi Arabia*

Introduction and Aims: Chronic infection with the HCV is common amongst patients on dialysis. While the associated liver disease is usually relatively mild during dialysis, disease progression can accelerate upon immunosuppression after kidney transplantation, and liver complications remain a significant cause of mortality in HCV-positive kidney transplant recipients meanwhile IFN therapy after transplantation stimulates graft rejection. Pegylated-interferon (PEG-IFN) has reduced clearance rate, increased stability, and prolonged systemic exposure. However till now there is relatively little information on the efficacy and tolerability of PEG-IFN in dialysis patients.
Methods: Male or female patients within the age range 18–65 years with ESRD who had been on dialysis in Prince Salman Center for Kidney disease for longer than 6 months and tested positive for HCV RNA on repeated occasions were included.
Liver biopsy, viral genotyping, qualitative and quantitative PCR was carried out before starting therapy. Patients were treated with PEG-IFN alpha-2a at a dose of 135 ug subcutaneously once a week. Treatment would be continued for a total duration of 48 weeks. Follow up would continue for at least 24 weeks after stopping treatment. Ptints were evaluated at baseline, at weeks 1, 2, 4, 6, 8, then every 4 weeks until 6 months after therapy. Investigations at each follow up included Hgb, WBC and platelet counts, liver biochemistry including ALT, AST, alkaline phosphatase, bilirubin and albumin. Ribavirin was added with dose modification whenever the CBC allows.
Results: Our study included 13 patients (8 males and 5 females). Nine patients completed 48 weeks of therapy, (5 males and 4 females). Their mean age was (43.67±14.01 years), Six months after termination of therapy: five (55.5%) of them were sustained virological responders while four (44.4%) were resistant to therapy. Their ALT and AST dropped from 69.08±17.48 IU/dl and 34.17±17.97 IU/dl before starting therapy to 25.50±16.80 IU/dl and 18.88±13.92 IU/dl after termination (P=0.08 and 0.05 respectively). Their hgb levels dropped from 11.05±1.43 to 9.48±1.24 gm/dl (P=0.3), wbcs from (6.82±2.6 K/UL) to (4.1±2.34 K/UL) P=0.57, Neutrophil count dropped from (7.12±2.31 to 3.63±143) P=0.07 and platelet count from (194.56±129.78 K/UL) to (152.33±107.66) P=0.39. When sustained responder were compared to resistant patients no difference was observed apart from higher ALT and AST in resistant patients that was not statistically significant. Liver biopsy and viral titer significantly improved after therapy in responder patients. None of the initially responders to IFN therapy underwent a virological relapse.
Conclusions: Pegylated Interferon was fairly tolerated among our HD patients. Hematological disturbances appeared to be the most important adverse effects. A sustained response rate up to 55.5% can be obtained with Pegylated IFN therapy which is advised to be started while the patient is still on haemodialysis awaiting renal transplantation.

MP061 RENAL FAILURE REQUIRING RENAL REPLACEMENT THERAPY IN PATIENTS WITH CARDIOMYOPATHY: PROGNOSIS AND DETERMINANTS OF OUTCOME

Gregor Lindner[1], Edith Doberer[1], Nikolaus Kneidinger[2], Walter Hoerl[1], Wilfred Druml[1]. [1]*Department for Nephrology and Dialysis, Medical University of Vienna, Vienna, Austria;* [2]*Intensive Care Unit 13H1, Medical University of Vienna, Vienna, Austria*

Introduction and Aims: The aim of the study was to assess the impact of renal replacement therapy dependent (sub-) acute renal failure (ARF) in patients with cardiomyopathy (CMP) on outcome.
Methods: In a retrospective analysis, otherwise stable patients with cardiomyopathy (without cardiogenic shock) admitted to the acute dialysis unit for renal replacement therapy for ARF were analyzed. Demography and morbidity (age, sex, BMI, cause of ARF, cause of death, type of CMP,

co-morbidities), and data on a daily basis (serum electrolytes; serum osmolality; parameters of renal function (creatinine and BUN), liver function parameters, markers of inflammation (C-reactive protein), blood cell count, blood pressure, heart rate, systolic and diastolic blood pressure and the fluid balance after dialysis) were recorded. Cardiac function was assed by echocardiography, levels of brain-natriuretic peptide and troponin T. Univariate regression analysis was performed to assess the impact of various parameters on outcome.

Results: 46 patients with CMP who developed dialysis dependent ARF were studied (mean age=68 yrs, SD=10.4; BMI=28.9, SD=12.4). Ischemic CMP was the leading subtype of CMP (26 cases). LVF was available for 35 patients. 9 patients had normal to moderately decreased LVF and 26 patients had severely impaired LVF. RVF (available for 23 pts) was normal to moderately impaired in 18 patients, and severely impaired in 5 patients. Mean BNP level (available for 14 pts.) was 20556 before start of dialysis. Prerenal ARF was the major cause of ARF, present in 25 cases. Mean serum creatinine at start of dialysis was 341 μmol/L, SD=145. In 14 patients renal function recovered. Mean survival time of patients was 205 days from the day of first dialysis session, SD=363. Except hemoglobin (p=0.03; hemoglobin <10g/dL indicated a better outcome!) and renal function recovery (p=0.04) none of the other factors had a significant influence on outcome.

Conclusions: The development of dialysis dependent ARF in patients with CMP is associated with an extremely grave prognosis. None of the factors usually associated with a poor outcome in CMP (such as anemia, inflammation, low BMI etc.) was significant in these patients, obviously, because the negative impact of ARF was so strong that it masked any other prognostic indicator. Recovery of renal function and unexpectedly, anemia were factors associated with an improved outcome.

MP062 COMPARISON BETWEEN PARAQUAT (PQ) ELIMINATION BY THE KIDNEY AND BY THE HEMOPERFUSION (HP)

Moon-Soo Kang, Hyo-Ook Gil, Jong-Oh Yang, Eun-Young Lee, Sae-Yong Hong. *Internal Medicine, Soonchunhyang University Hospital, Cheoan, Chung-nam, Republic of Korea*

Introduction and Aims: The mortality rate of acute paraquat (PQ) poisoning depends on the PQ concentration in the blood. The kidney has been known to eliminate PQ most effectively; that is, the renal clears the PQ more effectively than the creatinine. However, it has frequently been observed that the renal deteriorates early in acute PQ intoxication. This study was designed to compare the efficacy of PQ elimination between hemoperfusion (HP) and the kidney, with varying degrees of functional deterioration taken into account.

Methods: Ten patients with acute PQ intoxication were enrolled in this study. All the patients underwent HP for 3 hours with the same protocol, blood flow of 200 ml/min. Blood samples for both creatinine and PQ were drawn from both the artery and venous lines, through the tubing system: beginning at zero and every hour during the 3 hours of HP. Urine samples were also collected.

Eliminated PQ amount, by kidney (KE_{PQ}) and HP (HPE_{PQ}), was calculated as follows:

KE_{PQ} (mg) = uCo of $_{PQ}$*UV

(uCo of $_{PQ}$ = urine concentration of PQ, UV = Urine volume)

HPE_{PQ}(mg) = $C_{HP} * AUC$

(C_{HP} (HP Clearance) = Extraction Ratio * Blood Flow Rate * (1 – Hct))

(AUC = Area under the plasma PQ concentration-time curve).

Comparison of PQ elimination between that of kidney and HP

Case No.	Ccr (ml/min)	PQ Excretion (mg/3hr)	
		Kidney	HP
1	9.7	48.3	403.5
2	18.9	245.8	1655.7
3	29.2	29.3	77.2
4	36.0	64.2	77.9
5	60.1	158.4	102.3
6	97.2	59.9	57.4
7	110.0	64.7	39.4
8	117.4	69.8	89.9
9	133.3	8.6	6.3
10	177.0	4.9	4.6

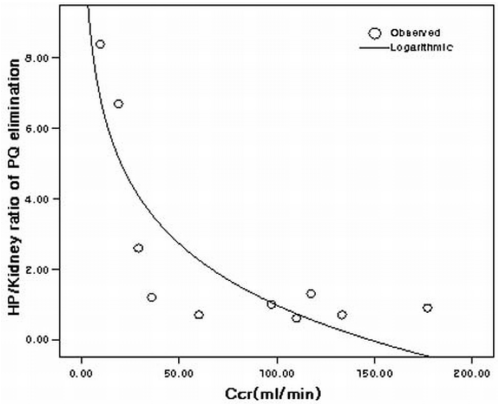


Figure 1. Comparison of PQ elimination between that of kidney and HP.

Results: In agreement with the previous reports, renal clearance of PQ during the HP session was considerably higher than that of creatinine in all of the subjects, regardless of renal function (98.6±53.8ml/min vs 79.8±56.0ml/min). As long as the renal function stays within the normal range, the renal PQ elimination rate was higher or equivocal than that of the HP (table1). However, as the creatinine clearance decreases, the PQ elimination via HP was as effective as several times of renal clearance (figure 1).

Conclusions: The renal, in its normal function, eliminates PQ as much as HP does. If the normal function slows down, the HP is then several times more effective than the kidney. In either case where the renal deteriorates earlier or PQ concentration is too high for the kidney, HP must then be the life saving modality.

MP063 RIFLE CLASSIFICATION FOR ACUTE KIDNEY INJURY IN PATIENTS WITH INCIPIENT SEPSIS AT ICU

Wim Van Biesen[1], Itir Yegenaga[2], Raymond Vanholder[1]. [1]*Renal Division, University Hospital Ghent, Ghent, Belgium;* [2]*Division of Nephrology, University of Kocaeli, Kocaeli, Turkey*

Introduction and Aims: The RIFLE criteria have been introduced as a uniform definition of acute kidney injury (AKI), offering a "gradation" of severity of kidney damage. RIFLE has been evaluated in different patient groups at risk for AKI, but not in patients with incipient sepsis. Therapeutic interventions need to be started very early in this patient group, as no proven therapy exists for established Acute Tubular Necrosis (ATN). A sensitive and specific diagnostic test is therefore of importance in this patient group. This study reports the prevalence of AKI as defined by RIFLE in patients at ICU who develop incipient sepsis.

Methods: All patients admitted to the ICU of the University Hospital Ghent during a 12 month time frame were daily screened for sepsis, defined according to the consensus of the ACCP/SCCM. From the first day they met these criteria, they were included in the study. Parameters necessary to calculate RIFLE score, Liano score and SHARF score were followed during the next 5 days.

Results: During the study period, 2442 patients were admitted to the ICU. Of these, 257 (10.5%) met the definition of sepsis during their stay. Of these 257 patients, 59 (22.9%), 48 (18.7%) and 46 (17.9%) met the criteria of the "R", "I", "F" definition in the RIFLE classification, in the 5 days after the diagnosis of sepsis (table).

Of the patients developing stage "F", 11 (23.9%) did so already on the first day, and of those developing it later, only 16 (34.8%) did have a "R" or "I" stage in the previous day. Of patients developing "R", only 11 (18.6%) did not develop "I" or "F" later on. SHARF and Liano score in patients with vs without AKI were 174±27 vs 168±29 (p=0.1) and 0.57±0.17 vs 0.59±0.29 (p= 0.7) respectively. Neither SHARF score (p=0.3) nor Liano score (p=0.4) were different in the 4 different stages.

Using the RIFLE criteria, 22.9% of patients with incipient sepsis develop AKI. This is a quite high prevalence, as we included patients on the first day of sepsis, thus far before patients became hemodynamically instable. This fits with the hypothesis that in septic patients, the pathophysiology of AKI is not primarily hemodynamic. Unfortunately, 2 out of 3 patients developed

"F" without having "R" previously. As a "preventive" warning system to start early therapy for AKI, RIFLE seems thus not to be of value in patients with sepsis.
Severity of disease by RIFLE did not correspond to two established scores for patients with AKI. This is in contrast to other reports in different patient groups. AKI in sepsis seems to be a yes/no disease, rather than a gradual process as e.g. in hemodynamically mediated AKI postoperatively. Again, it might indicate that AKI in sepsis is a different entity.
Conclusions: Using RIFLE classification, AKI is common in patients with incipient sepsis. AKI in sepsis seems to be present already at the very beginning of sepsis, and not to be related to hemodynamic conditions. Most patients with sepsis develop "F" without having "R" before. RIFLE can thus not be used to guide early start of treatment in septic patients.

MP064 MONITORING OF RENAL FUNCTION IN ASPHYXIATED NEWBORNS: IS IT SUFFICIENT TO USE SERUM CREATININE LEVEL ONLY?

Mohammad Bassiouny[1], Ayman Hammad[1], Hamed Zaghloul[2], Nasr Abd El Hafez[2], Ekbal Abo Hashem[3]. *[1]Peiatrics, Faculty of Medicine, Mansoura, Dakhlia, Egypt; [2]Mansoura University Children's Hospital, Mansoura, Dakhlia, Egypt; [3]Clinical Pathology, Faculty of Medicine, Mansoura, Dakhlia, Egypt*

Introduction and Aims: Diagnosis and monitoring of renal failure is difficult in neonates as many of the established clinical and biochemical parameters are unrelaiable in this age group. This study was done to evaluate glomerular and tubular functions in asphyxiated newborns and to find if cystatin C is superior to conventionally used creatinine in monitoring improvement in glomerular filtration rate (GFR) in these patients.
Methods: Serum creatinine (s.Cr) & cystatin C (s.Cys-C), urinary β_2 microglobulin (u.β_2 MG) and corrected creatinine clearance (c.Cr.cl) levels were assesed in 35 full term asphyxiated newborns on 3rd and again on 7th days postnatally. Patients were compared to 15 healthy controls of matched age and sex.
Results: In comparison to controls; patients -on the 3rd day- had significantly increased s.Cys-C [Median (IQR) 1.95 (1.35-2.74) Vs 3.25 (1.75-10.1) mg/L respectively; P<0.001], s.Cr [Median (IQR) 0.64 (0.3-0.95) Vs 0.92 (0.3-3.5) mg/dL respectively; P<0.001], u.β_2 MG [Median (IQR) 2.1 (0.4-2.9) Vs 3.55 (2.2-15.7) mg/dL respectively; P<0.001] and significantly decreased c.Cr.cl [Median (IQR) 25.71 (15.24-37.7) Vs 7.48 (5.44-18.5) ml/min/1.73m^2 respectively; P<0.001]. When these patients were re-evaluated on 7th day after conservative medical treatment; they showed a significant increase in c.Cr.cl (P<0.001) and a significant decrease in s.Cys-C (P<0.001) & u.β_2 MG (P<0.001). Interstingly; their s.Cr level did not change significantly (P = 0.494). c.Cr.cl level on 7th day was predicted more accurately from 3rd day s.Cys-C level (P<0.001 & accuracy 94.5%) rather than s.Cr level (P = 0.02 & accuracy 74.5% only).
Conclusions: Although GFR may increase within few days in asphyxiated neonates in response to conservative treatment; their s.Cr level may not reflect such improvement. s.Cys-C as a more sensitive marker of GFR can be better used to monitor early improvements in c.Cr.cl and predict short term renal outcome in these patients.

MP065 ACUTE RENAL FAILURE REQUIRING RENAL REPLACEMENT THERAPY IN ELDERLY PATIENTS

Nikolina Basic-Jukic, Bruna Brunetta-Gavranic, Petar Kes, Ivana Juric, Željka Mustapic, Vesna Furic-Cunko. *Department of Dialysis, University Hospital Zagreb, Zagreb, Croatia*

Introduction and Aims: Incidence of patients with acute renal failure requiring dialysis (ARF) is increasing, and despite the significant improvements in dialysis technology, their mortality rate remains high. Elderly patients require additional attention because of the numerous concomittant diseases which make them specially vulnerable. In the present study we investigated the incidence, etiology and outcome of patients with ARF older than 70 years.
Methods: During the period of one year we followed up prospectively all patients admitted to University hospital Zagreb for development of ARF. Patients aged 70 years or more were divided into community-acquired ARF (CAARF) and hospitally-acquired (HAARF) group. Demographic data, laboratory and clinical profiles were recorded. Patients were treated with continuous renal replacement therapy if hemodynamically instabile, with hemodialysis alone or with both methods depending on the current clinical status. $P < 0.05$ was considered statistically significant.
Results: Out of 62.951 consecutively admitted patients, 100 developed ARF (0.16%), 37 of them being older than 70 years. Twenty-five elderly patients had HAARF (67.56%), while 12 patients (32.44%) developed CAARF. Average age was 73.8, and 81.25 years, respectively (p=0.004). Patients from the HAARF had significantly more diabetes mellitus, arterial hypertension, and preexistent chronic renal failure. Sepsis was the most common cause of ARF in both groups, but its incidence was higher in HAARF group (62,5% vs. 41.7%, p=0.08), followed by ischemic and iatrogenic etiology. Significantly more patients with HAARF at beginning of the first dialysis required oxygen therapy, mechanical ventilation, inotropes and were already treated with loop diuretics. They were more often hospitalized in the intensive care unit (88% vs. 66.67%) and were surgically treated. 41.7% of patients from the HAARF group were treated only with CRRT, 20.8% with hemodialysis and 37.5% with both methods, compared to 25%, 66.7% and 8.3% in the CAARF group, respectively (p=0.0021). Number of dialysis sessions was 9.44 *vs*. 3.91% (p=0.0067). The overall mortality rate of elderly patients with HAARF was 76% and 33.3% in the CAARF group. Risk factors for mortality were demand for the inotrope treatment, oxygen therapy and mechanical ventilation at beginning of the first dialysis.
Conclusions: Elderly patients make large proportion of population with ARF. Despite the burden of concomitant diseases, these patients have fair perspective for survival and renal function recovery. Although patients from the CAARF group were significantly older than patients from the HAARF group, they had better prognosis. Our data demonstrate that an advanced age should not influence clinical judgment in management of patients with ARF.

MP066 EFFECT OF NON PULSATILE VS PULSATILE CARDIOPULMONARY BYPASS ON RENAL FUNCTION DURING MYOCARDIAL REVASCULARIZATION: A SECONDARY ANALYSIS IN ELDERLY WITH NORMAL PREOPERATIVE GLOMERULAR FILTRATE RATE

Pierangela Presta[1], Laura Fuiano[1], Francesco Onorati[2], Giuseppe Santarpino[2], Michele Andreucci[1], Pasquale Mastroroberto[2], Attilio Renzulli[2], Giorgio Fuiano[1]. *[1]Nephrology Unit, Magna Graecia University, Catanzaro, Italy; [2]Cardiac Surgery Unit, Magna Graecia University, Catanzaro, Italy*

Introduction and Aims: We have recently demonstrated that pulsatile cardiopulmonary bypass (CPB) obtained by automatic intra-aortic balloon pump (IABP) vs standard linear CPB is associated to better perioperative renal function in patients with normal or reduced glomerular filtrate rate (GFR). Since older subjects have a major risk of renal disease because of the different adaptation of the elderly kidney to acute ischemic injury, we have reanalyzed our data in order to evaluate the perioperative renal function in this subgroup of patients and the specific impact of the pulsatile CPB.
Methods: We performed a secondary analysis of the data of our recent study selecting patients with preoperative GFR $\geq$ 90 ml/min and stratifying them by age (65-75 years vs 50-64 years). Fifty patients met the selection criteria. Twenty-seven patients with age $\geq$ 50 years and < 65 years were randomized to non pulsatile CPB (N=12, Group A) or to pulsatile CPB (N=15, Group B) obtained by IABP. Twenty-three patients with age $\geq$ 65 years and $\leq$ 75 years were randomized to non pulsatile CPB (N=13, Group A) or to pulsatile CPB (N=10, Group B). GFR measured using the Modification of Diet in Renal Disease equation, daily diuresis, and lactatemia were compared among groups during pre- and perioperative period.
Results: Perioperative GFR adjusted for age was significantly lower in patients of Group A (81.746 ml/min/1.73 m^2, 95% CI: 79.361-84.132 ml/min/1.73 m^2) than in those of Group B (98.919 ml/min/1.73 m^2, 95% CI: 96.557-101.282 ml/min/1.73 m^2) and this difference was -17.173 ml/min/1.73 m^2 on average (P<0.001). By contrast, plasma lactate levels were significantly higher (+0.992 mMol/L on average; P<0.001) in Group A (2.618 mMol/L, 95% CI: 2.316-2.919 mMol/L) than in Group B (1.625 mMol/L, 95% CI: 1.327-1.924 mMol/L). No significant difference between

the two groups was observed for 24h-diuresis. Older patients showed a greater worsening in GFR than younger patients, while lactate and 24h diuresis were similar.
Conclusions: The renoprotective effect of pulsatile CPB is confirmed both in younger and older patients but our analysis does not demonstrate a major renal protection in older patients.

MP067 PATIENT AND RENAL OUTCOMES IN ATHEROEMBOLIC RENAL DISEASE (AERD): IMPACT OF DIALYSIS MODALITY

Francesco Scolari, Pietro Ravani, Rossella Gaggi, Cristiana Rollino, Marisa Santostefano, Loredana Colla, Francesca Valerio, Nadia Dallera, Battista Fabio Viola. *Chair of Nephrology, University of Brescia, Brescia, Italy; Division of Nephrology, Ospedale di Cremona, Cremona, Italy; Division of Nephrology, Ospedale Malpighi, Blogna, Italy; Division of Nephrology, Ospedale San Giovanni Bosco, Torino, Italy; Division of Nephrology, Ospedale Civile, Ravenna, Italy; Division of Nephrology, Ospedale Molinette, Torino, Italy; Chair of Nephrology, University of Brescia, Brescia, Italy; Division of Nephrology, Spedali Civil, Brescia, Italy*

Introduction and Aims: AERD is an increasing and still underdiagnosed cause of renal dysfunction in elderly patients. Anticoagulation is now recognized as one of the most important precipitating factors for AERD. In a minority of patients, AERD is characterized by the occurrence of a severe renal failure requiring dialysis. In this study, we sought to determine whether extracorporeal dialysis, which usually requires anticoagulation, is associated with worse patient and renal outcomes as compared to peritoneal dialysis.
Methods: Cases of AERD requiring acute dialysis were selected from the Italian Multicenter study (Scolari F et al, Circulation 2007) which enrolled 354 patients. Logistic regression was used to model the probability of renal function recovery as a function of dialysis type (HD vs. PD). Cox's regression was used to study the association of patient survival with the exposure of interest. Clinical characteristics including baseline levels of GFR were considered in the analyses.
Results: One-hundred and eleven cases of acute kidney injury requiring dialysis were followed for 2.9 years on average. The probability of renal function recovery (which occurred in 32 subjects) was similar by dialysis modality (29.4% among 85 subjects who had received HD and 26.9% among 26 subjects who had undergone PD; p value = 0.806).
During the follow-up 60 patients died, 15 among PD patients and 45 among HD patients. The relative risk for death was lower among those treated with PD although the estimated effect was not significant (HR 0.83, 95% CI 0.53, 1.3, P = 0.428). Adjustment for potential confounders did not change the result.
Conclusions: Our data suggest that in patients with AERD and renal failure requiring dialysis the potential for renal function recovery was not influenced by the dialysis modality. During follow-up, a high mortality rate was observed, reflective of the extensive cardiovascular disease of the affected patients. The lower although not significant relative risk for death observed in patients treated with PD requires confirmation in further studies.

MP068 IMPACT OF HEMOGLOBINLEVEL ON THE SURVIVAL OF PATIENTS WITH ACUTE RENAL FAILURE (ARF)

Carolina Gracia, Carolina Lentisco, Milagros Ortiz, Juan Carlos Herrero, Maria Sanchez, Olimpia Ortega, Aniana Oliet, Carmen Mon. *Nephrology, Severo Ochoa Hospital, Leganes, Madrid, Spain*

Introduction and Aims: This study was aimed at determining which mortality risk factors were present in ARF patients who were assessed in our Nephrology Service during hospital stay and after discharge.
Methods: We performed a retrospective cohort study of all adult hospitalizations during a 3 years period (2001-2003). A total of 187 patients with ARF were included of whom 63% were male and 36% female. According to classical definitions, ARF was considered as an increase on creatinine serum concentrations of a 30% from baseline value or an increase of 0.5 mg/dl with a previously normal level.
All patients were followed after discharge for at least one year with an average follow-up period of 408 days (SD 352 days). Several clinical and analytical parameters, already described in literature as ARF mortality prognostic factors, were collected from all patients included in the study during hospital stay and after discharge. Mortality risk factors and mortality were compared both during hospital stay and the follow-up period.
Analysis: p-values < 0.05 were taken as significant. All statistical tests were performed with spss 11.0
Results: During hospital stay the mortality was 12% (24 of 187 died). After the Logistic Regression Analysis the following were found to be the mortality prognostic factors: etiology [pre-renal ARF as a protective factor in comparison to parenquimatous and obstructive ARF; p: 0.01; β: 0.32; CI 95% (0.14-0.78)]; oliguria [(p: 0.04, β: 7.5; CI 95% (1.8-29.7)] and ICU stay [(p: 0.001; β: 9.54, CI 95% (2.7-33.5)].
163 patients were discharged. During the follow-up period the mortality was 23.3% (38 out of 163 died). Kaplan-Meier survival curves showed that cholesterol (log-rank: 0.04); haemoglobin (log-rank: 0.08) and Charlson comorbidity index (log-rank: 0.0081) were significant mortality prognostic factors.After adjustment all these factors by multivariable Cox regression models haemoglobin and Charlson comorbidity index were remained a significant predictors of long – term mortality: haemoglobin levels > 10.2 gr/dl (median value)[p: 0.027; β: 0.72; CI 95% (0.54-0.96)] and Charlson comorbidity index levels > 3 (median value) [p: 0.0001; β: 1.35; CI (1.15-16.05)].
Conclusions: Mortality prognostic factors during and after hospital stay were different. During hospital stay, parenquimatous and obstructive etiology, oliguria presence and ICU stay were the most relevant mortality predictors whereas during the follow-up period the Charlson comorbidity index (as was expected) and anemia was found to be a strong and independent predictor of long-term mortality in patients with ARF.

MP069 IMPAIRED RENAL FUNCTION DURING ANGIOSTATIC THERAPY WITH THE COX-II INHIBITOR ROFECOXIB, IN COMBINATION WITH PIOGLITAZONE AND TROFOSFAMID OR CAPEZITABINE IN PATIENTS WITH METASTATIC/ADVANCED CANCER

Stephan Reinhold[1], Albrecht Reichle[2], Sonja Leiminger[1], Günter Riegger[1], Bernhard Banas[1], Bernhard Krämer[1]. *[1]Klinik und Poliklinik für Innere Medizin II, University of Regensburg, Regensburg, Germany; [2]Abteilung für Hämatologie und Internistische Onkologie, University of Regensburg, Regensburg, Germany*

Introduction and Aims: Angiostatic/antiinflammatory therapy with COX-II inhibitors and pioglitazone seems to be a well tolerated and promising regimen in patients with metastatic cancer. COX-II inhibitors may have less gastrointestinal side effects than conventional non-steroidal antiphlogistic drugs but their impact on renal function seems to be similar. In the present analysis we report on the renal safety and tolerability of an orally administered treatment with rofecoxib and pioglitazone in a prospective trial in patients with advanced cancer.
Methods: 87 patients were treated up to 12 months (mean 19.54 weeks) in a Phase II trial with rofecoxib, pioglitazone and either capecitabine in a dose of 2.0 g bid (group A, gastrointestinal cancer, n=50) or trofosfamid 50mg tid (group B, non-gastrointestinal, n=37) and followed for further 6 months. The study was stopped because of withdrawal of rofecoxib from the market.
Results: Baseline serum creatinine concentration was 0.81 mg/dl (±0.28mg/dl). Renal function decreased in 75 patients (86%) in the first month ($p< 0.0001$). This decrease went along with clinical signs of volume expansion. No dialysis was required and the decreased renal function improved on average by 0.1 mg/dl within 2 months after discontinuation of the study medication. Glomerular filtration rate improved by 18ml/min within 2 months after discontinuation of the study medication.
Conclusions: Our data suggest that an antiangiogenic/antiinflammatory therapy with rofecoxib and pioglitazone combined with either pioglitazone or capezitabine results in a decrease of renal function in nearly every patient, especially in patients with preexisting renal insufficiency treated with diuretics or concomitant nephrotoxic medication, but after discontinuation renal function tended to recover.

MP070 HEMODIALYSIS TREATMENT AND OUTCOME IN PATIENTS WITH ACUTE RENAL FAILURE

Liljana Tozija, Zvezdana Antova, Vladimir Pusevski, Koco Cakalaroski, Aleksandar Sikole. *Clinic of Nephrology, Faculty of Medicine, Skopje, Macedonia, The Former Yugoslav Republic of*

Introduction and Aims: The syndrome of acute renal failure (ARF) is life treating condition with high mortality rate. Seen of this aspect, starting the early treatment with renal replacement therapy (RRT) is of the grate importance.
Methods: 112 patients with acute renal failure were included in prospective, monocentric, clinical study and 62 labaratory and clinical data titled as risk factors (rf) were analyzed. One of these rf was and treatment with hemodialysis (HD). The APACHE 2 score was determined to each patient on the admission in the Intensive care Unit (ICU). The patients were divided in two groups: dialyzed and non-dialyzed. The aim of the study was to estimate the survival rate of the patients with ARF who were treated with HD. All of the data were analyzed with descriptive and analytical methods using "Statistica 5" version.
Results: 61.6% of the 112 patients with ARF were male with mean age 44.28±16.57 years and 38.4% female with mean age 47.51±20.33 years participated in the study. 68 patients (60.71%) were HD treated, total 314 HD treatment were performed or 4.62 treatments to each patients. HD treatment was performed at every 1.68 day by the patients. The dialyzed group consisted ARF patients with worse APACHE score. According the age, univariance analysis of the data confirmed statistical significance of p=0.0075 between the survivors and non-survivors. That means the group of the survivors was younger with mean age 43.99±17.7 compared to non-survivors where the mean age was 53.96±17.3. The only statistical significancy to the outcomes was related with appearance of rf named as intradialytic complications (hypotension, bleeding). The mean value of that risk factor for the survivors is 0.352±0.7 and 1.048±1.3 for the non-survivors with p=0.004. Haemodialysis as rf in outcome was not with statistical significance (p=0.189)
Conclusions: ARF is very serious condition usually with unexpected outcome. The patients with worse prognosis assessing with Apache 2 and with HD treatment were with equal chances for survival as conservatively treated patients.

MP071 ELEVATED CREATININE KINASE LEVELS AND HYPOALBUMINEMIA AS RISK FACTORS FOR ACUTE RENAL FAILURE IN PATIENTS WITH RHABDOMYOLYSIS

Oana Rap, María José Soler, Eva Rodríguez, María Pau Valenzuela, Anna Oliveras, Susana Vazquez, María Antonia Orfila, Josep Lloveras. *Nephrology Department, Hospital del Mar, Universitat Autònoma de Barcelona, Barcelona, Spain*

Introduction and Aims: Rhabdomyolysis is a common cause of acute renal failure (ARF) and may be related to different predisposing factors. The predictive risk factors for the development of ARF in patients with rhabdomyolysis are not well known. The purpose of this study is to assess the predictive risk factors for ARF in patients with rhabdomyolysis.
Methods: Retrospective study of patients admitted with the diagnosis of rhabdomyolysis (CK levels > 5000 U/L) between January 1998 and December 2007. Patients with history of chronic kidney disease were excluded. The main clinical and analytical variables were assessed at the moment of the diagnosis. Continuous variables were dichotomized at the median. Differences between variables with or without renal failure were compared using the chi-squared test. Odds ratios and 95% confidence intervals (CI) were calculated using logistic regression analysis to assess the association between the proposed predictors and renal failure. (Statistical significance: $p<0.05$).
Results: In our group 93 (74%) of patients with rhabdomyolysis were men. The mean age was 53±20 years. The incidence of ARF was 60% (n=76). Twelve (9.5%) of those who developed renal failure required dialysis. In the univariate analyses, the development of ARF was associated with the presence of oliguria, disseminated intravascular coagulation, metabolic acidosis, hypoprothrombinemia, hypocalcemia, hypoalbuminemia, hyperkalemia and increased levels of CK, gamma glutamyl transferase, aspartate transaminase, alanine transaminase and lactate dehydrogenase. In a multivariate model, patients with admission CK levels higher than 12750 (OR: 5.4, CI 1.7-17.3, p=0.004), hypoalbuminemia (OR: 4.1, CI 1.1-12.6, p=0.013), metabolic acidosis (OR: 7.7, CI 2.2-27.8, p=0.001) and hypoprothrombinemia (OR: 4.1, CI 1.3-12.7, p=0.013) were at increased risk of developing ARF. For this model, the area under the curve (ROC) was 0.88.
Conclusions: The incidence of ARF in our study was 60%, elevated admission CK levels, hypoprothrombinemia, metabolic acidosis and hypoalbuminemia are independent risk factors for ARF in patients with rhabdomyolysis. Early identification of patients with rhabdomyolysis at high risk for renal failure may enable prompt and effective initiation of treatment.

MP072 ACUTE RENAL FAILURE SECONDARY TO MALARIA IN CHILDREN, PATTERN OF PRESENTATION AND FACTORS ASSOCIATED WITH POOR PROGNOSIS

Abdul-Karim Sheiban, Mohammed Siani. *Internal Medicine and Nephrology, Al-Thowra Teaching Hospital, Faculty of Medicine and Health Science, Sana'a University, Sana'a, Sana'a, Yemen*

Introduction and Aims: Yemeni physician reported an increasing rate of malarial cases with a typical clinical presentation and high mortality rate.The diagnostic tertian or quartan fever, rigor were not an important feature.Gastroenteritis, acute renal failure were more frequently encountered.The aims of the study were to outlines the changes in the clinical presentation and to identify the different factors affecting the prognosis.
Methods: Between January and December, we observed 64 children (mean age 8.3 years range 4.2 to 11.2 years) who required dialysis secondary to Falciparum Malaria. All were subjected to proper history taking, full clinical assessment.Their investigations included complete blood picture,blood film for malaria,renal &liver function tests,widal test,urine analysis,stool analysis and abdominal ultrasonography.All received anti-malarial treatment beside other supportive therapy as well as peritoneal dialysis.
Results: Out of these 28 died (43.8%).
The children who died (Group 1) compared to those who survived (Group 11) differed significantly in age (mean ± SD) (7.2±1.3) years vs. 9.2±2.1 years, $P<0.05$), serum creatinine at presentation (645±104 umol/L vs. 438±87 umol/L, $P<0.05$), plasma bilirubin (2.1±0.3 mg/dl vs.1.2±0.2 mg/dl, $P<0.02$), systolic BP (50±11 mmHg vs. 90±12mmHg, $P<0.01$), diastolic BP (20±4 mmHg vs. 60±9 mmHg, $P<0.01$), Hb level 5.3±0.4 g/dl vs. 8±1.3gm/dl, $P<0.02$), time from diagnosis to referral (5.3±1.3 days vs. 8.9±2.1 days, $P<0.05$), and urine output (200±49ml/24 hours vs. 600ml ±131 ml, $P<0.01$).
There was no significant difference in gender, alanine transaminase (ALT) level, degree of fever, plasma Na or plasma K.
Diarrhoea was present in 29% of the children who died and only in 11% of those who survived ($P<0.05$) and splenomegaly was found in 3% and 18% respectively.
Conclusions: It was concluded that in non immune patients ARF associated with malaria my present with ATN like features and carried the poor prognosis, and with non classical type of mild form of glomerulonephritis in immune patients with good prognosis.

MP073 ♦ RENAL FUNCTION DURING THE FIRST WEEKS FOLLOWING LUNG TRANSPLANTATION

Mads Hornum[1], Martin Iversen[2], Ida Steffensen[2], Jørn Carlsen[2], Peter Hovind[3], Bo Feldt-Rasmussen[1]. *[1]Nephrology; [2]Department of Medicine B, Div. of Lung Transplantation; [3]Department of Nuclear Medicine, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark*

Introduction and Aims: Our group has previously described an overall cumulative incidence of renal disease (K/DOQI Stage 5) of 22% among 390 adult lung transplanted (LTX) patients at 10 years in a National Center, and a 54% and 62% decline in measured GFR at 6 and 24 month after transplantation, respectively.
A high level of blood cyclosporine concentration is needed in these patients. We therefore decided to study renal function in the first weeks after lung transplantation.
Methods: 23 patients (12F/11M) age 47 (±14) years from a single

national lung transplantation center, 16 with Chronic obstructive pulmonary disease (COPD)/α-1-Antitrypsin (α1AT)-deficiency, 5 with Cystic Fibrosis (CF)/Bronchiectasis and 2 with Idiopathic Pulmonary Fibrosis (IPF)/Sarcoidosis, were included in an analysis of renal function at baseline before transplantation, and at 1,2,3 and 12 weeks after transplantation. Primary Graft Dysfunction (PGD) was assessed within 72 hours after transplantation by chest radiograph analysis according to ISHLT standard. The immune suppression treatment consisted of induction with antithymocyte-globulin (ATG), followed by a triple maintenance regimen of cyclosporine, azathioprine and prednisolone. Parameters of renal function included 51-Cr labeled EDTA clearance, measured at time zero and four hours by a single injection method, as a measure of glomerular filtration rate (mGFR) and Cockcroft-Gault estimated GFR (cGFR). Blood cyclosporine concentration measurements (B-CyA) were also included in the analyses.

Results: A total of 110 B-CyA, S-Creatinine and measured GFR values among 23 patients were included in all subsequent analyses. Mean mGFR before transplantation was on average 101±18 ml/min/1.73m^2 and declined to 65±22, 53±16 and 57±18 ml/min/1.73m^2 at one, three and twelve weeks after transplantation, respectively.

A 36% and 48% (P=0.0001) reduction in mean mGFR at one and three weeks after transplantation compared to baseline-values was observed.

A Bland Altman plot showed poor agreement between mGFR and cGFR with a mean difference of -27 ml/min/1.73m^2 and limits of agreements of ±59 ml/min.

In a repeated measures ANOVA, Time (P<0.0001) but not PGD (P=0.067) was an independent risk factor for a decline in mean mGFR after transplantation. Mean plasma creatinine before the transplantation and 12 weeks after increased from 0.061±17μmol/l to 0.094±32μmol/l (P=0.0001). The decline in mean mGFR coincided with a rise in B-CyA-concentration, which is in accordance with data previously described by our study group.

Conclusions: These data for the first time demonstrate, with a plasma clearance technique, that renal function decreases dramatically during the first weeks after transplantation.

We also demonstrate the poor agreement between calculated and measured GFR in these patients.

Studies on prophylactic renoprotective treatments with the potential to protect renal function in these patients are urgently needed

MP074 ★ CATECHOL-O-METHYLTRANSFERASE (COMT) LL GENOTYPE PREDISPOSES FOR ACUTE RENAL FAILURE IN CARDIAC SURGERY PATIENTS

Anja Haase-Fielitz[1], Michael Haase[1], Rinaldo Bellomo[2], Wolf-Hagen Schunck[3], Gavin Lambert[4], Duska Dragun[1]. *[1]Department of Nephrology and Intensive Care Medicine, Charité University Berlin, Berlin, Germany; [2]Intensive Care, Austin Health, Melbourne, Australia; [3]Cytochrome P450 and Endoplasmic Reticulum, Max Delbrück Center for Molecular Medicine, Berlin, Germany; [4]Sympathicoadrenal System, Baker Heart Research Institute, Melbourne, Australia*

Introduction and Aims: There is evidence that polymorphisms in inflammatory and vasomotor genes may account for acute renal failure (ARF) after cardiac surgery. Catechol-O-methyltransferase (COMT) is a regulatory enzyme of catecholamine degradation in proximal tubular epithelial cells - target cell in ARF. We hypothesised that the COMT LL (low activity) genotype might be associated with increased risk of ARF compared to COMT HH (high activity) genotype.

Methods: In 260 consecutive, elective cardiac surgical patients undergoing cardiopulmonary bypass, we prospectively determined COMT genotype, pre- and postoperative plasma creatinine concentration and recorded intra- and postoperative variables. ARF was defined as increase in plasma creatinine greater than 50% from baseline to peak value during the first five postoperative days.

Results: COMT LL and HH patients were comparable with regard to pre-morbidities and intra-operative characteristics. A higher proportion of COMT LL genotype patients developed ARF compared to HH (31.3% vs. 13.7%); P=0.013, OR 2.87 (1.22-6.71). Absolute and relative increase in plasma creatinine was higher in LL carriers compared to HH (p=0.024; p=0.027). We found LL genotype as an independent risk factor for postoperative ARF; P=0.037, OR 2.28 (1.05-4.93). Also, 7.8% of LL patients and none of HH patients required postoperative renal replacement therapy; P=0.020. COMT LL genotype patients had a longer stay in intensive care; P=0.019 and in hospital; P=0.045.

Conclusions: COMT LL genotype appears to predispose for postoperative ARF in cardiac surgical patients. COMT-genotyping may help in pre-operative risk-assessment and lead to initiation of preventive treatments. (ClinicalTrials.gov, NCT00334009)

MP075 NOVEL AND CONVENTIONAL RENAL BIOMARKERS IN ADULT CARDIAC SURGERY

Michael Haase[1], Rinaldo Bellomo[2], David Story[3], Duska Dragun[1], Anja Haase-Fielitz[1]. *[1]Department of Nephrology and Intensive Care Medicine, Charité University Medicine Berlin, Berlin, Germany; [2]Department of Intensive Care, Austin Health, Melbourne, Australia; [3]Department of Anesthesiology, Austin Health, Melbourne, Australia*

Introduction and Aims: To investigate the predictive value of novel and conventional renal biomarkers for acute kidney injury (AKI) in a cohort of adult cardiac surgery patients.

Methods: We enrolled one-hundred elective adult cardiac surgery patients in a single-center, prospective observational study at a tertiary hospital. We measured the plasma concentration of neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, creatinine and urea at baseline, on arrival in the intensive care unit (ICU) and at 24 hours after commencement of cardiopulmonary bypass (CPB). We assessed such biomarkers in relation to postoperative AKI within the first five postoperative days.

Results: Twenty-three patients developed AKI postoperatively. Plasma NGAL, cystatin C and creatinine concentrations on arrival in ICU were significantly higher in patients who subsequently developed AKI (P<0.05). The area under the receiver operating characteristic curve (AUCROC) on arrival in ICU and at 24 hours after CPB was 0.784 (P=0.001) and 0.871 (P<0.001) for plasma NGAL, 0.832 (P<0.001) and 0.840 (P<0.001) for plasma cystatin C and 0.679 (P=0.024) and 0.861 (P<0.001) for plasma creatinine. The combination of renal biomarkers improved the AUCROC for the prediction of AKI at 24 hours after CPB (AUC 0.910; p<0.001). Plasma NGAL and plasma cystatin C on arrival in ICU independently predicted AKI (P=0.027; P=0.019) whereas other renal biomarkers did not.

Conclusions: Measurement of plasma NGAL and plasma cystatin C on arrival in the ICU is valuable for early diagnosis of AKI in adult cardiac surgery patients.

MP076 APACHE II SCORE MEASURED AT THE TIME OF THE FIRST EXTRACORPOREAL TREATMENT (Apa-HD) IS A RELIABLE MORTALITY PREDICTOR IN ALL PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING DIALYSIS (AKI-D)

Paola Inguaggiato, Giorgio Canepari, Graziella Gigliola, Silvio Meinero, Carlo Ferrando, Carmelo Sicuso, Albino Dutto, Marco Formica. *Nephrology and Dialysis, S. Croce-Carle Hospital, Cuneo, Italy*

Introduction and Aims: Apache II score is an accurate measure of illness severity and a strong predictor of in-hospital mortality (HM). It is usually measured within 24 hours after admission in intensive care unit (Apa-ADM). The aim of this study was to demonstrate that Apa-HD is as valuable as Apa-ADM in all patients with AKI-D.

Methods: In this prospective study on 46 consecutive critically ill patients (pts) with AKI-D we assessed: diagnosis, Apa-ADM, Apa-HD, Apa-HD/Apa-ADM ratio, timing of AKI-D (early <72 hrs, late >72 hrs after admission), length of dialysis (LOD), number of extracorporeal treatments (NET) (either continuous or intermittent), length of stay (LOS), renal outcome (defined as dialysis requirement), HM.

Results: Pts were 33 male and 13 female, 71±11 years old; 21 were surgical pts (45.7%); 17 pts had sepsis at the time of AKI-D diagnosis (37%); mean Apa-ADM was 25±8, mean Apa-HD 28±7, mean Apa-HD/Apa-ADM ratio 1.2±0,8; 18 pts had early AKI-D (39.1%); mean LOD was 9 days, mean NET 8±7 treatments, mean LOS 28±21 days; 20 pts recovered renal function (43.5%), 1 pts was on chronic dialysis at discharge (2.2%); HM was 56.5%. Both Apa-ADM and Apa-HD, but not Apa-HD/Apa-ADM ratio, significantly correlates with renal outcome (both p<0.005) and mortality (p<0.005 and p<0.025 respectively). Apa-ADM and Apa-HD did not differ

significantly. No correlation in Apa-HD was observed between pts with or without surgery, sepsis or early AKI-D. Apa-HD did not correlate with LOS, LOD and NET; indeed, LOD and NET significantly correlates with LOS ($p<0.05$).

Conclusions: Severity scores are often unavailable in critically ill pts at the time of nephrological consultation, but it is common opinion that a valid tool in mortality prediction may help in stratifying AKI-D pts. In our opinion, Apa-HD is a reliable score that can be easily measured by the nephrologist together with extracorporeal treatment prescription, and that may fulfill the need of a global evaluation of clinical severity in all types of critically ill pts starting dialysis.

MP077 A CLINICAL SCORE TO PREDICT POSTOPERATIVE RENAL FAILURE AFTER AORTIC ANEURYSMS SURGERY

Anna Zalewska[1], Marian Janowski[2], Marcin Zmudzinski[1], Julia Popowska-Drojecka[1], Marek Muszytowski[1], Marek Jackowski[2].
[1]Department of Nephrology and Internal Disease, Ludwik Rydygier Hospital, Torun, Poland; [2]Department of General Surgery, Gastroenterology and Oncology, Ludwik Rydygier Hospital, Collegium Medicum Nicolaus Copernicus University, Torun, Poland

Introduction and Aims: Acute renal failure (ARF) is one of the most serious complications after aortic aneurysm (AA) surgery. The occurrence of ARF increases the risk of postoperative death. Therefore it is important to be able to predict the incidence of renal function deterioration before the aortic aneurysym surgery. The aim of this study was to propose a clinical score to predict postoperative ARF.

Methods: The incidence of postoperative ARF was analyzed retrospectively in 84 patients (average age 67.3±12.1, range 47-83 years) in the regional hospital in Torun from 2003 to 2007. We examined the association between the incidence of ARF and age, gender, morphology of the aneurysm, coronary artery disease (CAD), hypertension (HT), arteriosclerosis obliterans (AO), diabetes mellitus (DM), preoperative renal function and surgery duration. Postoperative ARF was defined as postoperative serum creatinine (sCr) levels increased by $>$ 1.5 times or postoperative GFR (using the MDRD equation) decreased by $>$ 25%. ARF was classified into three groups: mild, moderate and severe. The score ranged between 0 and 10 points. Four risk categories of increasing severity (score 0 to 2; 3 to 5; 6 to 8 and 9 to 10) were formed.

Results: Postoperative ARF occurred in 18 patients (21.4%). Patients with ARF were older than the patients without ARF. 13 patients had a history of hypertension and 6 patients previously undergone AO treatment. Before the surgery ARF had been diagnosed in six patients and chronic RF in two. In 5 patients with mild or moderate preoperative ARF the renal function improved after the surgery.

Two patients with severe ARF (2,4% of the total of AA surgery pts) required hemodialysis treatment. 5 patients died and the mortality rate was higher than in the group of patients without ARF. ARF score (points): age $>$ 70 years (2); hypertension (1); arteriosclerosis obliterans (1);dissecting aneurysm (1); preoperative creatinine 1.2 to $<$ 2.1 mg/dl (2); preoperative creatinine $\geq$ 2.1 mg/dl (5).

Conclusions: In conclusion, a score is accurate in predicting ARF after abdominal aortic aneurysms surgery. The score may be useful in planning future clinical trials of early diagnosis and intervention in ARF.

MP078 ACUTE KIDNEY INJURY, MORTALITY, IN HOSPITALIZED PATIENTS OF CHINA

Ling Qiu[1], Limeng Chen[2], Xuemei Li[2], Xinqi Cheng[1], Xuewang Li[2].
[1]Division of Laboratory Medicine, Peking Union Medical College Hospital, Chinese Academy of Medicine Science, Beijing, China; [2]Division of Nephrology

Introduction and Aims: Acute kidney injury (AKI) has been reported in 5 to 7% of hospitalized patients on the basis of several single-center reports. But the marginal effects of AKI on in-hospital mortality, have not been well described in China. In the context of a computer-based intervention in which data were collected on kidney function, severity of illness, drug prescription, and outcomes in hospitalized patients, we linked changes in serum creatinine (SCr) with in-hospital mortality. We hypothesized that relatively small changes in SCr would be common and associated with adverse outcomes, even after adjustment for severity of disease.

Methods: The study was conducted at a 1800-bed urban academic medical center in Beijing, China. Data were obtained for a study to examine the modality of hospitalized patients, effects of serial SCr determinations were collected on a consecutive series of hospitalized patients between June 2006 and May 2007. Routinely available demographic factors, specific drug prescriptions, the mortality of patients in Intensive Care Unit (ICU) were also collected. The presence and degree of AKI were assessed using absolute and relative increases from baseline to peak SCr concentration during hospitalization. Continuous variables are described as mean ± SD or median with interquartile range and compared with *t* test or the Wilcoxon rank sum test, when appropriate. Categorical variables are described as proportions and compared with the X^2 test. We used logistic regression to estimate the odds of death with AKI, adjusting for associations with age, gender, ICD-9-CM (*International Classification of Diseases, Ninth Revision, Clinical Modification)* group, and CKD.

Results: A consecutive sample of 36,855 adults who were admitted to an urban academic medical hospital, including 15,233 who had two or more SCr determinations, was evaluated. Large increases in SCr concentration were relatively rare (e.g., $>$or=2.0 mg/dl in 1.7% patients).The modest increase in Scr concentration were common (e.g., $>$or=0.5 mg/dl in 11.2% patients). The incidence of hospital-acquired AKI was not rare (8.46%, Scr increasing $>$or=50%).Patients with AKI were significantly older, had lower baseline creatinine clearances, and had higher severity of illness. The fraction of admissions with AKI differed significantly by ICD-9-CM category ($P < 0.001$). The incidence of AKI (e.g., increase in SCr 50%) was highest among patients with injury and poisoning (16.7%), infectious diseases (16.0%), diseases of blood and blood forming organs (16.1%). In-hospital mortality of patients with AKI in ICU was 23.3%, that was significant higher than mortality of without AKI, the adjusted OR for death associate AKI was 2.7 ($p<0.01$).

Conclusions: The incidence of AKI in hospitalized patients of China estimated by analyzing of SCr changes was significant higher than expected. AKI is associated with significantly increased mortality and costs across a broad spectrum of conditions. Prevention and effective treatment of hospital-acquired AKI should be a national priority.

MP079 PREDICTORS OF ACUTE RENAL FAILURE FOLLOWING CARDIAC SURGERY

Mohammadreza Ardalan[1], Jalal Etemadi[1], Naser Safaie[2], Mohammadzakaria Pezeshki[3], Mohammadali Mohajel Shoja[4].
[1]Nephrology Department, [2]Cardiac Surgery Department, [3]Faculty of Medicine, [4]Tuberculosis and Lung Disease Reserch Center, Tabriz University of Medical Sciences, Tabriz, Estern Azarbayejan, Iran

Introduction and Aims: Acute renal failure (ARF) following cardiac surgery occurs in 1 to 10% of patients. Patients who develop ARF have higher rates of mortality. This study was undertaken to estimate the role of perioperative variables in predicting of post cardiac surgery ARF.

Methods: We studied a cohort of 398 adult patients who underwent cardiac surgery at our institution between February 1, 2004 and February 1, 2006. Adult patients ($>$18 yr) who were scheduled for cardiac valvular surgery, coronary artery bypass grafting (CABG) and both, with or without cardiopulmonary bypass (CPB) were included. Exclusion criteria were death within two days of operation (n = 8), incomplete patient data, and preexisting renal dysfunction and dialysis requirement or a baseline serum creatinine $>$ 4 mg/dl. Age, sex, left ventricular ejection fraction, diabetes, preoperative presence of proteinuria (on dipstick), type of surgery (CABG, valvular, combined CABG and valvular), use of CPB and duration of surgery were recorded. A logistic regression analysis was performed to assess independent contribution of variables in the risk of ARF.

Results: A binary logistic regression revealed age was an independent predictor of ARF ($P < 0.05$). When both all variables were included in a multinominal logistic regression model, preoperative proteinuria independently predicted ARF (Odds ratio=3.91, 95%CI: 1.55-9.91, P=0.004).

Conclusions: Our results revealed that special considerations should be given to elderly and patients with proteinuria when managing post cardiac surgery ARF.

MP080 AN ASSESSMENT OF THE ACUTE KIDNEY INJURY NETWORK (AKIN) CRITERIA FOR ACUTE KIDNEY INJURY IN THE CRITICALLY ILL PATIENTS

Sara Gonçalves[1], José António Lopes[1], Paulo Fernandes[1], Sofia Jorge[1], António Alvarez[2], Zélia Costa e Silva[2], Carlos França[2], Mateus Martins Prata[1]. *[1]Nephrology and Renal Transplantation, Hospital de Santa Maria, Lisboa, Portugal; [2]Intensive Medicine, Hospital de Santa Maria, Lisboa, Portugal*

Introduction and Aims: Based on the pre-existing RIFLE criteria, the Acute Kidney Injury Network (AKIN) group has recently formulated a new classification for acute kidney injury (AKI). As far as we know, the clinical utility of the AKIN classification in the Intensive Care Unit (ICU) setting has not yet been validated. We sought to ascertain the ability of the AKIN classification in predicting ICU mortality.
Methods: Patients admitted to the Department of Intensive Medicine of our Hospital between January 2004 and February 2005 were retrospectively evaluated. Maximum AKIN within the first three days of hospitalization was considered. Chronic kidney disease patients undergoing dialysis and renal transplant recipients were excluded from the analysis.
Results: A total of 379 patients (mean age: 59,04±19,63 years, 231 men) were studied. One-hundred seventy-six patients (46,4%) developed AKI. Overall mortality was 25%, and it was higher according to renal function deterioration (no AKI, 8,4%; AKIN 1, 37,3%; AKIN 2, 42,4%; AKIN 3, 52,9%, $P<0,0001$). After adjusting for age, gender, race, medical versus surgical admission, comorbidity, and illness severity evaluated by SAPS II, AKIN 1 (odds ratio 5,77; 95% confidence interval 2,81-11,83; $P<0,0001$), AKIN 2 (odds ratio 6,61; 95% confidence interval 2,67-16,38; $P<0,0001$) and AKIN 3 (odds ratio 8,31; 95% confidence interval 3,91-17,65;$P<0,0001$) emerged as independent predictors of ICU mortality.
Conclusions: AKIN classification appears to provide a useful prognostic stratification of the critically ill patients.

MP081 N-ACETYL CYSTEINE FOR PREVENTION OF CISPLATIN INDUCED NEPHROTOXICITY

Pratik Das. *Nephrology, B.P. Poddar Hospital, Kolkata, West Bengal, India*

Introduction and Aims: To evaluate the impact of N-Acetyl cysteine on prevention of cisplatin induced nephrotoxicity
Methods: 16 patients of Cervical cancer and 18 patients of head & neck cancer with normal renal function (Cr.Cl > 90 ml/min) were included in the study. None of them was on additional nephrotoxic agent. First cycle of chemo was given without N-acetyl cysteine (ie.cisplatin 30 mg/m^2 on D1 in head & neck Ca & 25 mg/m^2 on D1 to D3 in Ca cervix). The Cr.Cl was estimated on D7,D14 & D21.Those who remained stable with Cr.Cl > 90ml/min, were included in the next cycle. 12 Ca cervix & 15 head&neck Ca were eligible for 2nd cycle where similar chemo therapy was repeated with 5 days additional course of N-acetyl cysteine, 600 mg orally bd (1 day prior to 1 day after in 3 day course & 2 day prior to 2 day after in 1 day course). Cr.Cl measured on D7,D14 & D21. Renal functions were compared between two cycles (each cycle = 21 days)
Results: In 1st cycle without N-acetyle cysteine, 4 patients of Ca cervix and 3 patients of Ca head & neck showed significant fall of Cr.Cl by more than 25%. Of them, 1 patient in each group recovered in three weeks. In next cycle, none of the patient with head & neck Ca & only one patient of Ca cervix showed fall in Cr.Cl by more than 25% but recovered by 3 weeks. Mean Cr.Cl at D7,D14 & D21 in 1st cycle is significantly lower than 2nd cycle.
Conclusions: N-acetyl cysteine provides adequate protection against nephrotoxicity by cisplatin. Chances & severity of renal failure are significantly reduced by N-acetyl cysteine.

Lab methods, progression & risk factors for CKD 2

MP082 RISK FACTORS FOR PROGRESSION TO END STAGE RENAL FAILURE IN LITHIUM TREATED PATIENTS

Vivian Yiu, Stephan Brincat, Joble Joseph, Nicholas Mansfield, Chris Jones, Sui Phin Kon, Satish Jayawardene. *Department of Renal Medicine, King's College Hospital, London, United Kingdom*

Introduction and Aims: Lithium has been used as a mood stabiliser in affective disorders (uni and bipolar) since 1949. Frequent complications include acute toxicity, nephrogenic diabetes insipidus and chronic tubulo-interstitial nephritis. *Aim:* To determine the prevalence of end stage renal failure (ESRF) secondary to lithium treatment in our local population and the risk factors which lead to progression to ESRF.
Methods: This retrospective study analysed the incidence of lithium-induced nephrotoxicity amongst all patients attending the Renal Unit at King's College Hospital between 1996 and 2007.
Results: 26 patients treated with lithium were identified. 18 were male, 19 were Caucasian; 18 were hypertensive and 8 were diabetic; mean age at presentation was 64.7 years; mean follow-up was 2.93 years; mean duration of lithium therapy was 20 years (5-50 years); mean eGFR (using MDRD formula) at presentation was 31ml/min (6-73ml/min). 10 patients had proteinuria but no patients had haematuria. 5 patients underwent renal biopsy, which showed evidence of interstitial fibrosis in all cases and FSGS in 2 cases. 6 patients reached ESRF. The only two risk factors which were significantly associated with progression to ESRF were hypertension and diabetes (p=0.04 and 0.01 respectively). Age, duration of lithium treatment, discontinuation of treatment and creatinine at presentation did correlate with progression to ESRF, but did not reach statistical significance. On subgroup analysis comparing discontinuation versus continuation of lithium therapy, there was no significant difference in progression to ESRF (11% v 14%).
Conclusions: The prevalence of lithium-induced ESRF in our population is negligible at 0.2%. Poor prognostic factors include the presence of hypertension and diabetes. Bearing in mind a 20 fold increase in suicide risk after withdrawal of lithium, the decision to discontinue treatment in the presence of lithium-induced nephrotoxicity remains controversial and potentially harmful.

MP083 THE GLOMERULAR FILTRATION RATE IN PATIENTS WITH BREAST CANCER TREATED BY RADIATION AND CHEMOTHERAPY FOLLOWED BY TAMOXIFEN-DOES TAMOXIFEN INFLUENCE RENAL FUNCTION IN PATIENTS WITH BREAST CANCER?

G. Gluhovschi[1], S. Velciov[1], S. Curescu[2], T. Nicola[3], C. Gluhovschi[1], F. Bob[1], V. Trandafirescu[1], L. Petrica[1], G. Bozdog[1], M. Tveici[1], C. Vernic[4]. *[1]Nephrology, University of Medicine and Pharmacy, Timisoara, Romania; [2]Oncology, University of Medicine and Pharmacy, Timisoara, Romania; [3]Surgical Oncology, University of Medicine and Pharmacy, Timisoara, Romania; [4]Medical Informatics and Biostatistics, University of Medicine and Pharmacy, Timisoara, Romania*

Introduction and Aims: Patients (pts) with breast cancer are treated by radiation and chemotherapy. Pts with estrogen-positive receptors of the tumour are following afterwards treatment with Tamoxifen. Radiation and chemotherapy can have nephrotoxic effects, while a renoprotective effect has been ascribed to Tamoxifen. Tamoxifen, an oral selective estrogen receptor modulator, has proven useful in the treatment of retroperitoneal fibrosis due to its antifibrogenic actions. Some data in mice and rats have shown its renoprotective effects in experimental glomerulosclerosis by modulation of the mesangial cell phenotype. Tamoxifen could have protective effects on glomerular function and structure. Although this could also have important implications for women with chronic kidney diesase, data regarding the glomerular-specific effects of Tamoxifen in women are sparse. The aim of our study was to assess the effects of radiation and chemotherapy and of Tamoxifen on renal function in pts with breast cancer.
Methods: Two groups (A and B) of pts with breast cancer were enrolled into the study. Group A consisted of 50 pts, mean age: 57.64±9.34, who underwent treatment with Tamoxifen and group B, 26 pts, mean age:

50±9.83 who didn't receive Tamoxifen. Both groups underwent surgical tumor resection, radiation and chemotherapy, Tamoxifen being administered to group A due to the estrogen-positive status of the tumour. We followed up the GFR (MDRD) before radiation and chemotherapy and after this treatment. Thereafter we followed up the GFR in group A at 1, 2 and 3 years (y) of Tamoxifen and in group B at 1, 2 and 3 y of radiation and chemotherapy. Statistical analysis was done using Epi 6.04.

Results: In group A the GFR declined not significantly after radiation and chemotherapy and at 1 y of Tamoxifen. At 2 y of Tamoxifen, in the 18 surviving pts the GFR increased very significantly from 61.13±17.53 ml/min to 66.56±16.3 ml/min (p=0.009). At 3 y of Tamoxifen, the 12 surviving pts showed a preservation of the GFR. In group B the GFR declined from 88.14±14.63 ml/min (baseline) to 80.01±20.62 ml/min (p=0.0001) after radiation and chemotherapy. At 1 y after radiation and chemotherapy the GFR declined to 78.21±17.65 ml/min (p<0.001 as compared to baseline). At 2 y after radiation and chemotherapy in the 18 surviving pts the GFR declined to 70.94±13.39 ml/min (p<0.001 as compared to baseline). At 3 y in the 8 surviving pts the GFR declined to 61.36±9.17 ml/min (p=0.001 as compared to baseline).

Conclusions: Pts undergoing treatment with Tamoxifen (group A) showed a preservation of their renal function. In pts undergoing radiation and chemotherapy alone (group B) we noticed a decline of the Glomerular Filtration Rate.

MP084 FACTORS INFLUENCING THE BODY-LEAD BURDEN IN CHRONIC RENAL FAILURE AND HYPERTENSION

Mohamed M. Nasralla[1], Dawlat Belal[1], Mahmoud M. Nasralla[2].
[1]*Nephrology, Internal Med, School of Medicine, Cairo Univ., Cairo, Egypt;* [2]*Air Pollution, National Research Centre, Guiza, Egypt*

Introduction and Aims: Exposure to lead *(Pb)* has been a global health problem for decades. Renal effects of acute exposure to Pb as well as chronic high-level occupational exposure are well established. Controversy exists as to the role of low-level environmental exposure to Pb on the kidneys. Body-lead burden *(BLB),* is known to be elevated among renal failure patients and several explanations were proposed for this, though none is fully confirmed or uniformly accepted. These include: inadequate Pb excretion by the failing kidneys; cause-effect relation between Pb-exposure and renal failure of unknown cause; and an association with hypertension/hypertensive nephrosclerosis. A further proposed possibility is that increased bone-turnover due to 2^{ry} hyperparathyroidism, in renal failure, releases Pb from its dormant stores in bone. We tried to test these various hypotheses head-on, for the first time, in this study.

Methods: We included 84 subjects divided to 2 main groups. *Group 1:* 50 with pre-ESRD *(CKD2-4*) divided into 3 subgroups: 1a: 19 with CKD of known cause; 1b: 15 with hypertensive nephrosclerosis; 1c: 16 with CKD of unknown cause. *Group 2:* 34 matched controls with normal kidney functions including 18 normtensive and 16 with essential hypertension

All subjects were evaluated by inquiry about sources of environmental exposure to Pb, symptoms/signs suggestive of Pb toxicity, assessment of BLB by *EDTA lead-mobilisation test*, measurement of serum parathormone *(PTH)*, calcium, phosphorus, alkaline phosphatase, urea, creatinine, uric acid.

Those with occupational exposure to Pb, acute renal failure, malignant hypertension or renal replacement therapy were excluded.

Results: 34 CKD patients (68%) vs 1 control (2%) had a *positive Pb mobilisation test* (>600ug).Only 9 recalled a source of exposure to Pb, those had higher BLB (p0.038) and 3 had symptoms suggestive of Pb toxicity

BLB was higher in CKD patients compared to controls (<0.0001), there was no difference in BLB between different subgroups of CKD patients nor between normo- and hyper-tensive controls. *PTH* was higher among CKD patients than controls (p 0.001) with no differences between CKD subgroups. PTH was higher in hyper- than normo-tensive controls (p 0.012)

In CKD patients, BLB correlated positively with serum PTH (r 0.7, p 0.0001). This was true for all subgroups (1a: r 0.84, p <0.0001; 1b: r 0.56, p 0.04; 1c: r 0.7, p 0.02). Regarding the other studied parameters, BLB only correlated posititively with serum creatinine (r 0.4, p.007).

In controls, BLB did not correlate with any studied parameter.

Conclusions: We conclude that: a)BLB is elevated in CKD *irrespective* of the cause of renal failure b)BLB in CKD is *related to hyperparathyroidism* c) Higher serum creatinine was associated with higher BLB *(ie more Pb excretion in urine)* (probably due to higher PTH) d) absence of symptoms of Pb toxicity or failure to recall exposure to Pb donot exclude elevated BLB in renal patients.

These results support the hypothesis that elevated PTH releases Pb from its bone stores which may explain several manifestations of and modify treatment for hyperparathyroidism and the uremic syndrome.

MP085 THE EFFECT OF CELECOXIB ON PODOCYTE APOPTOSIS INDUCED BY PUROMYCIN AMINONUCLEOSIDE

Wei-xin Kong[1], Lu-lu Ding[1], Yong Gu[2], Hai-chun Yang[2], Shan-yan Lin[2].
[1]*Department of Nephrology, Suzhou Kowloon Hospital, Shanghai Jiaotong University Medical School, Suzhou, Jiangsu Province, China;* [2]*Department of Nephrology, Huashan Hospital, Fudan University, Shanghai, China*

Introduction and Aims: The podocyte is a highly specialized and terminally differentiated cell and the reduced podocyte number is caused by detachment of cells from the glomerular basement membrane and/or by apoptosis. The underlying mechanisms of which the specific cyclooxygenase-2 (COX-2) inhibitors have been shown to decrease proteinuria and retard progressive glomerular injury in some animal models have not been addressed formally. Accordingly, in this study we investigated the direct effect of celecoxib, a specific COX-2 inhibitor, on podocyte apoptosis induced by puromycin aminonucleoside (PA) and the mechanisms that underlie this effect in order to further search for clinical therapeutic target on chronic progressive glomerular injury.

Methods: Experiments were performed using early-passage growth-restricted, conditionally immortalized mouse podocytes. The expression of COX-2 in podocytes was measured by use of Western blot analysis. The effects of specific COX-2 inhibitors celecoxib on podocyte apoptosis induced by PA will be examined on the basis of podocyte culture.The conditionally immortalized mouse podocytes were studied and divided into six groups. Control (CON); puromycin aminonucleoside (PA); celecoxib (CELE); celecoxib+puromycin aminonucleoside (CELE+PA); dexamethasone (DEX); dexamethasone+puromycin aminonucleoside (DEX+ PA). Viable cell number was assessed by methylthiazoletetrazolium (MTT) assay using CellTiter 96 Non-Radioactive Cell Proliferation Assay kit and apoptosis was measured by staining with Hoechst 33342 at 0, 8, 24, and 48 h. To determine the activity of caspase-3, we used the BD ApoAlert Caspase Colorimetric Assay Kit, according to the manufacturer's instructions. Western blot analysis was performed to measure the protein levels of p53 and COX-2.

Results: 1.For passaging cells, podocytes were grown under growth restrictive conditions at 37 °C for 14 days. The COX-2 expression increased over time. The highest level was found at 24 hour. Afterwards it decreased gradually.2.The percentage of apoptotic cells significantly increased in the podocytes that were exposed to PA compared with control group. No significant change was found in both CELE and DEX groups. In contrast, both dexamethasone and celecoxib significantly reduced PA-induced apoptosis (P<0.05). There was no difference in viable podocyte number and the activity of caspase-3 among each group. Western blot analysis showed that PA increased the protein levels for p53 in immortalized mouse podocytes. PA-induced p53 was reduced by DEX and CELE (P<0.05). COX2 expression was seen in control group. It was elevated profoundly after 24 hours induced by PA and reduced by use of DEX and CELE (P<0.05).

Conclusions: The COX-2 expression in podocytes was time-dependent. Celecoxib prevents podocyte apoptosis induced by PA that is p53 dependent. The preventing effect of celecoxib on podocyte apoptosis may be potential interactions with COX-2 expression.

MP086 ARE CONCOMITANT SERUM LEVELS OF NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AND CYSTATIN C RELIABLE MARKERS FOR CONTRAST NEPHROPATHY IN PATIENTS UNDERGOING CORONARY ANGIOGRAPHY?

Mohamed El-Khatib, Amal El-Shehaby, Ahmed Abd El-Aziz. *The Departments of Internal Medicine, Medical Biochemistry and Intensive Care Unit, Al-Kasr Al-Aini Medical School, Cairo, Egypt*

Introduction and Aims: Since interventional cardiologists are being asked more frequently to perform coronary angiography on an increasing numbers of patients, contrast nephropathy is a more frequent and potentially serious complication of coronary angiography. Very few biomarkers exist for monitoring contrast induced nephropathy. Recently, serum neutrophil gelatinase-associated lipocalin (NGAL) represents a novel biomarker for early identification of acute kidney injury. The present work aimed to test the hypothesis that NGAL could represent an early biomarker for kidney injury and to assess the relationship between NGAL and the two gold standards for estimating acute kidney changes (serum creatinine and cystatin C), in patients with normal serum creatinine undergoing percutaneous coronary angiography.
Methods: The study was performed on thirty non-diabetic patients with normal serum creatinine, undergoing coronary angiography due to coronary artery disease. All patients were matched for age and body mass index. Following full clinical examination, fasting blood samples were withdrawn for estimation of blood glucose, glycosylated hemoglobin, lipid profile, creatinine as well as NGAL and cystatin C before coronary angiography. Another blood samples were taken 4 and 24 hours after coronary angiography for all patients for evaluation of serum creatinine, NGAL and cystatin C.
Results: There was a significant increase in mean serum NGAL level 4 hours and 24 hours after coronary interventions when compared to the baseline value before coronary angiography. Before coronary angiography, serum NGAL was positively correlated with serum creatinine, and cystatin C. In multiple regression analysis, serum creatinine was the only predictor of serum NGAL. Serum NGAL, 4 hour after coronary angiography, correlated with serum creatinine only in simple and multiple regression analysis. On the other hand, mean serum cystatin C level increased significantly only 24 hour after coronary angiography compared to the baseline value before coronary angiography. In a simple regression analysis, serum cystatin C correlated positively to systolic and diastolic blood pressure, serum creatinine, and serum NGAL before coronary angiography. In multiple regression analysis, serum creatinine and systolic blood pressure were the predictors of serum cystatin C.
Conclusions: Serum NGAL and cystatin C could be valuable in the detection of acute renal impairment after coronary angiography. However, current diagnostic methods such as, serum creatinine or cystatin C measurements only respond after renal function has deteriorated. Therefore, the presence of new early markers for renal injury such as NGAL, can initiate proper management of acute renal failure within hours rather than days of the insult. It seems likely that the interest in NGAL will center chiefly on its role as a marker of kidney damage, where its early and marked response to the insult makes it one of the best markers of acute renal dysfunction.

MP087 VLDL-INDUCED TRIGLYCERIDE ACCUMULATION IN HUMAN MESANGIAL CELLS IS MAINLY MEDIATED BY LIPOPROTEIN LIPASE

Jing Li, Hang Li, Yu-bing Wen, Xue-wang. Li. *Division of Nephrology, Department of Internal Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Introduction and Aims: Lipoprotein lipase (LPL) expressed in the arterial wall plays a key role in atherogenesis by actions of enzymolysis and molecular bridge and, thereby, leading to the formation of lipid-loaded foam cells. Very low-density lipoprotein (VLDL) in vitro can induce foam cell formation in human mesangial cells. It is known that LPL is expressed by glomerular mesangial cells. This study was designed to investigate if LPL play a role in VLDL-induced lipid accumulation in human mesangial cells and its underlying mechanism.
Methods: Human wild type LPL (hLPLwt), catalytically inactive LPL (hLPL194) or control alkaline phosphatase (hAP) were expressed in human mesangial cell line (HMCLs) via adenoviral vectors. Orlistat, a specific inhibitor of the lipoidolytic activity of endogenous LPL, and heparanase, which degrades cell surface heparanase proteoglycan (HSPG), were also used to estimate the role of either enzymolysis action or "molecular bridge" action of LPL in the uptake of VLDL. Cellular lipid deposition was visualized by Oil Red O staining and analyzed quantitatively by standard enzymatic procedures. LPL protein expression and activity were measured by Western blot and a chemical analysis, respectively.
Results: VLDL induced triglyceride accumulation in HMCLs in time- and dose-dependent manner. Compared with Ad-hAP transfected HMCLs, cellular triglyceride content increased 4.55-fold (P=0.00) in Ad-hLPLwt transfected HMCLs and 1.52-fold (P= 0.01) in Ad-hLPL194 transfected HMCLs. Triglyceride accumulation in HMCLs in response to VLDL was mostly blocked by orlistat. cellular triglyceride content was reduced from 84.4054±1.7319μg/mg protein (DMSO group, DMSO was solvent of orlistat) to 62.6526±2.0883μg/mg protein (0.1μM orlistat, P=0.00), 46.4751±1.3543μg/mg protein (1μM orlistat, P=0.00) and 34.67122±0.8934μg/mg protein (10μM orlistat, P=0.00) in a dose-dependent manner. Pretreatment of the cells with heparanase slightly reduced cellular triglyceride accumulation in the present of high concentration of VLDL. LPL expression in HMCLs was also up-regulated by VLDL in a time –dependent manner.
Conclusions: VLDL-induced triglyceride accumulation in human mesangial cells is mainly mediated by LPL, and enzymolysis action of LPL could be major factor in this process. These results suggest that LPL may be an important factor participating in initiation and progression of VLDL–mediated lipid renal injury.

MP088 LEVELS OF OXIDANT STRESS INCREASE PROGRESSIVELY WITH RENAL FUNCTION LOSS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Ioannis Karamouzis[1], Pantelis Sarafidis[2], Stavros Iliadis[1], Michael Karamouzis[1], Anna-Bettina Haidich[3], Athanasios Sioulis[2], Athanasios Triantos[1], Norma Vavatsi-Christaki[1], Dimitrios Grekas[2]. *[1]Laboratory of Biological Chemistry, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Section of Nephrology and Hypertension, 1st Department of Medicine, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Laboratory of Hygiene, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Introduction and Aims: Increased oxidative stress in chronic kidney disease is suggested to be both a cause and an effect of renal injury. However, the evolution of oxidant stress from early stages of renal function decline is not fully clear. This study aimed to determine the oxidant stress status in patients with chronic kidney disease.
Methods: We evaluated a total of 85 consecutive patients with chronic kidney disease that had visited for first time the Nephrology Outpatient Clinic of a University Hospital within a period of 12 months. Patients were divided in those with chronic kidney disease stage 1-2, those with chronic kidney disease stage 3 and those with chronic kidney disease stage 4, according to current guidelines. A total of 29 matched healthy subjects were also evaluated. Plasma levels of 15-F_{2t}-IsoProstane (15-F_{2t}-IsoP), which is a highly accurate *in vivo* marker of oxidative stress were measured in all participants.
Results: Plasma 15-F_{2t}-IsoP levels displayed a progressive increase from 47,11±32,25 pg/ml in healthy subjects to 259,73±62,11 pg/ml in patients with chronic kidney disease stage 1-2, 317,45±107,61 pg/ml in patients with chronic kidney disease stage 3, and 412,82±99,76 pg/ml in patients with chronic kidney disease stage 4 (p<0.001 with ANOVA). Correlation analysis the total population of chronic kidney disease patients revealed that plasma 15-F_{2t}-IsoP levels were strongly and inversely correlated with eGFR levels (r= -0.65, p<0.001).
Conclusions: This study shows that 15-F_{2t}-IsoP levels are increasing progressively with advancing chronic kidney disease stages. Increase in oxidative stress is strongly associated with loss of renal function.

MP089 PLASMA TOTAL ANTIOXIDANT CAPACITY AND SERUM VITAMIN E LEVELS REMAIN STABLE WITH ADVANCING STAGES OF CHRONIC KIDNEY DISEASE

Ioannis Karamouzis[1], Pantelis Sarafidis[2], Michael Karamouzis[1], Stavros Iliadis[1], Anna-Bettina Haidich[3], Athanasios Sioulis[2], Athanasios Triantos[1], Norma Vavatsi-Christaki[1], Dimitrios Grekas[2]. *[1]Laboratory of Biological Chemistry, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Section of Nephrology and Hypertension, 1st Department of Medicine, AHEPA Hospital Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Laboratory of Hygiene, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Introduction and Aims: Studies on the antioxidant reserve in patients with chronic kidney disease are relatively limited and report contradictory results. This aim of this study was to examine the antioxidant reserve in vivo in predialysis patients with chronic kidney disease.
Methods: A total of consecutive 85 predialysis patients with chronic kidney disease divided in groups according to chronic kidney disease stage, as well as 29 healthy subjects were evaluated. All participants gave blood samples for the measurement of (a) plasma total antioxidant capacity (TAC) determined with a standardised assay, corrected for interferences from uric acid, bilirubin, and albumin levels and (b) serum levels of vitamin E.
Results: Plasma TAC remained stable with advancing chronic kidney disease stages (healthy subjects 1.05±0.08 mmol/l; chronic kidney disease Stage 1-2, 1.05±0.08 mmol/l; chronic kidney disease Stage 3, 1.05±0.10 mmol/l; chronic kidney disease Stage 4, 1.07±0.14 mmol/l); there were no significant differences in comparisons by pairs or with the use of ANOVA between groups. Vitamin E levels were higher in healthy subjects compared to any other group (31.09±6.16 μmol/l, $p<0.001$) but did not differ significantly between the groups of predialysis patients (chronic kidney disease Stage 1-2, 22.86±3.27 μmol/l; chronic kidney disease Stage 3, 22.56±4.89 μmol/l; chronic kidney disease Stage 4, 20.84±1.81 μmol/l).
Conclusions: In this study plasma TAC levels remained normal and vitamin E remained stable with advancing chronic kidney disease stages. The antioxidant reserve of the body does not seem to change with the loss of renal function.

MP090 NON TRADITIONAL CARDIOVASCULAR RISK FACTORS IN EARLY STAGES OF CHRONIC KIDNEY DISEASE. ROLE OF OLMESARTAN TREATMENT

Soledad García de Vinuesa[1], Marian Goicoechea[1], Victoria Cachofeiro[2], Vicente Lahera[2], Ursula Verdalles[1], Ines Aragoncillo[1], José Luño[1]. *[1]Nephrology, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]Physiology, Universidad Complutense, Madrid, Spain*

Introduction and Aims: In addition to the classical cardiovascular (CV) risk factors, recently other new non traditional factors such as inflammation, oxidative stress and homocysteine, among others, were found to be significantly associated with CV mortality in advance stages of CKD patients. However, the prevalence of increased oxidative stress and inflammation in early stages of CKD has not been fully investigated. The aim of this study was to investigate the prevalence of these newly emerging CV risk factors in a cohort of patients with mild to moderate CKD compared to a healthy subject cohort. At the same time we investigate the potential efficacy of olmesartan, an angiotensin receptor blocker (ARB) in this situation, since ARBs have been shown to act as antioxidant and anti-inflammatory agents in experimental models.
Methods: The study participants were 52 non diabetic and non previously treated with RAS blocking drugs, CKD patients (Mean eGFR: 42±17 ml/min). Olmesartan was administered at a 40 mg dose for 16 weeks. Before and after olmesartan treatment, inflammatory biomarkers (hs-CRP, IL-6), oxidative parameters: antioxidant capacity (TAC), lipid peroxidation (LPO), Oxidized LDL (ox-LDL) and homocysteine plasma levels were measured. Baseline data were compared with data obtained in 25 healthy control persons with similar age and normal renal function.
Results: The biomarkers of oxidative stress (LPO and ox-LDL), inflammation parameters (hs-CRP, IL-6) and homocysteine levels were significantly higher in CKD patients compared with control subjects, but TAC did not differed significantly between CKD patients and healthy subjects. In linear regression analysis LPO was significantly associated with chronic inflammation (hs-CRP), but not with renal function (eGRF). Olmesartan treatment resulted in a significant decrease of hs-CRP levels and fibrinogen but not any significant differences in oxidative stress parameters or homocysteine levels were observed after olmesartan therapy.
Conclusions: These data demonstrate increased oxidative stress without modification in the total antioxidant capacity in early stages of CKD that is significantly associated with an inflammation status but does not closely correlate with the level of GFR. Short term olmesartan treatment is able to improve the inflammation status but not the oxidative stress.
Disclosure: A grant from Pfizer was received to measure the lab. determinations.

MP091 THE EFFECT OF KETOANALOGS OF ESSENTIAL AMINO ACIDS SUPPLEMENTED LOW PROTEIN DIET ON THE PROGRESSION OF CHRONIC KIDNEY DISEASE

Dong Ki Kim[1], Jung Tak Park[1], Tae Ik Chang[1], Eun Young Kim[1], Hyun-Wook Kim[1], Jae Hyun Chang[1], Sun Young Park[1], Sung Jin Moon[1], Beom Seok Kim[1], Kyu Hun Choi[1], Ho Yung Lee[1], Dae-Suk Han[1], Sug Kyun Shin[2]. *[1]Department of Internal Medicine, The Institute of Kidney Disease, Yonsei University, College of Medicine, Seoul, Republic of Korea; [2]Department of Internal Medicine and Kidney Center, NHIC Ilsan Hospital, Ilsan, Republic of Korea*

Introduction and Aims: Low protein diet (LPD) is prescribed as a conservative treatment in patients with chronic kidney disease (CKD) to improve uremic symptoms and to slow the progression of renal dysfunction. However, deleterious effects of LPD on nutritional status and obscure clinical outcomes have raised concern. We investigated whether LPD supplemented with ketoanalogs retards progression of CKD and maintains nutritional status.
Methods: Data were collected retrospectively from 120 predialytic CKD patients to whom a supplemented LPD with ketoanalogs was administered for at least 6 months. Measurements of decline rate of glomerular filtration rate (GFR), clinical and biochemical parameters before (pre LPD+KA period) and after ketoanalogs supplemented LPD (LPD+KA period) were compared.
Results: GFR-time slope and reciprocal creatinine-time slope increased significantly during the LPD+KA period in both diabetic and non-diabetic patients. Mean total cholesterol and triglyceride levels decreased during the LPD+KA period. However, levels of albumin and protein did not change. Responders defined as patients who showed an increase in GFR-time slope during the LPD+KA period had higher prevalence of diabetes and a higher serum albumin level during the pre LPD+KA period. On multivariate analysis, responsiveness to LPD with ketoanalogs supplementation was independently related to diabetes and higher levels of albumin in the pre LPD+KA period.
Conclusions: LPD supplemented with ketoanalogs have beneficial effect for preserving GFR in CKD patients, and the nutritional status before staring the dietary treatment is thought to be an independent factor of this effect.

MP092 FUNCTIONAL ROLE OF INDUCIBLE NITRIC OXIDE SYNTHASE (iNOS) ON THE CORE BINDING FACTOR 1 (CBFA-1) EXPRESSION IN VASCULAR SMOOTH MUSCLE CELLS

Maria Aparecida da Gloria[1], Elisa Mieko Suemitsu Higa[1,2], Aluizio Barbosa de Carvalho[1]. *[1]Nephrology; [2]Emergency, UNIFESP/Escola Paulista de Medicina, Sao Paulo, SP, Brazil*

Introduction and Aims: Medial vascular calcification seen in uremia is considered to be a process mediated by vascular smooth muscle cells (VSMC), very similar to that of bone formation. The Cbfa-1 expression is required for the differentiation of VSMCs into osteoblastic-like cells. Although nitric oxide synthase (NOS) expression has been detected in osteoblast-like cells, the role of NO (nitric oxide) in their function is controversial. Thus, the objective of this study is to investigate the effects of inducible NOS (iNOS) on the Cbfa-1 expression of VSMC.
Methods: Renal VSMCs were cultured from adult male Wistar rats and incubated with DMEM plus 10% sera pooled from healthy individuals (CTL), lipopolysaccharide (LPS, 100 μg/ml), β-glycerophosphate (BGF,

12mM), BGF+LPS, aminoguanidine (AG, 30mM) and LPS+AG groups. iNOS and Cbfa-1 expressions were analyzed by RT-PCR.
Results: Cbfa-1 expression decreased 70% in the AG and increased 50% in the LPS when compared to CTL group. In the LPS, Cbfa-1 increased 70% when compared to LPS+AG group. In the LPS+AG, iNOS was decreased (44%) when compared to LPS group. Cell viability for all groups was $P>0.05$.
Conclusions: Our study showed that iNOS may have a functional role on the expression of Cbfa-1 in rVSMCs.

MP093 EVALUATION OF GLOMERULAR FILTRATION RATE (GFR) IN OBESE PATIENTS: WHICH FORMULAS?

Farideh Alenabi[1], Francois Chantrel[1], Xavier Parent[2], Claire Trivin[1], Sandrine Muller[1], Bernadette Faller[1]. *[1]Nephrologie, Hopital Pasteur, Colmar, France; [2]Biochimie, Hopital Pasteur, Colmar, France*

Introduction and Aims: Measurement of glomerular filtration rate (GFR) is time consuming and cumbersome. Several formulas have been developed to predict GFR using serum creatinine (Cr) concentrations and demographic characteristics. However, few studies have been performed to discern the best formula to estimate GFR in obese patients. In this study, we compared GFR measured by plasmatic Iohexol clearance to urinary clearance and estimated formulas.
Methods: In 21 obese patients (BMI>30), we compared the Cockcroft-Gault formula (CG), Normalized Cockcroft-Gault for BSA (CG/1.73m^2), MDRD equations (full and simplified) and urinay creatinine clearance (UV/P) to GFR measured by iohexol clearance using five venous samples (140min to 250min after an intravenous bolus). Statistical analysis was done by correlation studies, accuracy evaluation ie P30 values (percentage of results in a ±30% interval of GFR ([CG-GFR]/GFR%) and Bland-Altman procedure.
Results: Patients (M= 9, F=12),mean age was 62.5±11.9 years, all patients were obese BMI>30: mean BMI was 37.9 [31.7-51.1], mean BSA was 2.19m^2 [1.7-2.8]. Median plasmatic creatinine was 188±148 µmol/l [59-594]. The mean measured iohexol clearance GFR was 38.9±26.ml/min/1.73m^2 [4.4-95.8]. As previously reported CG strongly overestimates GFR with a mean 77.9±57ml/min, thus mean bias was 38±36 ml/min, correlation remains significant (r=0.91 p<0.00). After normalization of CG by BSA overestimation GFR decreases to 22.8±22 ml/min with a better correlation (r=0.93 p<0.00). Bland and Altman plot of CG and CG/1.73 compared to Iohexol shows increase of bias for higher GFR. Mean measured urinary clearance (UV/P) was 55.86±39.ml/min/1.73 m^2 thus mean bias was 15.6±19 ml/min/1.73 m^2, correlation remains significant (r=0.87 p<0.00), as with CG formulas overestimation increased with higher GFR values (Bland and Altman plot). With MDRD formulas mean clearance were 47.7±32.5ml/mn/1.73m^2 [9.6-123] and not different for MDRDs (simplified) 49.6±33.6 ml/mn/1.73m^2. Mean bias were 8.7±12.4ml/mn.1.73m^2 and 10.7±13.1 ml/mn/1.73m^2 for MDRD and MDRDs respectively. The accuracy of formulas assessed by P30 was 20%, 28.7%, 57%, and 40% for CG, CG-1.73, MDRD and MDRDs, UV/P respectively. MDRD and MDRDs show the best correlation with Iohexol clearance (r= 0.94 and 0.93 p<0.00).
Conclusions: Our study confirms a large overestimation of CG in obese patients, normalization by BSA or utilisation of measured creatinine clearance did not reach better accuracy of estimation of GFR in this population. MDRD formulas simplified or not seems more relevant for estimation of GFR as overestimation is not clinical significant and seems not related to the range of GFR concern.

MP094 EFFECT OF CHOLECALCIFEROL SUPPLEMENTATION ON INTRACELLULAR CALCIUM STATUS IN CKD PATIENTS

Ingrid Lajdová[1], Viera Spustová[1], Adrián Okša[1], Kornélia Štefíková[1], Dušan Chorvát Jr[2], Alžbeta Chorvátová[3], Rastislav Dzúrik[1]. *[1]Department of Clinical and Experimental Pharmacotherapy, Slovak Medical University, Bratislava, Slovakia (Slovak Republic); [2]International Laser Centre, Bratislava, Slovakia (Slovak Republic); [3]Research Centre, CHU Sainte-Justine, Department of Pediatrics, University of Montreal, Montreal, QC, Canada*

Introduction and Aims: The elevation of free cytosolic calcium concentration ($[Ca^{2+}]_i$) has been associated with cellular dysfunction in various conditions, such as diabetes mellitus, hypertension, hyperparathyroidism, and chronic kidney disease (CKD). In particular, chronic renal failure has been referred to as a state of cell calcium toxicity. The aim of this study was to investigate the status of $[Ca^{2+}]_i$ and intracellular calcium reserves in peripheral blood mononuclear cells (PBMCs) of CKD patients, and to determine the effect of vitamin D3 (cholecalciferol) supplementation on these parameters.
Methods: The study involved 57 CKD patients (stages 2-3 K/DOQI) and 70 healthy volunteers. All patients were randomized to cholecalciferol treatment with 5000 IU/week (27 patients) or 20000 IU/week (30 patients) for 12 months. PBMCs were separated by Ficoll density centrifugation and $[Ca^{2+}]_i$ was determined by spectrofluorometry using Fluo-3 AM fluorescent dye. Intracellular calcium reserves were emptied using thapsigargin (Tg), a specific inhibitor of endoplasmic reticulum Ca^{2+}-ATPase. 2-Aminoethyldiphenyl borate (2APB) was used to examine the capacitative calcium entry. All experiments were carried out at 37°C. Results are expressed as medians (95% CI).
Results: $[Ca^{2+}]_i$ of CKD patients was substantially higher in comparison with healthy subjects: 124 (118-126) nmol/l vs 102 (98-103) nmol/l, p<0.001. The calcium concentration in Tg-sensitive stores was also significantly increased in CKD patients [186 (173-240) nmol/l vs 118 (113-137) nmol/l, p<0.01]. A 12-months vitamin D3 supplementation with both doses caused a significant decrease in $[Ca^{2+}]_i$ (5000 IU/week, 123 vs 106 nmol/l, p<0.001; 20000 IU/week 125 vs 107 nmol/l, p< 0.001; a difference between the doses not significant). No significant changes in intracellular calcium reserves were found in CKD patients after vitamin D3 supplementation (5000 IU/week 185 vs 158 nmol/l, NS; 20000 IU/week 168 vs 194 nmol/l, NS). The intracellular calcium status was not affected by the capacitative calcium entry (81 vs 64 nmol/l, NS).
Conclusions: Our results demonstrate that 1) $[Ca^{2+}]_i$ was significantly increased already in early stages of CKD; 2) after vitamin D3 supplementation, the elevated $[Ca^{2+}]_i$ in CKD patients returned to values comparable with those in healthy subjects, indicating a favourable effect even of a nutritional cholecalciferol dose; 3) the effect of vitamin D3 on the intracellular calcium status was not dose dependent.
This work was supported by Slovak Research and Development Agency under the contract No. APVT-21-033002

MP095 SUSTAINED REMISSION OF PROTEINURIA PRESERVES RENAL FUNCTION IN ALL HISTOLOGICAL PATTERNS OF KIDNEY DISEASE

Giacomina Loriga, Daniela Mannoni, Rossana Faedda, Giovanni Soro, Andrea Ercole Satta. *Department of Internal Medicine, University of Sassari, Sassari, Sardinia, Italy*

Introduction and Aims: Proteinuria is a modifiable risk factor for progression of kidney disease. In chronic proteinuric patients treatment should be target to obtain a total remission of proteinuria (< 0.5 g/24h), but the extent in which this goal is achieved in the different histological patterns of kidney disease and in what degree proteinuria remission influences the renal outcome in clinical practice, has not been well described. Moreover the presence of diabetes may influence renal outcome, as than the response to antiproteinuric treatment.
Methods: We followed for two years sixty proteinuric patients, 11 of which whit diabetes, with a mean basal proteinuria of 1.4±1.8 g/24h. Among the 60 patients, 41 have a histological diagnosis of kidney disease: 26 of which with primary glomerulonephritis (14 IgA Nephropathy), 8 with glomerulonephritis secondary to systemic lupus eritematosus, 4 with diabetic nephropathy, 3 with interstitial nephritis.
Results: During follow-up only 50% of subjects reaching total remission of proteinuria and glomerular filtration rate (GFR) declined at -2.9±8.66 ml/min/year overall. Among the 30 patients with < 0.5 g/24h of sustained proteinuria, the rate of decline was -1.2±9.46 ml/min/year, almost 3-fold slower than the mean rate and near to physiological decline of renal function. The rate of decline increased with the amount of proteinuria, such that patients who achieved only a partial remission (n = 15, proteinuria > 0.5 and < 1 g/24h) showing a rate of GFR decline slightly higher than patients with total remission (-1.37±4.64 ml/min/year). Contrarily in those with sustained proteinuria were ≥ 1 g/24h (n = 15) the rate

of decline was -7.7±8.12 ml/min/year, about 7-fold faster than those with total remission. Histological patterns and presence of diabetes were equally distributed in the tree subgroups, suggesting a relatively small contribute of histological pattern in renal outcome, with the exception of IgA Nephropathy in which the rate of GFR decline was almost twofold of mean rate (-4.6±8.79 ml/min/year), despite the same percentage of proteinuria remission.

Conclusions: Data underscore the importance of achieved therapeutic target in preserve renal function. Also suggests that the histological diagnosis should advise in management of patients with worse renal prognosis.

MP096 191 CASES OF ACUTE PYELONEPHRITIS (APN): MONOCENTRIC CLINICAL EXPERIENCE

Cristiana Rollino[1], Giulietta Beltrame[1], Michela Ferro[1], Giacomo Quattrocchio[1], Manuela Sandrone[2], Francesco Quarello[1]. *[1]Nephrology, S. G. Bosco Hospital, Turin, Italy; [2]Radiology, S. G. Bosco Hospital, Turin, Italy*

Introduction and Aims: APN is a frequent parthologic condition: we observed 42 cases of APN both 2005 and in 2006 (8.6% and 7.2% of hospitalized patients respectively).

Methods: We created a file on which we recorded data of patients hospitalized in our department from January 1999 to October 2005 (191 patients -pts-,172 women and 19 men, mean age 38.1±18.5 years, (16-82 years).

Results: Clinical characteristics were: right/left kidney involvement 1.4; bilateral cases 24 (12.5%); renal transplantation 7; body temperature 39±0.68°C; leukocytes 15353±6626/mm^3; duration of leukocytosis 7.9±20.2 days; pyuria (as defined by WBC>10/hmf) 107/185 (57.8%); C Reactive Protein (CRP) 12.5±5.9 mg/dl.

Predisposing factors have been found in 58 pts (30,3%).

Urine culture was positive in 41/175 cases (23.4%) (E. coli 37 pts, Klebsiella pneumoniae 2, S. aureus 1, Enteroccocchi 1); blood cultures in 28/137 pts (20.4%) (E. coli 24, Acinetobacter 1, Proteus 1, S. saprophyticus 1, S hominis 1). Concordance between blood and urine cultures was 76%.

Ultrasound sonography was performed in 181/191 pt (94.7%): it was normal in 113 pt (62.4%), suggestive for APN in 68 pts (37.5%). CT was performed in 152/191 pts (79.5%): normal in 25 pts (16.4%) and confirming APN in 127 (83.5%). Concordance between CT and echography was 46%. In 38 cases NMR was done: normal in 12 pts (31.5%) and suggestive for APN in 26 (68.4%). Among pts with positive CT or NMR, urine culture was positive in 26 (20.4%). Thirty-four out of 152 pts (22.3%) submitted to CT presented a renal abscess. Only 6% of these abscesses was suspected at ultrasound examination. Pts with and without abscesses did not differ as regards elevation (39.1°C vs 39.1°C) and duration of fever (6.7 vs 6.8 days), entity (17.2 vs 14.9×10^3/μl) and duration of leukocytosis (4.9 vs 4.9 days), pyuria (57.5% vs 55.3%), CRP (10.9 vs 13.1 mg/dl), predisposing factors.

Conclusions: In conclusion, CT has low concordance with ultrasound sonography, which has low sensitivity in detecting abscesses. Evolution into an abscess is frequent and clinically unsuspectable. Hence, CT or NMR performance is necessary for precise diagnosis and appropriate treatment. This is strengthened by the fact that urine cultures are not always positive in APN pts because of different reasons (previous antibiotic treatment, bacteria not detected by routine tests -Ureaplasma urealyticum, Mycoplasma-, laboratory cut-off for positive cultures).

MP097 IMPACT OF CHRONIC KIDNEY DISEASE AND CONTRAST-INDUCED NEPHROPATHY ON LONG-TERM PROGNOSTIC AFTER CORONARY ARTERY ANGIOGRAPHY

Tomonori Kimura, Yoshitsugu Obi, Kazuhiro Sato, Terumasa Hayashi. *Nephrology, Rinku General Medical Center, Izumisano Municipal Hospital, Izumisano, Osaka, Japan*

Introduction and Aims: The incidence and prognostic implications of chronic kidney disease (CKD) and contrast-induced nephropathy (CIN) are unknown in patients undergoing coronary artery angiography (CAG).

Methods: Clinical and outcome data on 616 patients undergoing CAG and/or percutaneous coronary intervention (PCI) in 2004 were retrospectively collected. Patients undergoing dialysis therapy were excluded. CIN was defined as a relative rise in Cre ≥ 25%, or as an absolute increase ≥ 0.5mg/dL. Estimated glomerular filtration ratios (eGFR) was calculated and adjusted by Japanese coefficient.

Results: 244 patients (39.6%) showed CKD with their eGFR under 50mL/min. CIN occurred in 60 (9.7%) patients, and 25 patients of them (41.7%) were CKD. The cumulative two-year survival of patients with CKD was 64.3% for those who had CIN and 90.9% for those who did not have CIN ($p < 0.001$), and in patients without CKD there were no significant difference for those with and without CIN (96.5% and 96.5%, $p = 0.27$). Cox regression analysis identified CIN (odds ratio [OR], 2.58; 95% CI, 1.25 to 5.29), CKD (OR, 2.03; 95% CI, 1.10 to 3.77) and age (OR, 1.06; 95% CI, 1.02 to 1.10) as the independent risk factors of mortality.

Conclusions: CKD combined with CIN is associated with increased adverse outcomes after CAG. More attention and possible prophylactic means should be paid in the use of contrast medium in CKD patients.

MP098 IS THERE ANY ASSOCIATION BETWEEN SPINA BIFIDA OCCULTA AND PRIMARY VESICOURETERAL REFLUX IN CHILDREN

Seyed Taher Esfahani[1], Mehrzad Mehdizadeh[2]. *[1]Department of Pediatric Nephrology, Tehran University of Medical Sciences, Tehran, Iran; [2]Department of Radiology, Tehran University of Medical Sciences, Tehran, Iran*

Introduction and Aims: Spina bifida occulta (SBO) is a congenital disorder of incomplete closure of the spinal arch at 1 or more levels. The association of spina bifida occulta and urodynamic abnormalities of bladder and urethra is reported. Also some studies have shown higher prevalence of voiding dysfunction in children with vesicoureteral reflux (VUR). The aim of this study was to evaluate the association of SBO and primary vesicoureteral reflux in children.

Methods: 660 children with the first attach of febrile urinary tract infection underwent a standard voiding cystourethrography (VCUG) to detect reflux and other anomalies of lower urinary tract and vertebral column. Reflux grading was done according to the international reflux grading system. We compared the prevalence of SBO with the prevalence of VUR. For statistcal analysis SPSS13 software and Chi-square tests *were used.*

Results: The age of the children was between 1-14 years (mean 3.5±3.31). 253 were girls and 407 were boys. Of the 660 children, 197 (29.8%) had VUR and 463 (70.2%) did not. Of the 660 children, 156 (23.6%) had SBO and 504 (76.4%) did not. The sites of SBO were S1=89 (13.5%), L5=7 (1.1%), L5-S1=60 (9.1%). Of the 156 children who had SBO, 50 (32.1%) had VUR. Of the 504 Children who had not SBO, 147 (29.2%) had VUR. Chi-square test showed that there is no significant correlation between the presence of spina bifida occulta and VUR (p-value =0.473).

Conclusions: Presence of spina bifida occulta in children with primary VUR is probably a coincidental finding and its true significance in children with primary VUR is not established.

MP099 NICOTINE USE INCREASES CYSTATIN C PRODUCTION RATE AND NON-RENAL CLEARANCE

Per Sjöström[1], Martin Tidman[1], Ian Jones[2]. *[1]Department of Medicine, Örebro University Hospital, Örebro, Sweden; [2]Department of Clinical Chemistry, Örebro University Hospital, Örebro, Sweden*

Introduction and Aims: We have found that nicotine use significantly increases serum concentration of cystatin C (s-Cys) in HD patients with no residual renal function from 6.7±0.8 to 7.5±0.9 mg/L (P = 0,0008). This means that nicotine reduces the non-renal clearance (CL_{nr}) or increases the production rate of cystatin C (Cys_{pr}) as the renal clearance is zero in these patients. The aim of this study is to determine the effect of nicotine use upon Cys_{pr} and CL_{nr} in patients with a wide range of GFR and ascertain whether or not nicotine use necessitates a modification of our Cys C-eGFR formula.

Methods: S-Cys was measured in 352 patients referred to our laboratory for GFR-determination by plasma clearance of iohexol (CL-ioh). Nicotine metabolites in serum were used to identify nicotine users.

All patients			Age	B height	B weight	CL-ioh	s-Cys
Women	130	Mean	57.9	172.0	80.7	45.4	2.0
Men	122	SD	15.0	18.2	18.2	28.2	1.1
Nicotine users							
Women	28	Mean	55.0	172.9	79.8	49.5	1.9
Men	59	SD	13.4	9.4	15.8	28.5	1.0
Nicotine non-user							
Women	102	Mean	58.9	171.7	81.0	44.0	2.1
Men	163	SD	15.4	10.0	19.0	28.0	1.1

Results: see table.
Based upon eGFR = Cys_{pr}/s-Cys – CL_{nr} and regression analysis we found the following formulae:
All patients: eGFR = 92.2/S.cys - 13.8
Nicotine non-users: eGFR = 89.3/S.cys - 12.6
Nicotine users: eGFR = 100.4/S-cys - 17.3
Conclusions: The constants of the formulae show, that both Cys_{pr} and CL_{nr} increase with nicotine use, which counteract each other's effect on eGFR. The eGFR values calculated with the nicotine user or non-user formulae in an s-Cys interval from 1 to 5 mg/L will not differ more than 5 ml/min/1.73 m^2 from those calculated with the eGFR formula derived from all patients. The formulae give the same eGFR = 23 ml/min/1.73 m^2 at S-Cys = 2.5 mg/L. Thus, the same eGFR formula can be used for nicotine users and non-users.

MP100 PROTEOMIC ANALYSIS OF A PODOCYTE VESICLES-ENRICHED FRACTION FROM HUMAN NORMAL AND PATHOLOGICAL URINES

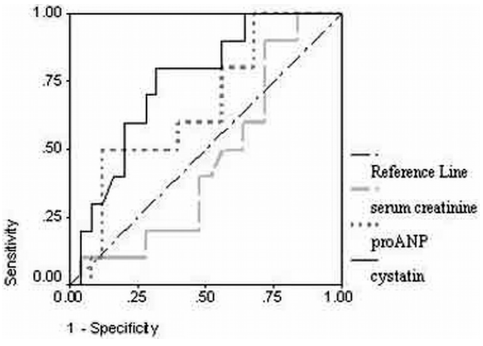
Pierre Lescuyer[1], Agnes Pernin[1], Alexandre Hainard[1], Jennifer A. Burgess[1], Jurg A. Schifferli[2], Denis F. Hochstrasser[1], Solange Moll[1].
[1]*Biomedical Proteomics Research Group, Department of Genetic and Laboratory Medicine, University Hospital, Geneva, Geneva, Switzerland;* [2]*Laboratory of Immunonephrology, University Hospital, Basel, Basel, Switzerland*

Introduction and Aims: Podocytes are known to release vesicles into urine in physiological conditions. This vesiculation process seems to be increased in pathological conditions such as glomerulopathies. Podocyte vesicles-enriched fractions of urine were therefore the starting material for proteomic analysis and identification of potential biomarkers of glomerular diseases.
Methods: We prepared a podocyte vesicles-enriched fraction from normal (19 healthy donors) and pathological (10 patients with biopsy-proven renal diseases) urine samples using an immunoadsorption method based on the specific binding to complement receptor 1 (CR-1), a surface marker of podocyte vesicles.
Results: We demonstrated the presence of vesicles on anti-CR1-coated beads using electron microscopy, and detected a 13-20 fold increase of podocalyxin, a podocyte specific marker, in podocyte vesicles-enriched fractions using Western blot and densitometry. We identified 76 unique proteins using SDS-PAGE and LC-MS/MS techniques. Several were previously described as potential markers of glomerulopathies. Interestingly, one protein, the serum paraoxonase/arylesterase 1 (PON-1), was newly identified in human urine. We confirmed the presence of PON-1 protein in normal human urines (Western blot), and demonstrated both PON-1 protein and mRNA expression in the normal human kidney (immunohistochemistry and RT-PCR).
Conclusions: These results suggest the potential benefit of enriching urines in podocyte vesicles for the discovery of kidney disease biomarkers.

MP101 CYSTATIN C AND PROATRIAL NATRIURETIC PEPTIDE (1-98) AS MARKERS OF RENAL FUNCTION IN ACUTE RENAL FAILURE

Saeed Abdelwhab[1], Samah Elshinawy[2]. [1]*Nephrology, Faculty of Medicine Ain Shams University, Cairo, Egypt;* [2]*Clinical Pathology, Faculty of Medicine Menofiyah University, Cairo, Egypt*

Introduction and Aims: Acute renal failure (ARF) is associated with high mortality. The serum concentration of cystatin C and proatrial natriuretic peptide have recently been proposed as better indicators of glomerular filtration rate (GFR) than plasma creatinine. Little is known about these markers in acute renal failure. We assessed serum cystatin C and proatrial natriuretic peptide as markers of renal function in acute renal failure (ARF) and its prognostic value in ARF patients
Methods: 35 patients with acute renal failure (group one), and 35 healthy control subjects (group two).For all complete history and full clinical examination, routine biochemical tests, Serum creatinine, BUN daily, Plasma cystatin c {using a particle-enhanced immunoassay (PET)} and proatrialnatriuretic peptide (1-98) {using radioimmunoassay} repeated every other day. Multiple regression analysis was performed to test independent predictors of replacement therapy and mortality. The positive predictive value for ARF and mortality was calculated by ROC analysis.
Results: Comparing group one and control group shows significant difference as regard serum cystatin ($p < 0.05$), proatrial natriuretic peptide ($p < 0.05$), serum albumin ($p < 0.05$), serum creatinine ($p < 0.05$).ROC curve analysis for sensitivity of different marker for early detection of renal impairment (GFR <80 mg/ml/min) shows area under the curve 0.99 for cystatin, 0.98 for serum creatinine and 0.97 for proANP there is no statistically significant differences between different makers. Linear regression study for renal replacement therapy shows significant correlation with serum cystatin ($t = 3.5$, $p = 0.002$) but no correlation with serum creatinine ($t = 1.9$, $p = 0.6$) or pro ANP ($t = 0.28$, $p = 0.78$).
ROC curve study for estimation of ability of different variable to predict the need for replacement therapy shows the greatest area under the curve for cystatin (= 0.750), followed by proANP (= 0.656, 95%), then serum creatinine (= 0.546).
Linear regression study for mortality shows only pro ANP is significant predictor for mortality ($t = 2.1$, $p = 0.044$).



Conclusions: Cystatin is similar to serum creatinine in early detection of acute renal failure.
Cystatin C was superior to serum creatinine, BUN, pro ANP, and GFR in differentiating acute renal failure patients who subsequently required RRT from those who did not. Neither serum creatinine nor cystatin c can predict mortality in patients with acute renal failure and only proANP gives significant predictive value for mortality in acute renal failure. These findings can help in early intervention for those patients at risk to develop complications or in need for replacement therapy.

MP102 PREVALENCE OF CHRONIC KIDNEY DISEASE IN PRIMARY CARE PATIENTS FROM A SPANISH HEALTH AREA

Pedro J. Labrador[1], Montaña Jiménez[2], Teresa Mengotti[2], Jorge Labrador[1], Flor Vicente[2], Emilio Fuentes[2], Javier Martín-Oncina[2].
[1]*Nephrology, Virgen del Puerto Hospital, Plasencia, Caceres, Spain;* [2]*Biochemical Lab., Virgen del Puerto Hospital, Plasencia, Caceres, Spain*

Introduction and Aims: Chronic kidney disease (CKD) is becoming a public health burden. Early detection of renal dysfunction is critical to its clinical management. Many factors affect serum creatinine concentration so creatinine-based equations are recommended to estimate glomerular filtration rate (GFR). The aim of this study was to investigate the prevalence of CKD in patients attended in Primary Care of a Spanish public health area.
Methods: This is a ten months descriptive study. The GFR was estimated using the MDRD-4 equation in all Primary Care patients over 18 years

living in our reference area, in who serum creatinine concentration was asking for. Kidney function was classified by the NFK-K/DOQI stages. We also examined cholesterol levels and presence of hyperglycaemia.

Results: GFR was estimated in 27.742 analyses from 23.574 patients attending Primary Care centers (27.8% of our reference population). When a single patient had two or more analyses, the lower serum creatinine was selected for the study.

A GFR <60mL/min/1.73m^2 was present in 2.110 patients (8.95%), 67.9% women. These patients age 27 to 107 years (mean 77±9.9), serum creatinine was 1.26±0.43 mg/dL and GFR 48.5±9.5 mL/min/1.73m^2. According to K/DOQI stages, 8.48% stage 3, 0.43% stage 4, and 0.04% stage 5. Glycaemia >126 mg/dL was found in 16.5% and between 102 to 125 mg/dL in 26.1%. An LDL-cholesterol level >100 mg/dL was present in 57.9%.

The prevalence of CKD according to sex and age groups is shown in figure 1.

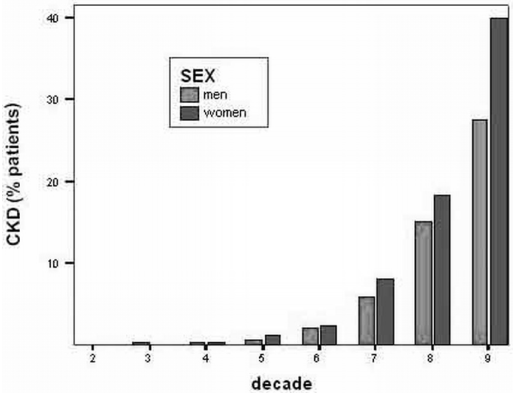


Figure 1. Prevalence of CKD by sex and age (decades of life groups)

Conclusions: This study show the high prevalence of patients with GFR <60mL/min/1.73m^2 in Primary Care patients, mostly women. And the substantial prevalence of impairment glycaemic metabolism and hypercholesterolemia among these patients. Prevalence of CKD increases with age in an exponential form.

MP103 EVALUATION OF INTRARENAL BLOOD FLOW IN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME (PAPS) NEPHROPATHY

T.V. Kirsanova, N.L. Koslovskaya, E.N. Platova, V.I. Sadovnikov, L.A. Belyaeva. *Moscow Sechenov Medical Academy, Moscow, Russian Federation*

Introduction and Aims: The nephropathy in PAPS corresponds to kidney disease associated with vaso-oclusive process in intrarenal vessels as a result of acute thromboses together with chronic arterial and arteriolar lesions leading to renal ischemia and progressive loss of renal function

The fine-needle biopsy is the only method that proves the diagnosis APSN. There are some contraindications as thrombocytopenia and intake of anticoagulants.

The aim of our study was to investigate the features of renal perfusion in PAPSN pts by ultrasound Doppler examination and to acess possibility of this non-invasive method in an identification and interpretation of small vessel occlusion considering this method to be alternative diagnostic method.

Methods: The study included 18 adult subjects (11 female,7 male) 21-53 years old (mean age 37 years): 10 PAPS pts according to Sapporo criteria (gr. 1) and 8 volunteers (gr. 2). Renal disorder in PAPS pts was defined as combinations of the following parametres: urine protein >0.2 g/24 h, GFR <80 ml/min, diastolic blood pressure >90 mmHg and serum creatinine > 1,4 mg/dl.

The intrarenal blood flow was investigated by Duplex Doppler ultrasound examination using ALOKA 1700. We measured systolic (Vps) and diastolic (Ved) velocities in segmental,interlobar and arcuate arteries at least at 5 pulse beats of arteries in each kidney The resistance parameter, RI, was determined as follows RI = (Vps - Ved)/Vps.

Results: All volunteers have the same waveforms, velocities and RI from signals of all pulse beats of each interlobar and arcuate arteries.

There was no any difference in velocities and RI in segmental and renalis arteries in pts of the 1t and 2d gr.

We noted an absence or decrease of a colour Doppler flow of an arcuate and more distal arterias in PAPSpts.

The blood flow parameters in gr.1 pts were lower than those in 2nd gr.pts in interlobar (0,29±0,06) and arcuate arteries (0,19±0,06) (p<0,05)

In all PAPSN patients the blood flow in distal renal vessels was irregular.

The RI in gr.1 varied in all pulse beats on interlobar and arcuate arteries from 0.48 to 0,59, in comparison with gr. 2, where RI and wave form were identical (see the table).

The intrarenal blood flow in interlobar and arcuate arteries

	Interlobar arteries		Arcuate arteries	
	RI max	RImin	RI max	RImin
Gr.1 (n=10)	0.58±0.035	0.5±0.033	0.56±0.024	0.48±0.02
Gr.2 (n=8)	0.59±0.04		0.58±0.04	

Conclusions: The absence or decrease of a colour Doppler flow of an arcuate and more distal arterial signal seems to be a marker of renal ischaemia. The cause of renal ischemia is more likely the thrombotic occlusion of intrarenal vessels.

The "patchy" decreasing of resistivity index (RI) in distal vessels suggests the presence of occlusive lesions as a result of thrombotic microangiopathy (TMA) due to arteriovenous bloodflow bypassing.

The doppler ultrasonography allows to detect the occlusion of distal small-caliber kidney vessels due to TMA and this method may be used as a non-ivasive method instead a biopsy.

MP104 INFLAMMATION, CARDIAC GEOMETRY AND FUNCTION IN THE PROGRESSION OF CHRONIC KIDNEY DISEASE (CKD)

Evangelia Dounousi[1], Aikaterini Papagianni[2], Konstantinos Pappas[1], Kyriakos Ioannou[3], Konstantinos Katopodis[1], Ioannis Tsouchnikas[3], Athanasios Kitsos[1], Kostas Siamopoulos[1], Dimitrios Tsakiris[3]. *[1]Dept. of Nephrology, University Hospital of Ioannina; [2]Dept. of Nephrology, "Hippokration" Hospital, Thessaloniki; [3]Dept. of Nephrology, General Hospital of Veria, Greece*

Introduction and Aims: In recent years CKD has been viewed as a chronic inflammatory state contributing to endothelial dysfunction in these patients who present with increased cardiovascular morbidity and mortality. There are few reports suggesting that the damaging effect of chronic inflammation on cardiac remodeling may start early in the course of CKD but the exact timing is not clear. The aim of this study was to investigate the association between markers of inflammation and endothelial dysfunction with echocardiography findings in patients with CKD stages 1 to 4.

Methods: In a cross-sectional study we assessed 216 steady patients from the out-patient clinics of two hospitals. Their mean age was 64.8 years old (range 25-88 years) and there were 113 males (52%). The most common primary renal diseases were hypertensive nephrosclerosis (16%), diabetes (14%), glomerulonephtitis (10%) and interstitial nephritis (11%). The distribution of the patients in CKD stages according to Cockcroft formula were, CKD 1: n=29 (14%) with a mean GFR 112±22 ml/min, CKD 2: n=59 (27%), mean GFR 76±8 ml/min, CKD 3: n=80 (37%), mean GFR 43±9 ml/min and CKD 4: n=48 (22%), mean GFR 24±4 ml/min. In these patients at their recruitment we assessed serum levels of CRP, plasma levels of VCAM-1, ICAM-1, IL-6, TNFα, fibrinogen, VEGF, PAI and vWF, and we carried out a 2-mode echocardiogram.

Results: VCAM-1, TNFα and fibrinogen increased significantly as CKD stages were advancing (ANOVA, p<0.001, p<0.02 and p<0.001 respectively), while levels of PAI showed a marked decrease during progression of CKD (p<0.001). CRP and IL-6 showed an increasing trend, which just failed to reach significance, but ICAM-1, VEGF and vWF did not show any significant changes. There was a significant positive association between CKD stages and LVmass/BSA, PW thickness, IVS and relative wall thickness (RWT) (ANOVA, p<0.001, 0.005, <0.02 and <0.02 respectively). In contrast, LVEDD, LVESD, EF, FS and E/A did not change significantly. There was a significant correlation between LVmass/BSA and levels of VCAM-1, TNFα and IL-6 (Spearman, ρ<0.01) and between CRP and

RWT, posterior wall thickness and intraventricular septum ($\rho<0.01$, $\rho<0.01$ and $\rho<0.05$ respectively).
Conclusions: It appears that certain markers of inflammation and endothelial dysfunction are altered early during the progression of CKD and they correlate significantly with cardiac remodeling and LV hypertrophy. These findings suggest that inflammation and endothelial dysfunction should be assessed during the early stages of CKD in order to minimize the cardiovascular burden in these patients.

MP105 *NIGELLA SATIVA* OIL FOR PREVENTION OF CHRONIC CYCLOSPORINE NEPHROTOXICITY: AN EXPERIMENTAL MODEL

Ebru Uz[1], Omer Bayrak[2], Efkan Uz[3], Arif Kaya[4], Reyhan Bayrak[5], Burak Uz[4], Faruk Turgut[1], Nuket Bavbek[1], Mehmet Kanbay[1].
[1]Nephrology, [2]Urology, Fatih University Medical School, Ankara, Turkey; [3]Medical Biology and Genetics, Suleyman Demirel University Medical School, Isparta, Turkey; [4]Internal Medicine, [5]Pathology, Fatih University Medical School, Ankara, Turkey

Introduction and Aims: Lack of efficacy for the prevention of long-term allograft failure may in part be due to the side effects of Cyclosporine.
The major purpose of the current study is to examine the possible protective effects of *Nigella Sativa (NS)* in prevention of chronic CsA-induced nephrotoxicity.
Methods: Twenty-four male Wistar albino rats were used for this study. Animals were divided in four groups: Control (n=6), NS (n=6), CsA (n=6), CsA plus NS (n=6). NS oil was administered since the first day, while CsA treatment was performed for the last 21 day. Control rats received sunflower oil orally. The left kidney was used for further enzymatic analysis (SOD, CAT, MDA, GSH-Px, NO), the right kidney was used for histological examination.
Results: Results of NS group were similar with control in the all parameters. There was no significant difference among the groups the SOD activities. CsA produced a decrease in renal CAT content compared with the control group and the NS group (p= 0,0001). Co-administration of NS and CsA could not abrogate the CsA-induced CAT decrease, compared with the CsA group. GSH-Px levels were decreased in CsA group compared with NS group (p= 0.008). The CsA plus NS supplemented rats, this enzyme activities were significantly higher than the CsA administered rats (p= 0.001). MDA, NO levels in the kidney tissue were increased by the CsA management and NS prevented these increments at a statistically significant level ($p<0.0001$).
Histological studies of rat kidney in the control and NS only groups showed a normal morphological appearance. CsA-treated rats showed the typical histopathological features of chronic CsA nephrotoxicity. In our semiquantitative scoring system, the arteriolopathy, striped interstitial fibrosis and tubular atrophy with focal inflammatory cell accumulation was higher in the CsA group than the control group, whereas this was markedly decreased with NS treatment compared with the CsA group ($p<0.05$).
Conclusions: We have demonstrated for the first time *in vivo* that NSO protects kidney, possibly against oxygen free radicals, preventing renal dysfunction and morphological abnormalities associated with chronic CsA administration.

MP106 SERUM ALBUMIN, FIBRINOGEN AND ALBUMINURIA AS MARKERS OF INFLAMMATION AND CARDIAC REMODELLING DURING CHRONIC KIDNEY DISEASE PROGRESSION

Kyriakos Ioannou[1], Evangelia Dounousi[2], Kostantinos Pappas[2], Apostolos Kelesidis[1], Ioannis Tsouchnikas[1], Konstantinos Katopodis[2], Vasilios Vargemezis[3], Konstantinos Siamopoulos[2], Dimitrios Tsakiris[1].
[1]Department of Nephrology, General Hospital of Veria, Veria, Greece; [2]Department of Nehprology, University of Ioannina, Ioannina, Greece; [3]Department of Nephrology, University of Thrace, Alexandroupolis, Greece

Introduction and Aims: Serum albumin has been considered as a marker of nutrition status and serum fibrinogen may serve as an inflammation marker. Serum albumin levels during chronic kidney disease (CKD) may decrease and serum fibrinogen levels may increase due to increased hepatic synthesis, probably as a respond to albumin loss and to chronic inflammatory state. The aim of this study was to investigate the relation among serum albumin, fibrinogen, albuminuria and CRP in the course of CKD and their correlation with left ventricular mass index (LVMI).
Methods: In a cross-sectional study we studied 221 steady patients with CKD stages 1 to 4 from the out-patient clinics of two hospitals. Patients at the entry of the study were screened for serum albumin, fibrinogen, CRP levels and albuminuria and correlated to LVMI estimated with a 2-mode echocardiogram.
Results: Albuminuria increased significantly as CKD progressed (p=0.004) and serum albumin levels correlated negatively with the degree of albuminuria (p=0.025). However, serum albumin levels did not decrease significantly during CKD progression and this may be due to an increase in albumin synthesis. In contrast, fibrinogen levels increased significantly as eGFR decreased (p=0.000), and albuminuria increased above the levels of microalbuminuria (p=0.017). A negative correlation was observed between serum albumin and fibrinogen levels (p=0.001), especially when albumin was reduced under 3.5g/dL. Both albumin and fibrinogen levels correlated negatively (p=0.000) and positively (p=0.000) with CRP levels respectively, confirming their role as inflammation markers during CKD. With regards to the relationship of these markers with LVMI, we observed a negative correlation between albumin levels and LVMI (p=0.005) while fibrinogen levels correlated positively (p=0.000). Furthermore, a positive correlation with LVMI was also noted when albuminuria exceeded the levels of microalbuminuria (p=0.018), suggesting that during microalbuminuric stage, cardiac remodelling may still be reversible.
Conclusions: During CKD progression although albuminuria increased serum albumin remained stable, while fibrinogen levels showed a negative correlation with decreasing eGFR. Both serum albumin and fibrinogen correlated with CRP levels suggesting that they may serve as markers of the CKD inflammatory state. Fibrinogen levels increased as CKD progressed and albuminuria increased. Serum fibrinogen levels and albuminuria correlated positively with LVMI, while serum albumin levels showed a negative correlation with LVMI. These findings suggest that cardiac remodeling may present soon during CKD progression and screening for albuminuria and simple markers such as serum albumin, fibrinogen and CRP may reflect early changes in cardiac function.

MP107 MITRAL REGURGITATION IN PATIENTS WITH CHRONIC HEART FAILURE IS ASSOCIATED WITH DECREASE OF KIDNEY FUNCTION

Alexander Shutov, Elena Kurzina, Valery Serov, Tatjana Ivashkina.
Department of Internal Medicine, Ulyanovsk State University, Ulyanovsk, Russian Federation

Introduction and Aims: The mitral regurgitation (MR) is a consequence of adverse left ventricular remodeling that occurs with a structurally normal valve and it is a marker of adverse prognosis. Mitral annular calcification and MR are common in coronary artery disease (CAD). Valvular and perivalvular involvement in end-stage renal disease is commonly manifested as mitral annular calcification and it is common association with mitral regurgitation. However, relationship between MR and kidney function in patients with chronic heart failure (CHF) without severe decrease of kidney function is unknown. The aim of this study was to examine the interaction between kidney function and MR in patients with CHF.
Methods: 340 patients with chronic heart failure (200 males, 140 females, mean age was 58.0±12.9 years) were studied. 44 (13%) patients had arterial hypertension, 112 (33%) - CAD and 184 (54%) had CAD and arterial hypertension. I class (NYHA) of CHF was in 112 (33%), II class - 177 (52%), III class - 34 (10%), IV class -17 (5%). A history of myocardial infarction was reported for 180 (53%) patients. Chronic kidney disease was defined concordantly NKF K/DOQI, 2002.
Results: The ejection fraction was 56.9±10.5%. Systolic dysfunction was detected in 90 (26%) patients. Mitral regurgitation was revealed in 221 (65%). Patients with more severe MR differed from patients with mild or no MR in that they were older ($p<0.001$), and more likely had previously myocardial infarction ($p<0.001$), and lower ejection fraction ($p<0.001$). Glomerular filtration rate (GFR) was 68.8±20.9 ml/min/1.73m^2 (19.2-149.7 ml/min/1.73m^2). GFR was under 60 ml/min/1.73m^2 in 114 (34%) patients.

There was positive correlation between severity of MR and NYHA class of CHF (r= 0.35;p<0.001). The structural changes of mitral valvular, including of mild valvular thickening, were revealed in 228 (67%) patients. There was a negative correlation between GFR and severity of MR (r=-0.43;p<0.001). Multiple regression analysis shows that severity of MR was independently associated with decrease of kidney function.
Conclusions: Mitral regurgitation is frequent among patients with chronic heart failure due to CAD and arterial hypertension. The disturbances of structure of mitral valve more commonly detected in patients with CHF with GFR under 60 ml/min/1,73m^2. Mitral regurgitation is associated with decreased kidney function in patients with chronic heart failure.

MP108 SERUM URATE DISTRIBUTION IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE (CKD): AN OBSERVATIONAL STUDY

Kathryn Bostock, Kate Harris, Gopalakrishnan Venkat-Raman. *Wessex Renal & Transplant Service, Queen Alexandra Hospital, Portsmouth, Hampshire, United Kingdom*

Introduction and Aims: Hyperuricaemia has been linked to hypertension and cardiovascular disease, but its role in progression of renal impairment is unknown. It is thought to be just a marker of renal dysfunction, though it may possibly play a pathophysiological role. The aim of this study was to investigate the distribution of serum urate (SU) in relation to the different stages of CKD (including transplants) with a view to examining the relationship between SU and serum creatinine (SCr).
Methods: We searched our renal database (Proton) for random SU concentrations for all live patients (May 2007), grouped according to CKD stages (as defined by KDOQI) in the pre-dialysis population, renal transplant recipients (Tx), peritoneal dialysis (PD) and haemodialysis (HD) patients. The relationship between SU and SCr/glomerular filtration rate (GFR; MDRD equation) was assessed in CKD stages 1-5 by plotting the correlation coefficient. Analysis of variance (ANOVA) was employed to detect SU differences between the stages of CKD, between stage 5 CKD and the 2 dialysis modes. 2-way ANOVA was employed to detect differences between CKD and Tx (by stage).
Results: The raw data are presented in the Table. In CKD subjects, when stratified by stage, ANOVA revealed a highly significant direct correlation between SU and SCr. However,the correlation was strongest in stages 1-2, and was not significant between stages 3,4 and 5.SU did not differ significantly between CKD stage 5, HD and PD, though HD showed a trend towards lower SU. SU was significantly higher in Tx group, when compared to CKD 1-5 by stages, though the difference was much more pronounced at stages 1-2 than 3-5.

Serum urate in different stages of renal failure

Stages	n	GFR (ml/min)	SCr (mcmol/L)	SU (mmol/L)
CKD 1-2	88	82.3	119	0.36
CKD 3	138	46.7	147	0.42
CKD 4	141	23.5	249	0.45
CKD 5	75	10.6	441	0.43
PD	39	5.9	568	0.41
HD	137	6.3	594	0.39
Tx	414	41.5	250	0.44

Conclusions: This study shows that SU rises in the course of progressive renal failure, but this is largely confined to the earlier stages, raising interesting possibilities about the excretion of urate in advanced renal failure. These results do not support a pathopathophysiological role for SU in progression of CKD. Dialysis treatment on the whole does not seem to affect SU, though there was a trend for lower SU on HD, which might reflect better clearance on HD compared to PD. Transplantation is associated with higher SU, compared to CKD of corresponding stages, again most obvious in the earlier stages. This is most likely related to the use of ciclosporine as the major immunosuppressive agent in this population.

MP109 COMPARISON BETWEEN CREATININE CLEARANCE, CYSTATIN C, BETA2 MICROGLOBULIN AND TATI AS RENAL FUNCTION MARKERS IN PATIENTS WITH PROTEINURIA

Gianfranco Tramonti[1], Carmela Annichiarico[2], Paolo Lorusso[1], Ilaria Cipollini[1], Giuliano Mariani[2], Giuliano Barsotti[1]. [1]*Medicina Interna - Nefrologia, Università di Pisa, Pisa, Italy;* [2]*Oncologia - Medicina Nucleare, Università di Pisa, Pisa, Italy*

Introduction and Aims: Patients with proteinuria are at risk to develop renal failure. In order to assess the progression of renal damage, accurate evaluation of renal function is important in these patients. Creatinine clearance (CrCl) is usually used as marker of GFR. More recently it has been reported that CrCl as well as eGFR from MDRD equation overestimate GFR in nephrotic syndrome. Cystatin C has been proposed as the best available test of renal function. TATI is another LMW protein (6200 d) which resulted a promising marker of renal function. The aim of this research was the evaluation of cystatin C, beta2 microglobulin and TATI, compared to CrCl, as biomarkers of renal function in patients with different degrees of proteinuria and various stages of renal insufficiency.
Methods: The studied patients were 53 (M 23, F 30, age 53±15). GFR was measured by the bladder cumulative method using ^{99m}Tc-DTPA. Simultaneously with GFR measurement of blood levels of cystatin C (N Latex Cystatin C, Behring), Beta2 microglobulin (Immunotech) and TATI (Orion Diagnostica) were performed. CrCl and proteinuria were determined by 24 h urine collection.
Results: The results are expressed as ratio with GFR of CrCl and reciprocals of cystatin C (1/cyst), beta2 microglobulin (1/Beta2) and TATI (1/TATI). Patients were divided in two groups with 24 h proteinuria >2 g/die (n= 10, m=4.04) and <2 g/die (n= 43, m=0.78), respectively. The ratio CrCl/GFR resulted 1.47 in patients with proteinuria >2 g/die and 1.45 in those with proteinuria <2 g/die. In the same patients the ratio1/cyst/GFR was 0.017 and 0.018, 1/Beta2/GFR 0.009 and 0.012 and 1/TATI/GFR resulted 0.017 and 0.014, respectively.
Conclusions: These results confirm the GFR overestimation of CrCl in patients with proteinuria. Also TATI seems to overestimate GFR while cystatin C and beta2 microglobulin underestimate GFR in proteinuric patients. Thus, a different renal handling of creatinine and of LMW proteins in patients with proteinuria does occur. As consequence in patients with heavy proteinuria the progression of renal damage should be assessed by direct radioisotopic methods.

MP110 ★ SIMPLE CYSTATIN C FORMULA COMPARED TO SERUM CREATININE-BASED EQUATIONS FOR ESTIMATION OF GLOMERULAR FILTRATION RATE IN PATIENTS WITH DIABETES MELLITUS TYPE 2 AND CHRONIC KIDNEY DISEASE

Radovan Hojs, Sebastjan Bevc, Robert Ekart, Maksimiljan Gorenjak, Ludvik Puklavec. *Department of Nephrology, Clinic of Internal Medicine, University Medical Center Maribor, Maribor, Slovenia; Department of Nephrology, Clinic of Internal Medicine, University Medical Center Maribor, Maribor, Slovenia; Department of Nephrology, Clinic of Internal Medicine, University Medical Center Maribor, Maribor, Slovenia; Department of Clinical Chemistry, University Medical Center Maribor, Maribor, Slovenia; Department of Nuclear Medicine, Clinic of Internal Medicine, University Medical Center Maribor, Maribor, Slovenia*

Introduction and Aims: Estimation of the glomerular filtration rate (GFR) is essential for the evaluation of patients with chronic kidney disease (CKD). In clinical practice serum creatinine-based equations (cretinine formulas) like the Cockcroft-Gault (C&G) and Modification of diet in renal disease (MDRD) formulas are most widely used tests of renal function. Recently, serum cystatin C-based equations (cystatin formulas) were proposed as markers for estimation of GFR. Present study compare simple cystatin formula (100/cystatin C) and creatinine formulas in patients with diabetes mellitus type 2 (DM2) and CKD.
Methods: In this study, 113 adult patients with DM2 and CKD were enrolled. In each patient, serum creatinine was determined and GFR was calculated using the C&G and MDRD formulas. The serum cystatin C was determined by an immunonephelometric method and GFR has been

estimated with simple cystatin formula. GFR was also measured using ^{51}CrEDTA clearance, and the correlation, accuracy, bias and precision of different equations were determined. Ability to correctly estimate patient's GFR with different equations compared to ^{51}CrEDTA clearance below and above 60 ml/min/1.73m^2 was analyzed.

Results: The mean ^{51}CrEDTA clearance was 47 ml/min/1.73m^2; mean serum creatinine 240 mmol/l; mean serum cystatin C 2.53 mg/l. Statistically significant correlation between ^{51}CrEDTA clearance with C&G (r=0.852) and MDRD (r=0.921) formulas and simple cystatin formula (r=0.915) was found. The Receiver Operating Characteristic (ROC) curve analysis (cut-off for GFR 60 ml/min/1.73m^2) showed that simple cystatin formula had a higher diagnostic accuracy than C&G formula (P<0.04). The equations showed different bias. The C&G formula and simple cystatin formula overestimated measured GFR (15.4 and 37.4 ml/min/1.73m^2) opposite to MDRD formula where measured GFR was underestimated (-14 ml/min/1.73m^2). All equations lacked precision. It was 40.6 and 29.2 ml/min/1.73m^2 for C&G and MDRD formulas and 31.2 ml/min/1.73m^2 for simple cystatin formula. The SD was smaller for MDRD formula (P<0.003) and simple cystatin formula (P<0.001) compared to C&G formula. Analysis of ability to correctly predict patient's GFR showed that simple cystatin formula had highest prediction, but the differences were not significant (100/cystatin C 92% vs. MDRD formula 86.7% vs. C&G formula 85.8%).

Conclusions: Our results indicate that simple cystatin formula is reliable marker of GFR with high diagnostic accuracy and ability to predict GFR below and above 60/ml/min/1.73m^2 in patients with DM2 and CKD.

MP111 INCREASED PARITY AND GLOMERULAR FILTRATION RATE: IS THERE ANY ASSOCIATION?

Ilknur Inegol Gumus[1], Ebru Uz[2], Ayse Kargili[3], Nuket Bavbek Ruzgaresen[2], Burcu Yanik[4], Faruk Hilmi Turgut[2], Ali Akcay[2], Nilgun Turhan[1]. *[1]Obstetrics and Gynecology, Fatih University Medical School, Ankara, Turkey; [2]Nephrology, Fatih University Medical School, Ankara, Turkey; [3]Internal Medicine, Fatih University Medical School, Ankara, Turkey; [4]Physical Medicine and Rehabilitation, Fatih University Medical School, Ankara, Turkey*

Introduction and Aims: Renal size and weight increase during pregnancy due to an increase in renal vascular and interstitial volume. Glomerular filtration rate (GFR) begins to increase by as early as 6 weeks' gestation, with a peak of 50% over nonpregnant values by the end of the first trimester. Although there is limited data on the measurement of GFR after 36 weeks' gestation, GFR does not appear to decrease at term. The pregnancy-associated rise in GFR results in decreased serum creatinine and urea concentrations in pregnancy. There is no previously reported study about long-term effects of parity on renal functions. So we aimed to determine the effect of increased parity on glomerular filtration rate.

Methods: Five hundred women mean aged 52,57±8,08 years, without a history of hypertension, diabetes mellitus, renal disease or complicated pregnancy were involved in the study. They were divided into three groups. Group 1; women with no or 1 parity (n=75), Group 2; women with 2 or 3 parities (n=332), Group 3; women with 4 or more parities (n=91). Laboratory parameters including GFR and demographical data were compared between the 3 groups. GFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula.

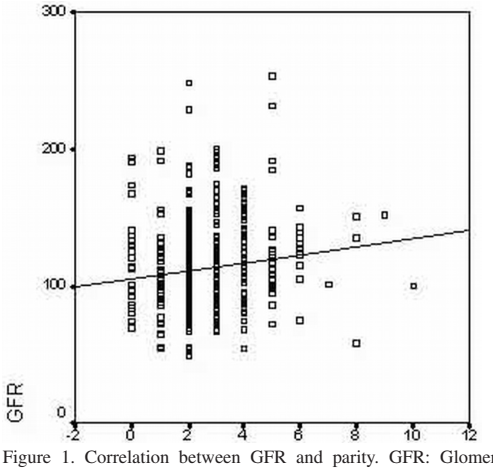


Figure 1. Correlation between GFR and parity. GFR: Glomerular Filtration Rate (r=0.0132, p=0.004)

Results: Mean ages were similar in all groups. Although blood urea nitrogen and creatinine were similar between the 3 groups, a statistically significant difference was found between the GFR values. Patients in group 3 had significantly higher GFR values compared to groups 1 and 2 (109,44±30,99, 110,76±30,22 and 121,92±34,73 mL/min/1.73 m^2 for groups 1,2 and 3 respectively) (p=0.008 for group 1 versus group 3; p=0.002 for group 1 versus group 3). Also there was a positive correlation between GFR levels and parity (r=0,132, p=0,004) (Figure 1).

Conclusions: It seems like that increased GFR in pregnancy does not return in post pregnancy period, and in the following years, especially in women with more parity.

MP112 INHIBITORY EFFECT OF RECEPTOR-ASSOCIATED PROTEIN ON MYELOMA LIGHT CHAIN INDUCED CYTOKINE RELEASE IN CULTURED HUMAN PROXIMAL TUBULAR CELLS

Sule Sengul[1], Sehsuvar Erturk[1], Vecihi Batuman[2]. *[1]Department of Nephrology, Ankara University School of Medicine, Ankara, Turkey; [2]Division of Nephrology, Tulane University School of Medicine, New Orleans, LA, USA*

Introduction and Aims: In proteinuric states increased inflammatory cytokine production through receptor-mediated endocytosis of filtered proteins by proximal tubule cells (PTCs) has been proposed as a major mechanism mediating tubulointerstitial fibrosis and progressive kidney disease. Myeloma light chains are endocytosed by the PTCs through the tandem endocytic receptors megalin/cubulin and targeted to degratative sites. Receptor associated protein (RAP) serves as a molecular chaperone/escort protein for megalin/cubilin to ensure transport of receptor-protein complex to degratative sites. In the present study, we studied the effects of different proteins on the production of inflammatory cytokines and the role of RAP in light chain induced inflammatory cytokine response in cultured human PTCs.

Methods: SV40 immortalized human PTCs were exposed to four different proteins (light chain, albumin, beta2-microglobulin and transferrin) for up to 24 h. Cytokines (interleukin (IL)-6 and 8) were determined by ELISA in the supernatants of PTCs. To test the effect of RAP on cytokine release and phosphorylation of MAPKs, cultured human PTCs were preincubated with recombinant RAP (1μM) for 1 hour and exposed to 25μM light chain for 4 h in the continous presence of RAP. Cytokines were measured in the supernatants by ELISA and phosphorylation of MAPKs were evaluated in the whole cell lysates by Western blotting.

Results: After 4-h exposure with 4 different proteins (light chain, albumin, transferrin and beta2-microglobulin), only myeloma light chain stimulated production of cytokines (IL-6 and 8, p<0.01) (Figure 1A,B). Coincubation with RAP significantly decreased cytokine responses (IL-6 and 8) by 25%percent (p<0.01) (Figure 2) and significantly inhibited phosphorylation of ERK1/2 and p38 pathways.

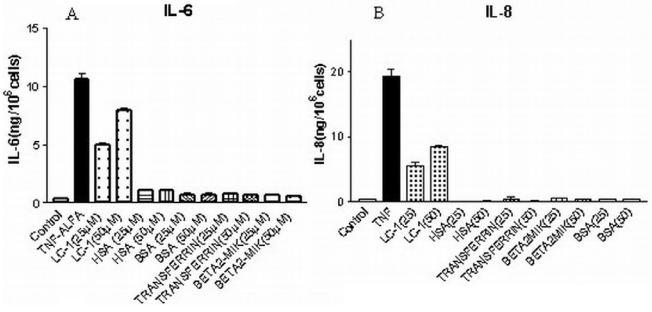


Figure 1A, B. Effect of four different proteins on IL-6 (panel A) and IL-8 (panel B) production.

Conclusions: Since RAP excess in the medium is known to inhibit receptor-mediated endocytosis, our results indicate that light chain endocytosis is essential for its cytokine effects, and blocking endocytosis protects

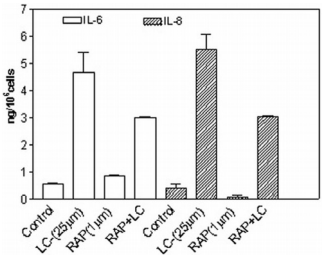


Figure 2. Inhibitory effect of RAP on LC-stimulated cytokine production.

cells from light chain induced cytotoxicity. This observation is consistent with our previous finding that blocking light chain endocytosis by either bafilomycin, or rendering medium hypertonic by sucrose, similarly resulted in inhbiting light chain induced cytokine responses. Maneuvers that inhibit light chain endocytosis may have therapeutic utility in preventing light chain cytotoxicity.

MP113 ★ FACTORS AFFECTING PROGRESSION OF ARTERIAL STIFFNESS IN CHRONIC KIDNEY DISEASE: AN OUT-PATIENTS BASED STUDY

Smeeta Sinha[1], Helen Eddington[1], Janet Hegarty[1], Beverley Lane[1], Robert Foley[2], Donal O'Donoghue[1], Rachel Middleton[1], Philip A. Kalra[1]. *[1]Deaprtment of Renal Medicine, Salford Royal Hospital Foundation NHS Trust, Salford, United Kingdom; [2]Chronic Disease Research Group and Department of Medicine, University of Minnesota, Minneapolis, USA*

Introduction and Aims: Patients with Chronic Kidney Disease (CKD) are known to have increased mortality from cardiovascular disease which cannot be attributed to traditional coronary risk factors alone. An increased vascular stiffness measurement is known to be a major contributing factor in dialysis patients. In this study we aimed to identify factors associated with the change in vascular stiffness measurements over 1 year in an out-patient based CKD population not on dialysis.
Methods: The Chronic Renal Insufficiency Standards Implementation Study (CRISIS) is a large prospective epidemiological study of patients with CKD stage 3-5. These patients are not yet on dialysis and are all managed in a clinic setting. The study commenced in 2002 but serial pulse wave measurements have been obtained since 2005. Phenotypic parameters including augmentation index (AI) have been collected annually. We have performed longitudinal analysis on 212 patients who have had 2 measurements of AI in order to evaluate the associations of progression of vascular stiffness.
Results: The mean age of the patients was 67±13 years, eGFR 32±14 ml/min, AI 28±10.2%, 35% were women, corrected calcium 2.26 mmol/l, phosphate 1.2 mmol/l, parathyroid hormone 88pg/ml and cholesterol 4.4 mmol/l and 14% were smokers. Deteriorating eGFR and increasing systolic blood pressure showed strong independent associations with increase in AI over the year. Baseline AI was found to be negatively associated with progression of AI (ie if severe vascular stiffness already present it was less likely to progress). Interestingly no statistical association was present between progression of AI and parathyroid hormone, phosphate, protein excretion, CRP or presence of diabetes.
Conclusions: To our knowledge this is the first longitudinal study of vascular stiffness in an unselected pre-dialysis CKD population. Our findings imply that in order to minimise progression of vascular stiffness in CKD attention should be focused upon optimally controlling systolic blood pressure and ameliorating progression of renal dysfunction.

MP114 FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ANEMIA IN STAGE 3 CHRONIC KIDNEY DISEASE. NADIR-3 STUDY. BASELINE DATA

J. Portolés, J.L. Gorriz, A. Martinez-Castelao, F. De Alvaro, F. García, V. Álvarez, J.M. Graña. *on Behalf of the NADIR-3 Study Group GEENDIAB, Sen, Spain*

Introduction and Aims: There is little information on the development of anemia in the early stages of kidney disease (CKD). Current clinical guidelines emphasize the importance of establishing an integrated program for CV risk reduction. However, we have few data on the degree of adherence to the guidelines in CKD 3.
The aim of this study was to analyze the development of renal anemia, its management and evolution, as well as associated factors, in a cohort of patients with stage 3 CKD (NKF/KDOQI™) without anemia, followed up in nephrology clinics. The secondary aims were to define the level of CV risk in these patients, such as proteinuria, arterial hypertension, LDL-cholesterol, malnutrition, smoking, and calcium-phosphorus, as well as establishing the differences between patients with diabetes mellitus (DM) and those without.
Methods: Prospective, multicenter (27 centers), epidemiological study with 2-year follow-up. Inclusion criteria: age (18-78 years), Cockcroft (30-59 mL/min) without anemia (EBPG-EDTA criteria) and informed consent. Consecutive, systematic sampling. Central website database with monitoring. Data at baseline, 6 months, and in the appearance of anemia with evolution on clinical analysis and treatment.
Results: 441 patients were included: age 63.7 years (range 22-78), 70.1% males. Etiology: glomerular 11.4%; interstitial 10.5%; vascular 29.4%; diabetes 17.3%; polycystic renal disease 7%. Comorbidity: 33.2% had diabetes (92.3% type 2) with glycoHb 6.2±1.6%; 68.7% dyslipidemia with LDL-cholesterol 110.6±33.3 mg/dL; and 93% had hypertension. The Charlson index was 3.4±2.1.
The baseline data were as follows: Cr 1.8±0.5 mg/dL; glomerular filtration rate (GFR) (Cockcroft) 42.9 mL/min; proteinuria 0.67±1 g/24 h; Hb 14.2±1.3 g/dL; iron 80.1±25.0 µg/dL; ferritin 131.7 ng/mL; TSI 30.2±30.4%. Seven percent of patients received oral iron supplements; 93% received antihypertensive drugs (52% ARB-II); 31% received antiplatelet drugs; and only 5% received vitamin D and binding agents with iPTH 96±63 pg/mL, calcium 9.6±0.5 mg/dL and phosphorus 3.5±0.6 mg/dL.
Diabetic patients showed a greater prevalence of prior CV events (48.2% vs 22.9%) and worse control of the majority modifiable CV risk factors: Smoking (14.0% vs 8.7%); Obesity (BMI> 30; 33.6% vs 25.3%), on target blood pressure (< 130/80 mmHg: 21.0% vs 28,1), daily proteinuria (0.8±1.1 vs 0.6±0.9 g/day). Diabetic patients present better lipid profile control (on-target: 60.1% vs 40.3%) and ACEI-IECAS use (85.3% vs 77.1).
Conclusions: The degree of risk factor control is greater than in other studies in the general population. Diabetic patients carried on higher CV risk. Knowledge of morbidity and mortality will help us to establish prevention and treatment strategies. The NADIR-3 study will contribute to establishing factors associated with the development of anemia.
Disclosure: This study was supported in part by a grant from Amgen, SA.

MP115 LONG-TERM OUTCOME OF PATIENTS WITH BALKAN ENDEMIC NEPHROPATHY

Danica Bukvic[1], Ivko Maric[1], Miodrag Milic[1], Aleksandra Arsenovic[1], Ljubica Djukanovic[2]. *[1]Institute for Endemic Nephropathy, Lazarevac, Serbia; [2]Academy of Medical Science, Beograd, Serbia*

Introduction and Aims: In 1992 the cross-sectional study was carried out in the Balkan endemic nephropathy (BEN) village of Šopic (Kolubara region). The study involved 1326 (86%) adult inhabitants and 119 patients in different stage of BEN were detected. In 2006 the outcome of these patients was examined with the aim to find out long term prognosis of BEN and factors associated with patient outcome.
Methods: In the period from 1992 to 2006, 47 patients died, 72 were invited to the control but 59 came and the outcome of remaining 13 patients remained unknown. The patients that came to the control were underwent the objective survey, laboratory analyses (routine analyses, proteinuria, alfa1-microglobulinuria, creatinine clearance (Ccr), fractional sodium excretion-FENa, percentage of tubular phosphate reabsorbtion-TRP) and ultrasound examination.
Results: In 1992 the 119 detected BEN patients were divided into four groups according to Ccr: (1) 84 patients with normal Ccr, (2) 11 patients with Ccr between 60 and 90 ml/min, (3) 10 patients with Ccr between 15 and 59 ml/min and (4) 14 with Ccr below 15 ml/min. Out of 84 patients from group 1, 21 (25%) patients died, one was on hemodialysis (HD), and in 52 patients that came to the control slightly lower kidney function and size in comparison to those in 1992 was found. From group 2, 7 patients (63%) died (3 on HD), 3 came to the control and their kidney function

and size decreased insignificantly in 14-year period. From group 3, 6 (60%) patients died (2 on HD), one was on HD, one maintained unchanged kidney function. One of the patients from group 4 was on HD and 13 (92%) died. Kaplan-Meier survival analysis showed that survival rate was consistently better for patients from group 1 that had normal CCr in 1992 than for three other groups with reduced Ccr. Eight patients who started HD were in the seventh decade of life and 42 patients died in the eighth decade of life and did not develop ESRD. The main causes of death were cardiovascular diseases (32%), upper urothelial tumors (11%) and other malignant diseases (6%). Multivariate logistic regression revealed Ccr, FENa, age, systolic blood pressure, cholesterol, TRP and proteinuria as significant risk factors of patient death.

Conclusions: In the fourteen year period, 8 out of 119 BEN patients detected in the village of Šopic started HD, 47 patients died (only 5 on HD), in 56 patients kidney function and size decreased insignificantly and the outcome of 13 patients was unknown. Cardiovascular diseases were the main causes of death and Ccr, FENa, age, systolic blood pressure, cholesterol, TRP and proteinuria were significant predictors of patient death.

MP116 BAROREFLEX SENSITIVITY IS NOT REDUCED BY ANTIHYPERTENSIVE THERAPY IN OLDER PEOPLE WITH CHRONIC KIDNEY DISEASE

Stephen John [1], Paul Owen [1], Jane Youde [2], Maarten Taal [1], Christopher McIntyre [1,3]. *[1]Department of Renal Medicine, Derby City General Hospital, Derby, United Kingdom; [2]Department of Medicine for the Elderly, Derbyshire Royal Infirmary, Derby, United Kingdom; [3]School of Graduate Entry Medicine and Health, University of Nottingham, Derby, United Kingdom*

Introduction and Aims: Baroreflex sensitivity (BRS) is a composite marker of autonomic function and is reduced in chronic kidney disease (CKD) and with advanced age. Concerns exist that the pursuit of a BP target optimised to reduce progression of CKD in the elderly might be undesirable, in terms of increasing falls propensity. Older patients have a propensity to falls which is exacerbated by impaired blood pressure (BP) control secondary to impaired BRS function. We are undertaking a study to investigate the effect of such an antihypertensive strategy on BRS in older people with CKD.

Methods: 12 non-diabetic patients with CKD stage 3-4 aged at least 70 years were recruited from primary and secondary care. Patients' antihypertensive therapy was washed out over 4 weeks before undergoing an integrated series of cardiovascular and functional assessments. Assessment was repeated after reintroduction of therapy to a target BP of 130/80. Patients were screened for postural hypotension during reintroduction. BRS was calculated by cross-correlation time-domain analysis of continuous digital BP trace. Central haemodynamics were assessed by applanation tonometry. Data are presented as mean±SD.

Results: Mean age was 75±5 years. Mean eGFR by 4-variable MDRD was 38±11 ml/min. Systolic and diastolic BP reduced with reintroduction of hypertensive therapy (145±18; 123±19mmHg; p=0.012, 80±11; 66±8mmHg; p<0.001). No patient developed postural hypotension. Rate-corrected augmentation index (AIx) reduced (21±8; 16.5±8%; p<0.01), central systolic and diastolic BP fell also (132±17; 111±19; p=0.01, 81±11; 66±11; p<0.001). BRS did not significantly alter (6.34±7.7ms/mmHg vs. 8.75±10.2ms/mmHg; p=0.12). A wide range of BRS was observed (1.61-21.9ms/mmHg).

Conclusions: Baseline BRS was mildly impaired (normal range 8-10ms/mmHg) and displayed marked variability. However, BRS did not reduce despite aggressive escalation of antihypertensive therapy to best-practice guidelines. Fears that pursuit of an optimal hypertensive strategy in older CKD patients would lead to impairment of vasomotor control appear unfounded – even patients with impaired BRS can demonstrate marked improvement with antihypertensive therapy. Further work is needed to characterise the range of BRS in this cohort and to evaluate the functional consequences of such a therapeutic strategy.

MP117 THE ROLE OF LEAN BODY MASS FOR GFR ESTIMATION IN PATIENTS WITH CKD WITH VARIOUS BMI

Sehmus Ozmen [1], Mehmet Ali Kaplan [1], Halil Kaya [2], Davut Akin [1], Ramazan Danis [1], Berfin Kizilkan [1], Orhan Yazanel [1]. *[1]Nephrology, Dicle University School of Medicine, Diyarbakir, Turkey; [2]Nuclear Medicine, Dicle University School of Medicine, Diyarbakir, Turkey*

Introduction and Aims: GFR is the main tool to diagnose, treat and follow up renal diseases. Formulae, designed for clinical use, have been investigated to predict GFR because gold standard method is difficult, expensive, and time-consuming (1). We aimed to investigate the role of lean body mass for GFR estimation in patients with chronic kidney disease with various body mass indices.

Methods: We enrolled 110 adult subjects referred for GFR measurement by 99mTc-DTPA renography into study. 24 hour Creatinine clearance (CCr), Clearance by Cockgroft-Gault, and MDRD formula were calculated in each patient. LBM and Fat Mass were measured Tanita Composition Analyzer, model TBF 300. Predictive factors were identified by linear regression analysis in each group defined by BMI. Subjects with a BMI <18.5 were defined as underweight (n=10), 18.5 to 24.9 as healthy weight (n=46), 25.0 to 29.9 as overweight (n=28), and >=30 as obese (n=26).

Results: Mean age was 47.0±16.9 years. GFR measured by DTPA, CrCl, Gault, and MDRD (4v) were 37±27, 42±30, 42±27, and 49±35 ml/min/1.73m^2, respectively. The predictive role of 1/Scr, age, serum albumin, amount of proteinuria, LBM, FM, LBM/SCR, and FM/SCr was investigated one-by-one in all BMI-groups. None of the factors were significant in underweight and healthy weight groups except 1/SCr (Table 1). LBM/SCr was independent predictive factors for both overweight and obese groups. Serum albumin and age of patient were also significant predictors of GFR in obese group but R^2 changed only 0.07 for each factor.

Table 1. Differences of R2 to predict GFR in subgroups

	Underweight	Healthy weight	Overweight	Obese
1/SCr	0.962	0.728	0.573	0.581
4vMDRD	0.940	0.775	0.717	0.586
CrCl	0.781	0.719	0.506	0.666
Gault	0.885	0.675	0.735	0.622

Significant Predictors in our study: 0.962 (1/Scr); 0.728 (1/Scr); 0.804 (LBM/SCr, albumin, age); 0.779 (LBM/SCr)

Conclusions: The explanatory role of SCr and formulas derived from SCr for GFR estimation decreases as BMI increases in chronic kidney disease. Although (4v)MDRD formula is recommended by guidelines (2), increasingly used in nephrology practice, and not including weight parameter, its explanatory role in GFR also surprisingly decreased in obese and overweight subjects. Therefore these formulas derived from SCr should be used cautiously in overweight and obese subjects. LBM measured by bioimpedans was independent predictive factor of GFR in obese and overweight subjects and add clinically important diagnostic value to 1/SCr. It needs to be investigated as a parameter in further studies trying to develop formula for estimating GFR in larger obese and overweight populations.

References: 1. Lamb EJ, Tomson CR, Roderick PJ. Estimating kidney function in adults using formulae. Ann Clin Biochem. 2005;42(Pt 5): 321-45.

2. National Kidney Foundation, K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1–S266.

MP118 LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AS A MAIN CARDIOVASCULAR DETERMINANT OF INCREASED BNP LEVEL IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Ivana Valocikova-Rosochova, Gabriel Valocik, Robert Roland, Beata Kristofova, Peter Mitro. *Internal Clinic I, P.J. Safarik University Hospital, Kosice, Slovakia (Slovak Republic); Internal Clinic III, P.J. Safarik University Hospital, Kosice, Slovakia (Slovak Republic)*

Introduction and Aims: Several studies have proved an increased cardiovascular morbidity and mortality in patients with chronic kidney disease

(CKD). However, BNP is a sensitive marker of impaired left ventricular (LV) function in CKD, it is not known if systolic or diastolic dysfunction of the LV contributes to its increased level.
The aim of this study was to assess the relation between BNP and several echocardiographic parameters of systolic and diastolic LV function in patients with different stages of chronic renal failure.
Methods: We studied 93 patients (51 males and 42 females with a mean age 60.83±15.32 years) with CKD in different stages of chronic renal failure (mean GFR 0.46±0.32 ml/s). Any of these patients had signs of congestive heart failure. Transthoracic echocardiography was performed and different parameters of systolic and diastolic function were assessed.
Results: In multiple linear regression analysis we found significant relation between BNP level and determinants of increased filling pressure of the LV such as transmitral flow propagation velocit Vp (p=0.02), early and late diastolic myocardial velocity as assessed by tissue Doppler echocardiography Em, and Am (both p=0.04), ratio of early transmitral diastolic flow and flow propagation velocity E/Vp (p=0.002), ratio of E/Em (p=0.006). There were no relations of BNP levels to other parameters, mainly determinants of systolic LV function such as LV ejection fraction (p=0.3), enddiastolic and endsystolic LV volumes (p=0.5, and 0.7), global myocardial performance index (p=0.9), systolic myocardial velocity Sm (p=0.5), and finally mean peak systolic strain and strain rate as assessed by speckle tracking echocardiography (p=0.5, and 0.9). Furthermore, there were no relations of BNP to left atrial volume and its indexed value (both p=0.6), and left ventricular mass and its indexed value (p=0.08, and 0.4).
Conclusions: Our results suggest that the main cardiovascular determinant of increased BNP level in patients with CKD is not systolic but diastolic LV dysfunction.

MP119 CIRCULATORY AND TISSUE RENIN-ANGIOTENSIN SYSTEM IN METABOLIC SYNDROME AND CHRONIC RENAL DISEASE

Tadashi Konoshita, Yasukazu Makino, Shigeyuki Wakahara, Isamu Miyamori. *Third Department of Internal Medicine, Fukui University School of Medicine, Eiheiji, Fukui, Japan*

Introduction and Aims: The renin-angiotensin system (RAS) plays important roles in the pathophysiology of cardiovascular and renal conditions. Purpose of this study is to evaluate the circulatory and renal tissue RAS in metabolic syndrome (Mets) and chronic renal disease (CKD).
Methods: First, we evaluated the relationship between Mets and circulatory RAS in 313 consecutive subjects (non-Mets 251 cases, Mets 62 cases) in our out-clinic. Second, we examined whether renal expressions of RAS differ between non-diabetics and diabetics. Subjects were 66 non-diabetics and 8 diabetics with biopsy-proven renal diseases. RNA levels from renal cortex were measured by real-time PCR for renin, (pro)renin receptor, angiotensinogen, ACE, ACE2, AT1 and AT2. At last, seventy-eight cases of biopsy-proven renal conditions were examined in details with the renal gene expressions of ACE and ACE2.
Results: As the results for the first part, compared to non-Mets cases, Mets cases showed significant high plasma renin activity (PRA). In 554 consecutive cases, logarithmic-transformed PRA showed significant positive correlation with serum triglyceride and HbA1c (r=0.091, p=0.040; r=0.169, p<0.001, respectively). We have identified cAMP response element and apolipoprotein regulating protein 1 binding element on human renin gene promoter (J Cell Biochem 2007) suggesting the relationship between Mets and RAS on transcriptional levels. As the results for the second part, a significant up-regulation was observed in ACE in diabetic renal tissue. The results suggest that renal tissue RAS might be activated in the respect of ACE up-regulation in spite of a tendency to low renin expression in diabetic nephropathy (Diabetes Care 2006). As the results for the last part, no significant correlation was observed between any clinico-pathological variables and either of the genes' expressions. However, a strong correlation was observed between the gene expressions of ACE and ACE2 (r=0.396, p<0.001). Moreover, the ACE/ACE2 ratio was significantly higher in subjects with hypertension (HT). Finally, stepwise regression analysis revealed that only HT is an independent confounding determinant of the ACE/ACE2 ratio. These data suggest that ACE2 might play an important role in maintaining a balanced status of local RAS synergistically with ACE confounded by the presence of HT (Endocrinology 2007).
Conclusions: Thus RAS may exert pivotal effects on cardiovascular and renal disease conditions in Mets and CKD.

Epidemiology and CKD 2

MP120 PEDIATRIC CHRONIC KIDNEY DISEASE STAGE 2-5 IN SERBIA

Amira Peco-Antic [1], Radovan Bogadanovic [2], Bilsana Mulic [3], Serbian Pediatric Nephrology Working Group. *[1]Department of Nephrology, University Children's Hospital, Belgrade, Serbia; [2]Department of Nephrology, Institute for Mother and Child Health Care, Belgrade, Serbia; [3]Department of Pediatrics, Medical Centre, Novi Pazar, Serbia*

Introduction and Aims: The SPEKID Registry is a prospective, population-based registry formed in Serbia in 2000 to provide current and reliable information concerning pediatric chronic kidney disease (CKD) stage 2 to 5 for planning pediatric renal replacement treatment and devising and monitoring strategies for prevention of chronic renal failure (CRF) in Serbia.
Methods: The index cases were defined using the following criteria: 1) Decreased GFR for at least 3 months; for children aged ≥ 1 year less than 90 ml/min/1,73m^2 and for younger ones as serum creatinine > mean +2SD; 2) age below 19 years at the time of registration, and 3) written informed consent for data collection, reporting and storage. The estimated numbers of people "at risk" for the morbidity analysis, derived from the 2002 republican census were 7,5 millions of general total population and 1,7 million of those younger than 19 years. All of the Serbian centres potentially involved in caring for children and adolescents with CRF were invited to report index cases. The children were reported on a prospective basis, but retrospective check-up were also performed.
Results: From January 2000 to December 2006, 205 children were registered. An average age of patients at the time of the registration was 8.4 years; boys were about 2 years younger than girls. Ratio of male to female was 1.97:1. A median follow-up of the patients after being registered was 5 years, while 25% of the patients were followed for 7 years. The mean annual incidence of CKD stage 2 to 5 was 10.04 per million child population (pmcp) ranging from 6.5 to 19.4 pmcp. The prevalence increased significantly during the study periods reaching 100.7 pmcp in December 2006. The mean annual incidence of terminal renal failure was 6.0 pmcp, while average point prevalence was 3 time greater. Congenital disorders contributed to more than two third of all causes of CRF. Eight children died during 7 years of the study period, 4 patients in non-terminal group and 4 patients on renal replacement therapy. The most common cause of the death was due to cardiovascular complications. The probability of survival was 92.9% at 7 years of the follow-up.
Conclusions: This is the first nation-wide prospective long-term study of incidence and etiology of pediatric CKD in Serbia. It demonstrated an increase in annual incidence of CRF in infants and increase in the prevalence of CRF in all age groups. Congenital renal malformations were the main cause of CRF in Serbian children. Therefore, the prevention should be directed at avoiding renal injury through improved and increased prenatal diagnosis and early postnatal care in targeted groups.

MP121 SAFE MR IMAGING IN ATHEROMATOUS RENOVASCULAR DISEASE IN THE LIGHT OF NEPHROGENIC SYSTEMIC FIBROSIS

Constantina Chrysochou [1], David Buckley [2], Alistair Cowie [3], Helen Eddington [1], Smeeta Sinha [1], Richard Hoefield [1], Philip A. Kalra [1]. *[1]Renal Department, Salford Royal Hospitals NHS Foundation Trust, Greater Manchester, Lancashire, United Kingdom; [2]Imaging Science and Biomedical Engineering, University of Manchester, Manchester, Lancashire, United Kingdom; [3]Radiology Department, Salford Royal Hospitals NHS Foundation Trust, Greater Manchester, Lancashire, United Kingdom*

Introduction and Aims: Nephrogenic systemic fibrosis (NSF) is a newly described condition and although rare, it may have devastating effects. The link with gadolinium exposure in patients with severe renal impairment has

impacted strongly on international radiology safety guidelines. Our centre has a longstanding research interest in atheromatous renovascular disease and we are accordingly big users of magnetic resonance angiography (MRA) which has traditionally been given at double dose (0.25 mmol/kg). Critical review of the literature suggests that the vast majority of cases of NSF have been dialysis dependent or non-dialysis dependent with severe renal failure, and thus we feel that not all patients with a GFR <30ml/min should be regarded as high risk. We aimed to analyse our hospital's experience and present our adjusted MR imaging (MRI) protocol taking into account the most recent guidance.
Methods: We obtained a list of all patients who had undergone MRA investigation for renal artery stenosis (RAS) since 1999. Their notes, records and cause of death were studied for any signs or symptoms suggestive of NSF following the MRA scan.
Results: Of 593 patients identified, 539 (355 males) were available for review. Follow up varied from 2 – 395 weeks (mean 127.9 weeks) and the mean age of the sample was 65 years (range 21-93, SD 13.8). 40 patients received Omniscan, and the remaining 499 Magnevist. Mean eGFR was 35.6ml/min (SD 22.5, range 5 - 133ml/min). 168 patients were classified as CKD 4 (31.5%) and 82 CKD 5 (15.4%) at the time of the scan. Thus 250 patients (46.8%) subjects had an eGFR <30ml/min, of which 27 were on dialysis. 24 (7 with CKD 4, 4 with CKD 5) patients had had two MRA's. 131 (24.3%) patients had died. None of the patients who had died and no other surviving patients had developed any signs or symptoms of NSF.
Conclusions: Despite these reassuring results, we have updated our MRI protocol in line with the latest literature. However, we challenge the latest guidelines relating to the safety of gadolinium enhanced MR (Gd-MR) studies in patients with CKD stage 4 by recommending that such patients might safely undergo Gd-MR, albeit using a macrocyclic gadolinium containing agent at half standard dose.

MP122 PREVALENCE OF HYPONATREMIA IN ADULTS AGED 55-70 YEARS INCLUDED IN THE SU.VI.MAX-2 STUDY FRENCH COHORT

S. Czernichow[1,2], E. Kesse[1], S. Péneau[1], S. Hercberg[1,2], P. Galan[1]. *[1]UMR (INSERM U557; INRA U1125; CNAM; UP13), Human Nutrition Research Center-IdF, Bobigny, France; [2]Public Health Department, Hôpital Avicenne (AP-HP), Bobigny, France*

Introduction and Aims: Hyponatremia is a common electrolyte disorder encountered in older people and is associated with morbidity and mortality in many chronic diseases. The most frequent form is dilutional hyponatremia which is associated with the excessive dilution of blood sodium following water retention. Symptoms of hyponatremia may be subtle or not attributed to hyponatremia and, if misdiagnosed or untreated, hyponatremia can lead to cognitive decline, irreversible neurological damage or death. The aim of this preliminary analysis was to estimate the prevalence of hyponatremia, and especially dilutional hyponatremia, in a subsample of subjects from the SU.VI.MAX-2 study, a cohort of the older (aged 48-73 years) general population in France.
Methods: Volunteer subjects from the SU.VI.MAX-2 Cohort (7200 subjects) were invited to attend one of the 72 hospitals involved in the study in order to evaluate: 1) nutritional status; 2) cognitive function; 3) overall clinical status; 4) posture equilibrium, quality of life and risk of osteoporotic fracture. A blood sample was taken at the time of consultation for subsequent laboratory analysis.
Results: In total, 496 subjects (mean age = 60.9±6.1 years, M/F = 187/309) were included in the sample; the mean serum sodium concentration and osmolality recorded were 139.9±4.1 mmol/L (range 120-147 mmol/L) and 299.6±8.7 mosm/L (range 256-325 mosm/L), respectively. Hyponatremia (serum sodium concentration ≤133 mmol/L) was diagnosed in 7.6% (n = 38, M/F = 20/18) of the subjects studied (mean = 128.9±3.5 mmol/L); the mean osmolality in this hyponatremic subgroup was 276.7±7.6 mosm/L. Twenty-four subjects (4.8%, M/F = 13/11) had a mean serum sodium concentration and osmolality ≤133 mmol/L and ≤280 mosm/L, respectively.
Conclusions: This initial analysis of a subsample of subjects from the SU.VI.MAX-2 cohort suggests that hyponatremia is prevalent in 7.6% of older French adults issued from the general population (4.8% for dilutional hyponatremia). Ongoing analysis of a larger sample of subjects (n = 2500) is expected to confirm this finding and should also provide insights into the impact of hyponatremia on cognitive function, gait, and quality of life.
Disclosure: This study was sponsored by sanofi-aventis.

MP123 THE ASSOCIATION BETWEEN SERUM CALCIUM, PHOSPHORUS, AND PARATHYROID HORMONE LEVELS WITH MORTALITY IN CHRONIC KIDNEY DISEASE: A META-ANALYSIS OF OBSERVATIONAL STUDIES

Suetonia Palmer[1], Giovanni Strippoli[2], Jonathan Craig[3]. *[1]Department of Medicine, University of Otago, Christchurch, Christchurch, New Zealand; [2]Department of Epidemiology and Pharmacology, Consorzio Mario Negri Sud, Santa Maria Imbaro, Chieti, Italy; [3]Centre for Kidney Research Excellence in Renal Medicine, The Children's Hospital at Westmead, Sydney, NSW, Australia*

Introduction and Aims: Randomised, controlled trials for management of altered calcium, phosphorus and parathyroid hormone levels in chronic kidney disease are numerous. Considerable controversy persists regarding the suitability of these parameters as the major end points for investigational studies, because such short-term biochemical responses to treatment are not yet validated as end points that are directly causal to long term outcomes, especially mortality and cardiovascular disease. Moreover, published guidelines for target levels of calcium, phosphorus and parathyroid hormone remain influential in current nephrology practice.
Methods: We performed a systematic review and meta-analysis of all available observational studies to characterise the association between calcium, phosphorus, and parathyroid hormone levels, and mortality in people with chronic kidney disease. We searched for observational studies in OVID Medline (to August, 2007). We extracted the frequency counts, adjusted hazard ratios (HR) or adjusted relative risks (RR) (and 95% confidence interval) for all cause mortality for each category of exposure for calcium, phosphorus, and PTH. Hierarchical linear models with second-order fractional polynomials were used to perform dose-response meta-analyses.
Results: We identified 35 observational studies examining mineral metabolism and subsequent patient-centred outcomes, following 197 175 people with CKD. The relationship between baseline serum phosphorus and all cause mortality was reported in 16 studies (159 193 patients). As serum phosphorus increased the risk for all cause mortality increased in an exponential curve, maximal at the highest levels of serum phosphorus. There appeared to be no clear "cut-point" of serum phosphorus above or below which the risk for mortality was clearly reduced. The relationship between serum calcium and all cause mortality was reported in 13 studies (137 743 people). The risk estimate for all cause mortality increased sharply above a serum calcium level of 9 mg/dl (2.25mmol/l) and was maximal at a serum calcium level of 11.5mg/dl (2.9mmol/l). The risk for all cause mortality following measurement of serum PTH levels was reported in 13 studies (144 911 people). The risk estimate for all cause mortality rose <5% overall with increasing PTH levels, between 150 and 900pg/ml (17-99pmol/l). No clear "cut-point" for PTH above which mortality was significantly increased was revealed by the dose-response analysis.
Conclusions: Large-scale observational studies provide support for the association between calcium, phosphorus and mortality in people with chornic kidney disease. However, the current target levels of these parameters set out in international treatment guidelines are not readily supported by the current observational data.

MP124 CHRONIC KIDNEY DISEASE AND MORTALITY RISK IN OLDER PEOPLE IN THE COMMUNITY

Dorothea Nitsch[1], Paul J. Roderick[2], Richard Atkins[1], Liam Smeeth[1], Richard Hubbard[3], Astrid Fletcher[1]. *[1]Department of Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom; [2]Applied Epidemiology Group, University of Southampton, Southampton, United Kingdom; [3]Department of Clinical Epidemiology, University of Nottingham, Nottingham, United Kingdom*

Introduction and Aims: Chronic kidney disease (CKD) is common in older people and most likely to be identified because of higher rates of routine blood testing. However the clinical significance of CKD is less clear in older people. The aim of this study was to examine whether CKD at older

ages (aged 75+) is independently associated with increased risk of all cause and cardiovascular mortality.

Methods: Cohort study of people aged 75 and over participating in a cluster randomised trial of health and social assessment of older people in the community between 1994-8 in the UK. There were 13177 (87%) participants in 53 general practices who had a serum creatinine measured in local laboratories at baseline. Estimated glomerular filtration rate (eGFR) was derived from the Modification of Diet in Renal Disease formula (MDRD). All patients were registered with the Office for National Statistics. Death certificates were obtained on all deaths. Analyses are based on deaths up to end November 2005 for any death and for ICD codes indicating cardiovascular disease as the underlying cause. Cox regression models were used to assess the effects of eGFR on mortality risk with adjustment for confounders (socio-demographic, cardiovascular risk, comorbidity, and for pathophysiological consequences of CKD such as low haemoglobin and high phosphate).

Results: After median follow-up of 7.3 yrs (IQR 3.8-8.8) 7633 (58%) had died, 42% from cardiovascular causes. In the first 2 years of follow-up compared to eGFR >60 ml/min/1.73m^2, the fully adjusted hazard ratios for all cause mortality for baseline CKD in bands 45-59, 30-44, <30 ml/min/1.73m^2 compared to eGFR >60 ml/min/1.73m^2 were in males 1.13 (0.93-1.37), 1.69 (1.26-2.28) and 3.87 (2.78-5.88) respectively and in females 1.14 (0.93-1.40), 1.33 (1.06-1.68) and 2.44 (1.68-3.56) respectively. The hazard ratios were greater in males and for cardiovascular mortality (in those without previous CVD), and were lower for mortality after 2 years though of the same pattern.

Conclusions: CKD is of independent prognostic significance in older people; compared to an eGFR over 60 ml/min/1.73m^2 as kidney function falls there is a graded increase in all cause and cardiovascular mortality risk which is more apparent once eGFR is less than 45 ml/min/1.73m^2.

MP125 TOTAL CHOLESTEROL IS NOT ASSOCIATED WITH SHORT-TERM AND LONG-TERM MORTALITY IN DIALYSIS PATIENTS: A MENDELIAN RANDOMIZATION STUDY

Marion Verduijn[1], Michal Chmielewski[2,5], Bengt Lindholm[2], Els W. Boeschoten[3], Raymond T. Krediet[4], Friedo W. Dekker[1]. *[1]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands; [2]Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; [3]Hans Mak Institute, Naarden, Netherlands; [4]Department of Nephrology, Academic Medical Center, Amsterdam, Netherlands; [5]Department of Nephrology, Transplantology and Internal Medicine, Medical University of Gdansk, Gdansk, Poland*

Introduction and Aims: In contrast to the general population, high total cholesterol (TC) levels tend to have a protective effect on mortality in ESRD patients. This may be a result of confounding or reverse causation. The aim of the study was to examine the association between TC and mortality in dialysis patients free from confounding and reverse causation by Mendelian randomization (MR) using the ApoE polymorphism.

Methods: Patients from a prospective multicenter cohort study among ESRD patients starting dialysis (NECOSAD) who were genotyped for ApoE and with a TC measurement available at 3 months after start of dialysis were included. Three TC categories were defined as 'desirable': ≤ 5.17 (ref.), 'borderline high': 5.17-6.22, and 'high': ≥ 6.22 mmol/L. The ApoE genotypes were grouped as E2+, E3 (ref.), and E4+. Hazard ratios (HRs) for 2 and 5 years of all-cause mortality were calculated for TC and ApoE.

Results: 787 patients were included (mean age (SD): 60 (15) years, 61% male, 63% HD, mean TC (SD): 5.1 (1.3) mmol/L). Patients with desirable TC were more often men, HD patients, and burdened by CVD. Moreover, Hb values were found to be lower, and higher Kt/V values were observed. Patients with high TC were found to be younger and had lower hsCRP values than the other patients. The baseline characteristics did not differ for ApoE, with exception of the TC levels with a mean (SD) of 4.86 (1.21), 5.04 (1.30), 5.22 (1.28) within E2+, E3, and E4+ patients, respectively (p-value: 0.045). The HRs for mortality are shown in Table 1.

Conclusions: Although a protective effect of high TC levels on short-term mortality is suggested after adjustment for possible confounders, no association of TC levels with short-term and long-term mortality was found when estimated by MR using ApoE. This confirms that low TC is only a marker of near death, and that the association between lower TC and mortality is caused by reverse causation and/or residual confounding.

Tabale 1. Mortality risks for TC and ApoE

		2 years follow up				
TC	N	crude HR	adjusted HR*	ApoE	N	crude HR
Desirable	457	1	1	E2	132	0.93 (0.61-1.43)
Borderline high	200	0.89 (0.62-1.26)	1.10 (0.77-1.59)	E3	458	1
High	130	0.41 (0.23-0.71)	0.64 (0.37-1.13)	E4	181	1.11 (0.77-1.59)

		5 years follow up				
TC	N	crude HR	adjusted HR*	ApoE	N	crude HR
Desirable	457	1	1	E2	132	1.00 (0.73-1.35)
Borderline high	200	0.85 (0.65-1.11)	0.97 (0.73-1.27)	E3	458	1
High	130	0.56 (0.39-0.79)	0.90 (0.63-1.36)	E4	181	0.90 (0.68-1.19)

*Adjusted for age, gender, primary kidney disease, CVD, and DM.

MP126 ESTIMATING GLOMERULAR FILTRATION RATE IN CHRONIC KIDNEY DISEASE: COMPARISONS BETWEEN SERUM CREATININE AND CYSTATIN C-BASED FORMULAE

You-Sang Ko[1], Jang-Won Seo[2], Tae-Jin Park[2], Su-Jin Kim[2], Young-Soo Song[2], Seong-Gyun Kim[2], Ji-Eun Oh[2], Young-Ki Lee[2], Jong-Woo Yoon[2], Ja-Ryong Koo[2], Hyung-Jik Kim[2], Jung-Woo Noh[2]. *[1]Department of Internal Medicine, College of Medicine, Hallym Unversity, Seoul, Republic of Korea; [2]Department of Internal Medicine, College of Medicine, Hallym Unversity and Kidney Research Institute, Seoul, Republic of Korea*

Introduction and Aims: Current KDIGO and NKF-K/DOQI guidelines recommend that patients with chronic kidney disease (CKD) should be calssified in stages 1-5 based on creatinine-based GFR prediction equation of the Modification of Diet in Renal Disease (MDRD) formula. Cystatin C (Cys C) has been proposed as an alternative marker of renal function. Eventhough there are many kinds of Cys C-based equations for calculation of GFR, estimation of the GFR based on Cys C has received little attention. Recently, several Cys C-based equations were developed in different patient cohorts. The purpose of our study was the comparison of the serum Cys C-based GFR estimates with the serum creatinine-based equations (Cockcroft-Gault and MDRD formula) in various stages of CKD.

Methods: Serum creatinine and Cys C levels were simultaneously measured in 199 CKD patients. The Cys C level was determined by latex particle-enhanced turbidimetric immunoassays. We compared the calculated MDRD formula and Cockcroft-Gault formula with previously developed six Cys C-based GFR formulae in these patients, respectively. Cys C-based GFR estimates were calculated by each following formulae.

(#1) Cys C-based GFR = (78/Cys C [mg/L]) + 4,
(#2) Cys C-based GFR = (80.35/Cys C [mg/L]) – 4.32,
(#3) Cys C-based GFR = 77.239 × Cys C [mg/L]$^{-1.2623}$,
(#4) Cys C-based GFR = (86.7/Cys C [mg/L]) – 4.2,
(#5) Cys C-based GFR = 66.8 × Cys C [mg/L]$^{-1.30}$,
(#6) Cys C-based GFR = 76.6 × Cys C [mg/L]$^{-1.16}$.

Results: All kinds of Cys C-based GFR formulae correlated well with MDRD formula in patients with various stages of CKD. (Fig. 1). Correlation coefficients between MDRD formula and each of the Cys C-based GFR

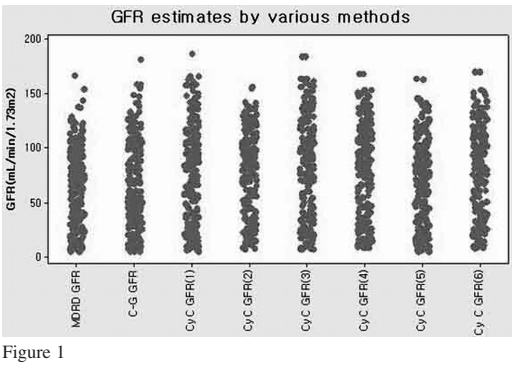


Figure 1

estimates were 0.899 (Cys C-based GFR (#1)), 0.891 (Cys C-based GFR (#2) and (#4)), 0.884 (Cys C-based GFR (#6)), 0.878 (Cys C-based GFR (#3)) and 0.876 (Cys C-based GFR (#5)), respectively ($p<0.01$). Correlation coefficients between MDRD formula and Cockroft-Gault GFR was also closely correlated with MDRD formula ($r=0.919$, $p<0.01$). The differences between the correlation coefficients did not reach statistical significance. Furthermore, Cys C-based GFR formulae had no difference with Cockroft-Gault equation.

Conclusions: Our study suggests that serum creatinine-based MDRD formula is a currently used standard calculated GFR but Cys C-based GFR formulae might also could be used for staging in CKD patients. Further studies are needed to investigate the relationships between calculated GFR estimates and measured GFR estimates in the same CKD populations.

MP127 CHRONIC KIDNEY DISEASE IN THAILAND: THE CROSS SECTIONAL HEALTH SURVEY IN A COMMUNITY-BASED POPULATION

Kriengsak Vareesangthip[1], Leena Ongajyooth[1], Wichai Aekplakorn[2], Panrasri Khonputsa[3], Mayura Kusoom[4]. *[1]Renal Division, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [2]Community Medicine Center, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [3]Setting Priorities Using Information on Cost-Effectiveness (SPICE) Projec, Ministry of Public Health, Bangkok, Thailand; [4]Medical Science Department, Ministry of Public Health, Bangkok, Thailand*

Introduction and Aims: To determine the prevalence of chronic kidney disease in Thai adults from National Health Examination Survey in 2004.

Methods: Data from a nationally representative sample of 3,117 individuals aged 15 years and older was collected using questionnaires, physical examination and blood samples. GFR was estimated using the Chinese modified Modification of Diet in Renal Disease Study equation. Chronic kidney Disease (CKD) stages was classified based on kidney Disease Outcome Quality Initiative (K/DOQI).

Results: The prevalence of CKD in Thai adults weighted to the 2004 Thai population by stage was 4.47% for stage 3, 0.11% and 0.11% for stage 4 and 5 respectively. Compared to non-CKD, individuals with CKD were older, having higher level of cholesterol, and blood pressure. The prevalence of cardiovascular risk factors were more common in those with CKD (stage 3-5) than those without, including hypertension (48.8% vs 15.4%), diabetes (18.6% vs 4.9%) and overweight (BMI>-25 kg/m^2, 24.0% vs 22.9% respectively).

Conclusions: The identification of CKD patients should be evaluated and monitored for appropriate intervention for progression to kidney disease from this screening.

MP128 ★ HIGH PREVALENCE OF CKD IN THE MIDDLE-AGED UK POPULATION: THE SCOTTISH HEART HEALTH STUDY AND THE BRITISH REGIONAL HEART STUDY

Keith McCullough[1,4], Goya Wannamethee[2], Hugh Tunstall-Pedoe[3], Alison MacLeod[4], Nicholas Fluck[1], W. Cairns Smith[5], Gordon Prescott[5], Izhar Khan[1], Tariq Ali[6], Corri Black[5]. *[1]Renal Unit, Aberdeen Royal Infirmary, United Kingdom; [2]Primary Care & Population Sciences, University College London, United Kingdom; [3]Cardiovascular Epidemiology Unit, University of Dundee, United Kingdom; [4]Medicine & Therapeutics, University of Aberdeen, United Kingdom; [5]Public Health, University of Aberdeen, United Kingdom; [6]Renal Unit, Kent & Canterbury Hospital, United Kingdom*

Introduction and Aims: The prevalence of low eGFR in unselected community populations has been reported from large studies in the US (NHANES III) and Norway (HUNT II). No comparable study in the UK has been reported previously. We examined data from 2 large historical heart cohort studies carried out in the UK, in which participants underwent measurement of serum creatinine at baseline, to explore the prevalence and cross-sectional co-morbidity associations of low eGFR.

Methods: The British Regional Heart Study (BRHS) considered 7735 men aged 40-59 years selected by random sampling from the registers of one general practice in each of 24 towns across mainland UK (1978-80). The Scottish Heart Health Study (SHHS) and overlapping WHO Monica Study considered 13067 men and women aged 25-70 years (87% aged 40-59 years) across 25 districts of Scotland by random sampling from general practice registers (1984-87). Creatinine values were standardised to reference methods, using method-specific slope and intercept equations for the assay types used, then the re-expressed version of the 4-variable MDRD equation for use with zero-biased assays was applied. Standardised prevalence rates were based on 1981 Census figures.

Results: Valid eGFRs were available for 7689 (99.4%) BRHS and 11704 (89.6%) SHHS participants. In both studies eGFR was normally distributed; amongst those with eGFR<60, eGFR was ≥45 in over 90% and there was a steep increase in prevalence with age. In the SHHS the normal distribution for women was shifted towards lower levels. Based on those aged 40-59 years, adjusted prevalence rates for eGFR<60 and eGFR<45, respectively, were 4.1% (95% CI: 3.7-4.6) and 0.35% (0.21-0.48) for British men; 2.8% (2.4-3.3) and 0.39% (0.22-0.56) for Scottish men; 8.5% (7.6-9.3) and 0.59% (0.38-0.81) for Scottish women; and 5.8% (5.3-6.2) and 0.49% (0.36-0.63) for Scottish men and women. For eGFR<60, statistically significant cross-sectional associations with hypertension and established coronary disease were observed, which persisted after correction for age in the BRHS, and age and sex in the SHHS; female sex remained more strongly associated than other factors in the SHHS.

Conclusions: Based on the BRHS and SHHS data, using comparable methodology, the prevalence of low eGFR in the UK appears higher than in the US and Norway (prevalence of Stage 3 CKD for men and women of 40-59 years was 1.8% in NHANES III, and 1.4% in HUNT II). Low eGFR is more common in women, who in general have lower mean eGFR than men, and is more common with advancing age. There is significant cross-sectional association with established coronary disease which was highly prevalent in the UK at the time of these studies.

Disclosure: Funded by the Chief Scientist Office (Scotland) small grant scheme 2006 -07.

MP129 REGRESSION OF LEFT VENTRICULAR HYPERTROPHY AND CHANGE IN MYOCARDIAL CONTRACTILITY BY ACE INHIBITION IN CHILDREN WITH CKD

Maria Chiara Matteucci[1], Stefano Picca[1], Marcello Chinali[3], Antonio Mastrostefano[1], Giovanni de Simone[3], Elke Wuhl[2], Franz Schaefer[2], and ESCAPE Trial Group. *[1]Pediatric Nephrology, Bambino Gesu' Hospital, Rome, Italy; [2]Pediatric Nephrology, University Hospital of Pediatric and Adolescent Medicine, Heidelberg, Germany; [3]Clinical and ExperimentalMedicine, Federico II University Hospital, Naples, Italy*

Introduction and Aims: We recently observed a high prevalence of left ventricular hypertrophy (LVH) and impaired LV contractility in children with stage II-III chronic kidney disease (CKD) (JASN 2006, JASN 2007). In a prospective open-label assessment in 84 children receiving fixed dose ACE inhibition (ramipril 6 mg/m^2/d) with or without additional antihypertensive medication, we evaluated by echocardiography left ventricular (LV) mass (LVM), geometry and myocardial mechanics at baseline and after 12 (N=65) or 24 months (N=55) of treatment.

Methods: LVH was defined by LVM index >38 g/m$^{2.7}$ and concentric geometry by relative wall thickness >0.375 (95th normal percentiles). LV systolic function was assessed at the midwall level by circumferential shortening (mS).

Results: Normalized 24h mean arterial blood pressure (BP) was reduced from 1.3±1.4 at baseline to 0.0±1.4 and -0.5±1.0 SDS after 12 and 24 months respectively. LVMI was reduced significantly after 12 (from 34.0±8.4 to 31.6±8.0 g/m$^{2.7}$, $p<0.02$) and 24 months (from 34.4±7.6 to 31.9±9.7, $p<0.05$). Of those patients presenting with LV hypertrophy at baseline, LVM regressed to the normal range in 10/19 (53%) after 12 months and in 10/18 (55%) after 24 months. The prevalence of concentric LV geometry remained unchanged (baseline: 8%, 12mo: 9%, 24mo: 7%). Age and afterload-corrected myocardial function increased from 90.6±12% to 99.0±10% and 93±15% to 100±13% at 12 ($p<0.001$)and 24 months ($p<0.005$). The changes in LVM and myocardial performance were independent of the randomized BP target and GFR. Change in LVM was correlated with change in hemoglobin level ($r=0.30$, $p<0.05$) and change in myocardial function with change in BP level ($r=0.39$, $p<0.05$).

Conclusions: In conclusion, fixed-dose ACE inhibition and tight blood pressure control induce regression of established LVH in the majority of children with stage II-III CKD. This is associated with a normalization of myocardial contractility.h

MP130 FACTORS ASSOCIATED WITH HIGH MORTALITY RATE IN CHRONIC KIDNEY DISEASE (CKD). RESULTS OF THE NATIONAL RENAL HEALTHCARE PROGRAM (NRHP) OF URUGUAY

Emma Schwedt, Laura Sola, Pablo Rios, Nelson Mazzuchi. *National Renal Healthcare Program, Renal Healthcare Program Honorary Committe, Montevideo, Uruguay*

Introduction and Aims: Data are lacking regarding the poor clinical outcomes in patients (P) stage I-V of CKD in non-renal replacement therapy. Late referral to nephrologist is reported to be associated with increased morbidity and mortality. Objective: To evaluate factors associated with mortality rate in patients with CKD.
Methods: The NRHP began in October 2004, is integrated to the Primary Care System in a reference-counter-reference system, facilitating the easy access to nephrologist and dietitian for P stage I to III, and for stage IV-V the assistance in CKD Clinics with a formal interdisciplinary team.
The baseline characteristics of the enrolled P (age, gender, nephropathy, time of follow-up, cardiovascular comorbidity), the frequency of P treated with ACEI's/ARB's and the causes of death were analized. The rate of death, end-stage renal disease (ESRD) and non-fatal cardiovascular (CV) events were estimated. CV morbidity and mortality per CKD stage was studied. Cox proportional hazard model was performed to evaluate factors associated with mortality.
Results: There were 1943 registered P, mean age 66±14 years, 47.9% females, mean time of folow-up 11.8 months (11.3-12.3), 21,8% had a late referral (CKD stage IV-V). The frequency of CV morbidity increased significantly by CKD stage (table I).
Mortality rate per 100 patient/years was 10.6 and by CKD stage was 3.7 in stage I-II, 9.8 in stage III and 19 in stage IV-V. The rate of ESRD was 5.3 per 100 patient/years and the rate of CV events was 12.3 per100 patient/years. The most frequent causes of death were: CV 47.9%, malignancy 17.4%, infection 13%, suicide 6.5%, others 15%.
In the follow-up, the frequency of P treated with ACEI's/ARB's increased from 61.9 to 66.3%. In the Cox proportional hazard model the variables significantly associated with mortality were: male gender, late referral, age over 65 years and CHF. Adjusted to age, gender, nephropathy, CKD stage and CV morbidity, P treated with ACEI's/ARB's had a 70% lower risk of death (p<0,001).

Table 1. Frequency of patients with CV comorbidity by CKD stage entering the program

	Stage I %	Stage II %	Stage III %	Stage IV %
Coronary Heart Disease (CHD)	8.9	15.2	22.3	26.7
Left-Ventricular Hypertrophy (LVH)	10.9	13.4	21.6	24.5
Congestive Heart Failure (CHF)	4.0	4.6	10.3	11.0
Stroke (S)	4.0	5.1	10.1	9.1
Peripheral Vascular Disease (PVD)	3.0	5.6	6.4	9.3

Conclusions: The rate of CV events and the rate of mortality were greater than the rate of ESRD. Late referral to nephrologist, male, age, and CHF were independent risk factors for death.

MP131 ★ IS CALIBRE A NEW INSIGHT IN RENAL ARTERY STENOSIS?

Luca Zanoli[1], Stefania Rastelli[1], Carmelita Marcantoni[2], Giovanni Tripepi[3], Massimo Matalone[2], Corrado Tamburino[4], Carmine Zoccali[3], Pietro Castellino[1]. *[1]Internal Medicine and Nephrology, University of Catania, Catania, Italy; [2]Nephrology and Dialysis, Cannizzaro Hospital, Catania, Italy; [3]IBIM-CNR, Ospedali Riuniti, Reggio Calabria, Italy; [4]Cardiology, University of Catania, Catania, Italy*

Introduction and Aims: Investigations of vessel morphology are focused on the assessment of the percentage of the renal artery stenosis (RASp). RASp is considered the main criterion of choice between a surgical and a medical treatment. Other features, such as the calibre, have been poorly investigated.
This study was planned to identify the independent predictors of CrCl < 60 mL/min in a high cardivascular risk population.
Methods: CrCl was estimated by Cockroft-Gault equation.
The renal artery calibre (RAC) was quantified with selective single-plane renal angiography as part of a diagnostic cardiac catheterization study.
The contrast-filled guiding catheter was used as calibration for vessel dimension calculation. The calibre (measured in the stenotic trait and in the reference diameter) was used for calculation of the sum of left to right RAC (LR-C) in all patients (pts).
Results: 737 pts were evaluated, the mean age was 64±10 years and 72% were males. CrCl was 82±29ml/min.
Angiographically evident RAS was present in 30% pts.
There were 42 pts with LR-C≤7mm: 41/42 pts of them with RAS (only 25 pts with RAS≥50%).
There was a relation (figure 1) between CrCl and LR-C.

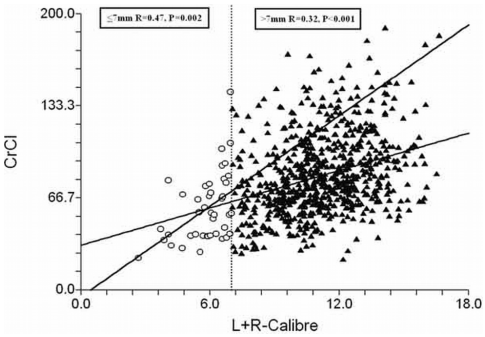
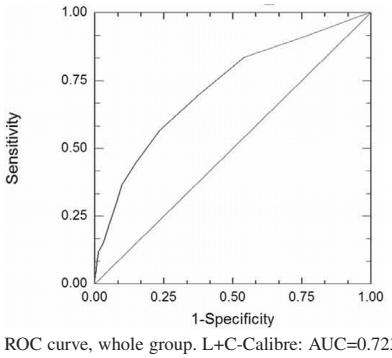


Figure 1. Scatter plot: CrCl Cockroft-Gault vs L+R-Calibre

On univariate logistic regression analysis, the LR-C was inversely related to CrCl<60ml/min [odds ratio (OR): 1 mm increase in LR-C: 0.69 (95% CI: 0.63-0.75, P<0.001) and the area under the ROC curve (AUC) was (figure2) 0.72 (P<0.001). In a multiple logistic regression model, including all univariate correlates of CrCl<60ml/min, age [OR (1 year increase): 1.14, 95% CI: 1.11-1.18, P<0.001], weight [OR (1 kg increase): 0.91, 95% CI: 0.89-0.93, P<0.001], and LR-C [OR (1 mm increase): 0.81, 95% CI: 0.73-0.89, P<0.001] maintained an independent association with CrCl <60ml/min and the AUC was 0.87.



ROC curve, whole group. L+C-Calibre: AUC=0.723

The independent association of LR-C for CrCl<60mL/min was also confirmed in the subgroup with LR-C≤7mm [OR: 0.37, 95% CI: 0.14-0.98, P<0.05].
Conclusions: Our analysis provide evidences of the existence of a critical luminal diameter in human renal arteries. Below this diameter, a significant reduction of CrCl is observed.
The relation between calibre and CrCl was strongest in smallest vessels.
LR-C is an independent predictor of CrCl, a better predictor of renal function than RASp, and can be helpful to identify a haemodynamically significant lesion.

MP132 MILD KIDNEY DISEASE MAY NOT BE AN INDEPENDENT RISK FACTOR FOR MORTALITY: FINDINGS FROM THE GRAMPIAN CKD STUDY GROUP

Laura Clark[1], Gordon Prescott[2], Cairns Smith[2], Nicholas Fluck[3], William Simpson[4], Alison MacLeod[1]. *[1]Medicine and Therapeutics, University of Aberdeen, Aberdeen, United Kingdom; [2]Public Health, University of Aberdeen, Aberdeen, United Kingdom; [3]Renal Unit, NHS Grampian, Aberdeen, United Kingdom; [4]Clinical Biochemistry, NHS Grampian, Aberdeen, United Kingdom*

Introduction and Aims: CKD is a major public health concern given its high prevalence and association with increased morbidity and mortality. We aimed to establish whether CKD itself is an independent risk factor for death and identify any other factors which are independently associated with death.

Methods: All patients with at least one creatinine $\geq$ 130μmol/L in females and $\geq$ 150μmol/L in males between 1/1/03 and 30/6/03 were identified. Patients were grouped according to whether they had ARF, ACRF, CKD (3 elevated creatinines spaced one month apart) or on RRT. 1918 patients were initially unclassified, as they did not fulfil our strict definition for CKD. To determine whether they had CKD all their available creatinine values from 1996 to 2005 were identified, as were markers of kidney damage from their case records. Those who had median eGFRs of <60mls/min/1.73m^2 and/or a marker of kidney damage present were defined as having mild CKD and those with median eGFRs $\geq$ 60mls/min/1.73m^2 with no marker present (n=129) as "No CKD"; 561 had an insufficient number of creatinines for diagnosis. Survival was determined as time from index creatinine to date of death or end of follow up (31/12/05). Independent factors associated with death were identified using a Cox proportional hazards regression model.

Results: 1228 patients were identified as having CKD. Median age was 80 years for those with CKD and 67 years for No CKD. Median eGFR for those with CKD was 43mls/min/1.73m^2. The commonest cause of death in those with CKD was cardiovascular disease. Cox proportional survival analysis showed that although other vascular co-morbidities were independently associated with increased risk of death CKD itself was not (Table). However, when including markers of kidney damage in the analysis those with persistent proteinuria (ACR/PCR) had a greater risk of death compared to those with normal urine (HR 1.90, CI 1.27-2.85, p=0.002).

Cox Regression Survival Analysis

Variable	Hazard Ratio	95% Confidence Interval		P Value
		Lower	Upper	
Age	1.042	1.032	1.051	<0.001
PVD	1.272	1.021	1.585	0.032
CCF	1.695	1.404	2.047	<0.001
Haem Malignancy	2.024	1.261	3.248	0.003
Non Haem Malignancy	1.496	1.239	1.807	<0.001
Dementia	1.700	1.342	2.153	<0.001
COPD	1.396	1.122	1.738	0.003
Chronic Liver Disease	2.895	1.764	4.753	<0.001
CKD Vs No CKD	0.805	0.596	1.087	0.157

Conclusions: Surprisingly this study shows that although other vascular co-morbidities are strongly predictive of death, "No CKD" CKD as defined by our strict criteria is not unless proteinuria is present. The K/DOQI eGFR CKD definition criteria is thus perhaps less useful at predicting risk of death, particularly in the elderly with mild CKD.

MP133 CLINICAL ASPECTS OF URINARY TRACT INFECTION IN THE ELDERLY

Luiz Paulo José Marques, Maria Helena Victor, Omar Rosa Santos. *Department of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil*

Introduction and Aims: The elderly population is now increasing in the world and, Urinary tract infection (UTI) is the most commom infection disease of the elderly and account for substantial morbidity and economic costs. UTI clinical presentation is often unusual in old people, which delays the diagnosis and when discovered its management poses problem. The aim of this study is to analyse the clinical characteristics of UTI in the elderly living in the community.

Methods: We studied 662 persons over 60 years old, 430 women and 232 men, who go to general practioners or nephrologist in Gaffreè and Guinle University Hospital. All of them collected a clean-voide urine for urinary Dip-Stick, sediment and culture. Pyuria was considered when $\geq$ 10 leukocyte/hpf and Significant Bacteriuria (SB) when $\geq$ 100000 cfu/ml. In the patients who presented positive urine culture, the urine examination was repeated after one and three months. UTI as defined by the presence of urinary symptoms, pyuria and SB and Assymptomatic Bacteriuria (AB) when only SB was presented.

Results: We found an overall SB prevalence of 18,5% in old people. SB was more prevalent in women (UTI 18,6% and AB 5,1%) than in men (UTI 8,6% and AB 0,4%) p<0,001. UTI clinical symptoms more frequent were pungent odor urine in 64,0%, disuria with urgency in 41,0% and frequency in 36,0%.

Diabetes was presented in 170 patients (76 men, 6 with ITU and, 94 women, 21 with ITU and 2 with AB) and did not incresead the risk of SB in old age people. In men the prevalence of UTI was signifcantly associated to prostatic hyperplasia (p<0,0001), E. Coli was responsible for 47,6% of the infections and the presence of Gram-positive bacilli was associated to urinary tract catheterization. Cytologic examination of vaginal smears was made in 39 women with SB and showed us hypotrophic smears in 100% and vaginitis or bacterial vaginosis in 74,3%. E.coli was responsible for SB in 79,4% of women. AB was not treated in this group of old people.

Conclusions: 1) UTI is more prevalent in old women and the clinical presentation was unusual, the more frequent symptom was pungent odor of urine. 2) Diabetes was not a predisponent factor for UTI in this eldery group and, the prostatic disease in men and the presence of vaginitis or bacterial vaginosis in women may act as a predisponent factor for Significant Bacteriuria.3) Its not necessary to treat Assymptomatic Bacteriuria in the elderly.

MP134 CHRONIC KIDNEY DISEASE – MINERAL AND BONE DISORDER (CKD-MBD): CONTROLLING AND CONTROLLED FACTORS

Ana Pires, Teresa Adragao, Jose Vinhas, Maria Joao Pais, Hugo Gil Ferreira. *Nephrology, Fernando Fonseca Hospital, Amadora, Portugal; Nephrology, Santa Cruz Hospital, Carnaxide, Portugal; Nephrology, S Bernardo Hospital, Setúbal, Portugal; CQFB, New University of Lisbon, Lisbon, Portugal*

Introduction and Aims: Biochemical alterations used to diagnose CKD-MBD are late phenomena that appear when compensatory mechanisms are no longer efficient. Understanding the pathogenesis of these perturbations may help to adequate treatment at an earlier phase. The objective of this study was to evaluate bone and mineral metabolism in non-dialysis patients.

Methods: We studied 1131 pts from CKD stage(S) 1 to 5 (MDRD equation). Laboratory data included serum levels of calcium (sCa) phosphorus (sP), iPTH, 25vitD and 1,25 vitD and urinary excretion fractions of calcium (UeFCa) and phosphate (UeFP). The range of variation (highest minus lowest value) (Δ) for each studied variable along CKD stages was calculated and expressed as a fraction of its corresponding value evaluated in pts with normal GFR. Curve fitting allowed the identification of inflexion points in the curves correlating GFR with studied variables.

Results: Pts were 67±15 years old, 53% male, 97% caucasian and 22% diabetic. Table 1 displays the prevalence of the main alterations (according to laboratory range for S1-2 and KDOQI for S3-5) and mean values of UeFCa and UeFP by CKD stage. The ΔsCa was 0.7; ΔsP was 2; Δ1,25vitD was 2; ΔiPTH was 8; ΔUeFCa was 7 and ΔUeFP was 6. GFR was

Table 1

	CKD S1 (n=60)	CKD S2 (n=102)	CKD S3 (n=455)	CKD S4 (n=344)	CKD S5 (n=170)	p
Hyperparathyroidism (%)	13	28	54	60	35	0.07
1,25vitD deficiency (%)	7	16	19	29	47	0.002
25vitD deficiency	43	21	25	28	58	0.2
Hyperphosphatemia (%)	0	1	4	13	26	<0.001
Hypocalcemia* (%)	0	3	5	11	22	<0.001
UeFCa (%)	0.9	1.0	0.8	1.2	2.4	<0.001
UeFP (%)	12.7	21.6	30.9	46.4	59.9	<0.001

*Serum calcium was corrected for albuminemia.

negatively correlated with iPTH (<0.001), sP (<0.001), UeFP (<0.001) and UeFCa (p=0.03) and positively correlated with sCa (<0.001), 25vitD (0.03) and 1,25vitD (<0.001). We found a clear point of inflexion on the curve correlation of GFR with UeFP, iPTH, UeCa and sP, respectively at GFR values of 45, 33, 28 and 25 ml/min/1.73m^2.

Conclusions: Along CKD stages, sCa and sP present the less range while PTH, calciuria and phosphaturia present a wide range of variation. Hypocalcemia and hyperphosphatemia are only significant from CKD S3 to S4 and S4 to S5. Increase in phosphate excretion fraction is an early indicator of the disturbance of mineral metabolism with steep increase of UeFP occurring with GFR of 45 ml/min/1.73m^2 and preceding steep increase in PTH. A perturbation in the Ca/P metabolism aims to maintain within normal range sCa and sP, acting as the controlled factors, at cost of very large variations on iPTH and Ca/P urinary excretions which behave as controlling factors.

MP135 CASE-FATALITY RATE (CFR) IN INCIDENT HEMODIALYSIS (HD) PATIENTS (PTS): COMPARISON BETWEEN ACETATE-FREE BIOFILTRATION (AFB) AND CONVENTIONAL HEMODIALYSIS (CHD)

Albino Poli[1], Nicola Tessitore[1], Oliviero Panzetta[2], William Mantovani[1], Juan Esteban[3], Gerard London[4], Bruno Perrone[5], Volker Wizemann[6], Klaus Neumann[7], Rafael Perez[8], Jorge Martinez Ara[8], Jose Louis Miguel[8], Antonio Santoro[9]. *[1]Verona, Italy; [2]Trieste, Italy; [3]Ourense, Spain; [4]Fleury, France; [5]Saintes, France; [6]Giessen, Germany; [7]Magdeburg, Germany; [8]Madrid, Spain; [9]Bologna, Italy*

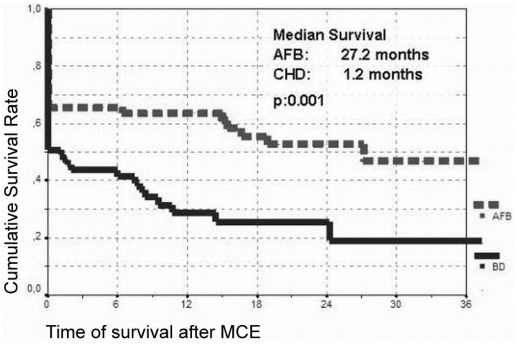
Introduction and Aims: CFR, i.e. the proportion of individuals contracting a disease who die of that disease, is an outcome commonly used to compare the effects of an intervention or a treatment on the fatality of a disease and to evaluate the performance among hospitals. We use CFR to compare the effects after major cardiovascular events (MCE, defined as cardiovascular death, non fatal myocardial infarction, stroke or symptomatic peripheral vascular disease) of AFB vs CHD from a controlled randomized european multicentric study in incident HD pts on 4-years mortality.

Methods: CFR was computed by dividing cardiovascular death by MCE that occurred during follow up. Cox hazard model was used to evaluate significant predictors of MCE among gender, baseline age, Ca-P product, left ventricular mass, predialysis systolic blood pressure (pSBP) subgroups (normotensive <140 mmHg, mild hypertensive 140-160 mmHg, severe hypertensive >160 mmHg), diabetes, history of cardiovascular (CV) disease and treatment (CHD or AFB).

Results: One-hundred-twenty-three pts (64 in BD and 59 in AFB) had a MCE, i.e a 4-y cumulative MCE rate of 33.3% in CHD and 34.7% in AFB (p=ns). Cox's analysis revealed that the occurrence of MCE was associated with diabetes (HR=1.83; 95% CI:1.23-2.73; p=0.012) and a history of cardiovascular disease (HR=1.53; 95% CI:1.10-2.31: p=0.040).

In the MCE pts, the cumulative CV mortality rate was 67.2% in BD and 45.8% in AFB (p=0.02).The initial MCE was fatal in 30 CHD and in 20 AFB pts (46.8% and 33.9%, respectively; p=ns). Figure below shows the Kaplan-Meier analysis of patient after MCE. Median survival of AFB arm was 27.2 months and 1.2 months in CHD.

Cox analysis showed that AFB was the only variable associated with a reduced risk of death in the event of a MCE (HR=0.56; 95% CI 0.32-0.98; p=0.040).



Conclusions: Our results suggest that, in incident HD pts, AFB is associated with a significant reduction in the fatality of CV events compared to CHD, though MCE rate is unaffected by the dialysis treatment modality. Further investigation is needed do understand the underlying mechanisms of this protective effect by AFB.

MP136 CHRONIC KIDNEY DISEASE IS A RISK FACTOR FOR CARDIOVASCULAR DISEASE AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

Charlotte Bebb[1], Nigel Sturrock[1], Richard Burden[1], Maarten Taal[2]. *[1]Renal Unit, Nottingham University Hospitals, Nottingham, United Kingdom; [2]Department of Renal Medicine, Derby City General Hospital, Derby, United Kingdom*

Introduction and Aims: Chronic kidney disease (CKD) has been identified as an independent risk factor for cardiovascular disease (CVD) in several large epidemiological studies but more detailed studies are required to investigate the importance of CKD relative to other cardiovascular risk factors in specific groups of patients. In this study we investigated CKD as a risk factor for CVD among 1465 subjects with type 2 diabetes.

Methods: Participants were recruited from 42 general practices in Nottinghamshire and underwent detailed assessment of their medical history as well as baseline anthropomorphic measurements and serum biochemistry. CVD was defined as any of: myocardial infarction, coronary artery bypass grafting, percutaneous coronary angioplasty, stroke, transient ischaemic attack, peripheral angioplasty or amputation. Subjects were followed up after 1 year and all new cardiovascular events recorded. GFR was estimated using the Cockroft-Gault formula.

Results: At baseline 560 (38.2%) subjects had CKD and 299 (20.4%) had a history of CVD. Subjects with a history of CVD evidenced significantly older age, higher urine albumin to creatinine ratio (ACR), lower estimated GFR (eGFR), lower cholesterol and higher pulse pressure. CVD was significantly more prevalent among subjects with CKD (152/560 vs. 147/905; χ^2=25.3; P<0.0001). This was also true for coronary artery disease, cerebrovascular disease and peripheral vascular disease when analysed separately. Logistic regression analysis identified higher age, higher urine ACR, lower eGFR and lower cholesterol as independent risk factors for CVD. Patients with CKD at baseline had a significantly higher incidence of a new cardiovascular event (24/513 vs. 20/849; χ^2=5.5; P=0.02) and new cardiovascular event or death over 1 year (33/522 vs. 28/857; χ^2=7.2; P=0.007). Logistic regression analysis identified past history of CVD as the most important determinant of new cardiovascular events. We therefore analysed a subgroup of 1088 subjects without a history of CVD at baseline separately. Those with CKD at baseline evidenced a higher incidence of a new cardiovascular event (14/375 vs. 10/713; χ^2=6.2; P=0.013) and new cardiovascular event or death over 1 year (19/380 vs. 14/717; χ^2=7.9; P=0.005). At baseline there were no significant differences between these groups with respect to gender, ethnicity, smoking status, body mass index, blood pressure, cholesterol or HBA_{1c}.

Conclusions: We conclude that CKD is a risk factor for CVD and death even in patients already at high risk as a result of diabetes.

MP137 METFORMIN, CHRONIC KIDNEY DISEASE, AND LACTIC ACIDOSIS: IS METFORMIN ABSOLUTELY CONTRAINDICATED?

M.C. McCloskey, J. Smyth, W. Marshall, N. Leonard. *Renal Unit, Ulster Hospital Dundonald, Belfast, United Kingdom*

Introduction and Aims: The UK prospective diabetes study showed that metformin was associated with a lower mortality from cardiovascular disease than sulphonylureas or insulin in obese patients with type 2 diabetes mellitus, as well as reduced all cause mortality. However, concerns remain about its side effects, especially the perceived risk of lactic acidosis in the presence of chronic kidney disease (CKD). This may result in many patients with type 2 diabetes being denied metformin therapy [1,2]. We aimed to assess the incidence of metformin induced lactic acidosis over a seven year period, within our hospital.

Methods: Data was retrieved from a computerised database, laboratory records and individual case note review for patients admitted over a 7-

year period, from 01/01/2000 until 31/12/2006. Diagnostic codes searched included metabolic acidosis, lactic acidosis, metformin, or glucophage. Renal function at presentation, at baseline, and the presence of a clearly identified precipitating illness were recorded. (N = 205 401)

Results: Three cases of lactic acidosis in patients prescribed metformin were identified. Each case had a precipitating illness; dehydration secondary to gastroenteritis in 2 cases and urinary sepsis in 1 case. Only one patient had baseline CKD (creatinine of 135mmol/l).

Conclusions: The incidence of metformin induced lactic acidosis reported in this study is significantly lower than predicted in the literature, which quotes an estimated incidence of 0–0.09 cases per 1000 pt years [1,2].

A Cochrane review of 206 comparative trials and cohort studies in patients with type 2 diabetes who were treated with metformin and had no contraindications to its use, found no evidence of increased risk of developing fatal/non-fatal lactic acidosis in metformin treated patients. They also found no difference in lactate concentrations between metformin and non-biguanide treated patients. Several reports found that physicians have increasingly ignored contraindications to prescribing metformin and yet the incidence of lactic acidosis has remained very low. The majority of case reports relating metformin to lactic acidosis report at least one other disease/acute illness that could result in lactic acidosis [1,2]. In our analysis each case had a precipitating illness.

Metformin provides a greater degree of cardiovascular protection than expected from antihyperglycaemic actions alone, and is the drug of choice for persons with type 2 diabetes. Further studies are required in order to accurately quantify the risk, if any, of metformin induced lactic acidosis in persons with CKD [1,2].

References: 1. Jones et al. Contraindications to the use of metformin. *BMJ* 2003; 326 (7379): 4

2. Tahrani et al. Metformin, heart failure, and lactic acidosis: is metformin absolutely contraindicated? *BMJ* 2007; 335: 508-512.

MP138 OUTCOMES IN PATIENTS WITH RENAL FAIULRE AND MULTIPLE MYELOMA

Shona Methven, Nicola Joss, Jonathan Fox. *Renal Unit, Glasgow Royal Infirmary, Glasgow, United Kingdom*

Introduction and Aims: Renal disease in multiple myeloma presents in a variety of ways. We present data on the severity of renal failure, frequency of renal biopsy, frequency of renal replacement therapy (RRT) and survival in patients diagnosed with multiple myeloma in a single centre.

Methods: Patients attending the Renal Unit between 1989 and March 2006 with a diagnosis of multiple myeloma were identified from the electronic patient record (EPR). Data was collated from the EPR and statistical analyses were carried out using Excel and SPSS for Windows version 11.5.

Results: *Baseline characteristics:* The characteristics of the patients, at the time of referral, are shown. 120 patients were identified, 60.7% were male.

Table 1. Baseline characteristics

	Mean Value	Standard deviation
Age (years)	65.5	11
Serum Creatinine (μmol/l)	400*	200, 716
eGFR (MDRD) (ml/min)	11.5*	6, 25
Haemoglobin (g/dl)	10	2.2
WCC ($\times 10^9$)	7.7	5.1
Platelets ($\times 10^9$)	185	100
Serum Albumin (g/l)	32.6	7.3
Adjusted Calcium (mmol/l)	2.4	0.3

*Median (Interquartile range).

Renal Failure at Time of Referral: A diagnosis of acute renal failure was made in 30 patients on the basis of recovery from RRT or a 20% fall in creatinine six weeks post referral. Of those with chronic renal failure, 37% of patients were referred at Chronic Kidney Disease stage 5.

Renal Biopsy: Thirty-four patients (27.9%) had a renal biopsy. The histological diagnoses are shown. There was no statistically significant difference in age, serum creatinine, eGFR, or serum albumin between the biopsy group and the non-biopsy group.

Renal Replacement Therapy and Renal Recovery: Fifty-three patients (43.4%) received RRT and 15 of those recovered renal function. Of those who did not receive renal replacement therapy, 15/69 patients (21.7%) showed evidence of renal recovery, as defined above. 19 patients were excluded as they died within 6 weeks of referral.

Table 2. Renal biopsy diagnosis

Histological Diagnosis	Number of patients
Cast nephropathy	13
AL amyloidosis	9
Light chain disease	3
Heavy chain disease	1
Acute interstitial nephritis	4
Acute interstitial nephritis plus cast nephropathy	1
Acute tubular necrosis	1
Acute tubular necrosis plus cast nephropathy	1
Acute tubular necrosis	2

Survival: Overall, median patient survival from time of referral was 13.7 months (95%CI 6.0, 21.3) with a 1-year survival of 52.1% and 5-year survival of 22.5%. Median survival in the group of patients who received RRT (from date of referral) was 23.0 months (95% CI 8.3, 37.8). In comparison, survival in the non-RRT group of patients was 16.5 months (95% CI 8.8, 24.3). There was no statistically significant difference between these groups (p=0.58).

Conclusions: A renal biopsy should not be systematically performed, however, it can be useful in predicting the reversibility of renal failure and to identify glomerular lesions in patients with albuminuria over 1g/day.

Renal failure in patients with multiple myeloma often presents late, frequently requires renal replacement therapy, and has a poor prognosis. However the prolongation of life achieved in the dialysis group such that the median survival was identical to those with milder renal failure is considered to be a significant benefit to these patients and justifies offering RRT.

MP139 EXPLANATION MODEL OF THE EVOLUTION OF THE END-STAGE RENAL DISEASE (ESRD) IN THE BASQUE COUNTRY, 1991-2002

Ramón María Saracho Rotaeche[1], María Teresa Rodrigo[1], Aurora Argoitia Urresti[1], Iñigo Moina Eguren[1], Fernando Viana Apraiz[1], Gorka García Eruzkin[1], Ildefonso Lampreabe Gaztelu[1], Gema Ariceta Iraola[1], Ramón Ruiz de Gauna[1], Román Aguirre[1], Antonio Maza[1], Ibon Martínez Arranz[2], Ángela Magaz Lago[2]. *[1]Basque Country Renal Registry, Bilbao, País Vasco, Spain; [2]Investigation and Studies, Grupo ALBOR-COHS, Bizkaia, País Vasco, Spain*

Introduction and Aims: The ESRD incidence is explained in The Basque Country among the years 1991 at 2002 through a Poisson regression model according to gender and age group at the start of Renal Replacement Therapy (RRT) and the evolution of these two variables in the general population from the Basque Country. This pattern is used to make a comparison between the observed cases since 2003 with the expected cases in the same years.

Methods: Incident patient residents in the Basque Country. New cases, 1991-2006, according to gender and age group (0-29 yrs, 30-44 yrs, 45-64 yrs, 65-74 yrs, >75 yrs). The population changes in 1991-2006 have been considered in the incidence rates.

Results: In the period 1991 to 2002 the risk increases in different measure according to age group, the observed increase in the relative risk (RR) of 1.5 (CI95% RR: 1.1-2.2) in the 65 to 75 years and of 7.1 (CI 95% RR: 3.1-16.9) in more 75 years old. Chi-square analysis of expected cases vs observed cases in 1992-2002 did not differ significantly ($\chi^2(119) = 138.35$, p=0.108).

Chi-square analysis of expected cases vs observed cases in 2003-2006 differ significantly ($\chi^2(39) = 96.37$, p=0.001). An overestimation (the proportion was 40%) in the number of incident patients exists in 2006.

Conclusions: A real increase on the risk exists between the years 1991 and 2002, but this increase seems not to remain in the last years. We could speak of a balance in the incidence rate in the Basque Country.

MP140 RENAL SCARRING IN CHILDREN ONE YEAR AFTER ACUTE PYELONPHRITIS: EVALUATION WITH DIMERCAPTOSUCCINIC ACID SCINTIGRAPHY

Neamatollah Ataei, Abbas Madani, Seyed Taher Esfahani. *Nephrology, Childrens Hospital Medical Center School of Medicine, Tehran, Iran*

Introduction and Aims: Early diagnosis, treatment, investigation and follow up of children with urinary tract infection (UTI) are needed to minimize renal scarring. The sites of new renal parenchymal scarring corresponded to those sites of acute pyelonephritis (APN) seen on initial technetium -99^{m}-labelled dimercaptosuccinic acid (DMSA) renal scans. The goal of this prospective study was to assess the occurrence of persistent renal parenchymal lesion in children, 1 year after admission with a first APN.
Methods: Fifty two patients (0boy, 52 girls) aged between 2 months and 12 years (mean 4 years -1 month) were included in the study. The progression of renal lesions was assessed by topographic analysis of each lesion. For all patients a voiding cystourethrography (VCUG) early in the course of the illness, generally within 5 -7 days of hospitalization and ultrasonography (US were done. A kidney with regular shape on DMSA and a tracer uptake which appeared to be homogenous was considered as normal. Single or multiple cortical defects and focal or diffuse patterns in one kidney were considered abnormal. We defined renal scars as persistent changes in the same location; complete or partial reversible lesions as complete or partial resolution of changes that had been observed on first DMSA; and new lesions not present during the acute phase of tract UTI. The involvement of each kidney was visually graded as mild (focal defect in uptake), moderate (uptake of renal radionuclide of 20 – 40%) and severe (shrunken kidney with uptake less than 20%).
Results: During the acute phase of UTI, renal parenchymal changes in DMSA were found in 49 out of 52 (94.23%) children. In the second assessment, renal parenchymal changes were found in 44 out of 49 (89.8%) children. In the third evaluation DMSA scan identified complete remission in 23%, mild involvement in 67% and moderate in 9.52% of children, and no patients had severe renal involvement. br]Topographic analysis of the 162 focal lesions showed that 24.3% were localized to the upper poles, 6.7% to the middle third, and 20.83% to the lower poles of the kidneys. In our experience, Vesicoureteral reflux (VUR) was found in 6/9 kidneys (66.6%) with evidence of APN on DMSA scan. It was absent also in 79/93 kidneys (84.9%) with renal involvement. In this series during the acute phase of study DMSA was found abnormal in 86 out of 104 (82.61%) renal unit, while US showed abnormality only in 18 out of 104 (17.14%) renal unit.
Conclusions: This study revealed a high frequency of changes on DMSA scan in 94.23% of children during the acute phase of UTI. Additionally, we found out complete or partial remission in majority of children (72%) one year after APN. The results of this study suggest that DMSA scan is more sensitive than US in detecting renal parenchymal inflammation in children with APN. No significant correlation was found between presence of VUR and renal parenchymal involvement.

MP141 ESTABLISHING CHRONICITY OF KIDNEY DISEASE TO PROVIDE A MORE ACCURATE PREVALENCE OF CHRONIC KIDNEY DISEASE (CKD)

Laura Clark[1], Gordon Prescott[2], William Simpson[3], Cairns Smith[2], Nicholas Fluck[4], Alison MacLeod[1], Tariq Ali[1]. *[1]Medicine & Therapeutics, University of Aberdeen, Aberdeen, United Kingdom; [2]Public Health, University of Aberdeen, Aberdeen, United Kingdom; [3]Clinical Biochemistry, NHS Grampian, Aberdeen, United Kingdom; [4]Renal Unit, NHS Grampian, Aberdeen, United Kingdom*

Introduction and Aims: CKD is now recognised to be a common condition. Despite this the epidemiology and natural history of CKD has not yet been fully explored. Previous studies may have overestimated the prevalence of CKD by relying on a single abnormal creatinine/eGFR measurement and few have referred to patients' case records to identify associated co-morbidities. The burden of CKD is, therefore, unclear. We aim to demonstrate with increased accuracy the prevalence of CKD and identify its associated co-morbidities.
Methods: 5751 patients were identified with at least one creatinine $\geq$ 130μmol/L in females and $\geq$150μmol/L in males (threshold values) in a 6 month period in 2003 in Grampian, Scotland (population 523390). Patients with ARF defined by ADQI (474) were excluded. 2315 patients had CKD defined by having 3 creatinines above the threshold spaced 1 month apart and another 324 were already on RRT. 1918 could be not be classified initially but 1228 of these had CKD defined by median eGFR values of $<$60mls/min/1.73m^2 and/or the presence of markers of kidney damage. Patients were staged according to their index creatinine (converted to eGFR using the abbreviated MDRD formula). Patient case records were searched for co-morbidities and for whether referral to a nephrologist had occurred.
Results: Of the 5751 patients 3955 patients were identified as having CKD, 474 patients (8%) had ARF, 632 (11%) were excluded as they were visitors or case records missing and the remaining 690 patients (12%) had no definite evidence of CKD using our criteria. 88695 people had a blood test for serum creatinine measurement during the 6 month identification period (16.9% of Grampian population). Therefore 4.5% of blood sample population had evidence of CKD (equivalent to a point prevalence of 9129 per million adult Grampian population, 5038 pmp when age/sex adjusted). The median age was 78.6 years and 65.8% were in Stage 3, 30.7% in Stage 4 and 3.4% in Stage 5 (RRT patients excluded). The commonest co-morbidities were ischaemic heart disease and hypertension (52% and 40%). The odds of being referred to a nephrologist were lower with increasing age (OR 0.94, CI 0.93-0.94, p$<$0.001) and higher in males and hypertensives (OR 1.73, CI 1.39-2.14, p$<$0.001 & OR 1.89, CI 1.53-2.35, p$<$0.001 respectively).
Conclusions: The prevalence of CKD in this predominantly elderly population is lower than other prevalence studies. This may be partly because the patients were selected due to having a blood test and at least one creatinine $\geq$130/150μmol/L. However we have used robust methods to ensure chronicity of disease and demonstrated that 20% of those with an elevated creatinine had no definite evidence of chronicity. Thus, other prevalence studies could be overestimating the prevalence of CKD by relying on only single creatinine measurements for diagnosis.

MP142 EFFECTS OF AN EXERCISE PROGRAMME ON UREMIC SYMPTOMS AND FUNCTIONAL PARAMETERS OF PATIENTS WITH RENAL FAILURE

George Kosmadakis[1], Alan Bevington[1], Alice Smith[1], Emma Clapp[1], Joao Viana[1], John Feehally[1]. *[1]John Walls Renal Unit, Department of Infection, Immunity & Inflammation, University of Leicester, Leicester, United Kingdom; [2]*

Introduction and Aims: Patients with renal failure suffer from poor physical functioning, muscle wasting and excessive tiredness. Their resulting severe deconditioning is associated with poor quality of life. Exercise has been shown to lead to improvements in parameters of physical performance as well as metabolic, functional and cardiovascular factors. The aim of the present study was to evaluate the effects of an exercise programme on the frequency and intrusiveness of 11 symptoms commonly associated with kidney diseases, as well as general concerns and parameters of physical, social, emotional and functional well-being.
Methods: Eight patients (7M and 1F) aged 51.9$\pm$14.1 years (range 30-73 years), 5 with Chronic Kidney Disease Stage 4 and 3 on Peritoneal Dialysis, exercised for 30 minutes at least 5 times a week for a total period of one month. The exercise programme consisted of brisk walking at a speed that was adjusted to correlate to a Borg Rating of Perceived Exertion Rate (RPE) of 12-14, and a heart rate range that was elicited by the target RPE. Before and after the exercise period haematological and biochemical parameters were measured as well as quality of life parameters in the form of the Leicester Uraemic Symptoms Score (LUSS) and FACIT-Sp: Functional Assessment of Chronic Illness therapy-Spirituality Scale Quality of Life (QOL) Tool (Pugh-Clarke et al. EDTNA-ERCA Journal 32,167-71,2006).
Results: After 30 days of exercise there were no significant changes in haematological parameters (Hemoglobin levels, White blood cell counts, Platelet counts) nor in the majority of biochemical parameters (Urea, Creatinine, eGFR measured with the MDRD formula, eCalcium, Phosphate, Calcium-Phosphate product, Sodium or Albumin). There was a small increase in serum Potassium levels (pre-exercise 4.4$\pm$0.5 meq/l vs post-exercise 4.7$\pm$0.6 meq/l, p=0.035). Nevertheless, there was a significant improvement in uremic symptoms (reduction of the LUSS (p=0.021)) and improvement in the part of FACIT-Sp that was concerned with emotional well-being of the patients (p=0.026).

Conclusions: As little as one month of medium intensity exercise therapy can improve the perceived uremic symptoms and the emotional well-being of patients with chronic kidney disease.

MP143 VITAMIN D LEVELS AND MORTALITY AMONG CHRONIC KIDNEY DISEASE (CKD) PATIENTS

Pietro Ravani[1], Paola Pecchini[1], Gianluigi Tripepi[2], Francesca Mallamaci[2], Fabio Malberti[1], Carmine Zoccali[2]. *[1]Divisione di Nefrologia e Dialisi, Istituti Ospitalieri, Cremona, Italy; [2]Fisiopatologia delle Malattie Renali, CNR-IBIM, Reggio Calabria, Italy*

Introduction and Aims: Vitamin D deficiency has been linked to cardiovascular disease and early mortality in hemodialysis patients. We sought to determine whether the same association exists also in an incident cohort of 170 CKD patients enrolled before they started dialysis.
Methods: Blood levels of 25-hydroxy-vitamin D (25D) were measured by RIA. Cox regression analysis was used to model time to death as a function of 25D levels. Covariates considered for adjustment included clinical characteristics, baseline glomerular filtration rate (GFR, MDRD formula), traditional cardiovascular risk factors, serum C reactive protein, fibrinogen, homocysteine, proteinuria, and concomitant therapies. Progression to dialysis was considered as a time-varying covariate.
Results: Mean age at enrolment was 70 (SD 11) years, 63% patients were male, 26% diabetic and 57% had background cardiovascular complications. Baseline GFR ranged from 10 to 90 (average:34±18) ml/min/1.73 m^2. At baseline, plasma levels of 25D were directly related to GFR (r=0.18, P=0.021). After a mean follow-up of 46.5 months (range 1.1, 82.1) 78 patients died (66% for cardiovascular causes). Of these patients 21 had previously started dialysis. Higher levels of 25D at baseline [HR per 1 ng/ml =0.96, 95% CI 0.94, 0.99] predicted longer patient survival. In the final adjusted model, levels of 25D higher that the median value (18 ng/ml) significantly predicted lower mortality rates as compared to values lower than the median [HR 0.56, 95% CI 0.35, 0.91].
Conclusions: In patients with moderate to severe CKD plasma 25-hydroxy-vitamin D is directly related to the GFR and represents a strong and independent inverse predictor of mortality. This novel finding confirms that Vitamin D is an important biomarker of cardiovascular disease in renal patients and further expands the implications of previous observations in End Stage Renal Disease.

MP144 EIGHTY YEARS-OLD OR OLDER PATIENTS REFERRED TO NEPHROLOGY IN A SPANISH HEALTH AREA

Pedro J. Labrador[1], Teresa Mengotti[2], Montaña Jimenez[2], Jorge Labrador[1], Flor Vicente[2], Emilio Fuentes[2], Javier Martin-Oncina[2]. *[1]Nephrology, Virgen del Puerto Hospital, Plasencia, Caceres, Spain; [2]Clinical Analysis, Virgen del Puerto Hospital, Plasencia, Caceres, Spain*

Introduction and Aims: Ageing in European population is a reality. So very older people are frequently referred to Nephrology care. The aim of this study was to study the characteristics of very elderly people referred to a Spanish Nephrology Department compared to younger people.
Methods: We studied all patients referred to our Nephrology Department in two years (between October 2005 and September 2007) from a reference Public Health Area population higher than 100.000 (20% older than 65 years). During the study period 976 patients were referred. Eighty years-old or older patients were 171 (17.5%), 56.7% women. Data from Primary Care referral or secondary care, referral causes, serum creatinine levels, estimated glomerular filtration rate (eGFR), K/DOQI stage, blood pressure, body mass index and obesity classification were analysed.
Results: Very elderly patients were referred with a lower mean eGFR (37 mL/min/1.73m^2, vs. 59 mL/min/1.73m^2). So 37.5% in this group were referred at 4-5 K/DOQI stages vs. 17.6% in younger group. Very older patients were mainly referred due to renal dysfunction (73.1%) while younger patients were by other causes (45.1%). Very elderly patients were 23.9% of patients from Primary Care vs. 14.1% from secondary care.
Patients over 80 had higher pulse pressure. Overweight and obesity were frequent in two groups and there was not difference between the groups.
Conclusions: One of every six Nephrology referred patients were very elderly. They were mainly referred due to impaired renal function, and from Primary Care. There were not differences in blood pressure control, except pulse pressure, or obesity between groups.
Overweight and obesity is present in 75% of patients referred to nephrology, independently of studied groups.

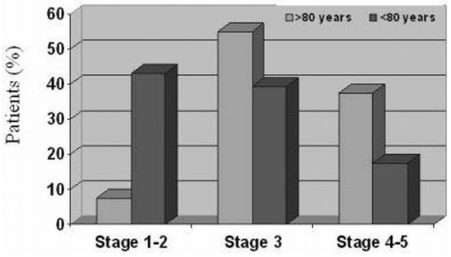


Figure 1. Distribution of patients according to K/DOQI stages.

	Eighty or older patients N=171	Patients under 80 N= 805
Age (years ± SD)	83.9 ± 3.4	60.8 ± 15.8
Creatinine (mg/dL)	1.76 ± 0.67	1.42 ± 0.79
MDRD (mL/min/1.73m2)	37.1 ± 16.3	58.6 ± 30.9
SBP (mmHg)	150 ± 28	145 ± 26
DBP (mmHg)	79 ± 14	83 ± 14
MBP (mmHg)	103 ± 17	103 ± 16
PP (mmHg)	72 ± 24	63 ± 21
BMI (kg/m2)	29.2 ± 5.4	29.4 ± 5.6
Overweight (%)	35.3	36.2
Obesity I (%)	30.7	29.2
Obesity II (%)	7.2	8.9
Obesity III (%)	3.9	4.8

Table 1. Demographic, laboratory and clinical data

Diabetes mellitus – Basic research 2

MP145 LATE BLOCKADE OF THE RENIN-ANGIOTENSIN SYSTEM IN THE OBESE ZUCKER RAT – EFFECTS OF ACE INHIBITION AND ANGIOTENSIN II TYPE 1 RECEPTOR ANTAGONISM

K. Sebekova[1], M. Lill[2], P. Boor[1], A. Heidland[3], K. Amann[2]. *[1]Slovak Medical University, Bratislava, Slovakia; [2]Univ. Erlangen-Nuernberg, Erlangen-Nuernberg, Germany; [3]Univ. Würzburg, Würzburg, Germany*

Introduction and Aims: The effects of the late administration of angiotensin (Ang) II converting enzyme inhibitor (ACEI), perindopril, and the Ang II receptor 1 blocker (ARB), candesartan, on renal function, renal morphology, blood pressure, metabolic and oxidative status were investigated in obese Zucker rats, an experimental model of type 2 diabetes mellitus associated nephropathy.
Methods: Forty 4-week-old obese Zucker rats were uninephrectomized, and fed a high protein diet to accelerate renal damage. After 16 weeks lag-period, rats were randomized into 4 groups (n=10 each) with comparable proteinuria: 1) control group (CTRL) sacrificed immediately for baseline data; and 3 groups daily gavaged for 8 weeks with either 2) placebo (PLAC; 1% water solution of hydroxyl-ethyl-cellulose -HEC); 3) perindopril (PER in HEC; 1 mg/kg/d) or 4) candesartan (CAN in HEC; 10 mg/kg/d). Renal function and morphology, metabolic parameters and those characterizing oxidative status (advanced oxidation protein products - AOPPs, erythrocyte glutathioneperoxidase activity - GPX) were determined.
Results: Both drugs reduced blood pressure (PER by 15.6%, CAN by 9.5%), and reversed proteinuria (PER to 32% and CAN to 37% of pre-treatment values, while in the OZR-PLAC rats 1.2-fold increase was observed). They

ameliorated the glomerulosclerosis injury score (CTRL: 1.13±0.18, PLAC: 1.71±0.22, p<0.01; PER: 1.19±0.38, CAN: 1.33±0.31, both p<0.001 vs. PLAC), mesangiolysis score (CTRL: 0.76±0.18, PLAC: 1.46±0.17, p<0.01; PER: 0.52±0.10, CAN: 0.81±0.41, both p<0.001 vs. PLAC), and preserved podocyte and endothelial cell numbers. CAN treatment resulted in a decline in circulating AOPP levels. Both drugs forestalled the in OZR-PLAC group decreased GPX activity in red blood cells.

Conclusions: The late intervention with perindopril and candesartan in established diabetic nephropathy in uninephrectomized obese Zucker rats halted the progression of renal injury, preserved glomerular cells and capillaries, and even induced a regression of mesangiolysis. These beneficial effects could partially be attributed to the blood pressure-lowering action of ACEI and ARB. In case of candesartan, additional mechanisms of salutary action are to be considered, such as reduction of oxidative stress and improved energy metabolism.

Disclosure: The study was supported in part by the Institut de Recherches Internationales Servier, Courbevoie, France, by the Deutsche Forschungsgemeinschaft (DFG, SFB423, project B8/Z2) and by the Verein zur Bekämpfung der Hochdruck- und Nierenkrankheiten Würzburg e.V., Germany.

MP146 INTIMA/TUNICA MEDIA THICKNESS IN DIABETIC RAT RENAL ARTERIOLE AND ITS RELATION TO BONE MATRIX PROTEINS AS WELL AS INFLAMMATORY FACTORS

Songmin Huang, Anju Zhao, Santao Ou, Zhejun Chen, Xueli Lai. *Department of Nephrology, West China Hospital of Sichuan University, Chengdu, Sichuan, China*

Introduction and Aims: To explore the effect of bone matrix proteins and inflammatory factors on diabetic rat renal arteriole.

Methods: Diabetic rat model was established by streptozotocin (STZ). Rats were divided into diabetic group (DN) and control group (N). Rats were sacrificed at 4^{th}, 12^{th} and 24^{th} week. The protein and mRNA expression of core-bind factor alpha-1 (Cbfa1),bone morphogenetic protein-2 (BMP-2),monocyte chemoattractant protein-1 (MCP-1)and matrix Gla Protein (MGP)in renal arteriole were detected by immunohistochemistry, hybridization in situ and Real-Time PCR at each time point.

Results: Immunohistochemistry stain and in-situ hybridization showed apparently higher Cbfa1,BMP-2 and MCP-1 expression in renal small arteryarteriole of DN group from 4 to 24 week comparing with N group, and reaching peaks at 24 week. Real-Time PCR showed that the level of MGP mRNA was evidently increased at 4^{th} week, slightly decreased at 8^{th} week and lowest at 24^{th} week in DN group; the level of BMP-2 mRNA began to increase from 4 to 24 week, and reached peak at 24^{th} week in DN group. Immunofluorescence-histochemistry indicated that the intima of renal arteriole showed red fluorescence, while tunica media showed green fluorescence. The ratio of intima and tunica media thickness had no difference in DN and DN-F group compared with N group at 4^{th} week; and show difference at 12^{th} week, then reached obvious level at 24^{th} week. A strong positive correlation between Cbfa1 and BMP-2 levels was found, Cbfa1 and BMP-2 were significantly negative correlated with MGP. No significant correlation was noticed among BMP-2, MGP and MCP-1. The ratio of intima and tunica media thickness showed obvious positive correlation with Cbfa1, BMP-2 and MCP-1.

Conclusions: Cbfa1 and BMP-2 expression could be noticed in renal arteriole in earlier stage of DN. The expression of MGP is gradually deceased with time. The ratio of intima and tunica media thickness remained unchanged in earlier period, then changed slightly in mid-period, and finally reached obvious level in later period of DN.

MP147 CD95 (Fas) EXPRESSION DISTURBANCES IN PATIENTS WITH DIABETIC NEPHROPATHY

Valentina Galchinskaya, Polina Semenovykh, Ivan Topchiy, Igor Kondakov, Anna Shitova. *Nephrology Department, Institute of Therapy Named after L. Malaya of AMS of Ukraine, Kharkov, Ukraine*

Introduction and Aims: Apoptosis, a mode of cell death which is mediated by the activation of the caspases and results in the cleavage of protein substrates and DNA fragmentation, has been proposed to cause loss of kidney cells in diabetic kidney disease. CD95 (Fas) antigen is a polypeptide that plays a role in the programmed sequence of events leading to apoptosis of various cell types. In this study we examined Fas expression on peripheral blood leukocytes from type II diabetic patients at different clinical stages of diabetic chronic kidney disease. As both metabolic and hemodynamic factors have been implicated in the pathogenesis of diabetic nephropathy we also examined the role of different clinical and biochemical parameters as potential predictors of apoptotic changes.

Methods: The investigation was done on freshly isolated peripheral blood-derived leukocytes from 55 patients with diabetic nephropathy and 10 healthy subjects. There were no significant differences in age and body weight between the groups. Peripheral blood leukocytes were isolated by standard techniques using Ficoll-Hypaque gradient density centrifugation. For stimulation assays, $1x10^6$cells from both patient groups and controls were preincubated with angiotensin II (10^{-7}M) and glucose-modified protein 50 (μg/ml). The cells were incubated with monoclonal antibodies to CD95 (anti-Fas), and the detection was accomplished by biotin-extravidin peroxidase method and light microscopy examination.

Results: CD95 (Fas)-positive cells were more numerous in both patient groups than in controls, irrespective of the experimental conditions, and their percentage was always significantly higher in chronic renal failure patients than in patients with earlier stages of diabetic nephropathy. Such pathogenic factors of diabetic nephropathy development as angiotensin II and glucose-modified protein significantly stimulate Fas expression but glycated protein showed more intensive stimulating effect. CD95 (Fas)-positive cells percentage under the influence of glycated protein reached 58,3±5,8%, while under angiotensin II - 40,2±4,6%, control – 29,8±3,1%. Significantly higher (67,5±5,9%) Fas expression was measured in cells with angiotensin II and glycated protein simultaneously. Last may testify to additivity of their effects and to different mechanisms of their influence on Fas expression.

Conclusions: Apoptotic activity was enhanced both in patients with early and in those with advanced clinical impairment. The development of diabetic nephropathy is accompanied by disturbances of Fas expression under angiotensin II and glucose-modified protein influence. These findings suggest that in diabetic nephropathy patients enhanced Fas expression is associated with chronic cell activation and induced by numerous stimuli including hyperglycemia, proteinuria, uremia, other metabolic and hemodynamic factors.

MP148 PROTECTIVE ROLE OF NEBIVOLOL AGAINST RENAL OXIDATIVE STRESS DAMAGE IN ZUCKER DIABETIC FATTY RATS

Jorge Toblli, Gabriel Cao, Leda Oliveri, Margarita Angerosa. *Laboratory of Experimental Medicine, Hospital Alemán, Buenos Ares, Argentina*

Introduction and Aims: One of the defects in metabolic syndrome (MS) and its associated diseases is excess cellular oxidative stress (OxS) and oxidative damage. Additionally, increased sympathetic nervous system activity is a recognized component in MS. In this study, we evaluated the possible benefit of nebivolol (N), a third-generation highly selective beta-blocker (BB) with additional vasodilating activity, versus the traditional BB atenolol (AT), regarding renal damage by OxS in a rat model of MS.

Methods: Three groups of ZDF rats and one of Lean Zucker rat (LZR) as control: During six months G1 (ZDF without treatment); G2 (ZDF N 10mg/kg/day); G3 (ZDF AT 100mg/kg/day) and G4 (LZR without treatment). Animals were killed at 6 months of treatment. In kidney homogenates, TBARS, GSH/GSSH ratio, CuZnSOD, Catalase and GPx were evaluated. LM and Immunohistochemistry (IHC) techniques using antibodies against Transforming Growth Factor-b1 (TGFb1) and endothelial nitric oxide synthase (eNOS) were also performed.

Results: At 6months: SBP (mmHg) G1 168±5, G2 134±3*, G3 132±4, G4 122±4**; CrCl. (ml/min) G1 2.1±0.2, G2 2.6±0.2*, G3 2.3±0.1, G4 3.2±0.2**. Proteinuria (mg/day) G1 267±27, G2 65±15*, G3 210±45, G4 7±2**. *versus ZDF and ZDF+AT p<0.01 **versus all groups p<0.01. Oxidative stress in kidney homogenates: TBARS (nmol MDA/mg prot) G1 212.2±26.2*, G2 140.7±9.9, G3 189.9±16.8**, G4 132.8±12.1; GSH/GSSG ratio G1 3.2±0.4, G2 6.9±0.3***, G3 4.0±0.6, G4 8.5±0.8*; CuZn SOD (U/mg prot) G1 1.2±0.2, G2 5.4±0.3***, G3 3.7±0.6, G4 10.3±0.9*; Catalase (U/mg prot) G1 34.9±6.9, G2 67.7±7.0***, G3 40.3±3.9, G4 83.0±9.6*, GPx (U/mg prot) G1 297.7±23.9, G2

237.9±20***, G3 285.9±11.2, G4 222.8±18.9***. *versus all groups p< 0.01 **versus ZDF+AT and LZR p< 0.01 ***versus ZDF and ZDF + AT p< 0.01. LM and IHC at 6months: Glomerulosclerosis (%) G1 29.0±7.2*, G2 8.1±2.9**, G3 16.0±3.3***, G4 2.8±1.8*. Tubulointerstitial Fibrosis (%) G1 16.0±3.2†, G2 6.8±3.7**, G3 13.0±3.8***, G4 2.0±1.5. TGFb1 (%) G1 27.0±3.8*, G2 6.6±1.6‡, G3 22.0±3.4***, G4 3.8±1.7. eNOS (%) G1 3.6±2.1*, G2 15.0±3.3‡, G3 6.4±1.5***, G4 14.0±1.5. * versus all groups p < 0.01 **versus ZDF+AT and LZR p< 0.01 ***versus LZR p< 0.01 †versus ZDF+N and LZR p< 0.01. ‡versus ZDF+AT.

Conclusions: Antioxidant defenses were preserved by N with a reduction in OxS parameters when compared with AT. These data suggest that beyond reducing blood pressure, N presents a real benefit against renal damage by OxS in this rat model of MS

MP149 ACE INHIBITION ESCAPE PHENOMENON IN PATIENTS WITH TYPE 2 DIABETES AND DIABETIC NEPHROPATHY

Natalia Trubitsyna, Gulnara Katsya, Svetlana Kuharenko, Elena Drozdova, Alexsandr Iliin, Andrey Alexsandrov, Minara Shamkhalova, Alexsandr Deev, Marina Shestakova. *Diabetic Nephropathy, Endocrinology Research Center, Moscow, Russian Federation*

Introduction and Aims: We evaluated the prevalence of the ACE inhibition escape phenomenon during long-term ACE inhibitors (ACEI) treatment in patients with type 2 diabetes and diabetic nephropathy (DN).

Methods: A total 62 patients (37 men, 25 women) with type 2 diabetes and DN who received ACEI were studied. Escape of ACE inhibition was defined as an increase in plasma angiotensin II (AII) more than 50,6 pg/ml. Upper limit of normal range was calculated (mean±1SD) from values of control subjects, who involved age-matched normotensive subjects without diabetes. Dietary salt intake was controlled.

Results: Duration of ACEI treatment was 6.6±3.4 years. Plasma AII level in control group was 34.5±16.1 pg/ml. Patients were divided into two groups according to their levels of AII: more than 50,6 pg/ml -escape group (EG), less than 50,6 pg/ml - non-escape group (NEG). ACE inhibition escape occurred in 24 patients (39%). There were no significant differences between the groups in age, duration of diabetes, albuminuria, lipid levels, 24-h blood pressure, duration of ACEI treatment, diabetes control, hypertension management, 24-h urinary sodium. Patients in EG had a significantly higher cardiac interventricular septum thickness (p=0.02), more often had hypo- and akinetic segments of myocardium (p=0.03). Also they showed lower 24-h urinary potassium excretion (p=0.03), higher level of plasma endothelin and a bit higher degree of renal insufficiency (not statistically significant). Plasma renin concentration was higher in the EG (p=0.004). AII did not correlate with aldosterone levels in both groups. Higher level of AII was associated with increase level of erythropoietin (RR 4,33, CI 95% (0,95-12,04), p<0,05) and plasma renin activity (RR 5,2, CI 95% (1,13-24,3), p=0,03) and low level of endothelin –1 (RR 0,21, CI 95% (0,05-0,88), p=0,03).

Conclusions: A relatively large percentage of type 2 diabetics with DN is affected by ACE inhibition escape. It may explain the lack of reno-and cardioprotective effect of renin-angiotensin-aldosterone system blockade. Higher level of AII was associated with increase level of erythropoietin and plasma renin activity and low level of endothelin –1.

MP150 GLUCOSE UPTAKE IN MESANGIAL CELLS (MC): ROLE OF GLUCOSE TRANSPORTERS AND ANGIOTENSIN II

Carine Arnoni, Carla Lima, Priscila Cristovam, Daniela Vidotti, Mirian Boim. *Medicine - Renal Division, Federal University of São Paulo, São Paulo, Brazil*

Introduction and Aims: Mesangial cells (MC) proliferation and overproduction of mesangial matrix play a central role in the pathogenesis of diabetic nephropathy (DN). MC dysfunction arises in part from abnormally high cellular glucose uptake and metabolism. MC express both insulin dependent (GLUT4) and mainly insulin-independent (GLUT1) glucose transporter. This study evaluated the time-dependent effect of high glucose concentration on the expression levels of glucose transporters GLUT1, GLUT4 and fibronectin, as well as the rate of glucose uptake by MC.

Methods: MC were exposed to normal (NG, 10 mM) or high (HG-30 mM) glucose during 1, 4, 12, 24 and 72 hr. Glucose uptake was measured by 2-deoxy-D-glucose (^{3}H-2DG) method in the absence and presence of insulin (1U/ml). mRNA expressions were estimated by real time PCR and the protein levels by western blot technique.

Results: HG induced an initial (1, 4 and 12 hr) rise in GLUT1 expression returning to control levels after 72 hr whereas GLUT4 was overexpressed in latter periods (24 and 72 hr). Fibronectin levels were increased in all periods under HG stimulus. HG exposure during 4 hr induced a 40% rise in glucose uptake which was unaffected by insulin treatment. In contrast after 72 of HG stimulus glucose uptake was increased by 50% only under insulin stimulus. These results suggest that the increase in glucose uptake was initially mediated by GLUT1 and after more prolonged periods it was also dependent of insulin and thus of GLUT4. HG stimulates angiotensin II (AII) synthesis in the MC and we observed that losartan blunted the effects of HG on GLUT1, GLUT4 and fibronectin expressions as well as on glucose uptake.

Conclusions: HG environment stimulates glucose uptake by both insulin-independent and –dependent mechanisms, making these cells highly susceptible to both hyperglycemia and hyperisulinemia. The beneficial effect of the AII receptor antagonists in the DN may involve an inhibition of glucose uptake by MC.

MP151 REGULATION OF THE (PRO) RENIN RECEPTOR IN MESANGIAL CELL UNDER HIGH GLUCOSE STIMULUS

Luciana Pereira, Carine Arnoni, Mirian Boim. *Medicine - Renal Division, Federal University of São Paulo, São Paulo, Brazil*

Introduction and Aims: Many evidences indicate that high glucose concentration (HG) stimulates angiotensin II (AII) synthesis in mesangial cells (MC). Local synthesized AII may play a key role in the MC proliferation and matriz expansion leading to glomerulosclerosis and diabetic nephropathy (DN). The (pro)renin receptor was identified in MC and binding of (pro)renin to its receptor triggers a nonproteolitic activation of (pro)renin contributing to increase AII synthesis in the cell surface. Also, the stimulation of the (pro)renin receptor induces activation of the extracellular signal-regulated MAP kinase 1 and 2 (ERK 1/2). The aim of the present study was to evaluated whether HG environment induces modifications on (pro)renin receptor, fibronectin and ERK2 mRNA and protein expressions in MC. In order see the (pro)renin receptor is regulated by intracellular levels of AII, the effect of the AT1 receptor blocker, losartan, was also evaluated.

Methods: Human mesangial cells (HMC) were exposed during 24 hr to standard glucose concentration (Control, 10 mM D-glucose), high glucose (HG, 30 mM D-glucose), Losartan (L, 100nM losartan) and high glucose+losartan (HG+L). The mRNA expression levels for (pro)renin receptor, fibronectin, b-actin and ERK2, were estimated by real-time RT-PCR. Protein levels were analyzed by Western Blot. Both total and phosphorilated forms of ERK2 were evaluated by Western Blot.

Results: The hyperglicemic environment significantly increased the expression levels of (pro)renin receptor (5-fold) and fibronectin (2-fold) mRNAs, but had no effect on ERK2 mRNA expression. Losartan caused a reduction in (pro)renin receptor and fibronectin mRNA levels either under normal or high glucose stimulus. The protein expression was coincident with the mRNA expression for (pro)renin receptor, fibronectin and total ERK2, however the active phosphorilated form of ERK2 was higher and the inactive form was lower in HG group. Losartan blunted these effects.

Conclusions: The overexpression of (pro)renin receptor may contributes to increase AII generation in MC under HG condition. The upregulation of this receptor appears to be mediated by intracellular levels of AII. The activation of ERK2 by (pro)renin receptor may have a role in the mesangial cell proliferation observed during the progression of diabetic nephropathy.

MP152 MOLECULAR MECHANISM INVOLVED IN PROTECTIVE EFFECT OF LYCOPENE AGAINST DIABETIC NEPHROPATHY IN RATS

Anurag Kuhad, Kanwaljit Chopra. *Pharmacology Research Laboratory, University Institute of Pharmaceutical Sciences, UGC Center of Advanced Studies, Panjab University, Chandigarh, India*

Introduction and Aims: Diabetic nephropathy is a serious microvascular complication and one of the main causes of end-stage renal disease. Clinical

and experimental studies have revealed that increased oxidative stress and inflammation are the major pathophysiological mechanisms which are involved in the etiology of diabetic nephropathy. Lycopene, a carotenoid mostly found in tomatoes and tomato products, is known to possess potent antioxidant and anti-inflammatory properties and thus we aimed to examine its effect on renal function, oxidative stress, TGF-β, TNF-α, NFκβ and nitric oxide in streptozotocin (STZ)-induced diabetic rats.

Methods: Diabetes was induced by a single intraperitoneal injection of STZ (65 mg/kg) in rats. After 4 weeks of STZ injection, rats were divided into six groups: the control rats, diabetic rats and diabetic rats treated with lycopene (1, 2 and 4 mg/kg, orally) and lycopene per se group, from week 4 up till week 6. At the termination of the experiments, urine albumin excretion, urine output, serum creatinine, blood urea nitrogen, creatinine and urea clearance were measured. The levels of the renal oxidative stress markers malonaldehyde and glutathione and the antioxidant enzymes superoxide dismutase and catalase were measured in kidney homogenate. Inflammation was assessed by estimating TGF-β, a profibrotic cytokine, TNF-α, and NFκβ in the serum and kidney of diabetic rats.

Results: STZ-injected rats showed significant increases in blood glucose, polyuria, proteinuria and a decrease in body weight compared with age-matched control rats. After 6 weeks, diabetic rats exhibited renal dysfunction, as evidenced by reduced creatinine and urea clearance, and proteinuria along with a marked increase in oxidative stress, as determined by lipid peroxidation and activities of key antioxidant enzymes. There was significant increase in TGF-β and NFκβ in the serum and kidney of diabetic rats. Treatment with lycopene significantly attenuated renal dysfunction, oxidative stress and inflammation in the diabetic rats.

Conclusions: Systemic hyperglycemia is the universal trigger for diabetic nephropathy. Alleviated glucose concentration leads to activation of polyol pathway, hexosamine pathway and associated activation of PKC. All these metabolic events together lead to increased cytokine and growth factor production. Glucose induced oxidative damage and PKC activation leads to production of TGF-β, a profibrotic cytokine. This cytokine is known to cause glomerular hypertrophy and extracellular matrix expansion. Chronic hyperglycemia has also cause a surge in TNF-α and NFκβ in microvascular tissues and initiates renal damage. Lycopene, a powerful antioxidant with a singlet-oxygen-quenching capacity and anti-inflammatory molecule, attenuated renal dysfunction, oxidative stress and inflammation in diabetic rats. These results were further substantiated with a marked decrease in TGF-β, TNF-α and NFκβ level. The present study points towards the possible antioxidative and anti-inflammatory mechanisms being responsible for the renoprotective action of lycopene.

MP153 TOLL-LIKE RECEPTOR 4 GENE POLYMORPHISMS AND EARLY ONSET OF DIABETIC RETINOPATHY IN TYPE 2 DIABETES PATIENTS

Monika Buraczynska, Iwona Baranowicz-Gaszczyk, Kinga Buraczynska, Andrzej Swatowski. *Nephrology, Univ. Medical School, Lublin, Poland*

Introduction and Aims: Toll-like receptor 4 (TLR4) is an important mediator of the innate immune response. It has been implicated in modulating susceptibility to atherosclerosis. Several studies suggested that type 2 diabetes might be associated with changes in the innate immune response. The aim of our study was to investigate whether the single nucleotide polymorphisms (*Asp*299*Gly* and *Thr*399*Ile*) in the toll-like receptor 4 gene are associated with microvascular diabetic complications.

Methods: The study group consisted of 864 patients with type 2 diabetes. Of this group 352 patients were diagnosed with diabetic retinopathy. The control group (A) involved 420 healthy individuals and group (B) 140 patients with type 2 diabetes lasting $\geq$ 10 years but free of retinopathy. All subjects were genotyped for the *Asp*299*Gly* and *Thr*399*Ile* polymorphisms by polymerase chain reaction (PCR) and subsequent cleavage with NcoI and HinfI restriction endonucleases, respectively. The TLR4 alleles were confirmed by automated sequencing.

Results: In the type 2 diabetes group 64 patients (7.4%) were heterozygous for the *Asp*299*Gly* polymorphism compared to 6.5% in healthy controls. For the *Thr*399*Ile* polymorphism there were 62 heterozygotes (7.2%) vs. 6.2% in healthy controls. In most cases, the minor alleles *Gly*299 and *Ile*399 co-segregated. The genotype distribution in the patients with no retinopathy after diabetes duration of $\geq$ 10 years was similar to that of healthy control group. Increased frequency of both heterozygous genotypes was observed in patients with retinopathy (11.2% for the *Asp*299*Gly*). The frequency of the G allele was significantly increased in the subgroup of patients with retinopathy, with diabetes duration less than 5 years (n=80). Fifty two percent of the G allele carriers and 3 of 4 homozygotes found were in this subgroup. Odds ratio for the G allele in this early onset subgroup was 5.0 with 95% CI 2.33-10.71 versus patients with no retinopathy after diabetes duration of $\geq$ 10 years. In contrast, in the entire retinopathy group, the odds ratio for the G allele was 1.88 with 95% CI 0.93-3.79. The multivariate logistic regression analysis revealed that in the studied population the G allele of the Asp299Gly polymorphism was an independent risk factor of early onset of diabetic retinopathy ($p<0.001$).

Conclusions: Our results suggest a novel association between the *Asp*299*Gly* polymorphism of the toll-like receptor 4 gene and an early onset of diabetic retinopathy in type 2 diabetes patients. The G allele of this polymorphism may be useful in identifying diabetic patients with increased risk of retinopathy.

MP154 THE RENAL PROTECTIVE EFFECT OF ASTRAGALUS MEMBRANACEUS IN ANIMAL MODELS OF DIABETES MELLITUS

Ju-Qian Zhang, Xi-Sheng Xie, Ping Fu. *Department of Nephrology, West China Hospital of Sichuan University, Chengdu, Sichuan, China*

Introduction and Aims: Diabetic Nephropathy (DN) has long been recognized as the leading cause of end-stage renal disease (ESRD) worldwide with enormous public health burden. But the efficacy of currently available medical interventions to delay, arrest or even reverse the progression of DN remains poor. Astragalus Membranaceus (Fisch) Bge. (AM) of the Leguminasae family is a widely used traditional herbal medicine, of which the saponins, flavonoids and polysaccharides are the main effective constituents. Recent experimental studies have shown the inhibitory effects of AM on oxidative stress in early DN. And AM has been applied as an adjuvant therapeutic approach in the management of DM and early DN in clinical settings with satisfactory safety profile in China. This systematic review attempted to assess the effectiveness and safety of AM as single herb in preventing or slowing down the progression of DN in diabetic animal models, to determine whether the evidence from animal studies of AM supported its use in clinical practice.

Methods: We conducted an electronic search of published studies, with handsearching through the reference lists of identified articles. We included all the randomized, controlled animal studies of AM treatment (including the effective components of AM) in any kind of animal model of DM or DN. Outcome measures included the glycemic status, renal functions, and mortality. Included studies should have adopted at least one measurement relevant to renal function. Methodological quality of included studies was appraised using a rating scale consisted of 6 items. 2 reviewers independently selected and graded the studies.

Results: Among 41 articles identified, a total of 13 reports of 11 animal researches that fulfilled the inclusion criteria were included in the review. The methodological quality of included studies was generally poor according to the scale. None of these studies stated the precise method of randomization, and none adopted blinding method. Only one study reported the number of death, and mentioned the specific cause of death as well. The large amount of heterogeneity existed in the 11 studies that cannot be explained by stratification of data prohibited the studies to be combined and analyzed quantitatively. 8 studies found statistically significant benefit of AM and Astragalus Polysaccharides in reducing the elevated GFR at 4-12 weeks after the induction of DM models, and the significantly decreased albuminuria was noted in 8 of the studies using AM, Astragalus Polysacchardies and Astragalus Saponin (AS) I. 4 studies that assessed the pathological changes of diabetic nephropathy observed evident ameliorating effects of AM and AS I in the GBM thickening and mesangial hyperplasia.

Conclusions: The significant effects of AM in partially reversing the glomerular hyperfiltration state, reducing the albuminuria and mitigating the pathological changes of early DN have been observed in animal researches. However, the heterogeneity and inadequate reporting of included studies compromised the quality of evidence, and the results from these studies should be extrapolated into clinical practice with great caution.

Diabetes mellitus – Clinical studies 2

MP155 PREVALENCE OF DECREASING OF GLOMERULAR FILTRATION RATE IN PATIENTS WITH DIABETES MELLITUS TYPE 1 AND TYPE 2

Irina I. Trofimenko[1], Vladimir A. Dobronravov[2], Natalia N. Bystrova[1], Julia V. Drozdova[1], Olga V. Galkina[3], Alexei V. Smirnov[2]. [1]*Department of Propedutics of Internal Diseases, Saint-Petersburg Pavlov State Medical University, Saint-Petersburg, Russian Federation;* [2]*Institute of Nephrology, Saint-Petersburg Pavlov State Medical University, Saint-Petersburg, Russian Federation;* [3]*Department of Clinical Laboratory Diagnostics, Saint-Petersburg Pavlov State Medical University, Saint-Petersburg, Russian Federation*

Introduction and Aims: The aim of this study was to determine the prevalence of the decreased glomerular filtration rate (GFR) in the population of patients (pts) with diabetes mellitus (DM) and the association of GFR with the level of albumin excretion rate (AER).
Methods: Estimated GFR (MDRD equation) and AER (by immunochemical method with monoclonal antibodies) were determined in 851 patients (pts) with diabetes mellitus (DM) (type 1 – 473 pts, type 2 – 378 pts).
Results: Normoalbuminuria (NAU) was found in 54%, microalbuminuria (MAU) in 16%, macroalbuminuria/overt proteinuria (PROT) – in 30% of pts with DM type 1. The decreased level of e-GFR (< 60 ml/min) was found in 775 cases. Interesting that CKD stages III–IV was determined in 8.3% of pts with NAU, in 6.4% of pts with MAU and 62.8% of pts with PROT. NAU was found in 33.6%, MAU – in 17.7%, PROT in 48.7% of pts with DM type 2. More than 40% of pts with DM type 2 with NAU and MAU had e-GFR <60 ml/min. Most of the pts with PROT (71.6%) had CKD stages III–V. In case of normal range of serum creatinine level e-GFR<60 ml/min was found in 7.6% of pts with DM type 1 and in 33% of pts with DM type 2.
Conclusions: The prevalence of the decreased e-GFR level in pts with DM with NAU and MAU is high. This fact demonstrates the importance of the usage of the value of eGFR as well as of AER in screening, dynamic observation and determination of the severity of kidney damage in patients with DM.

MP156 A COMBINATION TREATMENT OF AN ANGIOTENSIN-CONVERTING ENZYME INHIBITOR AND ANGIOTENSIN-RECEPTOR BLOCKER CAN INHIBIT PLASMA RENIN-ANGIOTENSIN SYSTEM MORE COMPLETELY AND PERSISTENTLY AS COMPARED WITH HIGH OR MODERATE DOSE ANGIOTENSIN-RECEPTOR BLOCKER TREATMENTS IN TYPE 2 DIABETIC NEPHROPATHY: NESTED COHORT STUDY OF CANDESARTAN-TRANDOLAPRIL TRIAL IN DIABETIC CKD (CAT TRIAL)

Naoyuki Nakao[1], Akira Fujimori[1], Hirohito Hasegawa[1], Hiroyuki Matsushima[2]. [1]*Division of Nephrolology and Dialysis Center, Kohnan-Rokko Island Hospital, Kobe, Hyogo, Japan;* [2]*Division of Nephrology, Kobe City Medical Center West Hospital, Kobe, Hyogo, Japan*

Introduction and Aims: We have recently reported a long-term better anti-proteinuric efficacy of a combination treatment of an ACEI and an ARB (trandolapril of 3 mg plus candesartan of 32 mg) as compared with a high or a moderate dose ARB (candesartan of 48 mg or of 32 mg) (www.associationhq.com/ISN/nexus/hypertension/pages/book.html). This finding may suggest an inhibition of the renin-angiotensin system (RAS) at multiple sites is better for a long-term outcome as compared with that at a single site, even though with a high-dose of ARB. To confirm this hypothesis, we have conducted a nested cohort study of the CAT trial inquiring for changes in systemic RAS activities with an incidence of aldosterone breakthrough (AB) event.
Methods: The CAT trial was a fixed-dose, open-label, and randomized prospective clinical trial exploring a long-term ant-proteinuric efficacy among three arms: candesartan plus trandolapril; a high dose candesartan; and a moderate does candesartan. We have sequentially measured plasma renin activity (PRA) and aldosterone concentration (PAC) levels in randomly selected 10 participants on each arm from baseline up to three years. AB was defined as an increased value compared with the pretreatment value.
Results: Similarly to the main results of the CAT trial, the combination had a better anti-proteinuric efficacy the other ARB-monotherapies at different doses throughout a median follow-up period of 2.4 years, despite of same degree of blood pressure reduction (-53 percent in the combination, -48 percent in high-dose candesartan and -39 percent in candesartan at moderate dose, P=0.001). PRA (ng/mL/hr) and PAC (ng/mL) at baseline and at 12 weeks after intervention were similar among three groups (P=0.01). At 24 weeks, PRA was six-times and significantly increased in combination and high-dose ARB treatments without any significant difference of them, while PAC values were similarly reduced among three groups. Thereafter, PAC and PAC were constant in the combination during a remaining study period. These biochemical markers, however, had tendencies to baseline values in ARB monotherapy groups (P=0.001 in PAC and P=0.04 among three groups). The incidences of AB in combination, high-dose ARB and medium-dose ARB were 20, 30, and 40 percent, respectively (P=0.01). After adjustment of baseline covariates, a positive relation between proteinuria and PAC and a negative one between proteinuria and PRA were significantly observed (P=0.02 and P=0.007, respectively). BA preceded a subsequent decrement of eGFR despite of investigating treatments.
Conclusions: To inhibit the RAS profoundly and persistently, an inhibition of multiple sites of the RAS is promising as compared with a single site inhibition.

MP157 CEREBROVASCULAR ACCIDENT IN TYPE 2 DIABETICS: DOES NEPHROPATHY ADVERSELY AFFECT OUTCOME?

Sachin Soni[1], Amit Nagarik[1], Rajashree Khot[2], Anuradha Raman[1]. [1]*Nephrology, Mediciti Hospitals, Hyderabad, Andhra Pradesh, India;* [2]*General Medicine, Government Medical College, Nagpur, Maharshtra, India*

Introduction and Aims: Diabetes mellitus, by virtue of its micro and macrovascular complications is a multisystem disease. In this analysis, conducted at tertiary care hospital we looked at clinical profile of stroke in type II diabetic patients with diabetic nephropathy compared diabetics without nephropathy.
Methods: Between January 2004 to December 2005, all diabetics admitted with stroke (Confirmed by computed tomography or magnetic resonance imaging) were included in this study. Diabetes was defined by standard criteria. Diabetic nephropathy was defined as "dipstick or micral strip" positive proteinuria with or without deranged creatinine in presence of diabetic retinopathy. Ophthalmoscopy was performed by single observer. Type of stroke (infarct or hemorrhage), lesion diameter and site of lesion were reported by radiologist. NIH (National Institute of Health) stroke score was calculated within 3 hours of admission. Comparison in two groups: Group I (with diabetic nephropathy) and Group II (Without diabetic nephropathy) was done with respect to demographic profile, duration of hospital stay, admission blood sugar levels, overall glycemic control (assessed with glycosylated hemoglobin), blood urea and serum creatinine levels and in hospital mortality. Statistical analysis was done using strata6 software for windows, p value of <0.05 was taken as statistically significant.
Results: During the study period 50 type 2 diabetic patients were confirmed to have stroke. 33 (66%) had diabetic nephropathy (Group I) while 17 (34%) were without nephropathy (Group II). Patients in Group I were younger compared with Group II (60.27 Vs 63.88 yrs; p- Not Significant). Group I patients had higher BMI, glycosylated hemoglobin levels and longer hospitals stay, but the difference was statistically not significant. Mean Systolic (157.9 Vs 159 mm Hg) and diastolic (96.43 Vs 95.76 mm Hg) blood pressure and admission blood sugar levels (211.4 Vs 198.4 mg/dl) were comparable in both groups. Group I patients had significantly higher NIH score (16.34 Vs 11.46; p<0.05), lesion diameter (36.87 mm Vs 23.11 mm; p< 0.05), blood urea (53.46 Vs 37.17 mg/dl; p<0.05) and serum creatinine (1.88 Vs 1.12 mg/dl; p<0.05) levels compared with Group II. Mortality was also higher in Group I (33% Vs 11.7%; p<0.01).
Conclusions: 1. Patients developing stroke are more likely to have diabetic nephropathy.
2. Patients with diabetic nephropathy develop stroke at younger age.
3. Severity of stroke is greater in patients with diabetic nephropathy.
4. Presence of nephropathy predicts higher mortality in diabetic stroke.

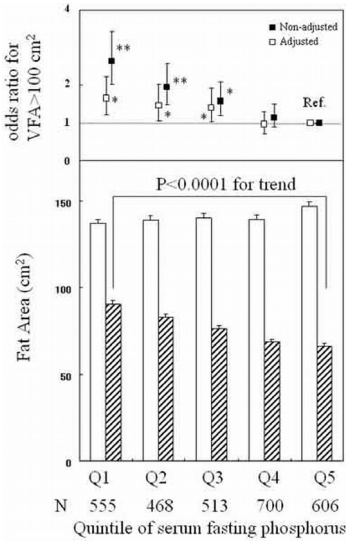
MP158 FASTING SERUM PHOSPHATE LEVEL: A POTENTIAL MARKER OF VISCERAL, BUT NOT SUBCUTANEOUS, FAT AREA

Takayuki Hamano[1], Masashi Fujita[2], Takahito Ito[1], Enyu Imai[1], Masafumi Kitakaze[3]. *[1]Nephrology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan; [2]Cardiovascular Medicine, Osaka University Graduate School of Medicine, Suita, Osaka, Japan; [3]Cardiovascular Division of Medicine, National Cardiovascular Center, Suita, Osaka, Japan*

Introduction and Aims: Although patients with metabolic syndrome (MetS) reportedly have significantly lower serum phosphate levels when compared to healthy individuals, the relationship between serum phosphate and central obesity in the general population remains unknown. Our aim in this study is to investigate the direct relationship between serum phosphate levels and abdominal fat distribution in subjects without MetS.

Methods: In this cross-sectional observational study, we enrolled 2,842 consecutive subjects without MetS, mostly office workers, who underwent health screening. All patients had visceral fat area (VFA) and subcutaneous fat area (SFA) measured by computed tomography (CT). We measured fasting serum phosphate, calcium, albumin, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, fasting plasma glucose (FPG), triglyceride (TG), uric acid (UA) and gamma-glutamyltransferase (GGT). We compared laboratory parameters, including MetS components, across each phosphate quintile by means of trend analysis with Jonckheere-Terpstra test. We employed a multiple logistic regression model to determine the impact of phosphate quintile on VFA>100 cm^2, adjusting for age, estimated GFR (eGFR), and other MetS components, i.e., blood pressure (BP), HDL, FPG and TG. To determine which clinical parameters are significant determinants of serum phosphate, we performed multiple linear regression analysis for serum phosphate.

Results: Mean age was similar among each quintile. Along with the increase in fasting serum phosphate levels, we observed significant stepwise decreases in BMI, systolic and diastolic BP, heart rate, FPG, TG, UA and GGT, while significant stepwise increases in HDL and LDL cholesterol were observed. Univariate analysis revealed a significant negative correlation between serum phosphate levels as a continuous variable and VFA (R = 0.2, P<0.0001), but not with SFA. Non-adjusted odds ratios for VFA>100cm^2 were 2.6 (95% confidence interval: 2.0-3.4, P<0.0001), 1.9 (1.5-2.6, P<0.0001), 1.6 (1.2-2.1, P=0.001), 1.1 (0.9-1.5, NS), and 1.0 (reference) for each serum phosphate quintile. This trend toward lower phosphate levels with larger VFA remained robust, even after adjustment for age, eGFR, and components of MetS. Conversely, multivariate regression analysis revealed that VFA, not SFA, made a significant negative contribution to serum phosphate.



Conclusions: Serum phosphate levels are significantly associated with VFA, but not with SFA, in the general population. Our results suggest a novel approach for detecting early abdominal fat gains without performing CT (before MetS criteria are met).

MP159 IMPACT OF BASELINE PROTEINURIA AND UNDERLYING DISEASE ON PROTEINURIA REDUCTION WITH HIGH DOSE CANDESARTAN IN THE SMART STUDY

Paul Rene de Cotret[1], Ellen Burgess[2], Norman Muirhead[3], the SMART Investigators. *[1]Université Laval, Québec, QC, Canada; [2]University of Calgary, Calgary, AB, Canada; [3]University of Western Ontario, London, ON, Canada*

Introduction and Aims: Despite the widespread use of ACEIs and ARBs, persistent proteinuria, an established risk factor for CKD, remains common in many patients. SMART (Supra Maximal Atacand Renal Trial) compared the effect on proteinuria of standard dose of candesartan, 16 mg, with higher doses, 64 or 128 mg, in patients with persistant proteinuria, ≥1g/24h, in spite of treatment with 16 mg for 8 weeks.

Methods: Canadian patients with persistant proteinuria, due to diabetes mellitus (53.9%), hypertensive nephrosclerosis (12.6%) or primary glomerular disease (33.5%), were recruited and stratified at baseline by 24h urine protein (UPr): 1-3g/24h (47, 51 and 47 patients for the 16, 64 and 128 mg) vs >3g/24h (35, 37 and 36 patients for the 16, 64 and 128 mg respectively). After randomization, double-blind treatment was started with 16, 64 or 128 mg for 30 weeks. Patients receiving 64 and 128 mg were compared to the 16 mg active control population.

Results: The baseline characteristics of the 269 randomized patients were: 79.6% male, mean age 55.3 yrs and mean BP 133/78 mmHg. Medians for serum creatinine 130 μmol/L, K^+ 4.5 mmol/L, eGFR 50 mL/min, and (UPr) 2.66 g/24hr.

Treatment with candesartan 128 mg led to a 33% further decrease in 24h UPr in the intention to treat analysis, with a 44% decrease in the per protocol population compared to 16 mg (see Table).

Candesartan 128 mg led to a 44% decrease for patients with baseline UPr 1-3g/24h, and a 25% decrease for those with >3g/24h.

Patients with type 2 diabetes had a similar response to candesartan 128 mg as non-diabetics, 28% and 37% respectively.

In patients with diabetes, baseline UPr was an important determinant of the response to high dose candesartan; diabetics with >3g/24h at baseline had a 19% fall in UPr at week 30 while those with 1-3g/24h had a 41% reduction. Among non-diabetics, UPr reduction was similar in the 1-3g/24h group and the >3g/24h group, 41% and 56% respectively.

High dose candesartan was well tolerated with no deaths reported and no dose limiting side effects or significant alterations in renal function or serum potassium. Changes in blood pressure during the study were minor and insufficient to explain the fall in proteinuria seen with high dose candesartan.

Proteinuria reduction after candesartan 128 mg vs 16 mg

Population		p-value
All patients	33%	0.0001
All patients - per protocol	44%	0.0001
1-3g/24h	44%	0.0001
>3g/24h	25%	0.0373
Subgroups		
Diabetics	28%	0.0118
1-3g/24h	41%	0.0183
>3g/24h	19%	0.2187
Non-diabetics	37%	0.0016
1-3g/24h	41%	0.0089
>3g/24h	56%	0.0065

p-values not adjusted for multiple comparisons.

Conclusions: High dose candesartan (128 mg) is a promising treatment for the reduction of residual proteinuria in a broad range proteinuric renal diseases. The results in the diabetic subgroup emphasize the need for early treatment.

Disclosure: The SMART study was financially supported by AstraZeneca Canada Inc.

MP160 CLASSIFICATION OF SUBCLASSES OF DIABETIC NEPHROPATHY (DN) BY SELDI-TOF/MS ANALYSIS OF HUMAN URINE

Massimo Papale[1], Salvatore Di Paolo[2], Annamaria Di Palma[3], Simona Magaldi[3], Valentina d'Onofrio[3], Maria Teresa Rocchetti[3], Marta Centra[4], Elena Ranieri[4], Mauro Cignarelli[5], Loreto Gesualdo[3]. *[1]Dept. of Bioagromed and INFM, University of Foggia/CNR Lecce, Foggia, Italy; [2]Division of Nephrology and Dialysis, Hospital "Dimiccoli", ASL BAT, Barletta, Italy; [3]Sect. of Nephrology, Dept. of Biomedical Sciences and Bioagromed, Faculty of Medicine, University of Foggia, Foggia, Italy; [4]Sect. of Clinical Pathology, Dept. of Biomedical Sciences, University of Foggia, Foggia, Italy; [5]Division of Endocrinology, Dept. of Medical Sciences, University of Foggia, Foggia*

Introduction and Aims: Diabetic Nephropathy (DN) is one of the most frequent causes of end stage renal disease (ESRD) worldwide. Renal injury in Type 2 diabetics shows a variable pattern of damage, ranging from typical glomerulosclerosis (class 1) to prevailing chronic vascular damage (class 2), to glomerulonephritides with or without the presence of diabetic glomerulosclerosis (class 3).[1] The above differences would likely play a key role on the prognosis and the specific treatment of renal damage in diabetics. SELDI-TOF/MS technology has raised a growing interest, due to its high-throughput nature, as a research tool for biomarker discovery over the last few years.

We used SELDI-TOF/MS technology to possibly identify a set of proteins which would allow to discriminate diabetics with chronic nephropathy, and, among them, class 1 from class 2 patients.

Methods: We recruited 31 renal biopsied pts [(6 class 1 and 10 class 2 diabetics, 8 pts with membranous nephropathy (MN) and 7 patients with nephroangiosclerosis]. Proteinuria ranged from 0.3 to 2.7 g/d in diabetics, from 0.9 to 25 g/d in MN pts and from 0.05 to 20g/d in nephroangiosclerosis. Ten μg urine protein from each subject were analysed by CM10 protein chip and the spectra were compared by Ciphergen express 3.0 software

Results: Four peaks (9.768, 10049, 6.227 and 21.444 m/z) were differently expressed (p-value < 0.05) between class 1 and class 2 DN. When MN pts were included in the analysis, only one among the above peaks (9.768 m/z) turned out to distinguish class 2 DN from MN pts. Finally, such peak was highly expressed in both class 2 DN and Nephroangiosclerosis pts, thus suggesting a specific association with chronic renal vascular damage.

Conclusions: SELDI-TOF/MS profiling of human urine allowed to distinguish diabetics with chronic nephropathy from pts with non-diabetic proteinuria, such as those with MN. Then, 4 peaks seemingly identified diabetics with renal chronic vascular changes and without diabetic glomerulosclerosis. Finally, one peak seems to be specifically associated with chronic vascular damage of both diabetic and nondiabetic kidney.

MP161 EFFECT OF SOCIO-ECONOMIC STATUS AND LIFESTYLE ON DIABETIC KIDNEY DISEASE PREVALENCE

Rufino Hdez J. Margarita[1], Maceira Cruz Benito[1], Garcia Rebollo Sagrario[1], Gonzalez Rinne Ana[1], Barbero Pablo[1], Martin Folgueras Tomas[2], Torres Ramirez Armando[1], Hernandez Marrero Domingo[1], Lorenzo Sellares Victor[1]. *[1]Nephrology Service, Hospital Universitario de Canarias, La Laguna, Santa Cruz de Tenerife, Canary Islands, Spain; [2]Endocrinology Service, Hospital Universitario de Canarias, La Laguna, Santa Cruz de Tenerife, Canary Islands, Spain*

Introduction and Aims: The prevalence of ESRD secondary to Diabetic Kidney Disease (DKD) in the Canary Island is alarmingly high in comparison with other european regions (70 pmp).

Aim: To study the extent to which environmental factors influences the prevalence of DKD in our community.

Methods: A total 207 type 2 diabetic patients from our health area were studied (66±8 years, 43%M). Patients were grouped according to renal complication. Control group (n=103): DM evolution >15y, absence of microalbuminuria and normal renal function. Study group (n=104): presence of DKD (time from diagnosis 13±8 years), GFR<60 ml/min and proteinuria >500 mg/day.

Information was collected by patients and family interviews. Questionnaire survey included: demographic data, socio economic status, educational level, relevant co-morbid conditions, proliferative retinopathy (yes/no), degree of compliance to diet and physical activity, and early (first ten years from diabetes diagnosis) diabetes education (yes/no).

Results: DKD prevalence was associated with: more prevalence of family history of CRF (30 vs 12%, p=0,0001), noncompliance with the diet recommendations (42% vs 11%, p=0,0001), physical activity (30% sedentarism vs 6%, p=0,0001), awareness of HbA1C test usefulness (4% vs 34%, p=0,0001), diabetic education (28% vs 55%, p=0,01), lower socio-economic status (51 vs 34%, p=0,02), more prevalence of diabetic retinopathy (91% vs 36%, p=0,0001), hypertension (60% vs 31%, p=0,0001), dyslipidemia (45% vs 27%, p=0,0001), cardiovascular comorbidity (47% vs 17%, p=0,0001) and vascular calcifications (74%vs 23%, p=0,0001), time to first primary care visit (2,5±0,7 vs 0,3±0,1y, p=0,0001), time to first uryanalysis (5,9±1 vs 2,4±0,5y, p=0,004), time on endocrinologic care (5,5±1 vs 12,4±0,7y, p=0,03), lower number of medical visits per year (3,6±0,4 vs 5,7±0,3, p=0,04) and more years of smoke habit coincident with diabetes evolution (6±1,2 vs 3,4±0,7y, p=0,03).

Conclusions: Environmental factors may account for the excess of prevalence of diabetic kidney disease. Effective prevention strategies need to be urgently implemented in our community, especially in people with lower socio-economic status.

Disclosure: this abstract was possible thanks to a grant given by: Ayudas a la Investigacion en Nefrologia de la Sociedad Espanola de Nefrologia and by the INTER-REG 05/MAC/2.3/A5. Diabetogen study.

MP162 COUPLED PLASMAFILTRATION ADSORPION: A NEW TECHNOLOGY FOR FREE LIGHT CHAIN REMOVAL

Sonia Pasquali[1], Elena Mancini[1], Lucia Barbara de Sanctis[1], Emanuele Mambelli[1], Marilou Wratten[2], Antonio Santoro[1]. *[1]Nephrology, Dyalisis and Hypertension, S. Orsola-Malpighi Hospital, Bologna, Italy; [2]Bellco, Mirandola, Modena, Italy*

Introduction and Aims: Circulating free light chains (LC) play a key role in the pathogenesis of acute renal failure due to multiple myeloma.

Free LC removal procedures have been advocated as a logical and rationale therapeutic approach in association with chemotherapy. However, conventional plasma exchange treatment showed no significant benefits questioning the efficacy of this procedure.

Methods: We studied an alternative approach utilizing an extracorporeal adsorbent treatment such as coupled plasmafiltration adsorption (CPFA).

This technique is based on the use of a double chamber filter. It allows separation of the plasma from whole blood and to filtrate the plasma across a cartridge containing an adsorbent resin. The resins utilized were hydrophobic divinylbenzene styrenic resins with an average bead diameter of 75 microns, an average pore diameter of 30 nm and a surface area of 700 m^2/g. We investigated the acute effect of CPFA treatment in 4 patients affected by renal failure due LC myeloma. The patients were treated for a 5 hour CPFA treatment; the session's number varied from 2 to 7.

Results: Serum free LC concentration was significantly reduced at each session with a progressive decrease at the end of the treatment (figure 1). The procedure was well tolerated and serum albumin levels maintained stable during each treatments.

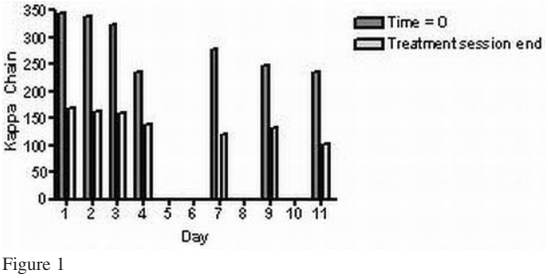


Figure 1

Conclusions: The preliminary results indicated:

- CPFA treatment could remove large quantitaties of free LC.
- This technique did not require albumin replacement in contrast to high permeability dialysis or plasma exchange.
- We need larger studies in order to identify the schedules of treatment and to verify its clinical utility in term of renal recovery.

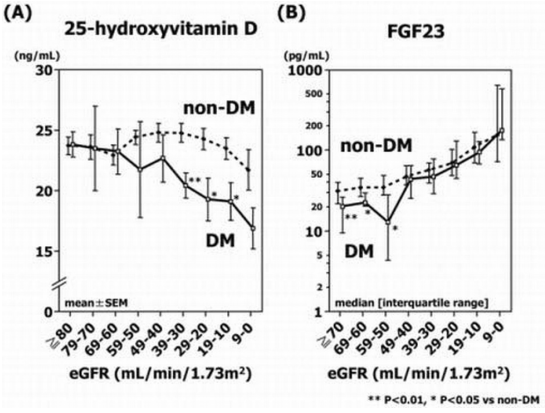
MP163 THE EFFECT OF DIABETES MELLITUS ON CKD-MBD (CHRONIC KIDNEY DISEASE – MINERAL AND BONE DISORDER) IN NON-DIALYZED PATIENTS

Naohiko Fujii[1], Takayuki Hamano[2], Satoshi Mikami[2], Isao Matsui[2], Kodo Tomida[2], Hirotaka Tanaka[2], Takahito Ito[2], Enyu Imai[2], Hiromi Rakugi[2]. *[1]Nephrology Department, Hyogo Prefectural Hospital, Nishinomiya, Nishinomiya, Hyogo, Japan; [2]Department of Nephrology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan*

Introduction and Aims: Diabetes mellitus (DM) itself disturbs bone and mineral metabolism. But little is known about the effect of DM on CKD-MBD (Chronic Kidney Disease - Mineral and Bone Disorder) in patients not on dialysis.

Methods: We performed a cross-sectional observational study (OVIDS-CKD; Osaka Vitamin D Study in CKD), enrolling CKD outpatients who had never received corticosteroid, vitamin D analogs, bisphosphonates, and other drugs affecting bone and mineral metabolism. We measured 1-84 parathyroid hormone (1-84PTH), 25-hydroxyvitamin D (25OHD), calcitriol (1,25D), fibroblast growth factor-23 (FGF23), serum calcium (Ca), phosphorus (P), creatinine (Cr), and albumin (Alb). We explored the differences in these parameters with or without DM and analyzed the effect of DM on the correlation between these parameters and renal function. We then extracted all DM subjects and sex-, age-, and eGFR-matched non-DM subjects to confirm the results.

Results: In total, 602 (393 males, mean age 61.8 years, eGFR 48.9±24.7 mL/min/1.73m^2) subjects were analyzed. In DM 25OHD decreased as renal function declined, whereas in non-DM it was constant (Fig. A). There was a significant statistical difference at eGFR<40 mL/min/1.73m^2 (P<0.05). 1-84PTH, however, did not show any difference between DM and non-DM, which was consistent with the tendency toward lower 1,25D levels in DM. In the higher eGFR range (eGFR≥50 mL/min/1.73m^2), DM had lower FGF23 than non-DM, but the difference disappeared in the lower eGFR (Fig. B). There was no difference in P. These results were confirmed with 224 sex-, age-, eGFR-matched extracted subjects.



Conclusions: Diabetic CKD patients have poorer vitamin D status than non-DM. Insufficient upregulation of PTH might deteriorate 1,25D deficiency in those subjects. Lower FGF23 in DM might reflect osteocyte dysfunction. DM might disturb the compensatory system in both parathyroid and bone.

MP164 OPTIMIZING GLYCEMIC CONTROL IN HEMODIALYZED DIABETIC PATIENTS

Rebeca Garcia-Agudo[1], Maria Jesus Moyano[1], Sami Aoufi[2], Cristobal Morales[1], Elena Jimenez-Vibora[3], Carlos Jarava[3], Nuria Del Toro[3], Berta Escalera[3], Mercedes Salgueira[1], Maria Jose Gomez[1], Alejandro Suarez-Benjumea[1], Clotilde Rios[1], Rosa Ortega[1], Javier Amor[1], Juan Polo[1], Jose Antonio Milan[1], Alfonso Palma[1]. *[1]Nephrology and Endocrinology Services and Investigation Unit, Virgen Macarena University Hospital, Seville, Spain; [2]Gastroenterology Service, Virgen del Rocio University Hospital, Seville, Spain; [3]Sierra Este Dialysis Centre, Seville, Spain; [4]Virgen de los Reyes Dialysis Centre, Seville, Spain*

Introduction and Aims: Diabetes mellitus constitutes a major end-stage renal disease health problem. Among risk factor reductions for mortality in dialysis patients with diabetes, improved glycemic control is widely recommended.

The hemoglobin A1c (HgbA1c) concentration is a marker of hyperglycemia and reflects average blood glucose concentration over 3 months in diabetic individuals.

Several factors impacting on end-stage renal disease glycemic management are known to exist, including pharmacodinamic effects of uremia, reduced erythrocyte survival, use of erythropoietin.

The aim was to analyze wether the HgbA1c correlates with the mean blood glucose on diabetic hemodialysis patients and wether it is a valid tool to monitor glycemic control in these patients.

Methods: We performed a data analysis of glycemic control and glycosylated hemoglobin on hemodialysis patients and diabetic patients without renal disease. We enrolled 33 diabetic patients receiving hemodialysis and 53 diabetic patients without renal disease for this study.

Results: Patients characteristics are shown in Table 1.

Table 1. Patients characteristics

	Diabetic patients on hemodialysis	Diabetic patients without renal disease	p
No. of patients	33	53	–
(%) male	66.7	40.4	0.0001
Age (years)	63.18	45.60	0.0001
Type I diabetes (%)	39.4	38.5	0.0001
Type II diabetes (%)	60.6	61.5	0.0001
Mean glycemia (mg/dl)	169.89	186.72	0.081
Mean glycemia on a non-hemodialysis day (mg/dl)	164.12	–	0.0001
Mean glycemia on a hemodialysis day (mg/dl)	163.52	–	0.0001
Mean HgbA1c (%)	7.03	8.22	0.02
Mean hemoglobin (g/dl)	11.34	–	0.014

Renal disease patients had seven glucose determinations on a hemodialysis day and seven on a non-hemodialysis day. All available blood glucose measurements on diabetic patients without renal disease drawn within the previous 90 days from the date of the HgbA1c were analyzed. Most patients had 14 or more determinations. A scatter plot generated by plotting the mean blood glucose versus HgbA1c indicated that the HgbA1c correlated with the mean blood glucose levels (DDCT criteria. Diabetes Care 2002;25:275-8) in 50.1% of the hemodialysis patients (p=0.027) and 60.8% of the diabetic patients without renal disease (p=0.002).

Conclusions: HgbA1c is the gold standard for evaluating risk of complications in patients with diabetes, but single measurements may not adequately reflect glycemic control for previous periods in diabetic hemodialyzed patients. It is prudent to individualize the HgbA1c target in end-stage renal disease and monitor glycemic control.

MP165 SIMILAR BLOOD PRESSURE CIRCADIAN PROFILE AND RENAL INVOLVEMENT IN WHITE COAT HYPERTENSIVES AND NORMOTENSIVES WITH CHRONIC KIDNEY DISEASE

Adrian Covic[1], Marilena Badea[1], Simona Hogas[1], Paul Gusbeth-Tatomir[1], Dragomir Nicolae Serban[2]. *[1]Nephrology Clinic, Parhon University Hospital, Iasi, Romania; [2]Physiology Department, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania*

Introduction and Aims: Ambulatory blood pressure monitoring (ABPM) has become an essential clinical and research procedure to evaluate blood pressure (BP). Relative to office-determined BP values, the following patterns are now recognised: white coat hypertension (WCH) when office blood pressure (OBP) >day-time ambulatory blood pressure (d-ABP), masked hypertension (MH) when d-ABP >OBP, sustained hypertension (SH) when both are abnormal, and normal blood pressure (N). However, different definitions are used to describe the same BP category. The aim of the present study was to describe, in a large chronic kidney disease (CKD) population, the prevalence of different BP patterns (see above) and their relation with glomerular filtration rate (GFR) and proteinuria.

Methods: ABPM and OBP were measured in 102 consecutive CKD patients (GFR < 90 ml/min., mean GFR = 73.6±39.5 ml/min/1.73 m^2.

Two previously reported accepted definitions for WCH were used: WCH_1 if OBP ≥130 mmH and ABP < 130 mmHg, and WCH_2 if OBP ≥ ABP + 20 mmHg; *MH* was considered when ABP > OBP +10mmHg and *SH* when both OBP and ABP ≥130mmHg. Normality was defined as: OBP and ABP < 130 mmHg (*N*).

Results: CKD is associated with a high prevalence of SH - 48.1% of the patients. WCH was also frequent - from 37.2% (WCH_1) to 51% (WCH_2). In contrast MH was seen in only 9.8% of the cases; 14.7% of our patients have normal BP values (N). Overall, a non-dipping pattern was recorded in 61.8% of this CKD population; irrespective of the definition used, WCH patients had a dipping profile (55-57% non-dippers, night/day BP ratio = 0.91-0.92) similar to normals (60% non-dippers, ratio = 0.92), but better than the MH or SH categories (67-70% non-dippers, ratio = 0.95-0.96, P<0.05). Compared to normals, patients with WCH had also a similar proteinuria prevalence = 23% (WCH1), 24% (WCH2) vs 20% (N) but significantly lower compared to ABPM hypertensives = 30% (MH) and 40% (SH), P<0.05. In contrast there was no difference in the level of GFR or distribution of different CKD stages between the five BP categories/patterns. Finally, a higher prevalence of diabetes was seen in WCH1 or WCH2 patients compared to normals or even to hypertensives (MH or SH): diabetes = 25 to 29% vs <10% respectively, P < 0.05.

Conclusions: WCH is frequent in CKD. Irrespective of the mode of definition, WCH subjects had a BP profile and proteinuria similar to normotensives, despite a higher prevalence of diabetics. GFR was not a predictor of WCH.

This work was supported from the Romanian state budget, by a research grant (PNCDI-II, program "IDEI", code ID_1156), under the contractual authority of UEFISCSU (contract no. 392/2.10.2007)

MP166 CENTRAL SLEEP APNEA IS HIGHLY PREVALENT IN CKD STAGE 3

Georg Fleischmann[1], Gundula Fillafer[1], Heike Matterer[1], Falko Skrabal[1], Peter Kotanko[2]. *[1]Department Internal Medicine, Krankenhaus der Barmherzigen Brueder, Graz, Austria; [2]Renal Research Institute, New York, NY, USA*

Introduction and Aims: Sleep apnea syndrome (SAS) is a well recognized complication in patients with dialysis-dependent chronic kidney disease (CKD). Hypertension, left ventricular hypertrophy and sympathetic overactivity are major clinical sequelae. SAS is less well studied in pre-dialysis CKD, and this study aimed to delineate the prevalence and nature of SAS in earlier CKD stages.

Methods: We investigated in a retrospective observational setting patients referred for clinically suspected SAS. Patients underwent a full-night standardized in-laboratory polysomnography. Glomerular filtration rate (eGFR; in mL/min/1.73 m^2) was computed using the abbreviated MDRD study equation. Patients were stratified by eGFR: GFR90+ (eGFR ≥ 90), CKD stage 2 (eGFR 60-89), and CKD stage 3 (eGFR 30-59). Groups were compared by ANCOVA with adjustment for age. Correlations were estimated by Spearman correlation coefficient. Data are expressed as mean (95% CI).

Results: A total of 158 Caucasian patients were studied (table 1). Total sleep time (TST) did not differ between the groups. eGFR correlated positively with the number of REM phases (r=0.267; P<0.001) and inversely (r= -0.18; P=0.024) with the number of central apneas (CA). CA frequency was increased in CKD stage 3 as compared to CKD stage 2 and GFR90+ (all P < 0.0001). Prevalence of obstructive apneas (OA) did not differ (table 1). Noteworthy, the number of REM phases was already significantly reduced patients with CKD stage 2 and compared with GFR90+.

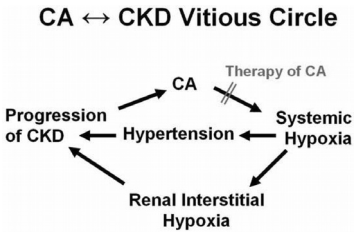


Figure 1

Conclusions: In patients with CKD stage 3 central apnea is significantly more prevalent compared to patients with eGRF ≥ 60 ml/min/1.73m^2. The cause of CA in CKD 3 patients is unknown and we hypothesize that that uremic toxins may play a role. SAS may contribute to renal damage by inducing hypertension and low blood oxygen saturation, which may in turn may affect particularly the renal medulla. These two processes may be part of a vicious cycle (figure 1). A high clinical index of suspicion for SAS in pre-dialysis patients may help to provide adequate diagnostic work-up and therapy.

MP167 DETERMINATION OF THE RATE OF ACHIEVING OPTIMAL BLOOD PRESSURE GOALS IN TYPE 2 DIABETICS FOLLOWED IN TERTIARY ACADEMIC CLINICS IN TEHRAN (A MULTICENTER STUDY)

Aria Jenabi, Aazam Moghiseh, Mosadegh Jabbari, Neda Ebrahimpour. *Nephrology Department, Rasool Akram Medical Center, Iran University of Medical Sciences, Tehran, Iran; Nephrology Department, Rasool Akram Medical Center, Iran University of Medical Sciences, Tehran, Iran*

Introduction and Aims: Hypertension is a common problem in diabetic patients and these patients are at increased risk for cardiovascular morbidity and mortality. BP control to new targets on the base of new guidelines [Joint National Committee on Hypertension 7 (JNC-7),K/DOQI), can prevent the onset and progression of diabetic microangiopathy and also major diabetic complications. The aim of present study was to investigate the rate of achieving these recommended goals for BP control in type 2 diabetics that were followed in three major tertiary academic clinics in Tehran, Iran.

Methods: In a multicenter cross-sectional study, a total of 671 patients (M/F=227/444) with type 2 diabetes from three tertiary academic clinics of endocrinology in Tehran, Iran were evaluated. The patients with the age 20 years or older and at least six months of receiving care from one of these centers were included.

The patients BP was measured in the last visit twice by an expert nurse after 5 minutes rest at sitting position with standardized methods. On the base of new goals of BP in diabetics (JNC-7 and K/DOQI guidelines), optimal systolic BP<130 and optimal diastolic BP<80 mmHg was considered. other data were collected include patient s age, sex, FBS, HbA1c, serum Cr, proteinuria, History of smoking, CVA,CAD, CHF, Retinopathy, Neuropathy, Nephropathy and also antihypertensive drugs. Finally these data were analyzed with spss13.1.

Results: The mean±SD of age was 56.59±11.88 yrs. The mean sys BP±SD was 132.84±21.04 mmHg and mean dia BP±SD was 81.16±11.49. A total of 304 (45.3%) of patients had sysBP 140 mmHg or diaBP 90 mmHg and 533 (79.4%) of patients had sysBP130 mmHg or diaBP80 mmHg. Only 20.6% of patients achieved the BP targets on the base of new guidelines (BP<130/80). and among the hypertensive patients (BP 130/80 or patients using antihypertensive drugs) (86.3%) only 392 patients (58.4%)

Abstract MP166 – Table 1. Baseline characteristics and polysomnography results

Variable	GFR90+ (N=70)	CKD Stage 2 (N=70)	CKD Stage 3 (N=18)	P-Value
Age	57 (55-60)	62 (59-66)	71 (67-75)	< 0.0001
Gender (% females)	27	56	17	0.001
eGFR (mL/min/1.73 m^2)	105 (102-108)	76 (74–78)	49 (45-53)	—
BMI (kg/m^2)	29 (28-31)	29 (28-31)	31 (28-34)	n.s.
CA (per TST)	6.7 (2.5-10.9)	6.4 (3.8-9.0)	42.9 (0-88.2)	< 0.001
OA (per TST)	41 (27-54)	35 (23-47)	48 (20-77)	n.s.
REM phases (per TST)	7.4 (6-8.7)	4.6 (3.8-5.4)	4.7 (3-6.4)	0.004
CA with O2 saturation drop >3% (per TST)	4.4 (.3-8.3)	2.5 (1.1-3.9)	38 (0-83)	<0.0001

n.s. - non significant.

were receiving anti hypertensive drugs. The meanSD of the number of antihypertensive drugs was 1.830.95 and 46.2% of patients were on monotherapy, 32.1% on dual therapy. The most common prescribed drugs were ACEI (36.4%) and the most common combination regimen was ACEI and beta blockers (28.6%) followed by ACEI and a diuretics (14%). On the other hand among patients receiving one, two, three or four drugs for hypertension control 87.3%, 88%, 88.7% and 95.75% respectively were not at BP target.

Conclusions: These data shows that treatment of hypertension in diabetic patients in these centers that are academic university centers not tight enough to reach optimal target especially on the base of new guidelines and because of importance of BP control in these patients to prevent major complications of diabetes it may be require to use some educational.

MP168 PROPYLENE GLYCOL – INDUCED RENAL TOXICITY FROM LORAZEPAM INFUSON

Daniela Chaparoska, Aleksandra Pivkova. *Department of Urgent Internal Medicine and Toxicology, Clinical Centre, Skopje, Macedonia, The Former Yugoslav Republic of; Department of Hematology, Skopje, Macedonia, The Former Yugoslav Republic of*

Introduction and Aims: Using data from patients who developed elevations in serum creatinine concentrations while receiving continuous -infusion lorazepam, we determinated the correlations between the magnitude of serum creatinine concentration rise and each of the following variables:serum propylene level,cumulative lorazepam dose,and duration of lorazepam administration.

Methods: Ten patients who developed elevations in serum creatinine concentrations while receiving continuous-infusion lorazepam.

The mean cumulative dose of lorazepam ws 4800 mg (range 190 - 11.000 mg),and the mean prolylene glycol level determined at the time of peak serum creatinine concentration was 1600 microg/ml (range 190-3600 mikrog/ml).

Results: Serum creatinine concentrations increased in all ten patients during lorezapam infusion and decreased in nine within 3 days after stopping infusion.A weak-to-moderate correlation existed between the magnitude of the rise in serum creatinine concentration and propylene glycol level. A weak-to-moderate correlation also was identified between cumulative lorazepam dose and serum creatinine concentration rise, and a strong-to-moderate was found between duration of magnitude of lorazepam infusion and magnitude of serum creatinine concentration rise.

Propylene glycol levels were strongly correlated with both serum osmolality and osmol gap.

Conclusions: The patients increased serum creatinine concentrations are likely to have resulted from exposure to propylene glycol as a result of a lorazepam infusion. Serum osmolality and osmol gap may be useful markers to propylene glycol toxicity.

MP169 CHRONICALLY ADMINISTERED IMMUNOTHERAPY WITH LOW-DOSE IL2 AND IFNα IN METASTATIC RENAL CELL CARCINOMA: A FEASIBLE OPTION FOR PATIENTS WITH A GOOD PROGNOSTIC PROFILE

Augusto Vaglio[1], Federico Alberici[1], Umberto Maggiore[1], Sebastiano Buti[2], Rodolfo Passalacqua[2], Carlo Buzio[1]. *[1]Clinical Medicine and Nephrology, University Hospital, Parma, Italy; [2]Oncology, Istituti Ospitalieri, Cremona, Italy*

Introduction and Aims: Immunotherapy with IL2 and IFNα still holds a role in the treatment of metastatic renal cell carcinoma (mRCC), despite the availability of new molecularly targeted therapies. However, its efficacy may depend on the prognostic profile of the patients. We report the results obtained using an original immunotherapy schedule with low-dose IL2 and IFNα, chronically administered in both responding and progressing patients, and assess its efficacy in different risk groups.

Methods: 138 consecutive mRCC patients were enrolled in this open, nonrandomised phase II study. IL2 was administered s.c. 5 days per week ($1*10^6$ IU/m^2, twice daily on days 1 and 2 and once daily on days 3-5) and IFNα i.m. twice weekly ($1.8*10^6$ IU/m^2, once a day on days 3 and 5); each immunotherapy cycle consisted of four consecutive weeks, and was repeated indefinitely in all patients at 4-month intervals irrespective of their response. Response was assessed at the end of the second cycle. The prognostic system by Negrier et al. (*Ann Oncol* 2002) was used to stratify patients into different risk groups: this system is based on 5 prognostic factors, i.e. performance status, disease-free interval, hemoglobin level, erythrocyte sedimentation rate/C-reactive protein level, and number of metastatic sites. The patients with 0-1 factor are included in the low risk, those with 2-3 factors in the intermediate risk, and those with 4-5 factors in the high risk group.

Results: 129 patients (93.5%) underwent nephrectomy before entering the trial. A total of 896 cycles were administered, with a median of 5 cycles per patient (range, 0.5-28). The median survival was 19.6 months (95% CI, 13.4-27.4) and the survival probabilities at 36 and 60 months 37% and 25%. Seven patients (5.1%) obtained a complete response and eight (5.8%) a partial response; 16 patients (11.6%) had stable disease and 87 (63%) progressive disease; 20 (14.5%) were not evaluable for response. The overall response rate was 10.9% based on an intent-to-treat analysis. Eleven patients (8%) showed a "late" response, i.e. an objective response or disease stabilization after an initial disease progression. Toxicity was limited to WHO grades 1 and 2 and never required hospitalization. 131 patients were eligible for the risk group analysis: 63, 48 and 20 were respectively included in the low, intermediate and high risk groups. The median survival was 65.1 months (95% CI, 48-82) in the low risk, 11.9 months (95% CI, 9-15) in the intermediate risk and 3.8 months (95% CI, 1-7) in the high risk groups ($p<0.00001$ low *vs* intermediate, $p<0.01$ intermediate *vs* high). The overall response rate was also higher in the low-risk than in the intermediate plus high-risk patients (19% *vs* 4.4%, p=0.008).

Conclusions: Chronically administered immunotherapy with IL2 and IFNα is a safe and effective treatment option for mRCC patients, particularly for those with a favourable prognostic profile.

MP170 FEMALE SEXUAL FUNCTION IN PATIENTS RECEIVING DIFFERENT TYPES OF RENAL REPLACEMENT THERAPY IN COMPARISON WITH HEALTHY WOMEN: PRELIMINARY RESULTS

Alpaslan Altunoglu, Demet Yavuz, Mujdat B. Canoz, Turan Colak, Beril Akman, Siren Sezer, Zubeyde Arat, F. Nurhan Ozdemir, Mehmet Haberal. *Nephrology, Baskent University Faculty of Medicine, Ankara, Turkey; General Surgery, Baskent University Faculty of Medicine, Ankara, Turkey*

Introduction and Aims: There are limited studies correlating possible sexual functional alterations related to the mode of renal replacement therapy among end stage renal disease (ESRD). In this study we performed a cross-sectional observational study to assess sexual function scores and biochemical variables that may have impact on female sexual dysfunction (FSD) in ESRD patients.

Methods: A total of 89 ESRD patients and 32 healthy women were recruited to the present cross-sectional study. The study was consisted of 32 renal transplantation (group I, mean age 37.0±9.1 years, mean post-transplant duration 66.0±60.7 months) and 37 hemodialysis (HD) (group II, mean age 43.1±7.2 years, mean ESRD duration 105.1±51.6 months) and 20 continuous ambulatory peritoneal dialysis (CAPD) (group III,mean age 39.0±10.2 years, mean ESRD duration 62.9±27.9 months) patients. Meanwhile; control group consisted of 32 healthy women (group IV, mean age 36.6±7.6 years). All groups were evaluated with following scales; The Female Sexual Function Index (FSFI) and Short Form (SF)-36 questionnaires, Beck Depression Inventory (BDI), and as well as their sexual history and partners is obtained. Statistical analysis were performed with one-way ANOVA and Student's t-test.

Results: The mean age of the above-mentioned groups were similar ($p>0.05$). Overall, total FSFI scores of women in groups I, II, III and IV were (50.53±26.03, 54.02±22.11, 49.68±24.34 and 71.78±18.32 respectively). The mean total FSFI score was not different in patients receiving different kinds of renal replacement therapy ($p>0.05$), while it was significant better in group IV ($p< 0.001$). In addition, physiological health domain of SF-36 was significantly better in healthy controls ($p<0,001$). The difference in terms of mean of BDI score did not reach to a statistical significance among groups ($p>0.05$).

Conclusions: In this cross-sectional study, we noted lower sexual function

and lower quality of life scores in patients with ESRD compared with healthy controls. It is worth mentioning that mode of renal replacement therapy have no impact on female sexual function. The cause of FSD in this group of patients is probably due to organic factors rather than psychogenic issues.

MP171 ETONOGESTREL IMPLANT IN WOMEN WITH DIABETES

Patrícia Branco, Rita Birne, Lisa Vicente, Zulmira Peerally, José Boavida. *Neprology, Portuguese Diabetic Association, Lisboa, Portugal*

Introduction and Aims: Etonogestrel contraceptive implant has shown to be a safe and effective contraceptive method in healthy women. But there are no studies addressing the use of the etonogestrel implant in women with diabetes and renal disease. The progestogen-only pill is an especially good contraceptive choice for diabetic women since it does not upset blood glucose control or carry any increased risk of vascular disease.
The primary objective of this study was to determine the impact of etonogestrel implant on glycometabolic control and on renal damage in women with type 1 diabetes. The secondary objective was to evaluate the acceptability of the method.
Methods: This is a prospective, single centre clinical trial, study of 23 women with insulin-treated diabetes type 1, who used etonogestrel implant for at least 1 year. Evaluation was performed before implant insertion and at 3, 6, 12, 24 and 36 months after implant insertion.
Results: Twenty three women entered the study but 1 was lost to follow-up. The mean age was 27,6 years ± 6.0 (range 12-37) years and the mean duration of diabetes was 13,7±6.6 years (range 1-25). 14/23 had retinopathy, 10/22 were hypertensive and 9/22 had dislipidemia. There were no contraceptive failures. Among users there were no increment of daily needs of insulin and no significant variation of HbA1c along the study (8.5 vs 8.25, p=ns). There were no significant changes of body mass index (26±3.8 vs 26.4±3.5 kg/m^2 p=ns) or in the lipidic profile with implant use. There were no differences on blood pressure (Pulse Pressure 52±17.9 vs 42.25±6.7, p= ns, Mean arterial Pressure 60.16±9.7 vs 58.16±5.5 mmHg). Comparing the baseline values, microalbuminuria was reduced from 13.92±12.6 to 10.42±12.0 mcg/min (p=0.008), and glomerular filtration rate evaluated by MDRD wasn't different (84.4±18.53 vs 81.88±18.31 ml/min, p=ns). Among women with vascular complications (18/23) there was no clinical cardiovascular events during the follow up. Menstrual changes were the most common side-effect noted.
Conclusions: In this group of women with diabetes the etonogestrel implant was a safe and well accepted contraceptive method, with little clinical impact on glycemic control, glomerular filtration rate or on arterial pressure This study shows that etonogestrel implant in young diabetic women,even with coexisting vascular disease, may reduce proteinuria, and may provide a good contraceptive choice.

MP172 GABAPENTIN IN THE TREATMENT OF PAIN IN HEMODIALYSIS PATIENTS

Huseyin Atalay, Ibrahim Guney, Yalcin Solak, H. Zeki Tonbul, Mehdi Yeksan, N.Yilmaz Selcuk, Suleyman Turk. *Nephrology, Selcuk University, Konya, Turkey*

Introduction and Aims: Although its high prevelance, pain induced by uremic neuropathy is usually underrecognized during diagnostic process and undertreated. In most of the patients, traditional drugs are ineffective.In this study we investigated the effect of gabapentin on neuropathic pain along with quality of life, sleep, anxiety and depression.
Methods: 22 patients with chronic renal failure who were on hemodialysis were included in our study.(10 males and 12 females, mean age 62±3.53) We administered 300 mg/day gabapentin for 8 weeks to patients in whom neuropathic pain was detected. We administered SF-36 Evaluation Test (Physical Component Score and Mental Component Score) for quality of life, Beck's Depression Inventory (BDI) for depression, Beck's Anxiety Inventory (BAI) and Short Form of McGill's Pain Questionnaire (SF-MPQ (VAS (Visual Analogue Score), PPI (Present Pain Intensity), total SF-MPQ)) before and after the treatment.
Results: With gabapentin treatment, we found a statistically significant decrease in pain scale scores. Total SF-MPQ decreased from 21.32±8.74 to 7.5±5.72, VAS scale decreased from 6.4±2.15 to 2.45±1.81, PPI decreased from 3.18±1.1 to 1.3±0.88. We also determened significant improvements in SF-36, BDI, BAI scales (p<0.001).

Effect of Gabapentin on Scales

Parameters	pretreatment	posttreatment	p value
SF-MPQ total	21.32±8.74	7.5±5.72	p<0.001
VAS	6.4±2.15	2.45±1.81	p<0.001
PPI	3.18±1.1	1.3±0.88	p<0.001
PCS	41.31±21.8	70.21±14.2	p<0.001
MCS	55.26±19.78	80.20±9.51	p<0.001
BDI	13.82±4.44	7.05±3.26	p<0.001
BAI	16.05±8.88	8.41±6.22	p<0.001

Conclusions: Gabapentin treatment improved pain which is a frequently encountered problem in hemodialysis patients and also made significant improvements in depression, anxiety and quality of life.

MP173 ASSOCIATION OF N-TERMINAL PRO B-TYPE NATRIURETIC PEPTIDE WITH DIASTOLIC DYSFUNCTION IN PATIENTS WITH DIABETIC NEPHROPATHY

Dimitris Xydakis[1], Apostolos Papadogiannakis[1], Maria Sfakianaki[2], Konstantinos Kostakis[1], Konstantinos Papachristoforou[1]. *[1]Nephrology Department, Venizeleio Hospital, Herakleio, Greece; [2]Internal Medicine Department, Venizeleio Hospital, Herakleio, Greece*

Introduction and Aims: The serum biomarker N-terminal proB-type natriuretic peptide (NT-proBNP), a cleaved fragment of the brain natriuretic peptide (BNP) precursor, is accepted as a standard marker for evaluating and monitoring cardiac injury characterized by myocardial wall stress. The aim of our study was to evaluate a possible relationship of NT-proBNP with diastolic left ventricular dysfunction in patients with diabetic nephropathy (DN).
Methods: We included 62 patients with diabetic nephropathy, 30 normotensive (group A) and 32 hypertensive (group B), matched on age, sex, BMI and years of diabetes. We excluded all patients with known cardiovascular disease, uncontrolled hypertension, acute illness on course and hypertension treatment other than ACE inhibitors.
All patients underwent in a routine blood chemistry control, assessment of NT-proBNP, echocardiography and determination of microalbuminuria.
Results: NT-proBNP plasma levels were statistically higher in group B than group A (93±22 pg/ml vs 51±18 pg/ml, p<0.001). Linear regression analysis showed that there was a significant positive correlation between plasma levels of NT-proBNP and microalbuminuria (p<0.05). Our data showed that levels of NT-proBNP were statistically related with left ventricular mass (r=51), left ventricular end-systolic diameter (r=46), end-systolic intraventricular septum thickness (r=58) and E/A ratio (r=48).
Conclusions: Our data suggest that patients with diabetic nephropathy and hypertension have higher levels of NT-proBNP than normotensive with DN. NT-proBNP is correlated with morphological parameters of left ventricular and with indices of diastolic dysfunction.
The determination of NT-proBNP can be used as a surrogate marker in the work up of DN in order to help identify DN patients with higher risk of diastolic dysfunction and left ventricular hypertrophy.

MP174 ADJUVANT LOW-DOSE IL2 PLUS IFNα IN OPERABLE RENAL CELL CARCINOMA: A PHASE III, RANDOMIZED, MULTICENTER TRIAL

Augusto Vaglio[1], Federico Alberici[1], Sebastiano Buti[2], Camillo Porta[3], Antonio Dal Canton[4], Domenico Potenzoni[5], Rodolfo Passalacqua[2], Caterina Caminiti[1], Carlo Buzio[1]. *[1]Clinical Medicine and Nephrology, University Hospital, Parma, Italy; [2]Oncology, Istituti Ospitalieri, Cremona, Italy; [3]Oncology, University Hospital, Pavia, Italy; [4]Nephrology, University Hospital, Pavia, Italy; [5]Urology, General Hospital, Fidenza, Italy*

Introduction and Aims: In non-metastatic, resected renal cell carcinoma, the standard approach is observation but about 30% of the patients develop metastases during the 5 years following nephrectomy. No trials have so far demonstrated any benefit with the use of adjuvant therapies. Immunotherapy

with low-dose IL2 plus IFNα is effective and well tolerated in patients with metastatic RCC. We investigated whether this immunotherapeutic approach may prevent the occurrence of metastases and prolong recurrence-free survival (RFS) in patients with operable RCC.
Methods: We enrolled patients with a biopsy-proven diagnosis of RCC, age <75, previous nephrectomy and no residual disease. Exclusion criteria were the presence of autoimmune diseases and severe arrhythmias. The patients were stratified according to the tumour stage and grade, and then randomized to treatment or observation. Treatment consisted of repeated cycles of IL2 and IFNα: IL2 was administered s.c. 5 days per week ($1*10^6$ IU/m^2, twice daily on days 1 and 2 and once daily on days 3-5) and IFNα i.m. twice weekly ($1.8*10^6$ IU/m^2, once a day on days 3 and 5); each immunotherapy cycle consisted of four consecutive weeks. The cycles were repeated every four months during the first 2 years and every 6 months for the following 3 years (total, 12 cycles during 5 years).
Results: A total of 310 patients were enrolled between 1996 and 2006, 7 were not eligible because of acute coronary disease: 151 patients were randomized to treatment and 152 to observation. The characteristics of the patients were comparable in the two groups. The median follow-up was 52 months, and the median number of immunotherapy cycles 6 per patient (range 0-16). 77 patients (25.4%) had disease recurrence and 59 (19.5%) died during the study period. RFS was longer in the treatment than in the observation arm, but the difference did not reach statistical significance (hazard ratio, HR 0.81, 95% CI 0.51-1.27, p=0.36). No differences were observed in overall survival. Subgroup analysis showed that the effect of immunotherapy was relevant in patients with age<60 y (p=0.13), tumour grade 1-2 (p=0.14), T3a tumours (p=0.16), and negative lymph nodes (p=0.07). Interaction analysis showed that immunotherapy significantly prolonged RFS in patients with two or more of the above factors (HR 0.44, 95% CI 0.24-0.82, p=0.002). Treatment-related toxicity was mainly limited to WHO grades 1-2.
Conclusions: Adjuvant immunotherapy with low-dose IL2 and IFNα does not prolong RFS in the whole population of patients with operable RCC. However, age<60, negative lymph nodes, T3a and grade 1-2 are predictive of benefit and, in the presence of two or more of these factors, immunotherapy significantly prevents disease recurrences.

Glomerulonephritis 2

MP175 ASSOCIATION OF MEGSIN 2093T-2180C HAPLOTYPE AT THE 3' UNTRANSLATED REGION WITH THE POOR RENAL SURVIVAL IN KOREAN IgA NEPHROPATHY PATIENTS

Chun Soo Lim[1,2], Sun Moon Kim[2], Yun Kyu Oh[1,2], Yon Su Kim[2], Jin Suk Han[2], Yoon Chul Jung[3]. *[1]Internal Medicine, Seoul National University Boramae Hospital, Seoul, Republic of Korea; [2]Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea; [3]Internal Medicine, Bundang Jesaeng Hospital, Sungnam, Gyunggi-do, Republic of Korea*

Introduction and Aims: Megsin, serine proteinase inhibitor, is a mesangial cell-predominant gene which belongs to the serpin superfamily. It has been reported that the expression of megsin is upregulated in IgA nephropathy (IgAN) and the upregulated expression coincides with mesangial proliferation and extracellular matrix expansion. In the present study, we evaluated the influence of the C2093T and C2180T polymorphism within the 3' untranslated region (3'UTR) of megsin gene on the development and progression of Korean IgAN patients.
Methods: Korean patients with biopsy-proven IgAN (N = 260) with a minimal follow-up of 4 years (mean ± SD: 103.0±52.4 months) were recruited. Healthy subjects with normal renal function, normal urinalysis and normotension (N = 315) were included as controls. The C2093T and C2180T polymorphisms were determined by the 5' nuclease allelic discrimination assay, and the haplotypes at the 3'UTR were constructed using the Phase program.
Results: The C2093T and C2180T genotype and allele frequencies were not different significantly between IgAN patients and controls. In C2093T polymorphism, patients with CC genotype showed a better outcome by Kaplan-Meier analysis in terms of renal survival (*P*=.027) than those with CT or TT genotypes. The megsin C2093T polymorphism remained an independent risk factor for progression after multivariate analysis (Cox regression model, HR for TT genotype: 3.52, 95% CI 1.69-7.34, *P*=.001; HR for CT genotype: 2.15, 95% CI 1.30-3.574, *P*=.003). In C2180T polymorphism, patients with TT genotype showed a better outcome by Kaplan-Meier analysis (*P* =.025) than those with CC or CT genotypes. The C2180T polymorphism was also an independent risk factor for progression (Cox regression model, HR for CC genotype: 4.05, 95% CI 1.93-8.51, *P*=.000; HR for CT genotype: 2.35, 95% CI 1.40-3.94, *P*=.003). The two alleles showed linkage disequilibrium in Phased haplotype [2093C-2180T; 347 (66.7%), 2093T-2180C; 166 (31.9%), 2093T-2180T; 6 (1.2%), 2093C-2180C; 1 (0.002%)]. The patients with 2093T-2180C haplotype showed a poor renal survival by Kaplan-Meier analysis (*P*=.028) compared to those with 2093C-2180T haplotype. The haplotype remained an independent risk factor for progression (Cox regression model, HR for 2093T-2180C haplotype: 2.01, 95% CI 1.44-2.81, *P*=.000).
Conclusions: Our results suggest that the 2093T-2180C haplotype at the 3'UTR of megsin gene is associated with rapid disease progression in Korean IgAN patients. This is the reverse of the results from the Chinese IgAN patients. Further studies are strongly needed to explicate the reasons of disparity.

MP176 THE EFFECT OF ALDOSTERON BLOCKADE IN PATIENTS WITH PERSISTENT NEPHROTIC RANGE PROTEINURIA AND MAXIMAL PATHOGENETIC TREATMENT

Adrian Covic, Mihaela Busuioc, Nicoleta Mardare. *Dialysis and Transplantation Centre, "Dr. C.I. Parhon" University Hospital, Iasi, Romania*

Introduction and Aims: Evidence is accumulating that dual therapy with angiotensin-converting enzyme inhibitors (ACEI) and either angiotensin II receptor blockers (ARB) or aldosterone receptor antagonists is more effective in reducing proteinuria than either agent used alone. In our study we prospectively followed up patients with persistent nephrotic syndrome despite immunosuppressive treatment and in which spironolactone treatment was introduced.
Methods: Study group included 15 patients with nephrotic syndrome and persistent > 3.5 g/24 hr proteinuria. These have been previously treated as per current best accepted evidence - with maximal doses of combination immunosuppressives (prednisone and cyclophosphamide/cyclosporine), for sufficient periods of time, combination of antihypertensives to maintain BP <130/85 mmHg including maximum approved doses of ACEI's. Demographic data, biochemical parameters (urea, creatinine, serum potassium), proteinuria and blood pressure were recorded at study entry. In all these patients without remission after a 6 months period of maximal treatment (as defined above), the imunosupressive treatment was stopped and low dose spironolactone (25mg/day) was introduced. Patients were followed for 3 months, with monthly clinical and laboratory evaluations being performed.
Results: Mean age in the study group was 40±14 years, 53.3% were women. The etiology of nephrotic syndrome was: minimal change disease in 2 pts., membranous GN in 4 pts., membranoproliferative GN in 6 pts. and IgA mesangial GN in 3 pts. Following spironolactone introduction, proteinuria decreased in 10 pts. and remained unchanged in 5 pts. However, overall, mean proteinuria decreased significantly over the study period from 8.7±5.5 g/24h to 5.6±4.2 g/24h (p = 0.041). In the same period, the mean creatinine level remained stable (1.01±0.33 mg/dl vs 1.06±0.43 mg/dl). In only one patient, during the second month of follow-up, spironolactone was stopped for 1 week because of important hyperkalemia (K+ = 7.3 mmol/dl) but without clinical or electrocardiographic manifestations.
Conclusions: The study reinforces the importance of aldosterone as a mediator of renal disease and confirms the efficiency of low dose spironolactone in combination with ACE inhibitors in reducing proteinuria in patients with nephrotic syndrome and persistent proteinuria.

MP177 THE ENDOTHELIAL PATTERN OF INJURY IN GLOMERULOPATHIES (GP) AS ASSESSED BY THE IMMUNOHISTOCHEMICAL (IHC) EXPRESSION OF VON WILLEBRAND FACTOR (vWF), CD31 AND CD34-ASSOCIATION TO MORPHOLOGICAL INDICES AND CLINICAL PARAMETERS

C. Gluhovschi[1], G. Gluhovschi[1], E. Potencz[2], D. Herman[2], V. Trandafirescu[1], A. Schiller[1], L. Petrica[1], S. Velciov[1], G. Bozdog[1], F. Bob[1], C. Vernic[3], D. Cioca[4]. *[1]Nephrology, [2]Pathology, [3]Medical Informatics and Biostatistics, University, Timisoara, Romania; [4]Immunology, Austrian Academy of Sciences, Innsbruck, Austria*

Introduction and Aims: An endothelial pattern of injury is the hallmark of malignant hypertension, hemolytic uremic syndrome or vasculitis. The aim was to assess glomerular and interstitial endothelial involvement by studying vWF, CD31 and CD34 in glomerulopathies (GP), as well as their relationship to morphological indices and clinical parameters.
Methods: A cross-sectional study of 36 patients (pts) with GP was performed. Mean age was: 46.44±12.97, 22M, 14F. Standard stains (HE, PAS and Trichrome Gömöri), as well as immunohistochemistry (IHC) (vWF, CD31, CD34) were done on kidney biopsy. Activity and chronicity of GP, as well as glomerular segmental sclerosis and interstitial fibrosis were evaluated according to a scoring system adapted from Neumann (NDT vol 20:96-104). IHC was graded on a scale ranging from 0 to 3. BP, proteinuria, serum Cr and GFR (MDRD) were measured. Statistical analysis (Spearman's rank correlation coefficient, ANOVA) was performed using EpiInfo 6.04, Epi 3.2.2. and SPSS 10.
Results: Histology: 3 pts: crescentic glomerulonephritis (2 primary, 1 vasculitis), 11 pts: FSGS (all primary), 5 pts: MN (1 SLE), 1 pt: membranoproliferative GP (lymphoma), 11 pts; mesangial proliferative GP (all primary), 5 pts: MCD (all primary). Comparing the different histopathological forms by ANOVA we found an extremely significant difference ($p<0.0001$) in the Activity Index (AI), an extremely significant difference ($p<0.0001$) in the Chronicity Index (CI), an extremely significant difference ($p<0.0001$) in glomerular segmental sclerosis, an extremely significant difference (p=0.0009) in interstitial fibrosis, a significant difference (p=0.0376) in proteinuria, a significant difference (p=0.0177) in GFR, a very significant difference (p=0.0037) in interstitial vessel (IV) CD34 immunoexpression and an extremely significant difference ($p<0.0001$) in interstitial vessel (IV) CD31 immunoexpression. Overall, across the 36 pts, correlations are shown in Table 1.

Table 1

Parameter	Parameter	Correlation Coefficient	p-value
CD34 glomerular endothelium (GE)	CD31 GE	r=0.60	p=0.001
CD34 GE	vWF GE	r=-0.18	p=0.19
Cd34 interstitial vesseles (IV)	CD31 IV	r=0.26	p=0.13
CD34 IV	CD31 IV	r=0.13	p=0.28
CD34 GE	CD34 IV	r=0.818	p<0.001
CD31 GE	CD31 IV	r=0.668	p=0.001
vWF GE	vWF IV	r=0.617	p=0.002

No correlation was found between either marker and glomerular segmental sclerosis, interstitial fibrosis, AI, CI and proteinuria. A fair degree of inverse correlation (r=-0.343; p=0.047) between CD34 IV immunoreactivity and GFR was found.
Conclusions: The markers CD34, CD31 and vWF are differentially affected and suggest microvasculature involvement. Loss of the markers was most evident in fibrosclerotic lesions.

MP178 PERSISTENCE OF SYMPTOMATIC CRYOGLOBULINEMIA AFTER THE DISAPPEARANCE OF HCV-RNA IN PATIENTS WITH CRYOGLOBULINEMIC MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (CMP-GN) TREATED WITH INTERFERON AND RIBAVIRIN

Enrique Morales, Elena Gutierrez-Solis, Gabriela Rosello, Eduardo Gutierrez, Eduardo Hernández, Esther González, Evangelina Mérida, Natalia Polanco, Manuel Praga. *Nephrology, H. 12 de Octubre, Madrid, Spain*

Introduction and Aims: Association between HCV infection and cryoglobulinemic membranoproliferative glomerulonephritis (CMP-GN) is a well known phenomenon. HCV infection is an stimulus for clonal B cell expansion that produce IgG-IgM cryoglobulins. Treatment with interferon/ribavirin is effective in a substantial proportion of patients (sustained undetectable HCV RNA). Long-term follow-up of patients with HCV-associated CMP-GN treated with antiviral therapy has been scarcely studied.
Methods: We have analyzed the outcome of 23 patients (15M, 8F; age 48.2±14.7 years, r 24-74) with HCV-associated CMP-GN.
Results: 15 patients were treated with interferon monotherapy or interferon-ribavirin combination. In 11 patients treatment was unsuccessful, due to intolerance to treatment or failure to achieve a sustained HCV-RNA disappearance. In these cases, cryoglobulinemic activity persisted, with recurrent flares of renal disease. In the remaining 4 patients, a durable virologic response was obtained after completion of antiviral therapy, with persistently undetectable HCV-RNA. Nevertheless, IgG-IgM cryoglobulins were detected for long periods in these patients. In two of them, cryoglobulins persisted for 2 and 6 years after the disappearance of HCV-RNA, although no clinical symptoms nor renal activity was observed. Another patient presented an oligoanuric renal failure 3 months after the disappearance of HCV-RNA; renal biopsy showed massive intraglomerular deposits of cryoglobulins together with high values of cryocrit. Renal function recovered after treatment with high-dose steroids, cyclophosphamide and plasmapheresis but the patient died because of infectious complications. The remaining patient showed a similar acute renal failure with massive cryoglobulin deposits, 9 months after HCV-RNA disappearance. Plasmapheresis and steroids were effective to recover renal function, but the patient continued to show recurrent flares of proteinuria, hematuria, skin purpura and renal function worsening. A cycle of rituximab was ineffective and steroids were needed to control cryoglobulinemic symptons. Thirty-six months after HCV-RNA disappearance, cryoglobulins are still detectable, although steroids have been slowly tapered off in the presence of normal renal function and minor urinary abnormalities.
Conclusions: In conclusion, symptomatic cryoglobulinemia can persist for long periods after successful treatment of HCV, even inducing cryoglobulinemic acute renal failure.

MP179 STEROIDS SHOULD BE STARTED RAPIDLY AFTER THE DIAGNOSIS OF DRUG-INDUCED ACUTE INTERSTITIAL NEPHRITIS

Esther González[1], Cristina Galeano[2], Covadonga Chevia[3], Patricia Sequera[4], Carmen Bernis[5], Emilio González-Parra[6], Ramón Delgado[7], Milagros Ortiz[8], M. Sanz[9], Marian Goicoechea[10], Manuel Praga[1]. *[1]Nephrology, H. 12 de Octubre; [2]H. Ramón y Cajal; [3]H. La Paz; [4]H. Principe de Asturias; [5]H. La Princesa; [6]H. Del Aire; [7]H. Ruber; [8]H. Severo Ochoa; [9]H. Getafe; [10]H. Gregorio Marañon, Madrid, Spain*

Introduction and Aims: The role of steroid treatment in drug-induced acute interstitial nephritis (DI-AIN) is a controversial issue.
Methods: We performed a multicenter retrospective study to analyse the influence of steroids in 61 patients with biopsy proven DI-AIN. Baseline renal function was available in all the patients. The responsible drug was an antibiotic in 34 patients (56%), a NSAIDs in 23 (37%) and other drugs in 4 patients. Fifty-two patients (Group 1) were treated with steroids (prednisone 1 mg/kg/day 8-12 weeks) 23±17 days (range 2-68) after the withdrawal of the offending drug and 9 patients (Group 2) were not.
Results: There were no significant baseline differences between Groups 1 and 2. Final serum creatinine (Scr) was significantly lower in Group 1 patients and a significantly higher proportion of Group 2 patients remained on chronic dialysis (44.4% vs 3.8%). Among Group 1 patients, 28 showed a complete recovery of baseline renal function after steroid treatment (Group 1a, final Scr 1.1±0.26 mg/dl) whereas in the remaining 24 patients renal function did not reach the baseline values (Group 1b, final Scr 3.23±2.7 mg/dl). There were no significant differences at baseline between groups 1a and 1b, and the duration and doses of steroids were similar. The onset of steroids after the withdrawal of the offending drug was significantly delayed in Group 1b patients (34±17 days) in comparison with Group 1a (13±10 days, $p<0.0001$). By multiple logistic regression analysis, a longer than 7 days interval between drug withdrawal and onset of steroid treatment was the only clinical factor that significantly increased the risk of an incomplete

recovery of renal function. A significant correlation between the delay in the onset of steroid treatment after drug withdrawal and the final Scr was observed (r=0.45, p<0.005). Renal biopsies, including three patients in whom a second renal biopsy was obtained, showed a progression of interstitial fibrosis related to the delay in steroid treatment. In twenty-three patients the drug responsible for the DI-AIN was identified as a NSAIDs As in the whole group of patients, the main difference between those patients who recovered baseline renal function and those who did not, was the interval between NSAIDs withdrawal and onset of steroid treatment (18.4±16 days vs 31.4±15, p<0.05).

Conclusions: In conclusion, steroids should be rapidly started after the diagnosis of DI-AIN, in order to avoid interstitial fibrosis and an incomplete recovery of renal function.

MP180 ADDITIVE ANTIPROTEINURIC EFFECT OF ALDOSTERONE ANTAGONISTS IN PATIENTS TREATED WITH ACEI AND ARB: A LONG-TERM FOLLOW-UP STUDY

Enrique Morales, Eduardo Gutierrez, Elena Gutierrez-Solis, Esther González, Natalia Polanco, Evangelina Mérida, Eduardo Hernández, Victor Gutierrez-Millet, Manuel Praga. *Nephrology, Hospital 12 de Octubre, Madrid, Spain*

Introduction and Aims: Dual blockade against the renin-angiotensin system with ACE inhibitors (ACEI) and angiotensin-II receptor blocker (ARB) is beneficial both in reducing proteinuria and in slowing the progression of chronic renal diseases. However, some patients still maintain significant proteinuria and progress to end stage renal disease despite dual blockade. We hypothesized that the administration of aldosterone receptor antagonists (ARA) may provide additional renal benefits to ACEI/ARB treatment.

Methods: We evaluated the long-term (16.8±13.3, 6-56 months) effects of ARA on proteinuria and renal function in 11 patients (10 males, 1 female) who maintained significant proteinuria values despite combined ACEI/ARB treatment. Diagnoses were focal glomeruloesclerosis in 4 patients, diabetic nephropathy in 2, IgA nephropathy in 2, nephroangiosclerosis in 2 and membranous glomerulonephritis in 1. We added spironolactone (25 mg/day) or eplerenone (25mg/day) to ACEI/ARB therapy in 6 patients (triple blockade ACEI/ARB/ARA)), whereas in the remaining five patients ARB was withdrawn (dual blockade ACEI/ARA). Evolution of urinary protein excretion, serum creatinine (SCr), glomerular filtration rate (GFR), serum potassium and blood pressure (BP) was analyzed.

Results: After 1 year of therapy, proteinuria had decreased from 4±1.7 to 1.6±1.4 g/24h (p<0.005) (proteinuria decrease 57.6% from the baseline). SCr and GFR remained stable throughout follow-up: initial values 1.57±0.96 mg/dl and 76±44 ml/min/1.73m^2 respectively, final values 1.59±1.4 and 70.8±43. There were not significant changes in BP and body weight. The addition of ARA was followed by a mild although significant rise in serum potassium levels (from 4.4±0.57 mEq/l at baseline to 4.87±0.24 after 12 months of treatment, p<0.05). However, no patient showed hyperkalemia episodes (serum potassium > 5.5 mEq/l) throughout follow-up.

Conclusions: In conclusion, the addition of ARA to patients treated with ACEI/ARB who maintain significant proteinuria induces an important proteinuria decrease. No episodes of hyperkalemia were detected, but close monitoring of serum potassium is advised.

MP181 INFLUENCE OF STEROID TREATMENT ON THE OUTCOME OF PATIENTS WITH ATHEROEMBOLIC RENAL DISEASE

Elena Gutierrez-Solis[1], Enrique Morales[1], Angel Rodriguez-Jornet[2], Carmen Vozmediano[3], J. Ibeas[2], Francisco Rivera[3], Francisco Javier Andreu[2], Manuel Praga[1]. *[1]Nephrology, H. 12 de Octubre, Madrid; [2]H. Parc Taulí, Sabadell; [3]H. General, Ciudad Real, Spain*

Introduction and Aims: Several studies have shown that the incidence of atheroembolic renal disease (ATR) is increasing. However, no prospective studies have been performed to analyze the effectiveness of therapeutic measures. Some recent studies have suggested that steroids can induce a beneficial influence on the final outcome of this disease.

Methods: We have gathered 45 patients with ATR (42 m, 3F; age 68.6± 9,9 y). History of smoking (93%) and hypertension (95%) was very common and most of them had previous cardiovascular events. The intervention that precipitated ATR was cardiac catheterization (40%), arteriography (27%) and onset of anticoagulation (9%), in the remaining patients no factors were identified.

Results: The commonest presentation was an acute renal failure (100%) accompanied by eosinophilia (66%) and skin lesions (60%). In 24 (53%) patients renal function worsened and started chronic dialysis. Thirty (67%) patients died. Fifteen (33%) patients were treated with steroids, whereas the remaining thirty received supportive therapy. Main differences between patients treated or not with steroids are shown in the Table.

	Steroid treatment (N=15)	No Steroids (N=30)	P
Age (years)	72.2±6.6 (63-89)	66.9±10.9 (44-84)	NS
Initial SCr (mg/dL)	4.6±2.2 (2-8.7)	4.4±2.7 (1.1-11)	NS
Final SCr (mg/dL)	5.7±2.3 (1.5-9.7)	4.9±2.9 (1.6-11)	NS
Chronic dialysis (%)	66.7	46.7	NS
Time to onset of dialysis (months)	3.7±3.8 (1-13)	4.4±11.9 (1-48)	NS
Death (%)	73.3	60	NS
Time to death (months)	9.7±8.1 (1-28)	28.6±36.2 (0-131)	NS

Conclusions: In conclusion, patients with ATR have a very poor renal prognosis and survival. Steroid treatment did not improve the final outcome of ATR patients and was associated to a tendency to a more rapid decline of renal function and poorer survival.

MP182 PROGNOSTIC VALUE OF MEASUREMENTS OF TRAIL SERUM CONCENTRATION AND URINARY EXCRETION IN PATIENTS WITH INFLAMMATORY AND NON-INFLAMMATORY PRIMARY GLOMERULONEPHRITIES

Rafal Zwiech, Feliks Kacprzyk. *Department of Kidney Transplantation, Medical University of Lodz, Lodz, Poland*

Introduction and Aims: TRAIL (TNF related apoptosis inducing ligand) may initiate apoptosis. Regarded as cancer cell apoptotic factor TRAIL has been extensively studied including autoimmune and glomerular disorders. Disregulation of apoptosis seems to be extremely important in inflammatory glomerulonethritis and may accelerate the progress of glomerular damage. The aim of the study was to assess whether serum (S) and/or urine (U) TRAIL measurements may be useful as the predicting factor in patients with inflammatory (i-GN) - mesangial proliferative (MGN), membrano-proliferative (MPGN), IgA nephropathy (IgAN), and non-inflammatory (ni-GN) - minimal change disease (MCD), focal glomerulosclerosis (FSGS), membranous nephropathy (MN), chronic glomerulonephritis.

Methods: Seventy nine patients (40 males, 39 females, mean age 42.7±21.3 years with biopsy-proven glomerular disease, i.e. ni-GN: MCD - 10 patients, FSGS - 11, MN – 11; and i-GN: MGN - 19, MPGN – 11, IgAN – 17) and clinical indications for immunosuppressive regiments therapy were included in this study. All of participants were treated with antihypertensive drugs (ACE-I and Ca blockers) and with statins. Mean values of blood pressure and lipids profile did not differ statistically. The control group comprised 10 healthy people. Serum concentration and urinary excretion of TRAIL had been measured using ELISA method before the treatment was instituted. After 12 months of therapy with steroids (initial pulse therapy with methylprednisolone - total dose of 1000 mg per 20 kg b.w. i.v. every other day followed by oral prednisone – 25 mg/day) and cyclophosphamide (0.6 g/m^2 b.s. i.v. once a month for 6 months) both groups i.e. ni-GN and i-GN, were divided into two subgroups according to the treatment results i.e. R– responders 26M, 28F (post-treatment proteinuria below 0.5 g/day and no increases of creatininemia) and NR – nonresponders 15M, 10F (above criteria not fulfilled). Furthermore, patients were matched so that both of subgroups present similar initial: interstitium volume, concentration of serum total protein, serum creatinine or proteinuria/Cr excretion and glomerular filtration.

Results: The obtained results are shown in the table. TRAIL serum concentrations and urinary excretion were higher in all patients than in control group (p<0.01). However TRAIL serum concentrations and urinary excretion did not differ statistically between R and NR subgroups in ni-GN (p=0.11), in i-GN serum concentrations and urinary excretion were higher in R than in NR subgroup (both p<0.05). No correlation between TRAIL urinary excretion and serum concentration was noticed.

		Inflammatory GN		Non-inflammatory GN	
	Healthy	R	NR	R	NR
Serum TRAIL (ng/ml) ± SD	112±31	2456±376.2	1789±321.6	1827±296.6	1767±267.1
Urinary TRAIL (ng/mg Cr) ± SD	2.6±0.9	42.3±30.1	18.0±20.1	33.2±28.8	31.1±30.4

Conclusions: To conclude higher TRAIL serum concentration and urinary exertion pointed better prognosis for remission in patients with inflammatory GN. Those assessments may be considered as a part of initial screening in patients with GN.

MP183 THE INFLUENCE OF IMMUNOSUPRESSIVE TREATMENT ON TRAIL SERUM CONCENTRATION AND URINARY EXCRETION IN PATIENTS WITH INFLAMMATORY AND NON-INFLAMMATORY PRIMARY GLOMERULONEPHRITIES

Rafal Zwiech, Feliks Kacprzyk. *Department of Kidney Transplantation, Medical University of Lodz, Lodz, Poland*

Introduction and Aims: TRAIL (TNF related apoptosis inducing ligand) has gained attention because this ligand seems to induce apoptosis. This was restricted to cancer cells but lately its presence in autoimmune diseases is discussed. Also primary glomerulonephritis – disease of still unknown origin are taken into account. TRAIL by modulating apoptosis subsequently may increase glomeruli regeneration rate and slower the progress of glomerulonephritis (GN). The aim of the study was to assess the influence of immunosuppresive treatment on serum and urine TRAIL in patients with inflammatory (ni-GN) - mesangial proliferative (MGN), membrano-proliferative (MPGN), IgA nephropathy (IgAN), and non-inflammatory (ni-GN) - minimal change disease (MCD), focal glomerulosclerosis (FSGS), membranous nephropathy (MN), chronic glomerulonephritis.
Methods: Seventy nine patients (40 males - M, 39 females - F, mean age 42.7±21.3 years) with biopsy-proven glomerular disease, i.e. ni-GN: MCD - 10 patients, FSGS - 11, MN – 11; and i-GN: MGN - 19, MPGN – 11, IgAN – 17, and clinical indications for immunosuppressive regiment therapy were included. The control group comprised 10 healthy age-matched subjects. All the patients received the identical immunosuppressive protocol which consisted of initial pulse therapy with methylprednisolone (total dose of 1000 mg per 20 kg b.w., 1000 mg i.v. every other day) followed by oral prednisone (20-25 mg/day) and cyclophosphamide (0.6 g/m^2 b.s. i.v.) once a month for 6 months. Serum concentration and urinary excretion of TRAIL were measured by ELISA before the treatment was instituted and after 12 months therapy. All of participants were treated with antihypertensive drugs (ACE-I and Ca blockers) and with statins. Mean values of blood pressure and lipids profile did not differ statistically.
Results: The obtained results are shown in the table. TRAIL serum concentration in patients was higher than in healthy participants ($p<0.01$) and no differences before and after treatment concentration in both subgroups were observed. Serum TRAIL were significantly higher in i-GN than ni-GN before and after treatment ($p<0.01$ both). TRAIL urinary excretion was also significantly higher in patients than in control group. Before treatment the urinary TRAIL was comparable in both subgroups ($p=0.81$) but after was higher in i-GN ($p<0.05$). TRAIL urinary excretion increased after treatment in i-GN and ni-GN (both $p<0.05$). No correlation between TRAIL urinary excretion and serum concentration was noticed.

Patients	Serum TRAIL (ng/ml) ± SD		Urinary TRAIL (ng/mg Cr) ± SD	
	before treatment	after treatment	before treatment	after treatment
ni-GN	1582.2±217.1	1587.8±311.2	33.0±30.3	76.8±37.6
i-GN	2250.1±340.5	1937.4±382.9	35.0±34.3	93.6±48.6
Healthy	112±31		2.6±0.9	

Conclusions: The immunosuppressive treatment reduced TRAIL serum concentration in i-GN but not in ni-GN and did not influence on its urinary excretion. Higher levels of TRIAL in body fluids in patients than in healthy subjects indicate that TRAIL plays a vital role in glomerular lesions formation especially in i-GN.

MP184 PATHOLOGICAL AND PROGNOSTIC VALUE OF URINARY NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) IN PROTEINURIC PATIENTS WITH WORSENING RENAL FUNCTION

Davide Bolignano, Giuseppe Coppolino, Susanna Campo, Antonio Lacquaniti, Michele Buemi. *Department of Internal Medicine, University of Messina, Messina, Italy*

Introduction and Aims: Whatever the cause of injury, a condition of persistent proteinuria can cause a tubular damage, representing a risk factor for the appearance of chronic renal failure. Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a protein released by kidney tubular cells in response to harmful stimuli, which can predict the onset of acute renal failure after several conditions potentially detrimental to the kidney. The aim of the present study was to analyse urinary NGAL levels (uNGAL) in a cohort of proteinuric patients affected by primitive membranous glomerulonephritis. After a 1 year follow-up, patients were re-evaluated to verify whether their baseline uNGAL levels may predict a different renal outcome.
Methods: We enrolled 23 patients with severe proteinuria (3.06±1.71 g/24h) and 20 healthy volunteers. NGAL was measured in urine using with ELISA. Statistical analysis of data was made using the unpaired two-tailed *t*-test, the Pearson correlation coefficient, the ROC analysis and the Fisher test, where appropriate.
Results: Patients showed uNGAL values significantly higher than controls (325.12±144.23 vs 8.25±4.33 ng/mL; $p<0.01$), directly correlated with daily proteinuria ($r=0.32$; $p=0.03$) and serum creatinine ($r=0.51$; $p=0.02$) and inversely correlated with GFR ($r=-0.55$; $p=0.05$). Patients were divided into two groups according to an uNGAL cut-off of 350 ng/mL, selected in a retrospective manner using ROC analysis. Patients with higher uNGAL levels (n=11; 48%) showed a significant worsening in serum creatinine (4.92±2.47 vs 2.06±1.12 mg/dL; $p<0.03$) and GFR (14.96±9.90 vs 58.16±21.65 mL/min; $p<0.04$) at the end of the follow up period, whereas those with lower uNGAL values (n=12; 52%) did not. Moreover, during the whole follow up period, 8/11 patients with higher baseline uNGAL (72%) manifested a decrease in GFR $\geq$ 50% of starting values vs only 1/12 patients (8%) with low uNGAL. Thus, a baseline uNGAL level $\geq$350 ng/mL was associated with a greater risk of a worsening in renal function (Risk Ratio 3.36; $p=0.003$).
Conclusions: Our results showed that severe proteinuria considerably influences the physiological balance of NGAL. Increased uNGAL levels could be the consequence of an augmented loss of circulating NGAL through the damaged glomeruli: this suggestion is supported by the strict correlation found between uNGAL and daily proteinuria. However, it cannot be excluded that tubular cells may actively produce uNGAL as a reaction to chronic damage induced by proteinuria: the correlation found between uNGAL and residual renal function seems to support this hypothesis. Previous studies have demonstrated that NGAL is able to predict a brief-term onset of acute renal failure after several events potentially detrimental to kidney, such as cardiac surgery or contrast administration. Our findings firstly suggest that NGAL may also have a prognostic value in the mid-term, predicting in our patients a chronic worsening of renal function within 1 year. This observation extends the importance of NGAL measurements to the field of chronic renal failure.

MP185 EFFECT OF A SINGLE INTRAVENOUS IMMUNOGLOBULIN INFUSION (IVIg) ON NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN (NGAL) LEVELS IN NEPHROTIC PATIENTS WITH NORMAL RENAL FUNCTION

Davide Bolignano, Giuseppe Coppolino, Susanna Campo, Caterina Bono, Michele Buemi. *Department of Internal Medicine, University of Messin, Messina, Italy*

Introduction and Aims: A significant reduction in daily proteinuria in patients affected by nephrotic syndrome represents a fundamental goal in preventing the progression of renal disease.
In fact, as well as a sign of renal impairment, severe proteinuria constitutes also a cause of tubular injury, which may lead to renal failure.
Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a protein produced by neutrophils but also released by tubular cells after harmful stimuli. In

the present study we aimed to evaluate serum and urinary NGAL levels in a small cohort of patients affected by nephrotic syndrome associated with membranous glomerulonephritis with conserved renal function. In the same subjects, NGAL values were further analyzed after a single high-dose bolus of intravenous immunoglobulin (IVIg), a new promising therapy of some renal diseases, in order to assess whether this treatment may influence the systemic NGAL balance.
Methods: We enrolled 15 patients with stable nephrotic proteinuria (3.95±1.99 g/24h) and conserved renal function (GFR 90.9±36.5 mL/min). Human polyclonal immunoglobulin was administered as a single intravenous bolus (0.4 g/kg). NGAL was measured in serum (sNGAL) and urine (uNGAL) at baseline, immediately after IVIg bolus and after 1 hour. 10 healthy subjects served as controls.
Results: In nephrotic patients, sNGAL and uNGAL values were markedly higher than in controls, being 370.1±180.5 vs 56.2±30.6 ng/mL ($p<0.01$) and 502.2±293.4 vs 7.3±6.1 ng/mL ($p<0.001$) respectively. Furthermore, a very strict correlation was found between sNGAL and uNGAL ($r=0.81$; $p<0.01$) and between uNGAL and daily proteinuria ($r=0.44$; $p<0.03$). Fractional excretion of NGAL (FeNGAL) was increased in patients vs controls and above the unity with a median level of 1.95 ($p<0.05$). Infusion of a single, high-dose bolus of IVIg has induced an impressive decrease from baseline in both serum- (194.1±121 vs. 370.1±180.5 ng/mL, $p<0.05$) and urinary-NGAL levels (153.3±108.6 vs 502.2±293.4 ng/mL, $p<0.03$).
Conclusions: Results obtained suggest that severe proteinuria dramatically influences NGAL balance, even if patients do not show a chronic renal impairment. Increased uNGAL could be the consequence of an augmented loss of circulating NGAL through the damaged glomeruli: this suggestion is supported by the correlations found between uNGAL and, respectively, sNGAL and daily proteinuria. However tubular cells, injured by persistent proteinuria, could be responsible for increased sNGAL and uNGAL levels through an active stress-induced production, as suggested by the increased FeNGAL level found in patients. Furthermore, other extra-renal cells (neutrophils, endothelium) may also give a significant contribution, as the expression of a systemic stress related to nephrotic syndrome, similarly to what previously described for other cytokines. This last hypothesis would further explicate the impressive decrease in NGAL values after infusion of IVIg, showing another proof of beneficial anti-inflammatory properties of this therapy in renal diseases.

MP186 COLLAPSING GLOMERULOPATHY: CLINICOPATHOLOGICAL FINDINGS OF 80 CASES

Sanjeev Sethi. *Laboratory Medicine and Pathology, Mayo Clinic, Rochester, USA*

Introduction and Aims: Collapsing glomerulopathy, a variant of focal segmental glomerulosclerosis (FSGS) has been associated with human immunodeficiency virus (HIV) infection. We reviewed all cases of collapsing FSGS received at the Department of Pathology, Mayo Clinic, between February 1995 and December 2006, to determine the relative frequency of other diseases associated with collapsing glomerulopathy.
Methods: A total of 80 cases were diagnosed in that time period. The mean age of the patients was 41.9 (±14.3) years. There were 43 males and 37 females. Eighteen patients were African-American.
Results: The medical history was positive for viral infections in 10 cases, autoimmune diseases in 10 cases and 10 cases were present following transplantation. Four patients were obese (BMI>30) and 4 patients were treated with Pamidronate. One case presented with thrombotic microangiopathy. There was no apparent cause in the remaining 41 cases. Viral infections included HIV infection in 5 cases and Hepatitis C infection in the other 5 cases. Auto-immune diseases included 4 cases of Systemic Lupus Erythematosus, 1 case of polyarteritis nodosum, 1 case of Sjögren's syndrome, 1 case of scleroderma and 3 cases with positive ANA titers. The 10 cases following transplantation included 6 in renal allografts (all *de novo*), 1 following cardiac transplantation, 2 following bone marrow transplantation for multiple myeloma and 1 followed liver transplantation.
Conclusions: In summary, this study shows a diverse group of disorders associated with collapsing glomerulopathy, all of which have an altered immune status. The common association of collapsing glomerulopathy was with viral infections (12.5%), transplant recipients (12.5%), and autoimmune disorders (12.5%).

MP187 EFFECTS OF SPIRONOLACTONE ON PROTEINURIA AND URINARY TGF-β1 IN IgA NEPHROPATHY

Chun-Gyoo Ihm, Tae Lee, Sang Lee, Mina Park, Ju Moon, Kyung Jeong. *Division of Nephrology, Kyung Hee University, Seoul, Republic of Korea*

Introduction and Aims: The activation of renin-angiotensin II-aldosterone system (RAAS) causes renal injury and fibrosis in IgA nephropathy (IgAN) mainly through the role of TGF-β. We and others observed that the measurement of urinary TGF-β is useful in evaluating the degree of renal injuries in patients with IgAN. The aim of the study was to evaluate the therapeutic effects of prednisolone (n=11), angiotensin II receptor blocker (ARB) (n=13), or spironolactone (n=11) on proteinuria and urinary TGF-β1 excretion in patients with IgAN (n=35).
Methods: Total TGF-β1 was measured by ELISA after acidification in morning urine specimens.
Results: The patients with IgAN had a higher urinary excretion of TGF-β1 than normal controls (n=13). Urinary TGF-β1 excretion was positively correlated with proteinuria and pathological grading but not with serum creatinine. After 8 weeks of spironolactone treatment (25 mg/day), no significant change in proteinuria was noticed (0.70±0.33 vs 0.53±0.32 g/gCr; $p>0.05$). A tendency of reduction in urinary TGF-β1 excretion was observed, but there were no significant differences (21.60±22.88 pg/mg Cr vs 7.11±4.52 pg/mg Cr; $p=0.06$). Treatment with prednisolone or ARB could significantly reduce the urinary excretion of protein and TGF-β1 ($p<0.05$). There was a significant correlation between the urinary TGF-β1 excretion and the serum aldosterone ($g=0.84$; $p=0.006$), but treatment with spironolactone abolished this correlation ($g=0.042$; $p=0.91$). No differences of blood pressure were found among treatment groups.
Conclusions: Spironolactone monotherapy may be deficient in the treatment of IgAN. Urinary excretion of TGF-β1 can be an indicator of response to RAAS blockade in patients with IgAN.

MP188 PROGNOSTIC FACTORS IN PATIENTS WITH LUPUS NEPHRITIS

Daniela Monova[1], Simeon Monov[1], Todor Todorov[2]. [1]*Department of Internal Diseases, Medical University, Sofia, Bulgaria;* [2]*Department of Pathoanathomy, Medical University, Sofia, Bulgaria*

Introduction and Aims: Renal involvement is one of the major determinants of the outcome in patients with systemic lupus erythematosus.
The objective of this study was to evaluate the prognostic significance of clinical and renal biopsy findings in patients with lupus nephritis. 209 patients (184 of them female) were included in the study.
Methods: We retrospective studied the age, gender, serum creatinine, estimated glomerular filtration rate, presence of hypertention, degree of proteinuria, duration of nephritis symptoms prior to biopsy, haematuria, serum albumin, complement components levels, renal histology, activity and chronicity index, haematocrit, haemoglobin, antinuclear antibodies titer, antibodies titer against double-standed deoxyribonucleic acid, antiphospholipid antibodies, urinalysis, and type of immunosuppression therapy. Mean age at biopsy was 34,7±11,3 years. Renal biopsies were classified according to the WHO criteria and examined for the presence of active and chronic histological changes. A variety of clinical and biopsy findings including several histological markers of chronic renal damage were identified by univariate and multivariate analyses.
Results: The median follow-up time was 14,8 years (0,5-23,0 yrs). In all cases, immunosuppressive treatment was initiated or intensified within one month following renal biopsy. The cumulative incidence of doubling serum creatinine or death after 3 and 5 years was 22,97% and 43,54%, respectively. In multivariate regression analyses, duration of nephritis symproms > 6 months prior to biopsy, serum creatinine > 140 μmol/l, anti-dsDNA titer, diffuse proliferative glomerulonephritis, tubular atrophy, emerged as the strongest combination of independent risk factors.
Patients reaching doubling serum creatinine had predominantly proliferative lupus nephritis ($P<0,001$) with nephrotic range proteinuria ($p<0,001$), higher activity index score ($p<0,05$), chronicity index score ($p<0,05$), serum creatinine ($P<0,05$) and mean arterial pressure ($P<0,05$), but lower baseline hematocrit ($P<0,05$) and complement C3 ($P<0,025$). Treatment with corticosteroids alone was also associated with poor outcome.
Conclusions: Our results confirm the negative prognostic impact of elevated

serum creatinine at the time of the kidney biopsy, class IV histopathology, high mean arterial pressure and nephrotic range proteinuria and tubular atrophy in lupus nephritis. Our data show that delay between onset of nephritis and renal biopsy constitutes an important risk factor of renal failure. Patients with SLE should have kidney biopsy as soon as clinical signs of nephritis are evident in order to accelerate treatment decisions and minimize risk of inflammation-induced irreversible kidney damage.

MP189 EFFECT OF TONSILLECTOMY PLUS STEROID PULSE THERAPY ON CLINICAL REMISSION IN PATIENTS WITH IgA NEPHROPATHY: A CONTROLLED STUDY

Hiroyuki Komatsu, Shouichi Fujimoto, Seiichiro Hara, Kazuhiro Yamada, Yuji Sato, Kazuo Kitamura. *Circulatory and Body Fluid Regulation, Department of Internal Medicine, Faculty of Medicine, University of Miyazaki, Kiyotake, Miyazaki, Japan*

Introduction and Aims: There are few evidences for the efficacy of tonsillectomy combined with steroid pulse therapy on IgA nephropathy with a well-designed study. We performed a prospective, non-randomized controlled study of the effects of the combined therapy vs. steroid pulse alone in patients with IgA nephropathy.
Methods: We enrolled 55 patients diagnosed with IgA nephropathy at renal biopsy between 1999 and 2003 and followed them up for 54.0±21.2 months. Thirty-five patients underwent tonsillectomy and received steroid pulse therapy (group C), and 20 received steroid pulse monotherapy (group M). Both groups received methylprednisolone (0.5 g/day) intravenously for three consecutive days, followed by oral prednisolone (initial dose, 0.5 mg/kg/day) that was tapered to zero over 12 months.
Study end-points were 100% increase in serum creatinine from the baseline levels or disappearance of urinary protein (UP) and/or occult blood (UOB) indicating clinical remission.
Results: At 24 months after the initial treatment, the percentage of disappearance of UP and UOB was higher in group C than in group M (UP, 76.5 vs. 41.2%, $p = 0.013$; UOB, 79.4 vs. 17.6%, $p < 0.001$), and the curative effect persisted until the final observation (UP, 65.7 vs. 35.0%, $p = 0.028$; UOB, 77.1 vs. 45.0%, $p = 0.016$). None of group C achieved a 100% increase in serum creatinine from the baseline level, whereas one patient in group M developed end-stage renal disease during the observation period. The histological findings from repeated biopsy specimens from 18 patients revealed that the extent of mesangial proliferation and distribution of IgA deposition were significantly reduced in group C, compared with group M. The Cox regression model with UP remission as a dependent variable showed that the combination therapy significantly impacted this parameter (Hazard ratio, 6.01; 95% CI, 1.98-18.2; $p = 0.002$).
Conclusions: Tonsillectomy combined with steroid pulse treatment can apparently induce clinical remission in patients with IgA nephropathy.

MP190 PROTEINS REGULATING BONE METABOLISM AND VASCULAR CALCIFICATION IN PATIENTS WITH NEPHROTIC SYNDROME

B. Przepiorkowska[1], T. Stompor[1], M. Krzanowski[1], E. Chowaniec[1], B. Kusnierz[2], W. Sulowicz[1]. *[1]Department of Nephrolgy; [2]Department of Clinical Biochemistry, Jagiellonian Uniwersity, Cracow, Poland*

Introduction and Aims: Vascular calcification and bone disorders are abundant pathologies found in chronic kidney disease (CKD) patients, especially in CKD stage 5. These abnormalities start to develop much earlier and are usually advanced in CKD 3-5. However, the exact "starting point" of developing these pathologies remains unknown. We hypothesized that glomerular disease with nephrotic syndrome can be associated with abnormal synthesis and/or urinary losses of proteins involved in bone metabolism and extraosseous calcification. The aim of this pilot study was to measure the serum levels of such proteins in patients with nephrotic syndrome.
Methods: Twenty one patients (11 F, mean age 41.5±16.6 years) underwent kidney biopsy due to recently diagnosed nephrotic syndrome. The following proteins considered as regulators of bone metabolism and extraosseous calcification were measured: matrix gla protein (MGP), osteocalcin (OC), osteoprotegerin (OPG), osteopontin (OP), fetuin A (FetuA) and FGF 23.
Results: Parameters characterizing the severity of nephrotic syndrome and levels of tested proteins with their reference values are presented in table 1.

Table 1

Parameter	Unit	Value	Ref. value
Tot. protein	g/L	58.3±14.8	60-80
albumin	g/L	33.0±11.1	35-55
Tot. chol.	mmol/L	6.8±1.79	3.6-5.2
Cl Cr	ml/min/1.73m^2	85.7±29.9	> 90
Proteinuria	g/L	5.37±4.26	–
Daily protein loss	g/24 h	8.98±4.9	–
MGP	nmol/L	5.0±1.14	0.7-7.0
OC	ng/mL	6.21±3.74	3.7-10.0
OPG	pmol/L	2.95 (2.1-11.3)*	1.8*
OP	nmol/L	129.7±68.4	49.2-175
FetuA	g/L	0.5±0.15	0.35-0.95
FGF 23	RU/mL**	118.4±212.0	N/A

*Median for reference population, **RU-relative units.

Analysis of correlations between serum protein, serum albumin, proteinuria, daily protein loss and tested regulatory proteins revealed some significant relationships only for FetuA (table 2). In addition, significant correlation has been found between ClCr and MGP ($R = 0.52$, $p = 0.04$).

Table 2

	Total protein	Albumin	Proteinuria	Daily protein loss
R	0.57	0.64	-0.36	−0.57
p	0.02	0.007	NS	0.02

Conclusions: Comparison of patients with daily protein loss below or above median (8.4 g/24 h) revealed the trend for lower FetuA in patients with higher protein loss (0.47±0.17 vs. 0.61±0.09 g/L; $p = 0.07$). Our preliminary results suggest that nephrotic range proteinuria does not impact on the serum levels of tested proteins involved in bone metabolism and vascular calcification, except for FetuA. Whether it may impact on an increased risk for bone resorption and/or vascular calcification needs further longterm observations.

MP191 MYELOPEROXIDASE-ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED RENAL VASCULITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Noriaki Kurita[1], Naobumi Mise[1], Akiko Fujii[2], Masaya Mori[2], Keiko Sai[1], Takahiro Nishi[1], Hitoshi Tagawa[1], Tokuichiro Sugimoto[1]. *[1]Department of Nephrology, Mitsui Memorial Hospital, Tokyo, Japan; [2]Department of Pathology, Mitsui Memorial Hospital, Tokyo, Japan*

Introduction and Aims: Myeloperoxidase (MPO)-antineutrophil cytoplasmic antibody (ANCA)-associated renal vasculitis (RV) often occurs in patients with rheumatoid arthritis (RA). We tried to clarify the clinical characteristics of the ANCA associated RV in patients with RA.
Methods: From 1992 to 2006 we experienced thirteen cases of MPO-ANCA-associated RV; 3 with RA (3 females; RA(+)) and 10 without RA (6 males and 4 females; RA(-)). Renal biopsy was performed in all RA(+) and six RA(-). We examined clinical and pathological parameters in the two groups.
Results: At the time of diagnosis the patients were significantly younger and the time duration from the symptoms onset was longer in RA(+) than in RA(-) (45 vs. 70 years; $P = 0.0005$, 495 vs. 147 days; $P = 0.003$, respectively). The estimated GFR by MDRD formula was comparable in the both groups (10.9 vs. 8.0 mL/min; $P = 0.26$), however the serum creatinine level was significantly lower in RA(+) than in RA(-) (3.4 vs. 8.2 mg/dL; $P = 0.034$). The RA(+) demonstrated lower Birmingham Vasculitis Activity Score and CRP value than RA(-) (12.3 vs. 19.4; $P = 0.0051$, 0.9 vs. 5.2 mg/dl; $p = 0.029$, respectively). The average duration of RA was 11 years in RA(+). Renal biopsy revealed a greater percentage of glomerular sclerosis in RA(+) than in RA(-), although the difference did not reach statistical significance (63 vs. 32%; $P = 0.16$).
Conclusions: MPO-ANCA-associated RV in RA appeared to develop at younger ages with RA duration of more than ten years. Longer periods were required until the diagnosis of RV, possibly because their extrarenal symptoms were obscure and they demonstrated relatively lower serum creatinine values for GFR, as RA patients had smaller muscle volume. This

difficulty of early diagnosis may also come from the slow progression of RV due to the immunosuppressive treatment in RA(+).

MP192 AUTOANTIBODIES AGAINST THE GLOBULAR FRAGMENTS OF THE INDIVIDUAL CHAINS OF C1q IN LUPUS NEPHRITIS

Vasil Vasilev[1], Ivanka Tsacheva[2], Boriana Deliyska[1], Violeta Stoianova[2], Maria Radanova[3], Maria Chorbadjieva[2], Svetla Petrova[2]. *[1]Medical University, Univ. Hosp. Queen Giovanna, Sofia, Bulgaria; [2]Sofia University Department of Biochemistry, Sofia University, Faculty Biology, Sofia, Bulgaria; [3]Department of Pharmacology, Medical University, Varna, Bulgaria*

Introduction and Aims: C1q is the recognition molecule of the classical pathway of complement activation. It is characteristically activated by binding to immune complexes.
Antibodies to C1q (C1qAb) are found in healthy people and increased levels are found more frequently in older age groups. The observation of anti-C1q antibodies in patients with systemic lupus erythematosus (SLE) has led to the establishment of a strong correlation between the titers of these antibodies and renal involvement in the patients.
The aim of the study was to detect the presence of autoantibodies against the globular fragments of each of the chains-A, B, C of C1q and to evaluate them according to the activity of SLE.
Methods: We analyzed by ELISA sera from 34 SLE patients with biopsy proved different classes lupus nephritis for the presence of autoantibodies against globular fragments of each of the chains - A, B and C, of C1q, using recombinant globular head regions of individual A, B and C chains of human C1q. For reference we examined sera from 62 healthy volunteers. Patients were divided in 2 groups according to the complex activity of disease-15 of them were in complete remission and 19 patients were with disease activity.
Results: Patients with remission were with lower levels of total anti-C1q antibodies and anti-globular antibodies, but there were not significant differences in the values compared with the group with activity of SLE. The rate of lower levels of antibody against fragments of chains A, B and C are higher in group with remission. The levels of antibodies against globular fragments of B and C chains of C1q correlate in group with remission ($r=0,903$, $p<0,05$) and in the group with activity of SLE ($r=0,712$, $p<0,05$).
Conclusions: We conclude that in lupus nephritis there were not only antibodies against total C1q, but also antibodies against globular fragments of each of the chains - A, B and C, of C1q. There were not significant differences in their levels according to the disease activity, but the SLE patients with remission more often have lower levels of antibodies against globular fragments of A, B, C chains of C1q.

MP193 RITUXIMAB FOR MULTIRELAPSING AND STEROID-DEPENDENT MINIMAL CHANGE NEFROPATHY (MCN)

Samiha Benedek, Annette Bruchfeld. *Division of Renal Medicine, Karolinska University Hospital at Huddinge, CLINTEC, Karolinska Institutet, Stockholm, Sweden*

Introduction and Aims: Minimal change nephropathy (MCN) accounts for 10 to 15 percent of cases of the nephrotic syndrome in adults, and is the most common cause of MCN-cases in children. It has been proposed that MCN reflects a disorder of T lymphocytes. Rituximab is a chimeric monoclonal antibody directed against CD20+ B cells with reported benefit in immune-mediated renal disease, possibly by indirectly regulating T-cell function. The aim of the present case series was to evaluate the use of Rituximab in MCN.
Methods: We present three female patients (52, 30 and 27 years of age) with multirelapsing MCN whilst on corticosteroid therapy. Patient 1 had suffered from >10 relapses in 14 years, and had received 6 courses of Cyclophosfamide 12 years earlier with minor effect and has remained steroid dependant. Pat 2 with a 10-year history of multirelapsing MCN was steroid free for 4 years. During the last year she had a major relapse and has been steroid-dependent since then. Pat 3, diagnosed 15 months ago is currently also steroid dependent with multiple relapses.
Pat 1 and pat 2 were given 2 courses of Rituximab 500mg i.v, the second dosage given two weeks after the initial treatment. Pat 3 is awaiting her second and final dosage.
Results: The CD 20 cell count was taken before each therapy. In pat 1 the peripheral CD 20 + B cell count fell to 0,03% after treatment, the figure being similar in pat 2. Before treatment this figure was 3% and 7% respectively. Since the completion of Rituximab therapy in pat 1 and 2 (10 and 3 months respectively) corticosteroids have been tapered. They are currently on low dose steroid therapy (2.5-5 mg/day) and are in complete remission without traces of albuminuria and hypoalbuminemia. Patient 3 with a CD 20 + B cell count of 13% prior to therapy is currently undergoing concomitant high dose steroid therapy which is to be tapered after the final dosage of rituximab.
Conclusions: Frequency of relapses and steroid dependency in MCN are therapeutic challenges to physicians. The current case series together with recent reports points to the fact that Rituximab may be of clinical use in the management of steroid-dependent multirelapsing MCN patients.

MP194 HASHIMOTO'S THYROIDITIS AND IgA NEPHROPATHY: AN UNDERESTIMATED ASSOCIATION?

Antonio Pasquariello[1], Maurizio Innocenti[1], Nadia Sami[2], Angelica Kanaki[2], Costanza Tattanelli[2], Daniela Campani[3], Luca Pollina[3], Giovanna Pasquariello[1], Vincenzo Panichi[2]. *[1]Division of Nephrology, S. Chiara Hospital, Pisa, Italy; [2]Department of Internal Medicine, University of Pisa, Pisa, Italy; [3]Department of Pathology, University of Pisa, Pisa, Italy*

Introduction and Aims: Various types of primary glomerulonephritis have been reported in association with autoimmune thyroiditis, but the most frequent is membranous glomerulonephritis (MGN). To establish the real association rate of Hashimoto's thyroiditis (HT) with IgA nephropathy (IgAN) and membranous glomerulonephritis, we studied prospectively 65 consecutive patients (Pts) with biopsy proven IgAN (42 M,25 F) and 86 consecutive Pts with MGN (49 M, 37 F) in our Division of Nephrology from June 2002 to November 2007.
Methods: In both groups we documented the number of patients presenting with a positive anamnesis of HT, and in this case we controlled the serum levels of TSH, free T4, free T3, antithyroglobulin antibodies and anti-thyroid peroxidase antibodies by laboratory analysis.
Results: Of the group with IgAN, eight female subjects (12.3%) aging from 26 to 70 years with a mean age of 41, revealed to suffer from autoimmune thyroiditis. All Pts had high serum levels of antithyroglobulin antibodies ranging from 327 to 873 UI/ml (vn < 34) or anti-thyroid peroxidase antibodies ranging from 315 to 927 UI/ml (nm < 12). In the second group of 86 Pts with MGN only one female subject suffered from HT (1.2%), and other two female Pts presented a nontoxic multinodular goiter.
Conclusions: The presence of two immunological disorders in the same patients cannot be considered a casual coincidence, but rather a consequential pathogenetic event. In both groups with autoimmune thyroiditis and glomerulonephritis the Pts were young women, and this datum reflects the prevalence of HT for the feminine gender (10 F/1 M). If we consider only the female Pts with IgAN the incidence rises further to 32%. Our results do not confirm the prevalence of MGN in patients with HT, but demonstrate a high incidence of IgAN secondary to autoimmune thyroiditis especially in young women. Since HT can have subclinical symptoms or normal thyroid function, we believe that the possibility of an underlying HT in female Pts with apparent IgAN should be investigated.

MP195 MPA-AUC AND ADVERSE DRUG REACTION IN LUPUS NEPHRITIS TREATED WITH MYCOPHENOLATE MOFETIL

Honglang Xie, Weixin Hu, Haitao Zhang, Hao Bao, Zhihong Liu, Leishi Li. *Research Institute of Nephrology, Jinling Hospital, Nanjing, Jiangsu, China*

Introduction and Aims: To retrospective assess the relationship between blood concentration of mycophenolate mofetil (MMF)and adverse drug reaction (ADR) in lupus nephritis (LN).
Methods: 162 cases of LN patients (143 female and 19 male) treated with MMF were included, with an average of 28.90 ± 12.57 years old. All patients received methylprednisolone (MP) pulse therapy, oral prednisone

and MMF therapy, with an initial MMF dose of 1.0~2.0g/d. Plasma total mycophenolic acid (MPA) concentration was detected (HPLC) and MPA-AUC was calculated according to MPA-C_0,$C_{0.5}$ and C_2. The relationship between MPA-AUC, C_0, $C_{0.5}$, C_2 and ADR were analyzed.
Results: (1) MMF dose corrected plasma totol MPA-AUC varied significantly among patients (9.18~137.2)mg.h/L.g, mean of (33.4±17.6)mg.h/L.g. (2)Within the 12 month of MMF therapy, a total of 40 (24.7%) ADR occurred in 32 (19.8%)patients. Infection occurred in 26 cases (16.0%), including pneumonia in 10 case (6.17%) and herpes zoster in 11 case (6.79%). 87.5% of ADR and 80.8% of infection occurred within 3 months of MMF treatment. The initial MPA-AUC (detected 1~2 week after intake of MMF) (52.4±16.6 vs 39.8±14.7, $p<0.01$)and MPA-C_0(2.5±1.5mg/L vs 1.7±1.0 mg/L, $p<0.05$) was significantly higher in patients with ADR.The incidence of ADR was significantly higher in the initial MPA-AUC>40 (mg.h/L) group (33.8% vs 18.2%,$P<0.01$.The incidence of ADR and infection were also markedly elevated in patients with MPA-AUC>40 (mg.h/L) during MMF treatment (18.0% vs 4.0% and 12.4% vs 2.0%, $p<0.01$ respectively). MPA-AUC level was higher than 40 (mg.h/L) in 90% of patients before onset of pneumonia. Furthermore, MPA-C_0 at the initial and during MMF treatment were both significantly higher when complicated with ADR and infection, but MPA-$C_{0.5h}$ and MPA-C_2 was not differed.
Conclusions: MPA-AUC and C_0 at the initial and during MMF treatment were related with ADR in LN patients. The incidence of ADR increased when MPA-AUC>40 (mg.h/L). The suggested initial MPA-AUC should be less than 40 (mg.h/L)in LN, but perspective study was needed.

MP196 CLINICAL AND IMMUNOLOGICAL FEATURES IN 1650 CHINESE PATIENTS WITH LUPUS NEPHRITIS

Weixin Hu, Chunbei Liu, Haiou Sun, Zhengzhao Liu, Honglang Xie, Huiping Chen, Zhihong Liu, Leishi Li. *Research Institute of Nephrology, Jingling Hospital, Nanjing University School of Medicine, Nanjing, Jiangsu, China*

Introduction and Aims: Lupus nephritis (LN) is the most common causes of secondary glomerulonephritis in China, however the epidemiology, clinical and immunological features have not yet been studied in the large sample of patients. This study was to analyze the main clinical manifestations and immunological features in 1650 Chinese LN patients with different histological classes.
Methods: 1650 patients in Jingling Hospital from 1986 to 2006 were included. All patients had renal biopsy, histological classification was categorized according to 2003 ISN/RPS classification (Class I and VI were not included in the study). The combined class of V with class IV or III were recorded as V+IV or V+III. Clinical features and immunological characteristics in different histological types of lupus nephritis were retrospectively analyzed.
Results: 1650 patients included 1483 (89.9%) females, 167 (10.1%) males, 80% of them were 18-50 years old (mean 27.0±8.2 years). The renal histological classes showed class II (13.0%), III (5.8%), IV (47.2%), V (15.7%), V+IV (12.9%) and V+III (5.3%). The proportion of class II (13.8%) and III (6.3%) in females was much higher than that in males (6.6% and 1.2% respectively, $P<0.05$), while class IV was more common in males than in females (68.2% vs 44.8%, $P<0.01$). The incidence of malar rash, fever, arthritis and anemia were much higher in class II than that in other types. The serositis, positive anti-dsDNA antibody and low C4 were more frequent in class IV and V+IV but less in class V. The skin vasculitis and serum ANCA (all were mpo-ANCA positive) were more common in class III (10.3%) and IV (5.3%). The anticardiolipin antibodies were found in all types but higher in class III (43.9%) while cryglobulinemia was more prominent in class V+III (64.6%), V+IV (54.6%) and V (53.4%). The patients with hematuria in class II (19.5%) and V (33.3%) were much less than that in class IV (81.4%), V+IV (81.2%), V+III (72.7%) and III (59.4%), while grass hematuria and RPGN were only found in class IV (10.9% and 24.4% respectively), V+IV (5.2%, 16.4%), V+III (6.8%,9.1%), III (6.3%,1.0%). The incidence of nephrotic syndrome was higher in class V+IV (40.4%) than that in class IV (20.5%), class V (34.0%) and V+III (31.8%).
Conclusions: Lupus nephritis class IV was the most common histological type in this study, class V combined with class IV or III was also common and should be identified. The sex difference influences the pattern of histological types. The correlation between histological class and clinical-immunological features might be associated with unique immunopathogenesis.

MP197 NITRIC OXIDE IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME

Magdalena Makowiecka, Anna Medynska, Katarzyna Kilis-Pstrusinska, Danuta Zwolinska. *Pediatric Nephrology, Medical University, Wroclaw, Poland*

Introduction and Aims: The pathogenesis of idiopathic nephrotic syndrome (INS), despite of many investigations, is still unknown. Nitric oxide (NO) is a free-radical gas, involved in numerous biological functions. It has been reported that free-radical particals could be responsible for endothelium injury. The role of NO in pathogenesis of glomerular diseases is controversial. High levels of NO production have been reported in animal models of glomerulonephritis. The aim of our study was to analyse plasma and urinary levels of nitrite/ nitrate (NOx) in children with INS.
Methods: The study group involved 20 children (14 boys, 6 girls) aged 2-17 years (mean 8,8) with diagnosis of INS. Control group included 15 patients (6 girls, 9 boys) aged 5-14 years (mean 8,85) with nocturnal enuresis. In all children renal function was normal. In children with INS urine and plasma samples were collected twice: in acute phase (before the initiation of corticosteroid treatment) and in remission. Most of NO in biologic fluids is oxidized to nitrite (NO_2^-) and nitrate (NO_3^-), the concentration of these stable anions have been used as a measure of NO production. We determined both nitrite and nitrate levels in samples using kit from R&D Systems. The results were expressed as sum of NO_2^- and NO_3^- (NOx).
Results: Mean NOx concentration in plasma obtained from children in acute phase of INS (111,064±4,02μmol/l) significantly decreased in the phase of remission (84,343±4,72μmol/l, $p<0.0001$), but was still enhanced comparing to the healthy controls (75,002±11,748μmol/l, $p=0.035$). No significant difference was found in urine NOx levels between children in relapse of INS (348,80±128,24μmol/g creat.) and in remission (291,69±151,93 μmol/g creat.). Urinary NOx excretion was significantly higher in INS patients, both in acute phase and in remission, compared to healthy children (201,51±12,76μmol/g creat., $p<0.0001$ and $p<0.019$, respectively). No correlation between NOx levels and proteinuria was found.
Conclusions: Persistently increased NOx concentration in children with INS, both in relapse and in remission, suggest that NO are not directly engaged in the pathomechanism of proteinuria. However, significantly higher NOx level in plasma and urine of INS patients imply that it may be involved in ongoing inflammation.

MP198 HEPATOCYTE GROWTH FACTOR (HGF) AND TRANSFORMING GROWTH FACTOR (TGF) EXPRESSION IN LUPUS NEPHRITIS. ROLE OF THE HGF/TGF RATIO AS A PROGNOSTIC FACTOR

Stefano Costanzi[1], Pietro Manuel Ferraro[1], Elisa Gremese[2], Gianfranco Zannoni[3], Vincenzo Arena[3], Silvia D'Alonzo[1], Gianfranco Ferraccioli[2]. *[1]Department of Nephrology, Catholic University of Sacred Heart, Rome, Italy; [2]Department of Rheumatology, Catholic University of Sacred Heart, Rome, Italy; [3]Department of Pathology, Catholic University of Sacred Heart, Rome, Italy*

Introduction and Aims: Several clinical and renal biopsy findings have been associated with an increased risk of renal failure in lupus nephritis. However, the prognostic value of different clinical and histological factors remains debated. Hepatocyte growth factor (HGF) and transforming growth factor (TGF-β1) are implicated in renal damage in several animal models. We sought to evaluate HGF and TGF-β1 expression in renal specimens of lupus nephritis patients and their role to predict the renal outcome at six months of immunosuppressant therapy.
Methods: 42 consecutive patients with newly diagnosed lupus nephritis were included in the study. Renal biopsy specimens were classified according to the WHO criteria and examined for the presence of active and chronic histological changes. Demographic (age, gender, time from SLE initial symptoms and diagnosis, time of follow-up), clinical (renal function, activity of SLE, renal biopsy), treatment and renal evolution data were collected.

Immunohistochemical expression of HGF and TGF-β1 was evaluated in tissue samples of kidneys and the results were evaluated following the Mizuno score.
We divided patients in two groups on the basis of the response to therapy at the 6th months in responders (R) and non responders (NR). A patient was considered responder if: 24h proteinuria < 1 gr and creatinine levels ameliorate from baseline.
Results: Characteristics of the 42 patients were: 35 women, 7 men; mean ± SD age at renal biopsy 36.1±11.9 years; mean disease duration 4.9±4.9 years; number of class II WHO nephritis = 2; class III WHO = 1; class IV WHO = 38; class V WHO = 1; mean activity index 8.0±4.4 and chronicity index 2.7±2.4. Immunohistochemistry confirmed that HGF and TGF-β1 are expressed in the tubuli but not in the glomeruli. We found an inverse correlation between HGF/TGFβ1 ratio and TGFβ1 score either for intensity (r: -0.64, p 0.04) either for extension (r: - 077, p <0.001). The TGFβ1 extension score directly correlated with cronicity index (r: 0.40, p 0.03). We did not find any correlation with clinical parameters of renal involvement (proteinuria, creatinine clearance) as well as serum complement levels and antiDNA antibodies. The 29 responder patients differed from the 13 non responders only for the HGF extension score (3.4±0.7 vs 1.9±0.8 p<0.001) and intensity score (2.4±0.7 vs 1.4±0.6 p <0.001) and HGF/TGF ratio either for extension (1.9±1.2 vs 0.8±0.5 p<0.001) and intensity score (1.8±1.5 vs 0.8±0.5 p =0.001). On the multivariate analysis, we found that the only parameter predictive of response was HGF/TGFβ1 extension score (p=0.02 OR 16.2, 95% CI 2.5-112.3). A cut-off value >1 for the ratio HGF/TGFβ1 was predictive of remission with a positive predictive value of 95% and with an OR of 15.2 (2.5-92) CI, p<0.0001.
Conclusions: HGF/TGFβ1 ratio at baseline seems to identify patients with a good response to standard SLE therapy.

MP199 FOLLOW-UP ANALYSIS OF PATIENTS WHO REACHED THE END-POINT DURING THE IgACE, A PLACEBO-CONTROLLED TRIAL OF ACE-INHIBITORS IN CHILDREN AND YOUNG ADULT PEOPLE WITH IgA NEPHROPATHY AND MODERATE PROTEINURIA

Licia Peruzzi[1], Rosanna Coppo[1], Alessandro Amore[1], Roberta Camilla[1], Rosario Stone[2], Bruno Ranchin[3], Giovanni Pavone[4], for the IgACE Trial Group. *[1]Nephrology, Dialysis, Transplant Unit, R. Margherita Hospital, Turin, Italy; [2]Unidade de Nefrologia,Serviço de Pediatria, Hospital de Santa Maria, Lisboa, Portugal; [3]Departement de Pediatrie, Hopital Edouard-Herriot, Lyon, France; [4]Pediatric Nephrology, Ospedale G Cristina, Palermo, Italy*

Introduction and Aims: We recently published (JASN 2007;18:1880-8) the results of an EC Biomedicine and Health Research, double-blind trial involving 23 Centers in Europe, which reported the effect of an Angiotensin converting enzyme inhibitor (ACE-I) in children and young people with IgA Nephropathy (IgAN), moderate proteinuria (>1g<3.5 g/day/1.73m^2) and creatinine clearance (CrCl) >50ml/min/1.73m^2. Sixty-six patients, 20.5 (9 –35) years old, were randomized to Benazepril, 0.2 mg/kg/day (ACE-I) or placebo (PL) and were followed in median for 38 months. A significant effect of ACE-I was observed for a composite end-point of >30% decrease of CrCl or worsening of proteinuria until ≥3.5g/day/1.73m^2 (P=0.035).
We aimed the present study at evaluating the follow-up of the patients who exited the IgACE trial because of worsening to the end-point.
Methods: The patients who reached the composite end-point of IgACE trial accounted for 1/32 (3.1%) in the ACE-I group, and 9/34 (26.5%) in the PL, and they were followed up to 7.5 (median 5) years.
Results: All the patients were given ACE-I. Steroid pulses (according to Pozzi's protocol) were also administered to 5/10 patients, followed-up for a median of 5.5 additional years (4-7.5). Their CrCl remained unchanged or slightly improved in spite of the clinical activity of the disease (CrCl before pulses: 62±12 versus 75±23 min/1.73m^2 at follow-up end), and their proteinuria significantly decreased steadily (from 3.8±1.1 g/day to 0.48±0.3 g/day, p<0.001). In 2/5 cases proteinuria went into complete and stable remission (<0.3 g/1,73 m^2/day). Five other cases who were in the PL group and exited the study after reaching the end-point were treated with ACE-I alone; 3 went into stable proteinuria remission, with CrCl > 80 ml/min/1.73m^2 after a follow-up of 3-7 years, one had a partial response to non-nephrotic proteinuria levels, while one case did not respond to ACE-I and to six months of oral steroids and progressed to end stage renal failure, with a biopsy showing progression of sclerosis.
Conclusions: In conclusion, apart from the benefit obtained by ACE-I in some previously placebo-receiving patients, the addition of pulse steroid therapy was able to obtain remission in 2/3 of the cases who failed to respond to ACE-I alone.

MP200 PRELIMINARY STUDY OF PROTEIN A IMMUNOADSORPTION AND MYCOPHENOLATE MOFETIL THERAPY IN PATIENTS WITH ANCA VASCULITIS AND RENAL INVOLVEMENT

Weixin Hu, Daxi Ji, Shijun Li, Zhihong Liu, Leishi Li. *Research Institute of Nephrology, Jinling Hospital, Nanjing, Jiangsu, China*

Introduction and Aims: To investigate the clinical efficacy of Protein A immunoadsorption (IA) in the treatment of ANCA-associated vasculitis (AAV) and its impact on the serum level of ANCA.
Methods: Six patients (3 male, 3 female, age 19–60 years) with active AAV (BVAS 15–22), diagnosed as microscopic polyangitis were studied. All patients had positive MPO-ANCA (27.4–849.05 RU/ml) and renal insufficiency (mean SCr 4.0±3.3 mg/dl), renal biopsy revealed crescent formation (51.0±27.1%). One patient was dialysis dependent. All patients received immunoadsorption treatment for five to ten sessions (4.5L plasma treated per session, every other day) as well as methylprednisolone (MP) pulse therapy followed by oral prednisone and mycophenolate mofetil (1.0-1.5g/d). Change of ANCA, BVAS and renal function was observed.
Results: After the first IA treatment, MPO-ANCA was eliminated in one patient. The ANCA levels of the other five patients were all significantly reduced, with the decrement of 52.6±14.0%(37.2%~70.4%) after the first IA treatment and 81.8±10.0% (67.8%~91.5%) from the baseline value after three IA sessions respectively. At the end of IA treatment, ANCA level was reduced to (9.6±6.3)% of the baseline (P<0.01). Renal function was much improved in one patient who was dialysis-dependent prior to IA treatment (SCr decreased from 10.5mg/dl to 4.1mg/dl), serum creatinine level decreased or remained stable in 4 patients, one patient had renal function recovered. During follow-up for 3 to 12 months, five patients got remission and one remained stable. Adverse events included hypotension (n=1) during IA treatment and bacterial pneumonia (n=1) during the follow-up.
Conclusions: Protein A immunoadsorption treatment could effectively decrease the serum ANCA level, control the disease activity and improve the renal function, further studies are required to evaluate the clinical efficacy and long-term effects on renal function.

MP201 MESANGIAL HYPERCELLULARITY DEVELOP ALDOSTERONE BREAKTHROUGH IN IMMUNOGLOBULIN A NEPHROPATHY DURING BLOCKADE OF RENIN-ANGIOTENSIN SYSTEM

Yoshio Horita[1], Satoko Kawasaki[1], Kouichiro Ostuka[1], Takashi Taguchi[2], Akira Furusu[3], Shigeru Kohno[3]. *[1]Division of Nephrology, Department of Medicine, National Hospital Organization, Nagasaki Medical Center, Omura, Nagasaki, Japan; [2]Department of Pathology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [3]Department of Molecular Microbiology and Immunology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

Introduction and Aims: The long-term effect of aldosterone was not inhibited in patients of chronic kidney disease, so the possibility of organ damage due to aldosterone breakthrough cannot be ignored, however the cause of breakthrough is unknown. We examine breakthrough and the relations of the renal injury.
Methods: We evaluated the aldosterone breakthrough of response to angiotensin converting enzyme inhibitors (ACEI) and/or angiotensin receptor blockers (ARB) administered for 12 months in 42 patients with chronic kidney disease such as proteinuric IgA nephropathy (IgAN). Histological scores were obtained on 252 glomeruli and 83 arteries formal score of glomerular hypercellularity, glomrulosclerosis, tubulointerstitial injury, arteriosclerosis and arteriolar hyalinosis.

Results: Although the overall plasma aldosterone concentrations (PAC) values did not change after any of the treatments administered for 12 months, they eventually increased in 22 of the 42 patients (52%; aldosterone breakthrough), and fell in the remainder (48%). Reduction of proteinuria after treatment ACEI and/or ARB was greater without breakthrough versus with breakthrough (-63±17 versus -43±15%, $P<0.05$). When patients were categorized with aldosterone breakthrough and without aldosterone breakthrough to ACEI and/or ARB, no difference between the two groups was detected in any clinical variable, whereas histology showed with aldosterone breakthrough higher score of glomerular hypercellularity (2.19±0.59 versus 1.62±0.52, $P<0.01$).
Conclusions: W suggests the predictor of aldosterone breakthrough after long-term treatment of ACEI and/or ARB in CKD associate with degree of mesangial hypercellularity.

MP202 15-DEOXY-DELTA(12,14)-PROSTAGLANDIN J2 AND PROINFLAMMATORY CYTOKINES IN IGA NEPHROPATHY

Sang Heon Song[1], Ihm Soo Kwak[1], Dong Won Lee[1], Byeong Yun Yang[1], Sung Joo Lee[2]. *[1]Internal Medicine, Pusan National University Hospital, Medical Research Institute, Busan, Republic of Korea; [2]Internal Medicine, Pusan Medical Center, Pusan, Republic of Korea*

Introduction and Aims: 15-deoxy-delta(12,14)-prostaglandin J2 (15d-PGJ2) is one of the derivatives of the prostaglandin D2 metabolism and is an endogenous natural ligand for PPAR-γ. 15d-PGJ2 have been reported that had an anti-inflammatory effect in vitro and in vivo studies. Also, the association between inflammatory variables and kidney injury has been increasingly studied over the past years. We hypothesized that 15d-PGJ2 had an important role in IgA nephropathy (IgAN) as inflammatory modulator. This study was performed to demonstrate a correlation among urinary 15d-PGJ2, proinflammatory cytokines (i.e. IL-23, IL-6, and TGF-β1), and CRP, and to determinate the contributors to prognostic score by proposed Wakai, et al (NDT, 2006) and proteinuria in IgAN patient. Additionally, this study was performed to find the difference between IgAN and minimal change disease (MCD).
Methods: Fifty-four patients with biopsy-proven IgAN were enrolled. For comparison with IgAN, five MCD patients were enrolled. Immunohistochemical stain for PPAR-γ in kidney tissue and measurements of urinary IL-6, IL-23, TGF-β1, 15d-PGJ2, and serum CRP were performed. Patients having IgAN were classified to four groups according to amount of 24hr proteinuria. Prognostic scores were checked using scoring system by proposed Wakai, et al (NDT 2006).
Results: There were no differences in proinflammatory cytokines, 15d-PGJ2, and other clinical parameters between PPAR-γ(+) and PPAR-γ(-) group. 15d-PGJ2 was negatively correlated with urinary IL-23 (r=- 0.293 p=0.031), TGF-β1 (r=- 0.427, $p<0.001$), and CRP (r=-0.444, $p<0.001$). Among proinflammatory cytokines and CRP, there were positive relationships each other except IL-23 and CRP. TGF-β1 in group having proteinuria more than 3gm/day was statistically higher than that in only hematuria group. But, in multivariate regression analysis, any relationship was not found between TGF-β1 and proteinuria. Prognostic score was correlated with IL-6, IL-23, TGF-β1, CRP, 15d-PGJ2, and 24hr proteinuria. 24hr proteinuria was correlated with IL-6 and 15d-PGJ2. In multivariate regression analysis, CRP, 15d-PGJ2, and 24hr proteinuria contributed to prognostic score, and only 15d-PGJ2 contributed to 24hr proteinuria. Last, urinary 15d-PGJ2 in IgAN was higher than that in MCD.
Conclusions: Endogenous 15d-PGJ2 was associated with inflammation and might be considered as an endogenous material which could delay the damage of kidney in IgA nephropathy. In the future, larger cohort and long-term follow-up studies will be needed to demonstrate the role of 15d-PGJ2 as prognostic indicator or marker of kidney damage.

MP203 DIFFERENT RESPONSES TO STEROID THERAPY MAY PREDICT HISTOPATHOLOGIC FEATURES OF IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN

Abass Madani[1], Nahid Rahimzadeh[1], Seyed Taher Esfahani[1], Nematollah Ataei[1], Bahar Madani[1], Fatemeh Mahjoub[2], Marzieh Hadadi[2]. *[1]Pediatric Nephrology Children's Hospital Medical Center Tehran University, Tehran, Central Tehran, Iran; [2]Pathology and Morbid Anatomy Children's Hospital Medical Center Tehran University, Tehran, Central Tehran, Iran*

Introduction and Aims: Oral steroid therapy is the most popular medication in treatment of childhood nephrosis.Even though the long prognosis of patients has proven to be different.The purpose of our study was determining the effect of steroid to induce remission and finding out the common histopathological aspect of patients with the diagnosis of steroid resistant,steroid dependent and frequently relapsing nephrotic syndrome.
Methods: We selected 238 children from out patient clinic in the period between:1995-2006.Their age ranged from 1-15 years and they were comprised 152 boys (63.8%)and 86 girls (36.2%).The initial oral steroid therapy for patients at the start of disease was the ISKDC protocol.The patients were followed between 12-144 months (median 51- months).
The mean age upon initial diagnosis was 4.5 years. Most patients were diagnosed between 2-3 years of age.
Thirty five of them had criteria for kidney biopsy before starting steroid therapy. Disease control was achived in 175 (86.2%) out of 203 patients with steroid therapy.
Results: The results of the therapy at the end of the follow up were: sustained remission 45 (25.7%),infrequently relapsing nephrotic syndrome (IFRNS) 44 (25.1%), frequently-relapsing nephrotic syndrome (FRNS) 39 (22.2%) and steroid-dependent nephrotic syndrome (SDNS) 47 (27%).Twenty eight out of 203 patients had steroid-resistent nephrotic syndrome (SRNS), (girls 15 and boys 13). For 18 of them kidney biopsy was undertaken,the most common histopathologic finding was focal segmental glomerular sclerosis (FSGS). It was surprising that the most common type of glomerulopathy among 26 children with the diagnosis of FRNS and SDNS were minimal change lesion (MCL).
Conclusions: Our study disclosed, that like others, the majority of children with idiopathic nephrotic syndrome (INS) were responsive to steroid therapy but relapses were more frequent than other studies (74.3% vs 60%). However they remained steroid sensitive during their next relapses.
The most common type of histopathological finding among patients with SRNS was FSGS (61%). While the MCL was common type in childeren with SDNS (61.2%) and FRNS (53.84).

MP204 SERUM AND URINARY LEPTIN, GHRELIN IN CHILDREN WITH NEPHROTIC SYNDROME

Meltem Dinleyici[1], Nurdan Kural[1], Bilal Yildiz[1], Ozkan Alatas[2]. *[1]Department of Pediatric Nephrology, Eskisehir Osmangazi University Faculty of Medicine, Eskisehir, Turkey; [2]Department of Biochemistry, Eskisehir Osmangazi University Faculty of Medicine, Eskisehir, Turkey*

Introduction and Aims: To the best of our literature knowledge, while limited reports were published about serum and urinary leptin levels in patients with nephrotic syndrome, serum and urinary ghrelin levels were not reported. The aim of this study was to evaluate serum and urinary leptin and ghrelin levels in children with primary idiopathic nephrotic syndrome, to compare these results between patients during relapse and remission phase and also to evaluate the possible role of leptin and ghrelin in pathogenesis of nephrotic syndrome.
Methods: Fourty-nine children with primary idiopathic nephrotic syndrome (25 children with relapse, 24 children in remission) which were followed-up in Pediatric Nephrology Unit, Eskisehir Osmangazi Univeristy Faculty of Medicine, enrolled. 28 age-sex matched healthy children served as controls. Serum and urinary leptin levels were determined with immunoenzymatic ELISA, serum and urinary ghrelin levels were determined by RIA method.
Results: Serum leptin levels were significantly lower in children with nephrotic syndrome during relaps phase than the children with nephrotic syndrome during remission and also controls (1.42±0.34 ng/dl and 3.60±0.70 ng/ml; $p<0.01$, 1.42±0.34 ng/ml and 5.27±4.67 ng/ml; $p<0.001$, consecu-

tively). Urinary leptin excretions were significantly higher in relapse group than the controls (0.40±0.11 ng/ml and 0.12±0.06 ng/ml, $p<0.01$). Serum ghrelin levels were similar between relapse, remission and control groups ($p>0.05$). Urinary ghrelin excretion were significantly higher in relapse group then remission group and controls (965.0 pg/ml (93-3711) and 679.7 pg/ml (93-3783); $p<0.05$, 965.0 pg/ml (93-3711) and 387.7 pg/ml (114-1214); $p<0.001$). Urinary ghrelin levels were also significantly higher in remission group than the controls (679.7 pg/ml (93-3783) and 387.7 pg/ml (114-1214); $p<0.01$). Serum leptin levels were positively correlated with serum albumin levels ($r=0.440$, $p<0.05$), and also negatively correlated with serum triglyceride levels during relapse phase in children with nephrotic syndrome. Urinary leptin levels and urinary ghrelin levels were positively correlated with proteinuria in relapse group.

Conclusions: In conclusion, we suggested that leptin might have a role in pathophysiology of nephrotic syndrome, and also associated with proteinuria, hypoproteinemia and hyperlipidemia. Urinary ghrelin excretion possibly increased due to low molecular weight, parallel to proteinuria. Unlike serum leptin levels, normal serum ghrelin levels could be associated with unknown compensation mechanism.

MP205 A COMPARISON STUDY BETWEEN MYCOPHENOLATE MOFETIL AND CYCLOPHOSPHAMIDE FOR TREATMENT OF PROLIFERATIVE LUPUS NEPHRITIS

Sung Jin Moon, Jung Tak Park, Tae Ik Chang, Eun Young Kim, Jung Eun Lee, Dong Ki Kim, Seung Hyeok Han, Jae Hyun Chang, Hyun-Wook Kim, Sun Young Park, Beom Suk Kim, Dae-Suk Han, Ho Yung Lee, Kyu Hun Choi. *Division of Nephrology, Department of Internal Medicine, The Institute of Kidney Disease, Yonsei University College of Medicine, Seoul, Korea*

Introduction and Aims: Mycophenolate mofetil (MMF) is a relatively specific inhibitor of lymphocyte proliferation. MMF has been used in the treatment of renal transplantation, lupus nephritis, and other autoimmune diseases. Our study was aimed to evaluate the efficacy of MMF compared with intravenous cyclophosphamide as induction therapy for proliferative lupus nephritis in Korea.

Methods: Forty-three patients who were diagnosed as proliferative lupus nephritis (WHO Class III and IV) between Jan 2000 and Dec 2005 were included. Nineteen patients were treated with oral MMF (initial dose, 1.0 g/day, increased to 2 g/day) and 24 patients with 0.75-1.0 g/m^2 of monthly intravenous cyclophosphamide (CP) followed by subsequent treatment of oral corticosteroid (initial dose 1 mg/kg/day, then slowly tapered down) for 6 months. Demographic and laboratory findings were reviewed retrospectively and were compared between the two groups. Complete remission (CR) was defined as no active sediments on urine analysis, urine protein/creatinine ratio (UPCR) < 0.3 g/g, normal serum albumin and stable serum creatinine levels. Partial remission (PR) was defined as UPCR between 0.3 and 2.9 g/g, serum albumin ≥ 3 g/dL, and stable serum creatinine.

Results: CR occurred in 7 out of the 19 patients (36.8%) treated with MMF and 8 out of the 24 patients (33.3%) treated with CP, which was not significantly different between the two groups ($p=0.66$). In addition, PR was achieved in 52.6% and 45.8% respectively. There were no significant differences in laboratory findings such as C-reactive protein, hemoglobin, platelet, erythrocyte sediment rate, serum albumin, C3, C4, UPCR and serum creatinine at the end of follow-up. In addition, both group had similar rates of adverse events.

Conclusions: Our study showed that in the treatment of lupus nephritis, MMF was as effective as IV cyclophosphamide with similar adverse effects. This finding suggests that MMF could be an alternative treatment of active lupus nephritis as induction therapy.

MP206 DOES HEYMANN NEPHRITIS REALLY REFLECT HUMAN MEMBRANOUS NEPHROPATHY?

Shao-yu Zhang [1], Vincent Audard [1,2], Dominique Desvaux [2], Marina Candelier [1], Philippe Lang [2], Dil Sahali [1,2]. *[1]Inserm U 841, Creteil, France; [2]Nephrology, Hopital Henri Mondor, Creteil, France*

Introduction and Aims: Idiopathic Membranous nephropathy (MN) defines a glomerular disease, of unknown etiology, commonly associated with a nephrotic syndrome and histologically characterized by diffuse thickening of the capillary loop as consequence of subepithelial immune deposits. The generation of an experimental model of MN established in rats by Heymann (HN) fifty years ago, represents the start-point of pathophysiological researches on MN. Megalin, a common component of the tubular and glomerular epithelial cell was identified as the target antigen of HN and provides the molecular basis of podocyte disease in MN. Active (AHN) and passive (PHN) type Heymann nephritis are induced by direct immunization of Lewis rats with crude preparation of brush border protein or by injection of rabbit anti-rat brush border antibodies, respectively. Both types closely mimic the human glomerular disease. The membrane attack complex of complement C5b-9/Mac is thought to play a crucial role in the induction of podocyte injury leading to proteinuria in this model. Proteinuria in PHN has been suggested to be entirely dependent on C5b-9/Mac. These data have been recently challenged by the development of an experimental model where AHN and PHN were induced in rat deficient in complement component C6 and cannot form Mac.

Methods: PHN was induced in male lewis by double injections of sheep anti-rat megalin antiserum. Cmip transgenic mice were produced using a targeting system based on the reconstitution of a functional X-linked HPRT locus. Activated RhoA and Rac1 pull-down kits were purchased from Cytoskeleton and assays performed following supplied protocols.

Results: We reported here that the gene encoding the cmaf inducing protein (cmip) is highly expressed, at the mRNA and protein level, in podocytes of patients with membranous nephropathy. We induced PHN by double injection of anti-megalin polyclonal antibody. Rats developed proteinuria that reached a peak at day 7 ($\geq$14 mg/24 hours). Immunofluorescence analyses showed a granular aspect along the glomerular capillary loops. Unexpectedly, despite several assays, immunofluorescence analyses did not detect cmip in glomeruli. The in vivo relevance of cmip induction was investigated in mice by targeted transgenesis. We found that selective induction of cmip in murine podocytes induces nephrotic proteinuria without morphological alterations. We showed that cmip interferes with physiological signaling in podocyte by turning off the signals connecting Fyn to nephrin and N-WASP. Furthermore, we demonstrated that cmip: i) inhibits in vitro RhoA activity while we did not observe changes in Rac1 activity; ii) upregulated in vitro and in vivo integrin linked kinase (ILK) and alters integrin-mediated cell-matrix interaction; iii) represses in vivo the VEGF expression at the mRNA and protein level.

Conclusions: These findings suggest that cmip plays a crucial role in podocyte disease of MN and questioned the relevance of HN as model of human membranous nephropathy.

MP207 LONG-TERM OUTCOME OF PATIENTS WITH SEVERE RENAL VASCULITIS TREATED WITH PLASMA EXCHANGE – SINGLE CENTRE EXPERIENCE

Zdenka Hruskova [1,2], Zuzana Rihova [1], Romana Rysava [1], Eva Jancova [1], Petra Koupilkova [1], Magdalena Mokrejsova [1], Jana Lachmanova [1], Miroslav Merta [1], Helena Mareckova [2], Vladimir Tesar [1]. *[1]Dpt. of Nephrology, General Teaching Hospital and First Faculty of Medicine, Charles University, Prague, Czech Republic; [2]Institute of Immunology and Microbiology, General Teaching Hospital and First Faculty of Medicine, Charles University, Prague, Czech Republic*

Introduction and Aims: In patients with systemic ANCA (Anti-Neutrophil Cytoplasmic Antibodies) - associated vasculitis (AAV), renal failure at presentation is connected with an increased risk of end-stage renal disease and death. A large international randomized study (MEPEX) has recently shown the benefit of plasma exchange (PE) in these patients. The aim of this retrospective analysis was to assess the long-term outcome of patients with severe renal vasculitis treated with PE in a single centre.

Methods: From 2001 to 2006, 40 patients (18 women, 22 men, median age 59.5 years, 12x antiPR3-ANCA and 28x antiMPO-ANCA positive) with severe renal AAV (i.e. with serum creatinine levels more than 500 umol/L) were treated with PE in our centre. In 13 patients, intra-alveolar haemorrhage was also present. Cyclophosphamide and corticosteroids were administered as induction therapy in all patients.

Results: The mean time of follow-up of our patients was 33 months (range 1-72 months). At three months after PE, 28 patients (70%) were alive and not dependent on dialysis. Patient survival rate at one year was 82.5%

and renal survival rate at one year was 67.5%. At the end of follow-up, 32 patients (80%) were alive and 24 of them dialysis independent, with median serum creatinine levels of 196 umol/L. The total renal survival rate at the end of follow-up was 60%. These numbers are similar to the results of the patients treated with PE within the MEPEX trial. In comparison with the MEPEX patients treated without the addition of PE, the rate of renal recovery in our group of patients is significantly higher. Adverse events of PE were generally rare and did not lead to premature treatment termination.
Conclusions: Our results confirm that addition of plasma exchange to standard immunosuppressive therapy helps to improve the long-term prognosis of patients with severe renal vasculitis and to increase the rate of renal recovery.

MP208 PRIMARY GLOMERULONEPHRITIS (PGN) IN THE ELDERLY

Cedomir Cuckovic, Nada Dimkovic, Vesna Maslarevic, Danica Vujic, Jovan Ikonomovski. *Clinical Department for Renal Diseases, Zvezdara University Medical Center, Belgrade, Serbia*

Introduction and Aims: Primary glomerulonephritis in elderly is not well described and there is no consensus about its prevalence, histology, diagnosis and therapy.This retrospective study was aimed to compare the histological finding, clinical presentation, therapy and outcome between older (>60 years) and younger group of patients (<60) with histologicaly confirmed primary glomerulonephritis (PGN).
Methods: Between 1999-2006, by percutaneous renal biopsy, PGN was confirmed in 123 patients and 29 patients were above 60 years of age (23.6%). Following parameters were recorded and compared between older (group A) and younger (group B) patients: biopsy findings, renal function, proteinuria, urinary sediment, blood preassure and outcome.
Results: In the elderly focal segmental glomerulosclerosis (FSGS) was diagnosed in 11 (37,9%) patients, membranous glomerulonephritis (MGN) in 8 (27,6%) and rapidly progressive glomerulonephritis (RPGN) in 4 (13,8%). Three patients developed acute postinfectious glomerulonephritis (10,3%), two (6,9%) mesangial proliferative glomerulonephritis (MEPGN), and one patient membranoproliferative glomerulonephritis (MPGN). In the group B leading types of PGN were MEPGN with IgA or IgM deposits (44/46,8%), FSGS (22/23,4%) and MGN (13/13,8%). Compared to patients younger than 60 years, at the time of renal biopsy patients older than 60 years had more often hypertension (79,3% vs. 52,1%) and renal failure (89,7% vs. 45,7%). Similar number of patients in both groups had microhematuria (65,5% vs. 68,1%). Proteinuria was significantly higher in the elderly (5,3 g/L vs. 3,3 g/L). In group A immunosuppressive therapy reduced proteinuria and improved renal function in 16 (55,2%) patients, 5 (17,2%) deteriorated renal failure and 3 (10,4%) developed ESRD. Five patients died from cardiovascular complications and severe infections. In group B 61 (64,9%) are in stabile remission, 21 (22,3%) deteriorated renal function and 7 (7,5%) developed ESRD. In this group five (5,3%) patients died.
Conclusions: In conclusion, the most frequent forms of PGN in the elderly are FSGS and MGN. PGN is more often associated with hypertension, renal failure and pronounced proteinuria in older patients than in younger ones. Good therapeutic response with respectable number of clinical improvement justifies early renal biopsy and immunosuppressive treatment in the elderly.

MP209 HISTOPATHOLOGICAL RENAL LESIONS IN ORTHOTOPIC LIVER TRANSPLANT RECIPIENTS WITH CHRONIC KIDNEY DYSFUNCTION

Lucia Barbara de Sanctis, Sonia Pasquali, Antonio Santoro. *Nephrology, Dialysis and Hypertension, S. Orsola-Malpighi Hospital, Bologna, Italy*

Introduction and Aims: Progressive renal function deterioration is a commonly recognized complication of orthotopic liver transplantation (OLT). Chronic calcineurin inhibitor therapy (CNI) has been implicated in the genesis of post-transplant chronic renal failure (CRF) due to its nephrotoxicity. Although presumed CNI toxicity is the main cause of renal failure in OLT patients, often suspected glomerular diseases remain an underestimated cause of renal dysfunction.
Methods: From 2002 to 2007 we evaluated 48 OLT (41 man, 8 women, mean age 54±10yrs, 20/48 HCV+, 6/48 HBV+) for renal complications at our Centre. The kidney injuries were 18.5% IRA (9 cases), 37.5% CRF stages II-III, 23.2% CRF stage IV, 20.8% urine abnormalities (5/10 cases of nephrotic proteinuria) with no biochemical evidence of renal dysfunction. In the long-term, the occurrence of renal dysfunction was observed after 5±2 yrs since the OLT, in 20% of cases it was accompanied by diabetes and in 18% by hypertension. A subset of patients with CKD occurring some time after the transplant (n=16/48 cases, 33%) underwent kidney biopsy. The renal biopsy was performed with the transcutaneous approach in 14 pts, and the transjugular technique in 2 pts.
Results: Most of the clinical diagnoses were CNI nephrotoxicity (n=18) histologically demonstrated at renal biopsy in 3 cases. Other histological diagnoses included membrano-proliferative glomerulonephritis (n=4) IgA mesangial glomerulonephritis (n=1) focal segmental glomeruloscerosis (n=4), diabetic nephropathy in combination with severe vascular injury (n=4).
Conclusions: These data suggest that even if nephropathy from calcineurin inhibitor is the most frequent form of renal damage, many other pathologies may underlie the functional and histological alterations observable after OLT. Hence, it is necessary in the dubious cases, in which elements in favour of CAN are lacking, to resort to the renal biopsy. In the patients with coagulation problems, the transjugular approach is to be preferred. The precocious identification of renal anomalies different from damage due to calcineurin inhibitors may indeed lead to targeted therapies that, if precocious, may provide definitive cares, and orient the choice of differentiated immunosuppressive therapy.

MP210 URINARY FIBRONECTIN AND COLLAGEN TYPE IV EXCRETIONS IN PATIENTS WITH PRIMARY CHRONIC GLOMERULONEPHRITIS

Ilona Idasiak-Piechocka, Andrzej Oko, Elzbieta Pawliczak, Stanislaw Czekalski. *Department of Nephrology, University of Medical Sciences, Poznan, Poland*

Introduction and Aims: The aim of the study was the estimation of urinary excretions of fibronectin and collagen type IV in patients with biopsy proven newly diagnosed primary glomerulonephritis (GN).
Methods: Fifty three untreated patients at the age of 38,2±10,1 years as a mean participated in the study. Nephrotic syndrome was diagnosed in 21 patients, 24 patients were in stage 1 of chronic kidney disease (CKD), 22 in stage 2 and 7 in stage 3. In the kidney biopsy specimens, the extend of glomerulosclerosis was assessed and the intensity of interstitial fibrosis was also evaluated. The concentrations of collagen type IV (coll.IV) and fibronectin (FIB) were measured by ELISA method in the first freshly voided morning urine sample.
Results: Urinary excretion of coll. IV was significantly higher (38,9±27,1 ng/gCr, p<0,05) but FIB excretion was lower (195,1±96,5 ng/gCr, NS) in 23 patients with more than 10% of sclerotized glomeruli in the biopsy specimen and more pronounced interstitial fibrosis compared to 30 patients with less marked morphological abnormalities (coll.IV 24,6±16,1 ng/gCr, FIB 239,0±162,4 ng/gCr, respectively). We did not observe signficant differences in urinary excretions of coll.IV and FIB depending on the stage of CKD. Immunossuppresive therapy (IMS) was introduced in 39 patients and in 14 patients only conservative treatment was recommended. Urinary excretions of coll. IV (54,6±32,4 ng/gCr) and FIB (250,6±135,6 ng/gCr) were significantly higher (p<0,05) in patients with poor response to IMS therapy when compared to healthy subjects (coll. IV 4,7±2,1; FIB 42,4±34,1 ng/gCr, respectively) and to patients on conservative therapy (coll.IV 27,9±19,2 ng/gCr, FIB 186,2±148,6 ng/gCr, respectively).
Conclusions: The results suggest that determinations of urinary coll. IV and FIB in patients with primary chronic GN may serve as the markers of disease activity and are usefull for the prognosis in patients on IMS therapy.

MP211 LONG-TERM OUTCOME OF PATIENTS WITH LUPUS NEPHRITIS

Nikoletta Nikolopoulou, John Droulias, Andreas Soloukides, Apostolou Theofanis, Vasilios Margelos, Dimitrios-Anestis Moutzouris, Valsamakis Hadjiconstantinou. *Nephrology, "Evangelismos" General Hospital, Athens, Attica, Greece*

Introduction and Aims: Few data regarding the very long term outcome of patients with lupus nephritis are available. The aim of the study was to monitor outcome of patients with biopsy proven lupus nephritis and estimate the progression of renal function in the very long term.
Methods: In the present study we report seventy-one patients (8males, 63 females) aged 27-62 years (median: 45) with biopsy-proven lupus nephritis who were followed for a median of 15 years (range: 1,5 - 26) in a single renal department between 1980-2006. Fifteen had impaired renal function at the time of biopsy. According to the biopsy findings, 41 patients were classified as class IV lupus nephritis, 11 as class V, 3 as class I, 11 as class III and 5 patients as class VI lupus nephritis. Thirty patients were treated with high doses of corticosteroids alone and 43 more severe cases with high doses of steroids plus immunosuppressive agents (cyclophosphamide, MMF, or azathioprine). This treatment was repeated in the event of a renal flare and followed by reduction to the minimal effective maintenance dose.
Results: Renal survival including patient death with functioning kidneys was 95% at 10 years and 84% at 20 years. Seven patients were lost to follow-up and 2 had died at various intervals while, at the end of the study period, 54 patients were in complete renal remission, 2 in partial remission, 2 in stage III or IV chronic kidney disease and 4 in renal replacement therapy. By multivariate analysis, the lack of achievement of complete renal remission and the occurrence of nephritic flares were found to be significantly correlated both with the risk of doubling plasma creatinine and death or dialysis. Those patients who entered complete renal remission had significantly less probability for developing nephritic flares.
Conclusions: We conclude that the long-term prognosis of the patients with lupus nephritis studied was quite satisfactory compared to that reported in the literature. Favorable factors for good long-term outcome were the achievement of complete renal remission, the absence of nephritic flares and their complete reversibility following appropriate treatment.

MP212 INFLUENCE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) GENE C-2578A POLYMORPHISM ON THE PROGRESSION OF IgA NEPHROPATHY

Christos Bantis[1,2], Peter Heering[1], Maria Stangou[2], Efstathios Alexopoulos[2], Dimitrios Memmos[2], Christina Schwandt[1], Lars-Christian Rump[1], Katrin Ivens[1]. *[1]Department of Nephrology, Heinrich-Heine University, Düsseldorf, Germany; [2]Department of Nephrology, Aristotle University, Thessaloniki, Greece*

Introduction and Aims: Vascular endothelial growth factor (VEGF) promotes endothelial cell proliferation and differentiation, mediates endothelium dependent vasodilatation and participates in interstitial remodelling. In the kidney VEGF is mainly expressed by podocytes, mesangial and tubular endothelial cells. Recently, the C-2578A polymorphism, located in the promoter region of the VEGF gene, has been associated with modified VEGF production. We evaluated its influence on the clinical course of IgA nephropathy (IgAN).
Methods: We studied n=138 patients with biopsy proven primary IgAN followed up for 7.1±6.1 years. The individual rate of progression of renal insufficiency was calculated as the slope of reciprocal serum creatinine versus time plot (linear regression). According to the slope of reciprocal serum creatinine ($\geq$ or$<$ -0.1 dl * mg^{-1} * $year^{-1}$) group A (slow progressors, n=90) and group B (fast progressors, n=48) were defined. One hundred volunteers were analysed as controls. VEGF gene C-2578A polymorphism was determined by PCR amplification.
Results: There was no significant difference in the genotype frequencies in patients (CC/CA: 76.8%, AA: 23.2%) and control subjects (CC/CA: 80%, AA: 20%, ns). Age, renal function, proteinuria and blood pressure did not differ significantly at the time of renal biopsy between patients with different genotypes (ns). VEGF gene C-2578A polymorphism influenced the progression of IgAN, with the CC/AA genotypes being associated with a worse prognosis: the rate of progression as estimated by the slope of the curve of reciprocal serum creatinine was higher among the -2578C allele carries (CC/CA genotypes: -0.162±0.46, AA: -0.068±0.068 dl * mg^{-1} * $year^{-1}$, p=0.023). Furthermore, the CC/CA genotypes were more frequent in the fast progressing group B (89.5%) than in group A (71.1%, p=0.030).
Conclusions: Our results suggest that VEGF gene C-2578A polymorphism is a progression marker in patients with IgA nephropathy.

MP213 DOES PARAOXONASE 1 ACTIVITY CHANGE IN PATIENTS WITH PRIMARY NEPHROTIC SYNDROME DURING STEROID TREATMENT? – PRELIMINARY RESULTS

Marcin Zietkiewicz[1], Agnieszka Stencel[2], Zbigniew Zdrojewski[1], Boleslaw Rutkowski[1]. *[1]Chair and Department of Nephrology, Transplantology and Internal Diseases, Medical University of Gdansk, Gdansk, Poland; [2]Department of Clinical Chemistry, Medical University of Gdansk, Gdansk, Poland*

Introduction and Aims: Hyperlipidaemia complicating nephrotic syndrome (NS) is characterized by elevated levels of total cholesterol, low density lipoprotein (LDL), very low density lipoprotein (VLDL), often with hypertriglyceridaemia and low level of high density lipoprotein (HDL). Both LDL and VLDL are apolipoprotein B-containing lipoproteins which are accepted as atherogenic. Oxidized-LDL (ox-LDL) has been suggested to play a fundamental role in atherogenesis. Paraoxonase1 (PON1) is a HDL-associated enzyme that prevents oxidative modification of LDL.
The aim of study is to determine whether paraoxonase activity is altered in patients with nephrotic syndrome compared to healthy population.
Methods: Eleven patients (4 F, 7 M) with nephrotic syndrome in course of primary glomerulonephritis were enrolled in the study. Also, 11 healthy persons (3 F, 8 M) were selected as a control group. Patients with NS had eGFR >60 ml/min and all were treated with pulses of methylprednisolone and oral prednisone. Serum triglyceride (TG), total cholesterol (TChol), LDL, HDL, uric acid (UA), C-reactive protein (CRP), apoprotein AI (ApoAI), apoprotein B (ApoB), total protein (TP) and albumin (ALB) levels were measured. Daily urine protein loss (DUPL) was also examined. PON1 activity was measured by spectrophotometry using paraoxon as substrate. In control group only PON1 activity was measured. In nephrotic group parameters were measured 3 times: before treatment (A), 5 days after starting treatment (B without DUPL) and 6 weeks after starting treatment with steroids (C).
Results: Mean PON1 activities in group with nephrotic syndrome were: at the time A: 177.1±124.88 U/L, B: 171.26±126.33 U/L, C: 174.9±123.02 U/L and in healthy group 172.6±113.95 U/L. Other results are presented in tables below.

Biochemical parameters (1)

	TChol	TG	LDL	HDL	TP	ALB
A	387.36	237.64	291.1	61.45	46.95	25.81
B	393.9	278.50	280.2	58.2	45.09	27.61
C	242.8	140.3	138.9	76.2	63.7	44.1
p	<0.05	<0.005	<0.05	<0.05	<0.005	<0.005

Biochemical parameters (2)

	ApoAI	ApoB	DUPL	CRP	UA
A	1.98	1.93	8.33	1.44	5.71
B	1.95	1.9	–	0.52	7.14
C	1.98	0.84	1.22	0.95	5.25
p	ns	<0.005	<0.05	<0.05	<0.05

Conclusions: In patients with nephrotic syndrome PON1 activity doesn't change during steroids treatment and was comparable to activity observed in healthy people.

MP214 ★ THROMBOMODULIN, VON WILLEBRAND FACTOR AND PLASMINOGEN ACTIVATOR INHIBITOR 1 AS MARKERS OF ENDOTHELIAL INJURY IN NEPHROTIC CHILDREN

Marcin Tkaczyk[1], Aneta Czupryniak[1], Michal Nowicki[1], Jolanta Lukamowicz[2], Danuta Owczarek[2], Ewa Swiatkowska[2], Romualda Rajska[2]. *[1]Dep. of Nephrology and Dialysis, Polish Mother's Memorial Hospital Research Institute, Lódz, Poland; [2]Central Laboratory, Polish Mother's Memorial Hospital Research Institute, Lódz, Poland*

Introduction and Aims: Nephrotic syndrome is considered as a risk factor for cardio-vascular events. The increased concentration of several atherogenic factors such as fibrinogen, cholesterol and inflammation are detected with significantly higher frequency than in general population. In children long-term cardiovascular outcome has not been described clearly and definitely. Endothelial function impairment may constitute a link between nephrotic syndrome and atherosclerosis in children. The aim of the study was to assess the endothelial dysfunction by detection of endothelium derived circulating particles.
Methods: We observed changes in plasma thrombomodulin (TBM), von Willebrand factor (vWF) and plasminogen activator inhibitor-1 (PAI-1) at different stages of idiopathic nephrotic syndrome in children and correlated them with clinical and biochemical parameters. The endothelium derived particles were assessed by ELISA test in plasma.
The study group included 132 nephrotic children (aged 2-18 y.) divided into four groups, i.e. in acute phase of the disease with proteinuria, during steroid-induced remission, steroid-free remission, and in long-term, steroid-free remission. Forty-one healthy children served as controls. In 15 children with severe clinical course treated with cyclosporine A intima-media thickness of carotic common artery was measured.
Results: The study detected increased markers of endothelial dysfunction (thrombomodulin, tissue plasminogen activator, tissue plasminogen activator inhibitor 1, von Willebrand factor activity) in children with idiopathic nephrotic relapse. Amongst these, the increase in TBM, PAI-1, vWF persisted in drug induced remission. These disturbances were accompanied by increased thrombinogenesis (thrombin-antithrombin complexes, F_{1+2} prothrombin fragments), especially in the first weeks of the relapse. In the correlation analysis, the detected disturbances were prominently dependent on the degree of proteinuria and serum albumin concentration. The insulinresistance was highest in early relapse of nephrotic syndrome, remained elevated in early remission, and decreased to normal levels later on. The homocysteine concentration was lowest in the group A when compared to healthy controls. The intima-media thickness in cyclosporine-A-treated children (15 s.) was significantly higher than in healthy children.
Conclusions: The study revealed that nephrotic children show markers of endothelial injury that are dependent on the disease activity. In the children with steroid-dependency on cyclosporine A treatment might be related to increased intima-media thickness.
This may lead to a hypothesis that children with severe clinical course of nephrotic syndrome may be at high risk of accelerated atherogenesis.
The study was supported by a grant of the Polish Ministry of Science KBN 2 P05E 034 26 and Polish Mother's Memorial Hospital Research Institute.

Immune and inflammatory mechanisms

MP215 TACHYKININ RECEPTOR BLOCKADE AMELIORATES KIDNEY INFLAMMATION DURING ANTI-THY 1.1 NEPHRITIS IN RATS BY PUTATIVE INHIBITION OF RENAL AFFERENT PEPTIDERGIC NERVE FIBER ACTIVITY

Roland Veelken[1], Karl Hilgers[1], Eva-Maria Vogel[1], Kerstin Amann[4], Gabriele Sass[2], Winfried Neuhuber[3], Gisa Tiegs[2]. *[1]Medizinische Klinik 4, Universität Erlangen-Nürnberg, Erlangen, Germany; [2]Pharmakologisches Institut, Universität Erlangen-Nürnberg, Erlangen, Germany; [3]Institut für Anatomie I, Universität Erlangen-Nürnberg, Erlangen, Germany; [4]Institut für Pathologie, Universität Erlangen-Nürnberg, Erlangen, Germany*

Introduction and Aims: Anti-Thy1.1 nephritis in rats characterized by severe inflammatory response after mesangiolysis induced by the antibody is aggravated by neurogenic mechanisms. We tested the hypothesis that tachykinin receptor blockade ameliorates kidney inflammation during Anti-Thy 1.1 nephritis in rats by putative inhibition of renal afferent peptidergic nerve fiber activity. This fibers use SP (and CGRP) as transmitters, express the respective receptors and can release the peptides from afferent nerve endings.
Methods: Anti-Thy1 nephritis was induced by i.v. injection of 1 mg/kg body weight ER4 antibody to Sprague-Dawley rats. One group of rats was pretreated with the tachykinin receptor antagonist aprepitant (5mg/kg i.p, 12h & 1h before ER4 antibody). Rats were sacrificed at 24h and 48h after anti-Thy1 induction, the kidneys were harvested. Inflammatory and proliferative changes were investigated by immunohistochemistry and real-time RT-PCR for the mRNA encoding the cytokine TNF-α. Respective renal innervation was investigated for by confocal microscopy.
Results: Rats suffering from anti-Thy1 nephritis exhibited albuminuria (64±6 μg/24h), infiltration of macrophages in the interstitium and glomeruli (25±3 and 3.5±0.6 cells per high-power field) as well as mesangiolysis (score 1.40±0.11). Pretreatment with aprepitand reduced significantly TNF-α expression in inflammed kidneys as compared to untreated Anti-Thy1.1 nephritic animals or SHAM controls (*24h:* 0.86±0.28 versus *2.93±0.31 or 1.0±0.88 respectively; *48h:* 2.6±1.4 versus *4.5±1.4 or 1.0±0.8 respectively, *$p<0.05$; n=6). All relevant strucutres ot the kidney (glomeruli, interstititum, vessels) were innervated with sympathetic as well as afferent nerve fibers.
Conclusions: Hence, we could demonstrate for the first time that tachykinin receptor blockade with aprepitant ameliorates inflammatory responses of the kidney in the anti-Thy1 model of glomerulonephritis in rats. This could be due to impaired renal afferent nerve input to the central nervous system regulating sympathetic outflow and to reduced neurogenic peptide release from nerve endings within the kidneys.

MP216 LYMPHOCYTE INHIBITION IS PROTECTIVE IN EXPERIMENTAL HYPERTENSIVE NEPHROPATHY

Stephanie Krämer, Eva Binder, Yingrui Wang-Rosenke, Tanja Loof, Sebastian Martini, Hans-H. Neumayer, Harm Peters. *Nephrology, Charité-Universitätsmedizin, Berlin, Germany*

Introduction and Aims: Chronic kidney disease is uniformly characterized by tissue infiltration with mononuclear cells independent of the underlying disease. In a model of immune-initiated progressive glomerulosclerosis, the lymphocyte migration inhibitor FTY720 has shown beneficial effects on renal fibrosis and loss of function. To test the hypothesis that this translates to hypertensive nephropathy (HN), FTY720 was administered to rats after 5/6 nephrectomy.
Methods: Subtotal nephrectomy was performed in male Wistar rats (250-280 g BW). Two days after surgery the following groups were formed: a) Sham operation (sham; n=4); b) HN (n=21) and c) HN+FTY720 in a dose of 0.3 mg/kg BW p.o (n=18). Therapy was continued for 6 weeks.
Results: As anticipated, FTY720 selectively reduced blood lymphocyte count by 83% ($p<0.001$ vs. HN) and renal lymphocyte infiltration (CD-3 positive cells) by 46% ($p<0.01$ vs. HN). With this lymphocytes inhibition achieved, glomerular histological matrix accumulation was 19% and the tubulointerstitial 26% lower in the treated vs. the untreated animals ($p<0.05$), respectively. Using Western blot analysis histology findings corresponded with reductions of 64% in collagen I, 58% in collagen III and 65% reduction in laminin cortical protein expression (all $p<0.01$ vs. HN). FTY720 treatment improved GFR by 15% and lowered proteinuria by 20%, while systolic blood was comparable in both HN-groups (HN 1615 vs. HN+FTY720 1605 mmHg, P=NS)
Conclusions: The present study shows that the lymphocyte migration inhibitor FTY720 limits significantly renal fibrosis both at a histological and molecular level in a model of hypertensive nephropathy. The results expand previous findings in experimental immune-initiated progressive glomerulosclerosis. Together both studies point to a more general active role that lymphocytes play in the progression of chronic renal disease independent of the underlying disorder.

MP217 INTRACELLULAR IMBALANCE OF NITRIC OXIDE AND MITOCHONDRIAL SUPEROXIDE LEAKAGE DURING THE HYPERPROTEINURIC PHASE OF PUROMYCIN NEPHROSIS

Aki Hirayama[1], Atsushi Ueda[2], Sohji Nagase[3], Takaaki Oteki[4], Yashige Kotake[5], Shigeru Owada[6], Kazumasa Aoyagi[1]. *[1]Center for Integrative Medicine, Tsukuba University of Technology, Tsukuba, Ibaraki, Japan; [2]Department of Internal Medicine, Namegata District General Hospital, Namegata, Ibaraki, Japan; [3]Nagase Naika, Moriya, Ibaraki, Japan; [4]Department of Nephrology, International University of Health and Welfare, Nasu-Shiobara, Tochigi, Japan; [5]Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; [6]Asao Clinic, Kawasaki, Kanagawa, Japan*

Introduction and Aims: In puromycin aminonucleoside (PAN)-induced nephrosis, remarkable productions of reactive oxygen species (ROS) occurs within 1 day of PAN administration, while its massive proteinuria is observed *day 7* to *9* of nephrosis. To clarify the movements and roles of ROS on this interval, we investigated 1)in vivo renal ROS production, 2)balances between mitochondria $O_2^{\cdot-}$ leakage and intracellular nitric oxide (NO) production. We also analyzed the microcharacterizations of the mitochondrial complex, which relates to the mitochondrial $O_2^{\cdot-}$ leakage.

Methods: The nephrosis was induced by the single administration of PAN. ROS were measured by an in vivo electron paramagnetic resonance (EPR) system using the acyl-protected hydroxylamine (ACP). Mitochondrial $O_2^{\cdot-}$ leakages were measured by X-band EPR using a spin trap 5-(2,2-dimethyl-1,3-propoxy cyclophosphoryl)-5-methyl-1-pyrroline N-oxide (CYPMPO), a new cyclic DEPMPO-type nitrone developed by us. NO was evaluated by the Griess method and EPR spin trapping with iron dithiocarbamate complexes. Mitochondrial complexes were characterized by a low temperature EPR (ltEPR).

Results: Rats increased proteinuria 4 days after the PAN injection reaching a maximum level around *day 7*. In vivo EPR detected increases of ROS on *day 1* of the PAN-treated kidney and decreases thereafter. The ROS mainly consisted of $O_2^{\cdot-}$, hydroxyl radical and H_2O_2. Spin trapping with CYPMPO detected mitochondrial $O_2^{\cdot-}$ leakages which conventional spin traps failed to note. Two peaks of $O_2^{\cdot-}$ leakage were observed on *day 1* and on *day 7 to 9*. The second peak of $O_2^{\cdot-}$ leakage was preceded by increases of intracellular NO, urinary and glomerular NOx arround *day 3*. ltEPR revealed the formation of dinitroxyl dithioilato iron complex (DNIC), a biomarker of the interaction of NO and Fe-S proteins in complex III, on *day 7* to *9*.

Conclusions: These results suggest that the increased NO induced by PAN decomposes mitochondrial Fe-S proteins to DNIC. Since EPR detects outermatrix $O_2^{\cdot-}$ leakage from complex III, this DNIC formation may lead to the increase of mitochondrial $O_2^{\cdot-}$ leakage and the hyperprotinuric phase of PAN nephrosis. The ROS producing mechanism in this phase is mainly depend on mitochondria, and different from the radical storm immediately induced by PAN.

MP218 THE ROLE OF THE MAMMALIAN TARGET OF RAPAMYCIN (mTOR) IN DENDRITIC CELLS

Michael Haidinger, Thomas Weichhart, Marko Poglitsch, Walter Hörl, Marcus Säemann. *Department of Internal Medicine III, Clinical Division of Nephrology & Dialysis, Medical University of Vienna, Vienna, Austria*

Introduction and Aims: Dendritic cells (DC) are professional antigen-presenting cells that are centrally positioned in the regulation of adaptive immune responses. Recent data indicate that mTOR may play a pivotal role in regulating innate immune cell function, however, mixed results are available about DC.

Methods: Here we systematically analyzed the influence of mTOR inhibition on both freshly isolated peripheral myeloid DC and compared them with monocyte-derived DC (mo-DC), which are *in vitro* generated from monocytes cultured with GM-CSF and IL-4.

Results: Analyzing peripheral myeloid DC activated with LPS, *Staphylococcus aureus cells*, PAM3Cys, or CD40-ligation we observed a strong cytokine deviation by mTOR inhibition exhibiting increased IL-12p40, IL-6 and TNF-a but suppressed IL-10 levels. Similarly, rapamycin differentially regulated a variety of activation markers including increased CD25, CD40, CD86, and HLA-DR, but did not affect CD80 and B7-H1 expression. In contrast mo-DC exhibited a globally suppressed phenotype after rapamycin exposure including inhibition of activation markers, defective cytokine production and allostimulatory capacity. Further investigating these dissimilarities, we found that IL-4 but not GM-CSF activated the mTOR pathway and specifically counteracted the effects of rapamycin. Analysis of the underlying signalling alterations revealed that IL-4 prevented the rapamycin-mediated hyperactivation of NF-kB.

Conclusions: Collectively, these data demonstrate that mTOR is a central negative regulator of peripheral DC activation, while their *in vitro* counterparts display a distorted phenotype after mTOR inhibition due the presence of specific mTOR pathway agonists.

MP219 TRIGLYCERIDE RICH LIPOPROTEINS CONTRIBUTE TO THE DECLINE IN RENAL FUNCTION IN EXPERIMENTAL CHRONIC RENAL FAILURE (CRF) RATS AND THE ORAL ADSORBENT AST-120 (KREMEZIN®) ALTERS THIS PROCESS

Shigeru Owada[1], AKI Hirayama[2], Atsushi Ueda[3], Soji Nagase[4], Sumie Goto[5], Fuyuhiko Nishijima[5]. *[1]Dialysis Center, Asao Clinic, Kawasaki, Kanagawa, Japan; [2]Internal Medicine, Tsukuba University of Technology, Tsukuba, Ibaragi, Japan; [3]Internal Medicine, Namegata Hospital, Namegata, Ibaragi, Japan; [4]Internal Medicine, Nagase Clinic, Moriya, Ibaragi, Japan; [5]Bio-Medical Research Center, Kureha Co., Ltd, Tokyo, Tokyo, Japan*

Introduction and Aims: We have developed a method for determining lipid profiles using agarose gel electrophoresis. Using increment of LDL negative charge (LDL-CMF), triglyceride (TG)/cholesterol (CH) ratio, LPO in the serum and HEL (hexanoyl-lysine) in the urine as oxidative stress markers, superoxide dismutase activity (SOD) in the kidney and EPR imaging of the kidney as a measure of the *in vivo* redox state and we assessed the protective effect of AST 120 in CRF rats.

Methods: CRF was induced in rats by renal artery ligation and 5 weeks later they were divided into three groups of 10 each. Group C was without treatment and Group K was treated with K orally once a day for 20 weeks. Group N was sham operated without K. Lipoprotein profiles was detected using rapid electrophoresis system (REP; Helena Co.,LTD), LPO was measured using fluorescence method and HEL was measured by ELISA. SOD activity was measured using X-band EPR spin trapping method. In vivo imaging was detected by low frequency in vivo EPR apparatus.

Results: Serum creatinine (mg/dl) levels were significantly decreased in group K compared to group C (N: 0.43±0.06, C: 1.05±0.21, K: 0.79±0.19). LDL-CMF (%) was unchanged in group N from 0 to 20 weeks (14±2→20±1). In group C and K, LDL-CMF was the same as that in group N at the 0 point but significantly increased at the end of the experiment (C:18±3→65±14, K: 27±8→45±20). The fasting LDL-TG (mg/dl) was significantly higher in group C (N:14.2±5.4→17.5±7.9, C: 15.0±4.5→44.0±9.9, K: 17.1±6.9→32.2±13.1). The TG/CH ratio compared to pre and post supplementation of diet was significantly higher in group C (N: 1.62±0.78→1.43±0.48, C: 1.99±0.62→2.59±0.78, K: 1.80±0.55→1.62±1.00). LPO levels (n mol/ml) in the serum was unchanged in group N from 0 to 20 weeks (1.20±0.41→1.04±0.45). In group C and K, LPO was the same as that in group N at the 0 point but significantly increased at the end of the experiment (C: 0.90±0.24→2.03±0.58, K: 0.92±0.32→1.49±0.47). Compared to group C, levels of LPO was significantly lower in group K at the end of experiment. HEL levels in the urine (nmol/mg-creatinine) was significantly increased in group C compare to group N and group K at the end of experiment (N: 3.67±0.84, C: 5.89±0.91, K: 4.71±0.62). SOD activities (U/g) in the kidney were significantly decreased in group C compared to group N (N: 3738±752, C:1054±278, K: 2243±350). The EPR imaging of the kidney, showing the clearance rate of free radicals, was prolonged in group C and T halves of free radicals (min) were significantly shorter in group K compared to group C (N:20±8, C: 50±21, K:18±10).

Conclusions: Our results suggest that improvement of LDL -CMF, the TG/CH ratio and the redox state induced by Kremedine® can delay the progression of CRF.

MP220 RAPAMYCIN ATTENUATES THE SEVERITY OF ESTABLISHED MURINE ADRIAMYCIN NEPHROPATHY

Sing Leung Lui[1,2], Ryan Tsang[2], Kwok Wah Chan[3], Florence Zhang[2], Sidney Tam[4], Susan Yung[2], Tak Mao Chan[2]. *[1]Medicine, The University of Hong Kong, Tung Wah Hospital, Hong Kong, Hong Kong; [2]Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong, Hong Kong; [3]Pathology, The University of Hong Kong, Queen Mary Hospital, Hong Kong, Hong Kong; [4]Clinical Biochemistry, Queen Mary Hospital, Hong Kong, Hong Kong*

Introduction and Aims: Progressive glomerulosclerosis and tubulointerstitial fibrosis are common features of most forms of chronic kidney diseases, irrespective of the underlying etiology. Therapeutic options for these pathological changes are limited. Rapamycin is an approved immunosuppressant for rejection prophylaxis in clinical transplantation. Recent studies suggest that rapamycin also possesses anti-fibrotic property. The aim of this study was to evaluate the effect of rapamycin on murine adriamycin nephropathy, a model of focal segmental glomerulosclerosis and tubulointerstitial inflammation with heavy proteinuria.
Methods: Adriamycin nephropathy was induced in 10-weeks old male Balb/c mice by a single intravenous injection of adriamycin (10mg/kg body weight) via a tail vein. The mice were treated with rapamycin (3mg/kg body weight) [N=12] or normal saline [N=12] once daily by oral gavage starting 1 week after the adriamycin injection when heavy albuminuria has been established and continued for 5 weeks. The severity of glomerulosclerosis and tubulointerstitial fibrosis in the two study groups were compared by means of survival, degree of albuminuria, serum urea and creatinine levels, renal histology and intra-renal expression of RANTES and Collagen I.
Results: At the time of sacrifice, 25% of the saline-treated mice versus 0% of the rapamycin-treated mice had died. The saline-treated mice had developed massive albuminuria and elevated serum urea and creatinine levels. Rapamycin treatment significantly reduced albuminuria and preserved renal function (Table 1). Kidney sections from saline-treated mice showed marked focal segmental glomerulosclerosis, tubular dilation with protein cast deposition and interstitial fibrosis. In contrast, the renal histology of the rapamycin-treated mice revealed relatively mild changes (Table 2). Rapamycin also significantly lowered the intra-renal expression of RANTES and Collagen I.

Table 1

	Saline-treated	Rapamycin-treated	P
Albuminuria (mg/dL)	24.0±8.4	3.9±0.2	<0.001
Serum Urea (mmol/L)	9.85±2.29	7.11±1.18	0.022
Serum Creatinine (μmol/L)	30.68±6.25	16.25±1.67	0.001

Table 2

Histological changes*	Saline-treated	Rapamycin-treated	P
Glomerulosclerosis	1.67±1.23	0.50±0.52	0.012
Tubular dilation	1.83±1.34	0.67±0.78	0.036
Interstitial fibrosis	2.00±1.21	0.58±0.67	0.008

*The histological changes for glomerulosclerosis, tubular dilation and interstitial fibrosis were scored semi-quantitatively on a 0 to 3 scale where 0 = absent, 1 = mild, 2 = moderate and 3 = severe. Values are means ± S.D.

Conclusions: Rapamycin is effective in attenuating the severity of adriamycin nephropathy in Balb/c mice. Rapamycin could be of therapeutic value in preventing the development of renal fibrosis in chronic proteinuric kidney diseases.

MP221 SYMMETRIC DIMETHYLARGININE: POTENTIAL SOURCE OF UREMIC VASCULAR DAMAGE BY ENHANCING CALCIUM FLUX AND ACTIVATION OF NFκB IN MONOCYTES

E. Schepers, G. Glorieux, A. Dhondt, R. Vanholder. *Internal Medicine, Renal Division, University Hospital Gent, Gent, Belgium*

Introduction and Aims: Chronic kidney disease (CKD) is a pro-inflammatory condition, whereby retained solutes have the potential to activate leukocytes and create vascular damage. Hence, identification of responsible compounds and mechanisms might help to develop therapies preventing vascular disease and subsequent morbidity and mortality. Since guanidines have previously been linked by us to leukocyte activation (Glorieux, KI, 2004), in the present study guanidinopropionic acid, guanidinobutyric acid (GBA), guanidine, guanidinoacetic acid, methylguanidine, symmetric (SDMA) and asymmetric dimethylarginine (ADMA) were evaluated for their effect on leukocytes.
Methods: Their influence on ROS production was evaluated in heparinized whole blood during fMLP stimulation reflecting the moderate inflammatory status in uremia. Subsequently the role of changes in leukocyte calcium influx induced by fMLP and of changes in NFκB activation were evaluated.
Results: Only SDMA and GBA significantly enhanced ROS production in both monocytes ($p < 0.04$) and granulocytes ($p < 0.01$). The effect of SDMA was abolished in EDTA anticoagulated blood which suggested the involvement of calcium. When evaluating the involved pathways it was found that in the presence of SDMA an increased influx of calcium caused a rise in monocytic intracellular calcium level ($p < 0.01$). Pre-incubation with captopril, known to inhibit the calcium influx, blocked the enhanced monocytic oxidative burst due to SDMA. Furthermore it was demonstrated that SDMA enhanced NFκB activation in monocytes ($p < 0.04$) which could be neutralized by N-acetylcysteine (NAC). In the presence of ADMA none of the described effects were observed.
Conclusions: In conclusion, SDMA, although previously considered biologically inert, has a pro-inflammatory effect in part related to increased calcium influx and in part to activation of NFκB. Inhibition of calcium influx by captopril and of NFκB activation by NAC neutralize this effect. These data add to the knowledge about pro-inflammatory mechanisms in uremia and about the pharmacologic strategies to cope with these effects.

MP222 EFFECT OF SELECTIVE PEROXISOME PROLIFERATOR–ACTIVATED RECEPTORγ MODULATOR WITHANGIOTENSIN RECEPTOR BLOCKING ACTIVITY ON CULTURED HUMAN MESANGIAL CELL (HMC)

Sung-Do Kim, Shung-Shin Park, Byoung-Soo Cho. *Dept. of Pediatrics, East West Kidney Diseases Research Institute, Seoul, Korea*

Introduction and Aims: Many studies have demonstrated that angiotensin receptor blockade (ARB) prevent renal progression in patients with diabetic nephropathy by inhibition of HMC proliferation and reduce of extracellular matrix expansion and glomerulosclerotic changes. Recently new Selective peroxisome proliferator–activated receptor (PPAR) γmodulator with angiotensin receptor blocking activity is emerging. Thus we investigated the effect of PPAR-r modulator with ARB on cultured HMC.
Methods: MC was grown in DMEM with 15% FBS and then telmisartan was treated on cultured MC. RNAs of HMC on 8 hours after PPAR-r modulator with ARB treatment were analyzed using affymetrix microarray chip. To validate the patterns of gene expression analyzed by the microarrays, some genes were selected and ELISA was performed.
Results: The present study demonstrates profile of gene expression after PPAR-r modulator with ARB treatment on human MC. Among genes, we found down-regulation of cytokine and chemokine associated genes after PPAR-r modulator with ARB treatment. IL-6, IL-8, IL-11, and MCP-1 production was significantly decreased by cytokine and chemokine ELISA.
Conclusions: Our results showed that cytokine and chemokine associated genes were down-regulated by PPAR-r modulator with ARB treatment on HMC. Further evaluation will be conducted to elucidate molecular mechanism of PPAR-r modulator with ARB on HMC.

MP223 NATURAL RESISTANCE-ASSOCIATED MACROPHAGE PROTEIN 1, Nramp1, WAS DOWNREGULATED IN POLYMORPHONUCLEAR LEUKOCYTES (PMNLs) FROM MAINTENANCE HEMODIALYSIS PATIENTS (mHD)

Yoshinaga Otaki, Masayoshi Nanami, Aritoshi Kida, Rie Kitamura, Katsukiyo Itou, Reiko Hata, Yukiko Hasuike, Takahiro Kuragano, Masaaki Izumi, Takeshi Nakanishi. *Internal Medicine Division of Kidney and Dialysis, Hyogo College of Medicine, Nishinomiya, Hyogo, Japan*

Introduction and Aims: In maintenance hemodialysis patients (mHD), the causes of susceptibility to infections have remained controversial. Intracellular iron had been suspected to affect the phagosomal activity. We have already

demonstrated that iron and ferritin contents of polymorphonuclear leukocytes (PMNLs) were increased significantly in mHD (AJKD 2004). Regarding intracellular iron distribution, Nramp1 functions in metal transport across the phagosomal membrane of macrophages and PMNLs, and defective Nramp1 causes sensitivity to several intracellular pathogens. In the present study, the expression of Nramp1 was examined in PMNLs from mHD.
Methods: 10 patients on mHD and 9 controls (C) were recruited in this study. PMNLs were obtained by differential centrifugation. For determining mRNA kevels of Nramp1 and Nramp2 in PMNLs, the quantitative PCR was performed using TaqMan real time PCR method. Nramp1 mRNA was normalized using the expression of GAPDH. For the analysis of Nramp1 protein, western blot analysis and immunohistochemistry were performed using anti Nramp1 polyclonal antibody.
Results: mRNA of Nramp2, e.g. divalent metal transporter 1 (DMT1), was not expressed significantly in PMNLs. The mRNA ratio of Nramp1/GAPDH in mHD was significantly decreased compared to C (0.23 vs 1.00). Western blot analysis showed that Nramp1 protein was also reduced in mHD. Immunohistochemistry demonstrated only faint staining of Nramp1 in PMNLs from mHD, but strong staining in cytosol of PMNLs from C.
Conclusions: This is the first report that the expression of Nramp1 in PMNLs from mHD was significantly downregulated compared to C, which might be one of the causes of the susceptibility to infections in mHD, those are Mycobacterium, Leishmania and Salmonella.

MP224 MODULATION OF TOLL-LIKE RECEPTORS EXPRESSION IN HUMAN MESANGIAL CELLS IN CULTURE IS MEDIATED BY ABERRANTLY GLYCOSYLATED POLYMERIC IgA

Elisa Loiacono[1], Valentina Minieri[1], Valentina Daprà[1], Emanuela Ricotti[2], Alda Alfarano[2], Roberta Camilla[1], Licia Peruzzi[1], Alessandro Amore[1], Rosanna Coppo[1]. *[1]Nephrology, Dialysis, Transplantation, R. Margherita Hospital, Turin, Italy; [2]Department of Pediatrics, University of Turin, Turin, Italy*

Introduction and Aims: At the ERA-EDTA meeting in 2007 we reported an increased expression of the toll-like receptor-4 (TLR-4) on peripheral blood mononuclear cells of patients with IgA nephropathy (IgAN), while no difference was found in TLR-3 or TLR-7 expression. TLRs are a family of receptors that recognizes pathogen associated molecular patterns and initiates the innate immune response. The engagement of TLRs by several exogenous and endogenous ligands may influence development and outcome of immunological glomerular diseases. Some TLRs are also expressed on mesangial cells, and are upregulated during the MRL 1pr/1pr SLE prone mice, increasing when inflammatory glomerular and interstitial lesions develop. We aimed this study at investigating the TLRs expressions in cultured human mesangial cells (MC) and their modification after contact with aberrantly glycosylated IgA, the IgA detected in renal deposits of human IgAN.
Methods: In cultured MC TLRs expression was detected in basal conditiona and after incubation in culture media additioned with in vitro prepared aberrantly glycosylated polymeric IgA (pIgA), obtained by treatment with selected glycosidases (neuraminidase, 0.1 U/mg pIgA and beta-galactosidase 0.1 U/200 μg pIgA). Effective pIgA desialylation and degalactosylation (deSia/deGal pIgA) was assessed by the binding to *Vicia Villosa* (specific for GalNac residues).
The expression of TLR-4, TLR-3 and TLR-7 were measured by Cell sorter (FACS) on MC cultured for 12 or 24 hours with complete medium supplemented with 20% fetal calf serum additioned with pIgA or deSia/deGal pIgA 50 μg/ml.
Results: The table reports the percentage of positive cells (+ve cells) and the mean peak position (PkPosX) of FACS analysis for each TLR investigated after 24 h incubation with probes.

Table 1

	TLR-4		TLR-3		TLR-7%	
	%+ve cells	PkPosX	%+ve cells	PkPosX	%+ve cells	PkPosX
Untreated cells	34.0±4	1.4±0.4	43.0±5	1.05±0.1	6.5±3	1.07±0.1
pIgA	34.2±5	2.4±0.3	41.4±4	1.05±0.1	2.8±1	1.01±0.2
deSia/deGal pIgA	46.8±4 *	3.2±0,8*	40.1±4	1.05±0.1	2.1±2	1.06±0.1

*p<0.05.

We observed a significant upregulation of TLR-4 in MC cultured with medium additioned with deSia/deGal pIgA in comparison to basal conditions and to incubation of native pIgA, while TLR3 and TLR7 (measured in permeabilized cells) were unmodified.
Conclusions: These data support the engagement of TLR-4 on the surface of mesangial cells by a direct or indirect effect of desialylated and degalactosylated pIgA, which are likely to act via interaction of uncovered sugar residues provided with lectinic domain.

MP225 MONONUCLEAR CELL ADENOSINE DEAMINASE IN PATIENTS WITH CHRONIC RENAL FAILURE

Saeed Abdelwhab[1], Gilan El Saadawi[2], Mamdouh Mahdi[1]. *[1]Internal Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt; [2]Department of Clinical Pathology, Faculty of Medicine, Ain Shams University, Cairo, Egypt*

Introduction and Aims: Infection is considered an important etiological factor for uremic syndrome. The cause of immunosuppression in renal failure patients in not exactly localized. Defect in mononuclear cell with disturbance related to adenosine metabolism was suggested as important contributor to immune dysfunction in patients with renal failure.
Methods: The study was carried out on 30 patients with chronic renal failure on regular hemodialysis (group 1), and 30 patients with chronic renal impairment in predialysis periods (group 2), and 30 healthy control subjects (group 3). Complete history taking including history of complications, especially infection necessitating treatment in the last 6 month, was done. Thorough clinical examination was performed. Echocardiography and nerve conduction studies were done to all patients. Mononuclear cell adenosine level (MCAD), and adenosine deaminase activity (MCADA) were measured.
Results: Mononuclear cell adenosine level was higher in group one than in group two and in both groups it was significantly higher than in the control group (32.3±6.9, 22.0±3.3, 11.8±1.2 pmol/$10^{(7)}$ cell respectively). Mononuclear cell adenosine deaminase activity (MCADA) was found to be significantly lower in group one than in group two and in both groups it was significantly lower than in the control group (185.3±43.1, 209.26±40.6, 647.2±78.7 pmol/$10^{(7)}$ respectively). MCAD was found to correlate positively to history of infection and negatively to ejection fraction in group one and two. There was positive correlation between MCAD and presence of neuropathy in group one (Pearson correlation = 0.52, $p < 0.005$) but not in group two (Pearson correlation = 0.4, $p > 0.05$).
Conclusions: Mononuclear cell adenosine deaminase is low in patients with chronic renal failure and decrease more with hemodialysis. This leads to high level of mononuclear cell adenosine which is related to development of infection, neuropathy, and myocardial depression in those patients

MP226 B7-1 AND HIF-1a EXPRESSION AND THE INFLUENCE ON THE CYTOSKELETON REARRANGEMENT IN HYPOXIA-RELATED GLOMERULAR PODOCYTES

Jer-Ming Chang[1,2,3], Hung-Chun Chen[2,3]. *[1]Department of Internal Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung, Taiwan; [2]Division of Nephrology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; [3]Faculty of Renal Care, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*

Introduction and Aims: Chronic hypoxia has been thought as a major factor in the deterioration of renal diseases. Hypoxia might cause cellular phenotypic changes through regulation of small GTPase and therefore cytoskeleton. In challenged podocytes, B7-1 expression mediates the actin cytoskeleton rearrangement and subsequent foot processes integrity. However, the involvement of B7-1/HIF-1α (and their interaction) and the alterations of podocytes cytoskeleton under hypoxic situation were not studied.
Methods: Mouse glomerular podocytes were cultivated in DMEM with 10% FCS. Hypoxia was simulated by 2% O_2-5%CO_2 balanced with nitrogen in the incubator. B7-1 and HIF-1α expression were examined by RT-PCR and Western blot. Fragments of B7-1 and HIF-1α were cloned into GFP and FLAG plasmids with standard procedures and transfected into HEK cell for further co-immunoprecipitation. Actin cytoskeleton (stress fiber) of the differentiated podocytes was stained by rhadamine-phalloidin and observed under fluorescence microscope. To knock down B7-1 in podocytes,

B7-1 siRNA was designed and cloned into the newly engineered lentiviral plasmid. Transfection of Lenti-B7-siRNA to podocytes was facilitated by Fugene-6 and stress fiber was examined.
Results: Under hypoxic environment, B7-1 and HIF-1α were upregulated in both mRNA and protein levels. B7-1 and HIF-1α interacts each other, which is demonstrated by co-immunoprecipitation. Unstimulated wild-type podocytes displayed abundant unbranched parallel stress fiber which was disrupted with LPS treatment, along with B7-1 upregulation. Influence of hypoxia simulated the phenotypic changes by LPS challenge to podocytes. Lentiviral-B7-siRNA decreased the B7 upregulation and protected the stress fiber from disruption under hypoxia situation.
Conclusions: B7-1 and HIF-1α expression were increased by LPS and hypoxia and they interact. Hypoxia disrupted the regularly displayed stress fiber and such a effect was B7-1-dependent, demonstrated by the protection of stress fiber disruption by lentiviral-B7-siRNA transfection. Small GTPases mighy participate in the regulation of the cytoskeleton rearrangement, but further study is necessary for confirmation.

MP227 DENDRITIC CELLS IN RENAL BIOPSIES OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

Benjamin Wilde[1,2], Pieter van Paassen[1], Jan Damoiseaux[1], Petra Heerings-Rewinkel[1], Henk van Rie[1], Oliver Witzke[2], Jan Willem Cohen Tervaert[1]. *[1]Department of Clinical and Experimental Immunology, University Hospital Maastricht, Maastricht, Netherlands; [2]Department of Nephrology, University Hospital Essen, Essen, Germany*

Introduction and Aims: Dendritic cells have an important role in maintaining immune tolerance and in the initiation of immune responses. Their involvement in ANCA-associated vasculitis (AAV) is unknown. In this study, the participation of dendritic cell subsets is investigated in renal biopsies of AAV patients.
Methods: 25 patients with biopsy-proven AAV and 5 healthy controls (HC) with normal renal histology were included. Renal biopsies were stained for mature (CD208), immature (CD209), plasmacytoid (CD303) and Langerhans (CD1a) dendritic cell subsets. Furthermore, T-cells were stained using a T-cell marker (CD3). The interstitial cellular infiltrate was graded semiquantitatively from 0+ (=absence of cells) to 3+ (=numerous cells). Within the glomeruli, an absolute count was performed for positive cells.
Results: CD208+ and CD209+ cells were found within patients' glomeruli but not in HC (1±0.3 vs. 0.08±0.1 cells/glom; 2±0.3 vs. 0.1±0.07 cells/glom). An average of 0.3±0.1 cell/glom expressed CD3 in patients while few cells were found in HC (0.1±0.7 cell/glom). Focal interstitial cellular infiltrates were observed in patients' biopsies but not in HC. Interstitial infiltration with CD3+ and CD209+ cells was assessed at an average of 1+; but some glomeruli and tubuli were surrounded by CD3+ and CD209+ cells forming clusters. Only few interstitial CD1a+, CD208+ and CD303+ cells were found in patients' specimen. Serial sections revealed that CD209+ cells were present in CD3+ rich areas.
Conclusions: Both mature and immature glomerular dendritic cells are found in renal biopsies of patients with AAV. Immature dendritic cells cluster with T-cells in interstitial infiltrates in these biopsies. Since dendritic cells form aggregates in T-cell areas, we hypothesize that these cells interact between each other e.g. are involved in lymphoid neogenesis.

MP228 THE EVALUATION OF URINE MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) IN CHILDREN WITH URINARY TRACT INFECTION: A POSSIBLE PREDICTOR OF ACUTE PYELONEPHRITIS AND PERSISTENT RENAL DAMAGE

Hasan Otukesh, Rozita Hoseini, Seyed Mohamad Fereshtehnejad, Sepideh Hekmat, Majid Chalian, Hamid Chalian, Reza Salamn Yazdi, Arash Bedayat. *Ali Asghar Children Hospital, Iran University, Tehran, Iran; Ali Asghar Children Hospital, Iran University, Tehran, Iran; Ali Asghar Children Hospital, Iran University, Tehran, Iran; Ali Asghar Children Hospital, Iran University, Tehran, Iran; Ali Asghar Children Hospital, Iran University, Tehran, of Iran*

Introduction and Aims: Macrophage migration inhibitory factor (MIF) is widely expressed and secreted in response to inflammatory stimuli, and plays an important role in renal tissue injury. However, the role of MIF was not evaluated in patients with pyelonephritis in any study. Therefore, the aim of our study was to compare urinary excretion of MIF in acute pyelonephritis, acute cystitis and also control group in order to find a non-invasive and sensitive method to differentiate them.
Methods: In this study 31 pediatric patients with urinary tract infection (25 patients with acute pyelonephritis, 8 patients with acute cystitis) and 40 healthy children were recruited. Urine MIF concentration was quantitated by ELISA and corrected for urine creatinine. The data were analyzed using SPSSv.13 software. Independent T-test, One Way ANOVA, correlation and Receiver Operating Curve (ROC) analysis were performed.
Results: The mean ratios of urine MIF/Cr were calculated as 66.14 (SEM=23.78)*pg/μmol creatinine* in acute pyelonephritis patients, 1.58 (SEM=0.59)*pg/μmol creatinine* in acute cystitis patients and 1.85 (SEM=0.35)*pg/μmol creatinine* in healthy individuals. It was significantly higher in pyelonephritis patients than the ones in acute cystitis patients (P=0.000) and control (P=0.000). ROC analysis demonstrated that urine MIF/Cr ratio could considered potentially useful index to detect acute pyelonephritis [P=0.000, Area under curve (AUC) = 0.959], and also the optimal cut-point of 5.39 *pg/μmol creatinine* for urine MIF/Cr ratio could potentially separates acute pyelonephritis patients from healthy individuals with sensitivity and specificity of 92% and 92.5%, respectively.
ROC analysis also demonstrated that urine MIF/Cr ratio could predict the persistence of renal damage (renal scarring) [P=0.05, Area under curve (AUC) = 0.85], and also the optimal cut-point of 71.1 *pg/μmol creatinine* for urine MIF/Cr ratio could potentially predicts renal scar with sensitivity and specificity of 100% and 75%, respectively.
Conclusions: To the best of our knowledge, urine MIF level of patients with cystitis, pyelonephritis and control group were compared with each other for the first time in our study. We showed that the urine MIF/Cr ratio can separate pyelonephritis from cystitis patients and also showed the high MIF/cr ratio an acute phase pf infection can predict renal scarring in future.

MP229 NON-ERYTHROPOIETIC EFFECTS OF ERYTHROPOIETIN BETA IN CRITICAL ILLNESS – A PILOT STUDY

David Hepburn[1], Sabine Eggert[1], Dafydd Thomas[1], Matthew Thomas[2], Iona Hilldrup[2], Kathie Wareham[2], Lisa Wakeman[3], Ashraf Mikhail[3]. *[1]Intensive Therapy Unit, [2]Clinical Research Unit, [3]Haematology, [4]Nephrology, Morriston Hospital, Swansea, United Kingdom*

Introduction and Aims: The Erythropoetin (Epo) receptor is widely expressed in non-haematological tissues, including the kidney. Epo is a cytokine with important anti-apoptotic activity, shown to prevent ischemia-reperfusion injury in the rat kidney, reducing glomerular dysfunction, tubular injury and apoptotic cell death.
Using Flow Cytometry, a rise Immature Reticulocyte Fraction (IRF) has been detected 12 hours post Epo injection. Previous methods of assessment of response to Epo have relied on changes in blood indices, some of which could take 2 to 4 weeks to be detected. The usefulness of IRF in assessing the response of Epo treatment in critically ill patients has yet to be defined. Our aims in this pilot study were to assess the possible effects of Epo-beta on renal function in these patients and to assess the effectiveness of IRF as a marker of response to Epo treatment.
Methods: Adult patients in a single mixed medical/surgical ITU with severe sepsis or pancreatitis in acute renal failure (whether requiring RRT or not) with Hb <10.5g/dl were included in the study. Patients with haematological malignancies, haemolytic anaemia, haemorrhage (e.g multiple trauma), and hypertensive emergencies were excluded. Patients received 6000iu/day of Epo-beta intravenously in three divided doses, for a total of seven days. Immature reticulocyte fraction was measured using Flow Cytometry, as well as serum creatinine, Hb concentration, reticulocyte concentration and percentage, and hourly urine output for fifteen days from the commencement of treatment. Results were analysed using Student's T-test and linear regression.
Results: A total of 5 patients were enrolled during the study period. Hb levels were maintained over the study period in all patients (9.6±1.2). A rise in IRF was noted within 24 hrs of Epo initiation, reached a statistical significance within 72 hours, maximum rise was achieved by day 7 of the study period. The rise in IRF was maintained throughout the study period (table I). The rise in IRF showed a strong positive correlation between the rise in urine output and (r=+0.7), and a negative correlation with the drop in

Table I

	Day 1	Day 2	Day 7	Day 15
IRF %	12 (5.8)	19.9 (8)	40 (7)	21 (5.3)
Reticulocyte count	36.3 (30.5)	31 (24.9)	85.3 (60.1)	112.8 (79.4)
Hb (g/dl)	9.4 (1.2)	9.3 (1.2)	9.3 (1.3)	9.6 (1.2)
Urine output (ml/Hour)	6 (5)	12 (11)	60 (32)	>100
Creatinine (umol/l)	400 (162)	318 (142)	139 (48)	103 (10)

serum creatinine (r= -0.6). No adverse events were noted. 30 day survival in the study group was 100%.

Conclusions: The action of Erythropoietin-beta in critically ill patients with renal failure appears to be effectively and rapidly reflected in changes in IRF measured by flow cytometry. The net fall in baseline serum creatinine and rise in urine output suggests that Epo-beta may have a protective effect on renal function in these patients. Larger group studies are needed.

Disclosure: This abstract was possible thanks to a grant given by Roche pharmaceuticals.

MP230 CHARACTERISTICS OF ANTI-NEPHRIN ANTIBODIES INDUCED BY THE NEPHRIN cDNA IMMUNIZATION WITH OR WITHOUT SIGNAL SEQUENCE

Shokichi Naito[1], Togo Aoyama[1], Nozomu Yamanaka[2], Tomoko Okamoto[1], Hiromi Tazaki[1], Kouju Kamata[1]. *[1]Internal Medicine, Kitasato University Graduate School of Medical Sciences, Sagamihara, Kanagawa, Japan; [2]Surgery, National Defense Medical Collage, Tokorozawa, Saitama, Japan*

Introduction and Aims: We previously reported the method for production of polyclonal anti-nephrin antibody by DNA immunization. In this experiment, we investigated the characteristics of the polyclonal anti-nephrin antibodies induced by the DNA immunization of nephrin fragments with or without signal sequence.

Methods: Five fragments of nephrin cDNA with or without signal sequence were inserted to pTARGET vector, respectively. Rats were administered with these vectors using gene-gun method. Sera derived from rats at 14 wks after DNA immunization were analyzed with Western blots, immunoprecipitation, flow cytometry and immunohistochemistry.

Results: Four of five different antibodies induced by the nephrin cDNA fragments without signal sequence reacted only to the fragments of nephrin protein without glycosylation, but not those with glycosylation. Four of five different antibodies induced by the nephrin cDNA fragments with signal sequence showed the binding with the nephrin protein fragments both those with and without glycosylation.

Conclusions: DNA immunization using nephrin cDNA with signal sequence produced the antibodies binding to the nephrin protein with and without glycosylation, while the antibodies induced by the cDNA without signal sequence only reacted with the protein without glycosylation.

MP231 ANTIBODIES TOWARDS OXIDISED PHOPHOLIPIDS AND INTERFERON-INDUCED PROTEINS IN MULTI-SYSTEM IMMUNOLOGICAL DISEASES

Roberta Fenoglio[1], Elisa Lazzarich[1], Marco Quaglia[1], Antonietta Rizzo[1], Andrea Airoldi[1], Matteo Vidali[3], Michele Mondini[2], Emanuele Albano[3], Marisa Gariglio[2], Piero Stratta[1]. *[1]Department of Clinical and Experimental Medicine - Nephrology, Amedeo Avogadro University, Novara, Italy; [2]Department of Medical Science - Microbiology, Amedeo Avogadro University, Novara, Italy; [3]General Pathology, Amedeo Avogadro University, Novara, Italy*

Introduction and Aims: Although the role of anti-phospholipid antibodies is well established, a more recent aspect relates to phospholipids oxidation and to the possibility that this phenomenon occurs in vivo representing the true responsible for the triggering of a humoral respose. Another emerging field of interest in immunological disorders is the research on interferon-induced proteins. Aims of the study were: 1) to assess the prevalence of anti-oxidised phospholipid antibodies and interferon-induced protein antibodies in a population of patient with systemic lupus erithematosus (SLE) or antiphospholipid syndrome (APS); 2) to evaluate the specificity of these antibodies for types of disease with peculiar clinical and laboratory features and 3) to analyse possible correlations between these two families of antibodies.

Methods: One-hundred fifty one patients were enrolled: 93 with SLE, 13 with secondary APS, 18 with primitive APS, 40 with primary or secondary glomerulopathies.We searched for anti-oxidised cardiolipin antibodies (CLOX), anti oxidised phophatidilserin (PSOX) and anti-IFI16, an interferon-induced protein. Immune reactivity towards CLOX, PSOX e IFI16 was determined by ELISA plates; previously phospholipids were oxidated under controlled condition, while IFI16 was subcloned in an expression vector.

Results: Anti-oxidised phospholipid antibodies were higher in primitive APS (50% CLOX e PSOX) and in SLE (45.6% CLOX, 35.48% PSOX) as compared with controls (7.5% CLOX, 2.5% PSOX) (p = 0.0001), while no significant difference was observed for anti-IFI 16 antibodies: 37.63% in SLE, 27.68% in primitive APS, 20% in controls (p = 0.12).

Anti-oxidised phospholipid antibodies did not completely correlate with the diagnosis of APS (69.23% PSOX, 92.31% CLOX in secondary APS; 50% PSOX and CLOX in primary APS) whereas they significantly correlated with disease duration.

Anti-IFI 16 were significantly associated with ANA antibodies (p = 0,045).Lastly, there was an almost complete correlation between positivity for anti-oxidised phospholipid antibodies CLOX and PSOX (100% in primary APS, 57% in SLE, 70% in secondary APS, p <0,001) and, unexpectedly, between anti-oxidised phospholipid antibodies and anti IFI16 (55,5% primary APS, 46% secondary APS, 37,5% SLE).

Conclusions: Anti-oxidised phospholipid antibodies were not present in all cases of APS but only in those with a longer history of disease.

Anti-IFI16 antibodies did not prove to be specific markers of SLE but they correlated with ANA positivity and coexisted/overlapped with anti-oxidised-phospholipid antibodies. Thus the diagnostic meaning of these antibodies in autoimmune disorders could lie in their capacity to identify a long-lasting disease rather than to differentiate between different forms of disease.

MP232 MESENCHYMAL STEM CELLS ACCELERATE GLOMERULAR HEALING IN ANTI THY1 NEPHRITIS BY MODULATION OF SCATTER FACTORS

Marilena Gregorini[1], Teresa Rampino[1], Chiara Teresa Balenzano[1], Giulia Bedino[1], Giovanni Piotti[1], Cristina Piacenza[1], Elisa Gabanti[1], Elisabetta Roscini[1], Pasquale Esposito[1], Grazia Soccio[1], Angelo Castellano[1], Francesca Bosio[1], Francesco Frassoni[2], Adalberto Ibatici[2], Antonio Dal Canton. *[1]Nephrology, Dialysis and Transplantation Unit, University and Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [2]Department of Hematology, Ospedale San Martino, Genova, Italy*

Introduction and Aims: Hepatocyte Growth Factor (HGF) and Macrophage Stimulating Protein (MSP) are two members of the Scatter Factor family involved in the pathogenesis of anti Thy 1 nephritis. The administration of HGF accelerates glomerular repair through the growth of endothelial cells and capillary regeneration, while the neutralization of MSP improves renal function and reduces tissue damage, stopping glomerular neutrophil and monocyte influx. Recently, we demonstrated that Mesenchymal Stem Cells (MSC) infusion ameliorates renal injury in anti Thy1 nephritis by a paracrine mechanism. We investigated whether the effects of MSC in anti Thy1 nephritis are mediated by Scatter Factors.

Methods: Anti Thy1 nephritis was induced in Sprague Dawely rats. Five groups of rats were studied. Group A: rats were infused with anti Thy1.1 mAb on day 0. Group B: rats were infused with anti Thy1.1 mAb on day 0 followed by MSC ($3x10^6$) on day 3. Group C rats were infused with anti Thy1.1 mAb on day 0 and rat mesangial cells on day 3. Group D: rats received saline solution on day 0 and MSC on day 3. Group E: rats received saline solution. The rats were sacrificed on day 7, 10, 14. Proteinuria and serum creatinine levels were measured. ED1, PCNA, c-met, MSP and Ron, were evaluated by immunohistochemistry.

Results: Infusion of MSC reduced proteinuria (day 10: A 123.6±43.8, B 43.9±30.4 mg/24h p<0.05) and serum creatinine levels (day 10: A 0.59±0.01; B 0.45±0.01 mg/dl, p<0.001). In B the number of ED-1 positive cells was significantly lower in comparison with A on day 7, and 10 (day 10 A: 6.7±1.3; B 4.1±0.5, p<0.05). On day 7,10 and 14 PCNA positive cells increased significantly in A, B and C in comparison with D

and E ($p<0.001$). However, on day 7 the number of PCNA positive cells was significantly lower in B than in A (B: 13±2; A 17±1.8, $p<0.05$). On the contrary on day 10 the number of PCNA positive cells was significantly lower in A than in B (A: 7±1,B: 14±1.2; $p<0.01$). The percentage of glomerular area staining for MSP was significantly lower in B than in A on day 7,10,14 (day 10 A: 60±10; B 30±10, $p<0.005$). The percentage of glomerular area staining for Ron was significantly lower in B than in A at day10 (day 10 B: 11.57±8.5%; A 30.67±12.25%, $p<0.005$). MSC induced overexpression of c-met in endothelial glomerular capillaries. The percentage of glomerular area staining for c-met was significantly higher in B than in A at day 10, 14 (day10 B: 88±13%; A 1.9±0.2%, $p<0.0001$). In groups C and D only some podocytes expressed c-met.

Conclusions: Our results suggest that the infusion of MSC ameliorates renal injury in anti- Thy1 nephritis through the modulation of the scatter factors. The downregulation of MSP/Ron may reduce glomerular inflammation and the upregulation of c-met may induce capillary regeneration

MP233 EPIGALLOCATECHIN-3-O-GALLATE (EGCG) SUPPRESSES TNF-α-INDUCED FRACTALKINE IN ENDOTHELIAL CELLS

Sung Kwang Park[1], Ae Sin Lee[1], Yu Jin Jung[1], Duk Hoon Kim[1], Kyung Pyo Kang[1], Sik Lee[1], Mi Jeong Sung[2], Won Kim[1]. *[1]Department of Internal Medicine and Renal Regeneration Laboratory, Chonbuk National University Medical School, Jeonju, Republic of Korea; [2]Food Function Research Center, Korea Food Research Institute, Song Nam, Republic of Korea*

Introduction and Aims: Fractalkine is a unique chemokine that functions as a chemoattractant as well as an adhesion molecule on endothelial cells activated by proinflammatory cytokines. Epigallocatechin-3-O-gallate (EGCG) is the main catechin, which is derived from *Camellia sinensis* plant. EGCG has been shown to have antioxidant, anti-atheosclerotic activity, and anti-inflammatiory activities. Its regulatory effects on expression of fractalkine in vascular endothelial cells and fractalkine receptor CX3CR1 in monocytes have not been studied. In this study, we evaluated the effects of EGCG on fractalkine expression in human umbilical vein endothelial cells and CX3CR1 expression in human monocyte in response to treatment with tumor necrosis factor (TNF)-α.

Methods: HUVECs were prepared from human umbilical cords by collagenase digestion. Fractalkine expression, NFκB activity and MAPK signaling pathway were evaluated by western blot analysis and flow cytometry. Monocyte adhesion assay were performed.

Results: TNF-α significantly induced fractalkine protein expression in endothelial cells. EGCG strongly suppressed TNF-α-induced fractalkine expression in endothelial cells through suppression of nuclear factor-κB activities and MAPK signal. EGCG decreased the number of TNF-α-induced fractalkine-positive endothelial cells and CX3CR1-positive cells determined by flow cytometric analysis. EGCG suppressed TNF-α-stimulated monocytes adhesion to human umbilical vein endothelial cells through MAPK signal.

Conclusions: EGCG may provide a new pharmacological approach for suppression of fractalkine/CX3CR1-mediated injury in inflammatory condition.

MP234 PROFIBROTIC EFFECTS OF MCP-1/CCR2 SYSTEM IN HIGH GLUCOSE-STIMULATED MESANGIAL CELLS

Seung Hyeok Han[1], Je Hyun Park[2], Soo Young Yoon[3], Jin Ji Li[2], Dong Sub Jung[2], Seung Jae Kwak[2], Jung Eun Lee[1], Dong Ki Kim[1], Dae Suk Han[1], Shin-Wook Kang[1]. *[1]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; [2]BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea; [3]Department of Internal Medicine, Kwandong University College of Medicine, Koyang, Kyungki-do, Korea*

Introduction and Aims: Monocyte chemoattractant protein-1 (MCP-1) is a potent chemokine that plays an important role in the recruitment of macrophages into the kidney, and its expression is known to be increased in various kidney diseases, including diabetic nephropathy (DN). However, the direct effect of MCP-1 on extracellular matrix (ECM) accumulation in mesangial cells (MC) has never been explored. This study was undertaken to investigate the role of MCP-1 and its receptor (C-C chemokine receptor-2; CCR2) on high glucose-induced fibronectin (FN) secretion in cultured MC.

Methods: Mouse MC were exposed to medium containing 5.6 mM glucose (NG), NG+24.4mM mannitol (NG+M), 30mM glucose (HG), TGF-β1 (2ng/ml), MCP-1 (10ng/ml) with or without dominant negative MCP-1 (mMCP-1,0.5mg/ml), CCR2 siRNA (10nM), or CCR2 inhibitor (RS102895,10mM). Transient transfection was performed by lipofectamine for 24 hours. Cell viability was measured by MTT assay, mouse and human MCP-1 levels and TGF-β1 by ELISA, CCR2 protein expression and secreted FN levels by Western blot.

Results: In mMCP-1-transfected cells exposed to HG, mouse MCP-1 levels were decreased by 69% compared to HG cells. In addition, transfection with CCR2 siRNA resulted in an increase in Cy3 fluorescence and inhibited HG-stimulated CCR2 protein expression. FN protein levels and TGF-β1 concentrations were significantly increased in HG-stimulated MC by 210% and 134%, respectively, compared to NG cells ($p<0.05$), and these increments were ameliorated by mMCP-1, CCR2 siRNA, and RS102895. MCP-1 also directly increased FN protein expression (1.8-fold) and TGF-β1 levels (1.4-fold) in MC ($p<0.05$), and these increments were ameliorated by CCR2 inhibition. On the other hand, TGF-β1-induced FN expression was abrogated by MCP-1 inhibition, while increased FN expression and MCP-1 levels by HG were inhibited by TGF-β neutralizing antibody.

Conclusions: These results suggest that an interaction between the MCP-1/CCR2 system and TGF-β1 may contribute to ECM accumulation in DN.

MP235 DYSREGULATED NEUTROPHIL APOPTOSIS AND MEMBRANE EXPRESSION OF PR3 AND CD177 IN ANCA-ASSOCIATED VASCULITIS

Mohamed Abdgawad, Lena Gunnarsson, Marten Segelmark, Thomas Hellmark. *Department of Nephrology, Lund University, Lund, Sweden*

Introduction and Aims: In previous studies, we have shown that plasma membrane bound proteinase 3 (mPR3) and CD177 are co-expressed on neutrophils in all individuals. mPR3 and CD177 are over expressed in vasculitis (AASV) and polycythemia vera (PV) patients. PR3 interfere with the process of apoptosis and there are studies linking mPR3 to neutrophil apoptosis and the pathogenesis of AASV.

The aim of this study were to investigate the rate of apoptosis and necrosis of neutrophils from AASV patients compared with renal transplant recipients, healthy individuals, PV-, and SLE patients.

Methods: Neutrophils were purified using density centrifugation. Plasma membrane bound CD177 and PR3 were measured using FACS. The purified neutrophils were cultured for 20h, labeled with Annexin V Alexa fluor 488 and 7-AAD, and the percentage of apoptotic, necrotic and live cells were measured by FACS.

Results: PMNs from AASV patients have a lower rate of apoptosis and higher rate of necrosis compared with healthy blood donors (apoptosis: 48.8% vs 64.5%, $P<0.0001$ and necrosis: 15% vs 11.7%, $P=0.0425$). Neutrophils from PV patients have lower rate of apoptosis (41.7%, $P=0.0037$) compared with healthy individuals. These findings were not seen in neutrophils from other disease controls i.e. renal transplant recipients and SLE patients. There was no association between the level of membrane expression of PR3 or CD177 and the apoptosis rate of neutrophils.

Conclusions: We find that neutrophils from AASV patients in stable remission exhibit a diminished rate of apoptosis compared with healthy blood donors. This difference can most probably not be explained by drug treatment, reduced renal function or general inflammation, as patients with SLE and renal transplants recipients did not differ from the healthy controls. AASV patients also exhibited an increased amount of necrotic cells compared with all control groups. The mechanisms underlying these phenomena are unknown but may include defects in the pathways of neutrophil apoptosis or cytokine environment.

MP236 ★ TRANSFERRIN RECEPTOR ENGAGEMENT BY POLYMERIC IgA1 INDUCES CELL PROLIFERATION AND CYTOKINE SECRETION THROUGH MAPK AND PI3K/Akt/mTOR PATHWAYS IN HUMAN MESANGIAL CELLS

Houda Tamouza[1,2], Meetu Tiwari[1,2], Manon Averty[1,2], Marie Demion[1,2], François Vrtovsnik[1,2], Pierre Launay[1,2], Marc Benhamou[1,2], Renato C. Monteiro[1,2], Ivan C. Moura[1,2]. [1]*INSERM U699, Paris, France;* [2]*University of Paris 7 - Denis Diderot, Paris, France*

Introduction and Aims: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide. The hallmark of the disease is glomerular deposition of circulating IgA-immune complexes accompanied by mesangial cell proliferation and matrix expansion. We previously identified the transferrin receptor (TfR/CD71) as the mesangial IgA receptor that is highly expressed in biopsies of IgAN patients and co-localizes with deposited IgA. We have shown that IgA/TfR interaction initiates a positive feedback loop inducing increased receptor expression, mesangial cell proliferation and release of inflammatory and fibrogenic cytokines. Understanding mesangial cell activation by IgA-bound TfR is therefore critical to design therapeutic strategies aiming at inhibiting mesangial cell activation in IgAN.
Methods: IgA-triggered mesangial cell activation was determined by standard biochemical methods (calcium mobilisation, protein tyrosine phosphorylation using commercially available monoclonal antibodies). Cytokine secretion was determined by ELISA. Cell proliferation was measured by [^{3}H]-thymidine incorporation.
Results: IgA but not apo or holo-transferrin leads to calcium mobilization in human mesangial cells. IgA/TfR triggering of mesangial cells involves the mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) and phosphatidylinositol 3-kinase (PI3K)/AKT pathways evidenced by the phosphorylation of these molecular effectors. Selective inhibition of these pathways with PD098059 (ERK inhibitor) and Wortmannin (PI3K inhibitor) demonstrated that they are involved in pro-inflammatory cytokines secretion and cell proliferation, respectively. Interestingly, PI3K/AKT led to the activation of the mammalian target of rapamycin (mTOR). Its specific inhibitor, rapamycin, confirmed that this pathway is critical for IgA-dependant mesangial cell proliferation.
Conclusions: This study identifies several new therapeutic targets within the IgA/TfR-triggered signaling pathways in mesangial cells that could be relevant in IgAN therapy.

MP237 EFFECTS OF CONTRAST MEDIA AND N-ACETYLCYSTEINE ON ENDOTHELIAL CELL MORPHOLOGY AND FUNCTION. AN IN VITRO STUDY

Nicoletta Ronda[1], Alessandra Palmisano[1], Guido Orlandini[2], Rita Gatti[2], Elisabetta Parenti[1], Aderville Cabassi[1], Enrico Fiaccadori[1]. [1]*Clinica Medica, Nefrologia e Scienze Prevenzione, Università degli Studi di Parma, Parma, Italy;* [2]*Dipartimento di Medicina Sperimentale, Università degli Studi di Parma, Parma, Italy*

Introduction and Aims: The use of contrast media (CM) is associated with increased risk of complications such as Acute Kidney Injury (AKI), and increased mortality and morbility, expecially in high risk patients. Moreover, a new systemic fibrosing disorder (Nephrogenic Systemic Fibrosis, NSF) has been recently described in patients with renal insufficiency or ESRD on dialysis, after contrast-enhanced magnetic resonance imaging using gadolinium-based CM (Gd-CM).
The mechanisms of CM toxicity are poorly understood and are likely to be multiple. Among them, a key role has been postulated for an acute systemic inflammatory response involving oxidative stress and endothelial cell (EC) activation and/or damage. Thus, preventive measures based on the administration of antioxidants have been proposed.
The aim of the study was to gather new information on the mechanisms of CM toxicity and the possible protective action of N-acetylcysteine (NAC).
Methods: We studied the *in vitro* effects of two iodinated CM (iodixanol and iomeprol) and of a Gd-CM (gadoterate meglumine) on cultured human endothelial cells (EC) from umbilical vein. Morphological modifications were detected in real time by confocal microscopy on living unfixed cells loaded with calcein^{AM} and incubated with CM. Secretion of the pro-inflammatory interleukin IL-6 was evaluated by ELISA on EC supernatants. The effects on IL-6 secretion of the co-incubation of EC with CM and NAC were also assessed.
Results: None of the CM modified EC viability at concentrations up to 4-fold those expected in the first hour after coronary artery radiologic procedures. However, EC exposure to CM induced relevant morphologic modifications, such as reduction of cell surface adhering to culture slides and to adjacent cells, increase in cell thickness, loss of intercellular junctions and exposure of intercellular matrix. Finally, secretion of IL-6 was increased in EC treated with iodinated CM in a dose-dependent fashion, and decreased by NAC (70% reduction) with no modification in cell viability.
Conclusions: The demonstration of the *in vitro* derangements of EC morphology resulting from exposure to CM and the ability of NAC to reduce IL-6 secretion by EC could be relevant to clarify CM toxicity mechanisms and to develop preventive strategies. In fact, a key role for EC activation has been postulated in the expansion phase of AKI; similarly, it has been suggested that the acute inflammatory phase triggered by Gd-CM could set the stage for progressive fibrosis in NSF. Finally, the morphologic changes of EC exposed to CM shown in the present study may be particularly relevant with respect to the highly specialized glomerular EC.

MP238 RESISTIN IN HEALTHY SUBJECTS AND HEMODIALYSIS PATIENTS: EFFECT ON NEUTROPHIL OXIDATIVE BURST

Gerald Cohen, Jana Raupachova, Robert Deicher, Walter H. Hörl. *Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria*

Introduction and Aims: The increased incidence of infections among patients with chronic kidney disease (CKD) is primarily a consequence of disturbed functions of neutrophils, cells of the first-line non-specific immune defense. Uremic toxins accumulating in the serum as a result of kidney failure play a main role in inhibiting neutrophil activities such as intracellular killing of microorganisms with reactive oxygen species (ROS) generated during the oxidative burst. Resistin, a 12.5 kDa protein primarily expressed in inflammatory cells in humans, is increased in sera of CKD patients. In the present study, we investigated the effect of hemodialysis (HD) treatment on resistin levels as well as the influence of resistin on the in vitro activation of the oxidative burst in neutrophils of healthy subjects and HD patients.
Methods: Resistin concentrations were determined with a sandwich enzyme immunoassay in sera of healthy subjects and uremic patients before and after a hemodialysis (HD) session. The stimulation of the neutrophil oxidative burst by E. coli or by phorbol 12-myristate 13-acetate (PMA) was assessed in whole blood by measuring the conversion of DHR123 to R123 using flow cytometry and is expressed as mean fluorescence activity (MFI).
Results: The resistin concentration in sera of healthy subjects was 13.0±1.5 ng/ml (n=23) and significantly elevated in HD patients (31.8±4.4 ng/ml; p=0.00003, n=8). Dialysis treatment did not lead to a decrease in the resistin concentration (35.2±5.7ng/ml; $p<0.00002$). The oxidative burst stimulated by E. coli was significantly inhibited in HD patients as compared to healthy subjects (MFI 12.3±2.0 vs. 24.6±4.5; p=0.0174). Dialysis did not improve neutrophil reactivity (MFI 12.4±1.7 after the HD session). Addition of resistin to blood of healthy subjects leading to uremic levels significantly decreased the stimulation of ROS production (MFI 17.7±3.2). A further increase in resistin concentration did not result in a stronger inhibition, i.e. reaching oxidative burst levels observed in uremia. This indicates that besides resistin other factors acting via different pathways contribute to the attenuated oxidative burst in uremia. Accordingly, addition of resistin to the blood of HD patients did not lead to a further decrease in ROS production. Similar results were obtained when PMA instead of E. coli was used as a stimulant.
Conclusions: Hemodialysis treatment is not able to decrease the elevated resistin levels or to improve the defect in the stimulation of neutrophil oxidative burst observed in HD patients. The increased level of resistin contributes to the decreased reactivity of neutrophils and as a consequence to the occurrence of infectious complications in uremia.

MP239 DINUCLEOSIDE POLYPHOSPHATES: NEWLY DETECTED UREMIC COMPOUNDS WITH AN IMPACT ON THE LEUKOCYTE OXIDATIVE BURST ACTIVITY

E. Schepers[1], V. Jankowski[2], G. Glorieux[1], J. Jankowski[2], R. Vanholder[1]. *[1]Internal Medicine, Renal Division, University Hospital Gent, Gent, Belgium; [2]Endocrinology and Nephrology, Charité Campus Benjamin Franklin, Berlin, Germany*

Introduction and Aims: Atherosclerosis is one of the major causes of death in end-stage renal failure. Dinucleoside polyphosphates (Np_nN's) are recently detected protein bound and middle molecular compounds (800-1200 D) known to play a role in cardiovascular physiology and pathology (Jankowski et al., Nat Med, 11;2:223-227, 2005). They act via a variety of purinoceptors and depending on the purinoceptor subtype they exert different effects on distinct cell functions. Diadenosine polyphosphates (Ap_nA; n = 3 to 6) are accumulated in platelets of hemodialysis patients. This study evaluates for the first time the impact of Np_nN's on leukocyte oxidative burst activity in whole blood.
Methods: First, purified Ap_3A to Ap_6A were tested at 10^{-4} M to investigate the effect of the number of phosphates on the production of reactive oxygen species. In a second phase the effect of the type of nucleoside was evaluated by adding Ap_4G, Gp_4G and Up_4A to whole blood. Oxidative burst activity was quantified by means of the Bursttest® at baseline and after stimulation with fMLP, E. coli and PMA.
Results: This study shows that especially lymphocytes are susceptible for the impact of the Ap_nA's. At baseline and after fMLP stimulation Ap_4A, Ap_5A and Ap_6A significantly ($p < 0.05$) enhance the lymphocyte total fluorescence intensity (TFI). In addition, incubation with Ap_3A, Ap_4A and Ap_5A stimulates the free radical production ($p < 0.05$) of PMA-stimulated lymphocytes. In general, mono- and granulocytes parallel the response of lymphocytes albeit with an inhibitory effect of Ap_6A on granulocytes at baseline. Regarding the type of nucleoside, Up_4A has the most important effects and for this molecule the impact on monocytes is even more important than that on lymphocytes.
Conclusions: Depending on the number of phosphates, the type of nucleoside and the type of leukocyte Np_nN's have a different impact on the oxidative burst activity at baseline and after stimulation. In general, these compounds have a leukocyte activating impact. Ap_4A has the most significant impact on lymphocytes while Up_4A especially stimulates monocytes.

MP240 CHANGES OF CYTOKINE EXPRESSION ACCORDING TO SLE ACTIVITY IN PATIENTS WITH LUPUS NEPHRITIS – A 20 MONTHS LONGITUDINAL STUDY

Kálmán Polner[1], Ágnes Haris[1], Barbara Érsek[2], Edit Búzás[2], György Nagy[2]. *[1]Department of Nephrology, St. Margit Hospital, Budapest, Hungary; [2]Department of Genetics, Cell and Immunbiology, Semmelweis University Medical School, Budapest, Hungary*

Introduction and Aims: Expression of several cytokines is dysregulated in SLE. The aim of our study was to follow cytokine production longitudinally, and determine the correlation between clinical activity and cytokine expression in patients with active and inactive lupus nephritis (LN).
Methods: Disease activity, assessed by SLEDAI scores and classical disease activity markers (CH50, C3, C4, antiC1q Ab, ds-DNA Ab levels), were followed and compared to interleukin-18 (IL-18), interleukin-21 (IL-21) and interferon-α (INF-α) levels for 20 months in 16 Caucasian patients (13 female, 3 male, age 32,7±9,6 years, duration of SLE 77 (19-204) months) with biopsy proven class III-IV-V LN. The "active" group (Gr I) consisted 8 patients who suffered relapses in the 20 months observational period. Group II consisted 4 patients whose lupus was clinically inactive, but classical antibody markers were elevated. Group III consisted 4 patients in clinical and serological remission. The cytokine levels were also measured in 11 healthy individuals (Controls). Routine laboratory values, serological tests and cytokines (ELISA methods) were determined four or five times during the observational period in each patient.
Results: The groups were demographically similar. The SLEDAI scores, ds-DNA Ab levels, and complements differed significantly among I-II-III groups. IL-18 was significantly higher ($p<0,01$) and IL-21 was significantly lower ($p<0,05$) in the patients than in healthy controls (Table). In the "active", group I patients, cytokine levels fluctuated during the 20 months, likely due to relapses and appropriate immunosuppressive treatments. In groups II and III lower and more stable cytokine concentrations were found. Cytokines showed significant correlations with the signs of disease activity, as IL-18 and SLEDAI ($r=0,37$, $p<0,005$), IL-18 and antiC1q Ab ($r=0,23$, $p<0,05$), IL-18 and urinary protein excretion ($r=0,27$, $p<0,05$), INF-α and ds-DNA Ab in the All patients group ($r=0,30$, $p<0,05$). INF-α and ds-DNA Ab even more closely correlated in the active patients' group (Gr I) ($r=0,37$, $p<0,05$). Interestingly, negative correlation was found between IL-21 and ds-DNA Ab in the All patients group ($r=-0,25$, $p<0,05$).

	IL-18 pg/ml	IL-21 pg/ml	TNF-α pg/ml	SLEDAI	ds-DNA Ab IU/ml
Gr I	1268±704[1,2]	563±452[4]	65±149	11,7±5,4[7,8]	346±337[9]
Gr II	813±490[1]	553±143[5]	47±50	4,1±2,7[7]	277±231[10]
Gr III	921±528	806±477	46±68	4,5±3,2[8]	43±44[9,10]
All patients	1082±647[3]	614±416[6]	56±116		
Controls	557±369[2,3]	944±346[4,5,6]	15±20		

1-1, 4-4, 6-6: $p<0,05$; 3-3: $p<0,01$; 2-2, 9-9: $p<0,005$; 10-10: $p<0,001$; 5-5: $p<0,0005$; 7-7, 8-8: $p<0,00001$.

Conclusions: Serum levels of IL-18 and INF-α are elevated in patients with LN, and these cytokines correlate with disease activity. On the contrary, the sickest the patients, the lowest the IL-21 were observed. Based on these results, further investigations are promising to clarify the roles of cytokines in the pathomechanism of LN, and also their applicability as diagnostic tools in lupus activity.

MP241 EVALUATION OF THE ANTI-INFLAMMATORY EFFECTS OF PARICALCITOL AND CALCITRIOL IN HUMAN MONOCYTES

Evelyne van Etten[1], Thierry C. Auperin[2], Femke Baeke[1], Lut Overbergh[1], Chantal Mathieu[1]. *[1]Experimental Medicine and Endocrinology (LEGENDO), Katholieke Universiteit Leuven (KUL), Leuven, Belgium; [2]Global Pharmaceuticals, Abbott Laboratories, Abbott Park, IL, USA*

Introduction and Aims: 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$, calcitriol) and 19-nor-$1,25(OH)_2D_2$ (paricalcitol) are vitamin D receptor activators (VDRAs) commonly used to manage hyperparathyroidism secondary to chronic kidney disease (CKD). Studies have shown that paricalcitol is ~10-fold less calcemic and ~3-fold less potent in suppressing PTH than calcitriol. Clinical observations show that VDRA therapy is associated with reduced morbidity and mortality in hemodialysis patients in the order of paricalcitol > calcitriol > no VDRA therapy, likely due to their differential effects on modulating factors associated with cardiovascular disease. An important factor contributing to the pathogenesis of cardiovascular disease is inflammation. The aim of this study was to compare the effects of paricalcitol and calcitriol on regulating the expression of inflammatory cytokines in IFNγ-stimulated human monocytes.
Methods: Monocytes were isolated by CD14-positive selection (Magnetic Cell Separation, MACS) from peripheral blood mononuclear cells (PBMCs) of healthy human volunteers and stimulated with IFNγ with or without paricalcitol or calcitriol at different concentrations. After 6, 9 and 12h IL12p40, TNFα, IL1, IL6 and 24-hydroxylase mRNA expression levels were determined by quantitative real-time RT-PCR. All conditions were performed in triplicate on monocytes from 5 different donors.
Results: The effect of paricalcitol on the expression of the inflammatory cytokines TNFα, IL1 and IL6 by human monocytes was comparable to that of calcitriol. The most affected target was IL12p40 with ~50% inhibition by both compounds at 10^{-8}M ($p<0.05$) after 9h and 12h incubation. Both compounds induced 24-hydroxylase expression.
Conclusions: These data show that the anti-inflammatory effects of paricalcitol on monocytes are as potent as those of calcitriol. In clinical settings, paricalcitol is commonly given at a 3-fold higher dose than calcitriol because of its wider therapeutic window. Thus, at equipotent PTH suppressing doses, paricalcitol will exert better effects on modulating inflammatory factors, which may offer an explanation why paricalcitol provides better mortality and morbidity benefits for CKD patients than calcitriol.

Haemodialysis 2

MP242 THE OPTIMAL ON-LINE HAEMODIAFILTRATION (OL-HDF) TECHNIQUE

Marco Gonella[1], Giovanni Calabrese[1], Isabella Quaglio[1], Claudio Baldin[2], Giuseppe Vagelli[1], Antonio Mazzotta[1], Silvia Berutti[1], Stefano Rindi[1], Piercarlo Deambrogio[2], Giovanni Cavalli[3]. *[1]Renal Unit, Ospedale S. Spirito, Casale Monferrato, Italy; [2]Laboratory of Clinical Pathology, Ospedale S. Spirito, Casale Monferrato, Italy; [3]GAMBRO S.p.A., Parma, Italy*

Introduction and Aims: OL-HDF has been associated with a lower mortality risk than HD. However, the postdilutional mode (POST HDF), performed using UF control, limits UF because of hemoconcentration; predilutional as well as mixed pre-postdilutional mode does not improve HDF efficiency. Thus, a possible improvement of UF was evaluated by performing POST HDF using the "TMP ultracontrol system".
Methods: Nine patients underwent two POST HDF sessions both using UF control (UF HDF) and TMP ultracontrol (TMP HDF). On UF HDF the infusion volume was established according to the maximum UF allowed by the system and TMP was the variable parameter; on TMP HDF, on the contrary, the maximum TMP was set authomatically and UF was the variable parameter. In all cases the technique was: monitor AK 200 Ultra (Gambro), high-flux 2.1 m^2 Polyamide membrane, session length 240 min, QB 350 and QD 500 ml/min respectively. In all the sessions, Clearance of BUN, Cr and Pi was determined by using Van Geelen's formula, B2M Clearance by Leypoldt's formula, and Hb, BUN, sCr, sPi and sB2M by standards methods. The mean value of each parameter was compared between the two different HDF techniques by using Student's t-test for paired data.
Results: The predialytic values did not result to be significantly different between the two POST-HDF techniques:

Table 1. The predialytic values on the two techniques

	Hb (g/dl)	BUN (mg/dl)	sCr (mg/dl)	sPi (mg/dl)	sB2M (mg/l)
UF HDF	11.6±1.1	113±32	8.3±1.3	5.2±1.1	26±3
TMP HDF	11.3±1.0	117±33	8.5±1.4	5.0±1.9	26±2

UF (ml/min) was significantly higher, and clearances (ml/min) were higher, although not significantly, on TMP control (TMP HDF) than on UF control (UF HDF):

Table 2. UF and Clearances in the two techniques

	UF TMP	p	TMP HDF
UF (ml/min)	64±14	<0.000	101±5
UrCl (ml/min)	283±16	<0.09	308±30
CrCl (ml/min)	197±19	<0.1	220±28
PiCl (ml/min)	171±23	<0.7	189±28
B2MCl (ml/min)	19±1	<0.18	20±2.0

Conclusions: TMP ultracontrol sharply improved UF in POST HDF while guaranteeing good rheologic conditions; the mild improvement of clearances could result in a positive long-term effect. Therefore, POST HDF with TMP ultracontrol seems to be the optimal strategy for performing HDF.

MP243 SLEEP DISTURBANCES IN PATIENTS TREATED WITH MAINTENANCE HEMODIALYSIS AND HEMODIAFILTRATION

Vincent Bourquin[1], Pierre-Alain Triverio[2], Marc Giovannini[3], Dominique Robert[3], Pierre-Yves Martin[1], Patrick Saudan[1]. *[1]Service de Nephrologie, Hopitaux Universitaire de Geneve, Geneve, Switzerland; [2]Service de Dialyse, Hopital de Sierre, Sierre, Switzerland; [3]Service de Dialyse, Hopital de la Providence, Neuchatel, Switzerland*

Introduction and Aims: Sleep disturbances and symptoms such as restless leg syndrome (RLS) and pruritus are common in patients with end-stage renal failure. The aim of this study was to determine the prevalence of these symptoms in our dialysed patients and whether there is a decreased prevalence in patients treated with on-line hemodiafiltration.
Methods: Cross-sectional study in 3 dialysis units in Western Switzerland assessing the presence of RLS, insomnia, risk for obstructive sleep apnea syndrome (OSAS) and pruritus with the help of validated questionnaires (RLSQ, Athens insomnia scale, Berlin questionnaire). Hemodialysis modalities were classified as conventional hemodialysis, hemodiafiltration and high-efficient hemodiafiltration (with > 15 L of replacement fluid per treatment).
Results: 101 patients answered the questionnaire, of whom 63 were treated with conventional hemodialysis, 17 with on-line hemodiafiltration, and 21 with high-efficiency hemodiafiltration. The three groups of patients did not differ in term of age, gender, co-morbidity score, body mass index, dialysis vintage and weekly dialysis time. Prevalence of RLS, insomnia, increased risk for OSAS and pruritus were 25, 71, 14 and 30% in the hemodialysis group, 24, 82, 24 and 27% in the hemodiafiltration group and 29, 48, 5 and 35% in the high-efficiency hemodiafiltration group respectively.
Conclusions: Though this is a small population of hemodialysis patients, these data do not reveal an advantage of hemodiafiltration over hemodialysis regarding the prevalence of RLS and pruritus. There is a trend towards less sleep disturbances in patients treated with high-efficiency HDF. These preliminary results need to be confirmed in a controlled interventional study.

MP244 EFFECTS OF A NEWLY DEVELOPED VITAMIN E-MODIFIED POLYSULFONE DIALYZER, VPS-H, ON OXIDATIVE STRESS IN HEMODIALYSIS PATIENTS

Hideki Nishimura, Masamichi Shibata, Takenori Funaki, Chieko Higuchi, Tsutomu Sanaka. *Internal Medicine, Tokyo Women's Medical University Medical Center East, Arakawa, Tokyo, Japan*

Introduction and Aims: To evaluate the effects on antioxidant capacity in hemodialysis patients of a newly developed polysulfone dialyzer, the VPS-H, which is more abundantly vitamin-E coated on the membrane than conventional dialyzers.
Methods: Sixteen stable hemodialysis patients (10 men; 16 women; mean age, 66.3±11.6 years) who gave informed consent and who had used polysulfone membrane dialyzers for more than 6 months before the study period participated in the experiment. All subjects were randomly divided into 2 groups: the VPS group (n=11), who changed to the VPS-H dialyzer from conventional polysulfone membrane dialyzers; and the Control group (n=5), who did not change. We measured oxidized LDL, antioxidant capacity (utilizing the reduction of Cu^{++}), pentosidine, and adiponectin before and 1, 3, 6, and 12 months after changing dialyzers. We also evaluated the clearance of VPS-15H compared with that of PS-13UW or PS-16UW. Patients' symptoms and complications during the study were also recorded. Drugs that influenced oxidative stress in the patients were not altered throughout the study period.
Results: No changes in symptoms or complications were observed. We did not see any appreciable differences in small solute clearance between VPS-15H and PS-UW, with the exception of BUN clearance by VPS-15H, which was lower than that of PS-16UW but not PS-13UW. Oxidized LDL was lower in the VPS group than the Control group from 1 month (VPS group vs. Control group; 0.68±0.16 vs. 1.07±0.17, respectively, $p<0.01$) through 12 months after the study start. Antioxidant capacity was significantly higher in the VPS group than the Control group as early as 6 months after the start (VPS group vs. Control group; 1.35±0.45 vs. 0.95±0.09, respectively, $P<0.05$). There were no significant differences in pentosidine and adiponectin.
Conclusions: VPS-H may ameliorate the oxidative stress in hemodialysis patients by reducing oxidized LDL and improving antioxidant capacity.

MP245 OXIDANT STRESS AND ANTIOXIDANT RESERVE STATUS IN PATIENTS WITH END-STAGE RENAL DISEASE UNDERGOING HEMODIALYSIS

Ioannis Karamouzis[1], Pantelis Sarafidis[2], Michael Karamouzis[1], Stavros Iliadis[1], Athanasios Sioulis[2], Pavlos Malindretos[2], Athanasios Triantos[1], Norma Vavatsi-Christaki[1], Dimitrios Grekas[2]. *[1]Laboratory of Biological Chemistry, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]1st Department of Medicine, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Introduction and Aims: An increase in oxidative stress has been previously

observed in patients with end-stage renal disease (ESRD). However, studies on the antioxidant reserve in these patients report contradictory results. The aim of this study was to examine *in vivo* the oxidant-antioxidant balance of patients with ESRD undergoing hemodialysis and compare it to healthy subjects using validated markers.

Methods: We evaluated a total of 31 consecutive patients with ESRD that started dialysis treatment in a Renal Dialysis Unit of a University Hospital within a period of 12 months and compared them with 29 carefully matched healthy subjects. All participants gave blood samples for the measurement of (a) plasma levels of 15-F_{2t}-IsoProstane (15-F_{2t}-IsoP) (b) plasma total antioxidant capacity (TAC) determined with a standardised assay, corrected for interferences from uric acid, bilirubin, and albumin levels and (c) serum levels of vitamin E.

Results: Plasma 15-F_{2t}-IsoP levels were more than 10 times higher in ESRD patients compared to healthy subjects (483,07±162,21 pg/ml vs 47,11±32,25 pg/ml, $p<0.001$). These elevated levels of ESRD patients presented a further slight increase during the hemodialysis procedure. In contrast, plasma TAC levels were slightly lower in ESRD patients than controls (0.94±0.16 mmol/l vs 1.05±0.08 mmol/l, $p<0.01$). Similarly, serum vitamin E levels were lower in ESRD patients than healthy subjects (26.85±1.54 μmol/l vs 31.09±6.16 μmol/l, $p<0.001$).

Conclusions: The enormous increase in oxidative stress in patients with ESRD on hemodialysis is not followed by any elevation of the antioxidant reserve, which remains slightly lower than normal. The deleterious effects of this shift in the oxidant-antioxidant balance remain to be fully elucidated.

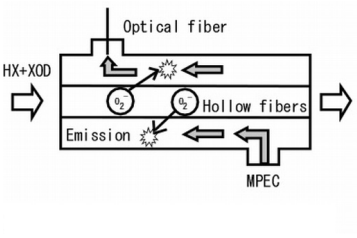
MP246 DEVELOPMENT OF A NOVEL DEVICE OF MEASURING CONCENTRATION OF O_2^- GENERATED BY CONTACT OF DIALYSIS MEMBRANE WITH BLOOD

Sumire Koga[1], Masato Matsuda[1], Ken-ichiro Yamamoto[2], Taiji Yakushiji[3], Makoto Fukuda[3], Takehiro Miyasaka[3], Kiyotaka Sakai[1].
[1]Department of Chemical Engineering, Waseda University, Shinjyuku-ku, Tokyo, Japan; [2]Waseda Institute for Advanced Study, Waseda University, Shinjyuku-ku, Tokyo, Japan; [3]Department of Medical Engineering, Himeji Dokkyo University, Himeji-shi, Hyogo, Japan

Introduction and Aims: Superoxide (O_2^-) is generated by the contact of dialysis membrane with the blood. Oxidative stress induced at higher O_2^- concentrations causes dialysis complications like dialysis amyloidosis. The objective of the present study is to develop a novel device of measuring O_2^- concentration by chemiluminescence which is packed with hollow fiber membranes and an optical fiber.

Methods: Either hypoxanthine (HX) aqueous solution (0 μM, 25 μM, 50 μM, 75 μM and 100 μM) inside hollow fibers or chemiluminescence probe: 2-methyl-6-p-methoxyphenylethynyl-imidazopyrazinone (MPEC) aqueous solution (15 μM) outside hollow fibers were caused to flow using a harvard pump at 0.5 ml/min. Intensity of chemiluminescence resulted from the reaction of O_2^- with MPEC was measured continuously on a photon detection unit connected to the optical fiber placed outside the hollow fibers (Fig. 1). After 180 s from measurement initiation, 1 ml of xanthineoxidase (XOD) aqueous solution (0.48 U/ml) was added to the HX aqueous solution and generated O_2^- was made to permeate through the hollow-fiber membranes. Chemiluminescence intensity was measured for 720 s.

Results: Injection of the XOD aqueous solution increased chemiluminescence intensity using 25 μM, 50 μM, 75 μM and 100 μM HX aqueous solutions. These results demonstrate that O_2^- can be detected by the newly-developed method of measuring O_2^- concentration. Peak areas for chemiluminescence intensity of 0, 221±53.4, 444±24.4, 682±53.7 and 861±171 (n = 3) were obtained at HX concentrations of 0 μM, 25 μM, 50 μM, 75 μM and 100 μM, respectively. Peak area gave a first-order good correlation with HX concentration (correlation coefficient 0.998) (Fig. 2). O_2^- concentration was dependent on HX concentration by the cytochrome C reduction method. These results indicate that O_2^- concentration is obtainable from data on peak area by the membrane permeation method we have developed.



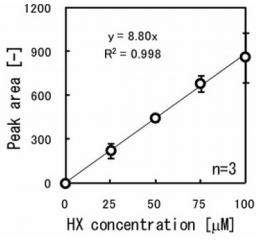


Fig. 1 (left). Newly-developed compact device of indirectly measuring O_2^- concentration. Fig. 2 (right). Peak area against HX concentration.

Conclusions: O_2^- concentration is measurable continuously with the newly-developed compact device using an optical fiber which has a potential of indirectly monitoring O_2^- concentration of the blood during hemodialysis treatments.

MP247 EFFECTIVE REMOVAL OF URAEMIC SOLUTES BY DIFFERENT CONVECTIVE STRATEGIES: A PROSPECTIVE CROSS-OVER TRIAL

Natalie Meert[1], Sunny Eloot[2], Marie-Anne Waterloos[1], Mieke Van Landschoot[1], Annemie Dhondt[1], Raymond Vanholder[1]. *[1]Nephrology, University Hospital Gent, Gent, Belgium; [2]Institute Biomedical Technology, University Gent, Gent, Belgium*

Introduction and Aims: Although different on-line convective removal strategies are available, studies comparing different options based on parallel protocols are scanty.

Methods: In this cross-over study we compared pre-dilution haemodiafiltration (pre-HDF, Polyflux 170), post-dilution haemodiafiltration (post-HDF, Polyflux 170) and pre-dilution haemofiltration (pre-HF, Polyflux 210) in 14 patients. Parallelism included the same blood flow (Q_b), dialysis time (t) and effective convection (22.9±1.7 vs 22.2±2.0 L, p=NS) in pre-HDF and post-HDF, and the same Q_b and t while comparing pre-HDF and pre-HF (1:1 dilution). With pre-HF, substitution was maximized to 72.9±8.2 L. We studied water soluble compounds (urea, creatinine, uric acid), protein bound compounds (hippuric acid, indole acetic acid, indoxylsulfate and p-cresylsulfate) and β_2-microglobulin (β_2M). Relative Removal and the Extraction Ratio over the entire session and the evolution of the concentration at the inlet and outlet of the dialyser were evaluated.

Results: Post-HDF was superior to pre-HDF for water soluble compounds and β_2-microglobulin, whereas there was no difference for protein bound compounds. Pre-HDF was superior to pre-HF for water soluble compounds and protein bound compounds. In contrast, removal of β_2-microglobulin for pre-HF was higher than for pre-HDF but it did not differ from that obtained with post-HDF.

Conclusions: It is concluded that post-dilution is superior to pre-dilution in HDF under conditions of similar convective removal, and HDF is superior to HF in pre-dilution, with the exception of removal of β_2-microglobulin. Overall, post-HDF is the most efficient convective strategy among those tested.

MP248 A PROSPECTIVE COMPARISON OF INTERNAL HEMODIAFILTRATION AND BICARBONATE DIALYSIS

Marco Righetti[1], Oliviero Filiberti[2], Andrea Ranghino[3], Gianmichele Ferrario[1], Gian Enrico Guida[2], Adalberto Tommasi[1].
[1]Nephrology and Dialysis Unit, Vimercate Hospital, Vimercate, Italy; [2]Nephrology and Dialysis Unit, S. Andrea Hospital, Vercelli, Italy; [3]Nephrology and Dialysis Unit, Novara Hospital, Novara, Italy

Introduction and Aims: It has been shown that internal hemodiafiltration (IHDF), a simple and low-cost technique like bicarbonate dialysis (BD), has an intradialytic capacity of small and medium molecules removal similar to other more complex mixed dialysis therapies. There are no clinical data about the long-term effects of IHDF. We are performing a trial to compare the effects of IHDF and standard BD on lots of laboratory and clinical parameters of prevalent hemodialysis patients.

Methods: We designed a prospective cross-over trial with a 2 periods, 2 treatments scheme. 24 dialysis patients were randomly assigned to 2 groups, one group receiving 6 months IHDF then 6 months BD and the other group BD followed by IHDF. BD was performed with low flux synthetic membranes having surface area similar to Toray polysulfone. Biochemical parameters were collected every month before the first dialysis session of the week. We present preliminary data for a mean follow-up of 10 months.

Results: Repeated measures analysis of variance has shown a trend towards a kt/V significantly higher during IHDF as compared to BD (1,61±0,03 vs 1,48±0,03; F value= 2,8; p= n.s.). Moreover, pre-dialysis urea levels were lower during IHDF as compared to BD (140±3 vs 153±4 mg/dl; p= n.s.). Beta 2-microglobulin net values and beta 2-microglobulin reduction rate were respectively lower (24,8±0,7 vs 28,6±0,6 mg/L) and higher (-18±7 vs 0,3±4%) in patients submitted to IHDF as compared to the patients on BD (F value= 4,8; p< 0,05). Pre-dialysis homocysteine values were similar in the 2 groups of treatment (IHDF vs BD: 22,1±0,7 vs 22,5±0,6 micromoles/L), even though homocysteine intradialytic removal was higher in IHDF as compared to BD. There were no differencies about data like haemoglobin, ESA consumption, iron parameters, vitamins B, calcium, phosphorus, parathormone, lipids, normalized protein catabolic rate, albumin, C-reactive protein, blood pressure values, dry weight, intradialytic hypotensive episodes.
Conclusions: After a medium-term follow-up pre-dialysis beta 2-microglobulin values were significantly lower in IHDF than BD. It might be necessary a longer follow-up and a larger study group for achieving statistically significant results concerning dialysis adequacy. IHDF might substitute BD because IHDF is a simple, low-cost dialysis therapy similar to BD, but with higher removal capacity.

MP249 INCREASED ULTRAFILTRATE VOLUMES IN POST DILUTIONAL ON-LINE HEMODIAFILTRATION BY SETTING A CONSTANT TRANSMEMBRANE PRESSURE CONTROL

Ezio Movilli, Giuliano Brunori, Battista Fabio Viola, Corrado Camerini, Roberto Zubani, Giuseppe Mazzola, Giovanni Cancarini. *Division of Nephrology, Spedali Civili and Section of Nephrology, University of Brescia, Brescia, Italy*

Introduction and Aims: On-line Hemodiafiltration (HDFol) is a dialysis technique that combines elevate diffusion rates with increasing convection volumes to increase the clearances of low molecular and middle molecular uremic toxins. High ultrafiltration (UF) volumes cause hemoconcentration, particularly in the post dilutional mode. The usual prescription mode of HDFol is to assign a preset constant UF volume to be exchanged during treatment (UFc). This causes transmembrane pressure (TMP) to increase steeply, potentially reducing total UF. Aim of this study has been to investigate if prescribing a fixed TMP (TMPc) instead of UFc could improve convective exchanges.
Methods: We studied 15 HD patients on post dilutional HDFol for at least 3 months (median 9 months). They were 12 men 3 women, mean age 65±8 years, in chronic HD treatment for 1-10.1 years (median: 4.4 years). During a 2 weeks period, we performed three consecutive HDFol sessions with UFc modality, and three consecutive HDFol with TMPc. The following parameters were assessed at each dialysis session: body weight (BW), dialysis body weight loss (BWL), total ultrafiltration rate (UF), TMP pre and post HDF. At the beginning of the study the following parameters were also assessed: Kt/V, total serum proteins (TP), hematocrit (Hct). Dialysis treatment time remained unchanged (median 4 hours; range: 3.5-4.5 hours). BWL, UF, TMP values are the mean of the three dialysis sessions either in UFc or TMPc. Data were analyzed by paired Student t test.
Results: BW was 79.6±18.1kg, Hct: 34.2±2.3%, Qb: 313±17 ml/min, TP: 6.6±0.3 g/dl, Kt/V: 1.30±0.13.
Data are reported in the table:

	BWL (kg)	UF/hour (ml)	TMPpre (mmHg)	TMPpost (mmHg)	UF tot (L)	Global UF (L) (UFtot+BWL)
UFc	3.3±1	2734±179	94.4±22.8	195.2±47.2	11.0±0.9	14.3±1.6
p	NS	<0.0001	NS	<0.0001	<0.0001	<0.0001
TMPc	3.3±1	3598±265	96.4±19.7	97.5±19.6	14.5±1.2	17.8±1.8

Conclusions: Changing from traditional UFc modality to TMPc modality in prescribing post dilutional HDFol, has determined a steady increase (31%) in the amount of UF/hour and total UF. This could be due to better preservation of membrane permeability in TMPc modality by preventing intradialytic TMP rise and consequent protein cake formation.

MP250 MID-DILUTION HEMODIAFILTRATION COMPARED WITH PRE- AND POST-DILUTION INFUSION MODES

Marta Arias, Francisco Maduell, Manel Vera, Nuria Serra, Miguel Blasco, Eduard Bergada, Aleix Cases, Josep M. Campistol. *Nephrology, Hospital Clínic, Barcelona, Spain*

Introduction and Aims: Hemodiafiltration (HDF) with elevated substitution fluid offers an optimal way to remove uremic toxins. Post-dilution infusion is more efficient for obtaining maximum clearances of small and larger solutes in comparison with pre-dilution mode. Mid-dilution infusion is a recent alternative which represents simultaneous pre- and post-dilution infusion that could be a highly effective technique to remove uremic toxins avoiding the disadvantages of post-dilutional infusion modes. The aim of this study was to compare, with the same membrane, mid-dilution with post- and pre-dilution modes, evaluating the efficiency in removing different low and middle molecules.
Methods: This prospective study was carried out in 20 patients (12 men and 8 women), 57.8±18 years old, stable in hemodialysis program and with good vascular access. The aetiology of their chronic renal failure was: 5 glomerulonephritis, 4 tubulo-interstitial nephropathy, 5 vascular disease, 2 polycystic kidney disease, 2 systemic diseases and 2 unknown. Each patient underwent three hemodialysis sessions, one with 1.7 m^2 polyphenylene and 200 ml/min pre-dilution infusion, one with 1.7 m^2 polyphenylene and 100 ml/min post-dilution infusion, and one with 1.9 m^2 polyphenylene and 200 ml/min mid-dilution infusion. The remaining dialysis parameters did not vary: Fresenius 4008 S monitor, dialysis time 269±32 minutes, blood flow 443±29, dialysate flow 800 ml/min. Pre and postdialysis urea, creatinine, β_2-microglobulin, mioglobin, prolactin and retinol binding protein (RBP) were measured to calculate their reduction ratio at each session.
Results: Convective volume was 53.1, 26.9 and 52.9 L in pre, post and mid-dilution infusion respectively. Urea and creatinine reduction ratio were slightly higher in post-dilution mode vs pre- and mid-dilution modes. The β_2-microglobulin (85.8±3%), mioglobin (73.6±11%) and prolactin reduction ratio (67.8±14%) with mid-dilution was significantly higher as compared to post-dilution mode (83.3±3, 68.4±10 and 62.8±8%, respectively) and pre-dilution mode (79.6±4, 54.9±12 and 51.8±10%, respectively). The RBP reduction ratio (29.2±9%) with mid-dilution was significantly higher as compared to post-dilution mode (23.5±10, p< 0.01) and pre-dilution mode (22.5±10%, p< 0.01).
Conclusions: On-line HDF with mid-dilution mode appears to be a good alternative technique which allows a higher convective volume with a better removal of β_2-microglobulin, mioglobin, prolactin and RBP in comparison with postdilution and showier in pre-dilution mode.

MP251 CARBAMYLATED HEMOGLOBIN AS AN INDICATOR TO HEMODIALYSIS ADEQUACY AND COMPLICATIONS

Saeed Abdel Wahab, Hossam Abdel Aziz, Tareq Yousef. *Department of Internal Medicine, Ain Shams University, Cairo, Egypt*

Introduction and Aims: Carbamylation is an irreversible process of non-enzymatic modification of proteins by the breakdown products of urea. The degree of carbamylation is a marker of urea exposure and has been proposed as an indicator of the control of uraemia by dialysis. Carbamylated proteins are considered an important part of uremic toxins and can be related to many uremic complications. Aim of the work: To study potential determinants of carbamylated hemoglobin (CarbHb). In addition, to investigate the relationship between CarbHb and established measures of dialysis adequacy, And to development of common complications of chronic renal failure such as ischemic heart disease and neuropathy.
Methods: We performed a cross-sectional study of patients with chronic renal failure classified into two groups; group one including patients on regular haemodialysis (HD) and group two including patients on conservative treatment, against normal control group (group 3). For all groups the following are done Complete history, thorough clinical examination, routine laboratory investigations ECG, efficiency of dialysis for group one using KT/V, nerve conduction study, resting ECG and Carbamylated hemoglobin level.
Results: In HD patients, CarbHb correlate with pre-dialysis BUN (r =0.395, P=0.019), serum albumin (r =0.721, P<0.001) and Kt/V ($r = -0.636$, $P<0.001$).

Also correlate with neuropathy (nerve conduction study) (r =-0.469, p =0.004) and ischemic change in resting ECG (r = -0.444, p =0.007).while in group two CarbHb correlate with BUN only (r =0.414, p= 0.013). Mean carbamylated hemoglobin in group one is 129.47±23.50 μg CV/g Hb, In group two is 88.09±9.41 μg CV/g Hb, while in group three is 30.7950±1.9395μg CV/g Hb. ROC curve for carbamylated hemoglobin with resting ECG in group one shows Area under the curve = 0.765, cut off 120.6 CV/g Hb shows sensitivity 81.8% and specificity of 66.7%. While in group two shows Area under the curve = 0.718 and at a cut off level 87.7 CV/g Hb shows sensitivity 100.0% and specificity 61.3%. ROC curve study for carbamylated hemoglobin and nerve affection was done for group one and two. Results for group one shows area under the ROC curve = 0.766 best criterion at cut off level 141.5 CV/g Hb with sensitivity100.0% and specificity 59%,while in group two shows Area under the ROC curve = 0.551, and best criterion at cut off 86.2 CV/g Hb with sensitivity 71.4% and specificity of 50.0%.

Conclusions: carbamylated hemoglobin is higher in uremic patients than normal control, and is higher in patients under regular hemodialysis than in patients under conservative treatment. In hemodialysis patients carbamylated hemoglobin correlate with KT/V and can be used as a supportive measure for adequacy of dialysis.the presence of complications like IHD and neuropathy in dialysis patients correlates with carbamylated hemoglobin which can be used as a marker for presence or tendency to develop these complications.

MP252 IMPACT OF DAILY HEMODIALYSIS (DH) ON UREA KINETIC MODELING (UKM) PARAMETERS IN PATIENTS SWITCHED FROM CONVENTIONAL HEMODIALYSIS TO DH

Jacek Pietrzyk[1], Przemyslaw Korohoda[2], Monika Miklaszewska[1], Roman Rumian[2], Lidia Krawentek[2], Dorota Drozdz[1], Katarzyna Zachwieja[1], Malgorzata Komorowska[3]. *[1]Dialysis Unit, University Children's Hospital, Cracow, Poland; [2]Electronics, Academy of Mining and Metallurgy (AGH), Cracow; [3]Dept. of Clinical Biochemistry, University Children's Hospital, Cracow*

Introduction and Aims: A large number of data shows beneficial effects of implementing daily hemodialysis (DH) upon the outcome in patients dialysed previously in a 3 times a week hemodialysis (HD) schedule. The mechanisms responsible for this phenomenon are still unclear, however, the time of low-flux DH sessions is shortened almost by half. Aim of the study: Evaluation of the effect of doubling the number of hemodialyses per week in patients upon kinetically calculated cellular clearance Kc, weekly eqKT/V/KT/V ratio, relative body weight decrease expressed as ultrafiltration to post-dialysis body weight ratio (Qf/BWt), % of recirculation (%R) and metabolic parameters: urea generation G and protein catabolic rate nPCR, respectively.

Methods: 7 chronically HD patients were subjected to DH for one week. Based upon output data from double-pool volume variable model equations and rebound, weekly KT/V, the time for each DH session was computed, with no change in KD (dialyser clearance). Kc and other kinetic parameters were estimated from optimization procedures performed according to the Nelder-Mead simplex method.

Results: By the use of almost similar dialyser clearances in 21 conventional and 42 DH modeling sessions, estimated Kc values were found to be significantly higher by 32.4% in DH (p=0.049). No differences in %R were noted. The relative body weight decrease expressed as the Qf/BWt ratio was found to be non-significantly increased in DH sessions, however – in both HD and DH treatment modalities – it strongly correlated with Kc (r = -0.653; p=0.006 and r=-0.552; p=0.0036, respectively). G increased in DH by 10.8% (4.8 vs. 5.38 mg/min; p = 0.106) and nPCR – by 8.6% (1.06 vs.1.16 g/kg/d; p=0.16). The correlation between nPCR and KT/V was found to be weak and non-significant (r=0.25; p=0.289).

Conclusions: An increased Kc observed in patients subjected to DH may result in better dialysis efficacy in patients switched into this treatment modality. Increased G and nPCR were also positive findings noted after one-week study.

MP253 BREATH ETHANE PEAKS DURING A SINGLE HAEMODIALYSIS SESSION AND IS ASSOCIATED WITH TIME ON DIALYSIS

Karen Stevenson[1], K. Radhakrishnan[1], C. Patterson[2], L. McMillan[2], K. Skelton[2], L. Buist[3], M. Padgett[2], P.G. Shiels[1]. *[1]Surgery, University of Glasgow, Glasgow, United Kingdom; [2]Department of Physics and Astronomy, University of Glasgow, Glasgow, United Kingdom; [3]Renal Unit, Western Infirmary Glasgow, Glasgow, United Kingdom*

Introduction and Aims: A growing body of evidence sugggests that oxidative stress is increased in haemodialysis patients and that dialysis itself is a contributory factor. The elevated oxidant stress, a result of increased production of reactive oxidant species (ROS) may be due to increased pro-inflammatory activity and reduced anti-oxidant mechanisms. As ROS are short lived transitory molecules surrogate markers of oxidant damage are needed. Identification of potential causes of oxidative damage such as dialyser membranes or dialysate have been proposed and therefore assessment of oxidative damage during a single dialysis session would be of interest. We have monitored oxidative stress levels during single dialysis sessions, using ethane production as a bio-marker. to investigate the cause and extent of the resulting oxidative damage.The aim of this study was to undertake a real time assessment of breath ethane production during haemodialysis in an end stage renal failure haemodialysis population.

Methods: Real-time laser spectroscopy was used to determine breath ethane levels in renal dialysis patients (n=24). Breath samples were collected using a simple single breath filling technique into SKC Tedlar sample bags. Each patient adopted the role of longitudinal control in this study and their breath ethane level was monitored regularly during the dialysis session.We have shown for the first time, that patients undergo significant breath ethane elevation at the beginning (within the first 10 minutes) of each dialysis session.

Results: A regression analysis of the data showed a trend towards increased ethane levels for patients on dialysis for shorter duration of time (r=0.656,R-Sq 43.3% p= 0.001). Multiple linear regression was undertaken to further assess these associations and revealed that peak ethane leves were significantly and independently associated with time period on dialysis (p<0.000), vascular access (p=0.013) and male sex (p=0.005). However whilst diabetes status had demonstrated a correlation with peak ethane levels (0.525, p=0.008) this was not independent of vascular access status. This multivariate linear model was significantly associated with Ln Peak Ethane levels (S=0.744, R-Sq = 80.8%).We have assessed for the first time the oxidative stress elevation resulting during a single dialysis session. We found a significant rise in oxidative stress during the first few minutes after commencement of dialysis.This rapid response gives new insight into the dynamics of the oxidative damage resulting from dialysis treatment.

Conclusions: We have assessed for the first time the oxidative stress elevation resulting during a single dialysis session. We found a significant rise in oxidative stress during the first few minutes after commencement of dialysis.This rapid response gives new insight into the dynamics of the oxidative damage resulting from dialysis treatment.

MP254 HEPATIC (ALBUMIN) DIALYSIS THERAPY WITH PROMETEUS^{R} IN PATIENTS WITH RARE CAUSES OF ACUTE LIVER FAILURE – A SERIES OF THREE CASES

Adrian Covic, Carmen Volovat, Paul Gusbeth-Tatomir, Ciresica Diaconescu, Cristina Birleanu, Luminita Voroneanu. *Nephrology Clinic, Parhon University Hospital, Iasi, Romania*

Introduction and Aims: Hepatic (albumin) dialysis has been extensively used in recent years in acute liver failure (ALF) and in severe liver cirrhosis as a "bridge" to liver transplantation. However, rare causes of ALF treated with albumin dialysis have been not well-described until yet.

Methods: We report three female adolescents/young patients referred to our clinic with acute liver failure (ALF) of initially unknown aetiology in two cases and with drug overdose in the third case. All patients were in second and third degree hepatic coma and were treated with hepatic dialysis with the Prometheus^{R} device.

Results: One 20-years old patient had solely a history of nausea lasting for three months. She had an ammonemia of 380 μg/dl, total bilirubin of 58.2 mg/dl (conjugated 47.2 mg/dl), ALAT 53 IU/l, serum creatinine

2 mg/dl, LDH 1220 IU/l, platelet count 98,000/ul. Two liver dialysis sessions with the Prometheus device of each 8 hours were done, with spectacular improvement of consciousness and biochemical parameters. A cornean Kayser-Fleischer ring has been noted at physical examination and the ceruloplasmin level was 150 mg/l. Therefore the diagnosis of Wilson's disease has been formulated (to our knowledge, the second case in the literature). Two additional Prometheus^R sessions were needed two weeks later, after which she was successful transplanted.

A second 17-years old patient, diagnosed recently with severe anemia and bleeding disorder, developed during hospitalization ALF and acute oliguric renal failure. She was subjected to two sessions of liver dialysis, with slight improvement of neurological signs; she subsequently developed severe sepsis and died five days after referral. Antimitochondrial antibodies were highly elevated and a post-mortem histological diagnosis of primitive billiary cirrhosis has been done.

A third 14-years old patient developed ALF after overdosed therapy with methotrexate, cotrimoxazol and non-steroidal drugs given for presumed dermatomyositis and tonsillitis. After 2 Prometheus sessions, she recovered spectacularly, with total bilirubin falling from 15.7 to 2.57 mg/dl and ALAT from 2141 to 442 IU/l. She was discharged after 6 days in good clinical condition.

Conclusions: The authors extensively discuss the diagnostic pitfalls of these three cases with acute liver failure due to rare causes and the usefulness of the Prometheus-system liver dialysis in these situations.

MP255 EFFECTS OF THE HEMODIALYSIS SESSION ON DIMETHYL-ARGININES PLASMA LEVELS

Adamasco Cupisti[1], Alessandro Saba[2], Cristina Consani[1], Vincenzo Panichi[1], Lisa Cavallini[1], Giuliano Barsotti[1]. [1]*Internal Medicine, Nephrology Unit, University of Pisa, Pisa, Italy;* [2]*Chemistry and Industrial Chemistry, University of Pisa, Pisa, Italy*

Introduction and Aims: Asymmetric dimethylarginine (ADMA), a nitric oxide synthetase inhibitor, is considered as a non-traditional cardiovascular risk factor which, together with symmetric dimethylarginine (SDMA), biological inactive substance, originate from methylated protein degradation. They are normally cleared by urine, thus the circulating levels are increased in uremic patients, but ADMA is additionally metabolized by dimethylaminohydrolase (DDAH), which is sensitive to oxidative stress and maybe to inflammation. L-arginine to ADMA molar ratio may reflect bio-availability of nitric oxide, but may also be a factor affecting the occurrence of intradialysis hypotension. The impact of hemodialysis treatment on ADMA levels is not yet defined, and also the role of diffusive or convective procedures is still controversial.

We aimed to investigate the effects of different hemodialysis techniques on L-arginine and on dimethylarginines plasma levels.

Methods: Thirty stable chronic uremic patients (20 m, 10 f, age 61±13 yrs), on maintenance hemodialysis treatment were recruited for the study and divided into three groups: 10 patients were on standard diffusive bicarbonate dialysis (HD), 10 patients were on Acetate-free-biofiltration (AFB), and 10 patients were on mid-dilution on-line hemodiafiltration (HDF). High biocompatible synthetic membranes were used. The groups were comparable as far as age, gender, Kt/V, nPCR and haemoglobin levels were concerned.

Before and after a single 4 hour hemodialysis session, serum levels of L-Arginine, ADMA and SDMA were measured by high-performance liquid chromatography (HPLC)-tandem mass spectrometry.

Results: As a whole, a significant decrease of L-Arginine (127±55 vs 73±32 μmol/L, $p<0.001$), ADMA (1.14±0.27 vs 0.65±0.17 μmol/L, $p<0.001$) and SDMA (3.49±1.00 vs 1.58±0.43 μmol/L, $p<0.001$) plasma levels occurred following hemodialysis treatments.

The average decrease of L-arginine was greater in HDF patients than in AFB (55.7% vs 22.9%, $p<0.01$) or HD (15.5%, $p<0.01$) patients; similarly, reduction of ADMA plasma levels was more consistent on HDF than on AFB (51.2%, vs 35.5%, $p<0.01$) or on HD (37.5%, $p<0.05$). Instead, no significant difference in SDMA reduction was observed among the three groups of patients (58.8%, 51.8%, and 47.6%, respectively). Of consequence, improving of L-arginine/ADMA ratio occurred with AFB and HD but not with HDF (as average 23%, 31%, - 11%, respectively, $p<0.05$).

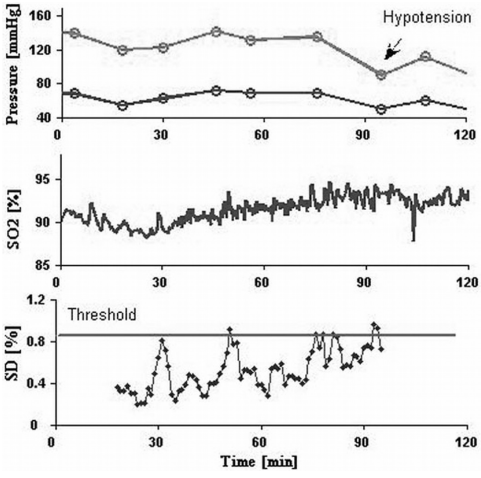
Conclusions: Our results demonstrate that significant decreases of L-arginine and dimethylarginines plasma levels occur following bicarbonate HD, AFB or on-line mid-dilution HDF. Namely, high flux convective treatment causes a significant reduction of ADMA and a more marked decrease of L-arginine, whereas SDMA changes are quite similar in the three studied groups. The clinical significance of these findings remains to be determined in the long run.

MP256 SHORT-TERM VARIABILITY OF OXYGEN SATURATION (SO_2) DURING HEMODIALYSIS (HD) IS A WARNING PARAMETER FOR HYPOTENSION APPEARANCE

Elena Mancini[1], Luca Corazza[2], Daniela C. Cannarile[1], Maria L Soverini[1], Silvio Cavalcanti[2], Antonio Santoro[1]. [1]*Nephrology, Dialysis, Hypertension, Policlinico S. Orsola-Malpighi, Bologna, Italy;* [2]*Laboratory of Cellular and Molecular Engineering, DEIS, University of Bologna, Bologna, Italy*

Introduction and Aims: Hypoxemia may be considered as a surrogate marker of hemodynamic instability. Continuous, non-invasive monitoring of SO_2 during HD is now possible, by means of sensors measuring SO_2 in blood entering the dialyzer. We analyzed the short-term variability of SO_2 correlated to conditions of hemodynamic instability during HD.

Methods: Twenty hypotension-prone pts where repeatedly monitored during their HD sessions in order to have, for each one, at least one session with hypotension and one without. SO_2 was recorded (sampling time = 5 s) from the *Hemox* sensor of the Formula 2000 (BellCo, I). Blood pressure, pre- and during HD (15-min interval), symptoms and time of their appearance, were collected. Data were analyzed off-line in order to define an algorythm, based on SO_2 behaviour, able to detect in advance the onset of hypotension episodes. Sessions were classified as *positive* with hypotension and *negativ*e without. The SO_2 time series was filtered with a digital low-pass filter to remove high frequency components. SO_2 data were extracted by shifting a 4-min long window, producing epochs overlapping by 75%. For each data window, long-term fluctuations having a period greater than the window-length were removed by linear regression and standard deviation (SD) was computed. In the *positive* sessions, the analysis was truncated at the hypotension onset. A critical threshold of 0.85% was set and the session with hypotension was predicted when the SD exceeded this threshold (Figure); the overshoot time (OT) was also calculated.



Results: On the basis of the hypotension presence, out of the 40 sessions considered for analysis, 20 were classified as *positive* and 20 *negative*. The incidence of the positive sessions was 2/2 in 7 pts, 1/2 in 6, and 0/2 in the remaining 7.

The off-line prediction, based on the SO_2 variability, was 88% (17 *positive* and 18 *negative* sessions). Notably, OT anticipated hypotension by 14.9 min. Hypotension prediction was correct in 85% of the 20 positive sections (17/20). The positive likelihood ratio (sensitivity/(1 – specificity)) was 8.5, indicating that the SO_2 variability index significantly increases the likelihood of a positive prediction.

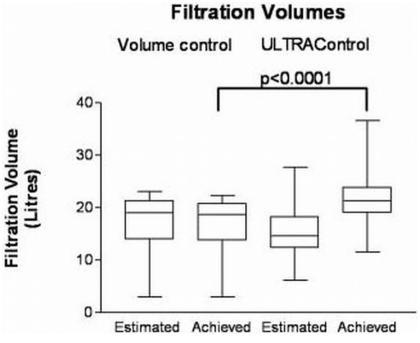
Conclusions: Intradialytic acute SO_2 changes anticipate hypotension, which is likely to be the result of the hypovolemia-induced decrease in cardiac

output and peripheral hypoperfusion. Continuous SO_2 monitoring variability may provide useful information for forecasting the hypotension onset. This study may pave the way to developing an alarm system including SO_2 changes as a warning variable, offering the chance of effecting preventive manoeuvres for the avoidance of hypotension.

MP257 HAEMODIAFILTRATION USING ULTRACONTROL ACHIEVES GREATER FILTRATION VOLUMES THAN HAEMODIAFILTRATION USING VOLUME CONTROL

Stuart Ross, Anne Allan, Colin Walker, Robert Peel, Stewart Lambie. *Department of Renal Medicine, Raigmore Hopital, Inverness, United Kingdom*

Introduction and Aims: Haemodiafiltration (HDF) combines convective as well as diffusive clearance of impurities from the bloodstream, and thereby increases clearance of middle and large molecules. Larger filtration volumes are likely to increase clearance of these molecules and thus enhance the benefits of HDF. Using ULTRAControl software (Gambro, Lund, Sweden) the transmembrane pressure (TMP) and achieved ultrafiltration (UF) rate are monitored and adjusted during HDF therapy to achieve optimal fluid removal within preset limits for TMP. This automates a function previously performed by estimation of achievable filtration volumes, this study aims to test whether this results in increased filtration volumes.
Methods: Ten patients dialysing with HDF were selected and studied for ten HDF sessions with estimation of achievable filtration volumes and then volume control, followed by ten sessions using ULTRAControl to optimise filtration volumes. The estimation of achievable filtration volume was derived from an algorithm based on haematocrit, time on treatment, UF volume and blood pump speed. ULTRAControl also estimates achievable filtration volume from initial data.
Results: The achieved filtration volume for a total of 97 sessions using volume control was 16.4±5.3 l (Mean ± SD), whereas with ULTRAControl it was 21.7±4.0 l ($p<0.0001$). The initial estimates produced by the two techniques were not significantly different at 16.8±5.4 l for volume control compared with 15.6±5.0 l for ULTRAControl. Blood Pump Speed did not differ significantly between the two techniques.



Conclusions: HDF using ULTRAControl achieves an increased filtration volume compared with HDF using volume control. Whether this increases middle molecule clearance or enhances patient benefit was not part of this study. Using ULTRAControl may also reduce nursing time and does reduce potential transcription errors in inputting the parameters required for estimation of filtration volumes when using volume control.

MP258 IONIC CLEARANCE-BASED Kt/V IN POSTDILUTION HEMODIAFILTRATION

Yvo Sijpkens[1], Veronique Joyeux[2], Lars-Göran Nilsson[3], Albert Jan Byvoet[1], Atman Haddj-Elmrabet[2]. *[1]Dept. of Nephrology, Leiden University Medical Center, Leiden, Netherlands; [2]Nephrology Unit, University Hospital Pontchaillou, Rennes, France; [3]Gambro Lundia AB, Lund, Sweden*

Introduction and Aims: Efficiency of dialysis can be assessed by the dialysis machine, using ionic clearance measurements. Ionic clearance corresponds closely to urea clearance and when the patient's estimated urea distribution volume (V) is entered the delivered Kt/V (iKt/V) is presented at treatment end. As part of a study evaluating on-line hemodiafiltration (HDF) therapy we assessed the within-patient variability of iKt/V (Diascan, Gambro) under stable treatment conditions and its relation to blood urea based Kt/V.
Methods: We enrolled 20 stable on-line HDF patients (male/female 13/7; age 58±21 years; body weight 72±10 kg; hematocrit, 38±4%). During a 4 week study period, iKt/V data were obtained for 207 postdilution HDF treatments with prescribed treatment time (236±14 minutes) and blood flow rate (311±33 ml/min) constant for each patient. V values from the Watson formulae were used for iKt/V calculations. For 37 of these treatments blood urea based eKt/V, calculated acc. to Daugirdas, was also obtained. The actual treated blood volume in the HDF treatments was 66±8 litres, and infusion and net UF volumes were 15±3 and 2.7±0.9 litres respectively.
Results: The overall mean iKt/V was 1.18±0.17. The within-patient variation in iKt/V, expressed as SD in per cent of mean value (SD/mean), was on average 6.6%. It was lower in patients (n=10) where treatment delivery was more stable in terms of treated blood volume (4.6±1.4%) compared to those where the treated blood volume varied more (8.9±2.0%; $p<0.001$). iKt/V levels correlated strongly with eKt/V (r=0.71; n=37) but were 6±11% lower in value ($p<0.01$).
Conclusions: When used in postdilution HDF the ionic clearance Kt/V function showed consistent results with a between-treatment variation of 5% when treatment conditions were stable. iKt/V values correlated closely with blood urea based eKt/V but were on average 6% lower. The choice of Watson V as input to the calculations may partly explain this difference.
Disclosure: this abstract was possible thanks to a grant given by Gambro.

MP259 TREATED BLOOD VOLUME AND HEMATOCRIT ARE MAJOR DETERMINANTS OF CONVECTIVE VOLUME IN HEMODIAFILTRATION

Veronique Joyeux[1], Yvo Sijpkens[2], Lars-Göran Nilsson[3], Atman Haddj-Elmrabet[1], Albert Jan Byvoet[2]. *[1]Nephrology Unit, University Hospital Pontchaillou, Rennes, France; [2]Dept. of Nephrology, Leiden University Medical Center, Leiden, Netherlands; [3]Gambro Lundia AB, Lund, Sweden*

Introduction and Aims: Recently an automated pressure control mode was introduced to simplify delivery of hemodiafiltration (HDF) treatments. Here, the machine sets a fixed operational trans-membrane pressure (TMP) based on a feedback loop of the achieved filtration. By eliminating the operator-dependent manual setting of infusion volume (in case of volume control) or TMP (in case of pressure control), this mode offers new opportunities to study factors that affect the convective volume in HDF.
Methods: We enrolled 20 stable HDF patients (male/female 13/7; age 58±21 years; body weight 72±10 kg). In 8-10 postdilution on-line HDF treatments per patient, performed in automated pressure control mode (ULTRA^{CONTROL}, Gambro), we recorded delivered infusion, net UF, and treated blood volume from the machine display at treatment end. For each treatment the automated TMP setting was repeated on an hourly basis. We measured pre-dialysis hematocrit and total plasma protein levels. We used a highly permeable dialyzer (1.7 or 2.1 m^2; Polyflux H, Gambro), a prescribed treatment time of 236±14 min, and a prescribed blood flow rate of 311±33 ml/min.
Results: The actual treated blood volume was 66±8 litres, corresponding to an effective mean blood flow rate of 294±32 ml/min. The automated TMP setting resulted in a TMP of 167±29 mmHg during the first treatment hour, rising to 234±62 mmHg for the last hour. The resulting convective volume was 18±3 L (net UF volume 3±1 L + infusion volume 15±3 L). Between patients the convective volume varied significantly between 11 and 23 litres and correlated with the treated blood volume ($r^2=0.74$). The per cent ratio of convective volume over treated blood volume (27±3%) correlated inversely with patients' pre-dialysis hematocrit level (38±4%; $r^2=0.42$), but not with their pre-dialysis total plasma protein level (67±4 g/L; $r^2=0.04$).
Conclusions: The treated blood volume, resulting from blood flow rate and treatment time, is the main determinant of the achievable convective volume in postdilution HDF therapy at constant TMP, given that a highly permeable dialysis membrane is used. In addition, interpatient variation of convective volume is largely explained by differences in hematocrit levels. The new automated pressure control mode appears to deliver simplified yet efficient HDF treatments.
Disclosure: this abstract was possible thanks to a grant given by Gambro.

MP260 ★ INFLUENCE OF USING A LOW-CALCIUM DIALYSATE ON ACHIEVING THE TARGET PARAMETERS OF CALCIUM-PHOSPHORUS METABOLISM IN A POPULATION OF HEMODIALYSIS PATIENTS

Adrian Dorin Zugravu[1], Simona Hildegard Stancu[1], Roxana Martinescu[2], Christian Klein[2], Gabriel Mircescu[1]. *[1]"Dr. Carol Davila" Clinical Hospital of Nephrology; "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [2]"Carol Davila" Fresenius NephroCare Dialysis Center, Bucharest, Romania*

Introduction and Aims: Dialysis patients have an increased cardiovascular morbidity and mortality, which are associated with the presence of vascular calcifications and abnormalities of the calcium-phosphorus metabolism. The study aims to assess the influence of using a low-calcium dialysate (AF13 - 1,25mEq/l calcium - Fresenius Medical Care, Germany) on the parameters of the mineral metabolism in a cohort of hemodialysis patients.
Methods: Corrected serum calcium, serum phosphate, calcium-phosphorus product and PTH were followed up in a cohort of 172 stable chronic hemodialysis patients for 9 months before and after starting using low-calcium dialysate. Low-calcium dialysate was used in patients with already high values of serum calcium, in which it is impossible to use vitamin D derivatives like calcitriol or to further increase the dose of calcium-based phosphate binder, because of resulting hypercalcemia.
Results: The study cohort comprises younger patients with a long dialysis vintage, more often with hypoparathyroidism, less often treated with vitamin D derivatives.

Table 1. Baseline characteristics of the study cohort

Male (%)	56.4%
Mean age (years)	55.1±12.6
Hemodialysis vintage (years)	10.7±9.6
Vitamin D therapy	18.6%
Hypoparathyroidism (%)	46%

Table 2. Parameters of mineral metabolism before and after using low-calcium dialysate

	Before AF13	After AF13	p
8,4<serum Ca<9,5mg/dl*	61%	76.2%	<0.05
Serum Ca>9,5mg/dl	13.4%	7%	<0.05
3,5<serum Pi<5,5mg/dl*	24.4%	32.6%	>0.05
Ca X Pi <55 (mg/dl)2 *	53.5%	53.5%	>0.05
3 normal parameters*	14%	26%	>0.05

*According to K/DOQI Guidelines.

Compared to the data available in the literature, there was a higher percentage of normocalcemic and a lower percentage of hypercalcemic patients. The percentage of normophosphatemic patients is marginally higher. Caution should be exerted, as hypocalcemia can develop in these patients and lead to hyperparathyroidism and further hypercalcemia.
Conclusions: Employing a low-calcium dialysate is useful in the attempt to reach the goals for the calcium-phosphorus metabolism parameters recommended by the guidelines. Nevertheless, other measures (non-calcium based phosphate binders, non-hypercalcemic vitamin D products, calcimimetics) are also needed in order to achieve the targets.
Reference: Kovesdy CP, Mehrotra R, Kalantar-Zadeh K. Battleground: Chronic Kidney Disorders Mineral and Bone Disease - Calcium Obsession, Vitamin D, and Binder Confusion. Clin J Am Soc Nephrol doi: 10.2215/CJN.03850907

MP261 RENAL REPLACEMENT THERAPY IN ACUTE HEPATIC FAILURE IN CHILDREN

Aurel Bizo, Cornel Aldea, Dan Delean, Cristina Muresan, Dana Olosutean, Andreea Munteanu. *Nefrologie Pediatrica, Spitalul Clinic de Urgenta Pentru Copii, Cluj-Napoca, Cluj, Romania*

Introduction and Aims: Toxic hepatic failure is associated with high mortality rate in pediatrics practice even under the adequate supportive treatment, including renal replacement therapy.
Mushroom intoxication, respectively with *Amanita Phalloides*, has the most important incidence for the geographical region where the study was performed.
Methods: Between 1997-2006 a number of 359 cases with mushroom intoxication were analysed. For 155 patients, diagnosis of hepatic failure was sustained on clinical basis and laboratory findings with a very high suspicion of *Amanita Phalloides* intoxication.
The supportive treatment was completed with one of the renal replacement therapy methods respectively hemoperfusion with active carbon, "plasma exchange", hepatic dialysis.
Selection criteria for one of above mentioned extrarenal purge methods depend on: Severe hepatic encephalopathy (GradeII-IV), Transaminase >3000U/I, blood coagulation changes, severely altered clinical status.
Results: From all suspected patients with *Amanita Phalloides* intoxication that has been treated combinely with hepatic supportive therapy and renal replacement therapy, a number of 51 (33%) died.
Conclusions: In our study group, unfavourabil prognostic factors were represented by major problems of blood coagulation, neurological disturbance, hepato-renal syndrom and cardio-vascular complications.

MP262 BENEFICIAL IMPACT OF LONGTERM WEEKLY (DE-NOVO) OZONIZATION ON MICROBIOLOGICAL PERMEATE WATER QUALITY IN AN OLDER PVC LOOP SYSTEM

Karl August Brensing[1], Peter Heidkamp[1], Peter Raab[1], Winfried Speuser[1], Alfred Nett[1], Eva Neugebauer[2], Anika Schielke[2], Miriam Moritz[2], Juergen Gebel[2], Martin Exner[2], Thomas Kistemann[2]. *[1]Dialysis Unit, Nephrology & Dialysis Center Bonn, Bonn, NRW, Germany; [2]Institute of Hygiene and Public Health, University of Bonn, Bonn, NRW, Germany*

Introduction and Aims: In hemodialysis (HD) patients optimal permeate water quality is crucial for good longterm outcome. However, frequent (weekly) disinfection procedures of water loops are limited by costs and chemical load. Otherwise, heat (>80°C) is not feasable for most currently installed water loops. Initiation of ozonization may overcome some caveats but longterm hygienic-microbiological efficiency data in established dialysis units are lacking.
Methods: Therefore, we studied after a three months baseline period for 9 months prospectively the effect of (de-novo) ozonization (once-weekly, dissolved ozon levels: 20-50 ppb for 1 h generated by an ozonizer test unit) in an 8-year old permeate loop system (standard PVC), which routinely fulfilled EU limits for colony forming units (=CFU < 100/ml, R2A agar, 7 days, 23°C). We analyzed twice monthly permeate water for endotoxin (sensitive limulus assay) and for CFU (water bacteria on R2A + mycobacteria on Middlebrook agars in 1 ml permeate and pseudomonas on Cetrimid + gram-neg. bacteria on MacConkey agars after membrane filtration of 100 ml permeate).
Results: Baseline period showed CFU of water bacteria (median: 16/ml, range: 0-330), mycobacteria (median: 0/ml, range: 0-28), pseudomonas (median: 0/100ml range: 0-432) and of gram-neg. bacteria (median: 0/100 ml, range: 0-406). After 3 months of ozonization all max. CFU results decreased (water bacteria: median: 17/ml, range: 0-79), mycobacteria (median: 0/ml, range: 0), pseudomonas (median: 1/100ml, range: 0-3) and gram-neg. bacteria (median: 0/100 ml, range: 0-1). After 9 months water bacteria remained similar (median: 19/ml, range: 2-77) but CFU levels for mycobacteria, pseudomonas and gram-neg. bacteria were constantly reduced to zero. In parallel, endotoxin levels decreased significantly from baseline values (median: 0.026 EU/ml, range: 0.012-0.31) to lower levels after 9 months (median: 0.019 EU/ml, range: 0.008-0.026; p<0.02).
Conclusions: 1. Our data show that (de-novo) ozonization (low-dose, weekly) reduces peak water bacteria by about 75% and eliminate potential human pathogens to zero even in an older PVC loop system. 2. Ozonization turned out to be safe and reliable after adequately adapted hydraulic and control systems. 3. Regular ozonization appears as new and cost-effective option for installed permeate water loops not suitable for heat approachs.

MP263 IMPROVEMENT OF LV SYSTOLIC FUNCTION BY COOLING OF DIALYSATE

Pratik Das. *Nephrology, B. P. Poddar Hospital, Kolkata, West Bengal, India*

Introduction and Aims: To evaluate effect of dialysate cooling on LV

systolic function in maintenance haemodialysis (MHD) patients with left ventricular systolic dysfunction.
Methods: 30 patients of MHD (3 per week) with LV ejection fraction < 50% on 2D echocardiography were randomly assigned in 2 groups. Both groups had comparable age, sex ratio,body weight, BP, Hb%, PCV,Ca, Ph,iPTH, serum iron, TIBC, ferritin and mean dose of ACE inhibitor, ARB, EPO. All parameters were repeated at 8,16 and 24 weeks. Group I received dialysis with dialysate temperature of 36 c and Group II with dialysate temperature of 37 c. Base line echo was done to all patients and was repeated at 8, 16 and 24 weeks. Patients with regional wall motion abnormality, h/o MI, angioplasty, CABG, CAG proved coronary artery disease, h/o typical anginal pain with ECG changes of IHD were excluded from the study. None of our patient were on nitrates.
Results: Base line echo in Group I showed LVEF (48.66±3.16)% and Group II (48.5±4.22)%. The same value at 8 weeks were (54.28±3.1)% in Group I and (50.8±2.8)% in Group II (NS). At 16 weeks and 24 weeks, LVEF were (59.6±2.6)% and (62.6±1.86)% respetively in Group I compared to (52.5±2.87)% and (52.9±3.8)% in Group II patients ($p<0.05$). One (1) patient died in Group I, none of the patient complained thermal symptoms. Hypotensive episodes are also significantly lower in Group I patients.
Conclusions: LV systolic function improves significantly on dialysis with cooling of dialysate in patients with global LV systolic dysfunction not due to coronary artery disease. It can be utilized as safely as a method of improving cardiac functions in CKD patients on dialysis.

MP264 START HEMODIALYSIS WITH ONCE-WEEKLY TREATMENT: QUALITY OF LIFE AND RESIDUAL RENAL FUNCTION

Carmelo Libetta, Pasquale Esposito, Vincenzo Sepe, Laura Cosmai, Valentina Portalupi, Michele Canevari, Elisa Margiotta, Antonio Dal Canton. *Nephrology, Dialysis and Transplantation, University and Fondazione IRCCS Policlinico S. Matteo, Pavia, Italy*

Introduction and Aims: The role of residual renal function (RRF) is well known in the peritoneal dialysis population as studies have clearly demonstrated a survival benefit with preservation of RRF. However, there are data suggesting that RRF is also important in hemodialysis (HD) patients. Diuretics appear to have a role in maximizing urine output and minimizing the need for aggressive ultrafiltration but did not influence the decline of RRF. Hemodialysis treatment is not easy to accept for patients with end-stage chronic renal failure, and could significantly affect their quality of life. Therefore in patients that start HD treatment we evaluated the clinical implication, RRF and quality of life of once-weekly hemodialysis (OWD).
Methods: 17 stable patients on regular dialysis treatment for at least 10 months were studied. Nine patients (age 69.1±9.7 yrs) were on standard bicarbonate dialysis (SHD), and 8 patients (age 67.3±6.4 yrs) were on once-weekly dialysis. The OWD treatment consisted of a 4-hour, high efficiency, euvolemic HD session per week. Blood and urine were collected just before the dialysis session at basal (BAS) and monthly of HD treatment. Serum levels of C-reactive protein (CRP), albumin and body mass index (BMI) were measured. RRF was assessed by average renal urea and creatinine clearances. The health related quality of life (HRQOL) of dialysis patients was evaluated every 3 months after the start of chronic dialysis treatment. HRQOL was measured using the Kidney Disease Quality of life questionnaire (KDQOL). The number of hospitalizations was also recorded.
Results: At beginning of observation there were not significantly differences in age, albumin, CRP and BMI between OWD and SHD. RRF In OWD group declined significantly after 6 months (BAS: 10.32±2.69, 6 months: 7.09±2.21 ml/min, $p<0.05$), whereas in SHD group 7 patients were anuric already after one month. From the KDQOL results scores significantly lower in OWD patients compared with SHD group both at six that at nine months ($p<0.05$). The number of hospitalizations was significantly lower in OWD when compared to SHD ($p<0.05$) during the first year of treatment. Albumin, CRP serum levels and BMI showed no significantly changes. Four patients of OWD group after 10 months were shifted to SHD.
Conclusions: In conclusion start HD with once-weekly treatment significantly better quality of life, reduces hospitalization, allows an easier acceptance of dialysis treatment and lenghten the presevation of the RRF.

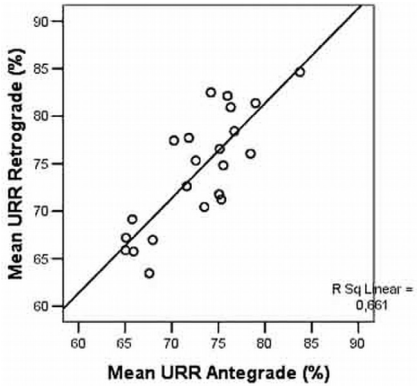
MP265 DOES THE DIRECTION ARTERIAL NEEDLE IN AV FISTULA CANNULATION AFFECT DIALYSIS ADEQUACY?

Sehmus Ozmen[1], Ali Kemal Kadiroglu[1], Cihan Akgul Ozmen[2], Ramazan Danis[1], Dede Sit[1], Davut Akin[1], Mehmet Emin Yilmaz[1].
[1]*Nephrology, Dicle University School of Medicine, Diyarbakir, Turkey;*
[2]*Radiology, Dicle University School of Medicine, Diyarbakir, Turkey*

Introduction and Aims: Dialysis adequacy is a challenge for nephrologists. The association between mortality and hemodialysis (HD) adequacy is well known. Many factors contribute to HD adequacy. However, there is no data investigating the role of direction of arterial needle placement in cannulation of arterivenous fistula (AVF). A very little difference in outcomes dependent upon direction of the cannulated needle was reported as a personal experience. Arterial needle placement can be in antegrade (up or in the direction of the blood flow) or retrograde (down or against the direction of the blood flow). Urea reduction rate (URR) is an acceptable way of measuring dialysis adequacy. We compared mean URR of HD patients when dialyzed via antegrade or retrograde arterial needle cannulation.
Methods: We enrolled 22 adults on maintenance hemodialysis for more than 6 months. They had no finding of AVF dysfunction on physical examination of AVF. All patients received conventional hemodialysis via a functioning AVF. The length of each dialysis was 5 hours and blood flow was 300 mL/min. Pre-dialysis and post-dialysis blood samples were obtained at the patient's midweek HD treatment 4 times a month for each direction. Arterial needle was placed in retrograde direction for the first month and converted to antegrade in the second month. The venous needle was always in the same direction as the blood flow. URR was calculated according the formula URR = 100 × (1 – postdialysis Urea/predialysis Urea). Doppler US of AVF was performed in all subjects. Mean of URR was calculated for each direction of cannulation. Results of antegrade and retrograde directions were compared by Wilcoxon Signed Ranks Test. $p<0.05$ was accepted to be significant.
Results: Mean age of patients was 36.2±12.4 years and mean hemoglobin was 10.9±0.9 g/dL. The urea and URR values are expressed in table1and Figure 1. All patients had an AVF blood flow above 600 ml/min on Doppler US. No problem of cannulation was observed during study period for both directions.

Serum Ure and URR of opposite arterial cannulation

	Retrograde Cannulation	Antegrade Cannulation	p
Pre-HD Urea (mg/dL)	141.8±24.2	154.4±37.0	0.101
Post-HD Urea (mg/dL)	36.7±11.0	40.6±10.1	0.108
URR (%)	74±6	73±5	0.123

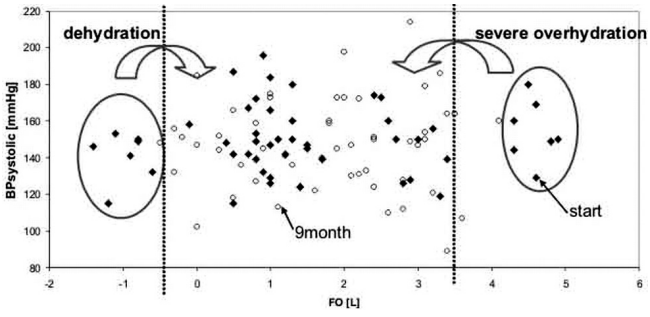


Conclusions: Although both directions of arterial needle placement are recommended by guidelines, no study addressing the effects of direction arterial needle on dialysis adequacy is present. Probably, ours is the first study investigating the issue. There is no difference between arterial needle directions regarding URR. Both antegrade and retrograde arterial needle placement may be preferred according to center experience without concern of HD adequacy.

MP266 OPTIMAL FLUID STATUS ASSESSED WITH BIOIMPEDANCE SPECTROSCOPY REDUCES IMES AND HOSPITALISATION IN HEMODIALYSIS PATIENTS

Machek Petr[1], Jirka Tomas[1], Moissl Ulrich[2], Wabel Peter[2], Chamney Paul[2]. [1]*Fresenius Medical Care Czech, Prag, Czech Republic;* [2]*Fresenius Medical Care D GmbH, Bad Homburg, Germany*

Introduction and Aims: The assessment of fluid status in patients on haemodialysis is one of the basic prerequisites for successful dialysis treatment. Long lasting fluid overload (FO) and high blood pressure (BP) in haemodialysis patients contribute significantly to the development of left ventricular hypertrophy (LVH), diastolic dysfunction and gradual heart failure, increasing hospitalization time. The other extreme, dehydration (as compared to a matched healthy subject), increases the risk of hypotensive events during dialysis. It was the aim of this study to firstly assess whether extreme fluid status can be identified and corrected, and secondly whether this reduction has an effect on hospitalisation and the number of morbid events.
Methods: To assess the degree of FO we studied 60 HD patients with the Body Composition Monitor (BCM, Fresenius Medical Care) over an average time of nine month. The patients were measured before the dialysis treatment and FO was provided by the BCM in litres (zero litres indicating normal hydration). Measurements were performed at least once a month, more frequent measurements were initiated if the dry weight had to be adjusted.Dry weight was gradually reduced in "severely overhydrated" patients who presented more than 3.5 L of FO. On the contrary the dry weight was gradually increased in patients with "significant dehydration" (FO pre dialysis less than -0.5 litres).
Results: 30% of all patients were either severely over- or dehydrated at initiation of the study. At the end of the study 50% of these patients had been returned to normal hydration status. The FO-distribution of all patients was reduced by more than 1 L (2 SD). In the interval of the intervention period no emergency dialysis because of pulmonary edema had to be performed, no heart attacks were observed and the number of intra-dialytic complications such as hypotension or spasms were reduced.

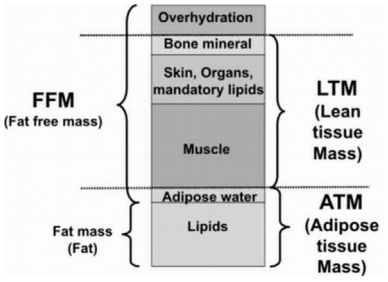


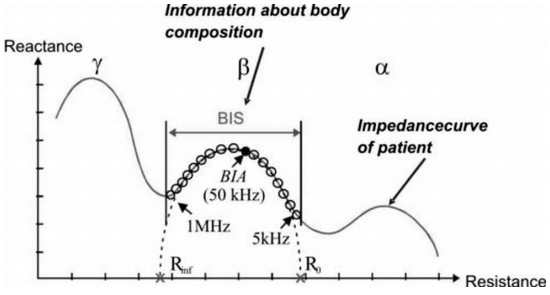
Conclusions: It is too early to assess the influence on the overall mortality after one year of monitoring. In our study we managed to prove that achieving a normal fluid status, avoiding severe over- or dehydration helps to improve the treatment quality with less IMEs and emergency dialysis. The target provided by the BCM is a invaluable help in the assessment of the fluid status of HD patients.
Disclosure: Authors are employees of Fresenius Medical Care.

MP267 BIOIMPEDANCE SPECTROSCOPY AND BIOIMPEDANCE ANALYSIS FOR DRY WEIGHT ASSESSMENT IN DIALYSIS PATIENTS: COMPARISON OF THE APPROACHE

Chamney Paul, Wiemann Katrin, Moissl Ulrich, Wabel Peter. *R&D IMM, Fresenius Medical Card D GmbH, Bad Homburg, Germany*

Introduction and Aims: The determination of the patient's dry weight as well as the assessment of his nutritional status are two issues nephrologists encounter during routine dialysis practise. Bioimpedance has been proposed as suitable method for addressing these aspects. There are two major approaches on the market, Bioimpedance analysis (BIA) and Bioimpednce spectroscopy (BIS). BIA involves the use of a single frequency (SF) measurement at 50 kHz while BIS performs measurements at multiple frequencies (MF). Furthermore there are differences in the methods used to calculate clinically relevant parameters such as total body water (TBW), fluid overload (FO) and Fat Free Mass (FFM). The purpose of the current analysis was to compare the performance of BIA and BIS based approaches.
Methods: We measured 34 patients with bioimpedance at single and multiple frequencies in whom change in post dialysis weight (PW) from baseline to follow-up exceeded 2.5 kg. Our hypothesis was that the change in PW was the consequence of a change in FO. Therefore only changes in PW occurring within one month were considered in order to minimise the effects of body composition changes. Using SF information (BIA), FFM was calculated by the Lukaski equation (Appl Physio 60, 1986) and TBW(SF) via Kushner (Am J Clin Nutr, 41, 1985). TBW was calculated from MF data using the equations of Moissl et al (Physiol Meas 27, 2006). A body composition model (Chamney et al. AJCN 85 2007) enabled lean tissue mass (LTM) and FO to be determined from MF data in addition. The advantage of LTM is that it is not influenced by changes in FO. Mean changes in these parameters from baseline to follow-up were calculated.
Results: ΔPW was found to be 3.6 kg $\pm$1.0. Via the BIS based approaches this ΔPW was reflected by ΔTBW(MF) of 2.6$\pm$1.2 L and ΔFO of 2.2$\pm$1.2 L. LTM remained stable 1.1$\pm$0.8 kg, (NS). By contrast the BIA measurements yielded ΔTBW(SF) of 4.7$\pm$2.5 L. Similarly a dramatic ΔFFM was observed (5.6$\pm$3.2 L).





Conclusions: Our results show that LTM via BIS is a reliable parameter for investigation of dialysis patients despite changes in post dialysis weight brought about by changes in fluid overload. In our study TBW calculated from SF measurements (BIA) exceeded the changes in weight and therefore appear implausible. Although approx half of the apparent changes in FFM (via BIA) might be attributed to fluid alone, it does not explain the full extent of the change. We suggest that FFM from BIA analysis can be misleading in dialysis patients.
Disclosure: Authors are employed by Fresenius Medical Care.

MP268 EFFECT OF SOLUTION VOLUME ON THERAPY EFFICACY FOR SHORT DAILY AND NOCTURNAL HEMODIALYSIS

Alp Akonur, Bradley J. Roynon, Shincy J. Maliekkal, Angelito Bernardo, Thomas D. Kelly, Ying-Cheng Lo. *Renal Division, Baxter Healthcare Corporation, McGaw Park, IL, USA*

Introduction and Aims: Recently, home hemodialysis (HHD) has attracted renewed interest as it may provide patients with improved clinical outcomes. As a result of this potential, new therapies such as short daily (SDHD) and nocturnal (NHD) hemodialysis have been promoted as alternatives to conventional in-center, three-times weekly therapy regimen. In this study, we investigated the effect of solution volume, therapy frequency, and

therapy duration on key clinical parameters for small and middle molecule clearances.

Methods: A two-compartment kinetic model (Ward et al, KI 2006, 69: 1431-1437) was used to simulate a variety of regimens for 22 L and 50 L solution volumes. Therapy frequencies from 3 to 6 times per week and therapy durations from 2 to 8 hours were considered. Model parameters for urea and beta2-microglobulin were obtained from previous studies (Clark et al, J Am Soc Nephrol 1999, 10: 601-609). An average patient with 40 L total body water was considered. In-vitro dialyzer clearances were measured in open and closed-loop fashion for urea and beta2-microglobulin respectively using Xenium 150 dialyzers. Peristaltic pumps were used to generate a blood flow rate of 300 ml/min and dialysate flow rates ranging from 46 to 417 ml/min. Standardized Kt/V (std Kt/V) for urea and mean pre-treatment concentration (MPC) for beta2-microglobulin were calculated. The std Kt/V was calculated as (G*T)/(MPC*V) where G is the urea generation rate, T is the total therapy time, and V is the urea distribution volume.

Results: The table shows simulation results in the form of a therapy map for 22 L and 50 L. Clearly, there are regions of the map where adequate results may not be achieved. With respect to urea, minimally adequate dialysis that KDOQI guidelines require is std Kt/V > 2.0. It is evident from the map that such adequacy may be easier to obtain with 50 L than 22 L. Specifically, for 2-hour therapy, SDHD requires 5 to 6 times per week dialysis with 22 L while 4 times dialysis may be sufficient with 50 L. On the other hand, 6-hour NHD may require 4-5 times a week with 22 L while 3 times per week may be enough with 50 L. There are no set guidelines for beta2-microglobulin, however, a previous study showed improved chance of survival with mid-week pre-dialysis concentration less than 27.5 mg/L (Cheung et al, Am Soc Nephrol, 17: 546-555, 2006). It is evident from the map that such improvement in beta2-microglobulin levels may be achieved only if 6 to 8-hour NHD therapies are performed 5-6 times per week.

22 L		2.0 hr	3.0 hr	4.0 hr	5.0 hr	6.0 hr	8.0 hr
M/W/F	3X	1.2	1.2	1.3	1.2	1.3	1.3
		40.5	38.4	36.9	35.5	34.3	32.4
M/W/F/Su	4X	1.5	1.6	1.7	1.7	1.8	1.8
		37.9	35.1	33.0	31.2	29.7	27.3
Except Tu/Sat	5X	1.9	2.0	2.1	2.1	2.2	2.2
		35.5	32.3	30.0	28.0	26.4	23.8
Except Sat	6X	2.3	2.4	2.5	2.5	2.7	2.7
		33.5	30.1	27.7	25.6	23.9	21.3

50 L		2.0 hr	3.0 hr	4.0 hr	5.0 hr	6.0 hr	8.0 hr
M/W/F	3X	1.5	1.8	2.0	2.1	2.2	2.2
		40.1	38.0	36.3	35.0	33.9	31.8
M/W/F/Su	4X	2.0	2.4	2.7	2.8	2.9	3.0
		37.3	34.5	32.3	30.6	29.1	26.6
Except Tu/Sat	5X	2.5	3.0	3.3	3.6	3.7	3.8
		34.9	31.7	29.2	27.4	25.8	23.1
Except Sat	6X	2.9	3.6	4.0	4.3	4.5	4.6
		32.9	29.5	26.9	25.0	23.3	20.6

Conclusions: We conclude that: (1) solution volume plays a critical role in achieving adequate clearances, (2) large solution volumes may provide greater flexibility in prescribing dialysis schedule, and (3) simultaneous adjustment of frequency and duration may be necessary to achieve optimum clearances.

Peritoneal dialysis 2

MP269 LEVELS AND DETERMINANTS OF PRO-HEPCIDIN IN PERITONEAL DIALYSIS AND HEMODIALYSIS PATIENTS

Faruk Turgut[1], Mehmet Kanbay[1], Mustafa Altay[2], Ebru Uz[1], Nuket Bavbek[1], Cemile Koca[3], Sema Secilmis[2], Murat Duranay[2], Ali Akcay[1], Adrian Covic[4]. *[1]Department of Nephrology, Fatih University School of Medicine, Ankara, Turkey; [2]Department of Nephrology, Ankara Research and Training Hospital, Ankara, Turkey; [3]Department of Biochemistry, Fatih University, School of Medicine, Ankara, Turkey; [4]Department of Nephrology, C.I. Parhon University Hospital, Dialysis and Transplantation Center, Iasi, Romania*

Introduction and Aims: Anemia is a major clinical problem in patients receiving dialysis therapy. Iron metabolism is impaired in chronic kidney disease. Hepcidin functions as a key regulator of iron absorption in response to body iron stores.

The aim of this study is to evaluate pro-hepcidin and hsCRP, albumin, iron parameters, and hemoglobin levels in peritoneal dialysis (PD) and hemodialysis (HD) patients.

Methods: We studied 85 PD (mean age 43.7±14.2), 43 HD (mean age 45.3±15.7) patients and a control group comprised of 41 healthy volunteers (mean age 39.6±11.6). Demographic characteristics of all patients were recorded. Pro-hepcidin and hsCRP were studied using commercially available kits. Iron status was assessed by measuring serum iron, transferrin saturation, and ferritin.

Results: Healthy volunteers, HD and PD patients did not differ significantly regarding age and BMI. Other relevant parameters of all three groups are shown in Table 1. Pro-hepcidin levels were significantly higher in patients receiving dialysis therapy than controls (Figure 1). HD patients had higher pro-hepcidin levels than PD patients, but this difference was not significant statistically (393.4±157.3 vs 361.3±40.1, p=0.19). In PD patients, there was a weak positive correlation between pro-hepcidin and creatinine (R=0.232, p=0.033). There were no correlations between pro-hepcidin levels and hsCRP, and albumin, and hemoglobin level and iron parameters in PD and HD patients.

Table 1. Comparison of some laboratory parameters for all three groups

Parameters	HD patients	PD patients	Healthy volunteers
Hemoglobin (g/dl)	11.7 ± 2.2*	11.4±1.8*	13.9±1.4
Ferritin (ng/dl)	742±425* †	432±267*	58.1 ± 60.4
TSAT (%)	41.1±23.1*	44.3±37.4*	20.5±9.4
hsCRP (mg/L)	2.0±2.7	1.1±1.5*	2.5±2.0
Albumin (g/dl)	4.2±1.3 †	3.6±0.5*	4.4±0.2
Parathyroid hormone (pg/ml)	501.0±419.0*	363.8±304.8**	39.3±7.0
Calcium (mg/dl)	9.3±0.8	9.2±0.8	9.2±1.4
Phosphorus (mg/dl)	5.6±1.7*	5.1±1.7*	3.3±0.4

*p<0.001 vs control, **p<0.05 vs control, †p<0.01 vs PD patients.

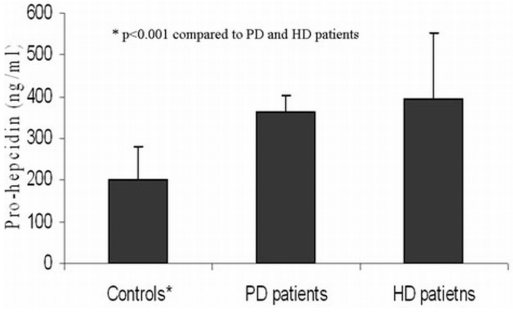


Figure 1. Srum pro-hepcidin levels.

Conclusions: Our results suggest that dialysis therapy is associated with elevated pro-hepcidin levels and not directly related to inflammation, malnutrition, indices of iron metabolism or hemoglobin levels. PD patients have relatively lower pro-hepcidin level than HD patients, but larger-scale studies are needed to determine a possible different impact of various dialytic modalities.

MP270 CLINICAL ROLE OF NT-pro BNP IN CAPD PATEINTS

Hyun Lee Kim, Jung Hoon Chung. *Internal Medicine, Chosun University College of Medicine, Gwangju, Republic of Korea*

Introduction and Aims: This study inquired the relationship between serum N-terminal pro-brain natriuretic peptide (NT-pro BNP) levels and left ventricular (LV) dysfunction and extracellular water (ECW%) in continuous ambulatory peritoneal dialysis (CAPD) patients.

Methods: We conducted a prospective study of 30 CAPD patients. Each patient was admitted to department of internal medicine, Chosun University Hospital between Febrary and Octorber, 2006. Echocardiography was performed using a HDI 5000 (Philips, USA), allowing M-mode, two-dimensional measurement. A multifrequency bioimpedance analyzer was used; ECW% was calculated as a percentage of total body water and was understood the index of volume load of CAPD patients.

Results: We conducted a prospective study of 30 CAPD patients: 19 males, 11 females: mean age 47±12 years. Underlying causes of renal failure are 14 with diabetes mellitus and 7 with hypertension and 9 with chronic glomerulonephritis. Mean serum NT-pro BNP level was 14236.56 (83-35000) pg/mL. LV mass index and LV ejection fraction (%) were 151.67±42.5g/m^2 and 57.48±12.9%. Mean Extracellular water (%) was 35.97±1.04%. Serum NT-pro BNP levels correlated positively with LV mass index (r=0.768, p=0.01), and Extracellular water (r=0.866, p=0.01) and negatively with LV ejection fraction (r=-0.808, p=0.01).
Conclusions: Serum NT-pro BNP levels significantly correlated with LV mass index, LV ejection fraction and extracellular water. Therefore, serum NT-pro BNP levels can be clinical predictive maker for LV hypertrophy, LV dysfunction and volume status in CAPD patients.

MP271 FREE WATER FRACTION IN PERITONEAL DIALYSIS PATIENTS WITH ULTRAFILTRATION FAILURE

Jacek Waniewski [1,2], Malgorzata Debowska [1], Bengt Lindholm [2]. [1] *Institute of Biocybernetics and Biomedical Engineering, Warsaw, Poland;* [2] *Karolinska Institutet, Department of Clinical Sciences, Technology and Intervention, Divisions of Baxter Novum and Renal Medicine, Stockholm, Sweden*

Introduction and Aims: Permanent ultrafiltration failure (UFF) is a common complication in long term PD patients with multifactorial etiology. Recently, theoretical and clinical studies have enabled the investigation of aquaporin function via free water transport, that is the part of transcapillary ultrafiltration that passes through water only permeable channels (aquaporins) and is therefore depleted from solutes, using detailed kinetics of fluid and sodium transport. The aim of this study was to provide more information about free water transport using a novel method via the estimation of sieving coefficient for sodium.
Methods: Aquaporin function was evaluated in 13 dwell studies performed in seven CAPD patients with UFF. In three patients, the peritoneal transport was studied also before the onset of UFF, and in three patients two studies were performed after the onset of UFF. Transcapillary ultrafiltration and fluid absorption rates K_E were assessed using radiolabelled albumin as a volume marker. Diffusive and convective transport rates of small solutes were estimated using the modified Babb – Randerson – Farrell model. Free water fraction, FWF, the fraction of fluid that passes through ultrasmall pores was estimated as FWF=1-S_{Na}, and free water transport, FWT, as FWT = (1 – S_{Na}) × CUF, where CUF is the cumulative transcapillary ultrafiltration and S_{Na} is sieving coefficient for sodium, according to Waniewski et al (2007).
Results: Five patients had increased diffusivity of small solutes, K_{BD}, one had increased fluid absorption K_E, and one both these complications. K_{BD} values for sodium were increased proportionally to K_{BD} for other small solutes except for two dwell studies. The initial decrease of sodium concentration in dialysis fluid (sodium dip) was pronounced in dwell studies before the onset of UFF, whereas in patients with UFF no sodium dip, or only a slight sodium dip, was observed. Transcapillary ultrafiltration at 60 min was decreased after the onset of UFF in five patients with high K_{BD}, but not in the patients with high K_E. FWF was reduced in four patients with high K_{BD} and in one patient with high values of both K_{BD} and K_E (FWF < 0.24), whereas it was normal in one patient with high K_{BD} and in one patient with high K_E (FWF > 0.33). FWT at 60 min was well correlated to FWF. In two patients total transcapillary ultrafiltration was normal in spite of low FWF and FWT at 60 min.
Conclusions: The high variability in UFF patterns, as found for the fluid transport parameters in this small group of patients, is in agreement with the previously reported values in a much larger patient population (Smit et al, 2004). Only one patient with high K_{BD} and one with high K_E had normal FWF, whereas in all other patients free water transport (reflecting impaired aquaporin function) was reduced during UFF.
Disclosure: Consultant for Baxter Healthcare Inc, IL.

MP272 INDIVIDUAL, DIFFUSIVE AND CONVECTIVE SMALL SOLUTE TRANSPORT PARAMETERS CHANGE WITH PERITONEAL DWELL TIME FOR HYPERTONIC GLUCOSE SOLUTION

Joanna Stachowska-Pietka [1], Jacek Waniewski [1,3], Edward Vonesh [2], Bengt Lindholm [3]. [1] *Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences, Warsaw, Poland;* [2] *Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA;* [3] *Divisions of Baxter Novum and Renal Medicine, Karolinska Institutet, Stockholm, Sweden*

Introduction and Aims: Diffusive mass transport parameters, K_{BD}, are typically increased during the initial time of a peritoneal dialysis exchange and this is thought to be due to vasodilatory effects of the dialysis fluid. The purpose of this study was to describe the individual variation caused by the vasodilation and to check whether convective solute transport and free water fraction (FWF) is also affected by this phenomenon.
Methods: Six hour dwell studies were performed in 35 CAPD patients using glucose 3.86% dialysis fluid with radiolabelled albumin (RISA) as a marker of dialysis fluid volume and peritoneal absorption rate. Solute transport parameters were estimated concomitantly as a function of dwell time with a stepwise procedure based on a membrane model. Diffusive mass transport coefficient, $K_{BD}(t)$, was evaluated for small solutes individually for each patient as a function of dwell time. The nonlinear mixed effect model was applied for fitting time-dependent curve to obtained K_{BD} values. The three-pore model was used for evaluation of A_0/dx from $K_{BD}(t)$ values of small solutes. Time-dependent sieving coefficient for sodium, $S_{Na}(t)$, was calculated using estimated values of $K_{BD}(t)$. FWF was estimated according to the three-pore model as FWF=1-$S_{Na}(t)$.
Results: Diffusive mass transport coefficients were found to be time-dependent, and described by an exponential decay function given by $K_{BD}(t) = K_{BDS}(1 + DK \times \exp(-k \times t))$. For urea, creatinine and glucose, respectively, we found that: the estimated steady state value of K_{BD}, K_{BDS}, was (mean±SE) 19.6±0.9, 9.4±0.7, and 9.3±0.4 mL/min; the initial increment of K_{BD} over the steady state value, DK, was 87±10% (range 23-217%), 98±14% (range 35-229%), and 124±14% (range 60-254%); and the decay time constant, k, which was not statistically different between patients, was equal 0.017, 0.021, and 0.024 min^{-1}. The average steady state value of time-dependent A_0/dx evaluated from $K_{BD}(t)$ for urea and creatinine according to the three-pore theory was 24165±3702 cm. Moreover, vasodilatory parameters (DK, k) did not depend on diffusive transport characteristics of small solutes (A_0/dx). The sodium sieving coefficient, S_{Na}, increased and FWF decreased during the initial 120 min of dwell time.
Conclusions: We conclude that diffusive mass transfer coefficient, sieving coefficient for small solutes as well as free water fraction, should be considered as time-dependent during the initial period of peritoneal exchanges with hypertonic glucose-based dialysis fluids. The initial increment of K_{BD}, DK, was highly variable between patients, whereas no such variability was found for the decay constant k. Furthermore, DK does not depend on the small solute transport status.
Disclosure: J. Stachowska-Pietka was supported by a grant from the Foundation for Polish Science. Bengt Lindholm is employed by Baxter.

MP273 ★ IS DIALYSATE SOLUBLE CD44 INVOLVED IN THE PATHOGENESIS OF ULTRAFILTRATION FAILURE IN PERITONEAL DIALYSIS PATIENTS?

Olga Stam, Anniek Vlijm, Dick Struijk, Raymond Krediet. *Nephrology, Academic Medical Center University of Amsterdam, Amsterdam, Netherlands*

Introduction and Aims: Chronic peritoneal dialysis (PD) may lead to morphological and functional changes of the peritoneal membrane. The most severe functional alteration is ultrafiltration failure (UFF), a condition in which PD patients are unable to remove excess fluid and waste products. Inflammatory processes are likely to be involved in the development of UFF. The soluble form of CD44 (sCD44; MW 78 kDa) - a family of type I transmembrane glycoproteins – shows an increased plasma-level in inflammatory processes. The objective of this study was to analyse whether sCD44 could be involved in the pathogenesis of UFF.
Methods: Serum and dialysate samples of 16 non-diabetic PD patients

obtained by a Standard peritoneal Permeability Analysis (SPA) were analysed. The PD patients were divided into 2 groups: PD patients without UFF (n=8) and PD patients with UFF (n=8). The duration of PD in the groups was not different (p=0.74). The diagnosis of UFF was based on netUFF < 400 ml/4 hrs with a 3.86% glucose solution. An ELISA was performed to determine the concentrations of sCD44 in serum and dialysate. Expected concentrations of sCD44 based on diffusion were calculated by using a transport line with diffusion rates of β-2-microglobulin (MW 12 kDa), albumin (MW 67 kDa), IgG (MW 146 kDa) and α-2-macroglobulin (MW 820 kDa). The expected sCD44 levels were subtracted from the actual measured sCD44 levels in order to determine local peritoneal production of sCD44. Differences between the two groups were analysed with an unpaired T-test. rGFR was determined as serum Cystatin C.
Results: Serum (S) and dialysate (D) values of sCD44 expressed as means ± standard deviation are shown in Table 1.

Table 1

Groups	S [sCD44] (mg/L)	D [sCD44] (mg/L)	D expected [sCD44] (mg/L)	Local production [sCD44] (mg/L)
No UFF	1.51 (0.34)	0.16 (0.06)*	0.01 (0.01)*	0.14 (0.05)*
UFF	1.87 (0.41)	0.23 (0.06)	0.02 (0.01)	0.21 (0.06)

*p<0.05.

Dialysate concentrations and local production of sCD44 were significantly higher in PD patients with UFF. No correlation was found between rGFR and serum sCD44 concentrations.
Conclusions: These results imply that almost all sCD44 (~90%) in dialysate is locally produced by peritoneal cells. The significantly higher dialysate concentrations and local production of sCD44 in PD patients with UFF suggest that sCD44 is involved in the pathogenesis of UFF. This finding requires confirmation in larger patient groups.

MP274 CLINICAL EVALUATION OF POLYMERASE CHAIN REACTION FOR RAPID DIAGNOSIS OF TUBERCULOSIS PERITONITIS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS

Stanley Lo[1], Siu Kim Chan[1], Chi Kwan Wong[1], Ching Kit Chan[1], Vincent Chow[1], Rodney Lee[2], Wing Cheung Yam[3], Ka Leung Mo[1], Kin Shing Wong[1]. *[1]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China; [2]Department of Microbiology, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China; [3]Department of Microbiology, The University of Hong Kong, Hong Kong SAR, China*

Introduction and Aims: Tuberculosis is prevalent in Hong Kong and mycobacterium tuberculosis (MTB) is not an uncommon etiological agent in CAPD patients with peritonitis. While acid-fast bacilli (AFB) culture results take 4-6 weeks and AFB smear is not sensitive for the diagnosis, polymerase chain reaction (PCR) is an emerging test for rapid diagnosis for TB peritonitis. Inhibitors of primers of PCR were believed to cause poor performance of MTB PCR in body fluid. However, reports for performance of PCR in diagnosing TB peritonitis are scanty.
Methods: The detailed results of PCR, AFB smear and culture for peritoneal dialysis fluid performed between 2005 and 2006 were obtained from the computer system of a cluster hospital tuberculosis laboratory. All the PCR were performed by a locally designed single-tube biotinylated nested PCR with microwell hybridization assay (bPCR-ELISA). Every PCR was confirmed by re-testing a specimen from the subsequent AFB culture.
Results: Of the 154 patients who were screened for AFB smear and culture between 2005 and 2006, 40 patients had the PDF tested for MTB PCR. AFB smears were negative in these 40 patients. AFB cultures were positive in 9 of the 40 patients and negative in 31 of these 40 patients. PCR was positive in 6 of the 9 culture-positive patients and it was negative in 31 of the 31 culture-negative patients. Taking AFB culture as gold standard of diagnosing tuberculous peritonitis, the sensitivity of MTB PCR was 67% (6/9), and the specificity of PCRMTB was 100% (31/31). One specimen that was tested to be negative by PCR MTB, turn out to be a case of atypical tuberculosis.

MTB PCR vs AFB culture

	PCR +ve	PCR -ve	
AFB culture +ve	6	3	9
AFB culture -ve	0	31	31

Conclusions: The MTB PCR has higher sensitivity and specificity in diagnosing TB peritonitis. While AFB smear is a poor test for early diagnosis, MTB PCR is a promising test for early diagnosis. As the PCR test is expensive and labor-intensive, it should be limited to cases with high clinical suspicion for TB peritonitis.

MP275 FREE CHOICE OF TECHNIQUE AND COMORBIDITY PREDICT EARLY MORTALITY IN PERITONEAL DIALYSIS

Jose Portoles[1], Gloria del Peso[2], M. Auxiliadora Bajo[2], M. Jose Fernandez-Reyes[3], GCDP[4]. *[1]Nephrology, Fundación Hospital Alcorcón, Madrid, Spain; [2]Nephrology, Hospital Universitario La Paz, Madrid, Spain; [3]Nephrology, Hospital General de Segovia, Segovia, Spain; [4]Nephrology, Grupo Centro de Diálisis Peritoneal, Madrid, Spain*

Introduction and Aims: Recent studies suggest that the survival rate of patients with chronic kidney disease who begin peritoneal dialysis (PD) is the same as or better than those that begin hemodialysis during the first two years of follow-up. In general, almost all studies indicate that age and the presence of diabetes at the beginning of treatment are the main factors associated with mortality in PD, with more controversy surrounding other factors such as peritoneal function or the dialysis dose. Our objective was to study the prognostic factors for mortalirty and admission in patients on PD.
Methods: A cohort of incident patients undergoing PD (2003-2006) in a reference area of 8.8 million people. Biannual data on individual characteristics, clinical and analytical progress, treatment and events are included.
Results: We included 489 patients (53.58 years, 61.6% male) with 3-year follow-up. They presented at inclussion: Charlson Index (ChI): 5.25; previous cardiovascular (CV) event: 23.7%; diabetes (DM): 19.1%; and hypertension (HT): 89.9%.
Annual hospitalization rate was 0.6 patients/year-at-risk. The variables that predict admission are (relative risk: RR): ChI (1.14 per point), DM (1.71), previous CV event (1.90). Anemia maintains significance when corrected for ChI: hemoglobin (Hb): 0.79 per 1g/dl Hb; and ChI: 1.15 per point.
Annual mortality rate was 5.4%. Those that die are older (67.47 vs. 52.78 years) with a higher ChI (8.7 vs. 5.0), lower initial Hb (11.5 vs. 12.2g/dL), with higher admissions and peritonitis annual rate, had more previous CV events (50.0% vs. 22.1%) and a higher DM prevalence (38.5% vs. 17.9%). The survival analysis identified prognostic factors (RR): ChI (1.51 per point); CV event (2.85); DM (2.52); age (1.06 per year); and obligatory referral to PD (6.54). The effect of CV events and DM persists after correction for age and that of choice of technique after correcting for ChI and/or age.
Conclusions: The ChI is useful for risk-estimation in PD-patients. Previous CV, DM and age are the most relevant risk factors. Control of anemia has prognostic value in admissions. Obligatory referral to PD is associated with higher mortality. The prognosis in PD depends on predialysis patient management.

MP276 INDUCED APOPTOSIS OF CULTURED CARDIOMYOCYTES BY PERITONITIS EFFLUENT FROM CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS

Ching-Yuang Lin. *Children's Medical Center, China Medical University Hospital, Taichung, Taiwan; Institute of Clinical Medical Science, China Medical University, Taichung, Taiwan*

Introduction and Aims: Cardiac disease is still the leading cause of death among patients receiving long-term continuous ambulatory peritoneal dialysis (CAPD) especially in patients with frequent peritonitis. Peritonitis toxins can be absorbed to the systemic circulation.
Purpose of this study: First, to test whether peritonitis effluent can induce apoptosis of cardiomyocytes in vitro. Second, to make certain that cultured H9c2 cell apoptosis via GATA-4 down regulation.
Methods: Fourteen peritonitis dialysate effluent patients' samples took at onset of peritonitis. Doxorubicin (Dox) used as positive control. Flow

cytometry has used for cell cycle and apoptotic stain. GATA-4 level was measured by real time RTPCR.
Results: The results showed that a significantly decreased cell proliferation of H9c2 treated with peritonitis effluent with dose response manner when compared with untreated group (O.D 0.354±0.2 vs. 1.951±0.4, $P<0.05$). The effect of peritonitis effluent on the cell cycle progression was study by flow cytometric analysis. When growth-arrested H9c2 cells were treated with peritonitis effluent, the cells remained in G2/M phase (27±5% vs. 10%±4%, $P<0.05$). Annexin V analysis showed peritonitis effluent can induce an apoptosis response (45% vs. 1%, $P<0.05$). Quantitative RT-PCR showed peritonitis effluent can induce GATA-4 depletion in H9c2 cells.
Conclusions: These results indicate that peritonitis effluent is a cardiotoxin & apoptosis-inducer which through GATA-4 depletion.

MP277 A CROSS-SECTIONAL STUDY WHICH MODALITY IS BETTER FOR PRESERVING ARTERIAL STIFFNESS OF UREMIC PATIENTS BETWEEN ON PERITONEAL DIALYSIS (PD) AND ON HEMODIALYSIS (HD)

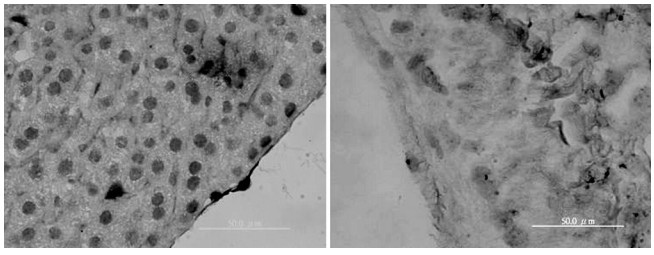
Hiroshi Kimura, Kentaro Nakai, Shuhei Miura, Atsuhiro Maeda, Kazuhito Takeda. *Nephrology, Aso-Iizuka Hospital, Iizuka, Fukuoka, Japan*

Introduction and Aims: Several articles have been reported that pulse wave velocity (PWV) is a predictor of mortality in patients with end-stage renal failure (ESRF). And Takeda et al. indicated that the possibility of long-term PD, especially more than 5 years' duration, was disadvantageous for preserving cardiac function as comparted with HD. But we have yet not known how about the duration within 5years on PD was disadvantageous, too. In order to conduct the validation, we made a comparison between arterial stiffness of patients on PD and on HD within 5 years' duration with some markers and we analized the number of effecting factors.
Methods: We investigated patients with ESRF on PD (n=20) and on HD (n=20) at the Kidney Center of Aso-Iizuka hospital. The patients age was 59.0±10.9 in the former and 60.6±9.2 years old in the latter. Womans' ratio of the groups was 35 and 50%. The duration of dialysis was 27.5±16.1 and 38.3±18.4 months. In each group 18 patients had glomerulonephritis, 1 had polycystic kidney disease and 1 had hypertensive nephrosclerosis. Arterial stiffness was estimated by Brachial-ankle pulse wave velocity (baPWV) and cardio-ankle vascular index (CAVI). BaPWV was measured with form PWV/ABI™(OMRON COLIN Co., Ltd.) and CAVI with VaSera™ (Fukuda Denshi Co., Ltd.). We tested the clinical data by multi linear regression analysis with the stastical soft ware, JMP6™(SAS Institute), business unit of SAS.
Results: Systolic blood pressure was lower in the patients on PD as compared with on HD (117±16 and 133±12 mmHg, $P<0.05$), but there was no significant difference in baPWV and CAVI between the two groups (1515±256 and 1781±560 cm/sec, 7.9±1.1 and 8.9±1.5, n.p.). Left ventricular mass index was no difference between PD and HD patients (108±21 and 115±28, n.p.), but cardiac-thoracic ratio, which was measured with X-ray film was lower in PD patients (44.8±3.0 and 48.6±4.5%, $P<0.05$).
Conclusions: Under well-controlled blood pressure and volume status, PD would not be disadvantageous for preserving arterial stiffness within 5 years' duration.

MP278 BONE MARROW DERIVED CELLS AND MESOTHELIAL REMODELING

Kuo-Su Chen[1], Chao-Hung Wang[1], Jim-Ray Chen[2], Tzung-Hai Yen[3], Ming-Jui Huang[1], Ching-Yuang Lin[4]. *[1]Department of Internal Medicine, Chang Gung Memorial Hospital, Keelung, Taiwan, Taiwan; [2]Department of Pathology, Chang Gung Memorial Hospital, Keelung, Taiwan, Taiwan; [3]Division of Nephrology, Chang Gung Memorial Hospital, Linko, Taiwan, Taiwan; [4]Children's Medical Center, China Medical University and Hospital, Taichung, Taiwan, Taiwan*

Introduction and Aims: Several hypotheses have been proposed regarding the cell origins of new mesothelium. Circulating precursors from the bone marrow are one of the proposed sources, however, no convincing data can support this postulation. The aim of this study is to examine whether bone marrow derived cells can contribute to the turnover of mesothelial cells.
Methods: Following total body irradiation with lethal doses, female wild-type mice (FVB/N) were injected with 5 X 10^6 whole bone marrow cells obtained from male eGFP transgenic mice through the tail vein. Recipient mice were euthanized at 2 week, 4 weeks, 6 weeks and 6 months after bone marrow transplantation respectively. Peritoneal tissues obtained from anterior abdominal walls, liver and small intestine were subject to immunohistochemical staining (IHC) for identification of eGFP protein and chromogenic in situ hybridization (CISH) for y-chromosome detection. Combined y-chromosome CISH and pan-cytokeratin immunostaining were performed to confirm the origin and expression of mesothelial phenotypes by donor marrow cells.
Results: eGFP protein-positive cells could be identified within the mesothelial layers of anterior abdominal walls, small intestine, mesentery and liver (Figure 1). However, the amount of positive cells was scanty, accounting for less than 1% of totally counted mesothelial cells in recipients either 2 wks, 4 wks, 6 wks or 6 months post-transplantation. The presence of donor marrow cells within mesothelium was again confirmed by the detection of y-chromosome marker in cells within mesothelium (Figure 2). Combined y-chromosome CISH and pan-cytokeratin immunostaining demonstrated that donor marrow cells incorporated into the mesothelial layer and expressed epithelial phenotype such as cytokeratin.



Conclusions: Bone marrow derived cells are possibly an alternative source of mesothelial progenitors, but its role in the process of mesothelial turnover is very minor. However, the exact role of bone marrow cells in the mesothelial remodeling require further studies using different models of acute peritoneal injuries.

MP279 DOES DURATION OF PRE-DIALYSIS RENAL SURVIVAL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AFFECT LONG-TERM OUTCOMES AFTER PERITONEAL DIALYSIS?

Tzung-Hai Yen, Chih-Chia Liang, Ja-Liang Lin, Chiz-Tzung Chang, Cheng-Chieh Hung, Chih-Wei Yang. *Department of Nephrology, Chang Gung Memorial Hospital, Taipei, Taiwan*

Introduction and Aims: To investigate whether the duration of pre-dialysis renal survival in patients with systemic lupus erythematosus (SLE) could affect their long-term outcomes after peritoneal dialysis (PD).
Methods: Out of the 35 patients with lupus nephritis, undergoing maintenance PD at Chang Gung Memorial Hospital, two distinct populations were identified. Ten patients suffered lupus nephritis and reached uremia in 3 years (short renal survival or renal survival < 3 years), whereas the other 25 patients reached uremia in more than 3 years (long renal survival or renal survival > 3 years). Data were analyzed with SPSS 11 for Mac OSX.
Results: In terms of demographics, the two groups did not different in age, sex, serum biochemistry, hematology, type of PD system used or duration of PD ($P>0.05$). Furthermore, there was no difference in nutritional status, inflammation status (high sensitivity C-reactive protein), adequacy of dialysis (Kt/V), volume status (cardiothoracic ration) or residual renal function ($P>0.05$). In addition, there was no difference in mortality (patient survival) or morbidity (technical survival and PD-related complications) (Logrank test, $P>0.05$). Before PD, patients with short renal survival had stronger lupus activity (C3 and C4) and receiving higher immunosuppressive medications than patients with long renal survival ($P<0.05$). However, the lupus activity was low and there was no difference in lupus activity or use of immunosuppressive medications between the two groups after PD ($P>0.05$).
Conclusions: Our data shows that the duration of pre-dialysis renal survival in patients with SLE did not significantly affect their long-term outcomes after PD. The burnout of lupus activity following PD might explain this finding.

MP280 CHANGE OF AQUAPORIN-1 EXPRESSION IN EPITHELIAL-TO-MESENCHYMAL TRANSITION OF PERITONEAL MESOTHELIAL CELLS AND IN ANIMAL PERITONEAL DIALYSIS MODEL

Sun-Hee Park, Hye Myung Ryu, Eun-Joo Oh, Soon-Youn Choi, Ji-Hyung Cho, In-Kyong Hur, Eun-Young Lee, Ji-Young Choi, Chan-Duck Kim, Yong-Lim Kim. *Nephrology and Internal Medicine, Kyungpook National University School of Medicine, Daegu, Republic of Korea*

Introduction and Aims: Aquaporin-1 (AQP-1) is a major water channel in peritoneum. Peritoneal fibrosis in PD is related to epithelial-to-mesenchymal transition (EMT) of peritoneal mesothelial cells. In this study, we explored the expression of AQP-1 in TGF-β1-induced EMT of peritoneal mesothelial cells and in animal PD model.
Methods: HPMCs were treated with TGF-β1 (3, 5ng/mL) for 48 h to induce EMT. The EMT process was monitored by the morphologic changes and the expression of α-SMA and E-cadherin. The expression of AQP-1 was evaluated by real time PCR and immunoblot analysis. For animal PD, male Sprague-Dawley (SD) rats were divided into 3 groups; Group NC, without catheter and not dialyzed (n=7); group CC, with catheter and not dialyzed (n=12); group D, with catheter and dialyzed with 4.25% glucose solution (Dianeal®, Baxter Healthcare Ltd, Singapore, n=12). Peritoneal transport rate was assessed at baseline and 8 week. Expression of α-SMA, E-cadherin and AQP-1 were assessed.
Results: After treatment with TGF-β1, HPMCs were changed to fibroblastoid cells and the expression of α-SMA was increased, whereas the expression of E-cadherin was decreased. AQP-1 mRNA significantly decreased in TGF-β1-treated HPMC compared to control. In animal PD, drain volume and D/D0 glucose at 8 week was significantly decreased in group D compared to group NC. D/P sodium in group D was significantly increased compared to group NC. The expression of α-SMA was increased and E-cadherin was decreased in group D compared to group NC. The expression of AQP-1 in group D was significantly decreased compared to group NC.
Conclusions: These results show that expression of AQP-1 was decreased in TGF-β1-induced EMT of peritoneal mesothelial cells and in animal PD model. It suggests that the change of AQP-1 along with increased solute transport characteristics, is related to the decreased ultrafiltration volume during PD.

MP281 THE EFFECTS OF L-PSICOSE ON THE PRODUCTION OF REACTIVE OXYGEN SPECIES AND MATRIX EXPANSION STIMULATED IN RESPONSE TO HIGH-GLUCOSE IN CULTURED RAT PERITONEAL MESOTHELIAL CELLS

Yoshiko Fujita, Hideyasu Kiyomoto, Hirofumi Hitomi, Keisuke Matsubara, Kumiko Moriwaki, Genei Ihara, Kumiko Kaifu, Chihiro Kurozumi, Tadashi Sofue, Yoko Nishijima, Masakazu Kohno. *Department of Cardiorenal and Cerebrovascular Medicine, Faculty of Medicine, Kagawa Univercity, Kita-gun, Miki-cho, Ikenobe, Kagawa, Japan*

Introduction and Aims: Peritoneal mesothelial cells (PMCs) are continuously exposed to high-glucose dialysate in peritoneal dialysis (PD). Although high concentration of glucose in dialysate is necessary to remove excess fluid, long exposure of non-physiological condition may deteriorate peritoneal membrane leading to quit PD therapy. Rare sugar is monosaccharide which seldom exists in nature, and more than 50 species of rare sugar have been discovered. It has been recently reported that some of them have protective effects for the tissue damages in several injury. Therefore, we investigated the effects of L-psicose, one of rare sugar, on PMCs injury.
Methods: Primary PMCs were collected from SD rat, and grew in M199 medium with 10%FBS until sub-confluent. Then, medium was switched to 83mM of glucose with or without 10% of L-psicose. The production of reactive oxygen species (ROS) was evaluated by dehydroethidium staining and lucigenin enhanced chemiluminescence assay. Matrix expansion was accessed by ^{3}H-labeled leucine incorporation into the PMCs. Gene expression of collagen type III was also measured by real time PCR.
Results: ROS production was increased in high-glucose medium by 1.5 fold compared to normal glucose. L-psicose containing medium prevented the production of ROS induced by high glucose. Matrix expansion was also increased in high glucose medium, and was inhibited by 10% L-psicose. Gene expression of collagen type III was also suppressed by L-psicose. Pre-treatment of DPI, a NADPH oxidase inhibitor, reduced the matrix expansion induced by high-glucose medium.
Conclusions: L-psicose has a potential preventive effect on PMCs from high-glucose induced ROS production, matrix expansion and collagen type III gene expression. Therefore, we conclude that L-psicose containing dialysate may be beneficial on PMCs to prevent the loss of function in PD therapy.

MP282 HbA1c IN NON-DIABETIC PERITONEAL DIALYSIS PATIENTS: WHICH RELATION WITH CLINICAL AND PRESCRIPTION PARAMETERS

M.J. Rocha, M.J. Carvalho, A. Rodrigues, A. Cabrita. *Nephrology, Hospital Geral de Santo António, Porto, Portugal*

Introduction and Aims: The use of glucose as the major osmotic agent in peritoneal dialysis (PD) solutions has raised concern about its long-term metabolic effects. Altered glucose profile, despite the absence of diabetes, has been reported in some PD populations and glycated haemoglobin (HbA1c) has been used as a marker. We performed a cross-sectional study on our non-diabetic PD patients to characterize the HbA1c distribution and its relationship to clinical parameters and to the PD prescription.
Methods: Fifty-three patients on stable PD prescription for more than 2 months (32F, 21M), aged 47±15 years, with a follow-up of 32±23 months were included. Thirty-three patients (62%) were anuric. Twenty-five patients (47%) were on CAPD; 15 patients (28%) used icodextrin for the long-dwell; no patient used the hypertonic PD fluid 3,86%. HbA1c was determined using HPLC. Body-mass index (BMI) was calculated. C-reactive protein (CRP) was used as a marker of inflammation. Lipid profile and albumin were measured. Peritoneal transport was assessed by the 4h-D/P creatinine in a 3,86% peritoneal equilibration test. Intraperitoneal daily glucose exposure was calculated from the dialysis regimen.
Results: Median HbA1c was 4,3% (3,6% -6,0%); references values from our laboratory 3,8 – 5,6%; only one patient had HbA1c above the cut-off point. Patients with higher (> than the median) HbA1c were older (54±10 *vs* 42±15 years; P=0,005) and more inflamed (log CRP -0.56±1.3 *vs* -1.5±1.3, P=0,014). Higher HbA1c was not statistically associated with the other tested variables: time of follow-up, BMI, lipid profile, albumin, residual renal function, peritoneal transport and intraperitoneal glucose exposure. We found strong positive correlations between HbA1c and age (R=0,35; P=0,009) and between HbA1c and log CRP (R=0,47; P<0,0001), and a weak albeit significant correlation between HbA1c and BMI (R=0,28; p=0,04). Obese patients had higher HbA1c levels (4,8±0,58 *vs* 4,3±0,43; P= 0,005), were more inflamed (0.03±1.5 vs -1.4 P=0.03) and had a higher intraperitoneal glucose exposure (2.0±0.3 vs 1.7±0.3% P=0.02.). HbA1c levels were not significantly different between patients on DPCA *vs* DPA nor between those with icodextrin *vs* no icodextrin prescription.
Conclusions: In our population, who does not have a high intraperitoneal glucose explosure, we did not find an adverse impact on carbohydrate metabolism associated with PD, as regards HbA1c. The association of HbA1c, even within normal range, with age, inflammation and obesity suggests it might identify a risk PD population, challenging PD prescription.

MP283 PERCUTANEOUS PLACEMENT OF THE PERITONEAL CATHETER USING THE SELDINGER TECHNIQUE

Jana Pafcugova, Marketa Hraskova, Julius Forejt, Miroslava Horackova. *Department of Nephrology, Faculty Hospital Motol, Prague, Czech Republic*

Introduction and Aims: Several techniques are used to insert the peritoneal dialysis catheter into the peritoneal cavity. Besides the surgical placement methods (minilaparotomy, laparoscopy), we also use the Seldinger technique in selected group of patients. We report our experiences with this type of catheter implantation which is safe, simple and reliable.
Methods: We performed twenty bedside catheter insertions in patients with no previous history of abdominal surgical intervention. We used the double-cuff Tenckhoff catheter in all twenty cases. The whole procedure was always carried out under the local anesthesia. We monitored the complications at

insertion (bleeding, bowel perforation) and incidence of complications such as catheter migration, exit site infection, tunnel infection, leakage and cuff dislocation within the next 12 months of the follow-up.

Results: The catheter insertion was successfully performed in all twenty patients. The only complication at insertion was an improperly placed catheter that had to be replaced under the sciascopic control. We had no complications in terms of bleeding or bowel perforation during the bedside procedure. The complications that occured during the follow-up period were catheter migration in four of 20 patients (20%), which was successfully managed by laparoscopic reposition, one episode of early leakage (5%), one episode of clotting (5%) managed by urokinase instillation, two episodes of cuff migration (10%). Concerning the early infectious complications, we dealt with two cases of exit site infection (10%) and no episode of tunnel infection. Early peritonitis episodes (within one month of catheter placement) did not occur. Our longest period of a functioning catheter has been 48months.

Conclusions: This technique shall not be a method of choice in patients with presumptive intra-abdominal adhesions and in cases of extreme obesity.

The percutaneous technique is preferable in patients with high risk of the general anesthesia. The blind bedside catheter insertion can be easily performed by nephrologists and in our opinion has a beneficial psychological effect on patient-physician relationship.

MP284 LONGITUDINAL ANALYSIS OF FLUID TRANSPORT AND THEIR DETERMINANTS IN PD PATIENTS

Annemieke Coester[1], Parikova Alena[2], Watske Smit[1,3], Dick Struijk[1,3], Raymond Krediet[1]. *[1]Internal Medicine, Division of Nephrology, Academic Medical Center, Amsterdam, Netherlands; [2]Internal Medicine, Division of Nephrology, Charles University, Prague, Czech Republic; [3]Dianet Foundation, Amsterdam-Utrecht, Netherlands*

Introduction and Aims: A decreased effectiveness of the glucose induced osmotic pressure in the induction of fluid flow to the peritoneal cavity, a so-called decreased glucose induced osmotic conductance (GOC), is an important cause of ultrafiltration (UF) failure, especially in long-term PD. It is associated with decreased free water transport (FWT). GOC results from the ultrafiltration coefficient (LpA), a membrane related property, and the reflection coefficient (sigma). Sigma depends largely on aquaporin-1 (AQP-1) function. The aim was to longitudinally analyse changes in fluid transport and their determinants in PD patients. The influence of determinants of fluid transport with time on PD was also analysed.

Methods: It was a single-center cohort study of consecutive incident PD patients (n=190) using conventional PD fluids who started with PD from 1995 until censoring of the data in 2004. Data included patient demographics and comorbidity at baseline. Primary kidney disease was also included. From those (n=150) with modified 3.86% peritoneal function tests (SPAs), done once yearly, solute and fluid transport kinetics and their determinants were analysed. Free water transport (FWT) was calculated from sodium kinetics and transcapillary UF. Solute transport was expressed as mass transfer area coefficients (MTAC) according to Waniewski *et al.* LpA and sigma from poresize modelling according to Rippe *et al.* Patients were stratified according to the number of available SPAs to detect possible confounders. A linear mixed model for repeated measurements was used for the longitudinal data.

Results: Baseline characteristics (Table). FWT at 60 min was similar in the group with 1 - 2 SPAs (153±69) and ≥3 SPAs (156±45, p=0.2) at the 1st SPA. Net UF, GOC, LpA and sigma were NS. The timecourse for FWT showed an increase, maximum at the 3rd SPA, followed by a decrease ($p<0.05$). This was also the case for GOC (p=0.5) and sigma (p=0.08). LpA showed a decreasing trend (p=0.5). The time-course of FWT was influenced by both sigma (p=0.06) and LpA ($p<0.01$). MTAC creatinine at the 1st SPA was NS, but higher in the group with 1 - 2 SPAs (10.2±4.0) compared to ≥3 SPAs (9.8±3.2, p=0.09). MTAC creatinine showed a U-shaped trend ($p<0.01$). Adding age and comorbidity to the models did NS change the results.

Table 1

	no SPA	1 -2 SPAs	≥ SPAs	p-value
Age (yrs)	57±16	56±15	53±16	0.3
Gender (m/f) (n)	22/18	43/34	48/25	0.4
Primary Kidney Disease				0.8
Renovascular (n)	14	18	20	
Glomerulonephritis (n)	6	12	11	
Other (n)	20	47	42	
Comorbidity score (Davies)				0.5
Low (n)	7	16	18	
Medium (n)	22	49	42	
High (n)	11	12	13	

Conclusions: The initial increase in FWT can result from upregulation of AQP-1, the decrease in FWT due to reduced AQP-1 function and increasing resistence of the peritoneal membrane. The U-shaped time-course of MTAC creatinine, also after correction for age and comorbidity, indicates the influence of vasoactive substances in the initial phase of PD and more permanent alterations afterwards.

MP285 SEVELAMER HYDROCHLORIDE VS LANTHANUM CARBONATE AS PHOSPHATE BINDERS IN PATIENTS ON PERITONEAL DIALYSIS

Ioannis Kakavas, George Chatzivasiliou, Penelope Kouki, Ioannis Kopelias, George Bougatsos, John T. Papadakis. *Nephrology Department, Hippokration General Hospital, Athens, Greece*

Introduction and Aims: Hyperphosphatemia and elevated calcium-phosphorus product (CaxP) have multiple adverse systemic effects and are associated with increased morbidity and mortality in dialysis patients. Sevelamer hydrochloride (SH) and lanthanum carbonate (LC), as calcium-free phosphate binders, reduce the levels of serum phosphorus, without increment of serum calcium. In this study we compare the efficacy, tolerability and safety of SH and LC on chronic peritoneal dialysis (PD) patients.

Methods: Thirteen stable patients (6 males, 7 females mean age 62.33±9,8 years) on PD for at least six months, with CrCl ≥ 55 lt/week, were enrolled in the study. After a two weeks washout period, SH was prescribed in a divided dose of 2400 mg/day, that was titrated to achieve serum phosphorus control (3,5-5,5 mg/dl).After four weeks of titration period SH was administrated for another twelve weeks. A washout period of two weeks was followed by a similar treatment schedule of LC, which was initially administrated in divided dose of 1600 mg/day that within four weeks titrated to a maintenance dose. The latter was given for another twelve weeks. During the study we estimated the following parameters: serum Calcium and Phosphorus, CaxP product, PTH, CRP, LDL-HDL cholesterol and dialysis adequacy (CrCl). Dietary intake of phosphorus, calcium, protein and Kilocalories did not change during the study, while dietary assessments were performed at two-time points during the maintenance period.

Results: All patients with both phosphate binders met the serum phosphorus and CaxP product targets (4.9±0.74 vs 4.5±0.68 mg/dl and 46.94±8.6 vs 44.10±6.36 mg^2/dl^2) for SH and LC respectively. During the maintenance period the required dose of LC was smaller than that of SH (2190±592.5 vs 4064±1880 mg/day). In terms of pills count, the number of pills that patients were required to take was also lower in the LC period (2.92±0.79 vs 5.09±2.35 pills/day). There was no differences among the other studied parameters during the SH and LC administration, while the CrCl remained stable. Neither SH nor LC administration caused differences at calcium levels (9.3±0.49 vs 9.4±0.67 mg/dl). One patient on LC discontinued the medication due to repeated vomiting.

Conclusions: This study demonstrates that Sevelamer Hydrochloride and Lanthanum Carbonate control equally serum phosphorus in patients on peritoneal dialysis without inducing hypercalcemia or increment of CaxP product.Both drugs are safe and well tolerated, however patients' compliance was better with Lanthanum carbonate due to the lower number of pills that they required to take.

MP286 PROGRESSION OF CARDIOVASCULAR CALCIFICATION IN PERITONEAL DIALYSIS PATIENTS

Maurizio Gallieni[1], C. Bocci[2], P. Borgatti[2], F. Caputo[2], F. Cavatorta[2], P. Coratelli[2], G. Deferrari[2], M. Farina[2], P. Gabella[2], M. Giannattasio[2], S. Greco[3], M. Mauro[2], G. Merico[3], A.R. Rocca[2], C. Ronco[2], C. Rugiu[2], A. Sacchetti[2], R. Scanziani[2], C. Spinelli[2], A. Stingone[2], ROCK PD Study Investigators[2]. *[1]Renal Unit, San Paolo Hospital, University of Milano, Milano, Italy; [2]ROCK-PD Study Investigators, Italy; [3]Medical Affairs, Dompe' Biotec, Milano, Italy*

Introduction and Aims: Hemodialysis patients are at increased risk for tissue calcifications as a result of deranged mineral metabolism. Few data are available for PD patients. We studied arterial and valvular calcifications in 335 PD patients during a 3 year long, multicenter, observational study.
Methods: Echocardiography and B-mode ultrasonography were used to detect the presence of calcification in 5 arteries and in 2 cardiac valves. A score (0 = no calcification to 7 = all sites calcified) was defined based on the presence/absence of calcification.
Results: Mean ± SD age was 61.0±14.0 years; dialysis vintage was 30±25 months, males 56%, CAPD 54%, APD 44%. At baseline, prevalence of calcification in each studied site ranged from 33% to 46%. The mean±SD global score was 2,77±2,33. Distribution of patients among score categories and its variation during the study were the following:
Baseline: score 0 = 24%; 1-2 = 28%; 3-4 = 21%; 5-6 = 20%; 7 = 8%.
12 months: score 0 = 18%; 1-2 = 21.5%; 3-4 = 26%; 5-6 = 25%; 7 = 9.5%.
24 months: score 0 = 14%; 1-2 = 25%; 3-4 = 22%; 5-6 = 27%; 7 = 12%.
36 months: score 0 = 10%; 1-2 = 20%; 3-4 = 27%; 5-6 = 28%; 7 = 15.5%.
Conclusions: Our data demonstrate a progressive worsening of cardiovascular calcifications over 36 months in PD patients. Ultrasonography can be used to assess progression of vascular calcification. Factors associated with progression of calcification are currently investigated.

MP287 RELATIONSHIP BETWEEN INFLAMMATORY MARKERS AND LEPTIN IN PERITONEAL DIALYSIS PATIENTS

Isabel Pinto[1], Ana Cabrita[1], Idalécio Bernardo[1], Herminio Carrasqueira[2], Marilia Faísca[3], Pedro Neves[1]. *[1]Nephrology, [2]Dietetics, [3]Biochemistry, Faro Hospital, Faro, Algarve, Portugal*

Introduction and Aims: Leptin is a protein hormone secreted by adipocytes regulating body fat and food intake.It has been reported that serum leptin levels are high in patients with chronic renal failure and this fact as been associated with malnutrition and inflammation in dialysis patients.
The present study was performed to investigate the potential relationship between plasma leptin concentrations and markers of malnutrition and inflammation in patients treated with Peritoneal Dialysis (PD).
Methods: We studied 28 stable patients (16 male,12 female) on PD. A group of 16 subjects (4 male,12 female) with normal renal function served as the control. We analysed several clinical, haematological, biochemical and inflammatory parameters. Nutritional status was assessed using Subjective Global Assessment (SGA), Protein Equivalent total Nitrogen Appearance (PNA) and Body Mass Index (BMI). Serum leptin level was detected by radioimmunoassay in μg/L.
Results: The mean age of the PD patients was 54±18 years.Mean PD duration was 25±20 months; 5 patients were on continuous ambulatory peritoneal dialysis (CAPD) and 23 patients on continuous cycling peritoneal dialysis (CCPD); 5 patients (17,9%) were diabetic.Serum leptin levels were significantly higher in PD patients compared with controls (29,9±28,37 vs 7±2,9 μg/L; p=0,000). Leptin levels of female patients were markedly higher than those found in men (44±36 vs 19±13,8; p=0,038). In a linear correlation model we found that C-reactive protein (hs-CRP) (r=0,69; p=0,000) and interleukin 6 (IL-6) (r=0,52; p=0,007) were positively correlated with the leptin levels. No significant correlation was seen between leptin concentration and residual renal function, duration of dialysis and nutritional indices. Serum leptin levels were higher in patients with higher BMI (BMI≥ 25 kg/m^2) (40±33 vs 16±13; p=0,02).
Conclusions: This study demonstrated that PD is associated with marked increased in serum leptin levels. We found a correlation between leptin levels and inflammatory parameters in our patients. As adipose tissue is the major secreting site of this adipokin our results suggest that adipose tissue plays an important role in the pathogenesis of inflammation in PD patients.

MP288 CIRCULATING ADMA IN CAPD AND IN HEMODIALYSIS PATIENTS REFLECTS THE UNDERLYING BURDEN OF RISK FACTORS AND IS LARGELY INDEPENDENT ON DIALYSIS REMOVAL

Giuseppe Enia[1], Francesco Marino[1], Renke Maas[2], Rainer Boeger[2]. *[1]CNR-IBIM, Clin. Epid. and Physiopath. of Renal Dis. and Hypert., Reggio Calabria, Italy; [2]Dpt of Pharmacol., Hamburg University, Hamburg, Germany*

Introduction and Aims: Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of NO synthase, has pro-atherogenic effects and predicts death and cardiovascular events in HD patients. However it is still unclear whether ADMA concentration is affected by dialysis modality because in the three small studies performed so far plasma levels of this methylarginine in CAPD patients were reported as decreased, increased or identical in comparison with HD patients.
Methods: To shed light on this issue, we compared plasma ADMA concentration in CAPD and HD patients on record in the CREED study database that includes a number of CAPD patients (n=50) twice higher than the whole collection of patients in previous studies as well as a large (n=225) number of HD patients. To compare the two dialysis modalities we also measured the average daily dialysis removal of ADMA in 6 CAPD patients and in 6 HD patients matched for age and receiving adequate dialysis dose (CAPD: median weekly Kt/V 1.88; HD: median Kt/V 1.34 per session in HD). ADMA was measured in the 24 h spent dialysate in CAPD patients and in the whole dialysate collected across a single dialysis session in HD patients and ADMA removal was estimated on a daily basis.
Results: Plasma ADMA was higher in CAPD patients (median 4.2 mMol/L IQ range 3.0-5.3) than in HD patients (median 2.51; IQ range 0.6-3.8; P<0.0001). Since risk factors and correlates of plasma ADMA in CAPD patients do not coincide with those in HD patients, we tested the effect of sequential multivariable adjustments on the between groups crude difference in plasma ADMA (1.7 mMol/L). Adjustment for traditional risk factors (age, sex, cholesterol, systolic pressure, diabetes) dialysis vintage and risk factors peculiar to ESRD (Hb and serum P) had no influence on this difference (1.7 μMol/L, P>0.0001). However sequential adjustment for serum Fibrinogen (0.7 μMol/L, P>0.0001) and Albumin (0.5 μMol/L, P>0.34) almost abolished the between groups difference which became largely non-significant. Daily removal of ADMA was higher (P=0.004) in HD patients (median 5.8 mMol IQ range 5.3-6.1) than in CAPD patients (median 3.6 mMol, IQ range 3.4-3.31. μMol/L). However, with both dialysis techniques the daily ADMA removal rate was just a minimal fraction of the estimated daily synthesis rate of ADMA in humans (300 μMol) (Achan V.ATVB 23:1455; 2003).
Conclusions: In the CREED study database ADMA levels are higher in CAPD than in HD patients. The higher ADMA levels observed in CAPD patients depend to a large extent on differences in confounding factors, Fibrinogen and Albumin being the strongest confounders. The ADMA removal rate by dialysis, although higher in HD patients, is just a small fraction of ongoing ADMA synthesis rate. Differences in plasma ADMA between HD and CAPD patients merely reflect underlying variations in Fibrinogen and Albumin, i.e. two risk factors for death and cardiovascular complications of paramount importance in the dialysis population.

MP289 HOW TO MODEL OSMOTIC EFFECT OF ICODEXTRIN IN PERITONEAL DIALYSIS (PD)?

Magda Galach[1], Jacek Waniewski[1], Andrzej Werynski[1], Philippe Freida[2]. *[1]Institute of Biocybernetics and Biomedical Eng., Polish Academy of Sciences, Warsaw, Poland; [2]Department of Nephrology, Louis Pasteur District Hospital, Cherbourg, France*

Introduction and Aims: Icodextrin is a mixture of several hundreds glucose polymers with molecular weight between 340 and 100000 Daltons. Mathematical modeling of its osmotic effect needs a definition of only a few fractions, which concentrations can be derived from chromatographic data (Rippe et al, 2000; Vonesh et al, 2006). However, the accuracy of the predictions for ultrafiltration that are based on a limited (5 – 8) number of fractions has not been checked.
Methods: The three pore model which was previously fitted to clinical data from icodextrin based dwell studies (Galach, Freida et al, 2007), was

applied for computer simulations of fluid ultrafiltration and small solute transport for the average transport pattern obtained for seven PD patients (Freida et al, 2007). The initial distribution of dextrin concentration in icodextrin solution was assumed lognormal and distribution parameters were fitted to the chromatographic data (Vonesh et al, 2006). The number of icodextrin fractions was varied from 1 to 50. The relative error in the variable X(n) simulated using n ($1 \leq n < 50$) fractions was described as the following percentage difference:

PercentageDiff = $100\% \cdot (X(n)-X(50))/X(50)$.

Results: The clinical and simulated net ultrafiltration after 15 hour dwell was 462 mL and practically the same volume was obtained with 16 and more icodextrin fractions. However, the volume was overestimated by 53% if using only one fraction, by 4% for five fractions, by 1% for ten fractions, and by 0.4% for 16 fractions (Figure 1). The number of fractions had no impact on simulated concentrations of small solutes.

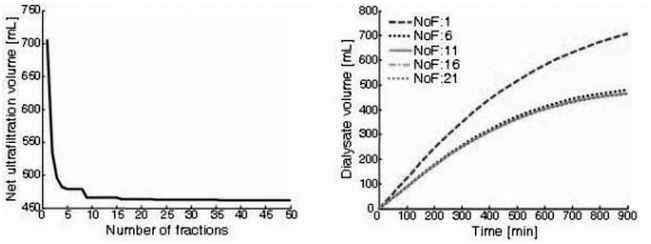


Figure 1. Cumulative net ultrafiltration volume after 15 h dwell as a function of number of fractions (left panel) and as a function of dwell time for selected number of fractions, NoF (right panel).

Conclusions: Osmotic effect of icodextrin can be well modeled by a small number of fractions. This number cannot however be too low. A good approximation can be obtained with five or more fractions, and using more than sixteen fractions do not effect the simulations of fluid ultrafiltration. Modeling of small solute transport is not influenced by the selected number of icodextrin fractions.

Disclosure: Consultant for Baxter HealthCare Inc., IL.

MP290 HYDRATION STATUS OF PATIENTS TREATED BY EITHER HEMODIALYSIS OR PERITONEAL DIALYSIS: A CROSS-SECTIONAL COMPARATIVE STUDY

Bertram Schmitt, Kay Herbrig, Frank Pistrosch, Jens Passauer. *Nephrology, Dept. of Medicine, Univ. Hospital Carl-Gustav-Carus, Dresden, Germany*

Introduction and Aims: Overhydration is regarded as an important factor contributing to hypertension and increased cardiovascular mortality in patients with end stage renal disease. Estimation of dry weight is therefore crucial in both hemodialysis (HD) and peritoneal dialysis (PD). At least during the first two years of treatment both dialysis modalities are considered to be equivalent. However, with decreasing residual diuresis tight volume control becomes more difficult in PD. The aim of this study was to assess the fluid status in a representative number of HD- and PD-patients in whom dry weight prescription was solely based on clinical grounds.

Methods: In 77 PD patients from 8 dialysis centres overhydration (OH) was measured by a newly developed bioimpedance spectroscopy (BIS) device containing a validated body composition model (Body Composition Monitor, Fresenius Medical Care). In addition blood pressure (BP), residual diuresis, number of antihypertensives and time on dialysis were recorded. Results were compared with data from 370 HD patients from 5 centres. In HD patients OH was measured just before a midweek session and time-averaged fluid overload (TAFO) was calculated ([pre-dialytic OH-post-dialytic OH]/2) assuming a linear increase in fluid overload during the dialysis-free interval.

Results: TAFO was slightly but significantly higher in PD than in HD (1.4 ± 2.2 vs. 0.9 ± 0.7 L, $p<0.05$) showing a higher degree of variability in PD. Systolic BP was comparable in both groups while diastolic BP was significantly higher in PD than in HD (83 ± 13 vs. 75 ± 13 mmHg, $p<0.001$). In PD significantly more anti-hypertensive drugs were prescribed.

Conclusions: In this study PD was inferior to HD with respect to volume control and use of anti-hypertensive drugs. BIS devices may help to determine the optimal time for a switch from PD to HD.

MP291 PERITONEAL CATHETER PLACEMENT: 2-TIME VERSUS STANDARD SURGICAL TECHNIQUE

Stefano Mangano, Luca Emilio Bernardi, Daniela Martinelli, Silvia Brenna, Daniela Pogliani, Paola Padovese, Giulia Tettamanti, Claudio Minoretti, Giuseppe Bonforte. *Nephrology and Dialysis Unit, Sant'Anna Hospital, Como, CO, Italy*

Introduction and Aims: Peritoneal dialysis is usually started after 3-6 weeks of peritoneal catheter insertion, which represents an obstacle to the initiation of peritoneal dialysis treatment in urgency. On the other hand, patients usually hardly accept early peritoneal catheter placement, due to the need of clinical controls and to aesthetic discomfort. Hence the risk of starting peritoneal dialysis treatment only after urgent haemodialysis treatment. For this reason we began to place peritoneal dialysis catheters in 2 times: initially, the peritoneal catheter was completely hidden inside the subcutaneous; when it was necessary to start peritoneal dialysis treatment, the outer segment of the catheter was externalised. Aim of this work was to compare the two different kind of catheter positioning.

Methods: From April, 2005 to May, 2007 we placed 46 double-cuffed, 23 with the standard surgical technique (Group A) and 23 with the 2-time technique (Group B).

Results: Group A: from April, 2005 to February, 2006, 23 patients (10 M, 13 F), mean age 61,7 years (range: 29,5-88,2), This patients were affected by end-stage renal disease (creatinine clearance 7 ± 3.7 ml/min). who underwent the standard surgical technique. These patients began peritoneal dialysis with full fill volumes after a mean break-in period of 31.4 days (range: 14-49). After 1 month of dialysis, residual diuresis was 929 ± 657 ml/24h and Kt/V was 2.3 ± 0.4. During the break-in, 7/23 patients started haemodialysis. Group B: from February, 2006 to May, 2007, 23 uraemic patients (creatinine clearance: $11{,}26 \pm 5.9$ ml/min) to the placement of a peritoneal catheter for dialysis with the 2-time technique. After a follow-up of 119,4 months in 23 patients, 10 patients began peritoneal dialysis after 3,6 months of catheter insertion without complications, the full peritoneal load (1890 ± 208 ml) was reached after 1.7 days (range: 1-9 days). One-month Kt/V was 2.3 ± 0.4. 13 patients are still followed-up under conservative treatment. All of the 23 patients have well tolerated the indwelling peritoneal catheter and there were no complications due to the peritoneal catheter itself. Particularly, in group B patients starting peritoneal dialysis, no leakage or infections, due to the surgery technique or the peritoneal catheter stay, were recorded. Only 1 patient had catheter malfunction due to an unfavourable pelvic anatomy (uterine prolapse treated with pessary and frequent urinary tract infections).

Conclusions: Our case series indicate that the "marsupialisation" technique seems to be effective in the clinical management of chronic renal failure patients to be addressed from conservative to peritoneal dialysis treatment. In fact, beyond avoiding the risk of leakage and the washing to keep the catheter open, it allows a viable dialysis access to start peritoneal dialysis in relatively urgent settings, since the catheter is easy to externalise and can be immediately used in case of rapid and/or unexpected worsening of renal function.

MP292 RISK FACTORS FOR AMBULATORY ARTERIAL STIFFNESS INDEX IN PERITONEAL DIALYSIS PATIENTS

Arzu Akgul[1], Ayse Bilgic[1], Zubeyde Arat[1], Nilufer Bayraktar[2], Siren Sezer[1], F. Nurhan Ozdemir[1]. [1]*Nephrology, Baskent University Faculty of Medicine, Ankara, Turkey;* [2]*Biochemistry, Baskent University Faculty of Medicine, Ankara, Turkey*

Introduction and Aims: Ambulatory arterial stiffness index (AASI), a measure based on the relative behavior of 24-hour systolic and diastolic blood pressure (BP), has been suggested as a marker of arterial stiffness and a predictor of cardiovascular mortality. Recently, several studies have demonstrated that low fetuin-A levels are associated with mortality in dialysis patients, possibly through regulation of vascular calcification. However, the effect of fetuin-A on arterial stifness remains is not well known. In this study, the relation between serum fetuin-A concentration and parameters of arterial stiffness was investigated in continuous ambulatory peritoneal dialysis (CAPD) patients.

Methods: In this cross-sectional study, we included 47 CAPD patients (14 male, age 42.5 ± 12.4 years, duration of CAPD 59.48 ± 27.74 months). The following data were analyzed for all patients such as demographic

features, 24-hour ambulatory BP, body mass index (BMI) serum levels of total cholesterol, HDL and LDL cholesterol, triglycerides, calcium, phosphorus, Calcium-phosphorus products (Ca x P), parathyroid hormone (PTH), fetuin-A and C-reactive protein (CRP). AASI was defined as 1 minus the regression slope of diastolic over systolic BP readings obtained from 24-hour recordings.
Results: We found that AASI was significantly correlated with duration of CAPD (r =.296, *p* =.04), serum Ca (r =.445, p=.002), CaxP (r =.316, *p*=.03), PTH (r =.411, *p*=.004) and fetuin-A level (r = -.307, *p*=.03). However, there was no correlation with mean arterial blood pressure, BMI, lipid parameters and CRP. Using multivariate linear regression analysis included all confounder, PTH (β =.363, *p*=.03) was identified as an independent factor influencing AASI.
Conclusions: Markers of vascular calcification associated with AASI that is a novel measure of arterial stiffness in CAPD patients. We found that PTH is an independent predictor of arterial stiffness development.

MP293 INITIAL PERITONEAL THICKNESS MEMBRANE IS A PREDICTOR OF HIGH PERITONEAL SOLUTE TRANSPORT RATE AND ULTRAFILTRATION FAILURE

Patrícia Matias[1], Patrícia Branco[1], Sância Ramos[2], Cristina Jorge[1], Rita Birne[1], António Martinho[3], Elisabete Costa[1], Margarida Gonçalves[1], Ana Paula Martins[2], Maria João Pais[1]. *[1]Dept. of Nephrology, Hospital de Santa Cruz - CHLO, Carnaxide, Portugal; [2]Dept. of Anatomopathology, Hospital de Santa Cruz - CHLO, Carnaxide, Portugal; [3]Dept. of Surgery, Hospital de Santa Cruz - CHLO, Carnaxide, Portugal*

Introduction and Aims: Loss of peritoneal function is the major factor leading to treatment failure in peritoneal dialysis (PD). Fibrosis and thickening of the peritoneal membrane is associated with loss of peritoneal function.
The aim of this retrospective study was to evaluate the relationship between peritoneal thickness, measured by peritoneum biopsy at the beginning of PD, and peritoneum functional parameters.
Methods: Charlson Comorbidity Index (CCI) was also measured at the beginning of PD. The patients were followed by semestral laboratorial data, PET evaluations and peritonitis were also recorded.
We studied 23 incident patients, with a mean age of 60.5±12.2 (33-77) years, 26% female and 30% diabetics. Mean follow-up time was 49.3±37.5 (3-165) months.
Results: Mean peritoneal thickness was 0.40±0.39 (0.02-1.5) mm. Peritoneal thickness was positively correlated with CCI (r= 0.43 p= 0.04), high transport status (r= 0.46, p= 0.03) and ultrafiltration failure (r= 0.48, p= 0.02). Peritoneal thickness was negatively correlated with albumin levels (r= -0.52, p= 0.01). Development of peritonitis and duration of PD treatment were not correlated with peritoneal thickness.
By logistic binary analysis, peritoneal thickness was a predictor of ultrafiltration failure (p= 0.03). On multivariate analysis, higher peritoneal thickness (> 0.8 mm) was associated with CCI (p=0.01), high transport status (p= 0.04) and ultrafiltration failure (p= 0.03).
Conclusions: Biopsy of the peritoneum at the beginning of PD (during PD catheter placement) is a simple and innocuous procedure, may predict loss of peritoneal function in PD patients and could help on PD prescription.

MP294 COURSE OF LEFT VENTRICULAR HYPERTROPHY IN PERITONEAL DIALYSIS PATIENTS: FOLLOW-UP STUDY

Hatice Keles[1], Sibel Turhan[2], Sim Kutlay[1], Gokhan Nergizoglu[1], Oktay Karatan[1], Kenan Ates[1]. *[1]Department of Nephrology, Ankara University Medical Faculty, Ankara, Turkey; [2]Department of Cardiology, Ankara University Medical Faculty, Ankara, Turkey*

Introduction and Aims: Left vetricular hypertrophy (LVH) is one of the most important predictors of mortality in patients with end stage renal failure. LVH was reported to progress frequently under chronic dialysis treatment. The aim of this study was to determine the course of left ventricular mass index (LVMI) and the factors affecting the variations in LVMI in chronic peritoneal dialysis (PD) patients.
Methods: A total of 54 patients consisting of 24 males and 30 females with a mean age of 45.2±11.8 years and taking PD for at least 6 months were included in this study. All the patients underwent echocardiographic examination initially and at the end of a median duration of 36 months follow-up. The mean measures of all blood pressures, hematological, biochemical and dialysis adequacy parameters were calculated between two evaluations. In addition, all the medications and associated diseases of patients were recorded. Paired and non-paired student T tests, chi square test and multivariate logistic regression test were used in the statistical analysis. More than 10% increase in LVMI between two measurements was defined as progression and more than 10% decrease in LVMI between two measurements was defined as regression.
Results: Table 1 shows demographic features of the patients. Throughout follow-up period (median 36 months, range: 6.5-124 months) mean LVMI decreased from 148.7±40.5 g/m^2 to 134.7±38.8 g/m^2 (p<0.05). LVH was detected in 75.4% of cases in the first measurement and in 70.2% of cases in the second measurement. we detected LVMI regression in 35.1% of cases and LVMI progression in 59.6% of cases. In patients with LVMI regression, mean hemoglobin, total creatinin clearence and residual renal function were significantly higher, LDL-cholesterol and C-reactive protein levels were significantly lower than those without regression. In addition, anti-HCV pozitivity was found to be significantly correlated with LVMI pregression. Change in LVMI did not correlated significantly with age, sex, co-morbidities, blood pressure and the mode of peritoneal dialysis. Multivariate regression analysis detected the levels of hemoglobin (OR: 3.38 (1.32-8.64), p=0.01), and LDL-cholesterol (OR: 0.96 (0.93-0.99), p=0.02) and the state of anti-HCV (OR: 0.16 (0.09-0.0[K1]), p=0.04) as independent predictors of LVMI.

Table 1. Demographic features of peritoneal dialysis patients included in the study

	N=54
Age (year), mean ± SD	45.2±11.8
Male, n (%)	24 (44)
Diabetes mellitus, n (%)	11 (20)
Hypertention, n (%)	39 (72)
Coronary heart disease, n (%)	11 (20)
Anti-HCV pozitivity, n (%)	12 (22)
HBsAg pozitivity, n (%)	3 (5)
CAPD/NIPD, n/n (%/%)	33/21 (61/38)

CAPD: Continious ambulatory peritoneal dialysis, APD: Automated peritoneal dialysis.

Conclusions: The progression of LVH in patients with PD is not an inevitable outcome. Improvement in LVH can be achieved particularly with the management of anemia and hyperlipidemia. Further studies with larger series are needed to determine the potential predictors of variations in LVH.

MP295 ACHIEVING TARGETS DEFINED BY CURRENT RECOMMENDATIONS: THE RESULTS OF THE BRAZILIAN MULTICENTRIC STUDY ON PERITONEAL DIALYSIS (BRAZPD)

Natalia Fernandes, Marcus Bastos, Luis Pereira, Marcia Franco, Sergio Haddad, Maria Regina Pinheiro, Teresa Faifer, Aparecida Visona, Elizabeth Tavares, Jaqueline Caramori, Edna Silva, Roberto Carvalho, Elcio Tavares-Filho, Jose C. Divino-Filho, Miguel Riella, Roberto Pecoits-Filho. *on Behalf of the Investigators BRAZPD, Brazil*

Introduction and Aims: Practice guidelines defined by scientific organizations are important tools to define goals for patient treatment. The Spanish Society of Nephrology (SEN) has established clinical targets for patients on dialysis, which define standards of care and are intended to reduce variability in practice patterns and improve clinical outcomes. Defining the proportion of patients who reach targets proposed in the guidelines is important to evaluate the quality of the treatment and the difficulties to achieve the goals. The aim of this study was to evaluate the proportion of patients who satisfied the current SEN guidelines in a cohort of patients on peritoneal dialysis (BRAZPD study).
Methods: Patients and Methods: The BRAZPD is a multi-center prospective cohort study that started in December, 2004. In this study, we studied all incidents and prevalent patients who were more than 3 months on peritoneal dialysis followed until February 2007, unless they had a renal transplantation, recovered renal function, were transferred to hemodialysis, or died. We evaluated demographic, laboratorial and clinical data. The variables blood pressure, haemoglobin, calcium and phosphate product

were compared with the SEN guidelines. Epidemiological profiles of those patients who did not achieve the goals were evaluated.
Results: The study included 3,226 patients in APD and CAPD, of whom 2,094 were incidents patients and the average follow up was 13,6 months. The mean age was 54±19 years, 52% were female, and 64% were Caucasian. Diabetes mellitus (36%) was the most frequent etiology of CKD. Target blood pressure was reached in 70% of patients. The prevalence of peritonitis was 1 episode/30 patients/month. Peritonitis with negative culture was observed in 40% of patients and the cure rate was 87%. The goal for hemoglobin was achieved in 49% of patients, whereas the goals for calcium, phosphate and calcium x phosphate product were 62%, 30% e 79%, respectively; 36% of the patients presented iPTH <150ρg/ml. Albumin was within the target in 66% of patients. The blood glucose was in the target range in 73% of patients. The total colesterol and triglycerides were within the target range in 61% and 62%, respectively. The diabetic patients were those in whom the goals were most difficult to be accomplished. The proposed level of hemoglobin was the most difficult one to be obtained, both in incident and prevalent patients, mainly in those who did not receive predialytic care (p<0,005). The drop out was 33%, mainly due to death (52%). Cardiovascular diseases were the most prevalent cause of death (40%).The incident and prevalent patient presented survival of 72% and 75%, respectively.
Conclusions: Our data allow us to conclude that the peritoneal dialysis therapy in Brazil is in to a great extent in agreement with the parameters established internationally.
Disclosure: This study was supported by a grant from Baxter Healthcare.

MP296 NEW BIOCOMPATIBLE PERITONEAL SOLUTIONS DISMINISH PERITONITIS INCIDENCE RATE

Luis Bolanos Cea, Teresa Cordal, Jose Ramon Criado, Rosa Ranero.
Nephrology, Hospital Xera-Calde, Lugo, Galicia, Spain

Introduction and Aims: New biocompatible peritoneal solutions with a low content of GDPs, have shown higher bactericide properties, mainly in ex vivo experiments,when compared with conventional ones. Data on how this findings affect peritonitis rates has not been fully elucidated. We aimed to analyse the peritonitis incidence rate in our Unit, comparing conventional and biocompatible solutions.
Methods: A retrospective, observational study was undertaken and a 58 month period from January/03 to November/07 was analyzed. During this period biocompatible peritoneal solutions were gradually introduced in our Unit attending to pain relieve during infusion or a higher biocompatible criteria. During this time no modification of either preventive or treatment peritonitis protocols was undertaken in our PD programe.
Results: 72 patients, 39 (54%) females and 33 (46%) males, with 52±1,9 years of age, received peritoneal dialysis being 14 (19%) diabetics. 21 (29%) were on CAPD and 51 (71%) on CCPD. Convention solutions were employed in 67 patients (Dianeal (r) 64; Sleep Safe (r) 3) and biocompatible solutions in 32 patients (Physioneal (r) 29; Gambrosol 2 and Bicavera 1). 48 peritonitis episodes were registered with conventional solutions (0,57 peritonitis patient- year) vs 20 peritonitis episodes with biocompatible solutions (0,46 peritonitis patient-year) (Chi- square= 8,01, p= 0,005). The waiting time for an event (peritonitis) with biocompatible solutions was significantly prolonged (2,18 years) (vs. 1,75 years, p= 0,005). The pattern of germs in peritonitis was not significantly modified. 19 peritonitis (40%) with conventional solutions required hospitalization and 6 (30%) with biocompatible ones (p= 0,46), with a shorter period of hospitalization (10,2 days) in the latter (vs 19,6 days, p< 0,05). Catheter removal was required in 1 case (5%) with biocompatible solutions (vs 11; 23%; p= 0,094).
Conclusions: New biocompatible solutions showed a significant decrement in our peritonitis incidence rate. Although the hospitalizations rate was not significantly modified, this period was shorten with biocompatible solutions. A trend towards a less catheter removal rate with biocompatible solutions was also observed.

MP297 A 2-YEAR CLINICAL EVALUATION OF POLYMERASE CHAIN REACTION FOR RAPID DIAGNOSIS OF TUBERCULOSIS PERITONITIS IN CHINESE CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS

Stanley Lo[1], Siu Kim Chan[1], Chi Kwan Wong[1], Ching Kit Chan[1], Vincent Chow[1], Rodney Lee[2], Wing Cheung Yam[3], Ka Leung Mo[1], Kin Shing Wong[1]. *[1]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China; [2]Department of Microbiology, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China; [3]Department of Microbiology, The University of Hong Kong, Hong Kong SAR, China*

Introduction and Aims: Tuberculosis is prevalent in Hong Kong and mycobacterium tuberculosis (MTB) is not an uncommon etiological agent in CAPD patients with peritonitis. While acid-fast bacilli (AFB) culture results take 4-6 weeks and AFB smear is not sensitive for the diagnosis, polymerase chain reaction (PCR) is an emerging test for rapid diagnosis for TB peritonitis. Inhibitors of primers of PCR were believed to cause poor performance of MTB PCR in body fluid. However, reports for performance of PCR in diagnosing TB peritonitis are scanty.
Methods: The detailed results of PCR, AFB smear and culture for peritoneal dialysis fluid performed between 2005 and 2006 were obtained from the computer system of a cluster hospital tuberculosis laboratory in Hong Kong. All the PCR were performed by a locally designed single-tube nested PCR with gel electrophoresis in a regional tuberculosis laboratory in Hong Kong (Hong Kong Eastern Cluster). Every PCR was confirmed by re-testing a specimen from the subsequent AFB culture.
Results: Of the 154 Chinese CAPD patients who were screened for AFB smear and culture between 2005 and 2006, 40 patients had the PDF tested for MTB PCR. AFB smears were negative in these 40 patients. AFB cultures were positive in 9 of the 40 patients and negative in 31 of these 40 patients. PCR was positive in 6 of the 9 culture-positive patients and it was negative in 31 of the 31 culture-negative patients. Taking AFB culture as gold standard of diagnosing tuberculous peritonitis, the sensitivity of MTB PCR was 67% (6/9), and the specificity of PCRMTB was 100% (31/31). One specimen that was tested to be negative by PCR MTB, turn out to be a case of atypical tuberculosis.

MTB PCR vs AFB culture

	PCR +ve	PCR -ve	
AFB culture +ve	6	3	9
AFB culture -ve	0	31	31

Conclusions: The MTB PCR has higher sensitivity and specificity in diagnosing TB peritonitis. While AFB smear is a poor test for early diagnosis, MTB PCR is a promising test for early diagnosis. As the PCR test is expensive and labor-intensive, it should be limited to cases with high clinical suspicion for TB peritonitis.

Cardiovascular complications 2

MP298 ★ THE ULTRA-STRUCTURAL HETEROGENEITY OF THE MINERAL PHASE IN HUMAN CALCIFIED ARTERIES

Steven Verberckmoes[1], Geert Behets[1], Susanne Jung[2], Dominik Müller[2], Uwe Querfeld[2], Georg Schlieper[3], Markus Ketteler[3], Dagmar-Christiane Fischer[4], Dieter Haffner[4], Patrick D'Haese[1]. *[1]Dept of Pathophysiology, University of Antwerp, Antwerp, Belgium; [2]Dept of Pediatric Nephrology, Charite Universitatsmedizin Berlin, Berlin, Germany; [3]Dept of Nephrology and Clinical Immunology, University Hospital of the RWTH Aachen, Aachen, Germany; [4]Department of Pediatrics, University Hospital Rostock, Rostock, Germany*

Introduction and Aims: A trans-differentiation of vascular smooth muscle cells to an osteogenic phenotype is a key event in the process of vascular media calcification (VC). Based on this fact it is generally accepted that the mineral deposited in the vascular wall has the physicochemical properties of hydroxyapatite (HA), the main mineral compound of bone. Previously, we were able to demonstrate a heterogeneity of the mineral phase deposited in the vessel wall of rats with either adenine induced renal failure or

vitamin D-treated 5/6 nephrectomized rats. In these models the mineral phase was identified not only as HA but also contained amorphous calcium (Ca) phosphate and magnesium (Mg) whitlockite. To further investigate the occurrence of such a heterogeneity in the human situation the mineral phase was identified in calcified artery samples from both uremic (N=11) and non-uremic patients (N=9) showing histological evidence of media and/or intima calcification.

Methods: Mineral identification was performed on 56 sample regions of 4μ-thick tissue sections from the 20 human artery samples by means of μ-X-ray-diffraction using an X-ray synchrotron beam of 2x7μ (Beam line ID18F of the European Synchrotron Radiation Facility, Grenoble, France). The mineral was identified by matching the integrated Debye diffractograms to a mineral database. Crystallinity was estimated by Scherrer analysis of the diffraction peak widths.

Results: In 8 sample regions HA was found as the only mineral phase. Interestingly, in 33 regions only whitlockite was found whilst 14 regions showed a mixture of whitlockite and HA. Amorphous Ca phosphate was found in only one region. No significant correlation was found between the presence of a particular mineral phase and the sample origin.

In contrast a significant difference ($p<0.05$) was found between the crystal size of HA vs. whitlockite in samples originating from both uremic patients and subjects with normal renal function. Moreover both the whitlockite and HA phase showed a more crystalline nature in samples of subjects with normal renal function vs those of uremic patients.

Conclusions: To which extent the presence of whitlockite can be related to an altered Mg metabolism is not clear. Since mineral crystallinity increases in a slow precipitation and further matures over time the discrepancy between HA and whitlockite can be the result of a much slower deposition rate and/or increased mineral age of the whitlockite phase. The same is true for the difference between the ectopic precipitates in uremic vs non-uremic samples. Here the physicochemical results suggest a much faster calcification in the uremic vs a non-uremic environment, an observation which underpins the rapid progression of VC in uremic patients.

MP299 EFFECTS OF ALDOSTERONE RECEPTORS BLOCKADE BY SPIRONOLACTONE ON MYOCARDIAL HYPERTROPHY IN SUBTOTALLY NEPHRECTOMIZED WISTAR RATS

Ashot Essaian[1], Aygul Karabayeva[1], Ivan Kayukov[1], Olga Beresneva[2], Maria Parastayeva[2], David Boterashvili[1]. *[1]Nephrology and Dialysis Department, Saint Petersburg Pavlov's State Medical University, Saint Petersburg, Russian Federation; [2]Nephrology Research Institute, Saint Petersburg Pavlov's State Medical University, Saint Petersburg, Russian Federation*

Introduction and Aims: Aldosterone can induce cardiovascular damage by induction of vascular smooth muscle cell hypertrophy, endothelial dysfunction and cardiac fibrosis due to activation of nonepithelial mineralocorticoid receptors. The aim of our study was to evaluate the influence of aldosterone receptors blockade by spironolactone on cardiac hypertrophy in Wistar rats with experimental uremia.

Methods: The cardiac hypertrophy index and plasma aldosterone concentration (PAC) were compared between three groups of male Wistar rats: group 1 (n=12) - 5/6 nephrectomized animals received spironolactone (0.2 mg daily), group 2 (n=11) – uremic control rats, and group 3 (n=14) – sham operated rats.

After 10 weeks of follow-up cardiac hypertrophy index (heart weight to body weight ratio) was calculated and PAC was assessed by immunoferment analysis

Results: Cardiac hypertrophy index did not significantly differ in group 1 and 3 (2.52 ± 0.06 and 2.35 ± 0.09, respectively; $p>0.05$), while in control uremic rats cardiac hypertrophy index was higher compared with both other groups (2.8 ± 0.11; $p<0.05$).

As a sequence of aldosterone receptors blockade by spironolactone, PAC was significantly higher in group 1 compared with group 3 (281.67 ± 39.02 pg/mL *vs* 145.42 ± 17.41, $p<0.05$). The difference between control (group 2) and sham operated (group 3) rats was not statistically significant ($207,55\pm32,86$ *vs* 145.42 ± 17.41 pg/mL, $p>0.05$).

Conclusions: Blockade of aldosterone receptors by spironolactone provide cardioprotive effect in experimental uremia in Wistar rats.

MP300 UREMIC TOXINS INCREASE MMP-2 AND MMP-9 ACTIVITY AND ALTER BASIC BIOLOGICAL FUNCTIONS OF CULTURED HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS (HUVEC)

Theodora Bita[1], Kalliopi Zafiropoulou[2], Evangelos Papachristou[1], Dimitrios Goumenos[1], Stella Karabina[2], Panagiotis Katsoris[2], Jannis Vlachojannis[1]. *[1]Internal Medicine - Nephrology, Patras University Hospital, Patras, Achaia, Greece; [2]Biology, University of Patras, Patras, Achaia, Greece*

Introduction and Aims: Endothelium has a structural as well as functional role. It responds to mechanical, metabolic and hormonal stimuli by secreting molecules which regulate vascular tone and activate inflammatory processes. End-stage renal disease (ESRD) is accompanied by accumulation of several uremic toxins leading to major metabolic and inflammatory disturbances. Endothelial cells are one of the major targets of uremic toxins causing dysfunction, vascular remodeling and atherosclerosis.

Metalloproteinases (MMPs) and their inhibitors (TIMPs) are secreted by endothelial cells and play an important role in degradation of extracellular matrix and destabilization of atheromatic plaques. Uremic toxicity causing endothelial dysfunction is accompanied by an imbalance between MMPs and TIMPs. This, results in disturbed processes involving development, angiogenesis and wound healing.

Investigation of the impact of uremic serum on basic biological functions of endothelial cells as well as the expression of MMP-2, MMP-9, TIMP-1, TIMP-2, elastin and collagen type IV, representing important components of extracellular matrix.

Methods: Primary cultures from human umbilical vein endothelial cells (HUVEC) incubated with serum from ESRD patients before (predialysis) and after (postdialysis) a 4h regular dialysis session were used. Ten ESRD patients (6 men, 4 women) 45 ± 8 years old, participated in this study. Risk factors for endothelial dysfunction (diabetes, hypertension, hyperlipidemia or smoking) were absent. Dialysis was performed using polysulphone filters ($1.7\ m^2$) and bicarbonate dialysate.

Basic biological functions of endothelial cells like proliferation, migration, wound healing as well as apoptosis were studied. In addition, expression of MMP-2, MMP-9, TIMP-1, TIMP-2, elastin and collagen type IV was also investigated.

Cell proliferation was determined with crystal violet method, apoptosis with flow cytometry and cell migration with transwell system.

Zymograms were used to detect MMP-2 and MMP-9 activity, Western Blot analysis for TIMP-1 and TIMP-2 protein expression and RT-PCR was performed for MMP-2, MMP-9, TIMP-1, TIMP-2, elastin and collagen type IV mRNA detection.

Results: Incubation of HUVEC with predialysis serum results in reduced proliferation, cell migration and wound healing capacity as well as increased apoptosis, compared to incubation with postdialysis serum. Predialysis serum also upregulates MMP-2 and MMP-9 and downregulates TIMP-1 and TIMP-2 expression and decreases both elastin and collagen type IV (mRNA and protein) compared to postdialysis serum.

Conclusions: Uremic serum alters basic biological functions of endothelial cells and causes an imbalance between synthesis and degradation of extracellular matrix components. The endothelial dysfunction that is in part improved by dialysis, is probably related to vascular remodeling observed in patients with ESRD.

MP301 COMPARISON OF ARTERIAL COMPLIANCE IN PATIENTS TREATED WITH HEMODIALYSIS AND PERITONEAL DIALYSIS IN THE EARLY AND LATE YEARS OF RENAL REPLACEMENT THERAPY

Grzegorz Wystrychowski, Ewa Zukowska-Szczechowska. *Department of Internal Medicine, Diabetology and Nephrology, Medical University of Silesia, Zabrze, Poland*

Introduction and Aims: A survival advantage of peritoneal dialysis (PD) over hemodialysis (HD) in the initial years of renal replacement therapy (RRT) and an opposite trend in the later years of RRT have been reported in numerous studies. The origin of these observations is not entirely clear. We aimed to assess whether arterial stiffness – an independent predictor/risk factor of cardiovascular mortality – differs between HD and PD patients in

the first two or in the subsequent years of RRT. If present, such variations might explain/contribute to the observed differences in mortality between the two populations.

Methods: All the centre's 100 eligible end stage renal disease patients treated with hemodialysis or peritoneal dialysis for at least 3 months have been studied. Exclusion criteria included acute clinical conditions, severe heart failure, arrhythmia, valve abnormalities, and switches between RRT modalities. The study group consisted of 31 HD and 18 PD patients dialysed for ≤2 years (15 M/16 F, aged 61.3±12.4 years and 11M/7F, aged 50.6±15.3 years, respectively), as well as 32 HD and 19 PD patients dialysed for >2 years (15 M/17 F, aged 55.7±12.1 years and 13M/6F, aged 58.4±14.1 years, respectively).

Large (C1) and small artery (C2) compliance indices were estimated non-invasively with use of modified Windkessel model analysis of pulse waveform (HDI/Pulse Wave CR-2000 Research Cardiovascular Profiling System) before HD procedure or with dialysate in peritoneal cavity in PD patients. Blood pressures and pulse rate were recorded, and major laboratory parameters were assessed.

C1 and C2 were compared between HD and PD patients of ≤2 or >2 years of RRT with univariate test, as well as by means of analysis of covariance with adjustment for independent correlates of arterial compliance, dissected in a cohort of 226 patients with stage 2-5 chronic kidney disease, as reported previously (WCN 2007). These included age, mean blood pressure, body surface area, as well as heart rate and use of angiotensin-inhibiting agent (C1) or serum CRP and diabetes duration >16 years (C2).

Results: There were no significant differences in the crude or adjusted values of C1 and C2 between both dialysis modalities in the first two or later years of RRT (table).

	Dialysis ≤2 years			Dialysis >2 years		
	HD	PD	*P*	HD	PD	*P*
C1 (crude) [ml/mmHg∗10]	8.1±3.5	9.5±3.2	0.16*	11.7±4.8	10.9±3.8	0.55*
C1 (adjusted)	8.3	9.3	0.23†	10.8	11.7	0.37†
C2 (crude) [ml/mmHg∗100]	2.9±2.2	3.2±1.4	0.10#	3.8±1.9	3.6±1.4	0.89#
lnC2 (adjusted)	0.92	1.07	0.30†	1.21	1.24	0.81†

*t-test; #Mann-Whitney U test; †ANCOVA.

Conclusions: Arterial compliance does not differ between patients treated with hemodialysis or peritoneal dialysis in the early, nor in the later years of renal replacement therapy. Variation in survival between both populations contingent on the duration of dialysis therapy seems not determined by arterial stiffness.

MP302 SERUM FETUIN-A CONCENTRATIONS ARE INVERSELY RELATED TO PROINFLAMMATORY CYTOKINE CONCENTRATIONS IN THE PATIENTS WITH CHRONIC RENAL FAILURE

Erkan Dervisoglu[1], Hale Kir[2], Betul Kalender[1], Ceyla Eraldemir[2], Cigdem Caglayan[3]. *[1]Nephrology, [2]Biochemistry, [3]Public Health, Kocaeli University, Kocaeli, Turkey*

Introduction and Aims: It is known that there is a close relationship between inflammation and vascular calcification. Several studies investigated the role of fetuin-A as a calcification inhibitor, but the number of studies in which the association of this glycoprotein with inflammation markers are limited. To understand the interdependence of inflammation with fetuin-A concentration, we aimed to investigate the relationship between serum fetuin-A and proinflammatory cytokines in patients with chronic renal failure (CRF).

Methods: Thirty-two patients on haemodialysis (HD), 32 conservatively managed chronic kidney disease (CKD) patients and a control group of 25 subjects with normal renal function were enrolled in this study. Serum fetuin-A, IL-1β, IL-6 and TNFα levels were measured by ELISA.

Results: In 64 CRF patients (on HD and with CKD), serum fetuin-A was significantly and inversely related to IL-1β (P = 0.000), IL-6 (P = 0.025) and TNFα (P = 0.007) respectively. In controls, we did not observe such correlation.

Conclusions: The negative correlation that we have found between serum fetuin-A and cytokine concentrations in CRF patients supports the hypothesis of inflammation-dependent down regulation of fetuin-A expression.

MP303 HIGHER ARTERIOVENOUS FISTULAE BLOOD FLOWS ARE ASSOCIATED WITH A LOWER LEVEL OF DIALYSIS INDUCED CARDIAC INJURY

Shvan Korsheed[1], James Burton[1], Christopher McIntyre[1,2]. *[1]Department of Renal Medicine, Derby City General Hospital, Derby, United Kingdom; [2]School of Graduate Entery Medicine and Health, University of Nottingham, Derby, United Kingdom*

Introduction and Aims: Native arteriovenous fistulae (AVF) remain the access of choice for haemodialysis (HD). Although associated with superior long term outcomes (c.f. catheter use), little is known about the haemodynamic consequences of AVFs. Repetitive myocardial injury (myocardial stunning) is an under recognised common consequence of HD, and is associated with dialysis related relative hypotension. The aim of this study was to examine the impact of AVF flow (QA) on dialysis induced cardiac injury.

Methods: We studied 50 chronic HD patients. All patients underwent echocardiography (and subsequent quantitative off line analysis) at baseline, during and post dialysis to assess left ventricular function and the development of regional wall motion abnormalities (RWMAs). QA was measured using ionic dialysance.

Patients were divided into QA tertiles (<500, mean 291±101 ml/min, 500-1000, mean 739±130 ml/min and >1000, mean 1623±220 ml/min).

Results: There were no significant differences between the groups for age, sex, diabetes or resting Ejection Fraction. Patients with QA > 1000 ml/min had a lower prevalence of left ventricular hypertrophy (55% vs. 76%, p=0.01). Dialysis induced myocardial stunning (seen in 70% of the patients studied) was significantly and sequentially reduced in those patients with higher QAs. This was seen in a lower number of segments and ventricular regions developing RWMAs, as well as a significantly reduced mean and cumulative percentage reduction in fractional shortening of those ventricular segments affected (-187±37%, -161±26% and -101±25% respectively, p=0.04).

Conclusions: Relatively higher AVF flows appear to be associated with an adaptive cardiovascular response reducing the propensity to HD induced cardiac injury.

MP304 ESTIMATION OF THE INFLUENCE OF THE PATIENT'S AGE AND DURATION OF UNDERGOING HEMODIALYSIS ON MINERAL AND BONE METABOLISM AS WELL AS INFLAMMATION STATUS IN PATIENTS WITH END STAGE RENAL DISEASE (ESRD)

Marek Kuzniewski[1], Danuta Fedak[2], Wladyslaw Sulowicz[1], Beata Kusnierz-Cabala[2], Paulina Dumnicka[2], Jerzy W. Naskalski[2], Mieczyslaw Pasowicz[3]. *[1]Department of Nephrology, Jagiellonian University, Cracow, Poland; [2]Department of Clinical Biochemistry, Jagiellonian University, Cracow, Poland; [3]Institute of Cardiology, Jagiellonian University, Cracow, Poland*

Introduction and Aims: ESRD multiplies the value of coronary artery calcium scores (CaSc), which together with the prolonged inflammation predict the risk of cardiovascular disease in patients on maintenance hemodialysis. ESRD per se and secondary hyperparathyroidism lead to the alterations of mineral, bone metabolism and induce bone mass lost. The coexsistance of those disorders and extraosseous calcification is a good proven picture of ESRD, called CKD-MBD (*Chronic Kidney Disease-Mineral and Bone Disorder*).

The aim of the study is to define which of selected biochemical parameters and imaging techniques characteristic for CKD-MBD depend on patient's age and/or duration of the dialysis treatment.

Methods: Studied group: 68 HD patient's (29 F, 39 M) aged 60,3±12,3 yrs, dialysed 3 times weekly for 24,5±4,8 months, based on reprocessed polysulphone dialysers, bicarbonate fluid and low molecular weight heparin as an antithrombotic agent.

Studied parameters: CaSc was assessed by multi-slice spiral computed tomography (MSCT), BMD was assessed by DEXA. CRP was measured by nephelometry, interleukin-6, tartrate-resistant acid phosphatase (TRAP), osteoprotegerin (OPG), bone alkaline phosphatase (bALP), fetuin A were measured by ELISA, iPTH by Nichols method, calcium, phosphorus and albumin by routine methods.

Results: All variables are presented in Tables 1 and 2.

Table 1. Comparison of selected parameters depending on duration of dialysis and patient's age

Patient's age		Selected parameters	Duration of dialysis	
r	p		r	p
NS	NS	CaSc	0,40	0,001
-0,34	0,01	BMD neck.	NS	NS
NS	NS	iPTH	0,30	0,02
NS	NS	Ca	0,49	0,00007
NS	NS	CaxPi	0,34	0,007

Table 2. Comparison of selected parameters depending on duration of dialysis and patient's age

Patient's age age		Selected parameters	Duration of dialysis	
r	p		r	p
-0,26	0,04	fetuin A	NS	NS
0,66	<0,00001	OPG	0,51	0,00003
NS	NS	bALP	0,29	0,02
NS	NS	TRAP	0,46	0,0002
-0,32	0,01	albumin	NS	NS
0,36	0,004	IL-6	NS	NS
0,30	0,02	CRP	NS	NS

Conclusions: 1. There is an existence of the relationship between the patient's age in one the hand and BMD, markers of inflammation (CRP, IL-6, albumin) and known extraosseous calcification inhibitors (fetuin A, OPG) on the other hand.
2. Diuration of maintenance hemodialysis has an influence on progression CaSc, secondary hyperparathyroidism and in consequence on mineral metabolism disturbances (iPTH, Ca, CaxPi).
3. High bone turnover is also a consequence of ESRD duration (bALP, TRAP, OPG).
4. Duration of patient's maintenance hemodialysis has no influence on the progression of chronic inflammation.

MP305 ABDOMINAL AORTIC CALCIFICATIONS IN HEMODIALYSIS PATIENTS: THE CONTRIBUTION OF TRADITIONAL AND UREMIA-RELATED RISK FACTORS

Gabriel Mircescu[1], Simona Stancu[1], Ligia Peterscu[1], Adrian Zugravu[1], Radu Dragulete[1], Carmen Barbulescu[2], Caterina Santimbrean[2], Elvira Rus[2], Roxana Martinescu[2], Christian Klein[2]. *[1] "Carol Davila" University of Medicine and Pharmacy and Clinical Hospital of Nephrology, Bucharest, Romania; [2] "Carol Davila" Fresenius NephroCare Dialysis Center, Bucharest, Romania*

Introduction and Aims: Vascular calcifications are associated with an adverse outcome in end-stage renal disease patients. They can be accurately quantified using computed tomography but simpler in-office techniques may provide equally useful information. The calcification score of abdominal aorta easily obtained by means of a plain abdominal X ray, showed a very good correlation with data obtained using more sophisticated methods like EBCT and is a predictor of general and cardiovascular mortality in HD patients. The aim of this study is to evaluate the contribution of traditional and uremia-related risk factors to abdominal aortic calcifications in HD patients.
Methods: We investigated 172 non-diabetic HD prevalent patients (gender M/F 56.4/43.6%, mean age 55.1±12.6, mean HD vintage 10.47±9.2 years), with glomerulonephritis as main cause of CKD - 52%. We estimated abdominal aortic calcification score on a plain abdominal X ray and evaluated cardiovascular traditional risk factors (gender, age, nutritional status by BMI and SGA, dyslipidemia using mean values of cholesterol and tryglicerides in the past 2 years, smoking and hypertension) and non traditional risk factors related to uremia (calcium-phosphate metabolism and inflammatory status evaluated by mean values of calcium, phosphorus, calcium-phosphorus product, PTH and CRP during the previous 2 years).
Results: Mean value of aortic calcification score was 6.9±7 (median 5, range 0-24). The distribution of patients according to quartiles of calcification score was: 32% patients with calcification score 0; 21.5% calcification score 1-5; 23.3% calcification score 5-12; 24.4% calcification score 12-24.Univariant analysis showed correlation of aortic calcifications with traditional risk factors: male gender ($p<0.005$), age ($p<0.0001$), smoking ($p<0.001$) and moderate/severe malnutrition ($p<0.0001$) and with uremia-related risk factors: macro inflammatory syndrome (CRP >10mg/l, $p<0.00001$), longer HD vintage ($p<0.0001$), mean calcemia ($p<0.05$), mean phosphatemia ($p<0.05$), mean calcium-phosphorus product ($p<0.05$) and marginally with the number of months with serum calcium and phosphorus values beyond K/DOKI guidelines ($p<0.07$). In multivariant analysis, only age ($r=4.3$, $p<0.0001$) and macro inflammatory syndrome ($r=11$, $p<0.0001$) were associated with aortic calcification.
Conclusions: Abdominal aortic calcifications are frequent in HD patients and were associated in our study especially with advanced age and macro inflammatory syndrome.

MP306 ASSOCIATION OF AORTIC CALCIFICATION SCORE WITH OTHER ATHEROSCLEROTIC DETERMINATIONS IN HD PATIENTS

Gabriel Mircescu[1], Simona Stancu[1], Ligia Peterescu[1], Adrian Zugravu[1], Radu Dragulete[1], Carmen Barbulescu[2], Caterina Santimbrean[2], Elvira Rus[2], Roxana Martinescu[2], Christian Klein[2]. *[1] "Carol Davila" University of Medicine and Pharmacy and Clinical Hospital of Nephrology, Bucharest, Romania; [2] "Carol Davila" Fresenius NephroCare Dialysis Center, Bucharest, Romania*

Introduction and Aims: Vascular calcifications in HD patients are negative prognostic factors for morbidity and mortality. Calcification score of abdominal aorta obtained on a plain abdominal X ray is a simple method for evaluation of vascular calcification in HD patients, and was positively correlated both with coronary calcification diagnosed by EBCT and pulse wave velocity measured by applanation tonometry. The aim of the study is to evaluate the association among abdominal aortic calcification score and other vascular changes in HD patients.
Methods: We investigated 172 non-diabetic prevalent HD patients (gender M/F 56.4/43.6%, mean age 55.1±12.6, mean HD vintage 10.47±9.2 years, with glomerulonephritis as main cause of CKD - 52%. We estimated abdominal aortic calcification score on a plain abdominal X ray, aortic button calcification on a chest X ray. Valvular calcification, carotid plaques and intima-media thickness (IMT) were assessed by sonography.
Results: See table.
In our study, the higher the aortic calcification score, the higher the number of atherosclerotic changes in other sites. The sensitivity and specificity for an aortic calcification score >12 was 74.4% and 44.9% for carotid plaques association; 75% and 64% for IMT>0.1mm; 74.4% and 63.9% for aortic button calcification; 74.4% and 38.1% for valvular calcifications. The area under the curve for aortic calcification score >12 associated with carotid plaques, aortic button calcification, IMT>0.1 and valvular calcification was 0.59, 0.69, 0.7 and 0.56, respectively. The likelihood ratio (95% confidence interval) for aortic calcification score >12 was 1.35 for carotid plaques, 2.06 for aortic button calcification, 2.5 for IMT >0.1mm and 1.2 for valvular calcification. The degree of aortic calcifications is best correlated with IMT, a surrogate marker itself for athero- and arteriosclerosis in HD patients and with aortic button calcification.

Abstract MP306 – Table 1

Parameter	Calcification score 0; 0; 53 patients (30%)	Calcification score 1-5; 37 patients (21.7%)	Calcification score 5-12; 40 patients (23.3%)	Calcification score 12-24; 42 patients (24.4%)	All (n=172) Mean calcification score 6.9±7 (median=5)	p
Patients with carotid plaques	16.7%	83.3%	100%	100%	64.7%	P<0.05 with score>12
Patients with aortic button calcification	15%	73%	87.5%	97.4%	63.9%	P<0.05 with score>12
Mean IMT, cm	0.06±0.013	0.1±0.008	0.1±0.01	0.115±0.02	0.091±0.02	P<0.05 with score>12
Valvular calcification	10%	14.3%	38%	42%	48%	P<0.05 with score>12

Conclusions: Determination of an aortic calcification score >12 by means of a plain X ray seems to be a simple, cost-effective and useful method which predicts extensive vascular and valvular calcifications in HD patients.

MP307 EXERCISE CAPACITY AND ISOKINETIC MUSCULAR FUNCTIONING IN MOBILE CHRONIC KIDNEY DISEASE PATIENTS

Laura Mason[1], Michael Kingsley[1], Emma Rees[1], Adrian Ionescu[2], Lisa Bastin[2], Ashraf Mikhail[2]. *[1]Swansea University, Swansea, United Kingdom; [2]Morriston Hospital, Swansea, United Kingdom*

Introduction and Aims: Decreased aerobic capacity, poor physical functioning and impaired muscle strength are commonly associated with Chronic Kidney Disease (CKD). Due to the large inter-individual differences within CKD patients, from relatively active kidney transplant candidates (mobile CKD patients) to those who are largely sedentary and depend on healthcare support. The current pilot study aimed to compare aerobic capacity, heart rate response to exercise and isokinetic muscular function of mobile CKD patients with an apparently healthy population.
Methods: We recruited six apparently healthy controls (age: 40.0±4.6 years, mass: 81.5±5.2 kg, height: 1.77±0.03 m) and four mobile CKD patients undergoing haemodialysis (age: 48.0±4.4 years, mass: 81.7±3.7 kg, height: 1.72±0.03 m) for the study. Within a week of health screening, all participants completed a symptom-limited incremental cycling test and isokinetic muscle function assessment on two separate testing days. The cycling protocol began at an intensity appropriate for each individual participant (15–50 W) and increased by 10 W every 2 minutes until exhaustion. Breath-by-breath respiratory parameters and heart rate data were recorded throughout the exercise protocol. Muscle function was assessed using an isokinetic dynamometer during concentric knee flexion and concentric knee extension at both $60° \cdot s^{-1}$ and $120° \cdot s^{-1}$.
Results: Significant differences were found between the groups in both peak work rate and peak oxygen consumption during the incremental cycling test (CKD: 93±12, Con: 223±7 W, $P = 0.010$; CKD: 17.9±1.5, Con: 36.0±2.5 $ml \cdot kg \cdot min^{-1}$, $P = 0.010$, respectively). Peak heart rates were similar during the cycling test (CKD: 149±14, Con: 172±6 $beats \cdot min^{-1}$; $P = 0.095$) and no differences were found in peak respiratory exchange ratio between groups (CKD: 1.07±0.07, Con: 1.13±0.05, $P = 0.352$). Although the average work per rep were similar between groups during knee extension and knee flexion at both isokinetic speeds ($P \geq 0.067$), a significant difference existed between groups for peak torque during knee extension at $60° \cdot s^{-1}$ (CKD: 57.5±13.5, Con: 94.7±6.7 Nm; $P = 0.038$).
Conclusions: These initial findings suggest that, even when the healthiest group of CKD patients is considered, CKD patients have reduced aerobic capacity and produce less peak torque during knee extensions when compared with a healthy control group. Decreased aerobic capacity and poor physical functioning have been shown to be closely linked with mortality and morbidity in CKD patients. These results suggest that an intervention which could improve peak oxygen consumption and increase local muscular strength could improve physical functioning and decrease hospitalisation rates in mobile CKD patients.

MP308 HELIOTHERAPY IMPROVE VITAMIN D AND REDUCE CaxP-PRODUCT IN HD PATIENTS

Rolfdieter Krause[1,2], Karin Mienert[2], Peter Winter[1], Rainer Stange[1], Hans-Hellmut Neumayer[2,3], Werner Hopfenmüller[4]. *[1]Clinic for Natural Medicine, Charité-Unversity Medicine, Berlin, Germany; [2]Nehrological Center Moabit, Kuratorium for Dialysis and Kidney Transplantation, Berlin, Germany; [3]Clinic for Nephrology CCM, Charité-University Medicine, Berlin, Germany; [4]Institute of Biostatistics and Clinical Epidemiology, Charité-University Medicine, Berlin, Germany*

Introduction and Aims: Enteral as well as parenteral substitution of (mainly active) vitamin D derivates often induce hypercalcemia and/or hyperphosphatemia in dialysis patients. Therefore often no adequate circulating levels of 25-hydroxy-vitamin D were reached. - The cutaneous production of Vitamin D by natural or artificial UV radiation do not increase the resorption of calcium and/or phosphate.
Aim of this prospective clinical pilot study was to control the vitamin-D-status and the serum levels of total calcium and of inorganic phosphate after serial UV(B) irradiation in HD patients.
Methods: 22 hemodialysis patints (10 f; median age 62.5 [35-83] yrs.; time on RRT 4.0 [0.5-6.0] yrs.) were irradiated with a sun-similar UV-(UV-B 3.5%) spectrum over a period of five months two times weekly during the routine hemodialysis session. Prior ands after 8, 14, 17, 21 weeks, resp. the serum levels of 25-hydroxy-vitamin D_3 (25-D3), of 1,25-dihydroxy-vitamin D_3 (1,25-D3), of calcium (Ca) and of inorganic phosphat (P) were controlled.
Results: Both 25-D3 and 1,25-D3 increased consecutive with maxima after 8 and 14 weeks, resp. up to 78 µg/l (+45%) and 23 ng/l (+95%). Ca decreased slowly (2.45 to 2.20 mmol/l), and P fall from 1.95 to 1,70 mmol/l, followoing the CaxP-product from 4.6 to 3.9 $mmol^2/l^2$ (- 9%).
Conclusions: Also in hemodialysis patients serial UV(B) radiation of only 15% of skin surface (= front of the legs) is able to increase and normalize 25-hydroxy- and 1,25-dihydroxy –vitamin D_3. In contrast to the established modes of vitamin D substitution heliotherapy shows no calcaemic side-effects.
Moreover, by the well-known pleiotropic effects of vitamin D regularly intermittend use of partial-body exposure to natural sun and/or sun-simulating artificial UV-source seems to be an effective alternative way to prevent and treat the common vitamin D deficiency in patients with chronic kidney disease and on dialysis.

MP309 THE INFLUENCE OF SPIRONOLACTONE TREATMENT ON ENDOTHELIAL FUNCTION IN ANURIC HEMODIALYSIS PATIENTS

Ashot Essaian[1], Aygul Karabaeva[1], Ivan Kayukov[1], Margarita Kadinskaya[2], Michael Timofeev[3], Alexandr Yenkin[4]. *[1]Nephrology and Dialysis Department FPO, Saint Petersburg Pavlov' State Medical University, Saint Petersburg, Russian Federation; [2]Department of Clinical Laboratory Diagnostics, Saint Petersburg Pavlov' State Medical University, Saint Petersburg, Russian Federation; [3]Division of Dialysis, City Hospital N 15, Saint Petersburg, Russian Federation; [4]Division of Dialysis, Leningrad Regional Hospital, Saint Petesburg, Russian Federation*

Introduction and Aims: The cardiovascular morbidity and mortality are significantly enhanced in chronic hemodialysis patients. Recently has suggested that aldosterone and specifically activation of the mineralocorticoid receptor (MR) in nonepithelial cells can induce cardiovascular damage by induction of vascular smooth muscle cell hypertrophy, endothelial dysfunction, and cardiac fibrosis that can be prevented by the simultaneously administered spironolactone. Such effects of aldosterone are realizing mainly by the modulation of plasminogen activator inhibitor type 1 (PAI-1) and endotelin-1 expression, and inhibition of tissue plasminogen activator (tPA). In anuric hemodialysis patients it is possible to blockade MR by spironolactone, without worrying about hyperkaliemia development.
The aim of our study was to assess the effect of aldosterone receptor blockade by spironolactone on plasma PAI-1, endotelin-1, and tPA levels in anuric hemodyalisis patients.
Methods: During the 6 months period 80 anuric hemodyalisis patients (mean age 50,74±9,44 years) have been studied, dividing in 2 groups. Group 1 patients (n= 38) in addition to standard therapy received spironolactone (25 mg once a day), group 2 (n=42) received only usual therapy. The levels of PAI-1 activity (assay with standardized commercial kits, Biopool Inc.), tPA and endotelin-1 (Immunoferment analysis) were measured before and following 6 months spironolactone treatment.
Results: The basal levels of PAI-1 were 5,68±0,42 U/ml and 5,02±0,05 U/ml, respectively (p>0.05), endotelin-1 - 0,62±0,075 and 0,558±0,070 fmol/L, respectively (p>0.05), and tPA - 5,03±0,3 and 4,79±0,26 ng/ml,

Table 1. Dynamics of PAI-1, tPA and Endotelin-1 in anuric hemodialysis patients before and after 6 months treatment

Parameters	Group 1 (n = 38)		Group 2 (n = 42)	
	Before	After	Before	After
PAI-1, U/ml	5,69±0,24	3,06±0,25*	5,02±0,16	4,99±0,26
tPA, ng/ml	5,03±0,3	5,64±0,3*	4,79±0,26	4,74±0,28
Endotelin-1, fmol/ml	0,62±0,04	0,25±0,01*	0,56±0,03	0,72±0,03&

*p<0,001, &p<0,01.

respectively (p>0.05) in group 1 and 2 (Table 1) and exceeded the normal values.
After 6 months of follow up in group 1 the levels of PAI-1and endotelin-1 decreased (3,1±0,11 U/ml, p < 0,0001), and tPA increased significantly, whereas in group 2 parameters of endothelial dysfunction remained unchanged (see table).
No patients developed hyperkalemia during the spironolactone treatment period.
Conclusions: In hemodialysis patients there is significant endothelial dysfunction. Spironolactone therapy (25 mg/day) improves such patients' endothelial function without induction of hyperkaliemia.

MP310 CALCIUM-PHOSPHATE BALANCE AND LEFT VENTRICULAR FUNCTION EVALUATED BY TISSUE DOPPLER IMAGING IN HEMODIALYSIS PATIENTS

Vladimir Dobronravov, Alexey Smirnov, Michail Volkov, Olga Degtyareva, Elena Shevyakova. *Research Institute of Nephrology, Saint-Petersburg Pavlov State Medical University, Saint-Petersburg, Russian Federation*

Introduction and Aims: Tissue Doppler imaging (TDI) is a new objective method that accurately quantifies left ventricle (LV) function compared with conventional echocardiography. Aim of this study is to determine association between left ventricular function and calcium-phosphate balance in patients on hemodialysis.
Methods: Conventional echocardiography and TVI images were recorded in 53 patients (29 men and 24 women), 51,6±12,9 years, hemodialysis duration 73,7±68,6 months. To evaluate LV function using TVI, we determined mitral annular velocities: early diastolic (Em), late diastolic (Am), peak systolic (Sm), the ratio Em/Am and average velocities of 12 LV segments: early diastolic (Es), late diastolic (As), peak systolic (Ss), the ratio Es/As. Serum intact parathyroid hormone (PTH), alkaline phosphatase, octeocalcin, C-telopeptides of type I collagen (crosslaps) were evaluated. Dual-energy X-ray absorptiometry (DEXA) was made and forearm bone mineral density was evaluated as T-score (BMD). We examined the length of abdominal aortic calcification (AAC) by radiographic detection.
Results: We found the prevalence of systolic dysfunction, evaluated by different methods: EF<55% (Simpson) in 13,3% pts, Sm<8 sm/sec in 15,1%, Ss<8 sm/sec in 49,1%, presence of at least 1 segment with Ss<8sm/sec in 100% of patients. Diastolic dysfunction was revealed by different methods of estimation: transmitral E/A<1 in 74,5% pts, Em/Am<1 in 58,5%, Es/As<1 in 50,9%, presence of segments with Es/As<1 in 94,3% of patients.
Es/As correlated directly with BMD (Rs=0,50;p=0,01) and inversely with AAC (Rs=-0,50;p=0,01). Em/Am correlated positively with BMD (Rs= 0,44; p=0,030) and negatively with AAC (Rs= 0,44; p=0,030).
Sm correlated positively with BMD (Rs=0,41;p=0,041) and negatively with PTH (Rs=-0,40;p=0,026), crosslaps (Rs=-0,36;p=0,027). We did not find relation between calcium-phosphate balance and LV function estimated by routine echocardiography methods.
Conclusions: TDI is more sensitive in evaluating LV dysfunction compared with routine echocardiograhy methods. We found that better diastolic and systolic LV function evaluated by tissue TDI was associated with higher BMD, less extent of vascular calcification, less severity of hyperparathyroidism.

MP311 25-HYDROXIVITAMIN D DEFICIENCY: A NEW CARDIOVASCULAR RISK FACTOR IN HEMODIALYSIS PATIENTS?

Teresa Adragao[1], Anibal Ferreira[2], Joao Frazao[3], Marie-Claude Monier-Faugere[4], Harmut Malluche[4]. *[1]Nephrology, Santa Cruz Hospital, Carnaxide, Lisbon, Portugal; [2]Nephrology, Curry Cabral Hospital, Lisbon, Portugal; [3]Nephrology Research and Development Unit, School of Medicine, Porto University, Oporto, Portugal; [4]Nephrology, Bone and Mineral Metabolism, University of Kentucky, Lexington, USA*

Introduction and Aims: Vitamin D deficiency may be associated with development of cardiac ventricular hypertrophy as demonstrated in Vitamin D receptor knock-out mice. The objective of this study was to evaluate, in a group of hemodialysis (HD) patients, relationships between 25-hydroxivitamin D (25-vitD) levels with markers of cardiovascular disease: vascular calcification, pulse pressure (PP), pulse wave velocity (PWV) and Left Ventricular Mass Index (LVMI).
Methods: We studied 48 patients (26 M and 22 F) treated with HD for 65±54 months. Biochemical evaluation was time averaged for 12 months before cardiovascular evaluation. Vascular calcifications were evaluated by a plain X-Ray score and by Coronary Agatston score using Helical Computed Tomography (HCT). PWV was assessed with Sphygmocor. LVMI was evaluated with M Mode Echocardiography.
Results: Deficiency in 25-vitD (<15 ng/mL) was present in 17 patients (35%). There was no correlation between 25-vitD and 1,25-vitD levels. In univariate analysis, deficiency of 25-vitD was associated with lower albumin levels (p<0.001), higher pulse pressure (PP) (p=0.034), higher PWV (p=0.014), higher LVMI (p=0.021) and more calcifications either by plain X-ray (p=0.02) or by HCT (p=0.005). In multivariate analysis, 25-vitD deficiency was independently associated with LVMI increase (p=0.043), PP increase (p=0.027) and vascular calcifications evaluated either by plain X-ray (p=0.023) or HCT (p=0.020).
Conclusions: Deficiency of 25-vit D was an independent predictor of LVMI increase, PP increase and vascular calcifications. These data suggest that 25-vitD deficiency is associated with and may predispose to cardiovascular disease in dialysis patients.

MP312 CARDIAC VALVE CALCIFICATION IN DIALYSIS PATIENTS IS ASSOCIATED WITH LOW BONE MINERAL DENSITY

Vladimir Dobronravov, Alexey Smirnov, Michail Volkov, Olga Degtyareva, Elena Shevyakova, Irina Trofimenko, Irina Panina. *Research Institute of Nephrology, Saint-Petersburg Pavlov State Medical University, Saint-Petersburg, Russian Federation*

Introduction and Aims: Cardiac valve calcification (CVC) occurs frequently in dialysis population and is associated with unfavorable prognosis. The purpose of this work is to determine factors associated with cardiac valve calcification with focus on bone pathology.
Methods: An echocardiography was performed in 131 pts, 75 males, 56 females, age 51,7±12,6 yrs, hemodialysis vintage 77,7±75,6 months. Ultrasonography of common carotid arteries was made to determine intima-media thickness (IMT). Bone mineral density (BMD) of spine, hip and forearm was measured by dual energy X-ray absorptiometry in 63 pts.
Results: CVC was revealed in 38,9% pts: aortic valve calcification in 3,8%, mitral valve calcification– 13,0% and both valves in 22,1%. Using WHO criteria, osteoporosis of forearm was revealed in 32,4% pts, osteopenia – 30,9%, normal BMD in 36,8%. We compared groups of patients with and without CVC and found, that patients with CVC were older (p<0,001), have longer duration of dialysis (p<0,0034), more frequent presence of coronary heart disease (p<0,014), higher levels of iPTH (p=0,037), alkaline phosphatase (p=0,0034), increased IMT (p=0,014), lower forearm BMD (T-score; p=0,048), higher level of C-reactive protein (p=0,016), higher left atrium size (p=0,001), higher peak blood flow velocities through mitral (p<0,001) and aortic valves (p<0,001).
Conclusions: CVC was revealed in 38,9% of dialysis patients. CVC was associated with advanced age of pts, longer dialysis duration, hyperparathyroidism, more severe atherosclerosis. We determined the association between CVC and lower BMD of forearm.

MP313 THE EFFECT OF NOVEL DIRECT HEMOPERFUSION COLUMNS, AS-15 AND AS-25 IN THE CHRONIC RENAL FAILURE PATIENT WITH ATHEROSCLEROSIS OBLITERANS (ASO)/PERIPHERAL ARTERIAL DISEASE (PAD)

Akihiko Matsuda, Osamu Matsumura, Tomoya Ogawa, Yuki Kanayama, Yumiko Yamaguti, Zyukou Asakura, Tadaaki Maeda, Ayako Sekiguti, Yousuke Tayama, Hitosi Kato, Tetsuya Mitarai. *Artificial Kidney and Nephrology and Hypertension, Saitama Medical Center, Saitama Medical University, Kawagoe, Saitama, Japan*

Introduction and Aims: Atherosclerosis obliterans (ASO)/Peripheral arterial disease (PAD) has become major complicatons for chronic renal failure patients with the increase in the number of diabetes mellitus patients and/or eldery population.Our purpose in this study was to evaluate the therapeutic

effect and capability of novel direct hemoperfusion columns AS-15 and AS-25 in chronic renal failure patients accompanying ASO/PAD.

Methods: There were 5 patients (2 males and 3 females) recruited for this study. The mean patient age was 62.2 years (range 49-75 years). 3 patients were categorized as Fontaine stage II, 2 as Fontaine stage IV. 5 patients had DM and HD, and 1 had nephrosclerosis.

Two types of the column, AS-15 of which volume is 150 mL or AS-25 of 250 mL, were applied poperly depending on the body weight of the patients. Treatment was performed for 2h at a blood flow rate of 60-100 mL/min with heparin as the anticoagulant, and carried out two or three times a week for a total of 10-14 treatments. The primary endpoint for Fontaine stage II (F2) patients was the maximum walking distance and the initial claudication distance on treadmill and that for stage IV (F4) was the size of ulcer and the degree of granulation.

Results: In F2 patients, walking distance improved in all of the three patients. In F4 patients, ulcer improvement was observed in hemodialysis patients, but not in predialysis patients. mprovement in subjective symptoms usually occurred immediately after the treatment was started. Serum levels of LDL cholesterol, triglycerides, fibrinogen, and plasma viscosity were reduced by 20%, 50%, 20%, and 10%, respectively in a single treatmet, but no obvious difference was observed between at the beginning and the end of the treatment.Blood pressure decreased on occasion by 30 min after the treatment was started, then was stabilized subsequently.

Conclusions: The novel direct hemoperfusion therapy using AS-15 or AS-25 column revealed to be a safe, simple, and useful modality in chronic renal failure patients with ASO/PAD.

MP314 CARDIAC BIOMARKER ELEVATION IN HAEMODIALYSIS PATIENTS – A CARDIAC MAGNETIC RESONANCE IMAGING STUDY

Adam Hedley[1], Nagesh Anavekar[2], Maurice Molan[3], Francesco Ierino[1]. *[1]Department of Nephrology, [2]Department of Cardiology, [3]Department of Radiology, Austin Health, Heidelberg, Victoria, Australia*

Introduction and Aims: Cardiovascular disease remains the leading cause of mortality and morbidity in patients undergoing chronic haemodialysis. Elevated cardiac biomarker levels (troponin I and T, B-type natriuretic peptide (BNP) and N-terminal pro-BNP) have been shown to predict cardiovascular events and patient outcome. The pathophysiology underlying elevated cardiac biomarkers in patients on dialysis is poorly understood, however functional correlation with novel cardiac investigations such as cardiac magnetic resonance imaging (cMRI) and echocardiography should help address these questions. We hypothesized that elevated troponins would correlate with myocardial ischaemia, whereas BNP would correlate with left ventricular function.

Methods: Twenty-eight asymptomatic patients on chronic haemodialysis underwent cMRI and transthoracic echocardiography (TTE), focusing on left ventricular mass, systolic and diastolic function and ischaemia as identified by enhancement on T2 dark blood cMRI imaging. Cardiac biomarkers - troponin I and T (cTnI, cTnT), BNP and N-terminal pro BNP (NT-BNP) were also assayed.

Results: On cMRI, 21.4% of patients had evidence of myocardial ischaemia, whilst 14.3% of patients had evidence of left ventricular hypertrophy (defined as left ventricular mass index (LVMI) > 95 g/m^2 for females and > 113 g/m^2 for males). There was no significant correlation between cTnI or cTnT levels and ischaemic changes on cMRI. However there was a significant correlation with both cTnI and cTnT and LVMI measured by cMRI – r=0.501, p=0.007 for cTnI and r=0.564, p=0.002 for cTnT. The correlation occurred even though the majority of patients had a LVMI within the normal range. Further, cTnI, but not cTnT significantly correlated with left ventricular ejection fraction (LVEF) measured by TTE – r=-0.558, p=0.007 and r=-0.246, p=0.27 respectively. There was a significant correlation of LVEF with BNP (r=-0.428, p=0.047) and approached significance with NT-BNP (r=-0.409, p=0.058). Patients with left ventricular diastolic dysfunction (LVDD) on TTE tended to have higher BNP levels (mean 521 pg/ml with LVDD vs. 274 pg/ml without LVDD, p=0.19) and NT-BNP (mean 746 pg/ml with LVDD vs. 375 pg/ml without LVDD, p=0.082), Left atrial area (a surrogate indicator of LVDD) correlated with BNP (r=0.614, p<0.001) and NT-BNP (r=0.592, p=0.001) as well as cTnI (r=0.560, p=0.002). Markers of LVDD as well as left atrial area correlated with LVMI on cMRI – particularly LVMI versus tissue Doppler imaging (r = -0.515, p = 0.01) and LVMI versus left atrial area (r = 0.741, p < 0.001).

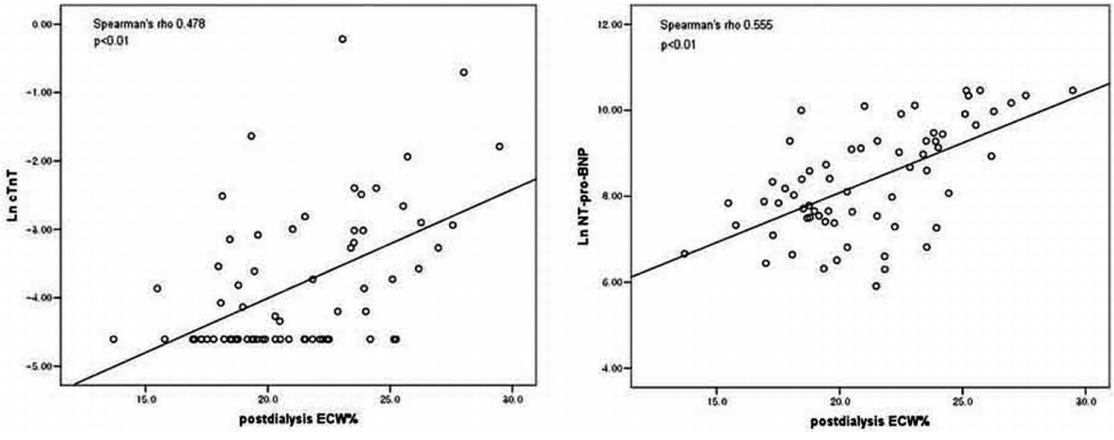
Conclusions: Our data suggest that pathophysiological factors related to increasing left ventricular mass are associated with raised troponins and that this correlation occurs when LVMI was in the normal range. BNP and NT-BNP both correlated inversely with LVEF and surrogates of LVDD. Ongoing studies will improve our understanding of cardiac pathophysiology in renal failure and the clinical utility of these cardiac biomarkers.

MP315 RELATIONSHIP OF CARDIAC TROPONIN T AND N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE TO BODY WATER ESTIMATED BY BIOIMPEDANCE ANALYSIS IN MAINTENANCE HAEMODIALYSIS PATIENTS WITHOUT ISCHEMIC HEART DISEASE

Jongha Park[1], Hyun Chul Chung[1], Min Soo Kim[1], Shin-Jae Kim[2], Yang Hun Park[3], Jai Won Chang[4], Jong Soo Lee[1]. *[1] Division of Nephrology, [2]Division of Cardiology, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea; [3]Park's Clinic, Busan, Korea; [4]Division of Nephrology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea*

Introduction and Aims: Many haemodialysis (HD) patients are in chronic volume overload state despite of maintaining dry weight adjusted clinically. It is one of causes for hypertension and left ventricular hypertrophy, which were associated with high cardiovascular (CV) mortality. Multifrequency segmental bioimpedance analysis (MF-SBIA) is a convenient, safe and reliable tool to assess the amount and distribution of body water. However, relationship of cardiac biomarkers as surrogates of CV mortality to body water measured by MF-SBIA has not been investigated sufficiently.

Methods: We conducted a cross-sectional analysis in stable maintenance HD patients without ischemic heart disease. Total body water% (TBW%, TBW as a percentage of body weight) and extracellular water% (ECW%, ECW



Abstract MP315 – Figure 1

as a percentage of body weight) were exposures, and cardiac troponin T (cTnT) and N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) were outcomes. Values of MF-SBIA were measured before and after HD with 10 min of an equilibration phase in supine position. We also measured TBW% and ECW% in healthy controls as reference.
Results: Seventy-four patients (age; median 50 yrs, interquartile range (IQR) 21, M:F=36:38) were recruited. Median pre-/post-HD TBW% and ECW% were 55.6% (IQR 11), 54.1% (13), 21.9% (5) and 20.7% (5), respectively. Median cTnT and NT-pro-BNP were 0.011 ng/mL (IQR 0.029) and 3,443 pg/mL (9,161). Significant positive associations were noted between cTnT quartiles and pre-/post-HD TBW% and pre-/post-HD ECW%. Similar trend was also showed among NT-pro-BNP quartiles. Post-HD ECW% was best correlated with Ln cTnT (Spearman's rho 0.478, $p<0.01$) and Ln NT-pro-BNP (Spearman's rho 0.555, $p<0.01$) among the body water indices (figure). In a multivariate regression analysis, post-HD ECW% was the strongest independent correlate of Ln cTnT ($p<0.01$) and Ln NT-pro-BNP ($p<0.01$). Compared with 95 percentiles value of ECW% in healthy controls (20.7% in male and 19.1% in female, n=184), 71.4% of male and 56.3% of female in this study were considered as overhydrated state.
Conclusions: Post-HD ECW% estimated by MF-SBIA was strongly related with cTnT and NT-pro-BNP considered as surrogates of CV mortality. A large proportion of asymptomatic HD patients were in overhydrated state based on post-HD ECW%. MF-SBIA may be useful tool adjusting dry weight for reducing CV mortality in HD patients.
Disclosure: This work was funded by Ulsan University Hospital (Biomedical Research Center Promotion Fund, UUH-2007-020).

MP316 DETERMINANTS OF LEFT VENTRICULAR HYPERTROPHY PROGRESSION IN HAEMODIALYSIS PATIENTS

Patrícia Matias[1,2], Carina Ferreira[1,2], Cristina Jorge[1,2], Inês Aires[1,2], Tiago Amaral[1,2], Célia Gil[1,2], Aníbal Ferreira[1,2]. [1]*Dialysis Clinic, Hemodial, Vila Franca de Xira, Portugal;* [2]*Dialysis Clinic, Dialverca, Forte da Casa, Portugal*

Introduction and Aims: Left ventricular hypertrophy (LVH) is an independent risk factor for morbidity and mortality in patients with CKD. The aim of this retrospective study was to asses the risk factors for LVH progression in prevalent haemodialysis (HD) patients.
Methods: All patients included in the study underwent baseline echocardiography and follow-up studies 18-24 months later. Left ventricular mass index (LVMI) was calculated using the Devereux formula and indexed to body surface area. Presence of LVH was defined on the basis of an LVMI greater than 125 g/m^2 for both men and women. Progressive LVH was defined as a follow-up LVMI greater than 105% of the baseline value. Clinical data included aetiology of renal failure, presence of diabetes mellitus (DM), pulse pressure (PP), interdialytic weight gain (IWG) and therapy with vitamin D. Laboratorial data considered were haemoglobin, C-reactive protein (CRP), albumin, serum calcium, phosphorus, iPTH, total cholesterol and triglycerides. The laboratorial values were obtained calculating the arithmetic media of four semester determinations. We studied 98 prevalent HD patients, mean age of 63.2±16.4 years, 51% female, 27% diabetic, with mean HD time (HDt) of 45.3±38.9 months. 48% of the pts were taking vit D (iv paricalcitol), with a mean dose of 7.2±3.9 μg/week). LVH was detected in 61% (n=60) of the patients and LVH progression occured in 53% (n=32) of those with LVH in the baseline evaluation. Uni and multivariate analysis were performed and a $p<0.05$ was considered significant.
Results: LVH progression was positively correlated with HDt ($r = 0.29$, $p = 0.002$), CRP ($r = 0.19$, $p = 0.03$), serum phosphorus ($r = 0.23$, $p = 0.008$), PP ($r = 0.31$, $p< 0.001$) and IWG ($r = 0.22$, $p = 0.01$). LVH progression was negatively correlated albumin ($r = -0.31$, $p< 0.001$) and vitamin D therapy ($r = -0.22$, $p = 0.009$). On multivariate analysis HDt ($p = 0.004$), serum phosphorus ($p = 0.01$), PP ($p< 0.001$) and IWG ($p = 0.02$) were all positive predictors of LVH progression. Albumin ($p< 0.001$) and vitamin D therapy ($p = 0.02$) were negative predictors of LVH progression.
Conclusions: LVH is highly prevalent in maintenance haemodialysis patients. In the follow-up echocardiography, LVH progressed in >50% of patients. Besides classical risk factors of progressive LVH, like HDt, IWG and PP, the inflammatory and nutritional state may also play a role in this pathology. The apparent protective effect of paricalcitol in the development of LVH is in accordance with animal data and retrospective studies, but needs confirmation in large prospective studies.

MP317 PLASMA BRAIN NATRIURETIC PEPTIDE (BNP) AND VASCULAR CALCIFICATIONS: ANY RELATIONSHIP?

Patrícia Matias[1,2], Carina Ferreira[1,2], Cristina Jorge[1,2], Marília Borges[3], Inês Aires[1,2], Tiago Amaral[1,2], Célia Gil[1,2], José Cortez[3], Aníbal Ferreira[1,2]. [1]*Dialysis Clinic, Hemodial, Vila Franca de Xira, Portugal;* [2]*Dialysis Clinic, Dialverca, Forte da Casa, Portugal;* [3]*Lab. Dr. Fernando Teixeira, Lisbon, Portugal*

Introduction and Aims: Vascular calcifications (VC) in haemodialysis (HD) patients are associated with arterial stiffening and development of cardiac dysfunction. The aim of this cross-sectional study was to evaluate the relationship between VC, traditional cardiovascular risk markers and brain natriuretic peptide (BNP).
Methods: VC were evaluated using a simple vascular calcification score (SVCS) based on plain radiographic films of pelvis and hands. We studied 223 prevalent HD patients, mean age of 62.7±15.3 years, 48% female, 27% diabetic, with mean HD time (HDt) of 42.9±39.3 months. Uni and multivariate analysis were performed and a $p<0.05$ was considered significant.
Results: BNP levels were high (573.98±696.34 pg/mL), comparing with general population with no cardiac insufficiency. Diabetes mellitus ($r = 0.15$, $p = 0.03$), C-reactive protein ($r = 0.13$, $p = 0.04$), pulse pressure (PP) ($r = 0.25$, $p< 0.001$), left ventricular mass index (LVMI) ($r = 0.33$, $p< 0.001$) and VC ($r = 0.17$, $p = 0.02$) were positively associated with BNP levels. Albumin ($r = -0.22$, $p = 0.003$) was negatively associated with BNP.
In multivariate analysis, BNP levels >800 pg/mL were independently associated with lower albumin levels ($p = 0.04$), PP ($p = 0.002$), LVMI ($p = 0.001$) and higher SVCS (≥ 3) ($p = 0.01$).
Conclusions: We found a significant association between BNP levels and VC. Both these factors have prognostic value in CKD patients. The link between these two factors still needs to be defined and this association needs to be confirmed in large prospective studies.

MP318 ★ TRADITIONAL (AGE, CARDIOVASCULAR HISTORY) AND NON-TRADITIONAL (HEMATOCRIT, FERRITIN) FACTORS ASSOCIATED WITH AORTIC CALCIFICATION IN PATIENTS WITH STABLE CHRONIC KIDNEY DISEASE STAGE 5D

Kathleen Claes[1], Sam Heye[2], Bert Bammens[1], Dirk Kuypers[1], Yves Vanrenterghem[1], Pieter Evenepoel[1]. [1]*Nephrology and Transplantation, UZ Gasthuisberg, Leuven, Belgium;* [2]*Radiology, UZ Gasthuisberg, Leuven, Belgium*

Introduction and Aims: Cardiovascular disease in association with artery calcification is the leading cause of death in patients with end-stage renal disease. Traditional cardiovascular risk factors are highly prevalent. In addition several non-traditional risk factors may contribute to accelerated atherosclerosis in these patients.
Methods: One hundred and three patients with CKD stage 5D (65 males, mean age 54 years) were enrolled in the present cross-sectional observational study at time of transplantation. Aortic calcifications were evaluated by means of a previously validated scoring system on lumbar X-ray (1). Linear regression analysis was used to evaluate associations between the aortic calcification score and several traditional (smoking status, BMI, lipid profile, hypertension, gender, age, history of cardiovascular disease, diabetes) and non-traditional risk factors (CRP, PTH, Ca, calcitriol, albumin, haematocrit). Also serum ferritin levels were included in the analysis, as a parameter of iron loading.
Results: In univariate analysis there was a significant correlation between age ($p<0.0001$), hematocrit ($p=0.01$), high serum ferritin ($p= 0.011$), hypertension ($p=0.0002$), history of cardiovascular disease ($p<0.0001$) and aortic calcification score. In the multivariate regression model, history of cardiovascular disease ($p<0.0001$), age ($p=0.001$), serum ferritin ($p=0.043$), and hematocrit ($p=0.035$) were found to be independently associated with the aortic calcification score. These variables explain 45% of the variation of the aortic calcification score.
Conclusions: In this cohort of 103 CKD stage 5D patients both traditional

(age, cardiovascular history) and non-traditional (ferritin, hematocrit) risk factors were associated with aortic calcifications. High serum ferritin levels are associated with a high aortic calcification score, independent from several traditional and non-traditional cardiovascular risk factors. Our data lend support to studies warning for the dangers of excessive iron loading in CKD patients.

References: L. Kauppila, Atherosclerosis, Volume 132, 2, p 245-250

MP319 RELATIONSHIP OF MINERAL METABOLISM ABNORMALITIES AND RISK OF CARDIOVASCULAR OUTCOMES (MORTALITY, MORBIDITY AND HOSPITALIZATION) IN DIALYSIS PATIENTS

Adrian Covic[1], Prajesh Kothawala[2], Myriam Bernal[2], Sean Robbins[3], David Goldsmith[4]. *[1]"C.I. Parhon" University Hospital, Iasi, Romania; [2]Cerner LifeSciences, CA, USA; [3]Amgen (Europe) GmbH, Zug, Switzerland; [4]Guy's Hospital, London, United Kingdom*

Introduction and Aims: Bone metabolism abnormalities are very common complications of end-stage renal disease (ESRD); control of mineral metabolism markers (PTH, phosphorus, calcium, Ca x P product) has been poor. Numerous studies suggest that mortality and morbidity may be favorably influenced by various therapies. In order to draw correct conclusions from the often contradictory data a critical appraisal of the current literature is long overdue. This study aimed to qualitatively describe the studies published to date.

Methods: Medline, EMBASE and Cochrane databases from 1980-December 2007 were searched. Studies assessing the epidemiological relationship of mineral metabolism markers and CV outcomes (mortality, congestive heart failure [CHF], myocardial infarction, stroke, acute coronary syndrome or hospitalization) in adult dialysis patients were included.

Results: 14 studies measured the risk of CV mortality (n=7), hospitalization (n=4) or morbidity (n=3) with mineral abnormalities. Methodologies varied across studies. Mineral markers were assessed as a dichotomous (n=7), continuous (n=5), or categorical variable (n=2). Risk assessment methods included hazard ratio (n=8), risk (n=4) or odds ratio (n=2). Studies analyzing mineral markers as categorical or dichotomous had varying reference levels to define the risk of outcomes, and the confounding factors adjusted across studies lacked consistency. Only 3 studies assessed the risk of CV outcomes with mineral levels beyond the European Best Practice Guidelines-suggested targets. Nine studies analyzed the relationship of phosphorus abnormalities with risk of CV mortality (n=5), hospitalization (n=3) and CHF (n=1). Hyperphosphatemia was significantly related with mortality and CHF in all studies and with hospitalization in 2 of the 3 studies assessing this outcome. Nine studies related Ca x P product increases to risk of CV mortality (n=5), hospitalization (n=3) or a composite of stroke, CHF and myocardial infarction (n=1). All studies reported a significant relationship between increases in Ca x P product and mortality/morbidity while 2 of the 3 studies assessing hospitalization showed a significantly increased risk. The effects of PTH levels on CV outcomes were assessed with respect to mortality (n=5) and hospitalization (n=4) only. Evidence on the risk of CV morbidity with changes in PTH levels is lacking. Most of the studies reported a significant increase in risk of CV mortality (n=4) and hospitalization (n=3) with raised PTH levels. Effects of hypercalcemia were evaluated for mortality (n=3), hospitalization (n=3) or CHF (n=2) and the risk of these outcomes were significantly increased in 2 studies each.

Conclusions: Methodological variations were evident across studies; still, the data support the existence of a significant relationship between mineral metabolism abnormalities and risk of CV morbidity. Decreasing this risk may require therapies effective in controlling all 4 markers of mineral metabolism.

Disclosure: I have financial dosclosures for Amgen, Roche, Novartis, Takeda, Fresenius Medical care.

MP320 RESISTIN INFLAMMATION AND CAROTID ARTERY ATHEROSCLEROSIS IN HAEMODIALYSIS PATIENTS

Yelda Cinar, Siren Sezer, Zubeyde Arat, F. Nurhan Ozdemir. *Nephrology, Baskent University Faculty of Medicine, Ankara, Turkey*

Introduction and Aims: Resistin is a peptide hormone that inhibits adipogenesis. A significant association between resistin concentration and inflammation, atherosclerosis has been demonstrated in non renal disease. However, it is known that high levels of resistin have been reported in chronic renal failure patients, but data on the role of resistin is scare in this patients.We aimed to quantify serum resistin levels and to explore correlations between resistin and inflammatory markers, carotid atherosclerosis in HD patients.

Methods: We studied 44 HD and compared their serum resistin with that of 17 age matched healthy controls. Besides resistin levels, the laboratory and demographic were studied. We recorded risk factors for cardiovascular disease. We used B-mode ultrasonography to determine carotid artery intima-media (IMT) thickness and the presence of atherosclerotic plaques by same radiologist.

Results: Serum resistin levels were higher in HD patients than in healthy controls ($p < 0.0001$). Our results revealed that plasma resistin positively correlated with age, hemoglobin, calcium and C-reactive protein (CRP) in HD patients and in control group positive correlation between resistin and creatinin, potassium, CRP as well as negative correlations between resistin and HDL. Only CRP was independent predictor of high resistin in HD patients. In a univariate regression model, serum resistin correlated with CRP in HD patients ($p < 0.0001$, $\beta = 4.52$, $r^2 = 0.38$). Compared with patients without the presence of atherosclerotic plaques, those with the presence of atherosclerotic plaques had higher resistin levels ($p < 0.0001$). Mean carotid IMT was significantly greater in HD patients than in controls ($P < 0.005$). In HD patients, carotid IMT was correlated positively with smoking (r=0.41, p=0.002), age (r=0.42, p=0.001), LDL (r=0.27, p=0.042), CRP (r=0.54, p=0.000), resistin (r=0.38, p=0.004) and the presence of the atherosclerotic plaques (r=0.49, p=0.000).

Conclusions: Serum resistin levels were increased and associated with inflammation and atherosclerosis in our HD group.

MP321 USE OF A POINT-OF-CARE PLATELET ASSAY IN THE HEMODIALYSIS POPULATION: PRECISION, REPRODUCIBILITY, AND CORRELATION WITH THE GOLD STANDARD

Yin Ping Liew[1], Rachel Fissell[1], Kandice Kottke-Marchant[2], Deepak L. Bhatt[3], Robert Heyka[1]. *[1]Nephrology and Hypertension, Cleveland Clinic; [2]Pathology and Laboratory Medicine, Cleveland Clinic; [3]Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA*

Introduction and Aims: Poor cardiovascular outcomes are associated with aspirin (ASA) resistance. The VerifyNow rapid platelet function assay is portable and convenient. Prior studies have shown that this assay is accurate, reproducible, and correlates well with the gold standard assay, optical aggregometry, in the healthy population. Accuracy of the VerifyNow assay in the hemodialysis (HD) population has not yet been assessed. This pilot study was conducted to assess the VerifyNow assay in the end-stage renal disease (ESRD): its precision, reproducibility, and correlation with the gold standard assay.

Methods: Twenty-five adult ESRD who were on HD for at least 2 months, and not on ASA or other medications known to interfere with platelet function, were enrolled. All patients had normal platelet function studies with recent platelet counts $\geq$150K/uL and Hgb $\geq$10g/dl. The VerifyNow assay platelet function result was reported in aspirin reaction units (ARUs) and the gold standard assay result was reported in % of platelet aggregation. Three measures from Ultegra per subject were used to evaluate reproducibility and precision, and the mean ARUs was correlated with the gold standard assay mean % platelet aggregation to adenosine diphosphate (ADP) and arachicdonic acid (AA). Precision of the mean ARUs was assessed via the coefficient of variation (CV) along with the 95% interval. The weighted mean of the Spearman correlation coefficients was used to evaluate the reproducibility, along with the percentage of the replicates that were within 30 ARUs of each other. Correlation between the VerifyNow and gold standard was reported using Spearman's correlation coefficient. Fisher's exact testing was used to compare the % of ARUs within normal range (631-676) to % of AA and ADP within normal range (AA: 66-100%; ADP: 70-100%).

Results: Mean age was 53$\pm$17 years with a mean Hgb 12 $\pm$1g/dl and a mean platelet count 260$\pm$76K/uL. The mean ARUs was 647 $\pm$ 26 with CV of 4% (95% CI 2.88% to 5.16%). The mean maximal ADP

aggregation was 84±10% and the mean maximal AA aggregation was 76±19%. The VerifyNow assay results were highly reproducible with 100% of the replicates within 30 ARUs (4.6% of 647) of each other and showed an overall weighted correlation coefficient of 0.65. Correlation between the VerifyNow assay and the gold standard assay was 0.50 (P=0.01). There was no statistically significant difference in % of ARUs within normal range when compared to % of ADP and AA within normal range: 92% ARUs vs. 92% AA (P >0.99), 92% ARUs vs. 92% ADP (P >0.99).

Conclusions: Point of care platelet assessment with the VerifyNow assay in this patients sample was precise. Values were highly reproducible and correlated with the gold standard assay. Future studies will use the VerifyNow assay in ESRD patients on ASA to measure prevalence of ASA resistance, determine antiplatelet effect of different doses of ASA, and examine associations between cardiovascular outcomes and ASA resistance.

MP322 SERUM FETUIN-A LEVELS, AORTIC CALCIFICATION AND MORTALITY IN CHRONIC HAEMODIALYSIS PATIENTS

Aikaterini Papagianni[1], Spyros Dovas[1], Efthimia Zafeiriadou[2], Konstantinos Tsinoglou[2], Anna-Maria Belechri[1], Christos Bantis[1], Georgios Efstratiadis[1], Efstathios Alexopoulos[1], Dimitrios Memmos[1]. *[1]Nephrology, Hippokration General Hospital, Thessaloniki, Greece; [2]Radiology, Hippokration General Hospital, Thessaloniki, Greece*

Introduction and Aims: Vascular calcification is a common complication in end-stage renal disease and is associated with the increased cardiovascular (CVD) mortality observed in these patients. The aim of this prospective study was to evaluate the associations between serum fetuin-A levels, aortic calcification and both all-cause and CVD mortality in stable chronic haemodialysis (HD) patients.

Methods: Eighty-five patients (45 male, mean age 58±17 years, mean HD duration 61±62 months) consecutively entered the study. Fourteen patients (15.6%) had diabetes mellitus and 28 patients (32.9%) had a clinical history of CVD. In all patients, the abdominal aorta was examined on consecutive noncontrast computed tomographic scans and aortic calcification index (ACI) was calculated as the proportion of aortic circumference covered by calcification. High sensitivity CRP (hsCRP) was measured by nephelometry. Serum fetuin-A was determined by sandwich immunoenzymometric assay using commercially available standard kits (BioVendor GmbH, Heildelberg Germany).

Results: During a mean follow-up period of 25 months (range 2 to 37 months), 24 patients died, most of CVD causes (54.2%). Compared with survivors, non-survivors had significantly lower median fetuin-A levels (0.447 vs 0.410 g/L, p=0.031) and significantly higher median ACI (78 vs 45%, p<0.0001). Kaplan-Meier analysis showed that compared with patients with fetuin-A levels >median (0.456 g/L, n=43), patients with fetuin-A <0.456 g/L displayed significantly higher all-cause and CVD mortality rate (log-rank 5.54, p=0.02 and log-rank 7.32, p=0.007, respectively). Kaplan-Meier analysis also showed that compared with patients with ACI <50% (n=35, 41% of the patients), patients with ACI >50% displayed significantly higher all-cause but only marginally significant CVD mortality rate (log-rank 8.86, p=0.003 and log-rank 3.84, p=0.05, respectively). Survival was also analyzed by univariate and multivariate Cox regression analyses. In univariate analyses, all-cause mortality was significantly associated with age (p=0.001), hsCRP (p<0.0001), serum albumin (p=0.01), fibrinogen (p=0.002), fetuin-A levels (p=0.047) and ACI (p=0.002). In multivariate analyses, all-cause mortality was significantly associated with age (p=0.007), hsCRP (p=0.019) and fetuin-A levels (p=0.023). CVD mortality was significantly associated with age (p=0.035), history of diabetes mellitus (p=0.034), hsCRP (p<0.0001), fibrinogen (p=0.008) and ACI (p=0.024), but not fetuin-A levels, in univariate analyses. In multivariate analyses, CVD mortality was significantly associated with hsCRP (p<0.0001), history of diabetes mellitus (p=0.004) and marginally with fetuin-A levels (p=0.052).

Conclusions: In chronic haemodialysis patients, serum fetuin-A levels predict all-cause mortality, while hsCRP appears to be a better predictor of CVD mortality in this group of patients.

MP323 PROGRESSION OF VASCULAR CALCIFICATION FROM THE START OF DIALYSIS TREATMENT

Marlies Noordzij[1], Willem Jan Bos[2], Elisabeth W. Boeschoten[3], Friedo W. Dekker[4], Raymond T. Krediet[5], Johanna C. Korevaar[1]. *[1]Department of Clinical Epidemiology, Biostatistics, and Bioinformatics, AMC, University of Amsterdam, Amsterdam, Netherlands; [2]Department of Internal Medicine, St. Antonius Hospital, Nieuwegein, Netherlands; [3]Hans Mak Institute, Naarden, Netherlands; [4]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands; [5]Department of Nephrology, AMC, University of Amsterdam, Amsterdam, Netherlands*

Introduction and Aims: Cardiovascular disease (CVD) is the leading cause of death in dialysis patients and the development of vascular calcification might play an important role in cardiovascular morbidity and mortality. We aimed to assess the prevalence of vascular calcification in the aortic arch of incident dialysis patients. In addition, we evaluated the progression of calcification over time.

Methods: 428 patients who started haemodialysis (HD) or peritoneal dialysis (PD) between 1997 and 2006 were included. Annual chest X-rays of these patients were screened for vascular calcification in the aortic arch and patients were scored as having no, moderate, or severe calcification. Progression of calcification was calculated by subtracting the first calcification score from the last available score. We used multivariate logistics regression to determine which clinical variables were associated with progression.

Results: Mean (SD) age was 61 (15) year, 63% were male and 62% were treated with HD. At baseline, 223 (52%) patients had moderate calcifications, 107 (25%) patients had severe calcifications and the remaining 98 (23%) patients had no calcifications. In 273 of 331 patients with no or moderate calcifications at baseline, X-rays were available for follow-up. The mean (SD) time between the first and last X-ray was 28 (22) months. We found that 82 patients (19%) had progression of vascular calcification during follow-up. After adjustment for age, sex, treatment modality, calcium, phosphorus, iPTH, albumin, and diabetes mellitus as primary kidney disease, we found that higher age (Odds Ratio [OR]: 1.04, 95% confidence interval [CI]: 1.02 to 1.06), calcium > 2.4 mmol/L (9.5 mg/dL, OR: 2.85, 95% CI: 1.28 to 6.34), and higher albumin level (OR: 1.07, 95%CI: 1.00 to 1.13) were statistically significantly associated with an increase in calcification score over time.

Conclusions: Vascular calcification in the aortic arch is widespread in HD and PD patients at the start of dialysis. Moreover, vascular calcification progressed during dialysis treatment in a fifth part of dialysis patients and progression was associated with higher age, hypercalcaemia and high albumin level.

Disclosure: This study was funded by unrestricted grants from the Dutch Kidney Foundation and Genzyme. The sponsors of the study were not involved in study design; in the collection, analysis, and interpretation of data. They were also not involved in the writing of the report; and in the decision to submit the report for publication.

MP324 CORONARY REVASCULARIZATION IN PREVALENT DIALYZED PATIENTS: A SINGLE-CENTRE EXPERIENCE

Paola David, Carlo Navino, Andreana De Mauri, Doriana Chiarinotti, Carlo Ruva, Mariangela De Maria, Federica Capurro, Andrea Ranghino, Martino De Leo. *S.C.O. Dialysis and Nephrology, A.O. Maggiore della Carità, Novara, Italy*

Introduction and Aims: Cardiovascular disease (CVD) and coronary arteries diseases (CAD) are the main cause of mortality (44-60%) and morbidity in dialyzed (HDpts) and kidney-transplanted patients (KTpts). Since many kidney recipients (13%) have already acquired CVD and CAD at transplantation time, clinicians have to perform a tight cardiac assessment in all HDpts, mainly in kidney transplant (KT) candidates. Finally, coronary revascularization should be performed in patients with inducible ischemia at the stress test, before graft procedure.

The aim of our retrospective study is to evaluate the efficacy of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) in HDpts and KTpts candidates. We further investigated risk factors for CAD and CVD mortality in our population.

Methods: We enrolled 256 hemodialyzed patients (HDpt) attending our centre from January 2001 to December 2005 (174 Male 88 Female; 67±15

years). 45 of them were checked to assess candidacy for KT. 21 subjects (19 M 2 F; 64,2 years, 69±71 months of dialysis) underwent to a CABG (13) and PTCA (8), because of angina or myocardial infarction or in presence of several risk factors requiring invasive evaluation (1 HDpts). We recorded also several clinical and humoral risk factors as diabetes, hypertension, previous CAD, serum lipids, homocysteine, parathormone. The mean follow-up period was 44 months.

Results: Among patients receiving PCI, revascularization was obtained in 90% and the restenosis rate was 1% at 1 year; mortality rate was 12% and 37% at 3 months and 5 years respectively.

Among patients receiving CABG revascularization was obtained in 100% and the restenosis rate was 17% at the end of the follow up; mortality rate was 23% and 46% at 3 months and 5 years respectively. According to the literature, 7 (14%) of 45 HDpts screened for KT received PCI (4) or CABG (3) successfully and in this group no deaths were observed.

In our population only high levels of serum omocisteynemia and parathormone correlated with CAD necessitating of an invasive correction.

9 of 21 treated pts died during the follow up. The time of dialysis before procedures and the time occurred between clinical symptoms or suspicious of acute coronary syndrome and revascularization procedure were significantly associated to the mortality rate.

Conclusions: Our study demonstrates that tight and early cardiac assessment in HDpts is mandatory to reduce CAD and CV mortality. Especially in kidney-transplant candidates, nephrologists must perform as soon as possible every hearth procedure to minimize CV risks not only for the "waiting in list period" but also for the life expectancy after kidney transplantation.

MP325 MAGNESIUM THERAPY HELPS TO IMPROVE CAROTID INTIMA MEDIA THICKNESS IN HEMODIALYSIS PATIENTS

Faruk Turgut[1], Mehmet Kanbay[1], Melike Rusen Metin[2], Ebru Uz[1], Nuket Bavbek[1], Ali Akcay[1]. *[1]Department of Nephrology, Fatih University School of Medicine, Ankara, Turkey; [2]Department of Radiology, Fatih University School of Medicine, Ankara, Turkey*

Introduction and Aims: Accelerated atherosclerosis is one of the primary causes of morbidity and mortality in hemodialysis (HD) patients. Magnesium is an important mineral acting natural calcium antagonist. There are some evidences that magnesium deficiency might be associated with increased atherosclerosis in HD patients. The aim of this study is to evaluate the effect of oral magnesium supplementation as a phosphate binder on carotid intima media thickness (IMT) in HD patients.

Methods: Forty four patients on maintenance HD (29 female and 15 male, mean age 57.1±16.8) were included to the study. Initially and 2 months later, serum calcium, phosphate, magnesium and parathyroid hormone levels were measured and IMT of both common carotids was assessed by B-mode ultrasound in each patient. Thirty two patients were given oral magnesium citrate as a phosphate binder for two months and 12 patients were included as control group which not given magnesium. Baseline and at 2 months values were compared between groups.

Results: There was no significant difference between initial and at two months values of groups regarding mean Kt/V, blood pressures, serum magnesium, calcium, phosphate and parathyroid hormone (Table 1). Bilateral carotid IMT was significantly improved in patients treated with magnesium citrate compared to initial values (0.97±0.3 vs 0.70±23 p=0.001 for left carotid artery and 0.95±0.3 vs 0.78±0.3, p=0.002 for right carotid artery). On the other hand, there were no significant changes in control subjects' carotid IMT (0.75±0.3 vs 0.80±0.2, p=0.6 for left carotid artery and 0.82±0.2 vs 0.85±0.3, p=0.5 for right carotid artery).

Table 1. Characteristics and some laboratory parameters of the patients

Variables	Magnesium group (n=30)	Control group (n=12)	p value
BMI (kg/m^2)	25.7±5.7	24.3±5.7	0.56
Duration on dialysis (month)	41.3±28.8	19.5±9.2	0.011
Baseline SBP (mmHg)	129.6±22.8	131.6±21.6	0.93
Baseline DBP (mmHg)	76.0±13.0	80.0±9.5	0.27
SBP at two months (mmHg)	127.6±20.9	126.6 ±23.4	0.73
DBP at two months (mmHg)	77.0±12.0	76.6±6.5	0.31
Baseline Kt/V	1.39±0.24	1.22±0.13	0.06
Kt/V at two months	1.51±0.87	1.32±0.17	0.63
Baseline magnesium (mg/dl)	2.46±0.45	2.15±0.32	0.02
Magnesium at two months (mg/dl)	2.69±0.39	2.38±0.40	0.04
Calcium (mg/dl)	9.4±0.9	8.7±0.5	0.013
Phosphate (mg/dl)	4.9±1.6	5.1±2.1	0.89
Parathyroid hormone (pg/ml)	392.7±346.4	198.2±133.7	0.079

BMI; Body mass index, SBP; Systolic blood pressure, DBP; Diastolic blood pressure.

Conclusions: Based on the present data, magnesium may play an important protective role in the progression of atherosclerosis in patients on dialysis; however, further studies are required to determine more definite results.

MP326 B-TYPE NATRIURETIC PEPTIDE AND PLASMA REFILLING IN DIALYSIS SESSION

Andreana De Mauri, Carlo Navino, Paola David, Doriana Chiarinotti, Carlo Ruva, Mariangela De Maria, Federica Capurro, Andrea Ranghino, Martino De Leo. *S.C.O. Dialysis and Nephrology, A.O. Maggiore della Carità, Novara, Italy*

Introduction and Aims: Cardiovascular disease (CVD) is the main cause of mortality and morbidity in dialyzed patients (HDpts). B-type natriuretic peptide (BNP) is a cardiac neurohormone released in response to the extracellular volume expansion and the blood pressure (BP) overload; it is a risk factor for heart failure and CVD. BNP is increased in HDpts because of impaired renal clearance and changes in plasma volume; several studies indicate that BNP is also useful to assess dry weight and vascular refilling in HDpts.

The aim of our study is to evaluate relationship between BNP and BP, net ultrafiltration (UF), the measures of refilling as the blood volume reduction rate (BV/WL) and the regulator of extracellular volume as renine-angiotensin-aldosterone system (RAAS).

Methods: We recruited HDpts older than 18 years, after a three-days wash out of RAAS inhibitors drugs. We recorded pre and post-HD BP and weight and the BV/WL (decline in blood volume divided by weight loss x 100), achieved by an online optical method based on the reflection of infrared light by erythrocyte membranes (Hemocontrol, Hospal, Italy). Serum BNP, aldosterone, renin, C-reactive protein (CRP), I-troponin (t-I) and routine biochemistry were measured before HD; BNP, aldosterone and renin were also measured after HD. For statistical analysis t-Student and Mann-Whitney test were used.

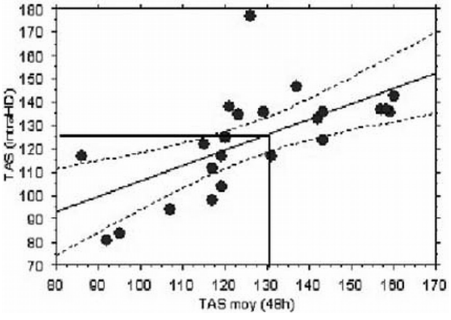
Results: We enrolled 27 pts, 14 (52%) males and 13 (48%) females, aged 70.2±14.4 years, receiving three weekly HD, 41% with diffusive and 59% with convective modality; 22 (81.5%) had hypertension and 14 (51.9%) diabetes. The causes of renal failure were diabetes (37%), nephroangiosclerosis (18.5%), glomerulopathy (11.1%), interestitial and cystic diseases (18.5%) and unknown (14.9%). Serum values were BNP preHD 476±741 and post 221±271 pg/ml (p=0.012); aldosterone preHD 358±382 and post 151±124 pg/ml (p=0.02), renin preHD 26±35 and post 25±27 mU/ml (p=ns). The mean BV/WL was -3.8±1.9% and UF 2.6±0.8l. Patients with BNP higher than median value (330 pg/ml) (group A) had higher preHD systolic BP (146±23vs128±22 mmHg, p=0.05), higher URR (71,4±16vs65,8±3,6%, p=0.04), more HD days (2136±1580vs992±1050, p=0.04), higher CRP (0,3±0,2vs1,1±1,8 mg/dl p=0.07) than patients with lower (group B). In the group A, more patients were diabetic (80vs16%, p=0.001), performed a convective treatment (73vs41%, p=0.04), had a preHD aldosterone lower than mean value (86vs50%, p=0.003), preHD t-I above normal range (60vs13%,p=0.002), URR >66% (86vs41%, p=0.01) and Kt/V >1.4 (80vs50%, p=0.05). Aldosterone, renin, tro-I, UF, BV/WL and other humoral parameters were not different between A and B.

Conclusions: Our study shows that BNP is elevated and declines after the HD session; HDpts have also hyperreninemic hyperaldosteronism with aldosterone decreasing after HD. BNP is correlated with diabetes, time of HD and aspecific increased levels of heart necrosis enzymes. The lack of correlation with UF, vascular refilling and RAAS may be explained by an unknown time needed to achieve the steady state of volume status.

MP327 INTRADIALYTIC BLOOD PRESSURE (BP) ANALYSED BY QCONTROL IS CORRELATED WITH INTERDIALYTIC BLOOD PRESSURE EVALUATED BY 48H-AMBULATORY BP MONITORING

Corina Stanescu[1], Ibrahim Moudachirou[1], Bernard Bene[2], Francoise Leonetti[1], Rehouni Boulahrouz[1], Philippe Le Cacheux[1], Christophe Charasse[1], Kim Seng Ang[1], Pierre Simon[1]. *[1]Departement of Nephrology, Y Le Foll Hospital, Saint-Brieuc, Brittany, France; [2]Gambro Industries, Lyon, France*

Introduction and Aims: Hypertension in chronic haemodialysis (HD) patients contributes significantly to cardio-vascular morbidity and mortality.Ambulatory BP monitoring (ABPM) is regarded as superior to random BP monitoring in predicting end-organ damage from elevated blood pressure. Generaly, BP is variable between HD sessions (interdialytic periods) and during HD sessions (peri and intradialytic period); interdialytic blood pressure is evaluated by 48h-ABPM, perdialytic BP (pre and post sessions) measured by nurse is assimilated to office or clinic BP; intradialytic BP can also be monitored and was assured in our HD centre by Qcontrol, software which processes periodicaly the database recorded on Exalis database (Integra monitors - Gambro Industries). The aim of our study was to evaluate a possible correlation between interdialytic BP measured by ABPM and intradialytic BP registred and analysed by Qcontrol.
Methods: This prospective study was performed between October 2005 and October 2006 including 23 HD patients (10 M and 13 F, mean age 70 years, 21 conventional HD and 2 daily HD); mean dry weight was 64 kg (42,5-89), mean interdialytic weight gain: 1,85 kg. For each patient, 48h-ABPM was performed by Spacelabs monitor with 160-180 succesive measures.Mean pre and post BP values were calculated on 30-40 sessions during 3 months; intradialytic BP were processed on the Integra monitors and recorded in Exalis database; the Qcontrol software processed periodically this database in order to display BP profile on 6 months; thus, we obtained 20 mesures/session and more than 600 mesures/patient on 3 months. Statistical analysis were performed with Statview.
Results: The average 48-h ABPM was 127/69 mmHg, diurne values 129/71mmHg and nocturne values 123/65 mmHg; the average pre HD sesssion Bp was 145/78 mmHg and post HD session BP 138/74 mmHg; the average intradialytic BP provided by Qcontrol was 124/67 mmHg; the comparison of BP values permits to find a strongly correlation between interdialytic BP and intradialytic BP ($p<0.0008$, $r=0.405$) (figure)



Conclusions: Qcontrol improves the BP monitoring during HD sessions. A strong correlation exists between intradialytic BP and interdialytic BP in haemodialysis patients, Q control permits to evaluate BP profile in this population.

MP328 CORONARY ARTERY DISEASE DIAGNOSIS IN HAEMODIALYSIS PATIENTS

Ines Aires[1], Patricia Matias[1], Ana Ferreira[1], Tiago Amaral[1], Cristina Jorge[1], Celia Gil[1], Luis Mourao[2], Anibal Ferreira[1]. *[1]NIDAN, Hemodial e Dialverca, VFX, Portugal; [2]UIV, Hospital Curry Cabral, Lisbon, Portugal*

Introduction and Aims: Cardiovascular disease is common in haemodialysis (HD) patients (pts). In addition to traditional risk factors, uraemia and dialysis specific factors contribute to vascular disease, which is associated with high mortality in this specific population. Non invasive testing of coronary artery disease (CAD) is important, especially in pts proposed for renal transplantation (Tx). In this study we investigated sensibility and specificity of myocardial stress scintigraphy (MS) and coronary angiography (CA) on CAD diagnosis.
Methods: We enrolled 198 prevalent pre-dilutional on-line haemodiafiltration pts. Eighty six pts had MS, 59,3% male, mean age 59,6±10,9 years, 34,9% diabetic. Mean chronic renal disease time was 6,1±5,4 years and mean HD time until MS was 22,3±27,4 months. MS was done for: renal Tx (26,7%); electrocardiogram abnormalities (25,6%); angina symptoms (20,9%); diabetes mellitus (15,1%) and non-cardiac ischemia (11,6%). In these 86 pts, left ventricular hypertrophy and cardiac valve calcification assessed by echocardiogram, were respectively present in 48,8% and 31,4%. Left ventricular mass index was calculated in 81 pts (mean 137±37 g/m^2). Vascular calcification (VC) was evaluated in 77 pts using a simple vascular calcification score based on plain radiographic films of hands and pelvis.
Results: MS was positive for CAD in 31,4% of pts. CA was performed in 26 pts, and coronary stenosis (positive if > 50%) was found in 57,7%. In diabetics, MS was positive in 40%. Seventy five percent of those submitted to CA had lesions. No relation was found between the cause of the exam request and MS and CA result. Uni and multivariate analysis were performed and a $p<0,05$ was considered significant. Age (r=0,03) and VC (r=0,03) positively correlated with positive MS. VC correlated with positive CA on uni and multivariate analysis (r=0,04; $p<0,05$). In our study, MS sensitivity was 73,3% and specificity 18,2%. Positive predictive value was 55% and negative predictive value was 33% (CI 95%).
Conclusions: In low risk pts VC can easily predict CAD. As MS sensitivity and specificity is low, CA is the best diagnostic test in HD pts and besides, it allows prompt therapeutic intervention.

MP329 EVALUATION OF CORONARY CALCIFICATION AND BONE MASS IN DIALYSIS PATIENTS WITH SEVERE HYPERPARATHYROIDISM (sHPT) ONE YEAR AFTER PARATHYROIDECTOMY (PTX)

Fabiana R. Hernandes, Fellype C. Barreto, Lillian Rocha, Maria Eugênia F. Canziani, Sérgio A. Draibe, Aluizio B. Carvalho. *Internal Medicine/Division of Nephrology, Federal University of São Paulo, São Paulo, Brazil*

Introduction and Aims: Coronary calcification (CAC) is an important cause of morbidity and mortality in dialysis patients. Severe secondary hyperparathyroidism (sHPT) has been implicated in its development. The aim of this study was to evaluate the progression of CAC in dialysis patients with sHPT one year after PTX.
Methods: Nineteen dialysis (HD18/PD01) patients (age: 45±11.2 years-old, 63% female, time on dialysis: 105±46.7 months) with sHPT (iPTH > 500 pg/mL) were submitted to coronary tomography, DEXA, laboratorial evaluation (ionized calcium, phosphorus, alkaline phosphatase, iPTH) at baseline (PTX) and after one year follow-up.
Results:

Baseline and one year follow-up data

	Baseline	One year follow-up	p
iCalcium (mmol/L)	1.33±0.10	1.19±0.10	< 0.001
Phosphorus (mg/dL)	6.8±2.1	5.3±1.6	< 0.006
Alk. phtase (U/L)	781±650	109±42	< 0.001
iPTH (pg/mL)	1987±551	75±77	< 0.001
CaS (AU)	722±1122	799±1171	< 0.05
BMD L2L4 (g/cm^2)	1.022±0.279	1.177±0.269	< 0.001
BMD Neck (g/cm^2)	0.821±0.211	0.971±0.234	< 0.001

CaS: calcium score; BMD: bone mineral density.

Delta CaS and BMD L_2L_4 were 76.5±153.7 AU and 0.155±0.106 g/cm^2. No association was found between delta CaS and delta BMD L_2L_4. The cumulative dosis of elemental calcium and calcitriol during the follow-up were 1.15±0.6 g/day and 1.03±0.8 mg/day, respectively. No correlation was observed between these parameters and delta CaS or BMD L_2L_4.
Conclusions: In dialysis patients, there was a worsening of CAC after one year of PTX in the presence of an improvement of bone mass.

MP330 ASSOCIATION BETWEEN ARTERIAL AUGMENTATION INDEX AND CALCIUM-, PHOSPHATE AND BONE METABOLISM IN HEMODIALYSIS PATIENTS

Zsofia Nemeth[1], Eszter Vamos[1], Csilla Almasi[1], Adrienn Marton[1], Klara Berta[2], Gyorgy Deak[1], Gabriella Beko[3], Andras Szabo[4], Petra Horony[1], Aniko Kovacs[1], Csaba Ambrus[1], Miklos Zsolt Molnar[1], Csaba Horvath[1], Istvan Mucsi[1,5]. *[1]1st Department of Medicine, Semmelweis University, Budapest, Hungary; [2]Fresenius Medical Care Hungary, Budapest, Hungary; [3]Central Diagnostic Laboratory, Semmelweis University, Budapest, Hungary; [4]1st Department of Pediatrics, Semmelweis University, Budapest, Hungary; [5]Nephrology, University of Toronto, Toronto, ON, Canada*

Introduction and Aims: An increasing attention has recently been directed towards the association between calcium, phosphate and bone metabolism and cardiovascular morbidity and vascular calcification in patients with chronic kidney disease. Arterial augmentation index (AIx) has been shown to predict cardiovascular morbidity and outcome in different CKD patient populations.
Here we analyzed the association between measures of calcium, phosphate and bone metabolism and AIx in hemodialysis patients.
Methods: Arterial augmentation index was assessed in 77 hemodialysis patients with a validated, small portable tonometer (PulsePen). Laboratory and socio-demographic information was collected from the charts. Bone densitometry was assessed by dual x-ray absorptiometry (DEXA), quantitative bone ultrasound (QUS) was also performed.
Results: Mean age was 60±12 years, median dialysis vintage 43 months. Fifty five percent of the patients were males, 35% were diabetics. Mean AIx was 12.55±6.55. AIx was significantly correlated with age (r=0.401, $p<0.001$). Significant negatíve correlation was found between AIx versus serum beta-2-microglobulin (r=-0.386, $p<0.001$), bone density measured at the radius (r=-0.387, $p<0.001$) and broad band ultrasound attenuation assessed by QUS (r=-0.300, $p<0.01$).
In multivariate analysis bone density measured at the radius remained independently associated with AIx after controlling for potential covariables.
Conclusions: These results are consistent with the hypothesis that disturbed bone metabolism is associated with increased arterial stiffness in patients on maintenance dialysis.

MP331 DIALYSIS MODALITY AS A RISK FACTOR IN P WAVE DISPERSION

Demet Yavuz, Alpaslan Altunoglu, Mujdat B. Canoz, Beril Akman, Siren Sezer, Zubeyde Arat, F. Nurhan Ozdemir. *Nephrology, Baskent University Faculty of Medicine, Ankara, Turkey*

Introduction and Aims: Atrial fibrillation is a frequent arrhythmia in patients with dialysis patients. Increased P wave dispersion (PWD) has been found to be associated with paroxysmal atrial fibrillation (AF). Our aim was to assess the factors affecting P wave duration/dispersion in non-diabetic ESRD patients on hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD).
Methods: Ninety (mean age: 50.8±12.4 years; male 45; mean dialysis duration:125.5±69.8 months) patients on HD and 51 (mean age:45.7±11.9 years; male 28; mean dialysis duration:100.1±56.5 months) patients on CAPD were enrolled in this study. CAPD patients used 1.36, 2.27 or 3.86% glucose containing 2000-3000 ml dialysate solutions (Baxter), with 4-5 times dwells daily. All HD patients were dialyzed on a 4-5 h, 3 times weekly schedule. The patients clinically evident atherosclerosis, pulmonary disease and those taking antiarrythmic drugs were excluded. The difference between maximum and minimum P wave duration was calculated and defined as P wave dispersion ($P_d = P_{max} - P_{min}$). Serum samples were obtained in each patient for serum BUN, creatinine, sodium, potassium, calcium, phosphate, total cholesterol, LDL, triglyceride, albumin, CRP, iPTH, hemoglobin, serum iron levels, iron binding capacity and ferritin levels predialysis for HD, out patient control time for CAPD patients. Possible P wave dispersion risk factors such as age, dialysis duration, hypertension, modality of dialysis, serum electrolyte-albumin-CRP and hemoglobin levels were analyzed. The analysis was evaluated in consideration with the interdialytic weight gain and mean blood pressure values of the patients.
Results: P wave dispersion and minimum P wave duration were negatively correlated in all patients (r=-0.348, p=0.001). P wave dispersion was significantly higher in hemodialysis than the CAPD patients (35.05±4.1 ms, 27.88±2.2 ms; $p<0.001$ respectively). P wave dispersion were positively correlated with serum sodium (r=0.224, p=0.008), uric acid (r=0.205, p=0.015), albumin (r=0.36, $p<0.001$), potassium (r=0.263, p=0.002) and negatively correlated with serum iron levels (r= -0.211, p=0.012), iron binding capacity (r= -0.166, p=0.049), total cholesterol (r= -0.405, $p<0.001$) and LDL (r= -0.368, $p<0.001$). When P wave dispersion risk factors were assessed with multivariate linear regression, significant differences was found in dialysis modalities (β=-7.525, $p<0.0001$).
Conclusions: Apart from the well-known risk factors, HD therapy modality can cause changes in P wave duration/dispersion and increase the risk of atrial fibrillation. CAPD therapy may be a better dialysis modality in high risk patient group for physiologic continuous ultrafiltration and blood pressure control.

MP332 SERUM PHOSPHATE CONTROL AND MORTALITY IN HEMODIALYSIS: RESULTS FROM THE RISCAVID STUDY

Sabrina Paoletti, Vincenzo Panichi, Roberto Bigazzi, Emanuela Mantuano, Sara Beati, Giada Bernabini, Valentina Marchetti, Giovanni Grazi, Giacomina Fontana, Giovanni Manca Rizza, Giuliano Barsotti, Roberto Palla. *RISCAVID Study Group, Italy*

Introduction and Aims: The RISCAVID (Cardiovascular risk in dialysis) study is a prospective, observational study that includes all haemodialysis (HD) patients afferent to all dialysis centres in the north-west part of Tuscany. Aim of the study is to elucidate the role of the various risk factors on mortality and morbidity in dialysed patients; in particular, the attention is here focused on mineral metabolism disorders in HD patients
Methods: The study started on June 2004. All prevalent patients in HD afferent to a dialysis centre in the north-west area of Tuscany were considered eligible for the study. At the time of enrolment demographic, clinical and laboratory data of the whole population were registered as well as comorbidity conditions (CV disease) that were established by anamnestic and instrumental information. The mineral metabolism was studied by the determination of serum phosphorus (P), calcium (Ca), calcium x phosphorus product (CaxP) and the intact parathyroid hormone (iPTH). In addition, the use of calcium supplements, as well as vitamin D, phosphate binders and cinacalcet were evaluated. The cohort was followed up for 24 months and overall mortality, CV mortality and CV major non fatal events (acute myocardial infarction, stroke and ictus) were registered.
Results: A total of 757 HD patients (mean age 66±14 years, mean dialytic vintage 70±76 months, diabetes 19%) were enrolled in the RISCAVID study. Our data confirm the high mortality rate in dialysed patients (all-cause mortality 12.9%/year; CV mortality 5.9%/year). The baseline data showed mean Ca level of 9.18±3.2 mg/dl, mean P level of 4.81±1.67 mg/dl, CaxP product of 47.2±18.3 mg^2/dl^2 and iPTH of 277±284 pg/dl. However, more than 30% of patients presented serum mineral concentrations out of the international guidelines ranges; in particular 29.8% of the population showed P value >5.5mg/dl whereas P was <3.5mg/d in 16.7% and CaxP product was >55 mg^2/dl^2 in 20.9% of patients. Elevated P levels (> 6.5 mg/dl) and an elevated CaxP product (> 65 mg^2/dl^2) are associated with an increased relative risk of CV mortality (Risk Ratio, RR, for fatal CV event 2.1, 95% interval confidence (IC) 1.3-3.4, and 3.2 respectively; $p<0.001$, 95% IC 1.6-5.9. It has to be underlined that also low P levels (< 3.5 mg/dl) are associated with an increased RR of non CV death (RR 1.6; $p<0.01$, 95% IC 1.0-2.6). Moreover, Cox regression analysis showed that - after adjustment for level of serum phosphorous, age, dialytic vintage and comorbidity - patients treated with Sevelamer hydrochloride during the 24 four-months follow-up were associated with a significantly lower mortality. ($p<0.001$).
Conclusions: In the RISCAVID study more than 30% of patients were shown to have mineral metabolism parameters out from the international guidelines values. Elevated levels of P and CaxP product are associated with an increased CV risk, whereas low P associated to elevated levels of CRP are tightly related to an increased risk of non CV death, probably due malnutrition.

MP333 CLOSE RELATION BETWEEN CORONARY ARTERIES CALCIUM SCORE AND COMMON CAROTID ARTERY INTIMA MEDIA THICKNESS IN HAEMODIALYSIS PATIENTS

Ilona Kurnatowska[1], Piotr Grzelak[2], Ludomir Stefanczyk[2], Michal Nowicki[1]. *[1]Department of Nephrology, Hypertension and Kidney Transplantation, Medical University, Lódz, Poland; [2]Department of Radiology and Diagnostic Imaging, Medical University, Lódz, Poland*

Introduction and Aims: Increased calcium deposition within the coronary artery walls (calcium score-CS) correlates with a higher risk of cardiovascular complications (CVC) in haemodialysis patients. Common carotid artery intima media thickness (IMT) is a simple test used for imaging atherosclerosis. The relation between IMT and CS is debatable and the latter measurement is much less accessible and expensive. The aim of this study was to assess CS and IMT in HD patients and evaluate the relationship between these parameters and HD duration, lipid profile, serum albumin and calcium-phosphate balance.
Methods: We performed a cross-sectional study in 47 HD patients (31 M, mean age 56.8±11.4 yrs, and 16 F mean age 56.0±7.5 yrs) with no history of major cardiovascular complications. The mean time on HD was 51.7±10.3 months. Serum lipids, calcium, phosphate, PTH, albumin and hemoglobin were measured before the mid-week dialysis session. IMT was measured with ultrasound and calcium score with multidetector computer tomography.
Results: The mean calcium score index in HD patients was 1055±232 (normal values < 400) and was higher in men (1285±286) than in women (545±334). IMT was 0.957±0.219 mm and was also higher in men (1.006±0.03 mm) than in women (0.85±0.05 mm). We found a significant positive correlation between CS and IMT r=0.70, p<0.001 as well as between the incidence of visible atherosclerosis plaque in the carotid arteries and calcium score R= 0.60, p<0.001, and IMT, respectively (R=0.76, p<0.001). We also found a positive correlation between the HD vintage and CS (r=0.32, p<0.03) and significant, but weaker, relationship between HD vintage and IMT (r=0.25, p<0.05). All correlations were stronger in females than in males. We did not observe any correlations between biochemical parameters and either CS or IMT.
Conclusions: IMT measurement may serve as a surrogate of calcium score in HD patients.

MP334 BIOIMPEDANCE DERIVED PARAMETERS ARE USEFUL INDICATORS FOR INCREASED ARTERIAL STIFFNESS, ENDOTHELIAL DYSFUNCTION AND CARDIAC SIZE IN HAEMODIALYSIS PATIENTS

Simona Hogas[1], Luminita Voroneanu[1], Paul Gusbeth-Tatomir[1], Dragomir Nicolae Serban[2], Adrian Covic[1]. *[1]FMC Nephrocare Dialysis Center, Parhon University Hospital, Iasi, Romania; [2]Physiology Department, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania*

Introduction and Aims: Cardiovascular (CV) morbidity and mortality is greatly enhanced in patients with end-stage renal disease (ESRD) compared to the non-renal populations. This is due,a mong other factors, to increased arterial stiffness as an expression of premature vascular aging. The aims of our study were to establish, in haemodialysis (HD) patients, the true relationship between fluid status (objectively assesed through echocardiographic and bioimpedance parameters), arterial stiffness and endothelial dysfunction.
Methods: We included 63 stable HD pacients (54.3±13.1 years old, 54% males), free of overt CDV disease. Pulse wave velocity (PWV) and augmentation index (AIx) were evaluated by applanation tonometry (AtCor device) before the HD session. Pre-HD bioimpedance parameters were measured (BIA-RJL 101A, Cyprus 1.1 software) to determine total body water - TBW, extracellular water - ECW, intracellular water - ICW). A phase angle (a parameter independent of weight, height and body fat) < six degrees was previously reported as abnormal (1), reflecting extracellular overhydration. Fluid status was evaluated through echocardiography by measuring inferior vena cava (IVC) diameter. Endothelium-dependent (ED) and endothelium-independent (EID) vascular reactivity were assessed by changes in AIx following inhaled salbutamol and sublingual nitroglycerin (GNT), respectively.
Results: PWV directly correlated with age and dialysis vintage (r = 0.51, and r = 0.71, respectively, P <0.05). On multiple regression analysis, age was the most important predictor of PWV; the model including age, dialysis duration and phase angle predicted 26% of the PWV variance (P = 0.001). Patients with a phase angle <6°, were significantly overhydrated (larger IVC, increased ECW and lower ICW), had stiffer arteries and greater left ventricle mass (LVM), compared with those with a phase angle >6°. Furthermore, both EID and ED vascular reactivity were more abnormal in patients with a phase angle < 6 (see Table 1).

Tabel 1. Relationship between bioimpedance and cardiovascular parameters

Parameters	Phase angle <6 (n =28)	Phase angle > 6 (n =35)	P
Age (years)	62.2±10.3	48.0±11.6	0.000
PWV (m/s)	10.1±3.2	7.6±2.2	0.001
IVC (mm)	18.9±3.4	16.3±3.3	0.031
LVM (g)	285.5±88.4	223.1±66.7	0.011
TBW (% BW)	58.6±7.1	58.6±6.8	0.981
ICW (% TBW)	51.7±3.7	59.3±7.2	0.000
ECW (% TBW)	48.2±3.7	40.6±7.2	0.002
EID: % change in AIx post GTN	83.0±11.0	70.0±9.3	0.05
EDD: % change in AIx post SAL	83.0±11.3	72.6±8.8	0.05

Conclusions: In HD patients, volume overload is an important contributor to increased arterial stiffness, abnormal vascular reactivity and LVM. Bioimpedance derived parameters are excellent discriminators for more abnormal cardiac and vascular profiles.

MP335 EVALUATION OF VASCULAR CALCIFICATIONS (VC) IN TRANSPLANTED (Tx) PATIENTS BY LUMBAR SPINE LATERAL X-RAY

Sandro Mazzaferro[1], Marzia Pasquali[1], Daniele Diacinti[2], Iacopo Carbone[2], Emanuela Algeri[2], Matteo Baldinelli[1], Giusi Barresi[1], Carmina Conte[1], Nicola Pirozzi[1], Francesco Pugliese[1]. *[1]Clinical Science, University "Sapienza", Rome, Italy; [2]Radiology, Univerity "Sapienza", Rome, Italy*

Introduction and Aims: The most important cause of mortality in uremia is represented by cardiovascular diseases, pathogenetically associated with VC. In particular coronary calcifications can be now accurately detected by EBCT or Multi Slice CT (MSCT), whose wide employment in these patients is precluded by costs and scarce diffusion. Alternatively lumbar spine lateral X-ray represents a widely accessible alternative to these sophisticated techniques. Interestingly, Kauppila et al (Atherosclerosis, 1997) has introduced a semi-quantitative assessment of lumbar aortic calcifications, with a score between 0 and 24 ($S_{0\text{-}24}$) which has been validated in a normal Framingham population as a useful marker of cardiovascular risk. Taking into account the differences existing between these two radiological techniques and the pathogenetic mechanisms of VC in normals and uremia, we judged useful to evaluate their correspondence in a special population of CRF patients.
Methods: We studied a total of 51 clinically stable renal Tx pts (45±12 y, 30M/21F, Tx age 6,5±5,4 y, dialysis age 4,7±4,3 y), by means of cardiac MSCT, lateral X-ray of lumbar spine and biochemical parameters of renal function (Cr, CCr), mineral metabolism (Ca, P, BALP, PTH, OPG) and inflammation (ESR, CRP, Fibrinogen). Severity of calcification was expressed as Agatston Score (AS) o Volume Score (VS) for coronary vessels, and as $S_{0\text{-}24}$ for lumbar aorta.
Results: Mean values (±SD) of the evaluated parameters: AS 570±1637; VS 498±1360; $S_{0\text{-}24}$ 3,6±5,5; Cr 1,8±0,6 mg/dl; CrCl 48±17 ml/min; Ca 9,8±0,9 mg/dl; P 3,2±0,9 mg/dl; PTH 165±165 pg/ml; BALP 32±21 U/L; ESR 21±18; CRP 0,49±0,73; Fibrinogen 353±75. Patients were significantly affected by VC with both MSCT (31/51) and $S_{0\text{-}24}$ (28/51), with potentially severe lesions (AS range = 0-9075; $S_{0\text{-}24}$ range = 0-19). Serum levels of PTH were increased, in front of normal BALP and OPG values. Aortic score was significantly related to coronary scores (vs AS: r=.613, p<0001; vs VS: r=.610; p<.001), age (r =.485, p<.0001) and OPG (r=.515; p<.0001). AS and VS also correlated significantly with age and OPG. However, despite these good correlations, diagnostic association was not optimal. In fact, considering coronary score as reference and $S_{0\text{-}24}$ as a test, we obtained a good sensibility (=0,83) but a low sensitivity (r=0,40).

Conclusions: In conclusion, aortic score correlates with coronary score, but the diagnostic value is not overlapping.

MP336 ARTERIES REMODELLING AS A MARKER OF A CORONARY ATHEROSCLEROSIS IN ASYMPTOMATIC RENAL TRANSPLANT RECIPIENTS

Galina Volgina, Natalia Gryabina. *Nephrology, Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; Intern Disease, Moscow State University of Medicine and Dentistry, Moscow, Russian Federation*

Introduction and Aims: Cardiovascular morbidity and mortality are common in renal transplant recipients (RTR) and are often attributed to accelerated atherosclerosis. There is not enough information concerning the prevalence of preclinical arterial wall alteration, their relationship with coronary artery atherosclerosis in asymptomatic RTR.
Methods: We studied 128 RTR (84 male, 44 female; mean age 43 [33; 52.5] years) and 15 age- and sex-matched healthy controls. The mean duration of the post-transplant period was 29,5 [11.5; 73.0] mo (range, 3–240 mo). Coronary heart disease (CHD) was detected *in* 63 (50.8%) of the patients. Intima-media thickness in CA and carotid plaque scores (CPS), renal arterial resistance index (RI) as well as left ventricular mass were examined by high resolution B-mode Doppler ultrasonography and by echocardiography.
Results: RTR with CHD in comparison with patients without CHD were older (P=0,007), more often had of type 2 diabetes mellitus (12.3% *vs* 1.6%, P<0.05) and cerebrovascular disease (27.7% *vs* 3.2%, P<0.001). Compared with control subjects, IMT of the CA (P<0.001) and frequency of CPS (P<0.001) were significantly higher in RTR without dependence from presence or absence CHD. At the same time IMT of the CA was higher in RTR with CHD (1.4 [1.2; 1.5] mm) than in asymptomatic patients (1.2 [1.1; 1.3] mm, P<0.003). We noticed that IMT CA was significantly associated with CPS (r=0.79, p<0.001), age (R=0.76; P<0.001), duration of post-transplantation period (R=0.27, P<0.002), proteinuria (r=0.29, p<0.05) and CRP (P<0.05). CPS (86.5% *vs* 27.1%, P<0.001), calcified lesion of CPS (45.9% *vs* 16.9%, P<0.005), worse graft function (Ccr 46.9 [32.2; 52.6] *vs* 56 [43.4; 61] ml/min per 1,73m^2, P<0.001) authentically more often were registered at RTR with CHD than in patients without CHD. There is a connection between CPS and atherosclerosis risk factors such as age (P<0.001), male sex (P=0,003), body mass index (P<0.013) and serum cholesterol level (P<0.001).
A total of 59 patients (46 percent) had a renal arterial resistance index (IR) of 80 or higher. Patients with IR values of 80 or higher were significantly older (P<0.001), had their transplants for a longer time (P=0.008), more severe proteinuria (P=0.05), IMT CA (P<0.001), frequency of CPS (P<0.001), worse graft function (P<0.001). IMT CA (r=0.45, P<0.01), CPS (r=0.58, P<0,001) and IR (r=0.45, P<0.01) were significantly related to left ventricular mass index.
Conclusions: The structural changes of large arteries and the heart leading to cardiovascular disease begin many years before the onset of clinically observable symptoms. This study shows a close association exists between asymptomatic carotid atherosclerosis and coronary artery atherosclerosis. The increase of intima-media thickness, carotid plaque scores, renal arterial resistance index are markers of early atherosclerosis and may be clinically useful for the systematic identification of renal transplant recipients with an increased risk of developing cardiovascular events.

MP337 INCREASED OXIDATIVE STRESS IN HEMODIALYSIS PATIENTS WITH HIGH RISK FOR SLEEP APNEA SYNDROME

Paik Seong Lim [1,2], Wen-Ching Chen [3], Po-I Chien [3]. *[1]Renal Medicine, Tungs' Taichung Metroharbor Hospital, Shalu, Taichung, Taiwan; [2]Department of Food & Nutrition, Providence University, Shalu, Taichung, Taiwan; [3]Dialysis Unit, God's Heart Hospital, Chiayi, Taiwan; [4]Nephrolgy, Tai Shin Hospital, Taichung, Taiwan*

Introduction and Aims: In recent years, sleep apnea syndrome (SAS) is widely considered to be a cardiovascular disease (CVD) risk factor. Although several plausible mechanisms have been put forth to explain such association in patients with SAS, oxidative stress has been suggested to play a major role. In patients with sleep apnea, the repetitive ischemic-reperfusion state causes excessive production of oxygen free radicals and may subsequently lead to oxidative injury of various biomolecules. Due to the high prevalence of SAS in dialysis patients, this possible uremia-specific CVD risk factor may definitely need more medical attention.
Methods: We, therefore, performed a case control study to investigate the relationship between oxidative stress and SAS in a group of dialysis patients, using some well established oxidative biomarkers.
Results: Our results showed that plasma nitrotyrosine, protein carbonyl and malonaldehyde levels were significantly elevated in patients with SAS. Markers of endothelial activation such as soluble CD40 ligand were also increased in this subgroup of patients. However, there was no significant difference in serum CRP levels between these groups.
Conclusions: In conclusion, the results indicate that patients with SAS manifest evidence for higher oxidative stress and endothelial activation. Thus, intermittent hypoxia, associated with recurrent apneas, represents a form of oxidative stress and low-grade chronic inflammatory state that may be associated with increased cardiovascular disease in these patients.

MP338 VITAMIN D LEVELS AND HYPERTENSION IN CHRONIC HEMODIALYSIS (CHD) PATIENTS

Ana Silva, Ana Cabrita, Anabela Guedes, Alexandre Baptista, Sandra Sampaio, Elsa Morgado, Isabel Pinto, Viriato Santos, Idalecio Bernardo, Pedro Neves. *Nephrology Department, Hospital Central Faro, Faro, Portugal*

Introduction and Aims: Vitamin D has been recently demonstrated to play a role in renin synthesis and therefore in blood pressure control. Vitamin D deficiency activates the RAA system leading to hypertension and left ventricular hypertrophy.
In this study, we evaluated the relationship between vitamin D levels, hypertension and the left ventricular mass index (LVMI) in a population of CHD patients.
Methods: We included 96 patients (m = 64; f = 32) with a mean age of 61,5 years in CHD for 51 months. Our population was divided in two groups: G-I (n = 59) – hypertensives; G-II (n = 37) – non-hypertensives, which were compared in relation to age, time on CHD, 1,25-dihydroxycolecalcipherol (vitamin D3) levels and LVMI.
Results: No differences were found concerning age and time on CHD. Patients in G-I showed lower levels of vitamin D3 (10,8 *vs* 16,4 pmol/L; p = 0,022) and increased LVMI values (172 vs136g/m^2; p= 0,001).
We could not find a linear correlation between blood pressure and vitamin D levels, probably because almost half of patients were under anti-hypertensive therapy. Vitamin D levels in hypertensive patients on ACEI's and/or ARB's (n = 31) were higher (11,8 *vs* 10,4 pmol/L), than in those without ACEI's or ARB's, though not reaching statistical significance. In patients without left ventricular hypertrophy (by LVMI criteria) there was a trend to higher vitamin D levels (15,1 *vs* 12,1 pmol/L).
Conclusions: The association of vitamin D deficiency and hypertension found in our CHD patients has already been described in the general population. To the best of our knowledge this is the first report of this association in CHD patients.

MP339 THE RELATIONSHIP BETWEEN VARIOUS TYPES OF ARTERIAL CALCIFICATION AND ATHEROSCLEROTIC LESIONS AND QT INTERVAL (ECG) DISPERSION IN HD PATIENTS

Saso Gelev [1], Goce Spasovski [1], Sonja Dzikova [1], Zoran Trajkovski [2], Vili Amitov [1], Aleksandar Sikole [1]. *[1]Department of Nephrology; [2]Institute of Radiology, University Clinical Center, Skopje, Macedonia, The Former Yugoslav Republic of*

Introduction and Aims: Hemodialysis (HD) patients may be at greater risk of cardiac arrhythmias and sudden death in post-HD period because of the increased QT interval dispersion on electrocardiograms (ECG). Aim of this study was to compare post-HD recorded QT interval duration in various groups of HD patients according to findings of the presence of arterial calcifications and atherosclerotic lesions.
Methods: In a cross-sectional study we examined 169 HD patients (100

male; mean age 54.1±22.6 years; HD duration 92.9±65.8 months). Primarily, we evaluated the presence of arterial intima (AIC) and arterial media calcifications (AMC) using plain radiography of the pelvis, as well as the presence of atherosclerotic lesions using high resolution B-mode ultrasonography of the common carotid (CCA) and femoral (FA) arteries. The cohort was stratified according to the variable of intima media thickness (IMT) in two equal groups at a cut level off 1.45 mm. Then we compared the QT interval duration (calculated from the post-HD recorded 12-lead ECG) among the groups of patients with different type of arterial calcifications and atherosclerotic lesions.

Results: The patients without arterial calcifications (n=44; 26.1%) had significantly ($p<0.05$) shorter QT (341.6±21.5 ms) and corrected QT (QTc) interval (404.5±25.5 ms) duration in comparison with the other two groups (AIC and AMC). There was no significant difference in QT (378.6±22.7 vs 375.3±24.1 ms) and QTc (462.2±25.4 vs 454.4±19.7 ms) interval duration between the patients with AIC (n=70; 41.4%) and AMC (n=55; 32.5%). A significantly ($p<0.05$) prolonged QT/QTc interval (377.6±23.7 vs 339.0±28.6 ms/459.1±22.5 vs 414.2±25.2 ms) was observed in the group with increased CCA intima media thickness (IMT) (1.70±0.22 mm) in comparison with those of decreased CCA-IMT (1.29±0.13 mm). Similarly, a significantly ($p<0.05$) prolonged QT/QTc interval (370.9±26.8 vs 334.0±19.5 ms/454.6±21.5 vs 412.7±22.8 ms) was found in the group with increased FA-IMT (1.68±0.18 mm) compared to those of decreased FA-IMT (1.26±0.16 mm). The same pattern of significantly ($p<0.05$) prolonged QT/QTc interval was also observed in the presence of carotid (367.5±26.7 vs 330.4±24.6 ms/460.2±19.9 vs 417.5±27.3 ms) and femoral (372.3±27.5 vs 333.0±25.4 ms/464.2±27.2 vs 411.8±26.8 ms) atherosclerotic plaques, as well as calcified carotid (381.4±29.1 vs 338.4±24.6 ms/461.9±27.6 vs 421.5±26.4 ms) and femoral (375.9±22.6 vs 332.3±18.8 ms/455.89±27.66 vs 411.31±31.13 ms) intimal plaques in patients with and without presence of atherosclerotic plaques, respectively.

Conclusions: Post-HD recorded QT/QTc interval is prolonged in HD patients with arterial calcifications and increased intima media thickness. The presence of AMC, AIC and carotid and femoral atherosclerosis may predispose hemodialysis patients to cardiac arrhythmias and sudden death.

MP340 IMPROVEMENT OF ARTERIAL STIFFNESS BY SWITCH TO EIGHT HOUR THRICE WEEKLY HEMODIALYSIS

Meltem Sezis[1], Gulperi Celik[1], Gulay Asci[1], Oner Ozdogan[1], Fatih Kircelli[1], Pinar Ergin[2], Murat Zengin[2], Meral Kayikcioglu[1], Ali Basci[1], Mehmet Ozkahya[1]. *[1]Nephrology & Cardiology, Ege University, Izmir, Turkey; [2]FMC Turkey Clinics*

Introduction and Aims: Arterial stiffness is proposed as a risk factor for cardiovascular mortality in hemodialysis (HD) patients. In this prospective, controlled study, we compared the changes in arterial stiffness parameters in 4-h and 8-h thrice weekly HD regimens.

Methods: Fifty-five prevalent HD patients were assigned to thrice weekly in-center nocturnal HD and sixty age-, gender-, diabetes status-, dialysis duration-matched HD patients to conventional HD. Interdialytic echocardiography and brachial pulse wave analysis (Sphygmocor, Atcor Medical) were performed at baseline and 12th month.

Student's t-test, chi square and multiple regressions were used for statistical analysis.

Results: There were no difference between groups regarding age, sex, diabetes and vintage of dialysis. Mean duration of follow-up was 12.4±5.0 months. Mean length of HD sessions were 240±20 min in 4-h group and 412±55 min in 8-h group ($p<0.001$) throughout follow-up.

Mean baseline augmentation index (AIx), subendocardial viability ratio (SEVR) and ejection duration (ED) were not different at baseline in both groups. Left atrial diameter (LAD), left ventricular end-diastolic diameter (LVED), left ventricular mass index (LVMI) and ejection fraction were also similar in groups (Table).

In follow-up systolic and diastolic blood pressures were similar in 4-h and 8-h groups.

At 12th month, subendocardial perfusion reflected by SEVR and diastolic dysfunction by ED improved in 8-h HD group, accompanied by regression of LVMI and LAD. PWV decreased in 8-h HD group, did not change in 4-h group. In 4-h HD group, an increase in AIx was observed (Table).

Parameters	Baseline		12th month	
	4-h group	8-h group	4-h group	8-h group
AIx (%)	28.8±9.7	27.9±12.3	31.5±10.8[a]	27.0±12.2
SEVR (%)	129±28	135±30	129±26	143±25[b]
ED(ms)	297±29	295±33	303±34	282±34[b]
PWV(m/s)	9.7±2.4	11.4±2.7	9.4±2.0	9.4±1.9[b]
LA (cm)	4.0±0.58	4.0±0.68	3.97±0.51	3.82±0.48[b]
LVED (cm)	4.36±0.84	4.36±0.76	4.50±0.67	4.15±0.54[b]
LVMI(g/m2)	147±69	156±68	137±42	116±33[b]
eKt/V	1.46±0.28	1.48±0.34	1.44±0.32	2.61±0.89[b]
Phoshorus (mg/dl)	4.9±1.2	4.7±1.2	4.9±1.1	3.9±0.8[b]
CaXP (mg^2/dl^2)	42±12	41±10	43±10	35±8.5[b]
Albumin (g/dl)	3.9±0.27	3.9±0.21	3.9±0.21	4.0±0.19[b]
CRP (mg/dl)	1.4±2.1	1.7±2.8	1.7±2.0[a]	1.4±1.5

a.p < 0.05 between baseline and 12th month
b.p < 0.01 between baseline and 12th month

In 8-h group, creatinine, phosphorus, CaxP product were lower, albumin and eKt/V were higher than 4-h group (Table).

Linear regression analysis revealed hs-CRP (t: -3.45; $p<0.01$) and mean duration of HD sessions (t: 2.73; $p<0.01$) as predictors of change in SEVR (Δ SEVR). Serum phosphorus level (t: 3.25; $p<0.01$ and t: 2.58; $p<0.01$) was found as a predictor for change in ED (Δ ED) and AIx (Δ AIx).

Percentage of patients with SEVR <100 were lower in 8-h group than in 4-h group (1.7 versus 14.8%, $p<0.01$).

Only serum phosphorus level (OR: 2.56, 95% CI: 1.11-5.89, $p<0.01$) and LVMI (OR: 1.02, 95% CI: 1.00-1.03) were found as risk factors for SEVR <100 in logistic regression analysis.

Conclusions: These data demonstrate that arterial stiffness is ameliorated by implementation of longer hemodialysis session, possibly through better phosphate control.

Disclosure: This study was supported by FMC.

MP341 SERUM 25-HYDROXYVITAMIN D STATUS AND CARDIOVASCULAR OUTCOMES IN CHRONIC PERITONEAL DIALYSIS PATIENTS: A PROSPECTIVE COHORT STUDY

Angela Y.M. Wang[1,2], Christopher W.K. Lam[3], John E. Sanderson[2,4], Mei Wang[1,2], Iris H.S. Chan[3], Siu-Fai Lui[2], Mandy M. Sea[2], Jean Woo[2]. *[1](Current) Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong, Hong Kong; [2]Medicine & Therapeutics, Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong, Hong Kong; [3]Chemical Pathology, Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong, Hong Kong; [4](Current) Cardiovascular Medicine, The Medical School, University of Birmingham, Edgbaston, Birmingham, United Kingdom*

Introduction and Aims: Cardiovascular disease is the leading cause of mortality in stage 5D chronic kidney disease (CKD) patients. There is also recent data to suggest a high prevalence of vitamin D deficiency in patients with CKD. The primary objective of this study is to evaluate the association between serum 25-hydroxyvitamin D status & clinical outcomes in stage 5 CKD patients receiving treatment with long-term peritoneal dialysis (PD). In addition, we evaluated the prevalence of serum 25-hydroxyvitamin D deficiency & factors relating to 25-hydroxyvitamin D status in these patients.

Methods: A single serum 25-hydroxyvitamin D [25(OH)D] level was measured in 230 PD patients who were prospectively followed up for 3 years or until death.

Results: Serum 25(OH)D level was deficient/insufficient (< 30ug/L) in 87% of the patients and was associated with diabetes, gender, declining residual renal function (RRF), age & left ventricular (LV) volume index by echocardiography. On univariate Cox regression analysis, log[serum 25(OH)D] was associated with fatal or non-fatal cardiovascular events (CVE) [P=0.016] but not all-cause mortality [P=0.91]. A significant increase in the CVE-free survival probability was observed across the four quartiles of increasing serum 25(OH)D (P=0.035; log-rank test). Adjusting for clinical & demographic parameters, every 1 unit increase in log-transformed serum 25(OH)D was associated with a 42% reduction in the hazard of CVE (95% CI, 0.36 – 0.94; P=0.027). However, the association was gradually lost when

additional stepwise adjustment was made for RRF (P=0.097), biochemical & nutritional parameters (P=0.104) & echocardiographic parameters including LV mass & volume index (P=0.62). In addition, patients with serum 25(OH)D > median (18.3ug/L) had significantly higher CVE-free survival probability than those ≤ 18.3ug/L in the stratified analysis for patients with LV mass index < median (P=0.029) or normal LV systolic function (P=0.011) but not among those with LV mass index ≥ median or LV systolic dysfunction.

Conclusions: A low serum 25-hydroxyvitamin D status is associated with an increased risk of CVE in chronic PD patients partly via its close relationships with RRF, LV hypertrophy and systolic dysfunction.

MP342 ARTERIAL STIFFNESS BUT NOT THE VASCULAR CALCIFICATION SCORE IS ALTERED IN THE EARLY STAGES OF CHRONIC KIDNEY DISEASE IN THE ABSENCE OF DIABETES

Emiliana Ferramosca[1], Elena Sestigiani[1], Marcora Mandreoli[1], Sonia Pasquali[1], Rossella Fattori[2], Antonio Santoro[1]. *[1]Nephrology Dialysis and Hypertension, S. Orsola-Malpighi Hospital, Bologna, Italy; [2]Radiology III Institute, S. Orsola-Malpighi Hospital, Bologna*

Introduction and Aims: Vascular calcification is common in patients suffering from advanced chronic kidney disease (CKD), yet little is known about vascular calcification and arterial stiffness in the early stages of renal dysfunction.

We evaluated, in patients suffering from CKD 3, the arterial vascular damage by means of the measurement of arterial stiffness and the coronary calcium score.

Methods: Eleven patients (7M, 4F, aged 64±7) with mild-to-moderate renal failure were enrolled. We deliberately excluded patients with diabetes and previous history of heart disease from this study; we did this in order to exclude the interference of other pathologies apart from functional kidney insufficiency in the genesis of vascular alterations. The cause of renal failure was nephroangiosclerosis (73%), membranous glomerulonephritis (18%), and interstitial nephritis (9%). All the patients underwent the assessment of: coronary calcification by means of multi-detector CT [expressed as calcium score (CS) according to Agatston score], arterial stiffness by pulse wave velocity measurement, common carotid intima-media thickness (IMT) by B-mode US scan, and left ventricular mass index by echocardiography. Renal function (GFR) was evaluated using the Cockroft and Gault formula. Blood samples were drawn for the measurement of serum creatinine, lipid profile, glycidic profile, electrolytes, Homa index, etc.

Results: The main results are summarized in the table below. Whilst the calcium score was abnormal in only one patient (the remaining patients had a CS <50HU), the PWV and IMT were high in all of them. No substantial alterations in the lipid profile and HOMA index were present.

Table 1

Variable	Mean±SD
GFR (ml/min)	40.6±10
Tot Cholesterol	198±35
LDL Cholesterol	111±29
HDL Cholesterol	53±16
Triglycerides	183±93
HOMA index (%)	1.9±1.5
PWV (m/sec)	10.5±1.6
ccIMT (mm)	0.8±1.2
LVM index (g/m^2)	110±41
CS (HU)*	0-1074

*Expressed as range.

Conclusions: In conclusion, our data, albeit obtained in a small number of patients, show that in the early stages of chronic renal failure, in the absence of diabetes and cardiac involvement, vascular calcification is only rarely present. On the contrary, arterial stiffening, as shown by PWV and IMT, starts very early, even in the presence of a normal lipid profile and insulin resistance.

Further studies in larger group are needed to confirm this results, as well as to understand at which moment or which factors are the ones that lead to the development of the extensive vascular calcification observable in the advanced stages of CKD.

MP343 FRACTURES AND QTc PROLONGATION IN HEMODIALYSIS PATIENTS: IS THERE A LINK?

Jesus Calviño[1], Isabel Rodriguez[2], Sonia Cillero[2], Pedro Villaverde[2], Gonzalo Peña[3], Ana Guitian[1], Francisco Valdes[1]. *[1]Nephrology, Hospital Juan Canalejo, A Coruña, Spain; [2]Nephrology, Hospital San Rafael, A Coruña, Spain; [3]Cardiology, Hospital San Rafael, A Coruña, Spain*

Introduction and Aims: Uremic bone disease is characterized by vascular and ectopic calcifications, bone mass reduction, fragility, and consequently a higher risk of fractures. Moreover, these patients often share conditions that may increase the risk of falling such as old age or the use of certain medications. We have recently reported a significant increase of the QTc interval with time on hemodialysis (HD) and its association with a higher frequency of vascular calcification. However, whether this increment can play a role in the development of fractures has not been previously analyzed.

Methods: 197 patients (128 males and 69 females) of 65±13.1 years. Routine EKG registries carried out at initiation and after 34 ± 22.7 months on HD were examined. Traumatic fracture reports were reviewed and its association with QTc interval variation as well as with other risk parameters (clinical, radiological and biochemical) was studied.

Results: Fractures were identified in 40 patients (20%). Localization was in the ribs (12 patients), hip (11 patients) and 17 in other areas. Patients with fractures were characterized by an older age (70±10.9 vs 64 ± 13.5 years, $p < 0.01$), antidepressant drug use (30 vs 16%), X-ray detected vascular calcification (90 vs 75%) and carpal tunnel surgery (10 vs 2%). These patients also showed a lower albumin level (3.3±0.40 vs 3.5 ± 0.45 g/dl) and higher rate of inflammation assessed by reactive C protein (2.2±1.81 vs 1.4±1.56 mg/dl, $p<0.05$). No significant association was found regarding calcium, phosphate and iPTH levels. QTc interval significantly increased after the period analyzed (from 422±30.1 to 436±33.2 ms, $p<0.01$). This increment was positively correlated with age ($r = 0.17$) and reactive protein C levels ($r = 0.23$). At the end of the study QTc interval was higher in those patients with fractures (448±40.8 vs 432±29.4 ms, $p<0.05$) and remained significant after multivariable analysis adjustment.

Conclusions: In the population examined, traumatic bone fractures occurred in 20% of the patients and was associated with several factors involved with falling such as age, poorer nutritional status (albumin), inflammation (reactive C protein), antidepressant drug use, and QTc interval increase. However, more studies are needed to assess if this increment (probably reflecting autonomic heart dysfunction) contributes to the higher risk of falls in these patients.

MP344 CONGESTIVE HEART FAILURE AND SERIAL MEASUREMENTS OF INFLAMMATORY MARKERS IN PREVALENT HEMODIALYSIS PATIENTS

Sunna Snaedal Jónsdóttir[1], Abdul Rashid Qureshi[1], Juan Jesus Carrero[1], Olof Heimbürger[1], Anders Danielsson[2], Bengt Fellström[3], Björn Wikström[3], Ingela Fehrman-Ekholm[4], Anders Alvestrand[1], Peter Stenvinkel[1], Peter Bárány[1]. *[1]Renal Medicine, Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; [2]Renal Medicine, Danderyds Hospital, Stockholm, Sweden; [3]Renal Medicine, Department of Medical Sciences, Uppsala University Hospital, Uppsala, Sweden; [4]Renal Unit, Sophiahemmet, Stockholm, Sweden*

Introduction and Aims: Patients with end stage renal failure have a high comorbidity and are prone to inflammation. Prevalence and incidence of congestive heart failure (CHF) are higher in dialysis patients compared to the general population. Inflammation has previously been linked to occurrence of CHF with a stronger relation in men than women. This 3-month study (the MIMICK study) was designed to assess CRP-variability within and in between patients and the relation between inflammation, comorbidity and intercurrent events in a group of non-selected, prevalent hemodialysis patients.

Methods: CRP was measured weekly for 12 weeks, IL-6 and TNF-α monthly in 228 hemodialysis patients. The median of all assessments in each individual was used for analysis. Information on comorbidity (CHF, ischaemic heart disease, malignancy, diabetes, systemic inflammatory disease, cerebral-and peripheral vascular disease and other significant diseases) was gathered from patients charts at study start. The diagnosis of CHF was based on clinical findings, chest x-ray and/or echocardiography.

The relationships between comorbidities and inflammatory markers were analyzed.
Results: A total of 228 subjects (44% females) were included; median age 66 years [range 23-87], median time on dialysis 29 months [range 1-378]. CHF was the comorbidity with the strongest association to inflammatory parameters. CRP and IL-6 were significantly higher in patients with CHF than those without CHF and the difference was most marked for CRP. TNF-α was not significantly different in patients with CHF compared to those without CHF.

Inflammatory parameters in hemodialysis patients with and without congestive heart failure

	CHF, n=48	No CHF, n=180	p-value
CRP, mg/L	9.6 (5.2-24.8)	5.2 (2.3-13.0)	<0.001
IL-6, pg/L	10.9 (7.4-19.8)	7.6 (5.1-13.5)	<0.01
TNF-alpha, pg/L	13.6 (11.1-16.3)	13.7 (11.4-16.5)	n.s.

Median (25-75 percentiles).

Conclusions: Concentrations of inflammatory markers are high and variable in hemodialysis patients and are strongly related to comorbidity. Previous reports on the connection between inflammation and congestive heart failure in dialysis patients are sparse. This study shows a strong relationship between CHF and serial measurements over 3 months of CRP and IL-6 in prevalent hemodialysis patients.
Disclosure: This research was supported by Amgen Inc.

MP345 DIALYSIS-INDUCED CHANGES OF THE VOLUME STATUS DOES NOT AFFECT PULSE WAVE VELOCITY

Emiliana Ferramosca[1], Elena Mancini[1], Daniela C. Cannarile[1], Eugenio R. Cosentino[2], Antonio Santoro[1]. *[1]Nephrology Dialysis and Hypertension, S. Orsola-Malpighi Hospital, Bologna, Italy; [2]Dept. of Internal Medicine and Biotechnology, S. Orsola-Malpighi Hospital, Bologna, Italy*

Introduction and Aims: Increased Pulse Wave Velocity (PWV), a marker of arterial stiffness, is considered a strong predictor of cardiovascular mortality both in general and in renal population. However, it is unknown if, in the dialysis (HD) patients, it may be affected by the rapid variations in the fluid status induced by the treatment.
Methods: We studied 13 patients (6 M, 7 F, 65±12 yrs), on thrice-weekly chronic HD treatment, in a study session after the longest interdialysis period. In each patient PWV was assessed pre- and post HD, by recording pulse waves at the right common carotid artery and the right femoral artery sequentially, by applanation tonometry (SphygmoCor®, AtCor, Sydney, Au). Impedentiometry-derived cardiac output (CO), blood volume (BV) changes, arterial pressure and heart rate were monitored. Brain Natriuretic Peptide (BNP) was also measured pre- and post-HD (direct cheminumilescence immunoassay, ADVIA Centaur BNP assay, Bayer Diagnostic, Tarrytown, NY, USA). The Watsons formula was used for the total body water (TBW) estimation.
Results: Results are summarized in the table.

	TBW (L)	CO (L/m)	PWV (m/s)	BNP (pg/ml)
Pre HD (meanSD)	43.01±8.6	5.02±1.05	11.7±2.7	729±339
Post HD (meanSD)	40.08±8.4	4.76±1.5	11.3±3.2	561±283
p	< 0.001	0.41	0.16	0.0006

Conclusions: All the dialysis sessions were free from acute hypotension episodes and/or muscular cramps. In spite of significant variations in TBW, PWV did not change significantly between pre-and post-HD. Changes of BNP, but not of PWV, correlated significantly with CO changes (R^2=0.5, $p<0.05$). Neither BNP nor PWV correlated significantly with the BV changes ($p>0.05$).
To conclude, PWV proved unaffected by the HD-induced volume status changes, thus its measurement seems confirmed as valid independently of the dialytic phase.

MP346 EFFECTS OF DIALYSIS ADEQUACY ON ECHOCARDIOGRAPHIC PARAMETERS OF LEFT VENTRICULAR STRUCTURE AND SYSTOLIC FUNCTION IN PATIENTS WITH NORMAL BASELINE LEFT VENTRICULAR SYSTOLIC FUNCTION – ONE-YEAR OBSERVATION

Miroslawa Janowska, Jan Dulawa, Marcin Drobisz, Piotr Strzelczyk. *Internal Medicine and Metabolic Diseases, Medical University of Silesia, Katowice, Poland*

Introduction and Aims: A compromise in left ventricle structure and systolic function affects the morbidity and mortality of chronically dialysed patients. The adequacy of renal replacement therapy is of key importance in improving prognosis.
Aim: Assessment of an effect of selected parameters of dialysis adequacy on echocardiographic characteristics of left ventricular structure and systolic function.
Methods: The study population included thirty-five chronically dialysed patients with normal baseline left ventricular systolic function. Ten parameters were used to assess dialysis adequacy: Kt/V, nPCR, serum albumine (Alb), haemoglobin (Hb), ferritin (Ferr), phosphorus (P), immunoreactive parathyroid hormone (iPTH), Ca x P product, predialysis systolic blood pressure (SBP), and interdialysis weight gain (IDWG %).
Each patient had an ECG, subsequently repeated after a period of 12 months. Changes in left ventricular parameters were assessed based on an analysis of the difference (Δ) between baseline and follow-up measurements. Nine structural (ie., LVEDD, IVST, PWT, LVMI/BSA, LVMI/$h^{2,7}$, RWT, MWT, LA, LA/h) and two functional (FS and LVEF%) characteristics were considered.
Results: Significant negative correlation was found between serum Alb and Δ LA ($r = -0.3823$, $p = 0.023$) and Δ LA/h ($r = -0.3890$, $p = 0.021$), as well as between nPCR and Δ IVST ($r = -0.4940$, $p = 0.003$), Δ PWT ($r = -0.4338$, $p = 0.009$), Δ LVMI/BSA ($r = -0.4301$, $p = 0.010$), Δ LVMI/$h^{2,7}$ ($r = -0.4479$, $p = 0.007$), and Δ MWT ($r = -0.5025$, $p = 0.002$). Significant positive correlations were observed between IDWG % and Δ IVST ($r = 0.4134$, $p = 0.014$), Δ LVMI/BSA ($r = 0.3557$, $p = 0.036$), Δ LVMI/$h^{2,7}$ ($r = 0.3746$, $p = 0.027$), Δ MWT ($r – 0.3942$, $p = 0.019$) and between Kt/V and Δ PWT ($r = 0.5357$, $p = 0.001$), Δ RWT ($r = 0.5035$, $p = 0.002$), and Δ MWT ($r = 0.4609$, $p = 0.005$). An analysis of correlations between the parameters of dialysis adequacy and Δ values of echocardiographic characteristics also revealed a significant positive correlation between Hgb and Δ LVEF% (r=0.3396, p=0.046), and between nPCR and Δ LVEF% ($r = 0.3639$, $p = 0.032$).
Conclusions: 1. Higher nutritional status parameters such as serum albumin and nPCR have a beneficial effect on left ventricular structure and systolic function in a dialysed patient; 2.The observed advantageous effect of less restrictive fluid regimen on left ventricular structure during one year might indicate some nutritional role of the parameter; 3. Better anaemia control improves left ventricular systolic function.

MP347 ★ PARICALCITOL AND CALCITRIOL EFFECT ON ATHEROSCLEROSIS AND HEART DISEASE IN UNINEPHRECTOMIZED ApoE -/- MICE

Luis Eduardo Becker[1,2,3], Nadezda Koleganova[2], Grzegorz Piecha[2,3], Aman Geldyyev[2], Irene L. Noronha[1], Ebberhard Ritz[3], Marie Luise Gross[2]. *[1]Internal Medicine, University of São Paulo, Sao Paulo, SP, Brazil; [2]Pathology, University of Heidelberg, Heidelberg, Germany; [3]Internal Medicine, University of Heidelberg, Heidelberg, Germany*

Introduction and Aims: Although VitD receptor activation has been proven to reduce cardiovascular morbidity and mortality in dialysis patients by reducing oxidative stress and atherosclerosis progression, the side effects of Calcitriol therapy limits its use. The study investigated the influence of a 10-week treatment with Paricalcitol or Calcitriol on cardiovascular disease in spontaneously atherosclerotic ApoE -/- mice submitted to uninephrectomy (UNX).
Methods: UNX and Sham-operated ApoE -/- mice (n=96) were divided into six groups according to pharmacological treatment: controls, which received vehicle 5×/week; Pacicalcitol (0.1μg/kg 5×/week); Calcitriol (0.03μg/kg 5×/week). Stereological analysis and immunohistochemistry

Abstract MP347 – Stereology, Sirius Red staining and PCR of the heart

Group	Capillary volume (%)	Capillary length density (mm/mm^2)	Collagen (Sirius Red) (score: 0-4)	TGFβ1 (ratios/GADPH)
Sham Control	4.86±0.58	5855±121$^{\&\&,\alpha}$	1.52±0.16	1.11±0,07
Sham Paricalcitol	4.98±0.74	5838±511$^{\&\&}$	1.43±0.14	0.75±0.1
Sham Calcitriol	4.74±0.28	5839±298$^{\&\&}$	1.43±0.14	1.2±0.19
UNX Control	4.44±0.55	5147±338	1.72±0.15$^{*,\S\S,\$\$}$	1.41±0.12§
UNX Paricalcitol	4.77±0.72	5610±727$^{\&}$	1.57±0.27	1.34±0.2
UNX Calcitriol	4.45±0.74	5538±314$^{\&}$	1.73±0.15$^{*,\S\S,\$\$}$	1.42±0.27§
p (ANOVA)	ns	p<0.01	p<0.01	p<0.05

Values are presented by mean±SD. *p<0.05 vs Sham Control; §p<0.05 vs Sham Paricalcitol; §§p<0.01vs Sham Paricalcitol; $^{\$\$}$p<0.01 vs Sham Calcitriol; $^{\&}$p<0.05 vs UNX Control; $^{\&\&}$p<0.01 vs UNX Control; $^{\alpha}$p<0.05 vs UNX Calcitriol.

were performed in the heart and aorta tissues. TGFβ1 mRNA expression in the heart was analized through RT-PCR. Immunohistochemical analysis was performed using a semiquantitative scoring system (0-4), or counted as positive cells/mm^2. Statistical analysis was performed using ANOVA.
Results: Capillary length density was significantly lower in UNX Control, but not in UNX Paricalcitol and UNX Calcitriol animals, when compared to shams. This was accompained by a higher collagen expression in UNX Control and UNX Calcitriol in comparison to shams. A higher TGFβ1 expression was observed in the UNX Control and UNX Calcitriol groups when compared to Sham Paricalcitol (table 1). In the aortas, a significantly lower wall/lumen ratio was observed in the Sham Control group when compared to UNX Control and UNX Calcitriol (0.057±0.002 vs. 0.064±0.005 and 0.075±0.013, p<0.01). In the latter, vascular calcifications accompanied by a significant presence of Runx2(cbfa1) positive cells were observed (1.33±2.19 cells/mm^2 - UNX Calcitriol vs. 0.19±0.22 - Sham Control, p<0.05).
Conclusions: 1) Both treatments were able to prevent the reduction in heart capillarization induced by the UNX model
2) At the dose of 0.1μg/kg Paricalcitol was superior to 0.03μg/kg Calcitriol by exerting this effect without inducing significant plaque calcification.
Disclosure: Becker L.E. is supported by an ISN-funded Fellowship Program. We also thank Abbott for supporting this study and for providing Paricalcitol and Calcitriol.

MP348 HOMOCYSTEINE, OXIDATIVE STRESS AND AGE CORRELATE WITH INTIMA-MEDIA THICKNESS AND CAROTID PLAQUES IN ESRD

Francesco Carluccio[1], Werner Siems[2], Alessandro Distante[3]. *[1]IFC-CNR Institute of Clinical Physiology Section of Lecce, CNR, Pisa, Italy; [2]Loges School of Physical Medicine and Gerontology, Bad Harzburg, Germany; [3]IFC-CNR Institute of Clinical Physiology Section of Lecce, CNR, Pisa, Italy*

Introduction and Aims: Previous research has shown that homocysteine plasma concentration (Hcy) correlates with both vascular functional abnormalities and the development of atherosclerosis. Increased oxidative stress has been hypothesized to mediate Hcy-induced vascular damage. In this study we evalueted the interrelationships between Hcy, in vivo indices of oxidative stress measured as plasma concentrations of 4-hydroxynonenal (HNE) and malondialdehyde (MDA), in vivo measurements of carotid artery atherosclerosis by measuring the carotid artery intima-media thickness (IMT), which has been accepted as a marker of total atherosclerotic burden, and carotid plaques.
Methods: We enrolled 28 patients on chronic (>12 months) haemodialysis due to End-Stage Renal Disease (ESRD). HNE was measured by DNPH derivatization, TLC separation of different groups of dinotrophenylhydrazones, and HPLC. MDA was measured according to the method of Wong et al. using TBA-conjugate formation and HPLC analysis. Parameters of carotid atherosclerosis were related to Hcy, duration of dialysis, age and parameters of oxidative stress. Patients were divided in two groups according to the presence or absence of plaques in carotid artery.
Results: All patients had increased values of Hcy in comparision with age-matched healthy control group. Furthermore, HNE and MDA were significantly increased.
The results of investigated parameters, according to this grouping, are shown in the following table:
Conclusions: Patients suffering from ESRD and extensive carotid atherosclerosis have higher values of Hcy and higher levels of oxidative stress which also might be a link between hyperhomocysteinemia and atherosclerosis. From this point of view, oxidative stress might be considered as an additional and emerging cardiovascular disease risk factor in chronic renal failure.

Vascular access 2

MP349 THE COMPARISON OF INTRALUMINAL WITH INTAVENONOUS ADMINISTRATION OF VANCOMYCIN IN PERMANENT HAEMODIALYSIS CATHETER ON THE RATE OF CATHETER REMOVAL

Ali Akbar Beigi, Sahar Khansoltani, Abdol Amir Atapour, Afrooz Eshaghian, Maryam Ghassami, Shahin Tavallai. *Vascular Surgery, Esfahan University of Medical Science, Esfahan, Iran; Nephrology, Esfahan University of Medical Science, Esfahan, Iran*

Introduction and Aims: Patients who use Permcath as the vascular access for long-term haemodialysis (HD) are occasionally confronted with catheter-related infections. Permcath infections can lead to catheter removal in HD patients. This is an important factor in morbidity and mortality of the patients. Successful use of a 'locked-in' antibiotic to treat unusual gram-negative and more common organisms (staphilococus) has reported good results in catheter infections. This study was designed to evaluate the impact of the intraluminal vancomycin in comparison with intravenous antibiotic administration.
Methods: This prospective experimental controlled study included 67 (37 males and 30 females) end-stage renal disease (ESRD) patients of diverse etiology enrolled for long-term HD from July 2004 to June 2007 at our tertiary care hospital. Those patients requiring permcath insertion for the maintenance or commencement of HD were eligible for the study. We exclude them, if they have allergy to vancomycin in the intervention group. The patient was divided to 2 groups. In the first group, 500 mg vancomycin (in 100 cc normal saline 0.9%) that was injected 50 ml via each lumen of permcath and antibiotic lock by the last 1.5 ml (each 48hours), with 1 gr IV Ceftriaxone (each 12hours) for 7 days, and then oral antibiotics was administered according to the culture fore three weeks. In the second group the routine intravenous antibiotic (500 mg intravenous Vancomycin + 100-150 mg Amikacin intravenous daily) prescribed. Our endpoint is to assessment of catheter removal. At the end, both groups compare by Fisher's Exact test to determine the effect of methods on catheter removal.
Results: Patients characteristics (age, sex, time of insertion of the catheter and number of dialysis per week) didn't differ between 2 groups. Of 28 patients in group 1, 1 catheter removal, and of 39 patients in group2, 22 catheter removals were done. There is a significant reduction of catheter removal in the first group (p<0.001).
Conclusions: This study has shown that administration of Vancomycin via permcath is more effective than intravenous, and increase life time of catheter.

MP350 FAR INFRARED THERAPY INHIBITS ENDOTHELIAL INFLAMMATION OF VASCULAR ACCESS VIA THE INDUCTION OF HEME OXYGENASE-1 IN HEMODIALYSIS PATIENTS

Chih-Ching Lin[1,3], Xiao-Ming Liu[2], Wu-Chang Yang[3,1], Shing-Jong Lin[4,1], William Durante[2]. *[1]School of Medicine, National Yang-Ming University, Taipei, Taiwan; [2]Department of Medical Pharmacology and Physiology, School of Medicine, University of Missouri-Columbia, Columbia, MO, USA; [3]Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; [4]Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*

Introduction and Aims: Survival of arteriovenous fistula (AVFs) in hemodialysis patients is associated with both far infrared (FIR) therapy and length polymorphisms of the heme oxygenase-1 (HO-1) promoter. In this study, we evaluated whether there is an interaction between FIR therapy and HO-1 in regulating vascular inflammation in human umbilical vein endothelial cells (HUVECs).
Methods: In HUVECs, the expression of HO-1 and NF-E2-related factor-2 (Nrf2), the promoter activity of HO-1 gene, tumor necrosis factor-α (TNF-α)-induced expression of E-selectin, vascular cell adhesion molecules-1 (VCAM-1), intercellular cell adhesion molecules-1 (ICAM-1), monocyte chemoattractant protein-1 (MCP-1), and interleukin-8 (IL-8) were evaluated in response to FIR by Western blotting, dual luciferase reporter assay, and monocyte adhesion study. We also evaluated whether the inhibition of HO-1 by tin protoporphyrin (SnPP) or HO-1 small interfering RNA (siRNA) would modulate the anti-inflammatory effect of FIR. We also evaluated the effect of FIR therapy on the inflammatory markers in hemodialysis patients.
Results: Treatment of HUVECs with FIR radiation stimulated HO-1 protein, mRNA, and promoter activity. HO-1 induction was dependent on the activation of the antioxidant responsive element, Nrf2, and was likely a consequence of heat stress. FIR radiation also inhibited TNF-α-mediated expression of E-selectin, VCAM-1, ICAM-1, monocyte chemoattractant protein-1, interleukin-8, and the cytokine-mediated adhesion of monocytes to Ecs.The anti-inflammatory action of FIR was mimicked by bilirubin and was reversed by the HO inhibitor, tin protoporphyrin-IX, or by the selective knockdown of HO-1. Finally, the anti-inflammatory effect of FIR was also observed in 20 hemodialysis patients.

The inflammatory markers of the 20 HD patients

	HD session without FIR	HD session with FIR	P value
hsCRP (mg/L)-BD	4.10±4.07	4.63±4.32	0.363
hsCRP (mg/L)-AD	4.34±4.26	3.98±2.93	0.593
Δ (AD-BD) hsCRP (mg/L)	0.24±0.43	-0.65±1.73	0.044
ICAM-1 (ng/mL)-BD	690±225	728±218	0.295
ICAM-1 (ng/mL)-AD	886±281	823±320	0.068
Δ (AD-BD) ICAM-1 (ng/mL)	196±128	95±190	0.005
VCAM-1 (ng/mL)-BD	1135±664	1164±676	0.675
VCAM-1 (ng/mL)-AD	1461±716	1243±667	0.037
&Δ (AD-BD) VCAM-1 (ng/mL)	326±249	79±107	<0.001

BD: before hemodialysis; AD: after hemodialysis.

Conclusions: These results demonstrate that FIR therapy exerts a potent anti-inflammatory effect via the induction of HO-1. The ability of FIR therapy to inhibit inflammation may play a critical role in preserving blood flow and patency of AVFs in hemodialysis patients.

MP351 RISK FACTORS FOR CATHETER THROMBOSIS: RESULTS OF A 2-YEAR PROSPECTIVE STUDY

Peter Thomson[1], Catherine Stirling[1], Jamie Traynor[2], Scott Morris[1], Robert Mactier[1]. *[1]Renal Unit, Glasgow Royal Infirmary, Glasgow, Lanarkshire, United Kingdom; [2]Renal Unit, Monklands Hospital, Airdrie, Lanarkshire, United Kingdom*

Introduction and Aims: One of the most common complications of central venous catheterisation is catheter thrombosis manifest by poor haemodialysis blood flows. In this study we describe our experience of catheter failure due to poor haemodialysis blood flow and evaluate potential risk association with underlying clinical and laboratory variables in a haemodialysis cohort.
Methods: Laboratory and clinical variables were recorded at catheter insertion and the clinical course was followed up to the point of catheter removal. An outcome event was defined as removal of a central venous catheter (CVC) in response to low haemodialysis blood flows that consistently impaired effective haemodialysis delivery despite anticoagulation and/or thrombolytic intervention.
Univariate analysis was used to test for association between clinical and laboratory variables and outcome. Significant univariates were then put forward for inclusion in a multivariate model to test for independent association.
Results: 44,528 catheter days of observation were accumulated over a 2-year study period during which time 365 patients underwent 823 central venous catheter insertions. A total of 131 catheters were removed due to poor haemodialysis blood flow (2.94 per 1000 catheter days).
Rates of catheter removal due to poor flow were 0.98 per 1000 catheter days in the tunnelled CVC (TCVC) group, 12.3 per 1000 catheter days in the internal jugular vein non-tunnelled CVC (NTCVC) group ($p<0.001$), and 37.6 per 1000 catheter days in the femoral vein NTCVC group ($p<0.001$). Internal jugular and femoral NTCVCs exchanged over a guidewire demonstrated failure rates of 20.2 ($p<0.001$) and 32.3 ($p<0.001$) per 1000 catheter days respectively. Low haemodialysis blood flow during the first dialysis following catheter insertion ($p<0.001$) and elevated levels of c-reactive protein (CRP) at the time of catheter insertion ($p<0.001$) were also significantly associated with outcome on univariate analysis. All other variables, amongst which included cause and duration of renal failure, modified charlson comorbidity scoring and antiplatelet use, were not significantly associated with catheter thrombosis.
Multivariate analysis demonstrated hazard ratios (HR) for the development of catheter failure due to poor flow with internal jugular NTCVCs of 4.65 ($p<0.001$), femoral NTCVCs of 9.23 ($p<0.001$), 5.56 ($p<0.001$) for internal jugular NTCVCs exchanged over a guidewire and 11.73 ($p<0.001$) for femoral NTCVCs exchanged over a guidewire. Elevated CRP demonstrated a HR of 1.004 ($p<0.001$) per unit increase.
Conclusions: There is a hierarchy of independent risk association for catheter failure due to poor haemodialysis blood flow across NTCVC sub-types. A heightened inflammatory state manifest by raised CRP at the time of catheter insertion was also independently associated with outcome. All other laboratory and clinical variables failed to demonstrate significant association with catheter failure. We recommend tunnelled central venous catheter insertion be performed where possible.

MP352 SMOOTH MUSCLE CHANGES IN THE CEPHALIC VEIN OF CHRONIC KIDNEY PATIENTS (CKD) BEFORE USE AS ARTERIOVENOUS FISTULA (AVF)

Mohammed Alhomrany[1], Mahmoud Wali[2], Refat Eid[3]. *[1]Medicine, King Khalid University, Abha, Aseer, Saudi Arabia; [2]Vascular Surgery, King Faisal Specialist Hospital, Jeddah, Makakh, Saudi Arabia; [3]Pathology, King Khalid University, Abha, Aseer, Saudi Arabia*

Introduction and Aims: Complications of arteriovenous fistula (AVF) occur in up to 35% of chronic kidney patients (CKD).The most frequent complication is thrombosis, usually from stenotic lesions in the venous outflow system. In the present study, we investigated the pre-existing smooth muscle changes in the cephalic vein of these patients.
Methods: Atotal of 17 cephalic vein specimens were collected from 3 normal controls and 14 CKD patients underwnt primary AVF creation on the chosen limb. After preparation, ultrathin sections were stained with uranyl and lead acetate and were examined under the transmission electron microscope (TEM).
Results: Compared with nornal controls, abnormal fibrous infiltration of the intima and media and varying degrees of smooth muscle degenerative changes were observed in all the cephalic vein sections of CKD patients. Smooth muscle cells (SMCs) lost their normal fusiform shape and were widely separated by increased amount of irregularly diposed, extracellular collagen fibres. Other cellular abnormalities include irregular cell membrane, granular cytoplasm, peri-and paranuclear vacuoles and mega mitochondria. SMCs also showed morphological expression of phagocytosis of collagen and elastic fibers as a sign of remodeling of the vein wall.
Conclusions: Pre-existing wall and smooth muscle changes were observed in all the cephalic vein sections of CKD patients, which may contribute to the later cmplications of AVFs.

MP353 ANATOMICAL CORRELATION OF A WELL FUNCTIONING ACCESS GRAFT FOR HAEMODIALYSIS

Pedro Ponce [1], Ana Mateus [1], Lidia Santos [2]. *[1]Nephrology, Hospital Garcia de Orta, Almada, Portugal; [2]Nephrology, Hospital Torres Novas, Torres Novas, Portugal*

Introduction and Aims: Despite a wide acceptance that vascular access (VA) haemodynamic surveillance should be performed, its real benefit has not yet been established. On the other hand, once detected, pre-emptive angioplasty of significant VA stenosis remains controversial.
This pilot study was designed to question the rational of our decision-making process in VA management.
Methods: Twelve consecutive adult patients dialysed through a PTFE graft for more than three months, were selected whenever all clinical and haemodynamic criteria (Dynamic Venous Pressure (DVP) < 150 mmHg and vascular access flow (Qa) measurement > 800ml/min) of a well functioning VA were met.
All the selected patients were submitted to a baseline diagnostic angiogram and cases with stenosis occluding more than 50% of the access lumen were counted.
Endovascular intervention was not performed in any of the patients, including those with stenosis.
Close clinical and haemodynamic follow-up monitoring were maintained during the next 6 months, with monthly Qa measurement and recording all access morbidity.
Results: The baseline diagnostic angiogram of the 12 patients revealed a venous anastomosis stenosis: (i) reducing more than 50% of the access lumen in 5 cases; (ii) 25 to 50% in 4 cases and (iii) no stenosis in 3 cases.
One patient with stenosis greater than 50% and another with stenosis between 25-50% had graft thrombosis during the follow-up period. None of the graft thrombosis could have been predicted from the previous month Qa evaluation. All the 4 patients with a stenosis higher than 50% that did not thrombose, had a normal Qa at the end of the follow-up period.
Conclusions: The data suggests that the presence of what we call a significant stenosis is not correlated with measured Qa and it might not be associated with early thrombosis deserving immediate intervention. Further studies are needed to clarify the best surveillance protocol and the role of pre-emptive intervention in significant stenosis.

MP354 EFFECT OF RADIAL ARTERY (RA) PATHOLOGY ON RADIOCEPHALIC FISTULA (RCF) FUNCTION FOR HEMODIALYSIS (HD). HISTOLOGIC ANALYSIS OF 37 PATIENTS

Ramon Roca-Tey, Ramon Bordes, Amelia Rivas, Omar Ibrik, Rosa Samon, Isabel Giménez, Román Martínez-Cercós, Jordi Viladoms. *Nephrology, Pathology & Vascular Surgery, Hospital de Mollet. CETIR Centre Mèdic., Barcelona, Spain*

Introduction and Aims: The aim of this prospective study was to investigate the impact of RA lesions on RCF function in chronic-renal failure (CRF) patients (pts) undergoing HD.
Methods: We performed RA biopsy (a 5-10 mm long segment of the RA wall) during the forearm RCF operation in 37 consecutive CRF pts (age 64.9±13.2 yr). All specimens of RA were stained with hematoxylin-eosin and analyzed with the light microscope by the same pathologist. From the microscopic RA study, we evaluated histopathologic changes and performed the following morphometric analysis: thickness of the intima (IT) and media (MT) layers, intima-media thickness IMT (IT + MT). Laboratory parameters: calcium, phosphorus, parathyroid hormone; calcium x phosphorus product was calculated. RCF outcome: functioning RCF 75.7% (28/37) or RCF not suitable for routine HD (non-functioning RCF, NFRCF) 24.3% (9/37). RCF function was evaluated measuring Q_A just after 1 month of successful RCF cannulation for HD by 2 needles at Q_b>250 ml/min. We determined Q_A by Delta-H method using the Crit-Line III monitor (ABF-mode, HemaMetrics, USA) (35.7%) or Doppler ultrasound performed by the same radiologist using a 5-10 MHz linear transducer (Sequoia machine, Siemens-Acuson) (64.3%).
Results: Prevalence of RA pathology: 29.7% (11/37). Histopathologic changes: medial calcifications (8/11, 72.7%), intimal atherosclerosis (1/11, 9.1%), combined calcifications and atherosclerosis (1/11, 9.1%), myxoid degeneration (1/11, 9.1%). Morphometric measurements (mm): IT 0.11 ± 0.22 (range, 0.02-1.02), MT 0.39±0.16 (range, 0.20-0.90), IMT 0.50±0.28 (range, 0.24-1.60). Mean Q_A (ml/min): 1154.7 ± 504.6 (range, 377-2269). Pts with RA pathology showed higher mean MT (0.54±0.19 *versus* 0.33±0.09 mm), higher mean IMT (0.76 ± 0.39 *versus* 0.39±0.10 mm) and lower mean Q_A (771.7±395.2 *versus* 1282.4±477.9 ml/min) compared to pts with healthy RA (hRA, 25/37, 67.6%) (p=0.01, p<0.001 and p=0.007, respectively). Pts with medial calcifications (9/37, 24.3%) had higher mean MT (0.58±0.18 *versus* 0.33±0.09 mm), higher mean IMT (0.73±0.37 *versus* 0.39±0.10 mm) and lower mean Q_A (662.0±265.9 *versus* 1282.4±477.9 ml/min) compared to pts with hRA (p<0.001, p=0.001 and p=0.005, respectively); no differences in mineral metabolism parameters were found when comparing both groups (for all comparisons, p=NS). Pts with NFRCF had higher mean MT (0.48±0.15 *versus* 0.36±0.15 mm) and tended to have higher mean IMT (0.64±0.39 *versus* 0.45±0.23 mm) compared to pts with FRCF (p=0.03 and p=0.07, respectively). Pts with diabetic nephropathy (8/37, 21.6%) showed lower mean Q_A (700.6±276.1 *versus* 1253.4±491.5 ml/min, p=0.018) and tended to have increased prevalence of RA calcification (50.0% *versus* 17.2%, p=0.08) compared with the remaining pts (29/37, 78.4%).
Conclusions: 1) One third of RA specimens analyzed had histopathological involvement. 2) The RCF function is impaired in pts with RA pathology. 3) The MT is predictive of RCF outcome.

MP355 FIVE YEARS OF VASCULAR ACCESS (VA) STENOSIS SURVEILLANCE BY BLOOD FLOW RATE (Q_A) MEASUREMENTS DURING HEMODIALYSIS (HD) USING THE DELTA-H METHOD

Ramon Roca-Tey, Rosa Samon, Omar Ibrik, Isabel Giménez, Román Martínez-Cercós, Jordi Viladoms. *Department of Nephrology and Vascular Surgery, Hospital de Mollet, Mollet del Vallès, Barcelona, Spain*

Introduction and Aims: The best method for early VA stenosis detection in ESRD patients (pts) is periodic Q_A measurement.
Methods: From June-2000 to June-2005, we prospectively monitored Q_A of 145 VA (arteriovenous fistula AVF 84.1% or graft 15.9%) during HD in 131 ESRD (age 62.6±13.5 yr) pts. Q_A was measured, at least every 4 months, within the first hour of the HD session by the Delta-H method using the Crit Line III Monitor. Baseline Q_A was calculated from two consecutive HD sessions (the values were averaged). All VA with absolute Q_A<700 ml/min or decreased >20% from baseline over time met the positive evaluation (PE) criteria and were referred for angiography (AG) plus subsequent elective VA intervention (angioplasty PTA or surgery) if VA stenosis≥50%. Mean arterial pressure MAP and Kt/V index were measured simultaneous with Q_A.
Results: We performed 950 Q_A measurements in 2.624 months of follow-up. Baseline and overall Q_A (ml/min): 1097.1±435.3 and 1166.6±473.1, respectively. Coefficient of variation for duplicate Q_A measurements: 7.3±5.9%. We found an inverse correlation between patient's age and baseline or overall Q_A (r=-0.37 and -0.38, respectively; p<0.001 for both correlations). Pts with diabetic nephropathy (19.1%)showed lower baseline (888.5±415.4 ml/min) and overall (929.7±411.3 ml/min) Q_A compared with the remaining pts (1140.7±430.6 and 1220.1±472.4 ml/min, respectively) (p=0.008 and 0.004, respectively). Radial AVF (78/145, 53.8%) showed lower baseline (971.7±450.2 ml/min) and overall (1070.5±499.8 ml/min) Q_A compared to the remaining VA (1243.0±369.8 and 1278.6±416.3 ml/min, respectively) (p<0.001 and 0.002, respectively). We found 54 cases of PE in 47 VA. AG was performed in 87% (47/54) cases of PE and most of them (43/47, 91.5%) showed significant VA stenosis (mean degree 80.5±12.9%). Positive predictive value, negative predictive value, sensitivity and specificity of Delta-H method for VA stenosis detection (%): 84.8, 91.9, 83.0 and 92.9, respectively. Twenty-five PE cases (25/43, 58.1%) underwent preventive intervention by PTA (24%) or surgery (76%). Q_A increased from 554.7±107.6 ml/min just before intervention to 977.9±359.9 ml/min just after intervention (n=21, ΔQ_A= 423.2±296.6 ml/min) (p<0.001). No difference was found when the highest recorded Q_A before intervention (889.8±409.5 ml/min) and Q_A post-intervention were compared (p=0.18). MAP not changed after intervention (93.4±13.3 *versus* 93.1±14.1 mmHg, p=0.95). Kt/V index improved from 1.43±0.21 before intervention to 1.49±0.21 after intervention

without any change in dialyser type or HD duration (p=0.006). Rate of VA thrombosis: 0.11 episodes per patient year at risk.
Conclusions: 1) The Delta-H technique is a method highly reproducible, accurate in early diagnosis of VA stenosis and useful in monitoring the hemodynamic effect of elective VA treatment. 2) The functional VA profile is related with patient's age and type of VA, and is worse in diabetic pts. 3) After elective intervention for stenosis, the functional VA status is restored and HD delivery is improved.

MP356 LESS THROMBOGENIC MICROPATTERNED POLYMER MODIFIED SURFACE IMPROVES TEMPORARY HEMODIALYSIS CATHETER SURVIVAL IN PATIENTS WITH END-STAGE RENAL DISEASE

Pascal Meier, Rachel Meier, Edouard Blanc. *Service of Nephrology, CHCVs Hôpital de Sion, Sion, Switzerland*

Introduction and Aims: Thrombosis is a major cause of HD catheter dysfunction. Surface properties turned out to play a key role for activation of the coagulation system and adhesion of clot components such as fibrin net or platelet aggregates. Recently, novel coating technology that provides the surface with a micropatterned structure of hydrophilic-hydrophobic domains in a polymer system containing hydrophobic polydimethylsiloxane blocks in a polyurethane net was proposed. We hypothesized that the improvement of blood–surface interaction by a reactive polymer film coating used *in vitro* might reduce thrombogenic events in the vascular access device and subsequently lead to prolonged catheter survival in the clinical setting.
Methods: We compared, in a randomized cross-over single-blinded study, the clinical application of two untunnelled temporary catheters (UTCs) namely one standard double lumen catheter (sDLC - GamCath GDK-1220) and one surface modified catheter (smDLC - GamCath Dolphin SM-GDK-1220) with identical geometry and flow design. All UTCs were inserted into the right internal jugular vein. None of the failed UTCs were brushed or exchanged over a guidewire. The other protocolled UTC was placed in a new site along the internal jugular vein. An overall of 50 stable chronic HD patients were included to obtain sufficient statistical power. No anticoagulation outside the dialysis session was allowed, and each patient was on platelet anti-aggregation using aspirin 100 mg/d. The primary endpoint was catheter survival. Efficacy endpoints were defined as the ability to complete HD and ability to achieve blood flow rates of $\geq$ 250 mL/min. Safety endpoints were defined as the occurrence of allergic reactions, infection or bleeding.
Results: The clinical investigation revealed that both number of days before UTCs removal according to clinical requirements and number of treatments per catheter were significantly higher with smDLC as compared with sDLC ([mean±SD] 36±17 *vs.* 19±8 days; 23 *vs.* 14 treatments; *p=0.01*). The mean±SD blood flow rate and the recirculation range were 298±27 mL/min. and 3-10% *vs.* 253±35 mL/min. and 5-12% for smDLC and sDLC, respectively (Qb: *p=0.01*). UTC malfunction occurred in 13% and 27% for smDLC and sDLC, respectively, giving an overall rate of 18 and 34 episodes per 1,000 UCT days at risk (*p=0.01*). Thrombosis of smDLC and sDLC was observed in 7.9 (2.4 episodes per 1,000 UCT days) *vs.* 20.9% (9.8 episodes per 1,000 UCT days), respectively (*p=0.001*). There was a significant difference in local infection rate with 1.1 for smDLC *vs.* 2.5 for sDLC local infection/1,000 UCT days (*p=0.002*), and 0.5 for smDLC *vs.* 1.3 for sDLC bacteremia/1,000 UCT days (*p=0.001*).
Conclusions: Micropatterned surface coating with a polyurethane polymer significantly increased smDLC survival and the number of treatments per catheter. Furthermore, these UCTs appear more efficient with lower dysfunction rate, and are a less risk for fibrin sleeves with better bacteriological barrier than sDLC.

MP357 MODIFICATION OF THE HEMODIALYSIS (HD) CATHETER SURFACE REDUCES BACTERIAL COLONIZATION: A RANDOMIZED CONTROLLED TRIAL

Ralf Schindler[1], Uwe Heemann[4], Ulrike Haug[3], Cosima Pohle[1], Reinhold Deppisch[3], Hermann Goehl[3], Markus Hollenbeck[2]. *[1]Nephrology and Intensive Care Medicine, Charite-Virchow Clinic, Berlin, Germany; [2]Klinik fuer Nephrologie und Rheumatologie, Knappschaftskrankenhaus, Bottrop, Germany; [3]Gambro Corporate Research, Hechingen, Germany; [4]Abteilung fuer Nephrologie, Klinikum Rechts der Isar, Munich, Germany*

Introduction and Aims: HD catheter-related blood stream infections are a major cause of morbidity and mortality in patients with acute and chronic renal failure.
Methods: We conducted a randomized, prospective, double-blind trial investigating the bacterial colonization of non-tunnelled HD catheters in 77 patients in need of temporary vascular access. A standard catheter (SC, Gambro) was compared to a surface-modified, bismuth-film coated catheter (FCC, Gambro). After removal of the catheter for any reason, both arterial and venous lumina were rinsed and the fluid cultured for detection of bacterial colony-forming units (CFU). The catheter tips were placed in a tube containing sterile saline, sonicated and the supernatant cultured. The results were expressed in CFU/ml as well as number of catheters with CFU above 100/ml.
Results: 77 patients in three hemodialysis units were randomized, 23 with acute, 49 with chronic renal failure and 5 patients were treated with plasma exchange. For all 3 conditions (sonic. catheters, art. and venous rinse fluids), the number of CFU/ml were lower with the use of FCC compared to SC (p=0.027, chi-square). Markers of inflammation (CRP, leukocytes) are currently being analyzed.

Colony forming units mean±SEM

	CFU Cath Sonic	CFU rinse art	CFU rinse ven	#cath CFU>100
SC n=39	62±35	57±16	19±16	7
FCC n=38	3.4±2	15±12	3.5±3	1

Conclusions: Surface modification with bismuth-film coating reduces the bacterial colonization of HD catheters in a clinical trial. These modified catheters may reduce the complications and costs due to catheter-related blood stream infections.
Disclosure: This study was supported by Gambro Corporte Research.

MP358 EVALUATION OF NEW MTHOD FOR MEASURING VASCULER ACCESS RECIRCULATION

Katsunobu Ando, Izumi Yoshida, Takayuki Uchida, Atsushi Horiguchi, Itsuro Nakajima, Yuki Sakuma, Takanori Komada, Kaoru Tabei. *Division of Nephrology, Department of Integrated Medicine, Saitama Medical Center, Jichi Medical University, Saitama, Japan*

Introduction and Aims: We evaluated the availability of the new method for measuring vascular access recirculation. This measurement is performed by a kind of a dilutional method using the marker produced by rapid ultrafiltration by dialysis machine.
Methods: Two optical monitors for measuring hematocrit were installed on the dialysis machine (DCS-27; NIKKISO CO., LTD). One of them was set to the extracorporeal venous line, and another was set to the extracorporeal arterial line. The measurement method is a kind of a dilutional method using the marker produced by rapid ultrafiltration by dialysis machine; brief ultrafiltration at higher rate is performed for 1sec (about 10ml or more) and a mass of concentrated blood in the venous line is produced. If vascular access recirculation occurs, some of the mass of concentrated blood will be measured by the monitor on the arterial line. Each value is integrated to the volume of blood through corresponding extracorporeal line. Vascular access recirculation is calculated by the ratio of the integration of the arterial variation to that of the venous one. Ultrafiltration volume and time required for 1 measurement is approximately 10mL and 4min, respectively. Operation is easy. Measurement is started by touching the key, and completes without any other operation, so results does not depend on the technique of the operator. Disposables, e.g. saline, syringes and so on are not needed.
3 times consecutive measurements of the rate of vascular access recirculation by the optical monitors were performed in 20 hemodialysis cases, and

standard measurements of vascular recirculation using urea and creatinine dilution methods were also performed at the same time. Dialysis shunt was used for vascular access in 18 cases, veins in arms in 1 case, and double-lumen catheter in the femoral vein, connected extracorporeal lines inversely in 1 case. Blood flow rate was between 100 to 230 mL/min. Used dialysers: membrane area was between 0.6 to 1.9m^2 and UFR was between 10.5 to 52mL/h/mmHg.
Results: In 53 measurements of standard vascular shunt with no postural change, difference of the results (absolute value) between the monitor and both dilution method were 4.0% and 3.2% respectively, and maximum difference of the results were 11.0% and 9.8% respectively. Regression analysis showed tight correlation between them ($p < 0.0001$).
In 1 measurement at dialysis shunt with postural change (to left lateral decubitus position), the difference between the monitor and urea dilution method was 16%, and creatinine dilution method was 12.6%. This result suggests that postural change influences the measurement. For making artificial recirculation, double-lumen catheter was connected extracorporeal lines inversely, and the average 3 measurements of recirculation is 92%.
Conclusions: We conclude that the new method for measuring vascular access recirculation by comparing the variation of the marker in the blood, produced by rapid ultrafiltration is available from the viewpoints of accuracy, easy operation, and unnecessity of disposables.

MP359 PREVALENCE AND FUNCTIONAL EFFECT OF ARTERIOVENOUS FISTULA (AVF) CALCIFICATIONS EVALUATED BY SPIRAL COMPUTED TOMOGRAPHY (CT) IN PATIENTS UNDERGOING CHRONIC HEMODIALYSIS (HD)

Ramon Roca-Tey, Rafael Páez, Amelia Rivas, Isabel Giménez, Rosa Samon, Omar Ibrik, Jordi Viladoms. *Departments of Nephrology and **CRC Hospital de Mollet, **CETIR Centre Mèdic, Barcelona, Spain*

Introduction and Aims: The aim of this cross-sectional study was to investigate the prevalence and functional effect of native AVF (feeding artery and/or arterialized vein) calcifications evaluated by CT in ESRD patients (pts) undergoing HD.
Methods: Forty-five AVF (radial 44.4% or brachial 55.6%, duration 65.3±12.6 months) without evidence of significant stenosis were evaluated by CT in 45 ESRD pts (age 63.8±13.1 yr; sex M: 71.1%, F: 28.9%; time on HD 53.1±8.1 months; diabetic nephropathy 15.6%). All AVF explorations were performed using the same multi-slice spiral CT scanner (HiSpeed Dual machine, GE Medical Systems). The severity of AVF calcifications was quantified by CT using the following criteria: grade I absence of calcifications, grade II isolated calcifications (<10 groups of calcification), grade III moderate calcifications (10-20 groups of calcification) and grade IV diffuse calcifications (>20 groups of calcification). Laboratory parameters: calcium, phosphorus, parathyroid hormone; calcium x phosphorus product was calculated. The same week of CT scanning, we evaluated AVF function measuring the blood flow rate (Q_A). We determined Q_A (1559.3±980.6 ml/min) by the Delta-H method (ABF-mode, HemaMetrics, USA) using the Crit-Line III monitor (68.9%) or Doppler ultrasound (31.1%) performed by the same radiologist using a 5-8 MHz linear transducer (Sequoia machine, Siemens-Acuson); mean arterial pressure MAP (94.7±16.3 mmHg) was recorded simultaneous with Q_A.
Results: Most pts not showed AVF calcification by CT scan (grade I 27/45, 60%). Forty percent of pts (18/45) demonstrated any degree of AVF calcification (grade II 13.3%, grade III 8.9%, grade IV 17.8%). Pts with brachial AVF showed higher Q_A compared to pts with radial AVF (1899.1±1131.8 *versus* 1134.5±516.4 ml/min, p=0.005), but MAP (91.2±15.8 *versus* 99.0±16.2 mmHg) and the prevalence of AVF calcification (32% *versus* 50%) were not different between both groups (p=0.11 and p=0.24, respectively).
Pts with evidence of any calcification on CT scanning (grade II, III or IV) had higher time on HD (84.6±63.1 *versus* 24.6±20.0 months), higher AVF duration (97.7±89.3 *versus* 34.6 ± 61.2 months) and similar Q_A (1488.3±678.9 *versus* 1606.6±1148.9 ml/min) compared with pts without AVF calcification (p=0.014, p=0.001 and p=0.69, respectively); no differences in MAP (95.4±13.8 *versus* 94.2±17.9 mmHg), prevalence of brachial AVF (44% *versus* 63%) or mineral metabolism parameters were found when comparing both groups (for all comparisons, p=NS). The same results were obtained when comparing pts with a high (grade III-IV: 26.7%) and a low (grade I-II: 73.3%) AVF calcification score, or when comparing pts with diffuse (grade IV) and without (grade I) AVF calcification.
Conclusions: 1) The prevalence of AVF calcification by CT scan was 40%. 2) The AVF calcification was related with time on HD and AVF duration. 3) The function of fully developed AVF suitable for routine HD was not impaired by the presence of calcifications.

MP360 USE OF CATHETERS IN INCIDENT HEMODIALYSIS (HD) PATIENTS

Giuseppe Pontoriero, Ferruccio Conte, Enzo Corghi, Aurelio Limido, Fabio Malberti, Donatella Spotti, Pietro Ravani. *Lombardy Dialysis and Transplant Registry, Milan, Lombardy, Italy*

Introduction and Aims: Permanent catheters are increasingly used in incident and prevalent HD patients. We studied the risk of catheter use over time in a large cohort of incident HD patients and factors known to influence the choice of vascular access.
Methods: An incident cohort of 3,054 patients who began HD treatment in Lombardy (Italy) between Jan 2001 and Dec 2005 was examined. Logistic regression was used to model the risk of having a catheter at the time of the first HD as a function of age, sex, diabetes, cardiovascular disease, and year of treatment. Trend modification by level of other covariates was formally tested using interaction terms. Centre effect was treated as a random effect.
Results: Between 2001 and 2005 catheter use progressively increased among incident patients. This occurred in the whole population – from 55% to 64%, as well as in non-diabetic relatively young males (age <55 years) – from 53% to 65%. In the final model, older age (OR 1.16 per decade, 95% CI 1.03 to 1.22) and more recent period (OR 1.09 per year, 95% CI 1.03 to 1.15; P for trend 0.004), but not gender, diabetes or cardiovascular disease, were significant predictors of carrying a catheter. There were no significant interaction terms.
Conclusions: Our data show a significant increasing use of catheters in patients new to HD. This trend occurred even in relatively young non-diabetic males. Therefore, older age and comorbid conditions are not the only factors affecting the choice of the vascular access for HD. More data on current practice patterns and patient characteristics are necessary to target intervention policies aimed at interrupting the declining use of the native arteriovenous fistula for HD.

MP361 ROLE OF ADDUCIN GENES IN ARTERIOVENOUS FISTULA PATENCY IN HEMODIALYSIS PATIENTS

Cristina Tantardini, Chiara Lanzani, Marco Melandri, Nunzia Casamassima, Simona Delli Carpini, Luisa Persichi, Donatella Spotti, Giuseppe Bianchi, Paolo Manunta. *Nephrology, Dialysis and Hypertension, San Raffaele Universty Hospital, Milan, Italy*

Introduction and Aims: In hemodialysis patients with an arteriovenous (AV) fistula, access failure is primarily due to fistula stenosis, which predisposes to thrombosis and subsequent access loss. The risk for access failure differs interindividually, an observation that is independent from vascular anatomy in a significant number of patients. Access patency is limited by the development of venous intimal hyperplasia, which predisposes to fistula stenosis and subsequent thrombosis. Adducin is a citoskeleton tetrameric protein, code by ADD1, ADD2, ADD3 genes, involved in signal transduction, cell-to-cell contact formation, and cell migration. Preliminary data indicate that the ADD1 460Trp allele is associated with enhanced production of reactive oxygen species in normal human cultured skin fibroblasts, providing an initial link between the ADD1 460Trp allele, oxidative stress, endothelial dysfunction and end-organ damage, such as increased intima media thickness. Recently three separate epidemiological studies suggest a role of the ADD1 460Trp allele as a plausible candidate for intima–media thickness. Aim: To determine whether ADD1, ADD2, ADD3 and ACE genes would be an independent factor or may have a genetic interaction for predicting patency of AV fistula in hemodialys patients.
Methods: One hundred three patients who had undergone placement of an AV fistula for initiation of hemodialysis treatment were genotyped for all gene polymorphisms. The primary end-point was time from fistula placement to access failure.

Results: The mean primary AV survival was 39.2±3.68 months. AV fistula patency neither differed between diabetic (40±5) and nondiabetic (38±5). Kaplan-Meier analysis of AV fistula patency stratified by ADD1 and ADD2 genotypes resulted in a 3 fold increased risk for vascular access failure (RR 2.99 CI 1.44-6.12, p = 0.02 after correction for AV type) in those patients carrying the wild type ADD1 and the mutate ADD2 allele. All the other analysis neither single genes or gene-genes interaction yield negative results.
Conclusions: These preliminary data suggest that the identification of relevant genes, ADD1 and ADD2, involved in remodeling process, may indicate a novel approaches for achieving higher patency rates.

MP362 VASCULAR ACCESS TYPE AND MORTALITY IN PATIENTS RETURNING TO HEMODIALYSIS AFTER A FAILED RENAL TRANSPLANT

Gustavo Laham, Gervasio Soler Pujol, Carlos Diaz, Ana Cusumano, Mario Davalos, Antonio Vilches. *Nephrology Section, Department of Medicine, FME-CEMIC Dialysis Unit, Centro de Educacion Medica e Investigaciones Clínicas (CEMIC), Ciudad de Buenos Aires, Buenos Aires, Argentina*

Introduction and Aims: Although the use of a catheter as a means for vascular access (VA) in patients (Pts) entering a hemodialysis program (HD) after failure of their native kidneys is associated with increased mortality. It is not known whether this association is also present in the case of failed renal transplants (Tx). The purpose of our study was to assess the relationship between the type of VA and mortality in Tx patients re-entering our HD program.
Methods: Between 1/1995 and 12/2006, 109 incident Pts started HD after a failed Tx. The cohort was divided into 2 groups according to the type of VA: 1) Planned VA (PVA), i.e. an A-V fistula or a graft; and, 2) Unplanned VA (UPVA), i.e. a catheter. Pts were censored at the time of re-transplantation or loss of follow up (FU). Co-morbid conditions were weighted using Khan's index based on age, presence of diabetes and organ-specific conditions. Cox regression analysis was used to establish mortality predictors and Kaplan-Meir's method for survival comparisons. Results are expressed as means, medians, interquartile ranges (IQR) and standard deviations (SD), as appropriate.
Results: Mean age was 43 years; 67.9% were males and median follow up was 56 months, IQR 15-94. Median Tx survival was 94 months, IQR 60-148, and the serum creatinine at the start of HD was 6.1 mg/dl ± 2.1. 41/109 Pts (37.6%) died during FU. There were significant differences in age ($p<0.02$), Khan index ($p<0.02$), time on HD after re-started on the program ($p<0.0001$), and survival when the PVA (n=69) and UPVA (n=40) groups were compared. Mortality was 27.5% and 55%, respectively, Log Rank test ($p<0.0001$). Multivariate Cox regression analysis showed that catheter use was independently associated with a greater mortality after adjusting for known confounders (age, Khan Index and donor type), Odds ratio 6.69; 95%; Confidence Interval 2.97-15.1.
Conclusions: For whatever reason an UPVA is independently associated with a greater mortality in Pts who start HD after Tx failure, and as nephrologists we should program a definitive VA in anticipation of this event in Pts with failing grafts.

MP363 AUTOGENOUS BRACHIOBASILIC FISTULA WITH BI-DIRECTIONAL FLOW: A FEASIBLE VASCULAR ACCESS IN COMORBID PATIENTS

Carlo Lomonte, Francesco Casucci, Maurizio Antonelli, Annalisa Teutonico, Pasquale Libutti, Carlo Basile. *Nephrology, Miulli General Hospital, Acquaviva delle Fonti, Italy*

Introduction and Aims: The brachiobasilic fistula (BB-AVF) is an excellent vascular access and should be considered before placing an upper arm graft in patients who cannot achieve a brachiocephalic AVF. However, in patients with comorbidities basilic vein in the forearm, albeit suitable for an AVF construction, usually is not utilized because of the poor quality of the forearm arteries and for topographic reasons. In the elbow, brachial artery and basilic vein are close together and the vessels diameters and wall morphology are better. We describe our experience in construction of the side-artery to side-vein anastomosis (S-S) BB-AVF with bi-directional flow, and compare this type with side-artery to end-vein (S-E) transposed BB-AVF.
Methods: The records of all patients undergoing autogenous brachiobasilic AVF with or without transposition between April 2003 and September 2007 were retrospectively evaluated.
Results: BB-AVF was the secondary or tertiary access in all patients; 23 of them were already receiving hemodialysis. Main comorbid conditions were: age > 65 years (26,6%), diabetes mellitus (16,6%), peripheral vascular disease (23%), long-term immunosuppressive therapy (23%) and time on dialysis >10 years (30%). Mean follow-up was 16 months (range: 3-42). Thirty patients (19 males and 11 females; mean age: 58±9 years) underwent 30 BB-AVF: 17 patients with adequate forearm basilic vein in S-S fashion and 13 S-E with vein transposition. Maturation rate was 93%, 28 fistulas were successfully used for dialysis, time to use was of 30 days (range:15-56) in the entire group: 24.5±6.3 in S-S and 37.7±9.1 in S-E fistulas ($p<0.01$). Primary patency rates were 78.6% at 1 year, 81.2% in S-S and 75% in S-E AVFs. Six surgery-related complications (five hematoma formation and one arm swelling) were recorded: 38.4% in the S-E and 5.8% in the S-S AVFs ($p<0.05$). No complications related to the reverse flow in the forearm basilic vein were observed.
Conclusions: In the context of an aggressive all-autogenous policy with regards to vascular access, the BB-AVF with S-S anastomosis should be considered before placement of a prosthetic graft. This type of AVF is technically easy to perform and shows an excellent patency rate, lower complications and a better maturation time with respect to the transposed BB-AVF, also in patients with comorbidity and high risk for access failure.

MP364 IMPACT OF ARTERIOVENOUS FISTULA ON LOAD OF LEFT VENTRICLE IN HEMODIALYSIS PATIENTS

Martin Valek, Frantisek Lopot, Vladimir Polakovic. *Department of Internal Medicine Strahov, General University Hospital, Prague, Czech Republic*

Introduction and Aims: Arteriovenous fistula (AVF) is considered one of the cardiovascular risk factors in hemodialysis patients. The aim of this study was to evaluate the impact of AVF on load of left ventricle (LLV) using a simple model calculation based on real data specifically in patients with high access blood flow AVF.
Methods: Vascular access blood flow (QVA), cardiac output (CO), and peripheral vascular resistance (PR) were determined by ultrasound dilution (Transonic Systems, Inc., USA). Load of left ventricle (LLV) was calculated using simplified formula: $LLV = PR*CO^2$. This total load was computationally divided into the part spent to run the flow QVA through the AVF (LLVAVF) and the flow (CO-AVF) through the vascular system (LLVS): $LLVAVF = PRAVF*QVA^2$, and system $LLVS = SPR*(CO-QVA)^2$, where PR=SPR*PRAVF/(SPR+PRAVF). Abbreviations: SPR - systemic peripheral vascular resistance, PRAVF - peripheral resistance of AVF.
The model calculation was first performed in a selected group of 14 patients with high access blood flow (QVA>1300 ml/min, group 1) and later extended for comparison by another group of 40 unselected patients with access blood flow (QVA range 200-1400 ml/min, 35 patients of those were with native AVF, group 2).
Results: Group 1: mean QVA was 2280 ml/min (range 1329-4306 ml/min), mean CO being 8.8 l/min (range 4.5-10.3 l/min), and mean LLV was 2.14 Watt, (range 0.9-4.28 Watt) whereas the LLVAVF was 0.55 Watt (range 0.3-1.6 Watt), representing on average 25.7% (range 13.8.-59.8%) of the total load of left ventricle.
Group 2: mean QVA and CO were 610 ml/min (range 284-1398 ml/min) and 5.93 l/min (range 3.2-11.9 l/min), respectively, giving the mean LLV of 1.2 Watt (range 0.7-1.7 Watt), with the LLVAVF component being 0.12 Watt (range 0.05-0.3 Watt). The LLVAVF thus represented on average 11.1% (range 3.9-24.7%) of the total LLV. While the LLVAVF positively correlated with QVA ($r=0.93$, $p<0.001$), no significant correlation was found between the total LLV and QVA ($r=0.19$, ns).
Conclusions: These computational results suggest that AVF in typical range of QVA (400-800 ml/min) shall not increase heart load significantly, and represents only 8-15% of the total LLV. However, in the high QVA group, the total LLV is nearly twofold, and AVF load reaches 25% of LLV.

Anaemia 2

MP365 ASSOCIATION BETWEEN NT-PROBNP LEVELS AND ANEMIA IN CAPD PATIENTS WITHOUT HEART FAILURE

Yang-Wook Kim[1], Seok Ju Park[1], Sun Woo Kang[1], Yeong Hoon Kim[1], Heok Jin Yoon[2]. *[1]Internal Medicine, Busan Paik Hospital, College of Medicine, Inje Univ., Busan; [2]Hanseo Hospital, Busan, Republic of Korea*

Introduction and Aims: N-terminal pro brain natriuretic peptide (NT-proBNP) provide information on cardiovascular morbidity and mortality in patients with normal renal function. It is useful for diagnosis of heart failure. However, NT-proBNP has the limitation in clinical practice because it can increase in patients with renal dysfunction. Anemia is an important comorbidity in patients with chronic renal failure (CRF), and it is a major contributor to morbidity and mortality in dialysis patients.
Recent studies indicate that anemia may also affect proBNP concentrations in patients with heart failure or stroke.
However, the impact of hemoglobin status on proBNP concentrations has not been established in CAPD patients without heart failure.
Methods: 26 patients (Male: 13, Female: 13) who starting CAPD treatment were enrolled in this prospective study. Left ventricular ejection fractions (LVEF), left ventricular mass index (LVMI) were assessed by echocardiography. Serum NT-proBNP, creatinin, Kt/V, hemoglobin, C-reactive protein (CRP), IPTH and extracelluar water (ECW %) with multifrequency bioimpedance analyzer were measured. Each parameters was assessed at the beginning of the peritoneal dialysis (PD) and then 6 months later.
Results: The mean age was 46±13 years. At the initiation of CAPD treatment, hemoglobin level, serum NT-proBNP, LVMI, LVEF, CRP, Kt/V, creatinine, iPTH, ECW% were 9.25±1.19 g/dL, 5454.6±9954.6 pg/dL, 230.26±70.53 gm/m^2, 62.99±8.11%, 2.51±5.49 mg/L, 2.1±0.5, 8.6±3.0 mg/dL, 246.2±248.1 pg/mL, 30.6±6.7%. Hemoglobin was inversely associated with log NT-proBNP (r: -0.46, $p<0.05$), but there were no correlations between NT-proBNP levels and CRP, Kt/V, LVEF, LVMI, creatinine, iPTH, ECW%.
After receiving CAPD treatment for more than 6 months, 12 patients were followed up, hemoglobin level, serum NT-proBNP, LVMI, LVEF, CRP, Kt/V, creatinin, ECW% were 10.2±1.9 g/dL, 1705.6±1196.6pg/dL, 209.3±60.6 gm/m^2, 64.1±5.6%, 0.1±0.13 mg/L, 2.21±0.46, 8.85±2.86 mg/dL, 263±276.3 pg/mL, 29.4±9.75%. In the correlation analysis, the serum NT-proBNP levels showed the relative correlation with LVMI (r: 0.59; p =0.04). The changes of plasma concentrations of were inversely related to anemia severity. (r: 0.6, $p<0.05$). However, the changes of LVMI did not correlate with that of NT-proBNP (r: 0.319, p=0.339) and of hemoglobin (r: -0.2, p=0.53).
Conclusions: The hemoglobin appeared to be inversely associated with NT-proBNP in CAPD patients without heart failure.
These data showed that NT-proBNP, as well as hemoglobin, may be an independent risk predictor, but also anemia should be taken into consideration during the interpretation of NT-proBNP levels in these patients.

MP366 COMPARATIVE PHARMACOKINETICS AND PHARMACODYNAMICS OF HX575 (BINOCRIT®/EPOETIN ALFA HEXAL®) AND EPOETIN ALFA (ERYPO/EPREX®) ADMINISTERED SUBCUTANEOUSLY (SC) TO HEALTHY VOLUNTEERS

Fritz Soergel[1], Ursula Thyroff-Friesinger[2], Andrea Vetter[2], Bernd Vens-Cappell[3], Martina Kinzig[1]. *[1]IBMP-Institute for Biomedical and Pharmaceutical Research, Nuernberg, Germany; [2]Hexal AG, Holzkirchen, Germany; [3]Scope International, Hamburg, Germany*

Introduction and Aims: The recombinant human epoetin HX575 (Sandoz Pharmaceuticals GmbH/Hexal AG) is the first biosimilar ESA (erythropoiesis-stimulating agent) with marketing authorisation in Europe. The primary objective of this study was the steady state pharmacokinetic and pharmacodynamic comparison of HX575 with a comparator epoetin alfa after multiple subcutaneous application to healthy volunteers.
Methods: In this open, randomized, parallel group study, 80 healthy male Caucasian volunteers were randomized in 1:1 ratio to either the biosimilar epoetin alfa HX575 or the comparator epoetin alfa (Eprex/Erypo®, Ortho Biotech) and treated subcutaneously at a dose of 100 IU/kg, three times weekly for 4 weeks. Epoetin plasma levels and anti-rhEPO antibodies were measured by ELISA methods, hemoglobin and other pharmacodynamic parameters by flow cytometry and routine clinical chemistry methods. As primary parameters, the absolute hemoglobin response (AUEC) for pharmacodynamics and AUC_τ and C_{max} of epoetin for pharmacokinetics were evaluated. Bioequivalence was confirmed statistically if the confidence intervals for the AUC_τ and C_{max} of epoetin at steady state was included in the classical bioequivalence range of 80-125%. For the pharmacodynamic surrogate parameter hemoglobin, an equivalence range of 96.8-103.2% was predefined for the parameter AUEC.
Results: 74 volunteers were included in the statistical evaluation, with a mean age of 36.8 (HX575) and 33.6 (reference) years respectively. The pharmacokinetic results at steady state are shown in Table 1.

Table 1. Pharmacokinetic parameters of HX575 vs. comparator epoetin alfa after multiple dose SC application

Parameter	HX575 (N = 37)		Comparator epoetin alfa (N = 37)	
	Mean	SD	Mean	SD
AUC 0-48,md [mIU/ml*h]	2044.9	587.9	2095.0	486.4
Cmax,md [mIU/mL]	82.410	48.690	82.817	34.056
t1/2,md [h]	18.28	8.50	18.16	7.52
Tmax,md [h]	8.74	6.15	9.20	5.42
Cmin,md [mU/mL]	19.226	5.968	20.780	5.396

Bioequivalence statistics showed that the 90% confidence intervals were within the tight boundaries (point estimators, 90% confidence interval): for $AUC_{0\text{-}48,md}$: 96.9% [CI 88.2-106.5%], $C_{max,md}$: 97.6% [CI 84.2-113.1%], $C_{min,md}$: 90.7% [CI 80.9-101.6], $t_{1/2,md}$: 97.9% [CI 81.0-118.2%],
Measurement of pharmacodynamic parameters showed no significant differences between groups in the surrogate parameter hemoglobin, fulfilling the predefined equivalence boundaries with a point estimator of 98.9% [90% CI: 97.7–100.2%].
Both products were well tolerated. No anti-rhEPO antibody formation was detected with either product.
Conclusions: Pharmacokinetics of HX575 and the comparator epoetin alfa were within the tight bioequivalence boundaries after multiple subcutaneous doses. The equivalence boundaries for the pharmacodynamic parameter hemoglobin were met. This study is a key part of the demonstration of the efficacy and safety profile of the biosimilar ESA, HX575.
Disclosure: The study results described in this abstract were part of the development program of the biosimilar ESA performed by Sandoz Pharmaceuticals GmbH & Hexal AG.

MP367 LONGTERM EFFICACY AND SAFETY OF HX575 (BINOCRIT®/EPOETIN ALFA HEXAL®) IN THE INTRAVENOUS (IV) TREATMENT OF ANAEMIA IN HAEMODIALYSIS PATIENTS

Marianne Haag-Weber[1], Ursula Thyroff-Friesinger[2], Andrea Vetter[2]. *[1]KfH Kuratorium für Dialyse und Nierentransplantation, Straubing, Germany; [2]Clinical Research, Hexal AG, Holzkirchen, Germany*

Introduction and Aims: The recombinant human epoetin HX575 (Sandoz Pharmaceuticals GmbH/Hexal AG) is the first biosimilar ESA (erythropoiesis-stimulating agent) with marketing authorisation in Europe. The primary objective of the study was the evaluation of the efficacy and safety of HX575 in the longterm intravenous treatment of anaemia in haemodialysis patients following a 1:1 dose conversion from the reference product (EPREX/ERYPO®, Ortho Biotech) to HX575. Efficacy in terms of therapeutic equivalence was assessed over 28 weeks. Particular focus was set on long-term safety data obtained over at least 12 months.
Methods: Haemodialysis patients with haemoglobin (Hb) levels of 10.0-13.0 g/dL were randomised to either continue their current intravenous epoetin alfa treatment or change to HX575. During treatment, epoetin dosages were titrated to maintain Hb values. The primary endpoint was the difference between treatment groups in the change of Hb levels between baseline (weeks -2 to 0) and evaluation period (weeks 25-28). Therapeutic equivalence was achieved if the mean absolute change in Hb levels between the two groups differed by less than ±0.5 g/dL.

Results: Therapeutic equivalence of HX575 and the comparator epoetin alfa, assessed during the first 28 weeks of the study, was statistically confirmed: mean changes in Hb levels were 0.147±0.092 g/dL in the HX575 and 0.063±0.117 g/dL in the comparator epoetin alfa group, with a difference between groups of 0.084 g/dL (95% confidence interval [-0.170; 0.338]). Hb levels and epoetin dosages remained stable throughout the entire study period of 56 weeks. The long-term safety profile of HX575 was similar to that of the comparator epoetin alfa. No antibody formation was detected.
Conclusions: This study demonstrated therapeutic equivalence of HX575 to the comparator epoetin alfa, together with a comparable safety profile. It can be concluded that both formulations are interchangeable for the intravenous treatment of anaemia in haemodialysis patients. This study is a key part in the demonstration of the safety profile and efficacy of the biosimilar ESA, HX575.
Disclosure: The study results described in the abstract were part of the development program of the biosimilar ESA performed by Sandoz Pharmaceuticals GmbH & Hexal AG.

MP368 PHARMACOKINETICS AND PHARMACODYNAMICS OF TWO EPOETINS: HX575 (BINOCRIT®/EPOETIN ALFA HEXAL®) AND EPOETIN BETA (NEORECORMON®) ADMINISTERED SUBCUTANEOUSLY (SC) TO HEALTHY VOLUNTEERS

Fritz Soergel[1], Ursula Thyroff-Friesinger[2], Andrea Vetter[2], Bernd Vens-Cappell[3], Martina Kinzig[1]. *[1]IBMP-Institute for Biomedical and Pharmaceutical Research, Nuernberg, Germany; [2]Hexal AG, Holzkirchen, Germany; [3]Scope International, Hamburg, Germany*

Introduction and Aims: The recombinant human epoetin HX575 (Sandoz Pharmaceuticals GmbH/Hexal AG) is the first biosimilar ESA (erythropoiesis-stimulating agent) with marketing authorisation in Europe. The primary objective of this study was the steady state pharmacokinetic and pharmacodynamic comparison of HX575 with epoetin beta after multiple subcutaneous application to healthy volunteers.
Methods: In this open, randomized, parallel group study, 80 healthy male Caucasian volunteers were randomized in 1:1 ratio to either HX575 or epoetin beta (NeoRecormon®, Roche) and treated subcutaneously at a dose of 100 IU/kg body weight, three times weekly for 4 weeks. Epoetin plasma levels and anti-rhEPO antibodies were measured by ELISA methods, hemoglobin and other pharmacodynamic parameters by flow cytometry and routine clinical chemistry methods. As primary parameters, the absolute hemoglobin response (AUEC) for pharmacodynamics and AUC_τ and C_{max} of epoetin for pharmacokinetics were evaluated. Bioequivalence was confirmed statistically if the confidence intervals for the AUC_τ and C_{max} of epoetin at steady state was included in the classical bioequivalence range of 80-125%. For the pharmacodynamic surrogate parameter hemoglobin, an equivalence range of 96.8-103.2% was predefined for the parameter AUEC.
Results: 73 volunteers were included in the statistical evaluation, with a mean age of 34.3 (HX575) and 31.5 (comparator) years respectively.

Table 1. Pharmacokinetic parameters of HX575 vs. comparator epoetin beta after multiple dose SC application

Parameter	HX575 (N = 36)		Comparator epoetin beta (N = 37)	
	Mean	SD	Mean	SD
AUC 0-48,md [mIU/ml*h]	1356	343.5		
Cmax,md [mIU/mL]	55.64	24.54	55.92	23.02
t1/2,md [h]	11.99	5.30	12.30	4.82
Tmax,md [h]	7.76	3.60	7.92	3.07
Cmin,md [mU/mL]	12.15	4.244	12.98	4.524

Plasma levels of both epoetins were well within bioequivalence boundaries, shown by the point estimators [90% confidence interval (CI)] $AUC_{0\text{-}48,md}$: 96.1% [86.4-106.9%], $C_{max,md}$: 98.5% [85.2-113.9%].
Measurement of the clinically relevant, surrogate parameters after administration of epoetin alfa and epoetin beta were also within dynamic equivalence boundaries, as shown by the point estimator of the AUEC of haemoglobin: 99.2% [CI 90%: 97.7-100.7%]. Both products were well tolerated. No anti-epoetin antibody formation was detected with either product.
Conclusions: Pharmacokinetic and pharmacodynamic results were within defined bioequivalence boundaries for HX575 and the comparator epoetin beta (NeoRecormon®). This suggests administration of the same dose of HX575 or NeoRecormon leads to comparable pharmacokinetic profiles resulting in a comparable increase in haemoglobin over a treatment period of 4 weeks. This study is a key part in the demonstration of efficacy and safety of the biosimilar ESA, HX575.
Disclosure: The study results described in this abstract were part of the development program of the biosimilar ESA performed by Sandoz Pharmaceuticals GmbH & Hexal AG.

MP369 COMPARATIVE PHARMACOKINETICS AND PHARMACODYNAMICS OF HX575 (BINOCRIT ®/EPOETIN ALFA HEXAL®) AND EPOETIN ALFA (ERYPO/EPREX®) ADMINISTERED INTRAVENOUSLY (IV) TO HEALTHY VOLUNTEERS

Fritz Soergel[1], Ursula Thyroff-Friesinger[2], Andrea Vetter[2], Bernd Vens-Cappell[3], Martina Kinzig[1]. *[1]IBMP-Institute for Biomedical and Pharmaceutical Research, Nuernberg, Germany; [2]Hexal AG, Holzkirchen, Germany; [3]Scope International, Hamburg, Germany*

Introduction and Aims: The recombinant human epoetin HX575 (Sandoz Pharmaceuticals GmbH/Hexal AG) is the first biosimilar ESA (erythropoiesis-stimulating agent) with marketing authorisation in Europe. The primary objective of this study was the steady state pharmacokinetic and pharmacodynamic comparison of HX575 with a comparator epoetin alfa after multiple intravenous application to healthy volunteers.
Methods: In this two-centre, open, randomized, parallel group study, 80 healthy male Caucasian volunteers were randomized in 1:1 ratio to either the biosimilar epoetin HX575 or the comparator epoetin alfa (Eprex/Erypo®, Ortho Biotech) and treated intravenously at a dose of 100 IU/kg three times weekly over 4 weeks. Epoetin plasma levels and anti-rhEPO antibodies were measured by ELISA methods, hemoglobin (Hb) and other blood cell parameters by flow cytometry and routine clinical chemistry methods. As primary parameters, the absolute hemoglobin response (AUEC) for pharmacodynamics and AUC_τ and C_{max} of epoetin for pharmacokinetics were evaluated. Bioequivalence was confirmed statistically if the confidence intervals for the AUC_τ and C_{max} of epoetin at steady state was included in the classical bioequivalence range of 80-125%. For the pharmacodynamic surrogate parameter AUEC of Hb, an equivalence range of 96.8-103.2% was predefined.
Results: 76 volunteers were included in the statistical evaluation, with a mean age of 32.6 (HX575) and 33.4 (comparator) years respectively.

Table 1. Pharmakinetic parameters of HX575 vs. comparator epoetin alfa after multiple dose IV application

Parameter	HX575 (N = 37)		Comparator epoetin alfa (N = 39)	
	Mean	SD	Mean	SD
AUC0-48, md [mIUxh/mL]	8422	2419	9224	1850
Cmax,md [mIU/mL]	2189	393.7	2262	422.0
t1/2,md [h]	4.14	1.71	4.74	2.00
tmax,md [h]	0.086	0.019	0.083	0.000
Cmin,md [mIU/mL]	9.007	2.821	8.682	2.218

Plasma levels of both epoetins were well within bioequivalence boundaries, shown by the point estimators [90% confidence interval (CI)] of $AUC_{0\text{-}48,md}$: 89.2% [82.5-96.2%], $C_{max,md}$ 97.5% [91.1-104.5%], $C_{min,md}$ 102.9% [92.8 - 114.1%].
Measurement of the pharmacodynamic parameters showed no significant differences between groups, as shown by the point estimators [90% CI] of the AUEC of haemoglobin: 99.9% [98.5-101.2%], which lay completely within the predefined equivalence boundaries. Both products were well tolerated. No anti-epoetin antibody formation was detected with either product.
Conclusions: Pharmacokinetic results were within bioequivalence boundaries for HX575 and the comparator epoetin alfa. Pharmacodynamic results suggested no significant differences between groups. Administration of the same dose of HX575 or Eprex/Erypo® leads to bioequivalent pharmacokinetic profiles and results in a comparable increase in haemoglobin over a

treatment period of 4 weeks. This study is a key part in the demonstration of the efficacy and safety profile of the biosimilar ESA, HX575.
Disclosure: The study results described in this abstract were part of the development program of the biosimilar ESA performed by Sandoz Pharmaceuticals GmbH & Hexal AG.

MP370 DARBEPOETIN ALFA (ARANESP®SURECLICK) ADMINISTERED ONCE MONTHLY (QM) IN PATIENTS WITH CHRONIC RENAL INSUFFICIENCY: 3 YEARS OF EXPERIENCE

António Sousa. *Serviço de Nefrologia, Hospital Doutor José Maria Grande, Portalegre, Portugal*

Introduction and Aims: Patients with chronic renal insufficiency (CRI) frequently experience anaemia, which can significantly affect their morbidity, mortality, and quality of life. Darbepoetin alfa (Darb-a), is effective for the treatment of anaemia in CRI by increasing the haemoglobin levels (Hb) and thus suppressing the need for red blood cells transfusions and also mitigating the anaemia associated symptoms. It can be administered once monthly in the maintenance phase in CRI (pre-dialysis) patients. SureClick is a Darb-a pre-filled device for subcutaneous (sc) administration that can be safely self-administrated.
Methods: Observational, open-label and non comparative study, aimed at evaluating both the efficacy and the safety of a 36 month length period of subcutaneous administration of Darb-a. CRI patients with adequate iron levels, a calculated creatinine clearance (Cr Cl) between 11 and 60 mL/min and Hb over 11 g/dL who had switch from Darb-a Q2W to QM were included in the study. The administered doses were adjusted according to the patients' Hb, to a target range of 11-13 g/dL. During the course of the study the majority of patients started treatment with SureClick.
Results: One hundred and twenty eight patients, 60.2% women, mean age 73.5±11.2 years with mean Cr Cl of 27.0±9.6 mL/min were evaluated. The most frequent etiologies for CRF were Nephroangiosclerosis (53.1%) and Diabetic Nephropathy (18.8%). The evaluated patients were followed for a mean period of 17.9±9.4 months (2287 cumulative months). The SureClick's use had a mean duration of 18.2±6.2 months (2161 cumulative months). The mean Darb-a administered doses were of 0.4±0.3; 0.4±0.2; 0.4±0.2; 0.3±0.2; and 0.4±0.3 μg/kg/week at baseline and at 6, 12, 24 and 36 months (p=0.156 baseline vs 36 months), respectively. At 6, 12, 24 and 36 months' follow-up, the percentage of evaluated patients was of 81.3%; 73.4%; 28.1%; and 7.0%, respectively. The corresponding mean Hb was, respectively, of 13.3±1.3; 12.8±1.2; 12.7±1.3; 12.6±1.3; and 12.1±0.4 g/dL. Fourteen patients (10.9%) maintained Hb values in accordance with the target range at all evaluations. In 715 patients' visits Darb-a dose was changed in 112 (15.7%), 87 to increase dose and 25 to decrease it. During the study, 18 patients died, 11 initiated dialysis and 8 were lost for follow up. No adverse effects were reported. Comparing patients who died or started replacement therapy with all the others, we found no statistically significant differences both in the Darb-a mean dose and in the mean Hb.
Conclusions: After 36 months of Darb-a administration, these patients' Hb levels were maintained, with no dose increase. The use of SureClick simplifies the process of administering Darb-a sc injections, increases the patients' quality of life, decreases the environmental burden, increasing the safety level of the therapeutics both for the patients and the health technicians.

MP371 HAEMOGLOBIN STABILITY IN CHRONIC KIDNEY DISEASE HEMODIALYSIS PATIENTS SWITCHED FROM DARBEPOETIN-ALFA TO EPOETIN-BETA

R. Neto[1], J.M. Frazao[1], M. Silva[2], J. Fazendeiro[2], M. Serafim[3], J. Pinheiro[3], M. Mota[4], C. Martins[5], M. Sarmento[5]. *[1]Centro Renal da Prelada, Porto, Portugal; [2]Fresenius Medical Care de Vila Nova de Gaia, Vila Nova de Gaia, Portugal; [3]Fresenius Medical Care de Fafe, Fafe, Portugal; [4]Clinica de Hemodialise Nossa Senhora da Franqueira, Barcelos, Portugal; [5]Centro Medico de Doencas Renais, Porto, Portugal*

Introduction and Aims: Both Erythropoiesis-Stimulating Agents (ESA), Darbepoetin alfa (DA) and Epoetin beta (EB), are effective for the treatment of Chronic Kidney Disease (CKD) induced anaemia, maintaining the haemoglobin levels (Hb) between 11.0 and 13.0 g/dL. There is evidence that DA is more cost-effective than EB. This study aimed to evaluate mean Hb and ESA dose change requirements in CKD hemodialysis patients who were switched from DA to EB.
Methods: A retrospective analysis was performed using data of patients with at least, 9 months on haemodialysis at the conversion moment from DA to EB, with stable hematocrit and adequate iron levels according to the European Best Practice Guidelines (EBPG).
The ESA conversion *ratio* used was of 1 μg DA to 200 IU EB. All patients who were being treated with IV DA once a week were switched to IV EB once, twice or thrice a week.Six months previous and subsequent to the therapeutic switch moment, the following data was collected for each patient: haemoglobin (Hb), hematocrit (HTC), serum ferritin (FT), serum iron (Fe), serum transferrin saturation (TS), DA and EB week doses, Kt/V, Reactive C protein (CRP) and intact PTH (iPTH).
Results: From 191 patients evaluated, 55 did not meet inclusion criteria (patients with mean FT inferior to 100 ng/ml, at least one of the 6 months periods of observation, and patients with mean TS inferior to 20%, at least at one 6 months period). One hundred and thirty six patients were included, 52.9% male, and with a mean age of 63.4±14.3 years. After the conversion, a significant increase ($p<0.005$) in the EB dose was necessary to maintain the target-Hb defined by the EBPG. Three and 6 months after the switch, the mean EB dose increased in 0.17% and 17.7% ($p=0.674$ and $p<0.001$), respectively. After the conversion, the Hb decreased from 12.2±1.4 g/dL (at the last DA month) to 11.3±1.2 g/dL ($p<0.001$) and 11.5±1.2 g/dL ($p<0.001$) at the third and sixth EB month, respectively. The TS and Kt/V levels where significantly different between the DA and the EB therapeutic periods ($p=0.008$ and $p=0.02$, respectively). No statistically significant differences between periods were observed in the iPTH, albumin or CRP levels.
Conclusions: Both these ESA are effective in the treatment of anaemia in CKD hemodialysis patients.
The *ratio* which was used (1:200) in converting the IV DA administered once a week into the IV EB administered once, twice or thrice a week seems not to have been adequate. Maintaining Hb in accordance with the target levels would require a *ratio* of around 1:300.
The significant necessary increase in EB dose which was observed in this study suggests that DA is more cost-effective than EB.

MP372 CHANGES IN SERUM PARATHYROID HORMONE DO NOT RELATE TO ERYTHROPOIETIN RESISTANCE INDEX IN MAINTENANCE HEMODIALYSIS PATIENTS

Anja Kruse, Stephan Thijssen, Peter Kotanko, Len Usvyat, Nathan W. Levin. *Renal Research Institute, New York, NY, USA*

Introduction and Aims: Hyperparathyroidism is common in patients with end stage renal disease and possibly related to erythropoietin (EPO) resistance. One mechanism underlying this relationship may be parathyroid hormone (PTH) mediated induction of bone marrow fibrosis. Furthermore, several reports have indicated that a drop in PTH levels following parathyroidectomy may associate with improved anemia control and lower EPO requirements, suggesting a reversible toxic effect of PTH on red blood cell production and/or survival (for review see 1). This study aimed to test the hypothesis that changes of iPTH and EPO resistance index show a positive correlation.
Methods: We conducted a retrospective database analysis in chronic hemodialysis patients receiving dialysis treatments in Renal Research Institute/New York Dialysis Services centers. All patients who were prescribed to start cinacalcet therapy during the study period were selected for analysis (n=574). Average serum intact PTH (iPTH), hemoglobin, and EPO-alpha dose per treatment were recorded for the month preceding cinacalcet prescription (baseline) and for months 3, 4, and 6 thereafter. EPO resistance index (ERI) was calculated as units of EPO per dialysis treatment per g/dL hemoglobin concentration. Changes in iPTH and ERI between baseline and months 3, 4, and 6 were calculated. Correlation between changes in iPTH and ERI were analyzed for the entire cohort and the following subgroups: a) PTH drop > 300 pg/mL to below 300 pg/mL b) PTH drop > 300 pg/mL to above 300 pg/mL c) PTH rise > 300 pg/mL.

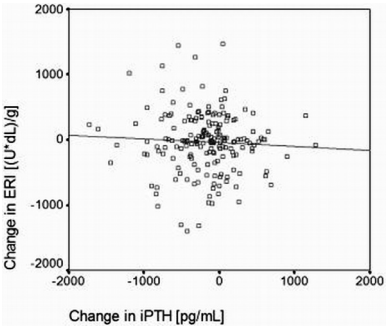


Figure 1

Results: No significant positive correlation was found between change in iPTH and change in ERI, irrespective of time point or subgroup analyzed. Figure 1 shows the correlation between change in iPTH and change in ERI from baseline to 3 months after cinacalcet prescription for the entire cohort.
Conclusions: The results of this short term study do not support the hypothesis that a drop in PTH is associated with decreased erythropoietin resistance in maintenance hemodialysis patients.
Reference: 1. Druecke T, NDT 16 [Suppl 7]: 25-28, 2001.

MP373 ★ DOES ROUTINE BLOOD SAMPLING CONTRIBUTE TO THE IRON REQUIREMENTS OF RENAL PATIENTS? A COMPARISON OF A HAEMODIALYSIS AND PERITONEAL DIALYSIS POPULATION

William Herrington, Ramesh Naik, Mobin Mohteshamzadeh, Emma Vaux, Lindsey Barker. *Renal Unit, Royal Berkshire Hospital, Reading, Berkshire, United Kingdom*

Introduction and Aims: All dialysis patients have routine blood tests to monitor anaemia, electrolyte balance, blood borne viruses and dialysis adequacy. Phlebotomy in our unit utilises the Vacutainer® system which removes a pre-specified volume of blood for each test. HD patients require more frequent iron administration than PD patients. HD patients have more frequent blood tests than PD patients.
The aim was to calculate the volume of blood and estimate the iron removed for routine blood samples from a population of peritoneal dialysis (PD) and haemodialysis (HD) patients in a single renal unit.
Methods: All dialysis patients (of at least 90 days) in a single renal unit from 01/01/2006 to 31/12/2006 were analysed. Data were collected retrospectively from a clinical computer database on patient demographics; number of blood tests; plasma haemoglobin (Hb) and ferritin levels; Erythropoiesis-stimulating agent (ESA) and intravenous (IV) iron dose and blood transfusion. From the data, annual volume of blood and iron removed were estimated.
Results: 224 HD and 118 PD patients were eligible for analysis, equivalent to 191 and 93 treatment years. Demographics showed 72% Caucasian, 63% male, 30% diabetic and HD patients were older than PD 63 v 58 years ($p<0.01$, paired t-test). The proportion on warfarin was similar (14%). Results are shown in Table 1.

Table 1

	HD n=224	PD n=118	
Annual blood sample volume	365 mls (291-508)	172 mls (125-247)	p<0.0001
Min unit requirement	216 mls	90 mls	
Annual Iron removed	141mg [116-185]	72 mg [50-95]	p<0.0001
Annual IV iron given	2000 mg [950-2950]	200 mg [0-600]	p<0.0001
Iron from transfusion	225mg	4.7mg	
Plasma ferritin	607 ug/l [456-756]	463 ug/l [375-602]	p<0.0001
Weekly Epo dose	7000U [5000-10000]	4000U [2000-6000]	p<0.0001
Haemoglobin	11.5 g/dl [10.7-12]	11.9 [10.9-12.6]	p<0.001

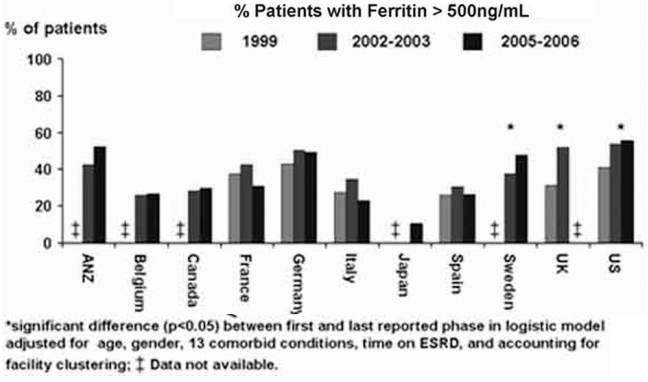
All median +IQR, Mann-Witney U test.

Conclusions: HD patients achieve a lower Hb with a higher ESA and IV iron requirement than PD patients. Routine blood sampling removes a significant amount of iron, twice as much in HD patients. This is more than would be required for standard unit monitoring but is small compared with the amount of IV iron received (6% HD and 35% PD). It is recognised that HD patients lose iron in the dialysis process but this is unlikely to account for all the difference and would not apply to PD patients. Other sources of iron loss such as occult gastrointestinal bleeding must be considered. A policy to reduce blood sampling to standard levels would not impact hugely on the IV iron requirement of HD patients.

MP374 PARENTERAL (IV) IRON DOSING TO HEMODIALYSIS (HD) PATIENTS WITH FERRITIN LEVELS > 500 ng/mL: THE DIALYSIS OUTCOMES AND PRACTICE PATTERNS STUDY (DOPPS)

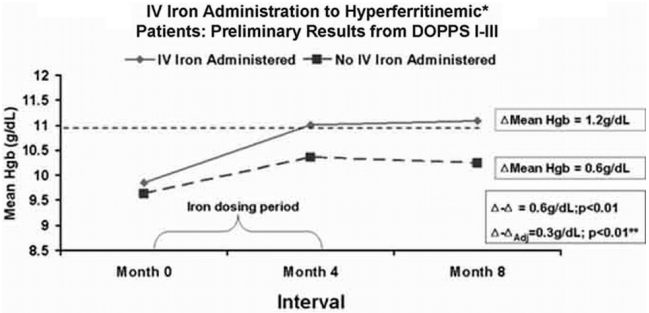
B.M. Robinson[1], M.K. Poler[1], A. Sen[2], T. Akiba[3], J.M. Cruz[4], F. Locatelli[5], A. Saito[6], F.K. Port[1]. *[1]Arbor Research Collaborative for Health, Ann Arbor, MI, USA; [2]University of Michigan, Ann Arbor, MI, USA; [3]Tokyo Women's Medical University, Tokyo, Japan; [4]Hosp General Univ, Valencia, Spain; [5]Ospedale A. Manzoni, Lecco, Italy; [6]Tokai University, Kanagawa, Japan*

Introduction and Aims: Clinical trials have demonstrated that IV iron dosing to patients with ferritin>500 ng/mL raises hemoglobin (Hgb) levels over 1-2 months. We used the DOPPS, an international observational study of HD, to examine prevalence of ferritin>500 ng/mL and associated IV iron dosing practices.
Methods: Laboratory values were from prevalent cross-sections of patients with ESRD >4 months receiving epoetin (EPO) in DOPPS I (1999; n=4,224), DOPPS II (2004; n=5,445) and DOPPS III (2006; n=4,217). Facility iron dosing practices were reported in the DOPPS III Medical Director Survey (n=177 facilities & 4,540 patients to date).
Results: *Ferritin levels:* The % of HD patients with ferritin >500 ng/mL is high in many countries and has increased significantly over recent years in SW, UK, and US.



*significant difference (p<0.05) between first and last reported phase in logistic model adjusted for age, gender, 13 comorbid conditions, time on ESRD, and accounting for facility clustering; ‡ Data not available.

IV iron dosing: Among DOPPS III patients with ferritin >500 ng/mL, the % receiving any IV iron over the next 4 months was 40% in Japan, 48% in Canada, and 61-80% in all other countries. Statistically significant increases over time were seen in the US (54 to 73% from DOPPS I to III) and the UK (59 to 69% from DOPPS I to II).
Hgb levels: IV iron dosing to patients with ferritin >500 ng/mL and TSAT <25% is associated with a sustained Hgb rise:



*Based on most recent lab values (TSAT<25, Ferritin >500, Hgb<11) preceding Month 0.; ΔHgb =Month8-Month0; N= 1,555 HD patients from all DOPPS receiving Epo; **mixed linear model adjusted for age, gender, 14 comorbid conditions, region, time on ESRD, Hgb, EPO dose, TSAT, ferritin, albumin, and accounting for facility clustering.

Facility patterns: In the US only, facilities that report routinely dosing IV iron to patients with ferritin >500 ng/mL tend to give more EPO [mean dose 22,000 units/month higher ($p<0.01$) in an adjusted mixed model] than facilities that report suspending IV iron. However, these facilities do not have significantly higher mean Hgb levels among all patients, or a higher % that meet clinical practice guidelines for Hgb levels.
Conclusions: The prevalence of ferritin >500 ng/mL varies internationally but is high in many countries. Dosing of IV iron to patients with ferritin >500 ng/mL is common and associated with a rise in Hgb levels (consistent with clinical trials), though the facility practice of IV iron dosing to such patients is not associated with higher facility-wide Hgb levels. The causal association, if any, between iron dosing to patients with ferritin >500 ng/mL and clinical outcomes merits further investigation.
Disclosure: The DOPPS is supported by research grants from Amgen, Inc. and Kirin Pharma Co., Ltd., without restrictions on publications.

MP375 THE EFFICACY AND SAFETY OF INTRAVENOUS FERRIC CARBOXYMALTOSE COMPARED TO IRON SUCROSE IN HAEMODIALYSIS PATIENTS WITH IRON DEFICIENCY ANAEMIA

Roland M. Schaefer, Nikolay N. Khasabov, Nikolay G. Todorov, Pieter Evenepoel. *Department of Internal Medicine, University of Muenster, Muenster, Germany; Department of Medicine, Russian State Postgraduate Medical Academy, Moscow, Russian Federation; Haemodialysis Unit, St Anna Hospital, Sofia, Bulgaria; Department of Nephrology, University Hospital Gasthuisberg, Leuven, Belgium*

Introduction and Aims: The use of intravenous (IV) iron is well established in haemodialysis (HD) patients with Iron Deficiency Anaemia (IDA). However, IV iron preparations differ in their individual characteristics. Novel compounds need to demonstrate their safety and efficacy by head-to-head comparison studies with current standard treatments. In this study, we compared the safety and efficacy of ferric carboxymaltose (FCM), a next generation IV iron formulation, with iron sucrose (ISC) in HD patients with IDA.
Methods: This was a multicentre, open-label, randomized study conducted in HD patients (18-80 years) with IDA defined as: Hb≤115g/L, a serum transferrin saturation (TfS)<20% or a serum ferritin <200μg/ml. Eligible patients were randomized to either IV FCM or ISC. Both drugs were administered into the haemodialysis venous line one hour after the start of each dialysis session. The dosing regimen was 200mg of either FCM given as a push injection or ISC given over 10 minutes, two to three times weekly until the total cumulative dose for each patient was reached. The maximum treatment period was 4 weeks and patients were followed for an additional 4 weeks. For patients prescribed EPO at baseline, the dose must have been stable during the study period. Primary response was defined as an Hb increase of at least 10g/L.
Results: The Per-Protocol population (N=183, 97 FCM and 86 ISC) is the basis of this analysis. Baseline characteristics and the mean iron deficit at baseline were similar in both groups. The mean duration of treatment was 15.8 and 16.2 days for the FCM and ISC groups, respectively. The primary response rate at week 4 was 46.4% and 37.2% for the FCM and ISC groups respectively. The mean Hb levels continued to increase during follow-up in both treatment groups: from 93g/L to 105.7g/L and from 93.4g/L to 103g/L for the FCM and ISC groups, respectively. Mean serum ferritin levels increased from baseline to week 2 (from 90.4μg/L to 723.4μg/L and from 93.1 μg/L to 549.6 μg/L for the FCM and ISC groups respectively). At the end of follow-up, the mean serum ferritin values were 465.3μg/L for the FCM group and 397.7for the ISC group. The percentage of patients who experienced at least one drug-related TEAE was lower in the FCM group (5%) than in the ISC group (10.2%). No serious TEAE or any of the TEAEs leading to discontinuation of treatment were considered drug related. Overall, there were no statistically significant differences in the other safety parameters between the two treatment groups.
Conclusions: Both FCM and ISC were well tolerated with no drug-related serious adverse events in either treatment group. There was a trend towards a better response of most efficacy parameters for patients allocated FCM. FCM administered by push injection can be considered to be at least as safe and effective as ICS for the treatment of HD patients with IDA.

MP376 INCIDENCE OF POST-TRANSPLANTATION ANAEMIA AND THE IMPACT OF IMMUNOSUPPRESSIVE THERAPY: PAEDIATRIC DATA FROM THE TRANCEPT OBSERVATIONAL STUDY

Pierre Merville[1], Uwe Heemann[2], Helio Tedesco da Silva[3], Lionel Rostaing[4], Corrado Bernasconi[5], Herwig-Ulf Meier-Kriesche[6]. *[1]Hopital Pellegrin, Bordeaux, France; [2]Technical University, Munich, Germany; [3]University of Sao Paulo, Sao Paulo, Brazil; [4]University Hospital, Toulouse, France; [5]F. Hoffmann-La Roche, Basel, Switzerland; [6]University of Florida, Gainesville, FL, USA*

Introduction and Aims: Transplantation is the preferred treatment for children with chronic kidney disease (CKD). Unfortunately, catch-up growth is suboptimal with traditional immunosuppressive regimens. New immunosuppressive regimens have helped to reduce loss of graft function due to rejection and minimised the use of steroids, enabling catch-up growth. Anaemia is a common complication in patients (pts) with renal transplants and immunosuppressive therapy may contribute to its prevalence.
Methods: TRANCEPT is a multicentre, observational, global study of long-term outcomes in pts with renal transplants. The study recruited 4399 pts of all ages who had been transplanted 6 months to ~20 years before enrolment and had renal function (GFR – determined by the Schwartz formula in paediatric pts) as primary analysis variable.
Here we analyse baseline data from 252 paediatric pts (<18 yr) to explore the relationship between Hb levels at enrolment and factors that may affect anaemia. Anaemia in children was defined as <5th percentile of mean Hb values adjusted for age and gender.
Results: The majority (68%) of the paediatric population were ≥12 years old at enrolment. Mean Hb (SD) was 12.1 (±2.0) g/dL and 68 (27%) pts had Hb ≤11 g/dL. However 44% of pts met the criterion for anaemia (table). Baseline Hb levels were related to age and graft type, patients with living vs cadaveric donor organs had higher mean Hb (12.5 vs 11.82 g/dL; p=0.0029). Gender did not significantly affect baseline Hb, and we found a slow decline in Hb after transplantation that was not significant. As reported previously, post-transplantation Hb values fell with decreasing renal function. A negative dose-effect relationship was noted for CsA, and this was confirmed in multivariate models that also included GFR. We observed lower Hb levels in pts receiving cyclosporine A vs tacrolimus or sirolimus (11.7, 12.5 and 12.9 g/dL, respectively; p=0.0039).

	No anaemia	Anaemia	Total patients
Age <6 years, n (%)	11 (58)	8 (42)	19 (100)
Age ≥6 to ≤12 years	31 (51)	30 (49)	61 (100)
Age ≥12 years	99 (58)	73 (42)	172 (100)
All	141 (56)	111 (44)	252 (100)

Conclusions: These are the first observational data on anaemia prevalence in paediatric transplant recipients. Children with decreasing graft function should be evaluated for anaemia and their immunosuppressive therapy re-evaluated if anaemia is present. Additional analyses are ongoing to elucidate inter-relationships between different immunosuppressive regimens, anaemia and renal function.
Disclosure: TranCept study funded by F.Hoffman - La Roche, Ltd, Basel Switzerland.

MP377 HEPCIDIN IN CHRONIC KIDNEY DISEASE – A NOVEL BIOMARKER ASSOCIATED WITH IRON STORE AND ERYTHROPOIESIS, RATHER THAN GFR

Takuya Uehata[1], Naohisa Tomosugi[2], Akihiro Shimomura[1], Kazunori Inoue[1], Daisuke Hayashi[1], Tetsuya Kaneko[1], Tatsuya Shoji[1], Noriyuki Okada[1], Yoshiharu Tsubakihara[1]. *[1]Kidney Disease and Hypertension, Osaka General Medical Center, Osaka, Japan; [2]Nephrology, Kanazawa Medical University, Kanazawa, Ishikawa, Japan*

Introduction and Aims: In the setting of chronic kidney disease (CKD), the role of hepcidin (Hn), a key iron regulatory hormone, is unknown. And the influence of decreased glomerular filtration rate (GFR) on Hn is unclear. The purpose of this study was to examine the relationship between Hn and GFR.
Methods: A cross-sectional study of 194 CKD patients with no inflammation and not on iron therapy was performed. Serum hepcidin-25 was measured

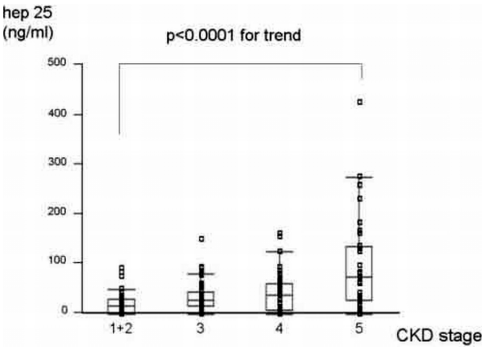
Abstract MP377 – Table 1. Characteristics

	CKD 1+2 (n=58)	CKD 3 (n=62)	CKD 4 (n=43)	CKD 5 (n=31)
MDRD-GFR (ml/min/1.73m^2)	79.2±15.1	43.6±8.3	22.3±4.5	9.9±3.6
Hepcidin (ng/ml)	15.7 (2.6-29.5)	26.0 (14.0-42.4)	38.3 (7.7-60.1)	74.3 (26.7-135.0)
Age (yr)	49.1±16.7	66.4±12.0	67.6±12.6	72.0±8.8
Sex (male)	25 (43.1%)	33 (53.2%)	26 (60.5%)	12 (38.7%)
Hemoglobin (g/dl)	13.6±1.6	13.2±1.7	11.8±2.0	10.4±1.3
Reticulocyte index	0.53±0.20	0.51±0.22	0.45±0.25	0.33±0.16
Ferritin (ng/ml)	57.7 (15.5-130.3)	76.7 (39.9-142.0)	105.0 (53.4-226.0)	111.0 (60.5-289.0)
% iron saturation	27.0±11.1	28.6±12.0	28.1±10.1	28.8±12.5
C-reactive protein (mg/dl)	0.04 (0.01-0.09)	0.08 (0.03-0.17)	0.05 (0.03-0.17)	0.13 (0.03-0.25)
IL-6 (pg/ml)	0.37 (0.20-0.70)	0.67 (0.42-1.21)	1.03 (0.53-1.66)	1.33 (0.89-2.70)
Albumin (g/dl)	4.1±0.4	4.1±0.4	3.8±0.4	3.9±0.3
EPO therapy	0 (0%)	5 (8.1%)	10 (23.3%)	21 (67.7%)

Mean ± SD, median (25–75%).

by liquid chromatography tandem mass spectrometry. Ferritin, % iron saturation, hemoglobin (Hb), reticulocyte index, C–reactive protein (CRP), interleukin–6 (IL–6) and albumin were measured. The reticulocyte index was calculated by correcting the reticulocyte count to a hematocrit of 45%. GFR was estimated using the abbreviated MDRD equation.

Results: Hn increased significantly by CKD stage ($p<0.0001$ for trend, see figure). Hn levels correlated with ferritin ($r=0.80$, $p<0.0001$), % iron saturation ($r=0.43$, $p<0.0001$), CRP ($r=0.18$, $p<0.01$) and IL−6 ($r=0.17$, $p<0.02$), while they inversely correlated with Hb ($r=-0.16$, $p<0.02$) and reticulocyte index ($r=-0.17$, $p<0.02$). A multivariate regression model using markers of renal function, iron status, erythropoiesis, anemia and inflammation revealed that Hn correlated with ferritin, reticulocyte index and sex. However there was no significant association between Hn and GFR.



Conclusions: These results suggest in CKD Hn may play a central role in iron store and erythropoiesis, but may be independent of renal function.

MP378 HEMODIALYSIS WITH AND WITHOUT INTRAVENOUS IRON INCREASE SERUM FREE DNA AS ASSESSED BY A NEWLY DEVELOPED CHEAP AND EASY TO PERFROM METHOD

David Tovbin[1], Hagit Goldshtein[2], Moshe Zlotnik[1], Amos Douvdevani[2]. *[1]Department of Nephrology; [2]Laboratory of Nephrology, Clinical Biochemistry Department, Soroka University Medical Center and Ben-Gurion University of the Negev, Beer-Sheva, Israel*

Introduction and Aims: Intravenous (IV) iron administration during hemodialysis (HD) sessions (IVIR) is required for iron availability, adequate erythropoeisis, anemia correction and improvement of HD patients' well being. However, IVIR may be associated (especially during infections or inflammation) with lipid, protein and DNA oxidation and an increase in infections, inflammation, oxidative stress, endothelial dysfunction and carotid intima-media thickness; a marker of atherosclerosis. Current available markers of oxidative stress and lipid, protein or DNA oxidation are cumbersome and expensive. However, a new fluorometric method developed in our laboratory for detection of free DNA in serum (SFD) was found to be easy to perform and cheap. SFD is associated with various pathologic conditions including inflammation, ischemia and cancer. SFD levels may be elevated in HD patients or increase during HD, but their relation to IVIR has not yet been reported. We hypothesized that our new method may be an easy and cheap way to assess markers and predictors for disease state and HD/IVIR-associated unwarranted effects. Thus, our aim in this preliminary study was to assess, by this new method, SFD levels in HD patients and their changes by HD and IVIR.

Methods: In a preliminary study, 8 chronic hospital-based HD unit patients who agreed to participate and signed an informed consent were evaluated for SFD, by a newly developed cheap and easy to perform fluorometric method. SFD levels were assessed at start and end of HD without and with (next session) IVIR.

Results: Pre-HD SFD levels in the 2 sessions were 26-293 and 26-203 ng/ml, and the absolute values of the actual and % differences between them were 15-143 ng/ml and 5-60% (<50% or 35 ng/ml in 6/8 patients). SFD levels increased significantly (Fig 1: $p<0.01$, >35 ng/ml in 6 patients) in both HD without (152±95 to 331±176 ng/ml) and with IVIR (117 ± 81 to 320±178 ng/ml), with % change of 205±96 (>80% in 6/8 patients) and 320±176 (>80% in all patients), respectively. IVIR-induced changes and post-IVIR SFD levels were significantly correlated with HD-induced changes and post-HD SFD levels ($p<0.05$, $r=0.76$, $p<0.05$, $r=0.83$, respectively).

Conclusions: Using this newly developed cheap and easy to perform method, SFD levels were similar before HD sessions, and increased prominently in most patients after HD with and without IVIR.

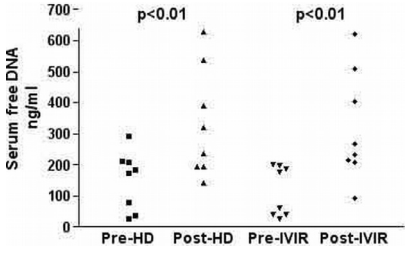


Figure 1. Changes in serum free DNA.

IVIR-associated SFD changes correlated with HD-associated SFD changes and did not suggest that IVIR had a prominent additive effect to HD on SFD. Assessment in HD patients during HD or IVIR, of the relation and predictive value of SFD to cumbersome and expensive inflammation and oxidative stress markers, is pending.

MP379 RELEVANT FACTORS IN HAEMOGLOBIN VARIABILITY ON HD PATIENTS

Vitor Ramalho, Beatriz Malvar, Pedro Pessegueiro, Manuel Amoedo, Carlos Pires, Joao Aniceto. *Nephrology Unit, Hospital Espirito Santo, Evora, Portugal*

Introduction and Aims: The haemoglobin (Hb) value in haemodialysis (HD) patients on erythropoiesis-stimulating agents (ESA) suffer fluctuations. This values are out of the target range for a considerably amount of time. This study objective was to evaluate the Hb variability and the main factors associated with it.

Methods: The study population included patients on regular HD for at least 6 months, on treatment with darbepoetin alfa. The Hb target range was 11,5 to 12,5g/dl. The dose was reduced or increased by 25% accordingly to Hb values. During 12 months the Hb values and fluctuations outside

Abstract MP379 – Table 1

Patients groups	Hb < 11,5	Hb > 12,5	Mean Hb in target range without fluctuations	Mean Hb in target range with 1-3 fluctuations	Mean Hb in target range with >4 fluctuations	p
Number of Patients (n)	14	12	32	23	23	p>0,05
Age (years)	71,5±13,7	66±12,7	70,6±11,3	76,6±11	70,2±15,2	p>0,05
Time on HD (months)	55,8±26,2	84,1±45	63±38,4	62,3±39	46,7±24,8	p>0,05
Morbid conditions*	4	6	11	8	12	p>0,05
Diabetes (n)	4	3	9	7	8	p>0,05
Cancer (n)	4	0	3	3	3	p>0,05
Hospitalizations (n)	14	2	1	8	7	p<0,05
Vascular acess problems (n)	13	4	8	17	22	p<0,05
EPO equivalent (u/kg.week)	141,1	47,8	58,2	66,8	116,7	p<0,05

*Number of patients with more than 2 morbid conditions.

the target range were registered. The patients were divided on 5 groups: (1) mean Hb <11,5; (2) mean Hb >12,5; (3) mean Hb in target range without fluctuations; (4) mean Hb in target range with 1-3 fluctuations; (5) mean Hb in target range with >4 fluctuations. The comorbid conditions, hospitalizations and vascular access problems were also evaluated. Results are presented in percents, mean and standard deviation. Statistical analysis was made with qui-square and Kruskal Wallis tests (p<0,05).

Results: 104 patients were included (53 men, mean age 71,4 ± 13 years old and 60,7±36 months on maintenance HD). The mean Hb value during the study was 12±1g/dl. There were 306 fluctuations registered. 75% of the patients had their Hb values on target, but only 32 (31%) had no fluctuations. Patients from the groups 1, 2, 4 and 5 remained outside of target values for an average period of time of 4,25 months. The 5 groups were similar on age and time on dialysis (pns). The patients on groups 1, 4 and 5 had more hospitalizations and vascular access problems (p<0,05). Darbepoetin consume was superior in groups 1 and 5 (p<0,05). There were no differences between the groups in terms of comorbid conditions, and particularly diabetes and cancer.

Conclusions: The Hb variability in HD patients on ESA is very common. Only 31% of patients kept their Hb values on target range without fluctuations. Changes on prescribed ESA, hospitalizations and vascular access problems were responsible for the Hb fluctuations in these patients.

MP380 CIRCULATING SOLUBLE TRANSFERRIN RECEPTOR (sTfR): A SIMPLE AND RELIABLE MARKER OF IRON STATUS IN HEMODIALYSED PATIENTS

John T. Papadakis[1], Konstantinos Koutroutsos[1], Ioannis Kopelias[1], Anthi Panagiotou[1], Lydia Plavoukou[2], Ioannis Kakavas[1], Irene Bosinakou[2]. *[1]Nephrology Department, [2]Haematology Department, Hippokration General Hospital, Athens, Greece*

Introduction and Aims: The main cause of hyporesponsiveness to erythropoetin (EPO) in haemodialysed patients is iron deficiency (ID). Detection of ID is of great value, since it can be easily corrected by intravenous iron administration. Iron deficiency may be attributed either to accelerated erythropoiesis and dialysis related blood loses that lead to depletion of iron stores (absolute ID), or to failure of adequate iron delivery to bone marrow in spite of apparently appropriate iron stores (functional ID). Transferin saturation (TSAT) and serum ferritin have been proven inadequate in the evaluation of iron status. The present study examines the diagnostic power of sTfR for the diagnosis of ID.

Methods: We enrolled 14 patients (males/females:7/7, age:63,43± 15,4 years) undergoing maintenance hemodialysis for 82,14±24 months that, for at least two months prior to the study period, were receiving a stable dose of EPO (mean dose: 100,72±26,9 IU/kg/week). Patients with recent bleeding episodes, inflammatory or infectious diseases, malignancies, hemoglobinopathies, overt hyperparathyroidism, aluminum overload, folate or B12 deficiencies, were excluded. Iron status was initially assessed by serum ferritin, TSAT and sTfR. According to serum ferritin (cutoff value: >100 ng/ml) and TSAT (cutoff value: >20%), all patients were iron repleted, while 9 out of 14 had high sTfR, (>1.5mg/l), a finding that suggests absolute ID. A loading dose of 1000 mg of iron gluconate was administered over a period of four weeks (100mg/dialysis session) in all patients and was followed by a maintenance dose of 50mg/week. EPO dosage was not altered throughout the study period. Responsiveness to iron loading was based on patients' Hb increment by more than 15%.

Results: Six weeks after the completion of iron loading 8/14 patients (57,14%) increased their serum Hb by more than 15% (mean increase: 2,19±1,06 g/dl). Seven out of 9 patients with initially high and 1/2 with initially low sTfR proved to be iron depleted by responding to iron loading. These findings indicate that sTfR has a 87,5% sensitivity and a 66,67% specificity for the diagnosis of absolute ID in patients that seemed to be iron repleted according to the traditional iron status markers.

Conclusions: In contrast to TSAT and serum ferritin, sTfR proved to be a sensitive and more reliable marker for the detection of ID in hemodialysed patients.

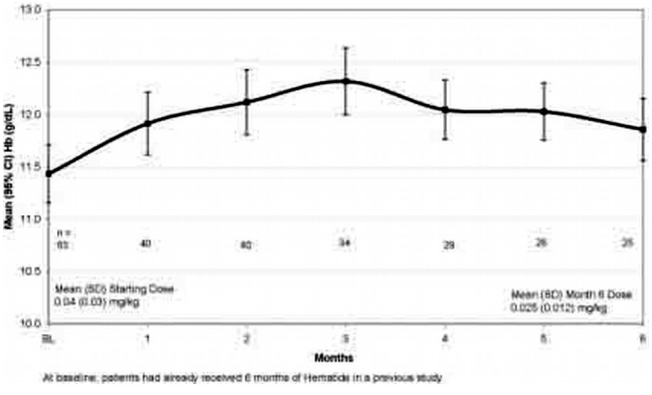
MP381 INTERIM EVALUATION OF LONG-TERM SAFETY AND TOLERABILITY OF HEMATIDE™ DURING MAINTENANCE TREATMENT OF ANAEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD)

Iain Macdougall[1], Luminita Ardelean[2], Adrian Covic[3], Vilpa DeSilva[4], Ovidiu Golea[5], Michal Nowicki[6], Michal Mysliwiec[7], Wladyslaw Sulowicz[8], Anne-Marie Duliege[9], Robert Leong[9], Andrzej Wiecek[10]. *[1]Department of Renal Medicine, King's College Hospital, London, United Kingdom; [2]Spitalul Clinic de Urgenta, Bucuresti, Romania; [3]Spitalul Clinic CI Parhon, Iasi, Romania; [4]Mayday University Hospital, Croydon, United Kingdom; [5]Spitalul Judetean Timisoara, Timisoara, Romania; [6]Department of Nephrology, Uniwersytecki Szpital Kliniczny, Lodz, Poland; [7]Wojewodzki Szpital Specjalistyczny, Bialystok, Poland; [8]Jagiellonian University, Cracow, Poland; [9]Affymax, Inc., Palo Alto, CA, USA; [10]Medical University of Silesia, Katowice, Poland*

Introduction and Aims: Hematide, a peptide-based erythropoiesis stimulating agent is being developed for treatment of anaemia associated with CKD.

Methods: This ongoing, open-label, long-term, roll-over study was designed to evaluate the safety and tolerability of up to 18 months of Hematide dosing during maintenance treatment of anaemia in patients with CKD. Patient eligibility included receipt of Hematide for at least 24 weeks in one of two previous Phase 2 studies and one haemoglobin (Hb) value ≥ 10.0 g/dL in the 4 weeks prior to study entry.

Results: The 63 enrolled patients (mean age: 63 years; 49% male) received Hematide via the same route (intravenous or subcutaneous) and frequency (every 4 weeks [Q4W]) used at the end of their previous study. Patients were monitored for adverse events (AEs), Hb concentration, dose adjustments,



vital signs, and laboratory values. Dose adjustment criteria were modified during the trial to reflect updates in KDOQI guidelines; the mean dose of Hematide at roll-over was 0.04±0.03 mg/kg and at 6 months was 0.025±0.012 mg/kg. The mean Hb at baseline was 11.4±0.3 g/dL and at 6 months was 11.9±0.3 g/dL. AEs were reported by 75% of patients; the most frequent AEs were back pain (14%), headache (14%), nasopharyngitis (13%), nausea (11%), hypertension (10%), and peripheral oedema (10%). Serious AEs were reported by 14 (22%) patients; diabetic ketoacidosis, and hyperkaelemia were each reported by 2 (3%) patients; all other serious AEs were each reported by one patient. No serious AEs were judged to be related to Hematide. Nine patients (14%) had an AE considered related to Hematide (most frequently headache reported by 5 patients [8%] and hypertension reported by 3 patients [5%]).

Conclusions: In data presented from this ongoing long-term study, patients received up to 12 months (including 6 months in their previous study) of Hematide Q4W, which was well tolerated. With dose adjustments, Hb concentrations were between 11 and 12 g/dL, 6 months following roll-over.

MP382 THE PHARMACOKINETICS, SAFETY AND TOLERABILITY OF FERRIC CARBOXYMALTOSE: DATA FROM A DOSE ESCALATING STUDY IN PATIENTS WITH IRON DEFICIENCY ANAEMIA

Peter Geisser, José Banké-Bochita. *R&D Division, Vifor (International) Inc., St. Gallen, Switzerland; Institute of Clinical Pharmacology, Parexel GmbH, Berlin, Germany*

Introduction and Aims: In iron deficiency anaemia (IDA), oral iron is often sub-therapeutic or poorly tolerated and current intravenous (IV) iron agents either have an immunogenic potential induced by dextran or dose limitations (acute labile iron toxicity). Ferric carboxymaltose (FCM) is a next generation IV iron formulation that has potential to overcome these limitations. In this study, we investigated the pharmacokinetics, safety and tolerability of escalating doses of FCM in IDA patients

Methods: This was a single-centre, randomised, double-blind, placebo-controlled, single-dose escalation study in patients with mild IDA investigating four dose groups (100, 500, 800 and 1000mg FCM or placebo). Patients in the first dose group were administered an IV bolus of 100mg FCM or placebo. Patients in the subsequent dose groups received an IV infusion over 15minutes. The decision to escalate to the next dose group was taken after reviewing the safety data for the previous dose level. Patients with mild IDA with a serum ferritin<20μg/L and Transferrin saturation (TfS)<16% were eligible

Results: 32 patients with a baseline Hb between 92 and 119g/L were included. Baseline serum ferritin was below 10μg/L in the majority of patients, but didn't exceed 16.96μg/L. Figure 1 shows the mean total serum iron concentration.

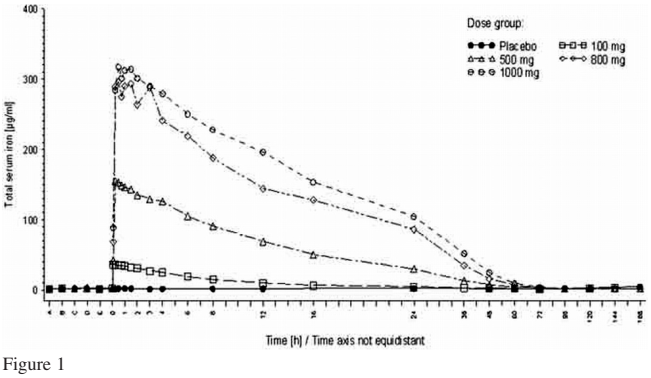


Figure 1

The overall serum exposure was similar across all dose groups, though somewhat lower after 100mg dose and estimates for T1/2 between 7.4 and 12.1 hours and for mean residence time (MRT) between 11.2 and 16.6 hours. A dose-dependent, but not dose-linear increase in ferritin concentrations was observed in all groups for the FCM treated patients compared to placebo with peak levels approximately 48 to 120 hours post-dose. The effect of FCM on serum transferrin levels or receptor concentrations didn't appear to be dose-dependent. Iron-binding capacity was transiently almost fully utilised after doses of 500, 800 and 1000mg. The elimination pattern for FCM essentially appeared to be mono-exponential. Safety laboratory assessments didn't show any significant abnormalities. In particular, liver enzyme activity, renal parameters, electrolytes were normal for all patients across the 4 dose groups. In total, 19 AEs occurred for 8 patients, of which three were considered drug-related for one patient allocated 100mg FCM and one patient allocated 1000mg FCM, respectively. There was no increase in the occurrence of AEs with increasing FCM doses

Conclusions: The pharmacokinetics of FCM at different doses were satisfactorily characterised by an observation period of 24 hours for 100 mg and 72 hours for the 500- to 1000mg doses. Overall, FCM was well tolerated across all dose ranges and may prove to be clinically useful for rapid and high-dose iron substitution

Disclosure: The first author is employed by Vifor (International) Inc.

MP383 SAFETY AND TOLERABILITY PROFILE OF FERRIC CARBOXYMALTOSE (FCM): DATA FROM THE FCM CLINICAL PROGRAM

Wajeh Y. Qunibi, Quinn Dinh, Joseph Benjamin. *Diabetes Institute, University of Texas Health Science Center and Texas Diabetes Institute, San Antonio, TX, USA; Clinical Research Development, Luitpold Pharmaceuticals Inc, Norristown, PA, USA; Temple University Hospital, Philadelphia, PA, USA*

Introduction and Aims: Available IV irons pose safety concerns and/or practical challenges to effective management of iron deficiency anemia (IDA). Iron dextran requires a test dose and carries the risk of anaphylaxis. Other IV irons (iron sucrose and ferric gluconate) are safer but typically require administration of small frequent doses which are inconvenient to patients. FCM is a new non-dextran IV iron agent that can be rapidly given over 15 minutes in a single dose up to 1000mg (Given to hemodialysis patients in divided doses of 200mg by rapid IV push). In the present study, we present the safety findings from the clinical trials conducted with FCM.

Methods: FCM was studied in 10 multi-centre, randomised controlled trials. The majority of studies compared FCM to oral iron ($FeSO_4$ as 325mg TID) in treating IDA in various patient populations (Chronic Kidney Disease (CKD), Gastrointestinal (GI) disorders, and women with heavy uterine bleeding or postpartum).

Results: The clinical program evaluated the safety and efficacy of FCM in patients with IDA. Of those receiving FCM (N=2095), 92% completed the study and approximately 94% received repletion dose of 1000mg. The discontinuation rate due to adverse events (AE) from FCM (1.5%) was slightly lower than that of oral iron (1.8%). No serious or life-threatening hypersensitivity (anaphylactic) Aes were reported with FCM. The most common drug-related AE with FCM was headache (Table 1). Two non-serious hypersensitivity Aes (0.1%), but no severe, symptomatic hypotension occurred. Mild to moderate transient skin changes (rashes, urticaria, and itching) had been observed.

Summary of reported Adverse Events

	FCM (N=2095) % of patients	Oral Iron (N=834) % of patients
One or more drug related AEs	15.2	26.1
One or more drug related serious AEs	0.0	0.0
Drug related AEs (incidence > 2%)		
Headache	2.3	2.2
Drug related AEs (incidence between 1 and 2%)		
Nausea	1.6	5.8
Rash	1.6	0.2
Decreased serum phosporus (transient, asymptomatic)	1.6	0.0
Local injection site reaction	1.5	NA
Constipation	1.0	11.3

AE, Adverse event.

Conclusions: Based on these safety data, we conclude that treatment with large single doses of FCM is safe and well tolerated

Disclosure: This study was supported by a research grant from American Regent/Luitpold Pharmaceuticals (Shirely New York, US).

MP384 PREVALENCE OF ANEMIA IN PATIENTS WITH DIABETIC NEPHROPATHY

Sergey Martynov, Marina Shestakova, Olga Vikulova, Larisa Koshel, Anastasia Severina, Natalya Trubitsyna. *Department of Diabetic Nephropathy and Dialysis, Endocrinology Scientific Center, Moscow, Russian Federation*

Introduction and Aims: Anemia is a common complication of chronic kidney disease (CKD) particularly in patients (pts) with chronic renal failure (CRF) in consequence of diabetic nephropathy (DN). The aims of the study to estimate the prevalence of anemia in pts with and without DN.

Methods: To evaluate the prevalence of anemia in DN we studied 1020 pts with type 1 37.5%) and type 2 62.5%) DM. Anemia was defined as hemoglobin (Hb) < 13.0 g/dl for men and Hb < 12.0 g/dl for women by the gender specific definition of WHO for pts without DN; and Hb < 13.5 g/dl for men and Hb <12.0 g/dl for women by the definition of anemia in CKD pts by National Kidney Foundation/Kidney Disease Outcome Quality Initiative (NKF/KDOQI) guideline for pts with diabetic kidney disease. Glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault formula. Evaluation of the distribution of anemia based on stages of CKD categories according NKF/KDOQI classification. Patients with GFR<15 ml/min and treated by erythropoietin-stimulating agents were not included. The clinical characteristics of pts are shown in Table 1.

Results: The prevalence of anemia in DN was 34.3% compare to 20.0% in absence of diabetic kidney disease ($p<0.001$). In type 1 DM anemia prevalence was significantly higher than in type 2 DM (44.7% and 27.3%, consequently ($p<0.001$)). In pts without DN the prevalence of anemia equitable to pts with kidney damage and normal GFR – 20.0% and 24.5%, consequently. In DN pts the prevalence of anemia significantly increases in pts with evident renal injury and achieves to 48.2% in proteinuric pts (n=195), that two time higher compared with person with microalbuminuria (n=315) (25.7%) ($p<0.001$). Anemia prevalence significantly increases then renal impairment progress (Fig.1). The Hb had close association with GFR level (R=0,28, p<0,001). The independent factors for Hb level by multiple logistic regression analysis were duration of diabetes, glycated hemoglobin, diastolic blood pressure and GFR ($p<0.001$).

The clinical characteristics of pts (n=1020)

	DM type 1 (n=382)	DM type 2 (n=638)
Age (years)	36.1±12.2	59.2±9.2**
Duration (years)	14.7±9.8	10.2±8.1**
Hb (g/l)	130.7±19.9	134.6±16.8*
GFR (ml/min)	120.3±45.1	114.1±38.2*
Nephropathy (%)	53.9	47.6

*p<0.01; **p<0.001.

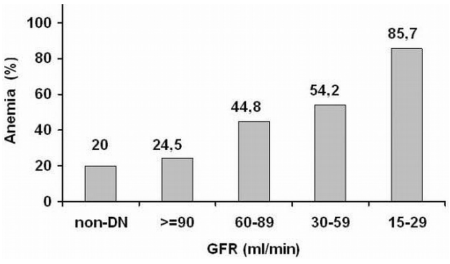


Figure 1. The prevalence of anemia in non-DN and DN patients (n=1020).

Conclusions: The prevalence of anemia in diabetic kidney disease related with advanced kidney damage and progression of CRF.

MP385 ANEMIA WITH ERYTHROPOIETIN DEFICIENCY IN DIABETIC NEPHROPATHY

Sergey Martynov, Marina Shestakova, Alexander Ilyin, Minara Shamhalova, Natalya Trubitsyna. *Department of Diabetic Nephropathy and Dialysis, Endocrinology Scientific Center, Moscow, Russian Federation*

Introduction and Aims: Diabetic nephropathy (DN) is associated with early development of anemia compared to chronic kidney disease (CKD) of other ethiology. The aim of the study is to evaluate serum EPO level and its response to anemia in patients (pts) with DN.

Methods: 94 pts with DN were studied (29 pts with type 1 and 65 with type 2 DM) - 48 males, 46 females, mean age 51.9±16.4). Among them 44 patients had microalbuminuria, 50 – macroalbuminuria. Glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault formula. Renal function was evaluated according to stage of CKD of NKF/KDOQI - 32 pts had GFR ≥90 ml/min, 30 pts had GFR 60-89 ml/min, 21 pts had GFR 30-59 ml/min and 11 pts were with GFR 15-29 ml/min. Anemia was defined as hemoglobin (Hb) < 13.5 g/dl in men and < 12.0 g/dl in women by the definition of anemia by NKF/KDOQI. The prevalence of anemia in total group was 43.6%. EPO was measured using ELISA and the laboratory normal range of serum EPO was 4.3-32.9 mIU/ml. Patients with GFR<15 ml/min and treated by erythropoietin-stimulating agents were not included.

Results: Mean EPO level was similar in pts with anemia and without anemia – 8.7±4.1 mUI/ml and 9.1±5.0 mIU/ml, consequently. We did not find significant differences of EPO concentration in anemic and non-anemic pts with microalbuminuria (9.4±4.9 mIU/ml and 8.8±3.9 mIU/ml, consequently) and macroalbuminuria (8.5±5.2 mIU/ml and 8.6±4.2 mIU/ml, consequently). Comparison of the level of EPO based on stages of CKD also did not find significant discrepancy in EPO value (Tabl.1). The significant inverse correlation of EPO and Hb was found for pts without anemia (R=-0.35; $p<0.01$) and pts with GFR ≥ 60 ml/min (R=-0.29; $p<0.05$) (Pic.1). And the intensity of correlation between EPO and Hb increased when GFR level enhanced: GFR ≥ 70 ml/min, R=-0.41; $p<0.01$, GFR ≥ 80 ml/min, R=-0.44; $p<0.01$ and at GFR ≥ 90 ml/min, R=-0.52; $p<0.01$. No correlation of EPO and Hb was observed in pts with GFR < 60 ml/min.

The serum EPO concentration (mIU/ml) in pts with DN (n=94)

GFR (ml/min)	Non-anemic pts (n=53)	Anemic pts (n=41)
≥90	8.8±5.4 (n=28)	11.2±6.1* (n=4)
60-89	9.9±5.0 (n=16)	8.3±3.4* (n=14)
30-59	8.9±4.0 (n=6)	8.6±4.5* (n=15)
15-29	7.6±2.4 (n=3)	8.3±3.6* (n=8)

*Not significantly different.

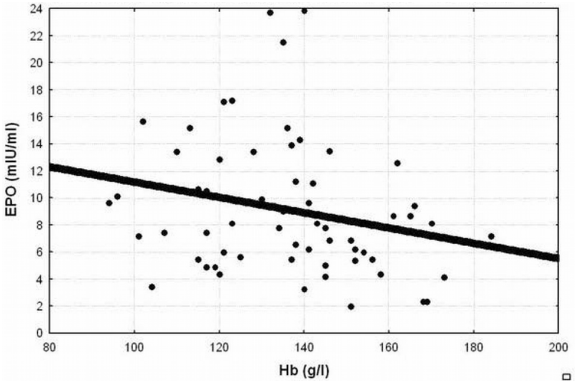


Figure 1. Distribution of individual EPO and Hb levels with linear regression analysis (DN patients with GFR≥60 ml/min (n=62).

Conclusions: DN is associated with low level of serum EPO in anemic pts in comparison with the non-anemic pts. In pts with anemia the renal EPO production is not elevated and remains inappropriately at the same level as in pts without anemia. Low response of EPO expression to anemia is observed when moderate decrease of GFR develops and mainly is related with early disturbance of EPO production by interstitial cells of kidneys and other factors which may affect to EPO metabolism in diabetes (neuropathy, inflammation, hyperglycemia and etc.).

MP386 EPOETIN ZETA: COMBINED SAFETY DATA FROM TWO CLINICAL STUDIES

Paul Scigalla[1], Rossen Koytchev[2]. [1]*CRC-International Clinical Research Consulting, Berlin, Germany;* [2]*CCDRD AG, Neuenhagen, Germany*

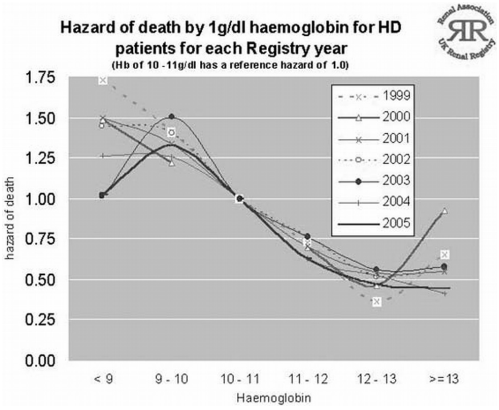
Introduction and Aims: We report combined safety data from two clinical trials using epoetin zeta (biosimilar), versus epoetin alfa, to correct and/or

maintain haemoglobin (Hb) concentration at >11 g/dL in patients with end-stage renal failure (ESRF) and anaemia, receiving chronic haemodialysis.
Methods: Two randomized, double-blind, multicentre, Phase III trials were conducted. Patients had anaemia at baseline (Hb <9.0 g/dL) (Trial I) or stable Hb of 10.5–12.5 g/dL with constant epoetin alfa dosing and no change in Hb >0.6 g/dL over 4 weeks (Trial II). Trial I: patients were randomized (1:1) to receive epoetin zeta or epoetin alfa intravenously, 1–3 times weekly, for 24 weeks to achieve Hb ≥11.0 g/dL. Trial II: patients were randomized (1:1) to receive epoetin zeta or epoetin alfa intravenously 1–3 times weekly to maintain stable Hb 10.5–12.5 g/dL. Treatment was administered after dialysis for 12 weeks then switched to the alternative treatment for a further 12 weeks. Safety endpoints were incidence of adverse events (AEs), tolerability ratings and occurrence of anti-erythropoietin (EPO) antibodies.
Results: Trial I: 305 and 304 patients (safety population) received epoetin zeta and epoetin alfa respectively; Trial II: 300 (155 + 145) and 304 (158 + 146) patients (safety population) received epoetin zeta and epoetin alfa respectively. Investigators rated tolerability as 'excellent' or 'good' for both products. Treatment-emergent AEs were reported by 600 patients (epoetin zeta: 693 AEs in 310 patients; epoetin alfa: 682 AEs in 290 patients). The most frequently reported AEs (>5% of patients) were hypertension, bronchitis and nasopharyngitis. Most AEs were assessed as mild (61.5%; n=845) or moderate (27.3%; n=376) in intensity and 95.6% (n=1315) were considered unrelated to study medication. No clinically significant difference in serious AEs (SAEs) was found between study groups (epoetin zeta: 165 SAEs in 97 patients; epoetin alfa: 171 SAEs in 105 patients). There were 32 deaths; 29 deaths (90.6%) were regarded as unlikely to be/not related to the study drugs. One death (3.1%) due to hypertensive crisis/haemorrhagic stroke was possibly related to epoetin zeta; two deaths (6.3%, one with epoetin zeta and one with epoetin alfa) were non-assessable. Overall, 57 patients withdrew from the trials due to a SAE: 57.9% (n=33) while receiving epoetin zeta. At baseline 15/912 patients (1.6%) tested positive for non-neutralizing anti-EPO antibodies; none developed antibodies during study treatment. There were no cases of pure red cell aplasia (PRCA).
Conclusions: Epoetin zeta is well tolerated. The similar frequency and intensity of treatment-emergent AEs indicate that the safety profile of epoetin zeta is comparable with epoetin alfa in patients with ESRF. No patients developed anti-EPO antibodies or PRCA during the studies, suggesting that the antibodies registered at baseline were either not inactivating or the titre was not high enough. Epoetin zeta offers a well-tolerated alternative to epoetin alfa in patients with CKD.
Disclosure: These studies were sponsored by STADA R&D GmbH, Bad Vilbel, Germany.

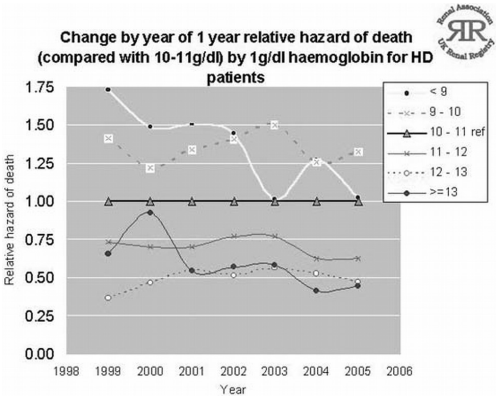
MP387 CHANGES BETWEEN 1999 AND 2005 IN THE RISK OF DEATH WITH HIGH OR LOW HAEMOGLOBINS IN UK HAEMODIALYSIS PATIENTS; DATA FROM 32,500 PATIENT YEARS OBSERVATION

David Ansell[1], Dan Ford[1], Donald Richardson[2]. [1]*UK Renal Registry, Bristol;* [2]*Renal Unit, York District Hospital, York, United Kingdom*

Introduction and Aims: There has been considerable interest in the new guidelines recommending that haemoglobin should be kept within a new upper limit target of under 13g/dl (12.5g/dl in the UK). This has been generated from concerns in randomised trials showing increased risk of thrombosis in patients with higher Hbs. This upper limit raises concerns, as the distribution of patient Hbs within a given renal unit are normally distributed and it is very difficult to narrow that distribution with a smaller 'tail' at both the top 'high Hb' and bottom 'low Hb' ends.
The risk of this new strategy is that it may generate an increase in the number of patients with a haemoglobin below 10 g/dl. Are the risks of a low haemoglobin equal to those of having a high haemoglobin?
Methods: The UK Renal Registry has been collecting quarterly Hb data since its outset, although patient numbers were small in 1997 and 1998 so we have only included data from 1999 to 2005. The data is collected via automated software data extraction process from hospital renal IT systems. All prevalent patients on HD within each of the sequential years were included. In 2005 cohort there were 8,500 prevalent patients included. The 4 quarterly Hb results for the year were meaned and relative risk of death in the following year (compared with an Hb 10.0 – 10.9 g/dl) was calculated adjusted for age, primary diagnosis and length of time on RRT.
Results: The relative risk of death for the different Hb groups appears to be consistent over the 7 year period. There is a lower risk of death with Hb > 10 g/dl.



The small numbers of patients in the <9 g/dl Hb group account for the variability seen in the relative hazard.



Conclusions: This stability in relative risk of death, is seen despite a large shift of patients from low Hbs to higher Hbs over this time period and this could indicate that it is related to achievement of Hb rather than a patient factor. Within the UK, average Hb in HD patients has continued to improve year on year. In 1999 there were 36% with Hb <10 and compared with 13% in 2005. Similarly in 1999 only 11% had an Hb >13 g/dl, compared with 22% in 2005.
This is observational data (not an randomised control trial) but it is not demonstrating a higher risk of death with achieving a higher Hb compared with the higher risk seen with a low Hb. Implementing an upper Hb limit may result in more patients having an Hb under 10 g/dl which is known to be related to an increased risk of death.

MP388 TIME OUTSIDE Hb-TARGET RANGES IN RESPECT OF OLD AND NEW K/DOQI GUIDELINES FOR ANEMIA MANAGEMENT

Hans-Joachim Müller[1], Patrick Biggar[2], Jan Galle[3], Lars-Christian Rump[4], Matthias Girndt[5], Hans-Gernot Asmus[6], Roland Winkler[7], Johann Braun[8], Johannes Mann[9], Christoph Wanner[10], Frank Dellanna[11]. [1]*Dept. of Nephrology, Klinikum Fulda, Germany;* [2]*KfH Nierenzentrum Coburg, Germany;* [3]*Dept. of Nephrology, Klinikum Lüdenscheid, Germany;* [4]*Dept. of Nephrology, University of Düsseldorf, Germany;* [5]*Dept. of Nephrology, University of Homburg, Germany;* [6]*KfH Nierenzentrum Berlin, Germany;* [7]*Dialysegemeinschaftspraxis Rostock, Germany;* [8]*KfH Nierenzentrum Nürnberg, Germany;* [9]*Dept. of Nephrology, Klinikum München-Schwabing, Germany;* [10]*Dept. of Nephrology, University of Würzburg, Germany;* [11]*Dialysegemeinschaftspraxis Düsseldorf, Germany*

Introduction and Aims: Quality management is an important fact in dialysis centers and guideline fulfillment is one important part of it.

Recently guidelines for anemia management have been changed and thus distribution of patients below, in and above target ranges (TR) may also have changed. Thus we analyzed in this study the changes in distribution of patients in the three different strata for old (11 – 13 g/dl) and new (10 – 12 g/dl) guidelines.

Methods: We performed a multi center (n = 26) retrospective study with data from the German AENEAS-database. All patients (n:901; age:65.3±14.2; m:512; diabetes:402) with 12 months Hb (2006) and ESA data with at least one Hb per month have been included. To calculate time outside TR all Hb consecutive values have been connected lineary and the intersection points with the lines representing the upper and lower limits have been calculated. Thus the time between two intersections represented the time below, inside or above TR. Time inside the three different groups have been compared for old and new guideline fulfillment.

Results: The mean observation period has been 343±6.7 days. The mean Hb value during the observation period was 11.76±0.85 g/dl (normally distributed). The median time for the different guidelines below TR has been 19% and 0% ($p<0.001$), in TR 62%, 50% (n.s.) and above 6%, 40% ($p<0.001$) respectively (F-Test).

Conclusions: In this quite well managed patients cohort the change of guidelines in anemia management would shift the time below targets significantly towards time above target without a significant increase of time in target. Thus no gain in fulfillment of guideline recommendations could be seen.

Disclosure: Supported by an unrestricted grant from Amgen.

MP389 IMMUNOGENICITY OF EPOETIN ZETA IN THE TREATMENT OF RENAL ANAEMIA

Nicole Casadevall[1], Arno Kromminga[2], Paul Scigalla[3]. *[1]Service d'Hématologie Biologique, Hôpital Hôtel-Dieu, Paris, France; [2]Institute for Immunology, Pathology and Molecular Medicine, Hamburg, Germany; [3]CRC-International Clinical Research Consulting, Berlin, Germany*

Introduction and Aims: Renal anaemia is a severe complication of chronic kidney disease, caused primarily by the inadequate production of erythropoietin. Recombinant human epoetin (EPO) has been used successfully for the treatment of renal anaemia for over a decade; however, safety concerns arose following increased reports of pure red cell aplasia (PRCA) due to neutralizing anti-erythropoietin antibodies. The recent development of biosimilar EPOs, including epoetin zeta, may provide equivalent clinical benefits with greater cost-effectiveness for this chronic condition. Two phase III studies were designed to compare the safety and efficacy of epoetin zeta and epoetin alfa in the treatment of renal anaemia. This analysis sought to investigate the immunogenicity of epoetin zeta.

Methods: Two randomized, double-blind, multicentre studies enrolled patients (18–75 years old) with end-stage renal failure, maintained on haemodialysis. In the correction study (CS), patients were required to have anaemia (haemoglobin [Hb] <9.0 g/dL despite optimal iron supplementation). Following an open run-in period of ≤6 weeks (including iron supplementation and anaemia work-up), patients were randomized (1:1) to receive epoetin zeta or epoetin alfa intravenously, 1–3 times weekly, for 24 weeks. In the maintenance crossover study (MS), patients had been on stable, adequate dialysis and receiving EPO for anaemia for at least 3 months. All patients received epoetin alfa during a 12- to 16-week open run-in phase. Those reaching a target Hb of 10.5–12.5 g/dL with constant epoetin alfa dosing and no change in Hb >0.6 g/dL over 4 weeks could enter the double-blind phase: 12 weeks of epoetin zeta or epoetin alfa intravenously, 1–3 times weekly after dialysis, followed by a switch to the alternative treatment for 12 weeks. Serum samples were taken at the beginning and end of each study to test for anti-erythropoietin antibodies, using immunoprecipitation.

Results: A total of 609 and 313 patients entered the double-blind phases of the CS and MS, respectively. Treatment efficacy was similar in both treatment arms in each study; mean Hb concentration fell within the predefined equivalence ranges. A total of 11 patients (1.8%) in the CS and 4 (1.28%) in the MS tested positive for anti-erythropoietin antibodies during the studies, all of whom had been positive at baseline. No other patients developed anti-erythropoietin antibodies during either study, no neutralizing anti-erythropoietin antibodies were detected and no cases of PRCA were reported. All 11 patients demonstrated a normal response to treatment.

Conclusions: Epoetin zeta, administered intravenously, was effective in correcting low Hb levels and in maintaining these improvements well within acceptable ranges in patients with renal anaemia. Treatment was not associated with the development of anti-erythropoietin antibodies and PRCA was not observed.

Disclosure: These studies were sponsored by STADA R&D GmbH, Bad Vilbel, Germany.

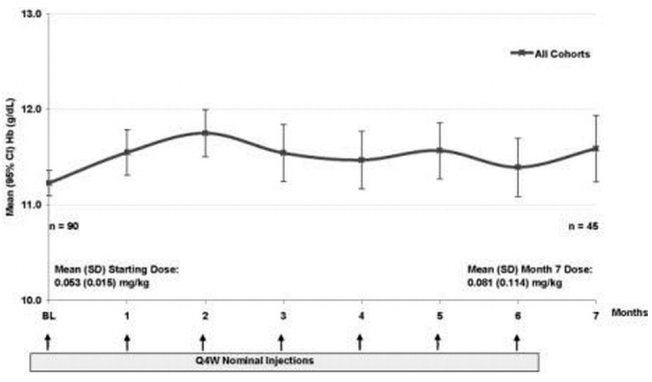
MP390 A PHASE 2, OPEN-LABEL, MULTI-CENTER, DOSE FINDING STUDY OF THE SAFETY, PHARMACODYNAMICS, AND PHARMACOKINETICS OF HEMATIDE™ FOR THE MAINTENANCE OF ANAEMIA IN HAEMODIALYSIS PATIENTS PREVIOUSLY TREATED WITH EPOETIN

Adrian Covic[1], Luminita Ardelean[2], Loris Manuelyan[3], Kiril Nenov[4], Pavlina Paunova[5], Vasil Tarnovo[6], Margarita Velkova[7], Marietta Franco[8], Robert Leong[8], Anne-Marie Duliege[8], Iain Macdougall[9]. *[1]Spitalul Clinic CI Parhon, Iasi, Romania; [2]Spitalul Clinic de Urgenta Bucuresti, Bucuresti, Romania; [3]Multiprofile Hospital for Active Treatment, Burgas, Bulgaria; [4]Multiprofile Hospital for Active Treatment St. Marina, Varna, Bulgaria; [5]Multiprofile Hospital for Active Treatment, Plovdic, Bulgaria; [6]University Multiprofile Hospital for Active Treatment, Pleven, Bulgaria; [7]Multiprofile District Hospital for Active Treatment, Veliko Tarnovo, Bulgaria; [8]Affymax, Inc., Palo Alto, CA, USA; [9]King's College Hospital, London, United Kingdom*

Introduction and Aims: Hematide, a novel synthetic PEGylated peptidic erythropoiesis stimulating agent, is being developed for treatment of anaemia associated with chronic kidney disease.

Methods: The study evaluated the dose range of intravenous (IV) or subcutaneous (SC) Hematide administered every 4 weeks (Q4W) that maintains haemoglobin (Hb) levels stable around baseline in haemodialysis patients whose Hb values were previously maintained on epoetin. Haemodialysis patients on epoetin therapy (≥ 50 and ≤ 200 U/kg/week) with a baseline Hb between 10 and 12.5 g/dL were enrolled in this ongoing open label dose-finding study. Patients were monitored for adverse events (AEs), Hb levels, dose adjustments, vital signs, and laboratory values.

Results: Ninety (90) patients (mean age of 52 years; 62% male) were enrolled in cohorts of 15 patients each. Patients were treated for 7 months with Hematide Q4W administered either IV (n=45) or SC (n=45). Patients in four of the cohorts (n=60) had a transition period during which epoetin was withheld for one week prior to administration of the first Hematide dose. Thirty-five patients (39%) reported at least one AE; AEs assessed to be possibly related to Hematide were reported in 9 patients, with the most frequent being increases in blood potassium levels (n=6) and headaches (n=3). Ten patients reported 12 serious AEs, including 3 deaths, none of which were attributed to Hematide. The mean Hb was 11.2 g/dL at baseline and 11.6 g/dL at 7 months. Patients who were dosed with Hematide after a transition period appeared to have less initial fluctuation in Hb levels compared to patients who made an immediate switch from epoetin to Hematide.



Conclusions: Based on the preliminary results from this on-going study, Hematide administered Q4W IV or SC in dialysis patients appears to be

well tolerated and maintains mean Hb concentrations between 11 and 12 g/dL throughout the study.

MP391 RESPONSE TO TREATMENT WITH IV IRON IN HEMODIALYSIS PATIENTS WITH HIGH SERUM FERRITIN AND LOW TRANSFERRIN SATURATION: IS THE SOLUBLE TRANSFERRIN RECEPTOR AN PREDICTOR OF THE RESPONSE?

Milagros Fernández Lucas[1], Jessica Amezquita[1], Jose Luis Teruel[1], Manuela Diaz[2], Nuria Rodriguez[1], Silvia Caldes[1], Judith Martins[1], Joaquin Ortuño[1]. [1]*Nephrology, Hospital Ramón y Cajal, Madrid, Spain;* [2]*Biochemistry, Hospital Ramón y Cajal, Madrd, Spain*

Introduction and Aims: Serum ferritin and transferrin saturation (TS) are the routine markers recommended by the current US and European Guidelines to achieve adequate iron stores in hemodialysis (HD) patients. The soluble transferrin receptor (s-TR) has been also advocated as a surrogate marker of iron status (iron deficiency or enhanced erythropoiesis may lead to an increase in s-TR).
Methods: We examined whether baseline iron markers and s-Tr predict the response of hemoglobin to treatment with iv iron. Sixty one patients were studied (95% received rh-EPO and 100 to 200 mg monthly iv ferric sucrose if ferritin was lower than < 500 ng/ml. Iron deficiency was defined as ferritin <200 ng/ml, TS <20% or both parameters (DOQUI-2007). Patients with such deficiency received 1gr of iron iv for 5 HD sessions.
Results: Iron status markers pre and post treatment with iv Fe are in the Table. In the group with high ferritin and low transferrin saturation, significantly higher transferrin saturation (15.2±3 vs 13.4±3.9 p=0.05) but not ferritin or s-TR levels predicted a significant increase in the haemoglobin (greater than 0.5 g/dl) but with minimal clinical significance.

	Ferritin<200 & TS<20% (n= 15)		Ferritin>200 & TS<20% (n= 14)	
	Pre	Post	Pre	Post
Hb	11.8±1.1	12.3±1.4, p=0,17	11.5±1.3	12.1±1.6, p= 0.08
Ferritin	106±48	286 ± 219, p=0.006	337±91	677±482, p= 0.014
TS	11±3.7	22±15, p=0.01	14±3.5	24±18, p=0.05
s-TR	1.89±0.5	1.55±0.6, p=0.01	1.76±0.4	1.62±0.5, p=0.16

Conclusions: We conclude that none of the studied markers is a good predictor of response to anemia treatment in this patient sub-population with high ferritin and low transferrin saturation.

Bone disease 2

MP392 HAS RECEPTOR THERAPY ANY ROLE IN THE HISTOPATHOLOGICAL ALTERATIONS OF PARATHYROID GLANDS IN REFRACTORY SECONDARY HYPERPARATHYROIDISM?

Carlo Lomonte[1], Luigi Vernaglione[2], Domenico Chimienti[1], Andrea Bruno[1], Savino Cocola[1], Annalisa Teutonico[1], Francesco Cazzato[1], Carlo Basile[1]. [1]*Division of Nephrology, Miulli General Hospital, Acquaviva delle Fonti, Bari, Italy;* [2]*Division of Nephrology, Hospital of Manduria, Manduria, Taranto, Italy*

Introduction and Aims: Nowadays, receptor therapy is the most adequate treatment of secondary hyperparathyroidism (SHPTH): calcitriol and vitamin D analogues act on vitamin D receptors (VDRs) and calcimimetics on calcium-sensing receptors (CaRs). Aim of the present study was to assess in hemodialysis patients affected by refractory SHPTH if an association exists between the histopathological alterations of parathyroid glands (i.e. nodular – NH - vs. diffuse hyperplasia and the expression of cell phenotypes) and the treatments with i.v. calcitriol, and/or cinacalcet and/or phosphate (P) binders.
Methods: Histological studies were performed on 82 parathyroid glands of 22 consecutive adult Caucasian hemodialysis patients (12 males and 10 females) referred for first parathyroidectomy (PTx). Besides defining the type of hyperplasia, a semiquantitative analysis was performed in order to assess the distribution of the two major cell populations, chief and oxyphil cells; it was expressed as oxyphil/chief cell ratio. The patients were subdivided into three groups according to the treatment of SHPTH: group A, consisting in 6 patients treated with cinacalcet, i.v. calcitriol and P binders; group B, consisting in 6 patients treated with i.v. calcitriol and P binders; group C, consisting in 10 patients treated with P binders only. The different treatments in the three groups were not due to the severity of SHPTH, but to the treatment preference of the individual dialysis centers before patients were referred for PTx.
Results: Sixty-eight glands removed out of 82 showed NH (82.9%). NH was more frequent in group A (95.6%) and B (95.5%) than in group C (67.6%) ($p < 0.05$). Oxyphil/chief cell ratio was significantly different when comparing the glands of the three groups (0.65±0.3 in group A, 0.36±0.4 in group B, 0.19±0.1 in group C, $p < 0.005$). The best fitted stepwise multiple regression analysis model ($R^2 = 0.550$; P = 0.0001) demonstrated that only cinacalcet treatment (B = 0.343; SE = 0.108; P = 0.005; 95% CI = 0.116; 0.570) and gender – females being associated with an increase of the ratio - (B = 0.283; SE = 0.101; P = 0.012; 95% CI = 0.070; 0.496) were predictors of the oxyphil/chief cell ratio.
Conclusions: There is an association between i.v. calcitriol therapy and the increase in the prevalence of NH of parathyroid glands and between cinacalcet therapy and the increase in the oxyphil/chief cell ratio. The meaning of the association between receptor therapy and the histopathological alterations of parathyroid glands in refractory SHPTH remains speculative and require the confirmation of further studies.

MP393 TREATMENT RESULTS OF BONE, MINERAL METABOLISM IN CHRONIC HEMODIALYSIS PATIENTS AND ITS ASSOCIATION WITH CHRONIC INFLAMMATION

Yu-Tze Tsai[1], Chien-Te Lee[1], Yih Su[2], Chien-Chun Kuo[1], Shang-Chih Liao[1]. [1]*Division of Nephrology, Medicine, Chang-Gung Memorial Hospital, Kaohsiung, Kaohsiung Hsien, Taiwan;* [2]*Department of International Trade, Cheng-Shiu University, Kaohsiung Hsien, Taiwan*

Introduction and Aims: Chronic inflammation is prevalent among chronic hemodialysis patients which strongly predicts long term outcome. Dysregulation of bone and mineral metabolism is a common complication that affects skeletal and cardiovascular systems. Failure to achieve treatment goal was associated with increased mortality. The relationship between these two abnormalities remains unclear. We aim to investigate the treatment result of bone and mineral metabolism in chronic hemodialysis (HD) patients according to KDOQI guidelines and to study the relationship between high sensitivity C reactive protein (hsCRP) and biomarkers of bone and mineral metabolism.
Methods: Demographic data and predialysis hsCRP, total calcium, phosphate, alkaline phosphatase (alk-p), parathyroid hormone (PTH) levels and calcium phosphate product (Ca × P) were measured in four hundred and forty eight HD patients. The treatment result was assessed based on KDOQI recommendation. Relationship between these variables and hsCRP were analyzed. Patients with higher hsCRP were identified and compared with other patients on biomarkers of the treatment results.
Results: About 50% of study patients achieved the recommend calcium and phosphate range. Only 23.7% patients had Ca × P ≥ 55 mg^2/dL^2. Ninety three patients (20.8%) achieved the recommend PTH range (150 – 300 pg/mL). Patients with higher Ca × P had higher hsCRP level (median: 3.86 mg/L *v.s.* 2.4 mg/L, $p < 0.05$). Correlation study revealed a positive correlation between hsCRP and calcium, phosphate and calcium phosphate product (all $p < 0.05$), but no relationship with PTH. Fifty patients (11.2%) achieved the four therapeutic goals and their hsCRP levels were significantly lower than other patients (median: 1.97 mg/dL *v.s* 2.71 mg/dL, $p < 0.05$). Patients with higher hsCRP levels (≥ 10mg/L) were older and associated with higher calcium, phosphate, Ca × P and lower albumin levels. Regression analysis found that serum albumin, Ca × P and alk-p were independent associated of hsCRP levels.
Conclusions: We conclude that the success rate of achieving recommended treatment goal in bone and mineral metabolism was not high. Higher Ca × P was associated with higher hsCRP level but patients with good treatment results had lower hsCRP levels. There was significant relationship between Ca × P, alk-p and hsCRP level, indicating an association between chronic inflammation and bone, mineral metabolism in HD patients.

MP394 EARLY: CINACALCET IN MODERATE SHPT IN A LARGE GERMAN PATIENT COHORT

Johann Braun[1], Helmut Reichel[2]. *[1]KfH Kuratorium für Dialyse und Nierentransplantation e.V., Nürnberg, Germany; [2]Nephrologisches Zentrum, Villingen-Schwenningen, Germany*

Introduction and Aims: Secondary hyperparathyroidism (sHPT) is common in chronic renal insufficiency and progresses over time. Conventional therapies often fail in terms of simultaneous KDOQI target achievement for PTH, Ca, P and Ca x P. The aim of this observational study was to characterize target achievement in dialysis patients with moderate sHPT treated with cinacalcet.

Methods: EARLY (EARLY = Evaluation of the use of cinacalcet for the treatment of moderate sHPT in hemodialysis and peritoneal dialysis patients) is a German multicenter observational study. Inclusion criteria were patients on dialysis, iPTH values of 300-800 pg/ml and no former use of cinacalcet. The primary endpoint was the percentage of patients in KDOQI target ranges for both PTH and Ca x P after 6 months treatment with cinacalcet.

Results: 6-month data were available for 468 patients (59.8% male, mean age 59.5 years). The most common underlying causes of kidney disease were chronic glomerulonephritis (26.5%), diabetic nephropathy (19.2%) and hypertensive nephrosclerosis (16.7%). Mean (± SD) values for PTH, P, Ca and CaxP are shown in the table: At 6 months, 33.1% of patients were in target for PTH (vs. 3.2% at baseline), 57.1% were in target for Ca x P (vs. 36.5% at baseline) and 21.4% reached the KDOQI target for both PTH and Ca x P (vs. <1% at baseline). More than half of patients received vitamin D, most patients received phosphate binders throughout the study. After 6 months, 45.7% of patients received a daily cinacalcet dose of 30 mg. The median daily dose was 47.1 mg/day.

	Baseline	6 months	Rel. difference (mo 6 vs baseline)
PTH [pg/ml]	625±295	376±297	−35.6%
P [mg/dl]	6.6±1.8	6.0±1.6	−6.1%
Ca [mg/dl]	9.4±0.9	8.8±0.9	−5.7%
CaxP [mg2/dl2]	62±17	53±15	−10.8%

Conclusions: These data suggest that a cinacalcet-based regimen for sHPT enables more patients to reach KDOQI targets as compared with conventional therapies. A high proportion of patients were in target for PTH and Ca x P after 6 months of cinacalcet treatment, however, better adherence to the common titration algorithm for cinacalcet might contribute to even higher KDOQI target achievement. Final results will be presented at the meeting.

Disclosure: Supported by Amgen - Prof. Braun: Honoraria - Amgen and Genzyme, advisory board - Amgen.

MP395 SEVELAMER THERAPY AND KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE (K/DOQI) TARGETS IN CKD 5 PATIENTS WITH DIABETES

Csaba Bereczki[1], Botond Csiky[2], Jozsef Balla[5], Erzsebet Ladanyi[2], Sandor Vido[3], Imre Kulcsar[3], Csaba Ambrus[2], Eva Kiss[4], Sandor Turi[2]. *[1]Dept. Paediatrics, University of Szeged, Szeged, Hungary; [2]FMC Magyarorszag, Hungary; [3]BBraun Avitum Magyarorszag, Hungary; [4]Gambro Magyarorszag, Hungary; [5]Dialysis Unit, Mediacal and Health Center Univ. Debrecen, Debrecen, Hungary*

Introduction and Aims: The hyperphosphatemia is associated directly with increased mortality and morbidity in chronic kidney disease (CKD). The risk is even higher in diabetic CKD patients.

The objective of the diabetes substudy of large, prospective, multicenter cohort (Hungarian Nationwide Sevelamer Study) was to determine the efficacy of Sevelamer in the diabetic CKD 5 patients with severe therapy resistant hyperphosphataemia.

Methods: 271 (15,9%) were diabetic out of involved 1695 CKD 5 patients. 197 (72,1%) were completed the study and analysed after 12-month Sevelamer (average dose: 4800 mg/day) therapy. The patients mean age was 60,1 years yrs.(12,1-82,6 years). The mortality rate (11,07%/year) was higher comparing to the non-diabetic group (10,2%/year) during the follow up, which indicates to the severe comorbidities in the diabetic patients studied.

Results: After 12-month Sevelamer therapy, the phosphorus level decreased from 2,38±0,48 to 1,97±0,51 mmol/L (p<0,001) and 32.9% of the patients achieved the K/DOQI target (1.12-1,76 mmol/L). The calcium level decreased from 2,33±0,24 to 2,27±0,36 mmol/L (p=0,011) and the number of patients, who achieved K/DOQI goal (2.1-2.37 mmol/L) increased from 38,7% to 63,87%. In majority of cases (84,9%), the baseline Ca x P product was higher than the K/DOQI target (<4,4 $mmol^2/l^2$) and after12-month therapy nearly the half of Sevelamertreated subjects (47,8%) achieved the it (p<0,001). Intact PTH level was lower than 300 pg/ml in all cases at the start of the study (inclusion criteria); it has not changed significantly during the follow-up.

Conclusions: These data indicate that Sevelamer treatment is effective in dialysed CKD patients with diabetes, but significant part of patients has not reached the recommended goals. Better patients compliance, higher doses of Sevelamer or combination therapies on bone mineral metabolism may be necessary to improve achievement of target levels.

Disclosure: Honorary consultant - Genzyme.

MP396 FIBROBLAST GROWTH FACTOR 23 IN PATIENTS WITH RENAL IMPAIRMENT

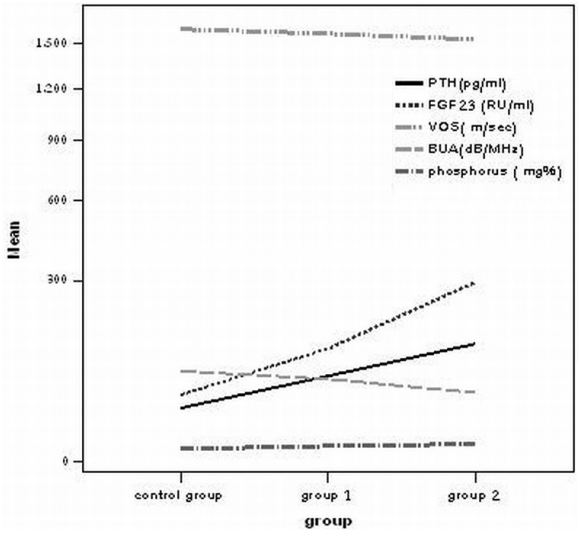
Saeed Afifi, Abdelbast Sharawy. *Nephrology, Ain Shams University, Cairo, Egypt*

Introduction and Aims: Secondary hyperparathyroidism is common in renal patients and is associated with increased mortality with the development of vascular calcification.

It would be useful to predict the development of hyperparathyroidism before treatment with active vitamin D agents. Fibroblast growth factor 23 (FGF23) is a newly identified humoral phosphaturic factor. Increased FGF23 levels are, at least partially, responsible for the reduction of 1, $25(OH)_{2D3}$ levels in the early phase of renal insufficiency and that this contributes to the development of secondary hyperparathyroidism in chronic and end-stage kidney disease.

Methods: The study was carried out on 45 subjects classified into three groups. Group one includes 15 patients with renal impairment, group two includes 15 patients with chronic renal failure on regular hemodialysis, and group three includes15 healthy control subjects. For the studied groups complete history and medical examination. Biochemical study includes renal function tests were done, serum calcium, phosphorus, alkaline phosphatase, calcitriol (by radioimmunoassay) and intact PTH level (by second-generation ELISA). Quantitative bone ultrasound and Fibroblast growth factor 23 (by two-site ELISA technique).

Results: Comparing group one and control group shows significant difference as regard PTH level (t = 8.21, p <0.001), BUA (t = -2.29, p =.03), VOS (t= -2.39 p =.02) and FGF23 (t=17.24, p < 0.001).Comparing group two and control group shows significant difference as regard PTH level (t = 17.04, p <0.001), BUA (t = -7.92, p =.03), VOS (t= -10.75, p =.02) and FGF23 (t =27.51, p < 0.001). Multiple regression analysis for PTH level in



patients with renal disease (group one and two) shows highest correlation with FGF23 (t =2.953, p= 0.007), followed by phosphorus level (t=2.916, p= 0.007). ROC curve study for PTH shows area under the curve for FGF232 is 0.976, phosphorus is 0.996, calcium is 0.124, and for Calcitriol is 0.052.
Conclusions: Our results show that FGF23 is high in patients with renal impairment and increase more with hemodialysis patients. In patient with renal disease FGF23 correlates with PTH and serum phosphorus level which indicates that FGF23 is related to hyperparathyroidism. ROC curve analysis shows that FGF23 is the best determinant for PTH level.we found that bone density in patient with renal disease correlate with PTH level, serum phosphorus, and serum calcium but no correlation with FGF23 level. We conclude that measurements of FGF23 levels in renal failure patients may help in deciding on an optimal treatment strategy and to predict secondary hyperparathyroidism.

MP397 CLINICAL FEATURES OF DIALYSIS PATIENTS WITH PARADOXICALLY REVERSED WHOLE PTH/INTACT PTH RATIO

Hirotaka Komaba[1], Yoko Takeda[1], Motoko Tanaka[2], Toshio Arakawa[3], Masafumi Fukagawa[1]. *[1]Division of Nephrology and Kidney Center, Kobe University School of Medicine, Kobe, Japan; [2]Akebono Clinic, Kumamoto, Japan; [3]Arakawa Renal Clinic, Takasago, Japan*

Introduction and Aims: The parathyroid hormone (PTH) levels detected by the third generation assays such as whole PTH assay are generally lower than those by the second generation assays such as intact PTH assay, because the latter also detect non-(1-84) PTH fragments accumulated in uraemic serum, mostly PTH (7-84). Rare exceptions to this rule have been reported in severe primary or secondary hyperparathyroidism and parathyroid carcinoma. In these patients, the existence of an N-form of PTH, distinct from PTH (1-84), has been demonstrated. This N-PTH is detectable by whole PTH assay but less well reactive in intact PTH assay.
Methods: Clinical features of 6 haemodialysis patients with reversed whole PTH/intact PTH ratio were analyzed and compared.
Results: All 6 patients demonstrated severe hyperparathyroidism with abnormally elevated whole PTH levels than intact PTH levels. A total of 5 patients demonstrated an enlargement of a single gland with hypervascularity, indicating sporadic primary adenoma or uraemic single nodule. The other patient had been performed total parathyroidectomy with forearm autograft, and later demonstrated recurrent hyperparathyroidism with reversed whole PTH/intact PTH ratio and enlargement of autografted parathyroid tissue. Among patients with single enlarged gland, 1 patient presented normalization of the whole PTH/intact PTH ratio after spontaneous remission due to autoinfarction of the gland. In other cases, surgical parathyroidectomy resulted in normalization of the whole PTH/intact PTH ratio, suggesting that the enlarged glands were responsible for the reversed whole PTH/intact PTH ratio.
Conclusions: These cases suggest that reversed ratio of whole PTH/intact PTH could be a marker for the severity of hyperparathyroidism and for the existence of single enlarged gland. Further studies are needed to elucidate the clinical significance of reversed whole PTH/intact PTH ratio in haemodialysis patients.

MP398 EARLY INITIATION OF CINACALCET (CN) FOR THE TREATMENT OF SECONDARY HYPERPARATHYROIDISM (SHPT) IN HEMODIALYSIS PATIENTS

Leonardo Lucchi, Lucia Stipo, Salvatore Perrone, Vittorio Albertazzi, Valentina Gatti, Alberto Albertazzi. *Nephrology and Dialysis, University Hospital, Modena, Italy*

Introduction and Aims: SHPT is a common complication in chronic kidney disease patients on hemodialysis (HD) and it is associated with adverse clinical outcomes. The calcimimetic CN has been shown to be an effective treatment for SHPT, significantly reducing serum PTH while simultaneously lowering Ca, P and Ca x P levels, thus increasing the proportion of patients achieving the KDOQI targets. The aim of this study was to evaluate the effect of early treatment with CN in HD patients with mild to moderate SHPT.
Methods: We evaluated 32 HD patients, age 59.8±12.4 years, dialysis duration 90.7±65.5 months. Inclusion criteria were iPTH > 300 pg/mL and serum Ca > 9.0 mg/dL. CN was started at 30 mg/day, the dose was than titrated to achieve iPTH < 300 pg/mL. Vitamin D and phosphate-binders were modulated to increase the achievement of KDOQI targets. Serum Ca (corrected), P, Ca x P, iPTH, were measured monthly.
Results: Results are reported in Table 1 below.
Conclusions: Early treatment with CN in HD patients with SHPT increases the proportion of patients achieving and maintaining KDOQI targets for bone mineral parameters. Early initiation of CN treatment allows the achievement and maintainance of targets with a lower dose of CN. The therapeutic effect of CN is better at 18 months compared with 12 months. The continued improvement in bone mineral parameters might suggests that long-term treatment with CN may attenuate the parathyroid hyperplasia that underlies SHPT. Future long-term studies are warranted.

MP399 EFFECT OF CALCIUM AND CALCITRIOL ON SIMULTANEOUS CaR AND VDR GENES EXPRESSION IN PARATHYROID GLANDS

Natalia Carrillo-Lopez, Daniel Alvarez-Hernandez, Ignacio Gonzalez-Suarez, Pablo Roman-Garcia, Diego Tuñon-Le Poultel, Jose Luis Fernandez-Martin, Jorge B. Cannata-Andia. *Bone and Mineral Research Unit. Instituto Reina Sofia de Investigacion, Universidad de Oviedo. Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*

Introduction and Aims: The regulatory mechanisms of parathyroid hormone are complex and involve among others calcium, calcitriol, the calcium sensing receptor (CaR) and the vitamin D receptor (VDR). The aim of this study was to assess the medium-long term effect of calcium and calcitriol on the simultaneous expression of CaR and VDR in parathyroid glands from rats.
Methods: To assess the effect of calcium, 6 independent experiments were performed using a total amount of 144 parathyroid glands removed from 4 months old male Wistar rats. Each experiment was carried out with 24 glands randomly divided into three different groups. The glands were washed for 8 hours and then cultured for additional 24 hours using a different calcium concentration in each group (0.6, 1.2 and 2.0 mM), changing the culture medium every twelve hours. To assess the effect of calcitriol, 6 independent experiments were performed using 96 parathyroid glands. Each

Abstract MP398 – Bone Mineral Parameters, dose of CN and Concomitant Medications

	Baseline	1 month	3 months	6 months	12 months	18 months
Patients number	32	32	32	32	30	27
Cinacalcet (mg/day)		30	33.8	33.8	37.6	38.3
iPTH (pg/mL)	609±345	305±163	205±104	209±69	195±58	199±44
Calcitriol (mcg/wk)	2.39±1.31	2.30±1.39	2.14±1.37	1.95±1.34	1.59±1.14	1.28±1.12
Serum Ca (mg/dL)	9.92±0.83	9.43±0.78	9.19±0.74	9.22±0.68	9.21±0.67	9.01±0.61
Serum P (mg/dL)	5.92±1.49	5.57±1.61	5.59±1.55	5.60±1.49	5.46±1.56	5.27±0.95
Ca x P (mg^2/dL^2)	58.3±13.8	52.2±14.6	51.2±13.9	51.4±12.6	51.6±15.1	47.5±9.7
Pts with iPTH < 300 pg/mL (%)	0	53.1	81.3	90.6	90.0	92.5
Pts with Ca x P < 55 (%)	37.5	65.6	65.6	65.6	65.5	86.8
Pts with no KDOQI target (%)	34.4	12.5	3.1	3.1	3.4	0
Pts within 1 KDOQI target (%)	28.1	6.3	18.8	9.4	24.1	13.3
Pts within 2 KDOQI target (%)	28.1	31.3	15.6	18.8	13.8	0
Pts within 3 KDOQI target (%)	9.4	34.4	34.4	43.8	10.3	40.0
Pts within 4 KDOQI target (%)	0	15.6	28.1	25.0	48.3	46.7

experiment was performed with 16 glands divided into 2 groups. The glands were washed for 8 hours and then cultured for additional 48 hours in a 0.6mM calcium medium containing 10^{-8}M calcitriol or vehicle, changing the culture medium every twelve hours. In both set of experiments (calcium and calcitriol), after the culture period, total RNA was extracted from the glands and CaR and VDR mRNA levels were measured by quantitative real-time PCR. The results were normalized against 18s expression and compared with the reference groups (0.6 mM calcium for calcium experiments and vehicle for calcitriol experiments). Statistical analysis was performed using non-parametric tests for two related samples (Wilcoxon test).

Results: No differences were found in the CaR mRNA expression among the 3 different calcium concentrations tested. By contrast, VDR mRNA levels increased when calcium concentration was increased (reference group- 0.6 mM calcium: 100%, 1.2 mM calcium: 163.5±26.6% and 2.0 mM calcium: 203.4±12.2%) achieving statistical signification only with the higher calcium concentration (p=0.043). Calcitriol significantly increased both, CaR (vehicle: 100.0% vs 10^{-8} M calcitriol: 212.8±39.9%; p=0.046) and VDR (vehicle: 100.0% vs 10^{-8} M calcitriol: 218.7±42.6%; p=0.028) mRNAs.

Conclusions: In summary, incubation with high calcium concentration was associated with significant increments in VDR gene expression but no changes in CaR expression. These results suggest that the activation of the CaR by high calcium may trigger a rapid and direct effect of calcium on VDR expression which seems to be independent of changes in CaR expression. On the other hand, calcitriol was able to increase both, VDR and CaR genes expression. These results support the hypothesis that calcitriol not only upregulates its receptor but also CaR expression even in the presence of low calcium concentration.

MP400 RESULTS OF A RANDOMISED, CROSS-OVER DESIGN STUDY OF SEVELAMER CARBONATE (RENVELA®) POWDER AND SEVELAMER HYDROCHLORIDE (RENAGEL®) TABLETS IN CHRONIC KIDNEY DISEASE PATIENTS ON HAEMODIALYSIS

Stanley Fan[1], Calum Ross[2], Sandip Mitra[3], Philip Kalra[4], Nick Pritchard[5]. *[1]Royal London Hospital, London, United Kingdom; [2]Norfolk and Norwich University Hospital, Norwich, United Kingdom; [3]Manchester Royal Infirmary, Manchester, United Kingdom; [4]Hope Hospital, Salford, United Kingdom; [5]Addenbrooke's Hospital, Cambridge, United Kingdom*

Introduction and Aims: Sevelamer carbonate (Renvela®) is a new, calcium- and metal-free phosphate binder with the same polymeric structure as sevelamer hydrochloride (Renagel®), in which carbonate replaces chloride as the anion. Sevelamer carbonate powder for oral suspension is mixed with water and taken orally, and provides an alternative formulation to tablets. The aim of this study was to demonstrate equivalence of sevelamer carbonate powder to sevelamer hydrochloride tablets, each dosed three times a day (TID) with meals, on the control of serum phosphorus levels in chronic kidney disease (CKD) patients on haemodialysis.

Methods: This was an open-label, randomised, cross-over study. Following a 2-week washout period and 4-week sevelamer hydrochloride tablet run-in period, 31 patients were randomly assigned on a 1:1 basis to treatment with either sevelamer hydrochloride tablets TID for 4 weeks followed by sevelamer carbonate powder TID for 4 weeks, or sevelamer carbonate powder TID for 4 weeks followed by sevelamer hydrochloride tablets TID for 4 weeks. The prescribed dose during the randomised treatment periods was individualised based on the final sevelamer hydrochloride tablet dose prescribed at the end of the run-in period.

Results: Equivalent control of serum phosphorus was established between sevelamer carbonate powder TID and sevelamer hydrochloride tablets TID (geometric least square mean ratio [sevelamer carbonate powder:sevelamer hydrochloride tablets] of 0.95 with a 90% CI of 0.87-1.03). The mean ± SD serum phosphorus was 1.6±0.5 mmol/L (5.0±1.5 mg/dL) during sevelamer carbonate powder treatment and 1.7±0.4 mmol/L (5.2±1.1 mg/dL) during sevelamer hydrochloride tablet treatment. Calcium-phosphorus product and lipid profiles were comparable between treatment groups.

From baseline (post sevelamer hydrochloride run-in period) to the end of randomised treatment, the mean ± SD change in serum bicarbonate was 2.7±3.7 mEq/L for sevelamer carbonate powder and 0.1±3.3 mEq/L for sevelamer hydrochloride tablets (p<0.001 between treatments). In other respects, the safety and tolerability profile of sevelamer carbonate powder and sevelamer hydrochloride tablets was similar.

The mean actual daily dose of sevelamer was 5.9 g/day for sevelamer carbonate powder and 6.5 g/day for sevelamer hydrochloride tablets. Compliance was 81% during sevelamer carbonate powder treatment and 83% during sevelamer hydrochloride tablet treatment.

Conclusions: Sevelamer carbonate powder TID and sevelamer hydrochloride tablets TID were equivalent in controlling serum phosphorus in CKD patients on haemodialysis.

MP401 SEVELAMER CARBONATE (RENVELA®): CONTROL OF SERUM PHOSPHORUS IN CHRONIC KIDNEY DISEASE (CKD) PATIENTS NOT ON DIALYSIS

M. Ketteler[1,7], M. Rix[2], S. Fan[3], N. Pritchard[4], O. Østergaard[5], P. Kalra[6]. *[1]RWTH University Hospital, Aachen, Germany; [2]Rigshospital, Copenhagen, Denmark; [3]Royal London Hospital, London, United Kingdom; [4]Addenbrookes Hospital, Cambridge, United Kingdom; [5]Roskilde Hospital, Roskilde, Denmark; [6]Hope Hospital, Salford, United Kingdom; [7]Klinikum Coburg, Coburg, Germany*

Introduction and Aims: Sevelamer carbonate (Renvela®) is a new, calcium- and metal-free phosphate binder with the same polymeric structure as sevelamer hydrochloride (Renagel®), in which carbonate replaces chloride as the anion. The aim of this study was to investigate the effects of sevelamer carbonate tablets dosed three times per day (TID) with meals on the control of serum phosphorus (P) in hyperphosphataemic (serum P>5.5 mg/dL) CKD patients not on dialysis.

Methods: This was a multi-centre, open-label, single-arm, dose titration study. Patients acted as their own controls by utilising pre- and post-treatment washout periods. The study consisted of a 2-week screening period, a 2-week washout period (only for patients on phosphate binders at screening), an 8-week sevelamer carbonate treatment period and a 2-week post-treatment washout period. Patients were initiated on sevelamer carbonate 4.8 g daily (2 x 800 mg tablets TID). The mean actual daily dose of sevelamer carbonate was 5.4±1.7 g.

Results: see Table 1.

From baseline to end of treatment, a statistically and clinically significant increase was seen in mean serum bicarbonate (1.3±2.9 mEq/L, p=0.005). The majority of adverse events were of mild or moderate intensity and no serious adverse events were considered related to treatment.

Conclusions: Sevelamer carbonate is an effective and well tolerated therapy for the control of serum phosphorus levels in hyperphosphataemic CKD patients not on dialysis.

Abstract MP401 – Table 1

Laboratory parameter	Pre-washout (N=27)[a]	Baseline (N=46)	Day 56/ET (N=46)	Change Baseline to Day 56/ET (N=46) *	Day 70 Post-washout (N=40)	Change Day 56 to Day 70 (N=40) *
P (mg/dL)	5.3±0.8	6.2±0.8	4.8±1.0	–1.4±1.0	6.5±1.3	1.7±1.1
Ca (mg/dL)[b]	9.1±0.9	8.5±0.9	8.8±0.8	0.3±0.5	8.6±0.6	–0.2±0.5 †
iPTH (pg/mL)[c]	208	341	319	–39§	362	63
Total cholesterol (mg/dL)	ND	173.2±42.0	137.2±36.4	–19.5±17.1%	165.5±47.0	23.0±20.9%
LDL Cholesterol (mg/dL)	ND	104.7±33.6	69.7±25.2	–31.9±18.1%	98.4±39.0	44.9±34.9%

*Wilcoxon signed rank test p< 0.001 unless otherwise indicated; §Wilcoxon signed rank test p=0.013; †Wilcoxon signed rank test p=0.007.
[a] Pre-washout only for patients on phosphate binders at screening; [b] Calcium (adjusted for albumin); [c] Median values.

MP402 CURRENT MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM IN 14 SWISS DIALYSIS UNITS: A BENCHMARK ANALYSIS WITH INTERNATIONAL DATA

Pierre-Yves Martin[1], Hans Saxenhofer[2], Zeew Glueck[3], Niklaus Hoefliger[6], Daniel Hertner[7], Ann-Kathrin Schwarzkopf[8], Maja Klein[9], Andrea Koflach[10], Markus Hugentobler[11], Hans Freudiger[4], Daniel Aerne[12], Marcel Schmid[13], Alois Staub[14], Rudolf P. Wüthrich[5]. *[1]Nephrology, University Hospital Geneva, Geneva; [2]Nephrology, Lindenhospital, Berne; [3]Nephrology, Spitalzentrum, Biel; [4]Centre de Dialyse, Permanence d'Onex, Onex; [5]Nephrology, University Hospital Zurich, Zurich; [6]Nephrology, Kantonspital Zug, Zug; [7]Regionalspital Altdorf, Schwytz; [8]Salemspital, Bern; [9]Rogionalspital, Emmental; [10]Hemodialysis Center, Zurich; [11]Kantonspital, Frauenfeld; [12]Spital, Lachen; [13]Hemodialysis Center, Visp; [14]Hemodialysis Center, Luzern, Switzerland*

Introduction and Aims: Secondary hyperparathyroidism (SHPT) is a progressive disease that can be treated by different therapeutic strategies. The objective of this ongoing project is to analyse SHPT therapeutic regimens in Swiss dialysis units and the achievement of all 4 KDOQI targets (PTH, P, Ca, CaxP) in these units and to compare the data with international results.
Methods: In this observational chart review, an analysis of SHPT parameters in 525 unselected dialysis patients was performed in 14 participating sites (17 to 66 patients/site). Information on baseline characteristics, laboratory values (PTH, P, Ca) and medications used to treat SHPT (phosphate binders, vitamin D, calcimimetics) was collected at the sites. The results were compared with data from DOPPS II (2002-2004; Dialysis Outcomes and Practice Pattern Study; n=8615) and COSMOS (2005-2008; Current Management Of SHPT – a Multicenter Observational Study; n=2495) as an international benchmark.
Results: 60.7% of the 525 patients were male, mean age (SD) was 66.4 (14.2) years and mean weight (SD) was 73.9 (17.2) kg; 93.3% received hemodialysis (HD) and 6.7% were on peritoneal dialysis (PD).

Percentage of patients within KDOQI targets in 14 Swiss dialysis centers, in comparison with DOPPS and COSMOS

	DOPPS n=8615	COSMOS n=2495	SWISS average 14 sites n=525
corr Ca (2.1-2.4 mmol/L)	40.5	53.5	68.2
P (1.13-1.78 mmol/L)	40.8	52.2	54.0
CaxP (<4.5 mmol2/L2)	56.5	75.6	76.2
iPTH (16.5-33.0 pmol/L)	22.2	32.4	29.3
PTH&CaxP within targets			23.5
All 4 parameters within targets	4.6		13.7

Of 525 patients, 55.6% were treated with vitamin D sterols (vs DOPPS: 52.2%; COSMOS: 45.0%) and 81.9% received at least one phosphate binder (vs DOPPS 81.1%; COSMOS 81.6%). Calcimimetics were used in 20.4% of the Swiss collective (vs COSMOS 2.4%)
Conclusions: This benchmark analysis highlights that KDOQI target levels are difficult to achieve. The results observed in Switzerland, however, are substantially better than those described in DOPPS or COSMOS. 13.7% of Swiss patients achieved all 4 KDOQI parameters, which is a 3-fold improvement compared with DOPPS in 2004. Apart from variations in baseline characteristics, reasons for the superior results in Switzerland could be a better awareness of guidelines recommendations and the enhanced integration of new therapies compared with DOPPS and COSMOS.

MP403 BONE HISTOLOGY AND KDOQI GUIDELINES FOR BONE METABOLISM AND DISEASE RELATIONSHIP IN CKD PATIENTS

Goce Spasovski[1], Saso Gelev[1], Adrian Covic[2], Raymond Vanholder[3], David Goldsmith[4]. *[1]Department of Nephrology, University Clinical Center, Skopje, Macedonia, The Former Yugoslav Republic of; [2]Nephrology Clinic, "Dr. C.I. Parhon" University Hospital, Iasi, Romania; [3]Department of Internal Medicine, Nephrology Section, University Hospital, Ghent, Belgium; [4]Renal Unit, Guy's Hospital, London, United Kingdom*

Introduction and Aims: The impact on bone histology of attaining the KDOQI thresholds for bone and mineral metabolism has not been assessed. The objective of this study was to analyse the association of achieving KDOQI targets for bone metabolism and bone histology in patients on hemodialysis (HD).
Methods: We prospectively followed 20 incident HD patients in our unit for a period of three years. 59 transiliac bone biopsies after double tetracycline labeling were performed at the recruitment (baseline; n=20), after 1 (n=20) and three years on HD (n=19). A monthly biochemistry for calcium and phosphate metabolism and PTH at 3 months interval was determined. Up to the end of the first year patients were treated with lanthanum carbonate (LC; n=10) or calcium carbonate (CC; n=10). Thereafter, all patients received regular treatment with calcium carbonate as a sole phosphate binder and vitamin D according to the standard routine clinical practice aiming to achieve KDOQI targets for bone and mineral metabolism as best as possible.
Results: Out of the total of 59 biopsies Mx bone disease was found to be the most frequent bone lesion in 37 (57.6%), followed by ABD in 11 (18.6%) and HPTH and osteomalacia in 9 (15.3%) and 2 (0.03%) of the biopsies, respectively. Only 2 biopsies at baseline, 6 at 1 year (LC=4; CC=2) and 2 at 3 years, or in total 10 biopsies (16.9%) were collected in patients conforming with the recommended ranges for serum calcium, phosphate and PTH levels. The histomorphometry of all these biopsies revealed a mixed (Mx) type of bone disease. The number of pts within PTH range of 150 - 300 pg/ml remained almost unchanged over the years, 4 at baseline, 6 at 1 year and 4 pts at 3 years on HD. Again, from these 14 pts (23.7%) the bone histology confirmed diagnosis of Mx bone lesion in 13 pts and only one patient was classified as hyperparathyroid bone disease. Conversely, the number of pts with PTH < 150 pg/ml increased from 6 at baseline and 7 after 1 year up to 15 after 3 years ($p<0.01$). The corresponding biopsies showed either ABD (n=11) or Mx histology (n=17). No biopsies showing ABD were found in patients with PTH ≥ 150 pg/ml.
Conclusions: Ten biopsies were obtained while biochemistry was compliant with KDOQI guideline for all parameters, all of them showing Mx bone histology. Hence, the Mx type of bone representing a mild abnormality that lies in between low and high-turnover lesions might be assumed to be the type of histologic bone disorder most conforming with the KDOQI thresholds. Over the years, an increased proportion of patients on HD have low bone turnover.
Disclosure: This study was partly sponsored as research project from SHIRE, UK.

MP404 EFFICACY OF PHOSPHORUS BINDING BETWEEN CHEWED AND CRUSHED LANTHANUM CARBONATE IN HEALTHY VOLUNTEERS

Darius Mason[1], Priscilla How[1], Jose Arruda[2], Alan Lau[1]. *[1]Pharmacy Practice, University of Illinois at Chicago, Chicago, IL, USA; [2]Medicine (Nephrology), University of Illinois at Chicago, Chicago, IL, USA*

Introduction and Aims: Lanthanum carbonate (LC) is an effective phosphorus (P) binder for the management of hyperphosphatemia and secondary hyperparathyroidism in chronic kidney disease. The manufacturer recommends that patients chew and take LC with or immediately after meals. However, certain patients are unable to chew the tablets or may prefer to crush the tablets and mix it with food. To date, it is not known if crushing LC prior to administration and taking it with food would be as efficacious as chewing it. As such, this study was conducted to compare the efficacy of P binding between chewed and crushed LC.
Methods: This was a randomized, open-label, crossover study. 11 healthy subjects (4 males, 7 females) were randomly assigned to receive: (A) A standardized meal that was controlled for the P content (32 mmol or 1 g of elemental P) which served as a dietary P load, (B) A single oral dose of LC 1 g (Fosrenol, Shire US Inc) that was chewed during the standardized meal and (C) A single oral dose of LC 1 g crushed into a fine powder using a pestle and mortar, mixed with 30 ml of applesauce and taken during the standardized meal. Serum P concentrations were obtained at baseline and hourly for up to eight hours after meal completion. Urine collection was also performed at 2-hour intervals to determine the amount of P excreted. The change in serum P concentrations, area under concentration-time curve (AUC), and urinary P excretion among the 3 arms were compared.
Results: Subjects who received chewed (B) and crushed (C) LC resulted in a smaller increase in serum P than those who received the meal alone (A) (Fig. 1). The increase in AUC from baseline for serum P were 4.7, 3.2, 3.3 mg.hr/dL for arms A, B and C, respectively (P= 0.047). Of the 7

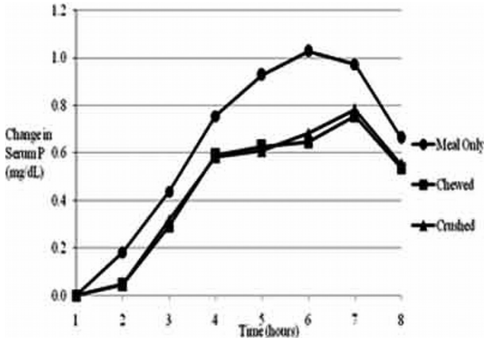


Figure 1

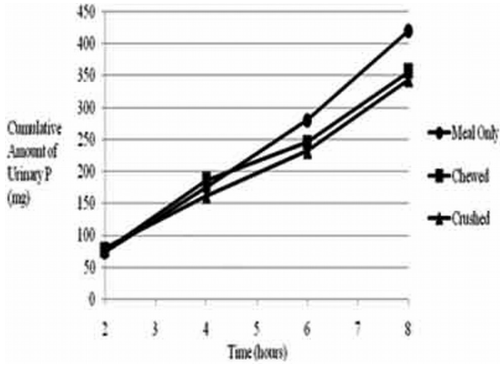


Figure 2

subjects with complete urine data (detectable urine P concentrations), the total amount of urine P excreted were 402, 356 and 344 mg for the control, chewed and crushed arms, respectively (P=NS). (Fig. 2)

Conclusions: The smaller change in serum P and AUC observed when LC was administered confirms that LC is an effective P binder. According to the changes in serum P and AUC observed, chewed and crushed LC are similarly efficacious in binding dietary P.

Disclosure: This study was supported in part by an unrestricted grant from Shire.

MP405 THE CALCIMIMETIC R-641 COMBINED WITH PTH TREATMENT REDUCES VASCULAR CALCIFICATION IN EXPERIMENTAL CKD AND PRESERVES RENAL FUNCTION

Thilo Krueger[1], Peter Boor[1], Vincent Brandenburg[1], Georg Schlieper[1], Markus Ketteler[2], Willi Jahnen-Dechent[3], Juergen Floege[1], Dave Martin[4], Ralf Westenfeld[1]. *[1]Nephrology and Clinical Immunology, University Clinic RWTH Aachen, Aachen, Germany; [2]Nephrology, Hospital Coburg, Coburg, Germany; [3]Dept. of Biomedical Engineering, University Clinic RWTH Aachen, Aachen, Germany; [4]Department of Metabolic Disorders, Amgen Inc., Thousand Oaks, CA, USA*

Introduction and Aims: Cardiovascular mortality and morbidity is increased in patients with end stage renal disease and associated with vascular calcification (VC). An elevated serum calcium phosphorus product and secondary hyperparathyroidism represent established risk factors for VC. Calcimimetics reduce PTH levels and have been shown to exert beneficial effects on VC and renal osteodystrophy. Nevertheless it is unclear whether these actions are mediated directly or indirectly via ameliorating bone metabolism after "PTH cycling". We investigated the effect of large amplitudes in serum PTH levels achieved by repetitive, sequential administration of a calcimimetic, AMG 641, and PTH on VC in a rat model of chronic renal failure.

Methods: Chronic kidney disease (CKD) was induced in rats by a diet containing 0.75% adenine for 4 weeks. Four treatment protocols then continued for a further 4 weeks in 10 rats each: AMG 641 + vehicle, PTH (1-34) alone, AMG 641 + PTH (1-34), or vehicle alone. AMG 641 (10 mg/kg body weight) or vehicle were administered every third day. In the AMG 641 + PTH group each AMG 641 dose was followed 48 hrs later by 80 μg/kg PTH or vehicle subcutaneously. Blood was collected weekly; blood pressure was obtained at the end of the experiment. Serum and urine parameters were measured using clinical laboratory techniques; PTH (1-84) by ELISA. VC was quantified by HCl extraction of the aorta and cresolphthalein assay. Only rats with established CKD were included in the analyses.

Results: Adenine treatment induced CKD as evidenced by doubling of creatinine serum levels in 65% of the rats. Administration of AMG 641 in adenine-fed rats reduced aortic calcium content to the range of healthy controls. PTH (1-34) treatment did not affect VC despite significant elevations of alkaline phosphatase serum levels. In the AMG 641 + PTH group the protective effect of AMG 641 against VC was still apparent but lost significance ($P = 0.1$). Combined AMG 641 + PTH treatment led to significantly reduced creatinine serum levels and albuminuria ($P < 0.01$). AMG 641 and AMG 641 + PTH treatment significantly reduced PTH serum levels compared to CKD rats. Only PTH (1-34) treated groups showed a significant reduction in blood pressure.

Conclusions: The calcimimetic AMG 641 attenuated the severity of secondary hyperparathyroidism in kidney failure and diminished the extent of VC. Additional treatment with PTH resulted in an improved kidney function and lower blood pressure. Large PTH amplitudes increased alkaline phosphatase levels which may indicate a higher osteoblast activity and thus a lower degree of renal osteodystrophy.

Disclosure: This project was kindly supported by a grant from Amgen Inc.

MP406 INCREASE IN BONE VOLUME IN NON-URAEMIC APOLIPOPROTEIN E-DEFICIENT (EKO) MICE AND EFFECT OF CHRONIC RENAL FAILURE (CRF)

Igor G. Nikolov[1,3], Nobuhiko Joki[1], Ognen Ivanovski[1], Olivier Phan[1], Thao Nguyen-Khoa[1,2], Bernard Lacour[2], Tilman B. Drueke[1], Ziad A. Massy[3], Luciene Machado dos Reis[4], Vanda Jorgetti[4]. *[1]Inserm U845, Necker Hospital, Paris, France; [2]Biochimie A, Necker Hospital, Paris, France; [3]Inserm ERI-12, UPJV, Amiens, France; [4]Nephrology, USP, São Paulo, Brazil*

Introduction and Aims: The EKO mouse has become a frequently used model to study the progression of atherosclerosis and its prevention. The EKO mouse with superimposed CRF develops, in addition to accelerated atherosclerosis, rapidly progressive arterial calcification both inside and outside of atheromatous plaques. Recent evidence points to links between vascular disease and bone disease.

Methods: We wished to examine possible bony changes in EKO mice and the effect of CRF there on, compared with C57/BL-6 wild-type mice (WT). CRF was induced surgically in 4 groups of 8-wk-old female mice (WT, WT+CRF, EKO, EKO+CRF, n=13-15 animals per group), using cortical electrocoagulation of one kidney and subsequent ablation of the other kidney.

Results: In EKO-CRF and WT-CRF mice, serum urea concentrations were comprised between 20 and 40 mM (normal, <10 mM). Serum Ca was significantly increased in both EKO-CRF and WT-CRF compared to non CRF mice whereas there was no significant difference for serum P (data not shown). The main results of bone histomorphometry are shown in the table.

Bone histomorphometry in non CRF and CRF wild type and EKO mice (means ± SE)

	WT	WT+CRF	EKO	EKO+CRF	p Type	p CRF
Bone volume, %	4.6±0.3	5.6±0.5	6.1±0.4	10.6±0.5	<0.001	<0.001
Osteoid surface, %	9.3±1.4	19.3±1.7	10.3±1.0	18.4±1.9	NS	<0.001
Osteoblast surface, %	6.7±1.1	15.4±1.4	8.3±0.8	12.7±1.1	NS	<0.001
Eroded surface, %	4.4±1.0	7.24±0.8	4.3±0.4	5.2±0.5	NS	<0.01
Osteoclast surface, %	1.4±0.3	2.1±0.3	1.3±0.2	1.5±0.2	NS	<0.05
Trabec. thickness, μm	26.5±2.1	29.4±1.1	28.5±1.0	37.4±1.1	<0.001	<0.001
Trabec. number, /mm	1.9±0.1	1.9±0.1	2.1±0.1	2.83±0.1	<0.001	<0.05
Osteoblast number, /mm^2	12.5±2.3	23.2±2.8	14.6±1.0	35.6±2.7	<0.01	<0.05
Osteoclast number, /mm^2	1.6±0.4	2.3±0.4	2.1±0.2	2.9±0.3	NS	<0.05

The main findings are that bone volume including trabecular thickness and number was increased in EKO compared with WT mice of young age and female gender. CRF led to a further increase in these two parameters. In addition, CRF stimulated osteoid, osteoblastic and osteoclastic parameters. An increase in mineralizing surface (p=0.02) and a borderline increase in bone formation rate (p=0.07) were observed in EKO+CRF, but not in WT+CRF mice.

Conclusions: Apolipoprotein E deficiency is associated with increased bone mass. The latter is further stimulated by chronic renal failure, which in addition induced features of osteitis fibrosa. The uraemic EKO mouse model could be useful for future physiologic and pharmacologic studies of linking CRF vascular and bone disease.

MP407 THE ECHO STUDY: THE USE OF CINACALCET (MIMPARA®/SENSIPAR®) IN PATIENTS RECEIVING/NOT RECEIVING VITAMIN D IN CLINICAL PRACTICE

Neil Ashman[1], Denis Fouque[2], Ana Baños[3], Chris Harris[3], Stefan Jacobson[4]. *[1]The Royal London Hospital, London, United Kingdom; [2]Hôpital Edouard Herriott, Lyon, France; [3]Amgen Europe GmbH, Zug, Switzerland; [4]Danderyd Hospital, Stockholm, Sweden*

Introduction and Aims: The use of vitamin D analogues (vit D) to control SHPT in dialysis patients may be limited by the development of hypercalcemia and hyperphosphatemia. To determine the impact of cinacalcet on PTH, P, and Ca among dialysis patients receiving or not receiving vitamin D, we analyzed data from ECHO, a pan-European observational study.
Methods: ECHO is a multicentre, observational study designed to collect data from approximately 2000 European dialysis patients with SHPT. Patients received cinacalcet at baseline for up to 12 months. We explored differences among patients who remained on vit D from baseline throughout study (vit D group) versus those who never received vit D (no vit D group).
Results: A total of 1282 patients were included in this analysis (881 pts [vit D] vs 401 pts [no vit D]). In the vit D group, median percent change in iPTH was higher (-50%) than the no vit D group (-41%.) with no difference in median cinacalcet dose (60 mg/day) at month 12. There was no difference in Ca or CaxP between groups at month 12, although the decrease in median percent change P was greater in the no vit D group (-12%, vs -6% for vit D group). Most patients in the vit D group received oral calcitriol or alfacalcidol at month 12; mean (SD) dose was 2.5 (1.7) μg/week and 4.3 (3.9) μg/week, respectively. More patients in the vit D group (60%) were receiving sevelamer at month 12 than in the no vit D group (47%), a decrease of -7% and -15%, respectively, from baseline. Although the proportion of patients receiving calcium-based phosphate binders was similar at baseline (42% and 41%) there was a greater increase in use in the vit D group (+10%) than in the no vit D group (+4%). No differences in mortality at one year were observed between the vit D group and the no vit D group (deaths: 6.2% vs 5.8%, respectively).

Biochemical parameter	Patients who received vit D throughout study			Patients who never received vit D		
	Median (Q1, Q2)		Percent change from baseline	Median (Q1, Q2)		Percent change from baseline
	Baseline	Month 12		Baseline	Month 12	
PTH (pg/mL)	754 (511,1095)	344 (217, 573)	-50	647 (457, 974)	388 (228, 707)	-41
P (mg/dL)	5.6 (4.6, 6.8)	5.3 (4.3, 6.2)	-6	6.2 (5.0, 7.5)	5.9 (4.6, 7.1)	-12
Ca (mg/dL)	9.8 (9.2, 10.4)	9.2 (8.6, 9.8)	-6	9.5 (9.0, 10.2)	8.9 (8.3, 9.7)	-5

Conclusions: Cinacalcet can effectively control SHPT in dialysis patients regardless of vit D use. The use of vit D in conjunction with cinacalcet is associated with a more profound reduction in PTH, but lesser P reduction than in patients not receiving vit D. Further randomized studies are required to confirm these findings.
Disclosure: This study was sponsored by Amgen.

MP408 ULTRASONOGRAPHY IN THE PRE-SURGICAL ASSESSMENT OF SEVERE SECONDARY HYPERPARATHYROIDISM

Mario Meola[1], Ilaria Petrucci[1], Massimiliano Barsotti[2], Mariano Grosso[3], Claudio Traino[3], Marco Puccini[4], Giuliano Barsotti[1]. *[1]Department of Internal Medicine, University of Pisa, Pisa, Italy; [2]Department of Oncology and Transplant Surgery, University of Pisa, Pisa, Italy; [3]Regional Centre of Nuclear Medicine, University of Pisa, Pisa, Italy; [4]Department of General Surgery, University of Pisa, Pisa, Italy*

Introduction and Aims: High-resolution sonography (US) can be used to study the parathyroid glands of uraemic patients with severe secondary hyperparathyroidism (s-HPT). The aim of this study was to define the sensitivity, specificity, positive and negative predictive values and the accuracy of the technique with respect to histological examination of patients with s-HPT who had received parathyroidectomy.
Methods: We studied 40 consecutive patients (20 F, 20 M, aged 51±14 years) attending our nephrology unit prior to parathyroidectomy. 29 patients were on maintenance haemodialysis (MHD) and 11 were under conservative treatment (CT). Biochemical parameters were: serum i-PTH 1236±652 pg/mL, serum Ca 9.8±1.8 mg/dL, serum P 5.7±1.9 mg/dL, CaxP 56±23 mg^2/dL^2. At sonography, glands with at least two diameters >5 mm and a volume <500 mm^3 were considered to have diffuse hyperplasia, whereas nodules with a diameter >1 cm and a volume >500 mm^3 were considered to be glands with nodular degeneration. The glandular volume was calculated in mm^3 using the formula for the volume of an irregular ellipsoid. Total parathyroidectomy was carried out using the traditional technique. 5 patients underwent subtotal parathyroidectomy. The anatomic fragments were fixed in formalin and analyzed to confirm the histological type of glandular hyperplasia.
Results: 41 glands were removed from CT patients and 103 glands from the MHD patients. US detected 24 glands with a mean volume of 522±564 mm^3 (range 35–1863 mm^3) in CT patients, and 83 glands with a mean volume of 559±753 mm^3 (range 35–4432 mm^3) in MHD patients. The sensitivity, specificity and positive predictive value of US were 74.7%, 64.6% and 94.8%. US had 100% of sensitivity and specificity in localizing glands with volume >500 mm^3. Colour Doppler imaging did not change the sensitivity and specificity of US, but it gave some semiquantitative parameters of glandular hyperfunction such as evidence of a vascular pole and a ray-like distribution of endonodular circulation.
Conclusions: US was able to identify glands of various sizes. For this reason, its main role may be the morphological monitoring of the progression of s-HPT rather than pre-surgical localization of hypertrophic glands.
Disclosure: Support for editing was provided by Amgen.

MP409 CINACALCET REDUCED GLANDULAR VOLUME IN PATIENTS WITH SHPT

Mario Meola, Ilaria Petrucci, Giuliano Barsotti. *Department of Internal Medicine, University of Pisa, Pisa, Italy*

Introduction and Aims: Secondary hyperparathyroidism (SHPT) is a progressive disease characterized by hyperplasia of the parathyroid glands. Preclinical studies show that calcimimetics prevent parathyroid gland hyperplasia in rodent models of chronic kidney disease (CKD). The aim of this study was to explore the effect of cinacalcet on parathyroid gland size in dialysis patients.
Methods: 8 haemodialysis patients were included with severe and uncontrolled SHPT. Patients couldn't undergo parathyroidectomy for clinical contraindications. Cinacalcet was administered with traditional therapies in an attempt to reach the KDOQI target ranges for PTH, P and Ca. Colour Doppler sonography was used to measure volumetric changes and semiquantitative parameters of glandular perfusion in the parathyroid glands against time.
Results: At baseline, 27 glands with solid and hypoechoic pattern were found. Mean volume was 720±908 mm^3. No complex anechoic areas were found, and they were all hypervascularized. After 2 years of follow-up, there was a significant decrease in mean iPTH (1273±381 pg/mL vs 268±99 pg/mL, $p < 0.0001$), mean phosphorus (5.5±1.3 mg/dL vs 4.4±0.9 mg/dL, $p = 0.05$) and mean CaxP (51.5±11 mg^2/dL^2 vs 40±7.8 mg^2/dL^2, $p = 0.03$). At the end of follow-up the number of hyperplastic glands did not vary but sonography revealed a decrease in glandular volume in 74% of cases. In addition, 44% of glands showed extensive complex anechoic areas, involving approximately 70-80% of their volume, suggestive of gland necrosis. 67% of glands became hypovascularised and 33% showed no vascular perfusion.
Conclusions: Cinacalcet improved biochemical parameters of SHPT, reduced parathyroid gland volume and reversed gland hypervascularisation in haemodialysis patients with severe SHPT. Long-term, randomized studies are warranted to confirm these findings.
Disclosure: Writing assistance was supported by Amgen.

MP410 THE ENDOGENOUS MODULATORS OF CA^{2+} TRANSPORTING ATP-ASE (PMCA) IN CHILDREN WITH CHRONIC KIDNEY DISEASE (CKD)

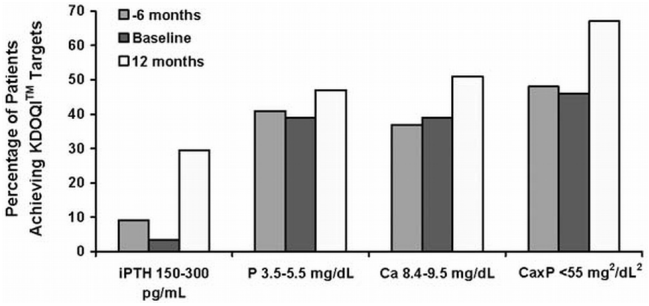
Dorota Polak-Jonkisz[1], Leszek Purzyc[2], Danuta Zwolinska[1], Krystyna Laszki-Szczachor[3]. *[1]Pediatric Nephrology, [2]Medical Biochemistry, [3]Pathophysiology, Medical University, Wroclaw, Poland*

Introduction and Aims: One of the disturbances associated with the development of CKD are changes in calcium-phosphate homeostasis, what manifests as an increase of free cytoplasmic calcium in erythrocytes [$Ca^{2+}{}_i$], which is regulated by the PMCA pomp. This pump's activity is directly modified by the "net" of mutually dependent on factors: proteinous and nonproteinous. *The aim of this study* was an assessment of endogenous protein modulators of PMCA (calmodulin and calpain-calpastatin system) in children with CKD relating to the different disease stages. The study was performed on 36 children with CKD, who were divided into 3 subgroups: I - 12 pts with CKD in III stage; II - 12 pts with CKD in IV stage; III - 12 treated with hemodialysis (study has been done before and after HD).The control group-consisted of 30 age and sex matched children.
Methods: The following parameters were determined in the serum: iPTH, P_i, Ca, urea, creatinine (cr); in red blood cells (RBC): free cytosolic calcium concentration (Ca_i^{2+}) and PMCA, bPMCA (basic PMCA), calmodulin (CALM), calpain (CANP), calpastatine (CAST).
Results: The results are presented in Table 1.
Conclusions: The increase of intracellular Ca_I^{2+} in children with progression chronic kidney disease is connected with decrease of activity of PMCA, what is probably the result of dysfunction the calpain-calpastatin system. This disturbances escalate with deteriorate kidney function and hemodialysis treatment is only partly normalizing it.

MP411 KDOQI™ TARGET ACHIEVEMENT IS IMPROVED WITH CINACALCET (MIMPARA[®]/SENSIPAR®) IN CLINICAL PRACTICE

Fabio Malberti[1], Heikki Saha[2], Ulrich Neyer[3], Ana Baños[4], Chris Harris[4], Miroslav Ryba[5]. *[1]AO Istituti Ospitalieri di Cremona, Cremona, Italy; [2]Tampere University Hospital, Tampere, Finland; [3]Landeskrankenhaus Feldkirch, Feldkirch, Austria; [4]Amgen Europe GmbH, Zug, Switzerland; [5]Krajska Nemocnice Liberec, Liberec, Czech Republic*

Introduction and Aims: In clinical studies, the calcimimetic cinacalcet simultaneously lowered parathyroid hormone (PTH) serum phosphorus (P) and calcium (Ca) in dialysis patients with SHPT [1,2]. ECHO is the first pan-European observational study to explore cinacalcet use in daily 'real-world' clinical practice.
Methods: ECHO is a multicentre, observational study designed to collect data from approximately 2000 European dialysis patients 6 months before initiating cinacalcet, at baseline (initiation of cinacalcet) and up to 12 months after cinacalcet. Relevant medical history, comorbidities, and laboratory data were collected via case report forms.
Results: A total of 1857 patients were included in this analysis; mean age±SD 58.1±15.0 years. 87% of patients were on haemodialysis. Patients generally had severely uncontrolled PTH (median=722pg/mL), P (median=5.9mg/dL) and Ca (median=9.7mg/dL) at baseline despite receiving standard care (vitamin D sterols [62% of patients] and phosphate binders [90% of patients]). The percentage of patients within KDOQI™ treatment targets (PTH, P, Ca and CaxP) increased from baseline to month 12 (+26%, +8%, +12% and +21%, respectively; figure). The median percent change in serum iPTH, P, Ca, and CaxP from baseline to month 12 was -49%, -8%, -6%, and -17%, respectively. A total of 61% and 66% of patients had ≥30% iPTH reduction from baseline at months 6 and 12 months, respectively. The median cinacalcet dose after 12 months was 60mg/day. In



general, vitamin D sterol use remained fairly stable throughout the study, but sevelamer use decreased by 14% and calcium-based phosphate binders increased by 7%. With regards to disease severity (</≥median), a higher proportion of patients achieved targets for PTH in the <722pg/mL group (n=909) by month 12 vs the ≥722pg/mL group [n=910] (38% vs 22%, respectively) whereas for CaxP the proportion of patients was comparable between groups.
Conclusions: Following cinacalcet, a higher percentage of patients achieved treatment targets for iPTH, P, Ca, and CaxP by month 12. The effectiveness of cinacalcet in clinical practice is consistent with findings from randomized, phase III clinical trials. Cinacalcet represents a significant advance in the treatment of SHPT.
References: 1. Block GA, et al. N Engl J Med 2004;350:1516-25.
2. Lindberg JS, et al. J Am Soc Nephrol 2005;16:800-7.
Disclosure: This study was sponsored by Amgen.

MP412 ARE CALCIFICATIONS UNDERDIAGNOSED IN EUROPEAN HAEMODIALYSIS PATIENTS? RESULTS FROM COSMOS

A. Ferreira[2], J.L. Fernández-Martín[1,2], P.R. Daffra[1,2], J. Floege[2], M. Ketteler[2], G. London[2], F. Locatelli[2], J.L. Gorriz[2], B. Rutkowski[2], V. Teplan[2], A. Covic[2], R. Kramar[2], J. Nagy[2], W.J. Bos[2], C. Tielemans[2], D. Verbeelen[2], D. Pavlovic[2], P.Y. Martin[2], Rudolf P. Wüthrich[2], M. Benedik[2], D. Goldsmith[2], D. Memos[2], J.B. Cannata-Andia[1,2], COSMOS Group. *[1]Bone and Mineral Research Unit. Instituto Reina Sofía de Investigación, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain; [2]COSMOS Group*

Introduction and Aims: In the past, the bone X-ray profile was used as a complimentary tool in the diagnosis of renal osteodystrophy; however, nowadays it plays mainly a role in the detection and evolution of calcifications. Currently there are no standardised procedures to investigate calcifications in haemodialysis patients.
The aim of the present study was to compare the reported prevalence of calcifications in the dialysis sites performing bone X-ray profile routinely versus sites not performing X-ray routinely in centres participating in COSMOS (Current Management of Secondary Hyperparathyroidism: A Multicentre Observational Study).
Methods: COSMOS is a prospective, pan-European, observational cohort study of haemodialysis patients, 18+ years of age. A representative sample of facilities and patients was identified using a stratified, random selection process. Approximately 5,900 patients in 21 countries were selected and will be followed for up to 3 years. At enrolment; site investigators entered detailed patient information including demographic data, medical history (including calcifications), and treatment data. Moreover, each site had to complete a form containing 21 questions related to the clinical management of secondary hyperparathyroidism including practice patterns such as the current use of bone X-ray profiles.

Abstract MP410 – Table 1

Parameters/Groups	PMCA [umol/Pi/mg/min]	bPMCA [umol/Pi/mg/min]	CAST [U/mg]	CANP [U/mg]	Cai2+ [nmol/L]	CALM [mg/l]
III	1,68±0,25	1,00±0,14	61,65±4,77a	55,90±5,75	138,20±1,99 a	2,63±0,29
IV	1,41±0,11	0,95±0,13	76,19±7,21	30,59±3,98	141,92±1,65	3,58 ±0.28
bHD	1,14±0,23	0,85±0,18	66,47±7,25	28,71±2,02	152,33±15,28	2,99±0,15
aHD	2,55±0,49	1,06±0,13	28,48±5,09	77,57±6,46	49,64±6,10	3,25±0,35
Control	3,13±0,20	1,84±0,15	18,09±2,07	44,12±4,23	26,77±1,44	4,54±0,301

Results: In this report, baseline data from 4135 patients (70.1% of expected sample) from 214 sites are presented. Overall, calcifications were reported in 42.5% of patients, vascular calcifications in 35.0%, valvular calcifications in 14.9%, soft tissue calcifications in 3.4% and calciphylaxis in 0.7%. It is important to stress that more than half of the dialysis sites (65.4%) do not perform bone X-ray profiles routinely. In fact, when the centres performing bone X-ray profiles routinely were analysed, the percentage of patients with calcifications was 52.8%, whereas in centres not performing bone X-rays routinely it was 37.2% ($p<0.000001$). Vascular and soft tissue calcification were reported also as less frequent in patients from sites not performing bone X-rays routinely (29.8% vs 45.0% and 2.1% vs 5.9% respectively, $p<0.0001$).
Conclusions: In summary, the baseline prevalence of calcifications was lower in centres not performing bone X-rays routinely. The lack of common and feasible protocols to investigate calcifications seems to be the main cause of the underdiagnosis of calcification.
Study supported by Amgen and Fundación Renal Iñigo Alvarez de Toledo.
Disclosure: Study supported by Amgen and Fundacion Renal Inigo Alvarez de Toledo.

Metabolic and other complications of ESRD 2

MP413 UREMIC PRURITUS IN END STAGE RENAL DISEASE (ESRD) PATIENTS

Toshiro Kamata, Hiroe Kamata, Kiyohide Fushimi. *Nishishinbashi Internal and Urological Clinic, Tokyo, Japan; Nishishinbashi Internal and Urological Clinic, Tokyo, Japan; Health Care Informatics, Tokyo Medical and Dental University, Graduate School of Medicine, Tokyo, Japan*

Introduction and Aims: Uremic pruritus is one of the most important and characteristic symptoms in End Stage Renal Disease (ESRD) patients. Past studies say 50-80% of ESRD patients complain of their itching. Some therapy has been suggested for pruritus, but the mechanism of pruritus in ESRD patients is still well unknown. In this study, we aimed to assess the relationships between the clinical symptom, laboratory findings, ordinary disease of ESRD patients etc. and uremic pruitus.
Methods: 118 ESRD patients (an average age was 61.57 ± 8.5 and an average duration of hemodialysis was 6.8 ± 3.8 years) underwent in this study. All of them were undergoing hemodialysis. All patients answered some questions about the assessment of their pruritus (localization, frequency, intensity etc.). Their own condition (gender, age, the duration of hemodialysis etc.) and laboratory findings (calcium, phosphate, intact PTH, blood urea nitrogen (BUN), creatinine, hemoglobin, hematocrit etc.) were investigated. Including some conditions in hemodialysis (erythropoietin, dialyzer, etc), we investigated whether correlation was found between their uremic pruritus and their physical condition, laboratory findings etc.
Results: 103 ESRD patients (87.3%) had experienced pruitus, and 98 ESRD patients (83.0%) complained their present pruritus. 70% of patients with pruitus complained of itching once or more a day and 40% of them complained of sleep disturbance. About laboratory findings, hypercalcemia ($Ca\geq9.8$mg/dl), hyperphosphatemia ($P\geq5.5$mg/dl), hyperparathyroidism (intact $PTH\geq360$pg/ml) and severe anemia ($Ht<21\%$) were considered as risk factors for uremic pruritus. The group which were used erythropoietin over 6,000IU per week complained their itching compared with another group. About their own condition or ordinary disease, male, old generation (over 50 years old), a long duration of dialysis (over 10 years) and diabete mallitus (DM) were recognized as a high risk for uremic pruritus. Other ordinary diseases except DM, some laboratory findings (natrium, blood urea nitrogen (BUN), creatinine etc.), dialysis time and the types of dialyzer membrane had no relationships with the severity of pruritus.
Conclusions: Gender, age, duration of hemodialysis, serum levels of calcium, pottasium, intact PTH (secondary hyperparathyroidism), and amount of erythropoietin had significant relationships with the serious uremic pruritus.

MP414 SERTRALINE USE FOR DEPRESSION CAUSES SEROTONIN SYNDROME IN MAINTENANCE DIALYSIS PATIENTS

Gulshan Kumar Mukhiya. *Department of Nephrology, Himalyan Institute Hospital Trust, Dehradun, Uttarakhand, India*

Introduction and Aims: Depression is common in end stage kidney disease (ESKD) patients on maintenance dialysis (MHD). Sertraline, a selective serotonin reuptake inhibitor (SSRI), has been found to be an effective therapy for depression. Our study aims to study the effect of Sertraline for the treatment of depression in ESKD patients on MHD.
Methods: We enrolled 12 ESKD patients on MHD for more than 3 months, who had moderate to severe depression (Goldberg's depression scale > 35). Sertraline was prescribed at a dose of 25mg/day. All patients had stable blood pressure $<150/90$mmHg with antihiypertensive medications and no evidence of overt heart disease at the start of therapy. All patients were clinically examined for the occurence of serotonin syndrome symptoms and signs on their scheduled dialysis days during Sertraline therapy.
Results: The age of enrolled patients ranged from 30 to 83 years. Half of them were males. In 11 patients, Sertraline was discontinued within 3 weeks as all of them developed symptoms related to hyperserotonin state. 7 patients (58.3%) complained of restlessness and became anxious and agitated. 5 patients (41.7%) developed myoclonic jerks whereas 3 patients (25%) complained of diarrhoea. 4 patients (33.3%) developed severe hypertension requiring an increase in antihypertensive drugs. 2 patients (16.7%) had hypotension following Sertraline and one of them, who developed severe serotonin syndrome developed intermittent atrial fibrillation. She presented to emergency with loss of consciousness preceded by agitation, tremors and myoclonic jerks of limbs. She was treated in intensive care unit. She recovered fully in 3 days after Seratonin withdrawl and supportive care.
Conclusions: Sertraline, an SSRI, at a dose of 25mg/day was not tolerated in majority of our patients. In one of patients, it produced life-threatening fatal serotonin syndrome. Serotonin syndrome has protean manifestations and unless clinical suspision is high, it can be missed.

MP415 LONG-TERM RETENTION OF GADOLINIUM IN THE SKIN OF RODENTS FOLLOWING THE ADMINISTRATION OF GADOLINIUM BASED CONTRAST AGENTS

Martin Sieber[1], Philipp Lengsfeld[2], Thomas Frenzel[1], Joachim Huetter[1], Hubertus Pietsch[1]. [1]*Contrast Media Research, Bayer Schering Pharma AG, Berlin, Germany;* [2]*Global Medical Affairs, Bayer Schering Pharma AG, Berlin, Germany*

Introduction and Aims: Nephrogenic systemic fibrosis (NSF) is an acquired, idiopathic disorder observed only in patients with severe renal dysfunction. The cuteneous findings in NSF patients are characterized by skin thickening, fibrosis, increase in cellularity, infiltration of CD34+ cells and increase in collagen bundles. Recently, several publications suggested a relationship between the administration of Gd -based CA (predominantly Gadodiamide (Omniscan®)) and the occurrence of NSF.
The aim of the study was to evaluate the possible long-term retention of Gadolinium (Gd) in the skin of rodents following administration of different GBCAs.
Methods: Gd-concentration in the skin was measured after application of linear non-ionic (Omniscan® and OptiMARK®); linear ionic (Magnevist®); macro-cyclic GBCAs (Gadovist®, ProHance® and Dotarem®) in Han-Wistar rats. The GBCAs were injected *i.v.* once daily at a dose of 2.5 mmol Gd/kg for 5 consecutive days. The Gd-concentration in skin biopsies was determined at various time points (up to 250 days *p.i.*) by ICP-MS.
Results: Regarding the Gd-concentration in the skin, we observed statically significant differences between the different GBCAs classes. For linear non-ionic compounds, accumulation during the injection period (5 days) and high Gd-concentration were maintained over time in the skin (up to 250 days). For the linear ionic compounds, a relatively lower Gd retention was observed over time in the skin. Beginning 40 days after the last injection, the Gd values in the skin observed after application of all macro-cyclic compounds were in the same range as observed in saline treated and in untreated animals.
Conclusions: We observed a correlation between the complex stability of GBCAs and the amount of residual Gd in the skin up to several months

after application of GBCAs. No long-term retention of Gd in the skin could be detected after application of macro-cyclic GBCAs.
Disclosure: All authors are employees of Bayer Schering Pharma AG.

MP416 THE EFFECTS OF DARBEPOETIN ALFA AND EPOETIN BETA ON OXIDATIVE STRESS IN CHRONIC HAEMODIALYSIS PATIENTS

Peter Monostori[1], Zsuzsanna Hracsko[2], Timea Boros[1], Eva Kiss[1], Eszter Karg[1], Ilona S. Varga[2], Ibolya Haszon[1], Viktoria Sumegi[1], Csaba Bereczki[1], Sandor Turi[1]. *[1]Department of Paediatrics, University of Szeged, Szeged, Hungary; [2]Department of Biochemistry and Molecular Biology, University of Szeged, Szeged, Hungary*

Introduction and Aims: The effects of the darbepoetin alfa (DA) and epoetin beta (EB) administration on various oxidative stress parameters were evaluated in a 12-week follow-up in hemodialysis (HD) patients.
Methods: The antecedent erythropoietin (EPO) treatment of 21 HD patients was suspended for 14 days. After that, 11 patients received EB two times a week and 10 patients DA once weekly, in identical weekly doses. Concentrations of the whole blood oxidized and reduced glutathione (GSSG, GSH) and erythrocyte malondialdehyde (E-MDA) and the activities of the erythrocyte superoxide dismutase (E-SOD), catalase (E-CAT), glutathione peroxidase (E-Glut-Px) and glutathione reductase (E-Glut-Red) were determined before the 14-day interval and also at weeks 0, 4, 8 and 12.
Results: In both study groups, the ratios GSSG/GSH and the E-MDA levels were increased at week 4 (all $p<0.05$ *vs.* the baseline) and returned to their baseline levels at week 12. The activity of E-SOD was decreased at week 4 in both groups ($p<0.05$ *vs.* the baseline) with a subsequent return to the baseline. As compared with its baseline level, the E-CAT activity was decreased at week 4 ($p<0.05$) and was increased at week 12 ($p<0.05$) in both groups. During the 12-week follow-up, the activity of E-Glut-Red decreased significantly ($p<0.05$) in both groups.
Conclusions: In terms of oxidative stress, the tendencies observed with DA and EB were similar, and were identical to those found in our previous study with epoetin alfa. In parallel with the increase of the ratio GSSG/GSH at week 4, the degree of the lipid peroxidation (as shown by the level of E-MDA) was also increased and the activities of E-SOD and E-CAT were decreased. All parameters returned to the baseline at the end of the 12-week follow-up. In summary, the early phase of both the DA and EB administration is accompanied by characteristic time-dependent changes in the oxidative indices in HD patients.

MP417 TWICE A WEEK HEMODIALYSIS – A SUB OPTIMAL MODALITY OF MAINTENANCE HEMODIALYSIS

Vishal Saxena, Sanjeev Gulati, Salil Jain, Saurabh Pokhariyal, Manisha Majumdar, Vijay Kher. *Nephrology, Fortis Institute of Nephrology and Transplant, New Delhi, Delhi, India*

Introduction and Aims: In a developing country like India where majority of CKD patient's on hemodialysis are self-funded, the frequency of hemodialysis has always been a point of debate. When the developed world is looking at daily dialysis, we Indians are still struggling with twice vs. thrice a week hemodialysis protocol.
Aim: To look at the difference in the patient characteristics between patients on twice a week vs. thrice a week hemodialysis.
Methods: The study included 59 patients consisting of 37 (63%) males and 22 (37%) females. The average age of patients was 65.3 years (range 19years to 79 years). Patient's who underwent minimum of four weeks of hemodialysis at our center were included. The median follow up was 153.5 days. Each hemodialysis session was of four-hour duration. Of the 59 patients, 42 (71%) patients were on thrice a week hemodialysis (Group B) and 17 (29%) were on twice a week (Group A) protocol. Hematological and biochemical parameters were monitored monthly and as & when clinically indicated. Intact PTH levels were done every 3 monthly. Co morbidities like malnutrition, coronary artery disease, cerebrovascular accidents, hyepr parathyroudism, hypertension were included and their scoring was done. Diabetes was not included. Table 1 summarizes our findings.
Results: There was no significant difference between the two groups when means of hemoglobin, TSAT, cumulative iron dose, EPO dose and intact PTH levels were compared.Dialysis dose (weekly Kt/V) in Group B was significantly higher as compared to Group A. There was significantly lower mortality in Group B despite lower mean serum albumin & higher co morbidity score, when compared to Group A.
Conclusions: Our study reveals that higher dialysis dose in thrice a week HD patients, results in significantly better survival as compared to patients on twice a week hemodialysis.

Table 1

Parameters	Group A (2/wk)	Group B (3/wk)	P value
WeekltKt/V	2.3	4.02	p<0.05
Albumin	3.24	2.93	p<0.05
Co morbidities	10	33	p<0.05
Mortality	4 (23.5%)	3 (7%)	p<0.05

MP418 INCREASED S-ADENOSYLHOMOCYSTEINE (SAH) CONCENTRATIONS AND DNA HYPOMETHYLATION IN CHRONIC KIDNEY DISEASE (CKD)

Alessandro Valli[1,2], Bjorn Anderstam[1], Mohamed Suliman[1], Abdul Rashid Qureshi[1], Tomas Ekstrom[3], Mohsen Karimi[3], Garibotto Giacomo[2], Juan Jesus Carrero[1], Jonas Axelsson[1], Peter Barany[1], Olof Heimburger[1], Bengt Lindholm[1], Peter Stenvinkel[1]. *[1]Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden; [2]Department of Internal Medicine, Nephrology Division, University of Medicine, Genoa, Italy; [3]Department of Molecular Medicine, Karolinska Institutet, Stockholm, Sweden*

Introduction and Aims: In chronic kidney disease (CKD) patients, the uremic milieu which typically includes inflammation and hyperhomocysteinemia may conceivably have an impact on epigenetic factors such as the degree of methylation of DNA. DNA hypomethylation induced by increases in S-adenosylhomocysteine (SAH) levels could be involved in homocysteine-related pathology. SAH is a powerful competitive inhibitor of S-adenosylmethionine-dependent methyltransferases, and it increases in CKD patients, suggesting an unbalanced methylation pathway metabolism. The aim of this study was to investigate whether DNA hypomethylation occurs in CKD patients and how the renal function could affect the trans-pathway.
Methods: The study included: 69 CKD stage 5 pts (56% males;) with median glomerular filtration rate (GFR) 6.0 (range 0.8-10.8) ml/min and median age 59 (25-70) years; 37 CKD stage 3-4 pts (78% males) with GFR 36 (15-52) ml/min and age 61 (27-80) years and 32 healthy subjects. Concentrations of S-adenosylmethionine (SAM), SAH and total homocysteine (tHcy) were determined using reversed phase HPLC coupled with fluorescence detector and global DNA methylation in peripheral blood leucocytes by Luminometric Methylation Assay (LUMA) yielding the ratio HpaII/EcoR1 where a high value denotes hypomethylation.
Results: Circulating serum levels of SAM and SAH were significantly increased in CKD 3-4 and CKD 5 groups compared with the controls ($P<0.001$). Whereas the SAM/SAH ratio was decreased in both the CKD 3-4 ($P<0.001$) and CKD 5 ($P<0.001$) patients, SAM and SAH levels were significantly higher in CKD 5 than in the CKD 3-4 patients ($P<0.001$). SAH was correlated with GFR in both groups CKD 3-4 and 5 (rho=-0.82; $P<0.001$, rho=-0.42; $P<0.001$, respectively). The concentrations of SAH were correlated with tHcy levels in CKD 3-4 ($P<0.01$; rho 0.47) and CKD 5 ($P<0.05$; rho 0.25) patients and with HpaII/EcoR1 in CKD stage 3-4 ($P<0.05$; rho 0.33) and CKD stage 5 ($P<0.05$; rho 0.28) patients.
Conclusions: The present study suggests that the increased concentration of the trans-methylation cycle intermediates SAH and SAM are related to the level of renal function. Furthermore, the decreased SAM/SAH ratio indicates that the trans-methylation pathway is unbalanced in CKD stage 3-5 patients. Finally, the positive association between SAH and HpaII/EcoR1 demonstrates that high levels of SAH are associated with DNA hypomethylation in CKD pts which may counterbalance the effects of inflammation induced hypermethylation.
Disclosure: B.L. is an employee of Baxter Healthcare Inc., Deerfield, IL, USA. The other authors do not declare other conflicts of interest.

MP419 THE EFFECT OF ON-LINE HEMODIAFILTRATION ON HEART RATE VARIABILITY IN END-STAGE RENAL DISEASE: 2-YEAR PROSPECTIVE STUDY

Soo-young Yoon[1], Sang Cheol Lee[1], Tae Woon Park[1], Sung Ja Yang[2]. *[1]Internal Medicine, College of Medicine, Kwandong University, Goyang, Republic of Korea; [2]Dialysis Room, Myongji Hospital, Goyang, Republic of Korea*

Introduction and Aims: The autonomic nervous system plays a central role in the maintenance of hemodynamic stability. Cardiac autonomic dysfunction may result in serious complications, such as sudden cardiac death. Heart rate variability (HRV) is significantly reduced in patients undergoing chronic hemodialysis, even in the absence of cardiovascular disease. The adequacy of hemodialysis is a predictor of improvement of cardiac autonomic nervous function in chronic uremia.
The aim of this study is to evaluate the effect of on-line HDF on autonomic nervous system in chronic hemodialysis patients.
Methods: We prospectively studied 11 chronic hemodialysis patients. Participants were 55% male, aged 56.5±16.0 (31-80) years, 18% diabetic, with 3-120 months of dialysis, and on high-flux hemodialysis thrice a week. We analyzed time-and frequency-domain measures of 24-h HRV during inter-dialytic period before post-dilution on-line HDF and thereafter six monthly for 24 months. Also, blood samples were drawn for routine laboratory assessments including hemoglobin, BUN, creatinine, calcium, phosphate, albumin, total cholesterol, triglyceride, uric acid, cystatin C, high sensitivity C-reactive protein (hsCRP), intact parathyroid hormone (i-PTH), and β_2-microglobulin (β_2-MG).
Results: After 24 months of on-line HDF, hemoglobin (8.8±1.5 to 10.9±1.2g/dl, $p<0.05$), albumin (3.5±0.3 to 3.7±0.3g/dl, $p<0.05$), and HDL cholesterol increased (28.3±3.8 to 33.2±7.6mg/dl, $p<0.05$). Triglyceride (185.7±105.6 to 119.0±17.8mg/dl, $p<0.05$) and β_2-MG decreased (42.1±10.5 to 25.3±3.5mg/l, $p<0.05$). And frequency-domain HRV parameters increased significantly compared with baseline (HF, 49.8±19.3 vs. 3.5±3.9 ms^2; LF, 95.5±34.2 vs. 20.7±7.7 ms^2; VLF, 558.5±50.3 vs. 75.4±79.9 ms^2; and LF/HF, 2.76±1.52 vs. 1.55±0.58 ms^2).

Changes of HRV parameters

	Baseline	12 months	24 months	p-value
Time-domain measures				
Mean NN (ms)	818.4±171.2	842.5±136.7	835.1±116.3	NS
SDNN (ms)	98.6±29.8	94.8±30.3	96.2±28.2	NS
Frequency-domain measures				
HF power (ms^2)	3.5±3.9	39.4±17.3	49.8±19.3	<0.05
LF power (ms^2)	20.7±7.7	82.6±44.5	95.5±34.2	<0.05
VLF power (ms^2)	75.4±79.9	429.5±80.3	558.5±50.3	<0.05
LF/HF (ms^2)	1.55±0.58	2.54±1.60	2.76±1.52	<0.05

NN, normal-to-normal R-R intervals; SDNN, the standard deviation of normal-to-normal R-R intervals during 24 h; HF, high frequency; LF, low frequency; VLF, very-low frequency; NS, not significant.

Conclusions: This study shows that on-line HDF can improve autonomic nervous system dysfunction in chronic hemodialysis patients.

MP420 RELATIONSHIP BEWEEN PLASMA LEVELS OF NITRIC OXIDE AND BLOOD PRESSURE IN HEMODIALYSIS PATIENTS

Monika Katko[1], Istvan Karpati[1], Laszlo Ujhelyi[1], Janos Matyus[1], Eva Csongradi[2], Gyorgy Paragh[2], Jozsef Balla[1], Zsuzsa Varga[1]. *[1]Division of Nephrology, Ist. Dept. of Medicine, [2]Division of Metabolism, Health and Medical Science Center University of Debrecen, Debrecen, Hungary*

Introduction and Aims: In regulation of blood pressure several vasoactive compounds play role. Nitric oxide (NO) is known as the most important vasodilator and endothelin-1 (ET-1) as a vasoconstrictor molecule. In non-kidney failure hypertensive patients decreased NO was observed. In hemodialysis (HD) patients contradictory results have been found considering relationship between NO levels and blood pressure. Therefore, we determined NO and ET-1 levels in 80 HD patients and 80 non-kidney failure patients (with the same ratio of hypertensive than in HD group) and relationship with systolic and diastolic blood pressure were analyzed.
Methods: NO was determined from the pretein free plasma using Griess reagent and ET-1 with commercially available kit (Biomedica, Wien, Austria).
Results: It was found that in hypertensive HD patients NO and CRP levels were significantly elevated, they had lower Hgb and Htc values than in normotensive HD patients or in controls. Results of correlation analysis showed that NO concentration was positively associated with systolic blood pressure (BPsys) ($r=0.456$, $p<0.01$) and negatively with Htc ($r=-0.3512$, $p<0.01$) values and was not related to ET-1 levels in HD patients. In contrast in non-kidney failure controls NO correlated negatively with BPsys ($r=-0.2849$, $p<0.04$), BPdias ($r=-0.3$, $p<0.04$) and ET-1 ($r=-0.376$, $p<0.01$) levels. BPsys of HD patients showed positive relationship with CRP ($r=0.336$, $p<0.02$) and rHuEPO dose ($r=263$, $p<0.05$), and negative with Hgb ($r=-0.376$, $p<0.02$) and Htc ($r=-0.42$, $p<0.001$) values. In case of non-kidney failre patients BPsys related to positively with ET-1 ($r=0.312$, $p<0.02$), serum cholesterol ($r=0.312$, $p<0.02$) levels, and BMI ($r=0.349$, $p<0.01$) values, and negatively with HDL-C ($r=-0.542$, $p<0.001$). rHuEPO dose was significantly higher in those HD patients who had Bpsys>140 Hgmm (28000 U/m), as BPsys<140 Hgmm (16000 U/m).
Conclusions: In conclusion, in hypertensive HD patients the elevated NO levels might be a part of a compensation mechanism showing endothel dysfuntion. This endothel dysfuction became more severe in anemia and microinflammation, and might relate to rHuEPO resistance.
Disclosure: The research was sponsored by Found of Hungarian Academy and (OTKA T 48596) and Hungarian Society of Nephrology.

MP421 THE EFFECT OF GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR ON IMMUNOLOGIC RESPONSE TO HEPATITIS B VACCINE IN CHRONIC HEMODIALYSIS PATIENTS

Farin Rashid Farokhi[1], Abdolrahim Khorasani[2], Jamileh Atapour[2], Fatemeh Dabiri[2], Sarah Shafii[2]. *[1]Nephrology, Shaheed Beheshti University of Medical Sciences, Tehran, Iran; [2]Internal Medicine, Kerman University of Medical Scinces, Kerman, Iran*

Introduction and Aims: Chronic hemodialysis patients are at increased risk of acquiring Hepatitis B virus (HBV) infection. So it is the main target of vaccination in them. Unfortunately, response rate to HBV vaccine in hemodialysis patients is lower than normal population due to immunosuppression of uremia, malnutrition or other causes. Use of adjuvant is one of the methods suggested to improve immune response to vaccine. Although documents are not sufficient for routine administration. In this study the effect of Granulocyte Macrophage Colony Stimulating Factor as an adjuvant for HBV vaccine in chronic hemodialysis patients has been evaluated.
Methods: Forty seven patients who completed the study were entered. They were referred to hemodialysis unit for initiation of chronic renal replacement therapy. These patients were clinically stable and HBS Ag negative with mean age of 51±14.2 and no previous history of HBV vaccination. They divided in two groups. There was no difference in age and sex distribution, mean body weight, the frequency of cigarette smoking and dialysis adequacy (KT/V) between two groups. The first dose of HBV vaccine, 40 microgram injected by intradeltoid route, was administrated in both groups. A dose of 4-5 micro/kg subcutaneous GMCSF were administrated 24 hours before vaccination in group 1 (23 patients) and distilled water was injected in group 2 as placebo. Second and third injections of vaccine were done after one and six months. HBS Ab titer, which was detected one month after first and last dose of vaccine, was compared between two group. SPSS software was used for statistical evaluation.
Results: HBV vaccine response rate (HBS ab titer> 10 miliIU/cc) was 38.4% and 63% in group 1 and 57.6% and 65% in group two in one month after first and last dose of vaccine, respectively. The difference between two group was significant in first month after vaccination, P value<0.05. Although there was not significant difference in response rate of two groups one month after last dose which was 7 months after first dose, the mean antibody titer was significantly higher in patients who recived GMCSF, 60±46.9 compared with 30.94±35.52, P<0.05.
Conclusions: So GMCSF can be effective in improvement of immune response to HBV vaccine but cost effectiveness of this method should be evaluated by other studies especially with considering low incidence of HBV infection in dialysis population by the wide use of infection control measures.

Disclosure: This study was supported by Research Center of Kerman University of Medical Sciences.

MP422 BETA-TRACE PROTEIN IS A MARKER OF RESIDUAL RENAL FUNCTION IN PATIENTS ON MAINTENANCE HAEMODIALYSIS

Karl August Brensing[1], Uwe Pöge[1], Thomas Gerhardt[2], Peter Raab[1], Birgit Stoffel-Wagner[3], Rainer Woitas[2]. *[1]Dialysis Unit, Nephrology & Dialysis Center Bonn, Bonn; [2]Dept. of Internal Medicine, [3]Dept. of Clinical Biochemistry, University of Bonn, Bonn, Germany*

Introduction and Aims: Beta-trace protein (BTP) has been proposed as an endogenous marker of the glomerular filtration rate that is virtually not affected by haemodialysis. Recently we proposed residual renal function (RRF) as the main contributor of BTP concentrations in dialysis patients. Consequently, we investigated the diagnostic performance of BTP for prediction of RRF measured by combined creatinine and urea clearance ($Cl_{residual}$).

Methods: BTP serum concentrations were determined by fully automated latex-enhanced immunonephelometric technique on a Behring Nephelometer II (Dade Behring, upper normal limit 0.74 mg/l). Interdialytic 24 hour urine sampling was used to calculate combined creatinine and urea clearance. Serum levels of BTP, creatinine and urea were analyzed before dialysis treatment in 129 patients of whom 47 patients were female. Overall, mean age was 64.5±12.7 (SD) years.

Results: Median urine volume, $Cl_{residual}$, BTP and creatinine were 260 (range: 0-3100) ml/day, 0.49 (range: 0-13.2) ml/min/1.73m^2, 10.0 (range: 2.9-25.1) mg/l and 9.0 (range: 3.0-15.8) mg/dl, respectively. $Cl_{residual}$ was subdivided into the following groups: 35.6% of patients without any diuresis (RRF=0) and 26.4, 16.3, 8.5, 8.5, 4.7% had a RRF between >0-2, 2-4, 4-6, 6-8 and above 8 ml/min/1.73m^2. The mean correspondending BTP and creatinine values were 13.2, 12.4, 7.5, 7.0, 5.5 and 6.0 mg/l and 11.0, 9.6, 7.6, 8.1 5.5, 6.5 mg/dl, respectively. Correlation of 1/BTP with $Cl_{residual}$ was significantly higher than correlation of 1/creatinine with $Cl_{residual}$ (r=0.78 vs. r=0.57, p=0.013). ROC analysis found highest AUC for BTP (0.97) with high sensitivity and specificity (97.1 and 83.1%, respectively, by using a BTP level of 8.0 mg/l) at a decision point of $Cl_{residual}$ =2ml/min/1.73m^2. The diagnostic performance of creatinine to detect low $Cl_{residual}$ was significantly inferior to BTP (AUC: 0.841; p<0.001 vs. BTP). Similar results with respect to sensitivity and specificity were found when ROC analyses were done by using urine volume as a marker of RRF (at a cut off of 300 ml/day sensitivity and specificity were 90.8 and 76.6%, respectively).

Conclusions: 1. BTP serum concentration is a marker of residual renal function in patients undergoing regular maintenance haemodialysis treatment. 2. In comparison to creatinine BTP offers a superior diagnostic performance to detect low or inexistent RRF. 3. BTP serum levels above 8 mg/l correspond to patients without clinically relevant RRF.

MP423 PERIOPERATIVE PROSTANOIDS ENHANCE CIRCULATING ENDOTHELIAL PROGENITOR CELLS MOBILIZATION IN HAEMODIALYSIS PATIENTS WITH SEVERE LIMB ISCHEMIA UNDERGOING PERIPHERAL REVASCULARIZATION

Giuseppe Coppolino, Davide Bolignano, Antoine Buemi, Antonio Lacquaniti, Michele Buemi. *Internal Medicine, University of Messina, Messina, Italy*

Introduction and Aims: The incidence of severe limb ischemia (SLI) is high among HD patients. Limb rescue rate after surgical revascularization is relatively poor compared with those with normal renal function. Prostanoids are an interesting category as adjuvant to revascularization. New vessels growth develops not exclusively by proliferation of endothelial cells in vascular extremities, but also by cells mobilized from the bone marrow (HSC), transformed into endothelial progenitor cells (EPC) contributing to both re endothelialization and neovascularization. Basal number of HSC and EPC is significantly reduced in HD patients and correlated with a subsequent defective neovascularization. We evaluated the effect of perioperative iloprost treatment on HSC and EPC in HD patients with SLI undergoing surgical revascularization. Vascular remodeling process was investigated through the amount of soluble adhesion molecules, markers of endothelial activation.

Methods: 30 HD patients with SLI undergoing peripheral revascularization were enrolled (20 treated with iloprost and 20 with placebo). Iloprost was administered as an intra-arterial bolus of 3000 ng over 1 to 3 minutes immediately after revascularization and in the same affected artery. Serum samples were taken before revascularization (T0), at 6 (T6) and 24 hours (T24) after infusion to measure sICAM-1, sE-selectin and sVCAM-1 and for quantification of HSC and EPC. Progenitors were identified by specific surface markers CD34+, CD133+ and VEGFR2+. Count was conducted using PROCOUNT™, performed in a TRUCOUNT™ tube and with a FACSort flow cytometer. Variance of groups was performed using a 1-way ANOVA followed by Fisher Test. Univariate correlations were made with Pearson coefficient.

Results: Before revascularization all patients showed a decreased number of HSC and EPC. After 6 hours, HSC augmented significantly respect to T0 in both groups. Iloprost group attained a significantly increase respect to placebo. HSC levels reduced drastically at T24. EPC augmented significantly respect to basal level after 24 hours. In iloprost group the increase was considerable respect to placebo group. A close negative correlation, assessed by Pearson coefficient (r), was found between HSC and EPC at T24 in iloprost group (R=0.82, P<0.01). Adhesion molecules had increased levels at T6 and T24 in both groups. Moreover, a close positive correlation, assessed by Pearson coefficient (r), was found between EPC and adhesion molecules in both groups but iloprost group maintained a better statistical association.

Conclusions: Revascularization stimulated HSC and EPC release from bone marrow but at different time: HSC suddenly at 6 hours and diminished to a minimal amount at T24, conversely, EPC increased significantly only at T24. This feature confirms that most HSC developed into EPC to promote neoangiogenesis. Iloprost treatment was able to amplify this mechanism validating recent findings (North TE, Nature 2007). Adhesion molecules as marker of endothelial activation and vascular development confirmed this tendency.

MP424 PENTRAXIN 3 (PTX3), A RAPID AND SENSITIVE MARKER OF INFLAMMATION INDUCED BY HEMODIALYSIS (HD)

Bodil Sjöberg, Björn Anderstam, Anders Alvestrand, Peter Bárány. *Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden*

Introduction and Aims: Patients (pts) with chronic kidney disease (CKD) often have elevated levels of inflammatory markers which together with several other non-traditional risk factors are thought to contribute to accelerated atherosclerosis and the exceedingly high mortality rate from cardiovascular disease (CVD). The HD procedure may induce inflammation and immune activation by e.g. blood-membrane interaction. The short pentraxin CRP, which is produced in the liver is the most studied inflammatory marker. The main inducer of CRP is interleukin-6 (IL-6). The long pentraxin PTX3 is produced by vascular endothelial cells and has been suggested as a novel diagnostic tool for CVD as it mainly reflects the inflammatory activity in the vasculature. Previous reports show that the concentration of PTX3 in plasma is increased in pts with CKD and that HD pts have the highest level of PTX3.

Methods: The aims of this study were to show how rapid and to what extent the plasma concentration of PTX3 increases during HD. Eleven stable HD patients with a mean age of 51.5±17 years were studied. Samples were taken at 0, 15, 30, 60 min, 2, 3 and 4 hours after start of HD treatment. PTX3

Increase of PTX3 during HD

Minute	PTX3 uncorrected	PTX3 corrected	SD (corr)	% change (corr)	p
0	7.5	7.5	4.2		
15	8.5	8.4	4.3	11	n.s.
30	9.3	9.0	4.5	20	<0.01
60	10.2	9.7	5.1	29	<0.01
120	11.1	10.0	5.1	34	<0.01
180	11.9	10.2	4.7	35	<0.01
240	12.7	10.4	4.7	38	<0.01

PTX3 values are presented with and without correction for UF. SD, % change and P-values are presented for corrected values. PTX3 is in pg/L.

was measured with a commercial ELISA (Perseus Preteomics Inc, Japan) and the concentrations during HD were corrected for the ultrafiltration.
Results: PTX3 concentrations increased in all patients during standard HD with low-flux filter. The increase is rapid and is significant 30 minutes after start of HD. The peak increase in concentration was median 54% [11-144%] after 180 min [30 to 240 minutes].
Conclusions: Compared to earlier observations of conventional markers, such as IL-6 and CRP, PTX3 appears to be a much more rapid and sensitive marker for studies of HD-induced acute inflammatory reactions. Analysis of plasma PTX3 during HD seems to be a sensitive tool to evaluate the inflammatory activity and its vascular effects in HD patients.

MP425 TOTAL MUSCLE CARNITINE CONTENT, EXERCISE CAPACITY AND CARDIOVASCULAR RESPONSE TO INTRAVENOUS L-CARNITINE SUPPLEMENTATION IN INCIDENT HAEMODIALYSIS PATIENTS

Paul Owen [1], Francis Stephens [3], William Priestman [1], Lindsay Chesterton [1], Christopher McIntyre [1,2]. *[1]Renal Medicine, Derby City General Hospital, Derby, United Kingdom; [2]School of Graduate Entry Medicine and Health, University of Nottingham, Derby, United Kingdom; [3]Centre for Integrated Systems Biology, University of Nottingham, Nottingham, United Kingdom*

Introduction and Aims: Progressively impaired exercise capacity and skeletal muscle carnitine deficiency are characteristics of prevalent haemodialysis (HD) patients. Such patients also have a vastly increased risk of cardiovascular disease. Lack of myocardial contractile reserve is an important determinant of the haemodynamic response to HD. Cardiac arrhythmias and myocardial dysfunction have been linked to secondary depletion of carnitine. The aim of this study was to determine whether intravenous supplementation of L-carnitine after each HD session could prevent the decline in muscle carnitine content and abbrogate the potential effects on exercise capacity and cardiovascular function in incident HD patients during their first year on dialysis.
Methods: Eight incident HD patients were recruited and randomised to receive either 10mg/kg L-carnitine iv or placebo following each HD session. On experimental visits before the first HD session and at 6 and 12 months after starting dialysis, muscle biopsy samples were obtained from vastus lateralis. These were analysed for total carnitine content (TC). In addition, an incremental shuttle walking test and isometric handgrip test were perfomed to assess exercise capacity. Cardiovascular function was assessed at the initial HD session and at 6 and 12 months using pulse wave analysis (Finometer). This non-invasive procedure involves continuous monitoring of digital arterial pressure and the full range of cardiovascular functional indices. The study groups were well matched for age and cause of end-stage-renal-disease.
Results: Muscle TC content remained stable in the treatment group (19.6 ± 1.3, 20.4 ± 1.4 and 20.3 ± 2.1 mmol·(kg dm)$^{-1}$ at 0, 6 and 12 months respectively), but declined in the placebo group by 15% at 6 months and 20% in one patient at 12 months. There were no differences in handgrip strength over the first year of HD in either group and no correlation between the change in muscle TC content and handgrip strength over 12 months. Total walking distance decreased in 2 control patients (by 30 and 60%) and 2 carnitine patients (by 20 and 40%) but increased in 2 carnitine patients (by 110 and 190%) at 12 months. There was a weak correlation between the change in muscle TC content and total walking distance over 12 months (r^2=0.73, p=0.06). No significant differences were observed between study groups over the twelve month period for the measured parameters: systolic and diastolic blood pressure, mean arterial pressure, stroke volume, cardiac output, total peripheral resistance and heart rate.
Conclusions: L-carnitine supplementation maintains muscle TC content in patients undergoing HD. The decrease in muscle carnitine content during the first 12 months of HD does not significantly affect muscle function nor does it provide any measurable benefit in cardiovascular function over this time period.

MP426 THE CORRELATION OF PREDIALYSIS iPTH WITH CHANGE IN PRE-POST SERUM CALCIUM IN PATIENTS HEMODIALYZED ON 1.25 MMOL/L DIALYSATE

Ciara Magee, Sinead Kinsella, Fiona Byrne, William D. Plant, Joseph A. Eustace. *Department of Nephrology, Cork University Hospital, Cork, Ireland*

Introduction and Aims: Low calcium dialysate (1.25 mmol/L) is associated with a negative intradialytic calcium balance in most HD patients (Sigrist et al J Ren Nutr 2006). We hypothesize that patients with low intact parathormone (iPTH) levels, who are more likely to have adynamic bone disease and, hence, decreased bone calcium fluxes, are predisposed to a greater decline in their serum calcium levels during dialysis.
Methods: We correlated (Spearman rank method,) pre-dialysis iPTH level, measured by first generation immunometric assay (Roche Elecsys®) with change in serum calcium (defined as post dialysis calcium minus the predialysis calcium) in 170 patients. The post dialysis value was measured using a standardized slow flow technique. Subjects were sampled on up to 5 separate occasions over a 1 year period. Change in serum calcium between groups were compared using the Mann Whitney U test. The association, significance and independence of Log (Ln) transformed iPTH with change in serum calcium was assesssed using linear regression. The model was adjusted for change in post minus pre serum albumin (as a measure of hemoconcentration during dialysis) and predialysis serum calcium level (a surrogate of serum-dialysate calcium gradient).
Results: 58% of subjects were male; 20% were diabetic; the mean (sd) age was 55.4 years (16.8); the median (Intra Quartile Range [IQR]) vintage was 3 years (1 - 5.75). The percentage of patients who had 1, 2, 3, 4, or 5 samples were 10%, 23%, 17%, 14% and 36% respectively. In each sample the iPTH was significantly correlated with change in serum calcium, mean (sem) correlation 0.34 (0.06), range (r=0.22, p= 0.02) to (r=0.56, p<0.001). In analyses using the most recent available result for each subject (n = 170), the median (IQR) iPTH was 267 ng/L (142-541), the mean (sd) predialysis calcium was 2.2 mmol/L (0.22), the median (IQR) change in post minus pre serum calcium was 0.01mmol/L (-0.1, 0.11), which was significantly correlated with the predialysis iPTH, r=0.22, p=0.02. The median (IQR) drop in serum calcium in patients with a predialysis iPTH <150 ng/L (n=45) was significantly greater than for those with a iPTH >300 ng/L (n=81): -0.04 mmol/L (-0.15, 0.07) vs. 0.06 mmol/L (-0.1, 0.18), p=0.02. On linear regression modeling, Ln (iPTH) was significantly and independently associated with change in serum calcium β =0.04, p= 0.001, adjusted for change in post minus pre serum albumin (β =0.02, p<0.001), and pre dialysis serum calcium (β = -0.50, p<0.001).
Conclusions: An iPTH < 150 ng/L is associated with a larger decline in serum calcium levels during dialysis, supporting the concept of decreased bone calcium fluxes in adynamic bone disease. Further investigations are warranted to examine whether the observed drop in serum calcium is associated with an increased frequency of intra-dialytic hypotension and whether this observation identifies a subgroup of patients at higher risk of vascular mineralization due to decreased bone calcium flux.

MP427 MALNUTRITION, INFLAMMATION, ATHEROSCLEROSIS AND CALCIFICATION (MIAC SYNDROME) NEGATIVELY INFLUENCE PERIPHERAL BLOOD FLOW DURING HEMODIALYSIS (HD)

Erik Mistrik [1], Sylvie Dusilova-Sulkova [1], Vladimir Blaha [1], Jiri Knizek [2], Lubos Sobotka [1]. *[1]Department of Gerontology, Nephrology and Metabolism, Charles University in Prague, Faculty Hospital and Medical Faculty in Hradec Kralove, Hradec Kralove, Czech Republic; [2]Department of Biophysics and Biostatistics, Charles University in Prague, Medical Faculty in Hradec Kralove, Hradec Kralove, Czech Republic*

Introduction and Aims: HD may induce perfusion changes due to blood volume decrease in response to ultrafiltration, but this phenomenon is not readily measurable. Disturbances of peripheral blood supply during HD may be underestimated (not recognized) contributing factor to ischemic complications in HD patients.
Methods: 31 patients (10 female, 21 male, 36-79 y, BMI= 28 ± 5.0) without any skin defects or apparent acute disease or infection were measured using Laser Doppler Line Scanner (LDLS®, Moor, Devon, UK) in 10

different areas of dorsum of each foot during HD with ultrafiltration (897±465 mL; mean loss of 1.4% preHD body weight, without hypotensive episode). The numbers of areas in lower and upper half with decreased, increased/not changed blood flow were compared using Fisher's exact test. The relation between skin blood flow change, nutrition (S-Albumin (S-Alb)); inflammation (C- reactive protein (CRP)) and calcium phosphate product (Ca x P) were evaluated using Spearman coefficient.
Results: Decrease of subcutaneous blood flow was apparent in 70% of evaluated areas.
The correlation of blood flow change was borderline with S-Alb (r=0.3, p=0.06). We found a significant correlation of mean Ca x P computed from 6 months preceding the measurement (r=-0.47, p=0.007) while it was only borderline (r=-0.34; p=0.06) if computed from three months measurements and there was no correlation if recent value was used (r=-0.27; p=0.15).
Similar results were obtained if the dorsal parts of hands were measured.

Number of areas with decrease/increase/no change compared according median based on:

	S-Alb 42 g/L	CRP 5 mg/L	Ca x P 5 mmol2/L2
Decrease (p)	<0.001	<0.001	<0.001
Increase/no change (p)	<0.001	<0.001	<0.001

Median served as cut-off value.

Conclusions: As serum albumin, CRP and calcium-phosphate product are considered markers of MIAC syndrome, we can suggest that MIAC syndrome negatively influences peripheral blood flow during HD with ultrafiltration.
Supported by research projects: MSM 0021620820, MSM 0021620819, IGA MH CR NR/9259-3.

MP428 PEDOMETERS AS A MEANS TO INCREASE PHYSICAL ACTIVITY IN CHRONIC HEMODIALYSIS PATIENTS

Katarzyna Murlikiewicz, Marta Augustyniak, Michal Nowicki. *Dept. Nephrology, Hypertension and Kidney Transplantation, Medical University, Lodz, Poland*

Introduction and Aims: Chronic hemodialysis patients are physically inactive and most of the interventions to promote physical activity in ESRD patients failed to show any sustained benefits due to poor compliance. In different non-CKD patient populations pedometers have been used to measure physical activity levels and as a means of increasing physical activity. We performed a study to examine whether pedometer use would lead to sustained (13-week) increases in physical activity in HD patients.
Methods: Thirty four chronic HD patients were included (17M and 17 F, age 58±10 yrs, HD vintage 5.1±5 yrs). All patients completed the self-reported physical activity questionnaires. They also received a pedometer and daily logbook to record their physical activities and a number of steps taken. Steps and daily activities were recorded at baseline and 3 months later at the end of the study each time constantly for 7 days between two mid-week dialyses (including a weekend activity). Between those recordings the same parameters were also recorded in two week intervals during 5 additional measurements between two mid-week dialyses in the same week. Additionally at baseline and at the final follow-up visit mean ESA dose, BMI, WHR were calculated and serum lipids, whole blood count, serum albumin and C-reactive protein were measured.
Results: We found a significant increase in self reported daily physical activity and in step counts. The number of steps taken daily by the patients during the weekdays increased constantly from visit to visit (from 2820±1813 at baseline to 3651±1721 at the final follow-up assessment; p<0.0001). Interestingly the increase of steps taken during the dialysis-free weekend intervals was not significant (3495±1799/day at baseline and 3680±1939/day at the end of the study; p=0.25). No change in body weight was recorded but there was an increase in mid-arm circumference (p=0.03), a decrease in total serum cholesterol (p=0.02), triglycerides (p=0.040), and an increase in blood hemoglobin (from 10,5±1.3 to 11.3±1.6 g/dl; p=0.04) despite no significant change in ESA requirements.
Conclusions: The study shows that pedometer use increases average daily steps taken by hemodialysis patients and this effect is maintained for at least 3 months.

MP429 PLASMA LEVELS OF AC-SDKP IN HEMODIALYSIS PATIENTS AND RELATIONSHIP WITH SYSTOLIC AND DIASTOLIC CARDIAC FUNCTION

Dimitra Biblaki[1], Alexandros Tselepis[2], Konstantinos Tellis[2], Georgios Paradelis[3], Eleni Papavasileiou[2], Nikolaos Papagalanis[1]. *[1]Nephrology, Red Cross Hospital, Athens, Greece; [2]Biochemistry Lab, Chemistry, University of Ioannina, Ioannina, Greece; [3]Cardiology, Red Cross Hospital, Athens, Greece*

Introduction and Aims: Ac-SDKP (N-acetyl-seryl-aspartyl-lysyl-proline) is a physiological negative regulator of hemopoiesis and is normally degraded by angiotensin converting enzyme (ACE).Plasma levels of Ac-SDKP are significantly increased in hemodialysis (HD) patients and this increase is even greater in ACE inhibitor-treated patients. Ac-SDKP has been shown to reduce fibrosis in myocardium.However administration of Ac-SDKP in experimental models of cardiac remodelling has also been shown to corelate with worsening of cardiac function. The aim of this study was to investigate the relationship between plasma levels of Ac-SDKP in HD patients and indices of cardiac function.
Methods: Twenty seven patients who underwent HD for at least 6 months were included in this study. None received ACE inhibitor as antihypertensive treatment.Blood drawn from the arterial needle of the fistula just before the start of hemodialysis session was collected in heparinized tubes.Blood was immediately mixed with solution of lisinopril 10^{-3} M/L,centrifigured and stored at -20°C until use.Ac-SDKP concentrations are assessed by a specific competitive enzyme immunoassay. All patients underwent cardiac triplex examination within 2 weeks after blood was drawn.Ejection fraction, the ratio of E to A wave (E/A), deceleration time (DT) and isovolemic relaxation time (IVRT) were measured. Results are expressed as mean ±SD.C oefficients of correlation were calculated using Spearman rank R.
Results: Plasma levels of Ac-SDKP in 27 HD patients before start of hemodialysis session were 1.42±0.47pmol/ml (mean ± SD). Ejection fraction was 67.1%±7.8%. Ac-SDKP concentration was inversely correlated to ejection fraction and this correlation was statistically significant (r = -0.44, P<0.05). E to A wave ratio was 0.98±0.49. Ac-SDKP was inversely correleted to E/A and this correlation was statistically significant (r = - 0.47, p <0.05). DT was 223.7±36.1 msec and correlated inversely with Ac-SDKP (r = -0.28) but without statistical significance. IVRT was 99.25±17.35 msec. A positive correlation (r = 0.22) was found between IVRT and Ac-SDKP levels but this correlation did not reach statistical significance.
Conclusions: In this study we investigated if any correlation exist between plasma levels of Ac-SDKP in HD patients (not on ACE inhibitors treatment) and indices of systolic and diastolic cardiac function.We have shown that increased levels of Ac-SDKP are correlated with poorer systolic function as this is expressed by a lower ejection fraction. Moreover we have shown that higher levels of Ac-SDKP are significantly correlated with lower values of E/A which is compatible with diastolic dysfunction.However we did not manage to show any significant correlation of Ac-SDKP levels with other indices of diastolic dysfunction (IVRT and DT) and this can partially attributed to the small number of patients included. Our results appear to confirm studies in experimental models that indicate that eventhough Ac-SDKP exerts anti-fibrotic properties does not seem to improve cardiac function.

Epidemiology and outcome 2

MP430 PREDICTORS OF MORTALITY AMONG INCIDENT NON-DIABETIC HEMODIALYSIS PATIENTS: A COHORT STUDY

Boris Bikbov, Natalia Tomilina. *Russian Dialysis Society, Moscow, Russian Federation*

Introduction and Aims: Death rate is extremely high among hemodialysis (HD) patients. In order to reveal predictors of mortality we performed an analysis of the individual data of the Russian Registry of Renal Replacement Therapy.
Methods: We included in analysis 2884 non-diabetic incident HD patients with completed demographic and laboratory parameters which started HD

treatment between 01/01/2000 and 31/12/2005. We analysed the influence of age, sex, diagnosis as well as initial values of blood pressure (BP), hemoglobin (Hb), serum albumin (Alb) and glomerular filtration rate (GFR) separately on 1- and 3-year survival. GFR was calculated by Cockcroft-Gault equitation.

Relative risks (RR) and their 95% confidence intervals (95% CI) were calculated in Cox proportional hazards model.

Results: Results of multivariable analysis of the influence of statisticaly significant predictors of mortality on 1- and 3- year survival are shown in Table 1.

Table 1. Influence of initial parameters at HD initiation on 1- and 3-year survival (multivariable Cox proportional hazards model)

Parameter	Number of patients in subgroup	1 year survival		3 year survival	
		RR	95% CI	RR	95% CI
Age, per 10 years	–	1.37*	1.24-1.52	1.33*	1.23-1.44
Diagnosis					
Glomerulonephritis	1590	Reference group		Reference group	
Vasculitis	83	2.04†	1.20-3.45	1.48	0.92-2.39
Glomerular filtration rate, ml/min					
0-5	326	1.91†	1.23-2.96	1.48§	1.06-2.05
5.1-10	1726	1.31	0.92-1.87	0.97	0.75-1.25
10.1-15	638	Reference group		Reference group	
15.1-20	137	2.07§	1.15-3.72	1.45	0.92-2.28
≥20.1	57	1.95	0.82-4.68	1.71	0.90-3.23
Systolic blood pressure, mm hg					
≤100	52	0.31	0.09-1.10	0.49	0.17-1.44
101-119	63	0.64	0.24-1.71	0.69	0.29-1.66
120-139	304	Reference group		Reference group	
140-159	717	1.29	0.72-2.31	1.89§	1.16-3.06
160-179	831	1.97	0.89-3.11	1.97§	1.17-3.34
≥180	917	2.27§	1.16-4.65	2.53§	1.44-4.42
Diastolic blood pressure, mm hg					
≤60	71	5.10†	1.94-13.37	4.50§	1.86-10.90
61-79	148	1.40	0.68-2.88	1.68	0.94-3.02
80-89	471	Reference group		Reference group	
90-99	691	0.94	0.59-1.48	0.88	0.61-1.26
100-109	901	0.78	0.47-1.27	0.92	0.63-1.35
≥110	602	0.84	0.48-1.48	0.96	0.62-1.49
Hemoglobin, g/l					
<80	1613	2.82†	1.47-5.44	2.28†	1.41-3.68
80-99,9	931	2.31§	1.19-4.51	2.08†	1.28-3.38
100-119,9	282	Reference group		Reference group	
≥120	58	1.12	0.24-5.24	1.63	0.60-4.40
Serum albumin, g/l					
≤35	1333	3.10*	2.15-4.48	2.26*	1.74-2.93
35.1-39.9	714	2.04†	1.34-4.48	1.47§	1.09-1.98
≥40	837	Reference group		Reference group	

*P<0.0005, †P<0.01, §P<0.05 in comparisson with reference group.

Conclusions: We confirmed that age, vasculitis, pre-dialysis very low GFR, anemia and hypoalbuminemia increased the RR of death. The most important finding that both very low diastolic BP (≤60 mm hg) and even moderately increased systolic BP (≥140 mm hg) at treatment initiation significantly impaired the long-term prognosis of life among incident HD patients.

MP431 FACTORS ASSOCIATED WITH MORTALITY IN INCIDENT END-STAGE RENAL DISEASE PATIENTS DIFFER BY DIABETES STATUS AND BY GENDER

Emmanuel Villar[1], Alexandre Karame[1], Pierre Trolliet[1], Agnes Caillette-Beaudoin[2], Remi Cahen[1], Rene Ecochard[3], Claire Pouteil-Noble[1], Michel Labeeuw[1]. *[1]Nephrology and Renal Transplantation, Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre Benite, France; [2]Centre Associatif Lyonnais de Dialyse (CALYDIAL), Centre Hospitalier Lucien Hussel, Vienne, France; [3]Department of Biostatistic, Hospices Civils de Lyon, Lyon, France*

Introduction and Aims: Females had poorer outcomes in end-stage renal disease (ESRD) patients with type 2 diabetes (T2DM). Gender had no effect on survival in ESRD patients without diabetes (noDM). We investigated patient characteristics associated with death after first dialysis by diabetes status and gender.

Methods: The 667 incident patients who started dialysis in two renal units covering the same geographical area between 01/011995 and 31/12/2006 were included (one academic hospital and one non-for-profit units). Baseline characteristics and details of renal replacement therapies were collected. Patients were followed until death or 31 December 2006. Multivariate survival analyses using Cox regression were adjusted for age, comorbid conditions and were stratified on first modality of dialysis, renal transplant during follow-up and renal unit. We checked for interactions between variables by including multiplicative terms in regressions. When significant, we performed subgroup analyses. Patients with type 1 diabetes (n=17) were excluded.

Results: We found significant interactions between cardiovascular comorbidities and diabetes status ($p<0.05$) with respect to death after first dialysis. In T2DM patient subgroup (n=210), we found a significant interaction between heart failure and gender (p=0.03). Factors associated with death by diabetes status and by gender are showed in Table 1.

Deaths from cardiovascular cause were 67 (39.1%) in noDM and 71 (54.6%) in T2DM patients (p=0.01), without significant difference between gender in both groups ($p>0.05$).

Conclusions: Mortality risks associated with cardiovascular diseases differed noticeably by diabetes status and by gender in these incident ESRD patients. Results deserve confirmations by epidemiological studies in larger cohorts and further explanatory studies.

MP432 COMPARISON OF OUTCOME AND QUALITY OF LIFE: HEMODIALYSIS VERSUS PERITONEAL DIALYSIS

Hamid Noshad[1], Nariman Nezami[2,3], Shahram Sadreddini[4], Yaghoub Salek Zamani[5], Javid Safa[1]. *[1]Department of Nephrology, Tabriz University of Medical Sciences, Tabriz, East Azerbaijan, Iran; [2]Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, East Azerbaijan, Iran; [3]Young Researchers Club, Tabriz, East Azerbaijan, Iran; [4]Department of Rheumatology, Tabriz University of Medical Sciences, Tabriz, East Azerbaijan, Iran; [5]Department of Physical Medicine and Rehabilitation, Tabriz University of Medical Sciences, Tabriz, East Azerbaijan, Iran*

Introduction and Aims: Ever since the Peritoneal Dialysis (PD) introduced as a renal replacement therapy, efficacy and complications of it, were compared with Hemodialysis (HD). The aim of this study was determination of PD efficacy and outcomes versus HD in our region.

Methods: We compared 60 patients on PD with 60 matched patients on HD in Tabriz Sina Hospital during 2004-2006. Patients' and technique survival,

Abstract MP431 – Table 1. Adjusted hazard ratio for death after first dialysis

	noDM	noDM	T2DM	T2DM
	Male n=287	Female n=153	Male n=123	Female n=87
Age (+1 year)	1.03 [1.02-1.05]*	1.08 [1.05-1.11]*	1.05 [1.02-1.08]*	1.06 [1.01-1.11]*
Heart failure	2.48 [1.60-3.83]*	1.47 [0.72-3.02]	1.91 [1.13-3.22]*	0.81 [0.44-1.48]
Coronaropathy	0.63 [0.40-1.01]	0.67 [0.32-1.42]	1.19 [0.67-2.09]	0.82 [0.44-1.53]
Peripheral vascular disease	1.05 [0.65-1.68]	0.89 [0.36-2.22]	1.96 [1.13-3.22]*	1.08 [0.59-2.00]
Cerebrovascular disease	1.61 [0.97-2.66]	1.71 [0.80-3.65]	1.49 [0.84-2.65]	0.71 [0.26-1.91]
Malignancy	1.06 [0.71-1.58]	1.69 [0.96-2.99]	1.69 [0.80-3.57]	1.26 [0.47-3.33]
Hepatic insufficiency	3.73 [1.69-8.26]*	–	–	–
Chronic lung disease	1.46 [0.80-2.66]	0.93 [0.41-2.13]	–	–

*p<0.05; –: variable not included (number of patients <5 with the given comorbidity).

and patients' quality of life were compared by means of health related quality of life questionnaire (GHQ-28).
Results: In our study, there wasn't significant difference in mean age and duration of dialysis between patients on PD and HD. Survival of diabetic patients was better in HD than PD but in non diabetic patients survival wasn't different between HD and PD. Among patients on PD, diabetics had higher mortality rate. Also mortality rate of diabetics on PD was 25% higher than the patients on HD, in non diabetic patients mortality on PD was 3% higher than HD. In all four axes of questionnaire including psychophysical dysfunction, Stress & sleep disorder, Social dysfunction and Major depression, PD patients had lower scores than HD (P values respectively; <0.001, <0.001, 0.002, <0.001) that means patients on PD had better quality of life than HD.

Quality of life on the basis of GHQ-28: HD vs. PD

		Dialysis type		
		HD	PD	P value
Psychophysical dysfunction	Nondiabetic	17.87±1.35	13.76±2.47	P<0.001
	Diabetic	16.68±2.45	13.45±1.97	P<0.001
	Total	17.46±2.67	13.57±1.34	P<0.001
Stress & sleep disorder	Nondiabetic	17.35±2.85	13.74±1.43	P<0.001
	Diabetic	6.74±1.24	11.46±2.986	P<0.001
	Total	16.64±1.56	12.75±2.13	P<0.001
Social dysfunction	Nondiabetic	16.58.±2.63	13.77±1.75	P<0.001
	Diabetic	15.58±1.54	11.65±1.36	P<0.001
	Total	16.13±1.38	12.42±1.76	P=0.002
Major depression	Nondiabetic	18.42±1.3	14.86±1.24	P<0.001
	Diabetic	17.57±1.35	12.85±1.59	P<0.001
	Total	18.22±2.03	13.76±2.1	P<0.001
Total Score	Nondiabetic	68.89±1.35	51.87±4.66	P<0.001
	Diabetic	66.48±1.93	47.21±2.74	P<0.001
	Total	67.06±1.86	50.57±2.1	P<0.001

Conclusions: In this study, patients' and technique survival and patients' QOL on PD was better than HD. Despite this finding, survival of diabetic patients was better in HD than PD and mortality was higher in diabetics on PD.

MP433 TIME DEPENDENT DIFFERENTIAL IMPACT OF TYPE 2 DIABETES BETWEEN GENDERS IN PATIENTS WITH END-STAGE RENAL DISEASE

Alexandre Karame [1], Michel Labeeuw [1], Pierre Trolliet [1], Agnes Caillette-Beaudoin [2], Remi Cahen [1], Rene Ecochard [3], Claire Pouteil-Noble [1], Emmanuel Villar [1]. *[1]Nephrology and Renal Transplantation, Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre Benite, France; [2]Centre Associatif Lyonnais de Dialyse (CALYDIAL), Centre Hospitalier Lucien Hussel, Vienne, France; [3]Department of Biostatistic, Hospices Civils de Lyon, Lyon, France*

Introduction and Aims: In the general population, mortality risk is lower among females than males. In patients with T2DM or end-stage renal disease (ESRD), females lost their survival advantage. We aim to explore the interaction between gender and T2DM with respect to ESRD patient mortality.
Methods: We analysed prospectively the 667 incident patients who started dialysis in two renal units covering the same geographical area between 1 January 1995 and 31 December 2006 (one academic hospital and one non-for-profit units). Baseline characteristics, renal replacement therapies including details of renal transplant were collected. Patients were followed until death or 31 December 2006. Multivariate analyses were adjusted for age, cardiovascular diseases, malignancy, and were stratified on first modality of dialysis, renal transplant during follow-up and renal unit. Shoenfeld's residual approach was used to explore adjusted time dependent effect of a variable on mortality after first dialysis. Cox regression analyses were used to determine adjusted effects of covariables on mortality by period of time after first dialysis. We checked for interactions between variables by including multiplicative terms in multivariate regressions. Patients with type 1 diabetes (n=17) were excluded.
Results: T2DM ESRD patients were 210 (females: 87, 41.4%) and patients without diabetes (noDM) were 440 (females: 153, 34.7%). There was a significant interaction between gender, diabetes status and time on dialysis (Figure 1, p=0.01).

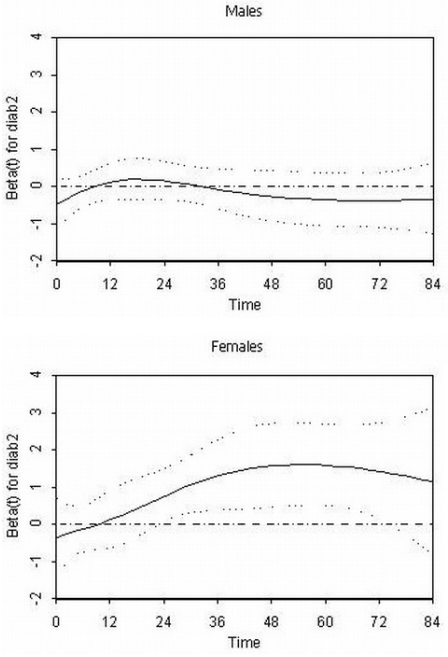


Figure 1

Within the first year after first dialysis, T2DM was not associated with death: in the whole cohort (n=650), adjusted hazard ratio (aHR) for death in T2DM versus noDM was 0.72 (p=0.10) without interaction between genders (p=0.48).
After the first year after first dialysis (n=455 one-year survivors), interaction between gender and diabetes status was significant (p=0.02). In males (n=292), T2DM was not associated with death (aHR for death in T2DM versus noDM: 0.94, p=0.78). In females (n=163), T2DM was significantly associated with death (aHR: 2.17, p=0.01). In T2DM patients, deaths from cardiovascular causes after the first year after first dialysis were 26 (57.7%) in males and 21 (58.3%) in females (p=0.86).
Conclusions: In this cohort, T2DM had an impact on mortality on dialysis only in females. This effect was time-dependent. These results deserve both further epidemiological studies in larger cohorts and explanatory studies.

MP434 NON-DIABETIC HEMODIALYSIS PATIENTS WITH CHRONIC VIRAL HEPATITIS HAVE LOWER SERUM FETUIN A LEVELS INDEPENDENT TO MALNUTRITION, INFLAMMATION AND ANEMIA

Hung Yuan Chen [1,2], Yen Lin Chiu [1,2], Shih Ping Hsu [1,2], Mei Fen Pai [1,2], Chun Fu Lai [1,2], Yu Sen Peng [1,2], Kuan Yu Hung [2], Kwan Dun Wu [2]. *[1]Division of Nephrology, Department of Internal Medicine, Far Eastern Memorial Hospital, Taipei, Taiwan; [2]Division of Nephrology, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan*

Introduction and Aims: Fetuin A, secreted in hepatocytes, links to cardiovascular mortality in dialysis patients. Its serum levels decreased in non-chronic kidney disease patients with severe liver diseases. However, the secretion of fetuin A in hemodialysis patients with chronic hepatitis, compared with individuals without viral hepatitis, has not been investigated yet.
Methods: One hundred and twenty-nine non-diabetic hemodialysis patients were recruited for this cross-sectional study. Thirty-nine patients had chronic hepatitis B or hepatitis C confirmed with serological and image investigation. We compared serum fetuin A, interleukin 6 (IL-6), highly sensitive C-reactive protein (hs-CRP), albumin, plasma hemoglobin levels, transferrin saturation (TSAT) and normalized protein catabolic rate (nPCR) in individuals with and without hepatitis.
Results: Sixty-seven women and sixty-two men aged 60±13 years were analyzed. The basic characteristics including age, gender, hemoglobin, TSAT, serum albumin, nPCR, hs-CRP and IL-6 were similar between individuals

with and without chronic hepatitis. Patients with chronic hepatitis had lower fetuin A than those without (0.88±0.19 v.s 0.97±0.27 g/L, P=0.027). In uni-variable regression analysis, fetuin A was negatively associated with chronic hepatitis (P=0.029), age (P<0.001), IL-6 (P=0.002) and positively associated with hemoglobin (P=0.007) and serum albumin (P<0.001). Fetuin A levels were not associated with parameters of liver function. In multi-variable analysis, after adjustment for albumin, hemoglobin, IL-6 and age, fetuin A was independently associated with chronic hepatitis (P=0.039, γ= -0.17).

Conclusions: Non-diabetic hemodialysis patients with chronic hepatitis have lower serum fetuin A concentration which is independently to malnutrition, inflammation and anemia. Chronic hepatitis leads to lower fetuin A concentration in these patients and probably contributes to CV mortality beyond the chronic inflammation.

MP435 THE TIME OF REFERRAL TO NEPHROLOGISTS: IMPACT ON THE INITIATION OF HAEMODYALISIS AND MORTALITY IN ESRD PATIENTS

Gjulsen Selim[1], Olivera Stojceva-Taneva[1], Ljubica Georgievska-Ismail[2], Saso Gelev[1], Pavlina Dzekova[1], Vili Amitov[1], Arben Asani[1], Lada Trajcevska[1], Svetlana Pavleska[1], Aleksandar Sikole[1]. *[1]Clinic of Nephrology, University "Ss. Cyril and Methodius", Macedonia, The Former Yugoslav Republic of; [2]University Institute for Heart Disease, University "Ss. Cyril and Methodius", Macedonia, The Former Yugoslav Republic of*

Introduction and Aims: The timing of referral to nephrologists is highly variable in patients with chronic kidney disease (CKD). Late nephrology referral of patients with CKD has been suggested to increase mortality after initiation of dialysis. The aim of this study was to assess the impact of nephrology referral on the initiation of haemodyalisis (HD) and mortality during HD treatment in end-stage renal disease (ESRD) patients who have died in our institution during a five years period.

Methods: We studied data from all 117 patients on HD treatment who died (after 90 days of HD treatment), in our institution, in the period between 01.01.2002 and 31.12.2006. Early (ER) and late referral (LR) were defined by the time of follow-up by a nephrologist greater than or less than 6 months, respectively, before initiation of hemodialysis.

Results: Out of a total of 117 patients, 37.6% started HD in the ER group and 62.4% in the LR group. At the start of HD, LR patients were older (56.97±14.88 vs 50.00±13.43; p=0.012), had higher proportion of temporary catheters (5.5% vs. 64%) and had significantly lower level of haemoglobin (77.51±14.30 g/L vs. 85.42±18.48; p=0.021) and diuresis (831.30±415.11ml vs. 1273±598.92; p=0.000), than ER patients. Creatinine clearance was less in the LR (7.67±3.86ml/min/1.73m^2) vs. the ER group (8.70±3.62ml/min/1.73m^2), but significantly not different. Correlation analysis showed that the months of nephrological follow-up correlated significantly with hemoglobin (R=0.207, p=0.04), creatinine clearance (R=0.241, p=0.01) and inversely with age (R=-0.248, p=0.007) and creatinine (R=-0.248, p=0.01). Cardiovascular disease (CVD), defined by a history of myocardial infarction, cerebral vascular disease, peripheral arteriopathy, and/or heart failure was also significantly more common among LR patients compared to ER (56%; 27%, p=0.002). During the hemodyalisis treatment until death, the LR group had significantly lower levels of hemoglobin and hematocrit (94.26±15.23g/L vs 11.18±13.25; p=0.015). According to echocardiography data, there were no significant differences in the left ventricular mass index (LVMI) between the LR and ER group at the time of dialysis initiation, but during the hemodialysis treatment the LR group had significantly greater LVMI than the ER group (232,96±92,48 g/m^2 vs.184,09±51,74 g/m^2; p=0,031). The time until death in months during dialysis treatment was significantly different between the LR and ER group, (69.51±64.03 vs.113.27±89.03, p=0.0025).

Conclusions: LR patients experienced a greater degree of anaemia and high prevalence of CVD at the time of dialysis initiation. Our data suggest that anaemia, CV damage and progression of left ventricular hypertrophy (LVH) in the LR patients during the haemodialysis treatment is associated with poor survival on haemodialysis.

MP436 REPLACEMENT THERAPY IN PATIENTS WITH ESRD AND LIVER CIRRHOSIS: COMPARISON OF HEMODIALYSIS WITH CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

Seung Ok Choi, Jae Won Yang, Jung Uk Choi, Min Soo Kim, Byoung Geun Han. *Nephrology, Yonsei University Wonju College of Medicine, Wonju, Gangwon, Korea*

Introduction and Aims: During hemodialysis (HD) in patients with end-stage renal disease (ESRD) and preexisting liver cirrhosis (LC), there is a risk of inadequate ultrafiltration due to either intradialytic hypotension or a coagulopathy causing complications from alteration of clotting factors and platelets. Peritoneal dialysis have several benefits over HD for cirrhotic patients including proper hemodynamic stability, avoidance of anticoagulants and direct removal of ascitic fluid. We compared the factors associated with the survival rates in patients with ESRD and LC undergoing dialysis.

Methods: We analyzed 41 ESRD patients with LC (HD 23 patients, PD 18 patients). Their age, sex, cause of renal disease, presence of diabetes, complication of cirrhosis, frequency of intradialytic hypotension, frequency of paracentesis, cause of death and laboratory findings at the beginning of dialysis were retrospectively analyzed. To investigate the factor affecting the patient survival rate, the survival rate was analyzed according to their cause of renal disease, cause of liver disease, initial modified Child-Pugh score, albumin level, hemoglobin level and residual renal function.

Results: Degree of ascites control and hemodynamic stability was more better in PD group, and peritonitis was less frequent in HD group. The survival duration was 36.2±30.2 month in HD group, and 25.8±26.5 month in PD group, but there was no significant difference in cumulative survival rate with the treatment modality. The patients with severe ascites at the beginning of dialysis, low albumin (serum albumin < 3.0 g/dl), high modified Child-Pugh score (MCP score ≥ 7) and low hemoglobin (Hb) level (Hb < 10 g/dl) had poor survival rate.

Conclusions: The multivariate analysis showed that age, the amount of ascites, the initial Hb level and the modified Child-Pugh score were risk factors for death. PD was an effective renal replacement therapy for patients with ESRD and LC. Patients with a modified Child-Pugh classification of A and B were not significantly different with regard to survival rates. Therefore, PD may be a safe and effective option for patients with ESRD and LC as well as hemodialysis.

MP437 ASSOCIATION OF COMORBIDITY AND QUALITY OF LIFE IN END-STAGE RENAL DISEASE PATIENTS ON HEMODIALYSIS

P. Malindretos[1], P. Sarafidis[1], A. Sioulis[1], S. Spaia[2], N. Zeggos[3], V. Kitos[4], Ch Koronis[5], Ch Kabouris[6], S.T. Vasiliou[1], P. Nikolaidis[1], D. Grekas[1]. *[1]Renal Unit, 1st Department of Internal Medicine, AHEPA University Hospital, Thessaloniki, Greece; [2]Department of Nephrology, 2nd IKA Hospital, Thessaloniki, Greece; [3]Renal Unit, Patsidis General Clinic, Larissa, Greece; [4]Renal Unit, Sarafianos General Clinic, Thessaloniki, Greece; [5]Renal Unit, Lefkada General Hospital, Lefkada, Greece; [6]Renal Unit, General Clinic of Thessaloniki, Thessaloniki, Greece*

Introduction and Aims: Data on the impact of comorbidity, estimated with validated indexes, on quality of life in chronic hemodialysis patients are limited. The aim of this study was to assess the relation between comorbidity and health related quality of life in chronic hemodialysis patients with the use of Index of Coexistent Disease (ICED).

Methods: This was a cross-sectional, multicenter study of prevalent hemodialysis patients. All participants filled the standard kidney disease quality of life short form (KDQOL-SF) questionnaire of quality of life. The comorbidity was assessed with the use of ICED, which is a valid index for this purpose.

Results: A total of 200 patients completed the questionnaire and were divided in 3 groups according to ICED score; group1 had ICED equal or less than 1; group 2 had ICED equal to 2; and group 3 had ICED equal to or greater than 3. Worsening of comorbidity (increase of ICED) was related with heavier burden of kidney disease (p=0.01), worse cognitive function (p=0.051), worse quality of social interaction (p=0.025), poorer sleep (p=0.008), poorer social support (p=0.026), worse physical functioning (p=0.024), worse emotional well being (p=0.025), decreased energy/fatigue

ratio (p=0,022), decreased overall health rating (p=0,04), decreased physical component summary (p=0.025), and decreased kidney disease component summary (p=0.009), as well as a trend towards increased pain (p=0,059).
Conclusions: Increase of the ICED index showed significant associations with various parameters of the KDQOL-SF questionnaire. These findings indicate that comorbidity seen in end-stage renal disease patients undergoing hemodialysis significantly affects various dimensions of health-related quality of life.

MP438 SOCIO-ECONOMICAL AND ETHICAL ASPECTS IN UNINSURED DIALYSIS PATIENTS – INDIAN EXPERIENCE

Visweswar Reddy Pachipala. *Nephrology, Bollineni Superspeciality Hospital, Nellore, Andhra Pradesh, India*

Introduction and Aims: End stage renal disease is becoming a common disease in India.The aim of our study is to analyze the socio economical and ethical aspects of dialysis dependent patients in a semi urban set up in India.
Methods: Over 7 year period (2001-2007), 500 ESRD patients were studied.Detailed analysis of dialysis case records,demographic and socioeconomic aspects was done.Standard statistical methods were used.
Results: There were 400 males,most common age being 45 years.Diabetic nephropathy is most common cause of ESRD.Educational status-illiterate 2%,school level 23%,pre degree 47%,degree 25%.Dialysis support is mostly given for the earning male members of the family in the age group between 18-50 years (90%).75% the patients offered dialysis only for initial 4-5 months. Thrice a week dialysis comprised only <10% of the total. 34% received complete course of Hepatitis B vaccination before initiating MHD. Dialysis schedule is highly irregular and is as demanded by the patient and family. *'Thrice weekly schedule leads to complications'*, a misconception seen in 95% even after explanation about dialysis adequacy. One third presents with complications like hyperkalemia, pulmonary edema, and uremic encephalopathy. For the majority (75%) fluid removal is an indication of dialysis adequacy. The average family size is 5.Divorce rate/living separately from the spouse is 27%. Prevalence of depression is 25.8% and required psychiatric counseling in all. The incidence of completed suicide is 0.6%.Attempted suicide is seen in 2% patients and is used as a mode to drag the attention and fiancial support.70% of patients are poor with an average income of 1600 USD per year. Awareness about the medical insurance is <5% and only 25% of educated and working classes are having knowledge about insurance. Most common cause for hospitalization is cardiovascular complication.Implementations of DOQI guide lines are highly restricted and impractical in 80%.Only 10% of patients were on Erythropoitin. Dialysis care is provided by the private hospitals in 95%.Government hospitals are unable to provide maintenance hemodialysis due to extremely limited resource allocation. Contributions from the non governmental, philanthropic and charitable organizations is negligible. Palliative dialysis done in 65% for complications, fluid over load and it depends on availability of money. Conflicts usually develops between the doctor and the patient & the doctor and the patient's attendants due differences of opinion, expectation, values, prognosis and outcome. Consideration of dialysis with drawl depends on the decision of the family and the financial aspects rather than the patient status.
Conclusions: Extremely poor financial status and social neglect are common in dialysis patients. Females and the patients between 18-60 years are highly neglected.Highly recommended to have an exclusive or a special renal/dialysis insurance.Active participation from non governmental, philanthropic charitable organizations and developed courtiers is extremely useful. Community level CKD prevention programs should be given priority in health planning These aspects should be strongly emphasized in nephrology residency training program.

MP439 COMPARISON OF MORTALITY BETWEEN DIABETIC NEPHROPATHY PATIENTS TREATED WITH HEMODIALYSIS AND PERITONEAL DIALYSIS (SINGLE CENTER STUDY)

Kyung Il Song, Soo Hee Kim. *Division of Nephrology, Internal Medicine, KangNung Asan Hospital,College of Medicine, University of Ulsan, KangNung City, Kang Won Do, Republic of Korea*

Introduction and Aims: Incidence of diabetes mellitus is on the rise and diabetic nephropathy (DN) is now the dominant cause of end-stage renal disease (ESRD) worldwide, We investigated the outcome of DN patients treated with renal replacement therapy (HD vs CAPD) at our institution.
Methods: A five-year comparison of DN patient survivals in CAPD and HD. Comparisons of patient survival were made for 41 CAPD and 69 HD patients undergoing dialysis between January 2001 and December 2006. Cox's proportional hazard regression model was used to compare patient survival, with an adjustment for pre-treatment prognostic differences. Only the patients' first treatments were considered.
Results: In HD group, the median age was 51 years, mean diabetic duration was 16.5 years and mean dialysis duration was 17.3 months. In CAPD group, the median age was 54.5 years, mean diabetic duration was 23 years and mean dialysis duration was 17.3 months. Overall 1, 3, and 5 years patient survival in HD group was 82.3%, 45.6% and 36.7%. Overall 1, 3, and 5 years patient survival in CAPD group was 80.1%, 43.2% and 32.4%. There was no statistical significance between CAPD and HD group (P >= 0.05 log-rank test). When adjusted for patient age, sex and other comorbid complicating conditions, adjusted 1, 3, and 5 years patient survival in HD group was 84.2%, 42.2% and 38% and adjusted 1, 3, and 5 years patient survival in CAPD group was 81.3%, 41.2% and 36.4%. There was no differences in the adjusted patient survival between HD and CAPD group (p>0.05). The most common cause of death in HD group was cardiovascular problems and sepsis due to peritonitis in CAPD group. The risk factors determining mortality in diabetic ESRD patients were patient age (RR=1.0484, p=0.0001) and serum alumin level (RR=0.5301, p=0.0017).
Conclusions: We conclude that there is no difference survival between HD and CAPD in diabetic ESRD patient and most importtant prognostic factors determining patient survival are patient's age and serum albumin level. Prospective randomized studies are needed to assign a cause-and-effect relationship between the choice of dialysis modality.

MP440 AN EPIDEMIOLOGICAL STUDY OF HAEMODIALYSIS PATIENTS BASED ON THE EUROPEAN FRESENIUS MEDICAL CARE (FMC) HAEMODIALYSIS NETWORK: THE ARO RESEARCH INITIATIVE

Alm DeFrancisco[1], P. Aljama[2], J. Kim[3], D. Marcelli[4]. *[1]Hospital Marques de Valdecilla de Santander, Santander, Spain; [2]Servicio de Nefrologia, Cordoba, Spain; [3]Amgen Ltd, London, United Kingdom; [4]Fresenius Medical Care, Bad Homburg, Germany*

Introduction and Aims: The ARO (Analysing data, Recognizing excellence, Optimizing outcomes) Chronic Kidney Disease Research Initiative was formed to characterize more fully practice patterns and clinical outcomes to support the informed use of therapies in European haemodialysis (HD) patients.
Methods: In an open-cohort design, patients were randomly selected from 172 participating FMC centres (approximately 25 sites/country; 50 patients/site). Altogether 11 114 patients (n=7105 prevalent, n=4009 incident) were followed for up to 2 years between Jan 2005 and Dec 2006 (>15,000 person-years). Incident patients received HD ≤6 months prior to follow-up. Data were collected for demographics, medical history, labs (by date), and medications (by date). Outcomes are available for cause-specific mortality and hospitalisations (ICD-10 codes available).
Results: Demographic and clinical characteristics vary across participating ARO countries (see Table). Prevalent patients (64% of ARO population) received HD for a mean (±SD) of 4.9±4.7yrs prior to the study. Most patients (69%) had fistula placement. The most common etiologies of chronic kidney disease were glomerular disease (15%), hypertension (12%), diabetic nephropathy (12%), cystic tubulo-interstitial disease (10%), kidney disease (5%), and other/unknown (46%). There is wide variation in the distribution of co-morbid disease across ARO countries.

Abstract MP440 – Table 1

Baseline Characteristics of Patients Treated at FMC Centres in Participating ARO Countries

Baseline variables*	Spain	Turkey	Portugal	Hungary	Italy	CEE†	France	UK	Total
Total subjects N(%)	1879(17)	1752(16)	1495(13)	1414(13)	1248(11)	1208(11)	1100(10)	1018(9)	11114(100)
Age Mean(SD)	66(15)	56(15)	64(15)	62(14)	66(14)	62(14)	61(17)	62(16)	62(15)
Female N(%)	702(37)	772(44)	607(41)	715(51)	521(42)	534(44)	421(38)	382(38)	4654(42)
BMI‡ Mean(SD)	25.2(4.6)	24.8(4.4)	25.0(4.3)	25.3(5.6)	25.3(4.7)	26.3(5.3)	24.8(5.1)	26.0(5.6)	25.3(5.0)
Prevalent N(%)	1028(55)	1181(67)	1063(71)	834(59)	890(71)	763(63)	686(62)	660(65)	7105(64)
Dialysis vintage for prevalent pts yrs Mean(SD)	5.0(5.1)	4.6(3.7)	5.1(4.3)	4.4(3.8)	6.3(6.1)	4.3(4.3)	4.6(5.5)	4.5(4.8)	4.9(4.7)
Follow-up yrs Mean(SD)									
Incident	0.9(0.6)	0.6(0.6)	1.0(0.7)	1.0(0.7)	1.0(0.7)	1.0(0.6)	1.1(0.7)	1.0(0.6)	0.9(0.7)
Prevalent	1.5(0.6)	1.5(0.6)	1.8(0.5)	1.5(0.6)	1.7(0.6)	1.7(0.6)	1.6(0.6)	1.6(0.6)	1.6(0.6)
Fistula N(%)									
Incident	548(69)	401(70)	261(62)	353(61)	292(82)	289(73)	158(89)	175(50)	2477(68)
Prevalent	692(68)	1054(89)	690(65)	624(76)	782(88)	592(82)	411(94)	457(70)	5302(78)
Smoker N(%)	514(37)	567(33)	243(18)	105(10)	472(42)	393(35)	145(25)	280(30)	2719(30)
Diabetes N(%)	239(13)	398(23)	320(21)	218(15)	251(20)	376(31)	132(12)	92(9)	2026(18)
CVD§ N(%)	806(43)	650(37)	673(45)	546(39)	440(35)	821(68)	335(30)	162(16)	4433(40)

* Missing data were omitted from the calculations
† CEE: Central Eastern European countries (Slovakia, Slovenia, Czech Republic, and Poland)
‡ BMI: Body Mass Index
§ CVD: Cardiovascular disease is defined as the presence of hypertension, myocardial infarction, angina, coronary artery disease, transient ischaemic attack, stroke, congestive heart failure, or peripheral vascular disease

Conclusions: Using granular real-life data obtained from FMC centres located across Europe, ARO is consistent with and complements other large epidemiological studies (DOPPS, COSMOS) designed to capture practice patterns in the European HD patient population.
Disclosure: A.L.M. de Francisco is a consultant for Amgen. This study is sponsored by Amgen Europe GmbH.

MP441 HAEMOGLOBIN LEVELS AND TIME TRENDS IN EUROPEAN HAEMODIALYSIS PATIENTS ASSESSED BY THE ARO RESEARCH INITIATIVE

K.-U. Eckardt[1], I.C. Macdougall[2], V. Belozeroff[3]. [1]*University of Erlangen-Nürnberg, Erlangen, Germany;* [2]*King's College Hospital, London, United Kingdom;* [3]*Amgen Inc, Thousand Oaks, USA*

Introduction and Aims: European (EU) Best Practice Guidelines for anaemia management in haemodialysis (HD) patients recommend haemoglobin (Hb) levels of > 11 g/dL, but data describing the achievement of these targets in clinical practice is limited. We assessed distributions of Hb levels and time trends in HD patients from the EU countries participating in the ARO (Analysing data, Recognising excellence, Optimising outcomes) research initiative.
Methods: ARO was formed to enable detailed investigation of chronic kidney disease management and support the informed use of therapies in EU HD patients. Data were collected via the EU Fresenius Medical Care (FMC) HD network. In an open-cohort design, patients were randomly selected from 172 FMC centers. Altogether 11,114 patients, including 4009 incident (≤6 months on HD) and 7105 prevalent patients (>6 months on HD) were followed for up to 2 years between Jan 2005 and Dec 2006. We summarised Hb distribution at enrollment by country, and assessed the percentage of patients moving between Hb categories over 1 year of follow-up.
Results: Distribution across Hb categories <11, 11-11.9, 12-12.9, and >13 g/dL at enrollment was 52%, 25%, 15%, 8% for incident and 32%, 29%, 23%, 16% for prevalent patients, with substantial variability across countries, particularly in the <11 g/dL category (Figures). Of the 4723 patients, who survived at least one year after baseline assessment and had Hb records available, between 32% and 45% of patients remained in their initial category, while the majority had moved up or down (Table).

Number (%) of patients moving across Hb categories over 1 year of follow-up

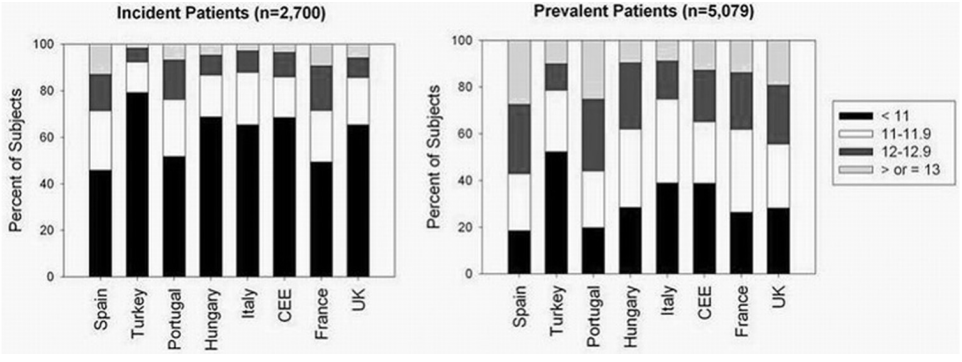
Hb at enrollment (g/dL)		Hb after 1 year (g/dL)			
Total	4723 (100.0)	<11	11– <12	12– <13	≥13
<11	1732 (36.7)	740 (42.7)	506 (29.2)	300 (17.3)	186 (10.7)
11– <12	1324 (28.0)	297 (22.4)	432 (32.6)	398 (30.1)	197 (14.9)
12– <13	998 (21.1)	143 (14.3)	281 (28.2)	325 (32.6)	249 (24.9)
≥13	669 (14.2)	63 (9.4)	126 (18.8)	182 (27.2)	298 (44.5)
	Total	1243 (26.3)	1345 (28.5)	1205 (25.5)	930 (19.7)

Conclusions: Distribution of Hb varies across EU countries, presumably reflecting differences in practice patterns and/or dialysis populations. As reported for the US dialysis population, HD patients tend to switch categories, indicating variability in Hb levels. Future research will examine the determinants of Hb variability and the association of this variability with the long term prognosis.
Disclosure: K.-U. Eckardt is a consultant for Amgen. This study is sponsored by Amgen Europe GmbH.

MP442 HABITUAL PHYSICAL ACTIVITY IN HAEMODIALYSIS PATIENTS. ASSOCIATIONS WITH CLINICAL AND DEMOGRAPHIC VARIABLES

Marta Lugo, Alicia Marini, Graciela Voronovitsky. *Quality of Life and Rehabilitation, Fresenius Medical Care Argentina, Buenos Aires, Argentina*

Introduction and Aims: Since sedentarism is a risk factor in dialysis patients it is important to quantify habitual physical activity (HPA), both to



Abstract MP441 – Figures

estimate its magnitude and to evaluate the progression of strategies to revert sedentarism. In the present study we measured HPA in a haemodialysis (HD) population, analyzed the domains in which it takes place and investigated whether there are associations with age, sex, etiology and inflammatory state.

Methods: Patients with less than 3 months in HD, motor, visual or mental disabilities were excluded (23% of the original population of 3 clinics) HPA was quantified in the remaining 162 HD patients, 59.9% male, Mean Age 59.6 - s.d. 15.5. Measurements of physical activity were obtained from anamnesis administered by a nutritionist, based on the International Physical Activity Questionnnaire (IPAQ) Long Form, which discriminates HPA performed in 4 domains: Work, Transportation, Home/Garden and Leisure. Results are expressed as metabolic equivalents per minute per week (MET-min-wk) and categorized as Low (<600 MET-min-wk), Moderate (600 to 1500) and High (>1500). C-Reactive Protein (CRP) determination by chemo luminiscence was used as inflammation marker. Statistics: descriptive, chi-square and multiple regression processed with SPSS 14.0

Results: HPA levels were Low in 51.2%, Moderate in 19.8% and High in 29.0% of patients. HPA falls abruptly around 60 years of age (p=0.000). There is no significant difference between sexes; yet most activity in women is performed at home while work is the domain in which men display more activity in this population. There are noticeable differences according to etiology: thus diabetics (not including those with other disabilities) are at the lower end of activity - 70.6% with Low activity and only 5% with High Activity - while a considerable proportion of patients with glomerulonephritis or policystic disease exhibited High Activity (37.9% and 41.2% respectively). Multiple regression analysis, controlling for age and diabetes, shows that CRP decreases with increasing levels of activity in MET-min-wk (p=0.009)

Conclusions: The analysis of habitual physical activity in HD patients indicates significant heterogeneity of behaviors according to distribution of age, etiology and prevalence of disabilities other than end stage renal disease. Age and inflammation (C-Reactive Protein) show statistically significant inverse associations with physical activity. IPAQ provides an interesting and accessible instrument; not restricted to leisure time, allowing comparisons with the monitoring of physical activity in the general population.

MP443 DETERMINANT FACTORS OF QUALITY OF LIFE (QoL) IN HEMODIALYSIS (HD) BY SF-36 SURVEY

Santiago Torales, M.I. Iglesias, M. Batlle, M. Coppola, M. Padin. *Head Office, Diaverum Argentina, Buenos Aires, Argentina*

Introduction and Aims: QoL is affected by many factors, as demographic, clinical and social/economic (SE) variables. In underdeveloped countries, the SE factors may play a significant role not well established yet. SF-36 survey shows cuantitative data about 8 wide dimensions of QoL, ordered in 2 generic categories: is a well-proved tool for QoL measurements in chronic diseases, and it could be applied to get adequate information in HD patients searching for this relations.

Methods: To determine factors that can influence QoL in HD using SF-36 subcategories and dimensions, the survey was realized in 143 ptes >18 y.o. prevalents in HD randomly selected from 3 clinics (with >100 patients) in a metropolitan area; the scores from each subcategories (physical=*P*; mental=*M*) and dimensions (physical function=*PF*; physical role=*PF*; pain=*PM*; global health=*GH*; vitality=*V*; social function=*SF*; emotional role=*ER*; mental health=*MH*) were considered as measures of QoL; other variables (*vr*) as age, gender, months in HD; diabetes (DBT); Hgb, KtV, nPCR, Ph, PTH and objective nutritional scale (mean from 3 previous months to survey) were recorded; educational and income levels, home conditions, family support (FS) and composition were also included, and asked at the same time of the survey. All QoL measurements were validated with Cronbach α test (Epidat®). Considering succesively as dependent variables QoL scores obtained, all other variables were adjusted to multiple regression models (InStat3®) searching for significant relations between them (p<0.05).

Results: General and SE results are displayed in Table 2. The results from regression models are shown in Table 1. Dimensions *V*, *GH* and *SF* were not significantly related with any applied model.

Conclusions: In this population, using SF-36, QoL was correlated with recognized objective factors as age, diabetes and Hgb. FS seems to play a significant role in social and psicological dimensions, perhaps acting as a neccesary net that sustains the other SE variables affected.

Table 1. Results from regression models

Dimensions	P	M	PF	PR	ER	PM	MH
Cronbach α	0.73	0.76	0.75	0.77	0.77	0.75	0.77
Scores	52.4	60.3	59.1	43.9	61.1	55.8	62.9
SD	17.6	18.7	29.8	40.1	41.1	25.9	20.8
IC 95%	49.5-55.3	57.3-63.4	54.1-63.9	37.3-50.4	54.3-67.9	51.5-60.1	59.5-66.3
r^2	0.228	0.186	0.266	0.206	0.191	0.189	0.186
p	0.002	0.017	0.001	0.006	0.012	0.014	0.016
vr1	age	FS	age	DBT	Hgb	age	FS
coeff	-0.35	0.25	-0.41	-0.31	0.24	-0.24	0.27
vr2	DBT	Hgb	DBT	age	FS	DBT	Hgb
coeff	-0.25	0.17	-0.23	-0.24	0.17	-0.22	0.20
vr3	Hgb			PTH	DBT	Hgb	
coeff	0.04			-0.04	-0.16	0.15	

Table 2. General, clinical and SE values

Variable	Mean	SD	SE variables	Value
Age	52.5	16.2	1st level education	72%
Gender	M	52%	2nd level education or more	28%
Months in HD	48.4	37.2	not working	78%
DBT	23%		working/studying	22%
Hgb	10.5	1.4	income less than ε350/month	94%
KtV	1.75	0.27	living with more than 3	59%
Ph	5.4	1.7	home conditions (0 to 7)	5.45 (±1.33)
PTH	726.3	435.9	family support (+)	78%
BMI	25.3	5.2		
alb	3.79	0.42		
nPCR	1.24	0.24		
Transferrin	224.2	62.2		

MP444 ★ BIOCOMPATIBLE LOW GLUCOSE DEGRADATION PRODUCTS DIALYSIS SOLUTION IMPROVES SURVIVAL IN CAPD PATIENT

Seung Hyeok Han[1], Jee Young Yun[2], Dae Joong Kim[3], Jun Young Do[4], Soon Bae Kim[5], Nam Ho Kim[6], Chul Whee Park[7], Joong Kyung Kim[8], Ki Hyun Kim[9], Dae Suk Han[10]. *[1]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea; [2]Baxter Healthcare Corporation, Seoul, Korea; [3]Department of Internal Medicine, Sungkyunkwan University, Samsung Medical Center, Seoul, Korea; [4]Internal Medicine, Yeungnam University, Seoul, Korea; [5]Department of Internal Medicine, Ulsan University, Asan Medicial Center, Seoul, Korea; [6]Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea; [7]Department of Internal Medicine, The Catholic University, Seoul, Korea; [8]Department of Internal Medicine, Bong Saeng Hospital, Busan, Korea; [9]Department of Internal Medicine, Dong-A University, Busan, Korea; [10]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea*

Introduction and Aims: Despite the proposed beneficial effects of low GDP PD fluid (PDF) on peritoneal membrane, there is limited clinical evidence regarding the patient outcomes of this PDF. This study aimed to investigate if biocompatible low GDP PDF could improve survival in CAPD patients.

Methods: A total of 2,163 incident PD patients from Jul 2003 to Dec 2006 were included from 54 centers in Korea. Outcome data were retrieved retrospectively from the Baxter Korea database. Of the patients, 1,672 were initiated on Dianeal (D) and 461 switched to Physioneal (P). In addition, 491 were initiated on P and 39 switched to D. Patient outcomes were compared by using intention to treat (ITT) and as treated (AT) analysis.

Results: There were no significant differences in gender and the proportion of diabetes and cardiovascular (CV) comorbidity at baseline between the two groups. However, P group was significantly younger (54 vs. 55 years, p<0.05) and used more Extraneal (E) PDF (42.8% vs. 34.7%, p<0.01) compared to D group. In an ITT analysis, Kaplan-Meier plots revealed that 4-yr patient survival was significantly higher (81.7% vs. 70.6%, p<0.01), and 4-yr CV mortality was significantly lower (11.3% vs. 18.3%, p<0.05) in P group, whereas 4-yr technique survival was similar in both groups (86.7% vs. 84.9%, p=0.298). In a multivariate Cox analysis adjusted for age, gender, diabetes, CV comorbidity, center size, socioeconomic status and E use, P use was significantly associated with a lower risk of death

(vs. D, HR 0.71, p<0.05). In addition, age (per 1-yr increase, HR 1.07, p<0.01), diabetes (vs. non-DM, HR 2.02, p<0.01) and CV comorbidity (vs. no, HR 1.37, p<0.05) were identified as significant predictors of death. The survival benefit of P persisted in an AT analysis (4-yr survival, 80.4% vs. 65.5%. p<0.01).
Conclusions: This study shows that biocompatible low GDP PDF might provide survival advantage over conventional PDF. To demonstrate our results, a large randomized prospective study will be needed.

MP445 A MODIFIED SOFA SCORE TO PREDICT HOSPITAL MORTALITY OF ACUTE RENAL FAILURE PATIENTS REQUIRING RENAL REPLACEMENT THERAPY: THE NSARF EXPERIENCE

Yu-Feng Lin[1], Wen-Je Ko[2], Vin-Cent Wu[1], Yung-Ming Chen[1], Ming-Shiou Wu[1], Tzong-Shinn Chu[1], Kung-Yu Hung[1], Tun-Jun Tsai[1], Kwan-Dun Wu[1]. *[1]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; [2]Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan*

Introduction and Aims: A predictive model for intensive care unit (ICU) mortality in post-operative acute renal failure (ARF) patients may aid clinicians' therapeutic decision making and research design.
Methods: To identify predictors of hospital mortality and develop a model using data available prior to renal replacement therapy, we conducted an observational study of 398 post-operative acute renal failure patients requiring renal replacement therapy. The derivation cohort consisted of 334 patients from January 2002 to December 2005. The validation cohort consisted of 64 patients from January 2006 to December 2006.
Results: The hospital mortality rates for the derivation cohort and validation cohort were 65.6% and 62.5%, respectively. Independent predictors of hospital mortality by a multivariable logistic regression analysis included generic sequential organ failure assessment (SOFA) score, serum lactate level, presence of sepsis, status post cardiopulmonary resuscitation, necessity of mechanical circulatory support, necessity of total parenteral nutrition, and age more than 75 years old. A modified SOFA score was constructed by a formula of serum lactate level (mmol/L)+2 x (generic SOFA score) + 8 (if mechanical circulatory support required)+ 10 (if age $\geq$ 75) +10 (if total parenteral nutrition required) +11 (if status post cardiopulmonary resuscitation)+ 14 (if positive sepsis sign). The area under the receiver operating characteristic curve of the model for the derivation cohort and validation cohort were 0.807 and 0.848, respectively. This modified SOFA score model stratified the patients into low risk (<36), intermediate risk (36-48), and high risk (>48) groups with accurate hospital mortality prediction (log-rank, $P<0.001$).
Conclusions: This validated score may assist clinicians in estimating mortality, making therapeutic decisions and planning clinical trials in post-operative acute renal failure patients requiring renal replacement therapy.

MP446 THE PRESENCE OF METABOLIC SYNDROME CORRELATES WITH INSULIN RESISTANCE, ADIPONECTIN AND C REACTIVE PROTEIN IN MAINTENANCE HAEMODIALYSIS PATIENTS

Shao-Yu Yang[1,3], Hung-Yuan Chen[2], Yu-Sen Peng[2], Yen-Ling Chiu[2], Chun-Fu Lai[2], Mei-Fen Pai[2], Shih-Ping Hsu[2], Kuan-Yu Hung[3], Kwan-Dun Wu[3]. *[1]Internal Medicine, National Taiwan University Hospital, Yun-Lin Branch, Douliu City, Yun-Lin County, Taiwan; [2]Internal Medicine, Far-Eastern Memorial Hospital, Taipei, Taiwan; [3]Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan*

Introduction and Aims: Modified Asian criteria of metabolic syndrome (MS) are well accepted for prediction of cardiovascular diseases in Asian general population. However, the studies of the modified criteria in haemodialysis (HD) patients are scarce. Insulin resistance is found to be common in HD patients, and is also an independent predictor of cardiovascular mortality in HD patients. We tried to examine the relationship between the insulin resistance and MS in HD patients by using the modified Asian criteria.
Methods: We included 331 patients receiving maintenance HD for more than 3 months, and used modified Asian criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) with different waist circumference cutoff value (80 cm in female and 90 cm in male) to define the presence of MS. Insulin resistance was evaluated by homeostasis model assessment (HOMA-IR) after overnight fasting. The levels of plasma adiponectin and C reactive protein (CRP) were also measured in these patients.
Results: Using the modified Asian criteria, 163 (49.24%) patients were identified as MS in our study. In patients with MS, the HOMA-IR was significantly higher (10.81±1.1 v.s. 4.3±0.4, p<0.001) than those without MS. On the other hand, in HD patients with MS, the plasma adiponectin levels were lower (11.4±1.0 v.s. 20.6±1.7 mg/L, p<0.001), and the CRP levels were higher (14.2±29.1 v.s. 6.9±11.9 mg/L, p=0.003). The HOMA-IR increased and adiponectin decreased as the components of MS increased (Figure 1 and 2).

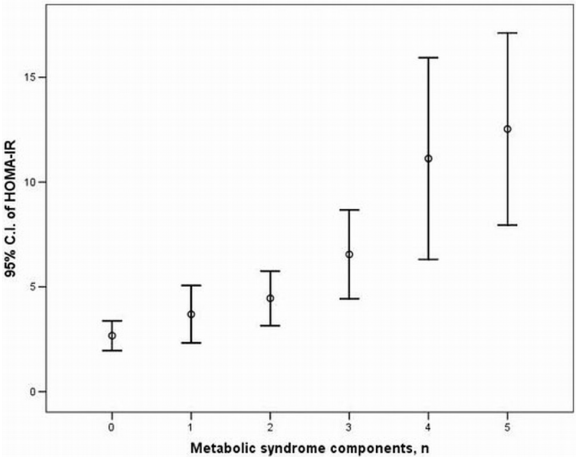


Figure 1

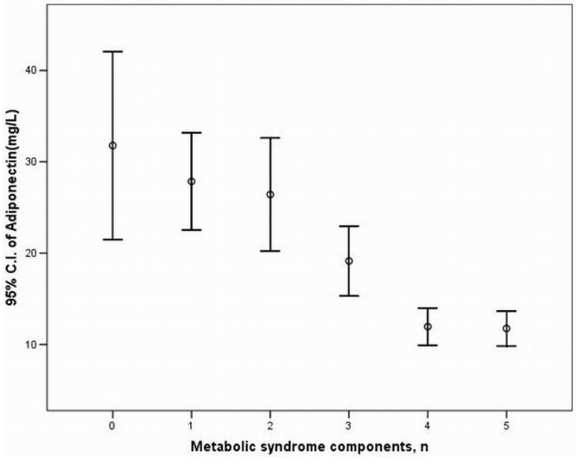


Figure 2

Conclusions: Using the modified Asian criteria, we found that the presence of MS correlates with insulin resistance, CRP, and adiponectin levels in maintenance HD patients. The identification of MS may be as important in HD patients as in the general population.
Disclosure: This abstract was supported by a grant from the Far-Eastern Memorial Hospital (FEMH-95-C-022).

MP447 ASSESSMENT OF NEEDS IN ELDERLY PATIENTS ON CHRONIC DIALYSIS

Renata Klak[1], Joanna Rymaszewska[2], Waclaw Weyde[1], Mariusz Kusztal[1], Magdalena Krajewska[1], Katarzyna Madziarska[1], Marian Klinger[1]. *[1]Nephrology and Transplantation Medicine, Wroclaw Medical University, Wroclaw, Poland; [2]Psychiatry, Wroclaw Medical University, Wroclaw, Poland*

Introduction and Aims: Recognizing the needs of elderly individuals on

maintenance dialysis is essential for effective care and for quality of life improvement. The questionnaire Short Camberwell Assessment of Need for the Elderly (Short CANE) is applicable in general population but was never used in elderly patients who underwent renal replacement therapy (RRT).
Aims of the study were (1) to identify the needs in elderly patients on maintenance dialysis (2) to assess reliability and accuracy of the polish version of Short - CANE.
Methods: The study population encompassed 30 patients over 65 y.o. (mean age 75.5±4.7) who were undergoing haemodialysis (HD; n=25) and peritoneal dialysis (PD; n=5) for at least 6 months (mean dialysis period 49.03±51,8 months). As an investigation instruments, Mini-Mental State Examination (MMSE) and polish version of Short CANE (24 needs' areas) with patients' and investigators' evaluations were used. In those patients who did not reach 19 points in MMSE, the patient' assessment was replaced by the caregiver' assessment.
Results: In general the Cronbach alpha coefficient calculated for 24 areas of Short CANE was high enough (mean α=0,854 for patient; α=0,72 for investigator) to meet psychometric criteria. An internal consistency in patients' and investigators' assessment of needs was also satisfactory (Cohen κ=0,62 for all areas ranging from 1,0 to –0,447 in specific areas). An exceptionally low internal consistency was found in following areas: physical health, violence, behavior, social life, close relationship, money and subsistence allowance.
The MMSE score ranges from 6 to 29 pts (mean 23,57±4,8). General number of needs in patients' assessment was 10,5 (SD=4,38), including 7,67 (SD=3,15) and 2,83 (SD= 2,93) for satisfied and unsatisfied needs respectively. The corresponding numbers of needs in investigators' assessment were 12,2 (SD=2,60), 8,83 (SD=2,67) and 3,33 (SD=3,27).
In investigators' assessment the number of unsatisfied patient needs varied depending on that who was the caregiver, i.e. higher number if child of the patient and lower if spouse.
The longer period of care the lower total number of needs, especially satisfied.
An inverse correlation was found between MMSE score and number of unsatisfied needs (r -0.35, p=0.05).
Individuals with unsatisfied needs in memory areas in patients' assessment showed markedly lower MMSE score, but in investigator' assessment the lowest MMSE was found also in other areas of unsatisfied needs (daily functioning, urination, violence, social life, close relationship).
Conclusions: An application of Short CANE in polish version showed acceptable psychometric parameters. The investigator's assessment of needs in elderly dialyzed patients seems more accurate in the case of low MMSE score because more unsatisfied areas can be identified. The recognition of satisfied and unsatisfied needs in many areas may be helpful in planning and effective care of elderly patients on RRT.

MP448 BURNOUT SYNDROME STUDY AMONG CAREGIVERS OF ELDERLY DIALYZED PATIENTS

Renata Klak [1], Joanna Rymaszewska [2], Waclaw Weyde [1], Mariusz Kusztal [1], Magdalena Krajewska [1], Katarzyna Madziarska [1], Marian Klinger [1]. *[1]Nephrology and Transplantation Medicine, Wroclaw Medical University, Wroclaw, Poland; [2]Psychiatry, Wroclaw Medical University, Wroclaw, Poland*

Introduction and Aims: The studies regarding caregivers were mostly conducted in relation to patients with dementia or those during palliative care so far. Until now there was no published study assessing burden of persons who take care of patients with end-stage renal disease (ESRD) and over 65 y.o.
The aim of this study was to evaluate incidence of the burnout syndrome among caregivers of elderly patients requiring renal replacement therapy (RRT; peritoneal dialysis or haemodialysis).
An influence of physical, emotional, and financial burdens on mental health of caregivers was assessed. Additionally, the relations between severity of patients' dementia symptoms as well as the period of care and caregivers' exertion were analyzed.
Methods: The study encompassed 30 caregivers of patients over 65 y.o. (mean age 75.5±4.7) who were undergoing haemodialysis (HD; n=25) and peritoneal dialysis (PD; n=5) (caregiver's age ranges between 38-82 y.o. and patients' age between 67-83 y.o.). Caregivers completed General Health Questionnaire (GHQ-12) and Questionnaire of Caregiver's Burden (QCB, Ochudlo et al.) whereas patients were screened for dementia using Mini – Mental State Examination (MMSE).
Results: The significant correlations were found between all GHQ-12 and QCB scales, especially in limitation subscale (r 0.53, p=0.002). In subscale "emotions" an inverse association between MMSE and QCB was observed (- r 0.31, p=0.027). In general QCB did not depend on caregivers' sex or source of income; however QCB limitation subscale showed an association with caregiver's age.
Among socio-demographic factors only patients' educational level positively correlated with better psychical state of the caregiver (p=0.05).
Conclusions: Caregivers' burnout markedly influenced their mental condition and daily life organization. An occurance of dementia syndrome in patients significantly escalates burnout in all areas. The psychophysical condition of the caregiver is an important element in complex RRT of elderly patient with ESRD.

MP449 CUMULATIVE INCIDENCE OF PERITONEAL DIALYSIS TECHNIQUE FAILURE: A REGIONAL HISTORICAL COHORT STUDY

Maurizio Nordio, Mariano Feriani, Antonio Piccoli, Barbara Rossi, Francesco Antonucci. *Dialysis and Transplantation Registry of Veneto Region, Italy*

Introduction and Aims: Despite a widespread consciousness that peritoneal dialysis (PD) is affected by an high failure rate, surprisingly only few studies measured this rate and mostly center-based. To estimate the incidence failure, an historical cohort of incident patients enrolled in Veneto Dialysis and Transplantation Registry between 1998 and 2004 was followed up to 31/12/2005.
Methods: PD failure, the principal outcome, was defined as switch to hemodialysis for any reason. Kidney transplantation and death were competitive events. Age (classified in 5 classes: $<$25, 25-45, 45-65, 65-75 and $\geq$75 yo), primary kidney disease and comorbidities (diabetes, ischemic heart disease, heart failure, hypertension, stroke, peripheral vascular disease, liver disease, cancer and pulmonary disease) were considered for possible associations to the primary outcome. Owing to the presence of competitive outcomes, Gray's method was used to estimate the cumulative incidence of PD failure. Gray and Fine's subdistribution proportional hazard model was used to estimate associations with predetermined risk factors.
Results: 763 subjects were followed up. The cumulative incidence of DP failure was 4.59% at the end of the first year, 11.19% at the second, 15.38% at the third, 18.45% at the fourth and 19.88% at five year. The cumulative incidence of kidney transplantation was 34.46% at five year and in the same period the cumulative incidence of death was 14.02%. With subdistribution proportional hazard model, only age was associated to PD failure with a subdistribution hazard ratio = 1.21 (95%CI: 1.03 - 1.42).
Conclusions: The cumulative incidence of PD technique failure in previous center-based studies was estimated at about 30 - 40% in five years. Our results are far better, probably because the cumulative incidence is obtained accounting for the competitive outcomes, while in other papers it wasn't and thus it resulted overestimated. In our population the first cause of drop out from PD is kidney transplantation, technique failure is the second one with an incidence not particularly worrying (about 20% in five years). These findings confirm that PD is suitable for medium and long term treatment. The risk of drop out increases by 20% passing from a class of age to the older one, this observation may reveal not only clinical, but also social problems.

MP450 PSYCHOLOGICAL DISCOMFORT, QUALITY OF LIFE AND CYTOKINE PROFILE IN HEMODIALYSIS PATIENTS

Vincenzo Montinaro, Grazia Iaffaldano, Simona Granata, F. Paolo Schena, Giovanni Pertosa. *Division of Nephrology, University of Bari, Bari, Italy*

Introduction and Aims: Psychological discomfort (depression and anxiety) along with physical co-morbidity affect quality of life (QOL) in HD patients. Blood-artificial surface interaction during HD induces an inflammatory response and increased release of cytokines by peripheral blood mononuclear cell (PBMC). Inflammatory cytokines play a relevant pathogenetic role in

major psychological disorders such as depression. The aim of this study was to assess the psychological discomfort and QOL in HD patients, and to correlate these conditions with the pattern of cytokine production.

Methods: 30 stable HD patients and 20 subject with chronic kidney disease (CKD) stage I–II K-DOQI as controls were enrolled. Psychological discomfort was assessed by the HADS (Hospital Anxiety Depression Scale) test, a 14-item test, which restitutes a global score (range 0-42), an anxiety subset score (ASS, range 0-21) and a depression subset score (DSS, range 0-21). ASS $\geq$ 8 and DSS $\geq$ 8 indicate presence of clinical relevant anxiety and depression, respectively. QOL was evaluated by the kidney disease QOL test (KDQOL; score from 0 to 100). Whole blood samples collected at beginning of HD session were diluted with RPMI/heparin (1:5) and incubated for 24 h in presence of E. coli LPS (10 ng/ml for IL-6 and 100 ng/ml for IL-1β and TNF-α). ELISA for these cytokines was performed on supernatants and the results expressed by normalizing cytokine concentrations per number of PBMC (ng/10^6 cells). Kt/V (Daugirdas formula) and serum albumin were also studied as markers of dialysis efficiency and malnutrition.

Results: HD patients showed an higher incidence of depression (50%) compared with controls (20%, $p<0.0001$), while incidence of anxiety was similar (43% vs. 45% in HD and controls respectively). QOL score was significantly lower in HD (63.7±14.8) compared to controls (74.9±11.9, p=0.006); QOL was inversely correlated with HADS total score, ASS and DSS ($p<0.0001$) in HD patients. Albumin levels and Kt/V values were similar in HD patients with either ASS$\geq$8 or <8 and DSS$\geq$8 or <8. Cytokine production by PBMC was significantly higher in HD patients, compared with controls (IL-1β 4.13±2.65 vs 2.78±1.81, p=0.05; IL-6 15.59±7.61 vs. 10.34±5.39, p=0.010; TNF-α 14.35±6.42 vs. 7.17±2.61, $p<0.0001$). HD patients with the HADS test positive for anxiety or depression showed higher IL-6 production by PBMC, compared with HD patients with HADS test negative for anxiety or depression. This increase was statistically significant for anxiety, not for depression (Table 1).

Table 1

Cytokine	ASS $\geq$ 8	ASS < 8	p	DSS $\geq$ 8	DSS < 8	p
IL-1β	4.11±3.19	4.15±2.25	NS	4.12±2.78	4.15±2.60	NS
IL-6	19.07±6.84	12.93±7.05	0.026	17.87±8.20	13.31±6.46	NS
TNF-α	15.58±6.70	13.40±6.23	NS	13.48±5.53	15.21±7.29	NS

Conclusions: In HD patients the psychological discomfort is relevant with both symptoms of depression and anxiety that affect negatively the QOL. These symptoms are independent of the efficiency of dialysis and nutrition status. On the contrary, inflammation-related production of cytokines, particularly IL-6, is linked to the presence of psychological discomfort in these patients.

MP451 ANALYSIS OF DIABETIC PATIENTS ON RENAL REPLACEMENT TREATMENT: COMPARISON OF TWO PERIODS OF CATALAN RENAL REGISTRY

Teresa Doñate[1], Emma Arcos[2], Jordi Comas[2], Beatriu Bayés[3], Roser Deulofeu[2], Renal Registry Committee[2]. *[1]Servei de Nefrologia, Fundació Puigvert, Barcelona, Catalunya, Spain; [2]Organització Catalana de Trasplantaments, Servei Català de la Salut, Barcelona, Catalunya, Spain; [3]Servei de Nefrologia, Hospital Germans Trias i Pujol, Badalona, Catalunya, Spain*

Introduction and Aims: In recent years we have observed a change in the profile of the patient on Renal Replacement Treatment (RRT) and in the actual treatment, predominantly within the diabetic population. The aim of the study is to compare diabetic patient initiating RRT in two different periods for (I) incidence and prevalence, (II) type of treatment, (III) associated cardiovascular disease and (IV) mortality according to age and type of treatment.

Methods: The two periods analysed were 1984-1994 and 1995-2005 and data from the Catalan Registry of Renal Patients was used.

Results: A total of 936 diabetic patients began RRT in the first period and 2957 patients in the second one. The incidence of diabetic patients on RRT has increased since 1984, moving from 3 patients pmp and 26.6 pmp between 1984 and 1994 to 32.3 pmp and 46 pmp during the years 1995 to 2005. Of the patients initiating RRT between 1995 and 2005, 28% were diabetics, 13 points above those beginning RRT in the period 1984-1994. During the period 1995-2005 the percentage of patients classified as diabetic nephropathy (ND) type I and ND type II diminished when compared with the first period, while diabetes as co-morbidity rose from 9.5% to 30.3%. In age groups, the percentage of new cases over 65 years increased from 43.6% to 65.3%, at the same time as younger patients decreased. Depending on treatment mode at the initiation of RRT, the percentage of patients on peritoneal dialysis fell from 15.8% to 8.3%. In relation to transplant, the proportion of diabetic patients aged between 45 and 65 years old receiving a renal transplant has increased from 4.9% to 18.2%. Greater cardiovascular co-morbidity at the initiation of RRT was observed in the period of 1995-2005, remaining till the end of the period. On the other hand, in the period of 1984-1994 cardiovascular co-morbidity was less frequent at the beginning of RRT and had increased considerable by the end of the period. The percentage of deaths found between the two periods were 51.6% and 57.4%.

Conclusions: Between 1995-2005 the number of diabetic patients initiating RRT increased. Although they were older and with more cardiovascular pathologies (at initiation) than from 1984-1994, no great differences in mortality rates between the two groups were observed. We believe this is due to improved prevention, better treatment of cardiovascular complications and technical advances.

MP452 SOLUBLE TWEAK AND MORTALITY IN INFLAMED PATIENTS UNDERGOING HEMODIALYSIS

Juan Jesus Carrero[1], Alberto Ortiz[2], Abdul Rashid Qureshi[1], Jose Luis Martin-Ventura[2], Peter Barany[1], Olof Heimburger[1], Belen Marron[2], George Metry[1], Sunna Snaedal-Jonsdottir[1], Bengt Lindholm[1], Jesus Egido[2], Luis M. Blanco-Colio[2], Peter Stenvinkel[1]. *[1]Renal Medicine and Baxter Novum, CLINTEC, Karolinska Institutet, Stockholm, Sweden; [2]Vascular and Renal Research Laboratory. Fundacion Jimenez Diaz, Autonoma University, Madrid, Spain*

Introduction and Aims: Chronic kidney disease is characterized by an exceptionally high mortality rate, primarily due to cardiovascular disease (CVD). Abnormal soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) plasma levels have recently been reported as a protein released by human atherosclerotic plaques. We have assessed sTWEAK plasma levels in hemodialysis (HD) patients and their relation with patients' outcome.

Methods: A cross-sectional study was conducted in 218 prevalent patients undergoing hemodialysis (121 male; 63±14 years). Biochemical markers of wasting and inflammation were measured in relation to sTWEAK levels. Overall mortality was assessed after a median of 31 (range 2-42) months. Causes of death were recorded and cardiovascular mortality was also assessed.

Results: Median sTWEAK plasma levels were 208 (range [165-272]) pg/mL, being these values lower in those patients with CVD. sTWEAK was negatively associated with inflammatory markers, such as C-reactive protein (ρ=-0.16, P= 0.01), interleukin-6 (ρ=-0.17, P=0.009), fibrinogen (ρ=-0.20, P=0.001) and white blood cell count (ρ=-0.14, P=0.04). Overall mortality was assessed after an average follow-up of 31 months, during which 81 patients died (34 from CVD). After controlling for potential confounding variables, patients in the upper tertile of sTWEAK plasma levels had an increased risk of cardiovascular and all-cause mortality. The association of sTWEAK with mortality was strongest in patients with inflammation (defined as IL-6>7.0 pg/mL), in whom the upper tertile of sTWEAK predicted cardiovascular [hazard ratio (95% confidence interval), 7.45 (1.98-27.9); p=0.02)] and all-cause [3.91 (1.80-8.45); p=0.0005] mortality. This group of patients also exhibited increased signs of muscle wasting (lower handgrip strength and insulin growth factor-1 levels).

Conclusions: Increased sTWEAK plasma concentrations are linked to increased cardiovascular and all-cause mortality in HD patients with signs of inflammation. Although these results need to be confirmed in larger cohorts, these findings suggest that the combined use of these biomarkers (sTWEAK and IL-6) may help to identify HD patients at a higher risk of death.

MP453 MEDICAL REHABILITATION IN FRAIL AND MULTI-COMORBID HD PATIENTS – GOALS AND EXPERIENCES

Rolfdieter Krause[1], Petra Rech[2], Karin Mienert[1], Christian Zippel[2]. *[1]Nephrological Center Moabit, Kuratorium for Dialysis and Kidney Transpalntation, Berlin, Germany; [2]Clinic for Geriatric Rehabilitation, Median Reha Group, Berlin, Germany*

Introduction and Aims: In Germany approx. 50% of the dialysis population is older than 65 years (up to 91 years). The mean Co-Morbidity-Score is 7,6 (up to 10,2). Therefore medical rehabilitation is of great importance in these patients, especially after hospitalisation.
The aim of the study was to analyze the outcome of patients with end-stage kidney disease after a follow-up stay with special rehabilitation activities.
Methods: 47 (25f) patients, 26 were diabetics, with a men age of 75.6 years (51 - 90 yrs.) on maintenance hemodialysis treatment had a median stay of 23.2 (range 18 - 29) days in a geriatric rehabilitation center. All patients were referred from acute care hospitals due to a variety of injuries: surgical interventions concerning of fractures of femoral bones (16), cardio surgical interventions after acute coronary syndromes (5), amputations of legs (9) and disorders of wounds healing (3). Often the Hct still was below the recommended range due to the acute injuries or treatment, resp.
The patients had daily exercising in condition to their acute injuries: generally a special physical and occupational therapy, intensive nursing care, speech therapy and/or psychological therapy in a multidisciplinary rehabilitation team.
Three times weekly (Tuesday, Thursday, Saturday afternoon) the patients had their routine hemodialysis session in a Nephrological Centre close to the Rehabilitation Clinic.
Results: 1. The Barthel-Index (as teh mostly used index for self-care activities) increased by 25% from 58.5. to 77.5 points. 2. 85% of the patients were able to go back to their own home without need of help for the daily-living-activities. 3. Only one patients needs assisted care at home, and only three patients has to be transferred to a nursing home.
Conclusions: Using individualized rehabilitation measures and procedures also in frail and multi-comorbid elderly hemodialysis patients an effective rehabilitation of daily-living-activities and mobility is practicable. A close interaction between the Rehabilitation Clinic and the Nephrological Centre can optimize the outcome. To stabilize the long-term rehabilitation effects home training instructions and regular activities also during the routine hemodialysis sessions are of great importance for the long-term outcome.

MP454 WHAT CAUSES A HIGHER SAFETY CLIMATE IN THE STAFF OF A DIALYSIS UNIT? REPORT OF AN EVALUATION IN A LARGE NETWORK

Attilio Di Benedetto[1], Manuela Moretti[1], Francesco Pelliccia[1], Wanda D'Orsi[1], Fernando Starace[1], Daniele Marcelli[2]. *[1]NephroCare Italy, Napoli, Italy; [2]NCC, Fresenius Medical Care, Bad Homburg, Germany*

Introduction and Aims: The perception of safety by front-line clinical staff is considered an important indicator on the implementation level of a safety culture. For this purpose the Institute for Healthcare Improvements developed the Safety Climate Survey questionnaire. Another questionnaire evaluating the implementation level of Universal Hygiene Precautions was submitted as well in order to check how an objective procedure influences staff opinion on the safety level. For this, a questionnaire developed by Gershon et al. was selected.
Methods: The questionnaires on Safety Climate and Universal Precautions, the former based on 19 questions, the latter on 14 questions, were submitted to the clinical personnel of a dialysis network located in the south of Italy. 307 staff members of 32 dialysis units were involved in the survey: 24.2% were physicians (thereof 37.6% Directors), 59.6% were Registered Nurses (thereof 21.1% Quality Responsible Head Nurses, QRHN), 14.7% Health-care Assistants (HCA) and 1.4% others. Job experience was remarkable with only 3.2% having less than 6 months, 4.2% between 6 and 12 months, 4.6% from 1 to 2 years, 17.5% from 3 to 7 years, 28.4% from 8 to 12 years, 32.6% from 13 to 20 years, 9.5% more than 21 years of experience in the field.
Results: Mean total score of the Safety Climate was 81.9%, significantly higher for Medical Directors (91.5%) and Head Nurses (87.4%) in respect to the staff physicians (82.4%), Registered Nurses (78.9%) and HCA (78.8%) ($p<0.01$). Job experience did not affect significantly (p=NS) the outcome of the survey. Mean scores reported by the various units differed significantly ($p<0.001$) ranging from a minimum of 45.3% to approximately 100%.
Mean total score of the application of Universal Precautions was 90.8% (SD: 11.0), not different between Medical Directors (92%), other physicians (91.4%) Head Nurses (93.2%) and staff nurses (91.4%). Only HCA reported a significantly ($p<0.05$) lower score (83.6%). The job experience did not affect significantly (p=NS) the outcome of the survey. Mean score reported by the various units differed significantly ($p<0.001$) ranging from a minimum of 80.5% to a maximum of 98.7%.
Using the center as statistical unit, Safety Climate scores were not significantly related with the score on the applications of Universal precautions (r=0.21, p=NS). The same result was confirmed using the job position or the experience (as categorical variable) as statistical unit. The direct correlation between the two questionnaires on the basis of an answer by the same person was not possible due to its anonymous nature.
Conclusions: In conclusion, the top management of the dialysis units, Medical Directors and QRHN, feel safer in their responsibilities in respect to other staff. Is this an effect of the delegation process moving the responsibility to the whole staff? It was also realized that a higher safety climate score is not a consequence of the stricter application of universal precautions or longer experience. It is likely that some other psycho-social or organizational variables are involved.
Disclosure: All authors are employed by the dialyis network mentioned in the abstract.

Renal transplantation – Basic research

MP455 ★ URINE PROTEOMICS PROFILING BY MATRIX-ASSISTED LASER DESORPTION/IONIZATION TIME OF FLIGHT MASS SPECTROMETRY AS A NON-INVASIVE DIAGNOSTIC TOOL IN CHRONIC ALLOGRAFT DYSFUNCTION

Luis F. Quintana[1], Amanda Solé[2], Susana Kalko[3], Elisenda Bañon[2], Joaquin Abian[4], Josep M. Campistol[1]. *[1]Servicio Nefrología y Trasplante Renal, Hospital Clinic, Barcelona; [2]Laboratorio Experimental Nefrología y Trasplante Renal, Hospital Clinic/IDIBAPS, Barcelona; [3]Unidad de Bioinformatica, Hospital Clinic/IDIBAPS, Barcelona; [4]Laboratorio de Proteomica, Universidad Autonoma de Barcelona/CSIC, Barcelona, Spain*

Introduction and Aims: Kidney transplantation is the treatment of choice for end-stage renal disease. However, over 50% of transplants fail, despite optimal immunosuppressive therapy, because of progressive chronic allo-graft dysfunction (CAD). Optimizing the differential diagnosis of CAD is essential to improve results and graft half-life.
The aim of this study was to evaluate whether solid phase extraction coupled with mass spectrometry detects differences in the urinary polypeptide pattern in patients with interstitial fibrosis and tubular atrophy (IF/TA) with any other specific etiology, patients with chronic active antibody-mediated rejection (CAAR) and two control populations.
Methods: We studied 36 individuals during the analysis, 18 were patients with CAD and 18 were controls. Patients were divided into two groups: 1) 8 patients (five men and three women) with interstitial fibrosis and tubular atrophy with no evidence of any specific aetiology (IF/TA= group 1). 2) Ten patients (7 men and 3 women) with chronic active antibody mediated rejection (CAAR= group 2). There were no clinical statistical differences between groups. All transplant cases received immunosuppressive treatment with a calcineurin inhibitor, mycophenolate mofetil and prednisone.
The control group was divided into two groups: 1) stable renal transplants: eight live donor recipients of a first renal graft (mean age 36,2, mean serum creatinine of 1,08 mg/dl and mean proteinuria 205,2 (176-273)mg/day). 2) Healthy: ten individuals; volunteers, (mean age 43 years; 7 men and 3 women, mean creatinine 0,91 mg/dl, GFR 110 ml/min, mean microalbuminuria/creatinuria 4 mg/g mean proteinuria/creatinuria 39 mg/g).
Results: CAD pattern had peak clusters in three regions corresponding to mass/charge (m/z) values of 2628 to 2922, 4307 to 4799 and 8303 to 8850 that always occurred together, whereas control urine protein had no peak clusters in these m/z regions. Moreover, the composition of urine proteome of the IF/TA group differed from that of the CAAR group.

Statistical analysis identified 800 m/z differential points without negative discriminative capacity between CAAR and IF/TA. Nevertheless, highly significant peak values ($q \leq 0.05$ and Fold change ≥ 1.2) were grouped in the following m/z values: 4925 to 5376, 6147, 7267, 13477 to 13864, 13932 to 14387, 14413 to 14596, 14785 to 15086, 15312 to 15346, 16250 to 16590, 16723 to 17592, and 17825 to 17994.
Conclusions: In conclusion, this study establishes for the first time a non-invasive diagnostic pattern for two histological lesions of CAD (IF/TA vs CAAR), with distinct graft outcome.

MP456 INVOLVEMENT OF PELVIC UROTHELIUM IN RENAL ALLOGRAFT REJECTION

Dan Phan[1], Gary Barone[2], Neriman Gokden[1]. *[1]Pathology, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [2]Transplant Surgery, University of Arkansas for Medical Sciences, Little Rock, AR, USA*

Introduction and Aims: Studies of renal allograft rejection focus almost exclusively on the donor cortex and medulla. Little attention is paid to the renal pelvic urothelium as a target of acute cellular rejection in the literature. We reviewed the nephrectomy specimens removed for irreversible renal allograft rejection for possible involvement of renal pelvis by acute cellular rejection (ACR).
Methods: Retrospectively, 31 renal allograft nephrectomies were identified between 1998 and September 2007 in surgical pathology files at a single academic institution. H&E- and PAS-stained slides were reviewed by 2 investigators (DP, NG) and those cases with intact renal pelvis were identified. Immunohistochemical (IHC) stains with prediluted antibodies (all from Ventana, Tucson, AZ) including CD3 for T-lymphocytes and CD20 for B-lymphocytes, and CD68 for macrophages were performed on the sections where the renal pelvis was available, using heat induced epitope retrieval and standard avidin-biotin techniques. The distribution of the infiltrates in pelvic urothelium (PU) and IHC staining patterns were tabulated and correlated with histologic findings in the cortex and medulla.
Results: Of 31 rejected kidneys, 22 had intact renal pelvis available for evaluation and IHC. 12 of 22 (55%) cases had multifocal and 10 of 22 (45%) had focal infiltration of PU by predominantly T-lymphocytes, and scattered macrophages and B-lymphocytes. 9 of 12 (75%) cases with multifocal PU infiltrates also had concomitant ACR, type I and/or type II and/or type III and 3 of 12 (25%) had concomitant chronic allograft nephropathy (CAN). 3 of 10 (33%) cases with focal PU infiltrates showed co-existent ACR, type I and/or II, and 7 of 10 (66%) had co-existent marked CAN. The degree of PU infiltrates correlated with that of renal parenchyma.
Conclusions: Rejection types of changes were present in renal PU in all cases, where renal pelvis was sampled. PU appears to be multifocally involved in 75% of acute rejection process, and is focally and less commonly involved in CAN cases (25%). In deep renal allograft biopsies containing PU and missing cortical tissue for evaluation, infiltration of PU by T-lymphocytes should be taken into account as evidence for possible co-existent acute cellular rejection in the cortex, particularly in cases where the PU infiltration is multifocal.

MP457 EFFECTS OF INOSINE MONOPHOSPHATE DEHYDROGENASE INHIBITION ON PLATELET-DERIVED GROWTH FACTOR-INDUCED FIBRONECTIN SECRETION AND CELLULAR OXYGEN SPECIES IN MOUSE MESANGIAL CELLS

Jehyun Park[1], Byung Jun So[2], Hee Chul Yu[3], Myoung Soo Kim[1], Yu Seun Kim[1]. *[1]Surgery, Yonsei University Medical Center, Seoul, Korea; [2]Surgery, Wonkang University Hospital, Iksan, Korea; [3]Surgery, Chonbuk University Hospital, Jeonju, Korea*

Introduction and Aims: Mesangial cell extracellular matrix (ECM) synthesis plays an important role in various renal diseases. Mycophenolic acid (MPA), which is an inhibitor of inosine monophosphate dehydrogenase (IMPDH), inhibits mesangial cell proliferation and ECM synthesis. However, the exact mechanism of MPA has not been clearly elucidated in mesangial cells. To examine the relative importance of IMPDH on the inhibitory action of MPA, this study compared the effects of MPA or IMPDH2 siRNA on platelet-derived growth factor (PDGF)-induced fibronectin secretion and cellular reactive oxygen species (ROS) by mouse mesangial cells (MMC).
Methods: MMC were stimulated with PDGF 10 ng/ml with or without MPA 0.1-10 μM, IMPDH2 siRNA 10-50 nM, or N-acetylcystein (NAC). IMPDH2 siRNA was transiently transfected by lipofectamine for 24 hours. MPA 0.1-10 μM, ribavirin 10-100 μM, and NAC 5 mM were administered 1 hour before the stimulation. Cell viability was measured by methylthiazoletetrazolium (MTT) assay, fibronectin secretion by Western blot analysis, and dichlorofluorescein (DCF)-sensitive cellular ROS by flow cytometry.
Results: PDGF 10 ng/ml effectively increased fibronectin secretion and cellular ROS in MMC. MPA and NAC at concentration without affecting basal level of fibronectin and cellular ROS ameliorated PDGF-induced fibronectin secretion and cellular ROS. However, IMPDH2 siRNA only partially reduced PDGF-induced fibronectin secretion and cellular ROS in MMC.
Conclusions: These results suggest that MPA may inhibit PDGF-induced fibronectin secretion partly through IMPDH2 or cellular ROS in MMC and that there may be other mechanisms on the inhibitory action of MPA in mesenchymal cells.

MP458 ★ MODULATION OF IMMUNO-PROTEASOME IN CIRCULATING LYMPHOMONOCYTES OF PATIENTS WITH IgA NEPHROPATHY AFTER TRANSPLANTATION

Roberta Camilla[1], Elisa Loiacono[1], Licia Peruzzi[1], Alessandro Amore[1], Alfarano Alda[2], Valentina Minieri[1], Valentina Daprà[1], Maurizio Salvadori[3], Elisabetta Bertoni[3], Giuseppe Montagnino[4], Roberta Giraudi[5], Giuseppe Segoloni[5], Chiara Venturelli[6], Francesco Scolari[6], Antonio Dal Canton[7], Rosanna Coppo[1]. *[1]Nephrology, Dialysis, Transplantation, R. Margherita Hospital, Turin; [2]Dept of Pediatrics, Univ. of Turin, Turin; [3]Transplantation Units of, Careggi Hospital, Florence; [4]Policlinico, Milan; [5]Univ. of Turin, Turin; [6]Univ. of Brescia, Brescia; [7]Univ. of Pavia, Pavia, Italy*

Introduction and Aims: The immuno-proteasome (iPS) derives from the effect of IFNγ and α on proteasome (PS), inducing substitution of 3 PS catalytic units β1, β2, β5 with low molecular weight proteins (LMP 2, LMP7) and endopeptidase-like complex (MECL1) conferring optimal catalytic property for professional presentation of peptides to MHC Class I and T lymphocyte response strengthening. In a previous study we demonstrated in IgA nephropathy patients (IgAN) a significant switch in peripheral lymphomonocytes (PBMC) of 2 PS mRNA subunits to the corresponding iPS (β2 to MECL1 and β5 to LMP7). Now we aimed at investigating the switch from PS to iPS in PBMC of IgAN patients which progressed to dialysis and transplantation (Tx).
Methods: In a prospective arm we investigated 8 subjects within the first 24h of kidney Tx and after 1 year. In a retrospective arm we studied 12 IgAN patients Tx >5 years before; 5 of them had IgAN recurrence evaluated by renal biopsy. PBMC mRNAs were tested with real-time PRC (Taqman) to assess semiquantitatively mRNA levels of PS constitutive α subunit, active (β1, β2, β5) and iPS (LMP2, LMP7 and MECL1).Data were expressed as ratio between normalized values to the housekeeping gene Abelson.
Results: In the prospective arm, MECL/β2 ratio proved significantly increased in IgAN at Tx vs both healthy controls (p=0.0002) and 56 IgAN patients with normal renal function (p<0.0001). After 12 months, MECL/β2 was significantly blunted (p=0.028) getting to the same level of IgAN patients with normal renal function. In the long term, as demonstrated in IgAN patients Tx since >5 years on the retrospective arm, MECL/β2

Abstract MP458 – Table 1

	HC	IgAN	IgAN at TX	IgAN TX at 12m	IgAN TX >5 years	IgAN RELAPSE	IgAN NO RELAPSE
MECL/beta2	1.02±0.30	1.49±0.89	6.17±6.24	1.30±0.11	2.35±1.12	2.83±1.26	1.73±0.46
LMP2/beta1	0.9±0.42	1.01±0.65	2.05±0.69	1.69±0.78	1.53±0.60	1.26±0.33	1.91±0.72
LMP7/beta5	1.07±0.33	1.73±1.36	1.09±0.27	1.33±0.55	1.32±0.44	1.37±0.42	1.23±0.51

increased again significantly compared to the levels reached after 12 months of Tx (p=0.02). Of interest, patients with recurrent IgAN had MECL/β2 significantly higher than non recurrent (p=0.049).No modification in the other iPS/PS ratio were observed during the course of renal Tx of patients with IgAN.

Conclusions: In conclusion, we observed a switch from PS to iPS mRNAs in PBMCs of patients with IgAN, particularly relevant in cases who progressed to dialysis. The switch from PS to iPS is modulated by immunosuppressive therapies after Tx and in patients with recurrence is significantly higher than in non recurrent.

MP459 IMPACT OF CYTOKINE GENE POLYMORPHISMS ON THE OUTCOME OF RENAL TRANSPLANTATION

Monika Buraczynska, Anna Bednarek-Skublewska, Iwona Baranowicz-Gaszczyk, Lucyna Jozwiak, Andrzej Ksiazek.
Nephrology, University Medical School, Lublin, Poland

Introduction and Aims: Immunologic pathways play an essential role in renal allograft dysfunction (ischemia-reperfusion injury, acute rejection, chronic rejection). These processes are mediated by cytokines and chemokines. Pretransplantation identification of patients at an increased risk for adverse events would allow individualized treatment strategies and improved long-term outcome. The aim of our study was to determine whether the single nucleotide polymorphisms (SNP) in the TNF-alpha, TGF-beta and IL-6 genes in kidney recipients influence the outcome of renal transplantation.

Methods: A total of 349 kidney transplant recipients and 300 healthy controls were genotyped for 3 single nucleotide polymorphisms: T869C in transforming growth factor-β (TGF-β), G -308A in tumor necrosis factor-α (TNF-α) and C -634G in interleukin-6 (IL-6). The genotyping was performed using a polymerase chain reaction (PCR) technique followed by digestion with restriction endonucleases (Pst I, Nco I and Bsr BI, respectively).

Results: For all three polymorphisms the allele and genotype frequencies were similar between the kidney transplant recipients and control subjects. Distribution of genotypes did not deviate from Hardy-Weinberg equilibrium in healthy controls or among patients. For the +869 TGF-β polymorphism, the low production genotype (carriers of the C allele) was associated with risk for acute and chronic rejection. In the subgroup of patients with this genotype, acute rejection rate was 53.2% compared to 26.1% in kidney recipients with high producer genotype ($p<0.01$). The low production genot pe was found in only 4% of patients with the graft functioning > 10 years. For the -308 TNF-α polymorphism, the carriers of the A allele had a significantly increased risk of acute kidney rejection, with OR 3.9, 95% CI 1.8-7.3. The combination of the -308A homozygous and heterozygous genotypes with low production genotype of the TGF-β polymorphism did not further increase risk of acute rejection (p=033). For the -634 IL-6 polymorphism only the preliminary study was performed. The heterozygous CG genotype of this polymorphism was observed in 26% of transplant recipients with acute rejection, compared to 12% in chronic rejection group ($p<0.05$). Interesting observation was that all acute rejection patients with this genotype had a longer time interval between the onset of ESRD and kidney transplantation.

Conclusions: We conclude that recipient TGF-β and TNF-α gene polymorphisms influence the outcome of renal transplantation. Both polymorphisms seem to be associated with increased risk of acute rejection and might help with identifying high risk renal transplant candidates.

MP460 ♦ NON-INVASIVE DETECTION OF ACUTE ALLOGRAFT REJECTION AFTER RAT RENAL TRANSPLANTATION BY FLUOR-DESOXY-GLUCOSE-SMALL-ANIMAL-POSITRON EMISSION TOMOGRAPHY

Stefan Reuter[1], Uta Schnoeckel[2], Michael Schaefers[2], Rita Schroeter[1], Eberhard Schlatter[1], Gert Gabriels[1]. *[1]Department of Internal Medicine D, University Muenster, Muenster, Germany; [2]Department of Nuclear Medicine, University Muenster, Muenster, Germany*

Introduction and Aims: Episodes of acute rejection (AR) are a negative prognostic factor for long-term renal graft survival. Therefore, a non-invasive tool for the detection of AR which can be applied in the early phase is desirable. AR is associated with graft infiltration and activation of leukocytes. They show a distinct accumulation of ^{18}F-Fluor-Desoxy-Glucose (^{18}F-FDG). The aim of the present study was to evaluate the relevance of ^{18}F-FDG-Positron emission tomography (PET) for detection and follow-up of acute rejection processes occurring in an allogeneic rat renal transplantation model.

Methods: 3h after after i.v. injection of 30 MBq ^{18}F-FDG into adult uni-nephrectomized, allogeneically transplanted rats (LBN to Lewis), tissue radioactivity was assessed in vivo by a small animal PET scanner (post operative day 1-4) and post mortem dissection (day 4). The mean radioactivity (counts per mm^3) tissue was compared between graft and native kidney. These results were confirmed by histological and autoradiographic analysis. Healthy and syngeneic transplanted rats served as controls.

Results: ^{18}F-FDG uptake of graft was elevated from the first post operative day (POD) on when compared to the native kidney (graft/native kidney: POD 1: 2.6±0.32; POD 2: 2.3±1.1; POD 3: 2.17±0.5; POD 4: 3.36±0.45; all results $p<0.05$; n=4-8). No differences between kidneys were found in healthy controls (n=5) and syngeneically transplanted kidneys (n=5). In vivo uptake of ^{18}F-FDG correlated with results obtained by microautoradiography (fig. 1) and inflammatory infiltrates observed in histology.

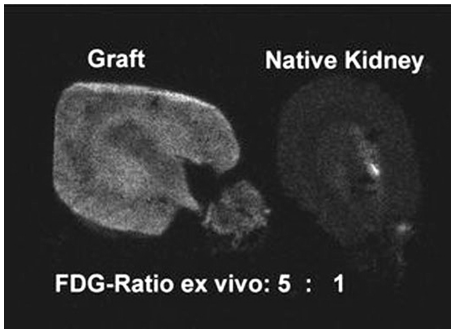


Figure 1. Microautoradiography obtained on postoperative day 4.

Conclusions: Assessment of renal ^{18}F-FDG-uptake is a new, non-invasive diagnostic tool for early detection and rating of the inflammatory process with AR in rat renal transplantation. This method may be useful to investigate the kinetics of acute rejection and response to therapeutic interventions.

MP461 ★ COMPARABILITY BETWEEN THE CMV SEROSTATUS AND THE PRESENCE OF CMV-SPECIFIC T CELLS IN SOLID ORGAN TRANSPLANT CANDIDATES: A CROSS-SECTIONAL OBSERVATIONAL CLINICAL STUDY

Amaryllis H. Van Craenenbroeck[1,2], Viggo F. Van Tendeloo[2], Tessa Braeckman[2], Jacques J. Sennesael[3], Zwi N. Berneman[2], Gert A. Verpooten[1]. *[1]Department of Nephrology-Hypertension, Antwerp University Hospital; [2]Vaccine & Infectious Disease Institute - Faculty of Medicine, University of Antwerp; [3]Department of Nephrology, University Hospital Brussel, Belgium*

Introduction and Aims: Cytomegalovirus (CMV) is a persistent herpes virus responsible for a major part of the opportunistic viral infections occurring in immunocompromised solid organ transplantation patients. Despite the availability of effective antiviral therapy, CMV disease remains an important cause of morbidity and mortality the first months after transplantation.

Considering the intracellular nature of CMV, cellular immunity plays an important role in controlling viral replication and proliferation. Detecting circulating CMVpp65 epitope-specific CD8$^+$ cytotoxic T lymphocytes by MHC I multimer analysis offers the opportunity to follow closely and in a direct manner the cellular immune response triggered by infection or reactivation. To determine the value of the presence of CMV-specific CD8$^+$ cytotoxic T lymphocytes as a monitoring instrument in different diagnostic and therapeutic settings (including cellular immunotherapy), it is useful to investigate the degree to which serostatus and T cellular response are comparable in the population of interest.

Methods: Peripheral blood samples were taken from 21 HLA-A2$^+$ candidates for renal transplantation. Both IgM and IgG were determined using a commercial ELISA kit. After isolating peripheral blood mononuclear cells (PBMCs), circulating CMV-specific CD8$^+$ T lymphocytes were detected *ex vivo* by staining with CMVpp65 (aa 495-503; NLVPMVATV) peptide-MHC I tetramers and subsequent flowcytometric analysis. The same staining and analysis protocol was then repeated on the PBMCs 7-10 days after *in vitro* challenge with CMVpp65 peptide.
Results: Seropositivity, defined as IgG > 0,4 IU/ml, was found in 9 of 21 subjects (43%). CMVpp65-specific CD8$^+$ T cells could be detected in 5/9 (55%) seropositive subjects. The percentage of tetramer-positive cells within the CD8$^+$ T cell population specifically recognizing the CMVpp65 epitope ranged from 1,02% to 2,06%.
A positive IgM titer was found in 2 of 21 subjects (9,5%). One of them showed an IgG titer < 0,4 IU/ml, the other one was seropositive. In both, CMVpp65-specific CD8$^+$ T cells were found (100%) within a range of 1,33% to 1,75% tetramer-positive cells of all CD8$^+$ T cells.
In 11 out of 11 subjects with an IgG value < 0,4 IU/ml and negative IgM titer, no CMVpp65-specific CD8$^+$ T cells could be detected.
In 4/5 of *ex vivo* tetramer-positive T cell samples, no expansion of CMVpp65-specific CD8$^+$ T cells could be detected following one round of *in vitro* stimulation with CMVpp65 peptide. Of the 12 seronegative subjects, one showed positive tetramer staining after *in vitro* peptide stimulation.
Conclusions: CMVpp65-specific CD8$^+$ T cells can be detected in 55% of CMV-seropositive candidates for solid organ transplantation. A mixed lymphocyte peptide coculture (MLPC) of 7-10 days does not result in expansion of CMV pp65-specific T cells as detected by MHC I multimer analysis.

MP462 SIROLIMUS, BUT NOT CALCINEURIN INHIBITORS, BLUNTS RENAL ISCHEMIA-REPERFUSION INJURY IN RATS

Fabrizio Grosjean, Ciro Esposito, Massimo Torreggiani, Vittoria Esposito, Filippo Mangione, Luigi Villa, Clara Migotto, Nicoletta Serpieri, Antonio Dal Canton. *Unit of Nephrology, Policlinico San Matteo, University of Pavia, Pavia, Italy*

Introduction and Aims: Immunosuppressive drugs may modulate the inflammatory response after ischemia-reperfusion injury (I/R) but may also contribute to renal damage We evaluated the effects of immunosuppressive drugs in a model of renal ischemia-reperfusion in rats.
Methods: Monolateral renal I/R was induced in Sprague-Dawley rats by clamping the right renal artery for 60 min. Rats were then randomized into four groups: A (n=5): cyclosporine; B (n=5) tacrolimus; C (n=5) sirolimus; group D (n=5) saline; E (n=4 sham operated rats, saline. Drugs serum levels were measured every 10 days to adjust the dose. After 30 days GFR, measured separately for each kidney, histological (H&E, PAS, Sirius red), immunohistochemical (ED-1, vimentin) and molecular analysis (TaqMan real-time PCR) were performed.
Results: In groups A and B ischemic kidney weight was reduced compared to controlateral ($p<0.001$) and with group CThere was no difference in body weight (bw) between groups A,B,C (352,0±28,8 vs 332,6±37,5 vs 371,8±28,6 vs 400,8±20,1 g, respectively), whereas bw of group D was slightly increased (400.8±20.1 g). Cyclosporine and tacrolimus levels were 419,3±134,4 and 13,2±6,7 ng/ml respectively. Treatment with calcineurin inhibitors lowered significantly the weight of ischemic kidney compared to the ischemic kidney of control and sham operated rats (1.3±0.2 vs 0.8±0.1 vs 2.0±0.1 vs 1.8±0.1 g, A, B, C, D, respectively, $p<0.01$, $p<0.001$). GFR of ischemic kidney was significantly reduced by cyclosporine and even more by tacrolimus compared to controlateral kidney (403.2±302.5 vs 1006±483.7 ml/min $p<0.05$; 125.8 ± 169.6 vs 567.3±374.1 ml/min $p<0.05$ A and B respectively). GFR of ischemic kidney was reduced by cyclosporine compared to control and sham operated rats (618.8±241.7 vs 736.8±350.2 ml/min C and D respectively) and was significantly reduced by tacrolimus compared with the same groups ($p<0.05$).Histological examination of ischemic kidneys showed diffuse interstitial infiltrate in I/R controls and tacrolimus treated rats. In cyclosporine treated rats there was a marked reduction of interstitial infiltrate with an increase of fibrosis and intimal thickening of small vessels. Controlateral kidneys and both kidneys in the sham operated group didi not show any changes. Real time PCR of mRNA extracted from renal cortex showed a significantly decrease of fibronectin and TGF-b expression measured as ischemic/controlateral kidney ratio in tacrolimus and cyclosporine treated rats.
Conclusions: In conclusion our study shows that the changes induced by ischemia-reperfusion are still present after 30 days in Sprague-Dawley rats. Calcineurin inhibitors may modulate I/R injury with changes in the interstitial infiltrate and in the expression of matrix components and fibrogenic factors.

MP463 CD4+CD25+Foxp3+ REGULATORY T CELLS BEFORE AND AFTER INDUCTION PHASE OF IMMUNOSUPPRESSION IN KIDNEY TRANSPLANT RECIPIENTS

Carmelo Libetta [1], Valentina Portalupi [1], Vincenzo Sepe [1], Massimo Abelli [2], Elisa Margiotta [1], Laura Cosmai [1], Michele Canevari [1], Federica Meloni [3], Monica Morosini [3], Antonio Dal Canton [1]. *[1] Unit of Nephrology Dialysis and Transplantation, University and IRCCS Policlinico San Matteo, Pavia, Italy; [2] Unit of Renal Transplantation, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [3] Unit of Respiratory Disease, University and IRCCS Policlinico San Matteo, Pavia, Italy*

Introduction and Aims: Immunosuppressive drugs are essential for the prevention of acute transplant rejection but some may not promote long-term tolerance. Tolerance to self-antigens is ensured naturally by several mechanisms; one major mechanism depends on the activity of regulatory T lymphocytes (Treg) particolarly CD4+CD25+ T cells. The transcription factor forkhead box protein 3 (Foxp3) has been identified as a molecular marker for Treg cells. The direct effects of immunosuppressive drugs on CD4+CD25+ cells are uncertain. In the clinical setting, basiliximab used in the induction phase of immunosuppression effectively reduced the number of acute rejection episodes. We studied the effects of the most widely used induction immunosuppressive regimes including calcineurin inhibition (cyclosporin, CsA), micophenolate Mofetil (MMF), steroids, monoclonal antibody anti-CD25 (Basiliximab) on the capacity of regulating human CD4+CD25+ cells in vivo.
Methods: Twenty recipients of first cadaveric kidney transplantation (14 males, 6 females) were enrolled into the study. All blood samples were collected before (PRE) kidney transplantation and after one month (POST). Blood was always collected from patients just before the assumption of immunosuppressive therapy and after overnight fasting. All transplanted patients did not present laboratory or clinical signs of both infection or acute rejection. The frequency of CD4+CD25+ and Foxp3+ T cells was determined by Fluorescence Activated Cell Sorter (FACS) analysis.
Results: The results are reported as mean ± SD:

	PRE (%)	POST (%)	PRE (n)	POST (%)
CD4+CD25+	8.4±4.6	0±0	585.7±384.5	0±0
CD4+CD25+Foxp3	1.39±0.96	0±0	93.3±61.1	0±0
lymphocytes Foxp3+	2.06±1.08	1.47±1.15	135.9±69.2*	77.2±63.4
CD4+	31.7±13.4	24.3±8.7	2208±1207*	1314±680
CD4+ Foxp3	3.9±2.1	2.4±2.0	264.1±150.8*	128.1±116.0

*$p<0.05$ vs POST.

Our results showed the absence of both CD4+CD25+ and CD4+CD25+Foxp3+ T cells just after tolerance induction. Instead, both the absolute number of peripheral CD4+Foxp3+ and total Foxp3+ lymphocytes were not significantly decreased after kidney transplantation when compared to PRE. The CD4/CD8 subpopulation did not decrease after transplantation.
Conclusions: These preliminary data suggest that CD4+CD25+ regulatory cells are completely suppressed by immunosuppressive induction therapy with basiliximab reducing significantly the total number of Foxp3+ lymphocytes.

MP464 Th1 IMMUNE RESPONSE AND ISCHEMIA-REPERFUSION (I-R) INJURY IN RENAL GRAFT RECIPIENTS WITH DELAYED GRAFT FUNCTION (DGF)

A. Loverre[1], M. Taveri[1], R. Verrienti[1], G. Zaza[1], M. Rossini[1], R. Melchiorre[1], G. Castellano[1], P. Ditonno[2], M. Battaglia[2], F.P. Selvaggi[2], A. Crovace[3], F.P. Schena[1], G. Grandaliano[1]. [1]*Nephrology, Dialysis and Transplant Unit, DETO, University of Bari, Bari, Italy;* [2]*Urology and Transplant Unit, DETO, University of Bari, Bari, Italy;* [3]*Veterinary Unit, DETO, University of Bari, Bari, Italy*

Introduction and Aims: I-R injury in transplanted kidney is a major cause of DGF, an event associated with an increased risk of acute rejection. Adaptative immunity was suggested to play a role in the pathogenesis of renal I-R injury, although the influence of the Th1/Th2 bias in this scenario is still debated. Thus, the aim of the present study was to evaluate the features of T cell response during I-R injury at the peripheral and tissue level in renal graft recipients with DGF.
Methods: The mRNA levels of specific Th1 (T-bet) and Th2 (GATA-3) transcription factors were evaluated in circulating lymphomonocyte of kidney transplant recipients with early graft function (EGF) (n=10) and DGF (n=10), before (T0) and 24 hours after transplantation (T24) by real time PCR. Infiltrating lymphocytes were characterized in graft biopsies of patients with DGF (n=40) and in a control group of patients with tubular damage by acute CNI toxicity (n=10) by immunohistochemistry. In addition, we evaluated the Th1/Th2 bias at the renal level in a pig model of I-R injury.
Results: T-bet/GATA-3 mRNA ratio was similar in the 2 groups of patients at T0. At T24 the DGF group presented a significantly higher increase of T-bet/GATA-3 ratio compared with the EGF group (798±346 vs 288±147% of T0, $p<0.001$). Moving to the tissue level, DGF patients presented a number of interstitial $CD4^+$ (8.0±5.1 vs 2.6±2.1, p=0.04) and $CD8^+$ (10.8±6.7 vs 4±2, p=0.02) T cells significantly higher compared to the control group, while no significant differences were observed in $CD20^+$ cells number between the two groups. Also at the tissue level the ratio between T-bet^+ and GATA-3^+ cells was significantly higher in the DGF compared with the control group (3.5±1.8 vs 1.1±0.9, respectively, p=0.005). To confirm that these changes were due to I-R, we investigated the presence of T-bet^+ and GATA-3^+ cells in a pig model of I-R injury. Interestingly, the ratio was significantly increased after 24 hours of reperfusion (basal 2.5±0.9 vs 24 hours 8.1±3.6; p=0.02).
Conclusions: In conclusion, our results suggest that kidney transplant recipients with DGF present a bias toward a Th1-driven immune response both at the peripheral and at the tissue level. This event, due to the I-R process, as suggested by the animal model, may represent a link between DGF and acute graft rejection.

MP465 IMMUNOHISTOCHEMICAL CHARACTERIZATION OF GLOMERULAR (G) AND TUBULOINTERSTITIAL (TI) INFILTRATE IN RENAL TRANSPLANT PATIENTS (Pts) WITH CHRONIC ALLOGRAFT DYSFUNCTION (CAD)

M. Rossini, C. Divella, A. Loverre, A. Schena, A. Maiorano, V. Gesualdo, G. Zaza, G. Grandaliano, F.P. Schena. *Nephrology, Dialysis and Transplant Unit, DETO, University of Bari, Bari, Italy*

Introduction and Aims: The term chronic allograft nephropathy (CAN) has been abolished by the last Banff Meeting Report (Am J Transplant, 2007) and 2 categories have been introduced for chronic changes: chronic active T cell-mediated rejection and chronic active humoral rejection (CAHR). Aim of the study was to review all cases of CAN diagnosed in the last 4 years and to identify immunohistochemical markers of chronic rejection.
Methods: A cohort of 79 CAD pts with biopsy-proven CAN was analyzed. Each case was reviewed and assigned into 3 groups according to Banff 2005 criteria: chronic rejection (CR), chronic calcineurin toxicity (CNIT) or chronic lesions not otherwise specified (NOS). CD4+, CD8+, CD20+, CD68+ cells and C4d deposits were assessed by immunohistochemistry.
Results: Twenty-eight pts were classified as CNIT, 34 as CR, 19 of which were CAHR, and 17 as NOS. Serum creatinine and 24h proteinuria at renal biopsy, extent of interstitial fibrosis and glomerulosclerosis were not significantly different among 3 groups (table). The number of $CD4^+$ cells was higher at TI level in CR compared to CNIT (Table, *p=.05). $CD8^+$ cells were higher at TI and G level in CR compared to CNIT (Table, *p=.05). TI and G $CD20^+$ cells were not different among the 3 groups (Table). The number of G $CD68^+$ cells was increased in CR compared to CNI and NOS (Table, *p=.05). No significant difference in CD20, CD4, CD8, CD68 expression was found at TI and G level between $C4d^+$ and $C4d^-$ cases of CR. CD68, CD8, CD4 but not CD20 expression at TI level correlated with TI fibrosis (R^2=.105,.077,.156, respectively, $p<.05$) at the univariate analysis. Only TI $CD4^+$ cells independently correlated with fibrosis at multiple regression analysis.

	CR	CNIT	NOS
SCr (mg/dl)	2.7±1.4	2.5±1.1	2.1 ±.8
24h prot (g/24h)	2.1±2.7	2.1±6.2	1.5±1.5
TI Fibrosis (%)	37.0±18.7	33.0 ±12.7	33.2±28.6
TI CD4 (cell/hpf)	15.5±13.9*	10.2±6.2*	11.4±12.1
GCD4 (cell/glom)	0.5±1.4	0.3±0.5	0.4±0.9
TI CD8 (cell/hpf)	31.02±18.7*	19.6±12.9*	24.6±17.7
G CD8 (cell/glom)	1.05±1.5*	0.2±0.3*	0.6±1.1
TI CD20 (cell/hpf)	9.7±10.8	8.6±9	7.9±9.7
G CD20 (cell/glom)	0.1±0.3	0.1±0.2	0.03±0.07
TI CD68 (cell/hpf)	15.5±13.9	10.2±6.2	11.4±12.1
G CD68 (cell/glom)	1.7±1.9* (**)	1±1.3*	0.4±0.5**

Conclusions: In conclusion, our data suggest that: 1. infiltrating $CD8^+$ cells may differentiate CR from CNIT; 2. infiltrating cell characterization might improve diagnostic/prognostic features of graft biopsy in CAD.

MP466 HYPOXIA IN THE PATHOGENESIS OF EXPERIMENTAL CHRONIC CYCLOSPORINE NEPHROLOGY

Pei Wang, Zhangsuo Liu, Hong Luo, Jin Ma. *Nephrology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan, China*

Introduction and Aims: It has been reported that hypoxia plays important role in the pathogenesis of kidney diseases, including acute rejection and acute cyclosporine A (CsA) nephrotoxicity. However, it hasn't been fully investigated that which role it has in the chronic cyclosporine nephropathy (CCN) although arteriole injury is prominent impairment of CCN. This study was designed to explore the role of hypoxia in CCN.
Methods: 72 Male Sprague-Dawley rats were randomly divided into three groups:1) group CsA was given low salt diet low (sodium concentration 0.14%) and CsA (15mg/kg.d, s.c.); 2) group ND was given normal diet (sodium concentration 0.53%,) and 3) group ND was given low salt diet. Six rats of each group were harvested at day 4, day 8, day 14 and day 28. Hypoxia was detected by hypoxyprobe pimonidazole, hypoxia inducible factor-1 alpha (HIF-1alpha), heme oxygenase-1(HO-1), vascular epithelial growth factor (VEGF) and connective tissue growth factor (CTGF) mRNA and protein expression was detected by RT-PCR and Western Blot.
Results: Hypoxia detected by pimozadole staining and HIF-1alpha mRNA expression was significantly elevated at day 4 and peaked at day 28, however, HIF-1alpha protein expression declined prominently at the same time period. mRNA expression of HO-1 and VEGF, two downstream gene of HIF-1alpha, decreased greatly at the four time period. CTGF mRNA and protein expression increased at day 28.
Conclusions: Our study indicated CsA prevented hypoxia adaptation by suppress HIF-1 transcriptional activity as it induce hypoxia. Such a mechanism may contribute to CCN.

MP467 OUTCOME OF 18 CASES OF SIMULTANEOUS KIDNEY AND DONOR SPECIFIC BONE MARROW TRANSPLANTATION

Gholamreza Pourmand, Abdolrasoul Mehrsai, Mohamadreza Nikoobakht, Mohsen Taherimahmoudi, Alireza Shahnazari. *Urology Research Center, Tehran, Iran*

Introduction and Aims: to evaluate the effect of simultaneous donor specific bone marrow transplantation on patient survival.
Methods: Since 1997, 81 patients received renal transplantation in our center and were followed up for presence and magnitude of michrochimerism using DRB1 region of HLA class by PCR. 18 of these patients were selected to receive donor's bone marrow. The bone marrow was extracted from iliac crest of the donor just prior to nephrectomy. The cell count was determined

and enough volume containing 3-5 million celis per kg weight of recipient was ingected just after the transplantation. The rest of the patients were regarded as control group. The blood sample of recipients were taken pre operatively and one week, 1, 3, 6, 12, 18, 24 months after operation.The blood sample donor were also taken before the operation. The samples were tested for urea, creatinine, sodium, potasium, calcium, phospher, blood cell count hemogiobin and cyclosporine A levels. Samples prior to operation were also tested for DRB1 alleles in both donor and recipients by PCR.Afterward the recipients samples taken at above mentioned intervals were tested for presence and persistence of donors DRB1 alleles.
Results: Our results indicates that creatinine levels at all intervals does not differ significantly in DMBT and control group. The rate of acute rejection is, however, lower in patients who received DMBT as compared to the control group (one case, 5.6% and 6 cases, 9.5% respectively). In control group 4 of the patients with acute rejection episode responded to therapy. The chronic rejection episodes were also lower in DBMT group (1 case, 5.5%). There were 7 cases of chronic rejection (11.1%) in control group. The graft survival rate was 94.4% in DBMT group and 87.3% in control group.
Conclusions: Our results shows that simultaneous DBMT and renal transplantation may have some positive effect on graft and patient's survival.

MP468 ASSOCIATION BETWEEN INTERLEUKIN-8, CXCR2, AND SELECTIN POLYMORPHISMS WITH ACUTE REJECTION IN KIDNEY TRANSPLANTATION

Han Ro[1], Young-Hwan Hwang[2], Jaeseok Yang[3], Kitae Bang[1], Kiwon Kim[4], Kook-Hwan Oh[1], Myoung Hee Park[5], Curie Ahn[1,6,7].
[1]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea; [2]Department of Internal Medicine, Eulji University School of Medicine, Seoul, Korea; [3]Department of Internal Medicine, Gachon University of Medicine and Science, Incheon, Korea; [4]Department of Nephrology, National Cancer Center, Goyang, Korea; [5]Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea; [6]Transplantation Research Institute, Seoul National University, Seoul, Korea; [7]Cancer Research Institute, Seoul National University, Seoul, Korea

Introduction and Aims: Leukocyte infiltration is a major component of the inflammatory response mediating tissue injury. Interleukin-8, CXCR2, and selectin play a key role in the process. Cellular invasion and cytokine release are important steps in the initiation of rejection. Acute renal graft rejection influences the results of kidney transplantation and thus remains the major obstacle in the success of renal transplantation. The purpose of the present study was to investigate associations between polymorphisms of these molecules and kidney graft rejection in Korea.
Methods: We genotyed IL8 -251A/T, CXCR2 -8939C/T, CXCR2 1208T/C, E-selectin -642A/G, and L-selectin 1402C/T in kidney transplant donor and recipients of Seoul National University Hospital transplant center. Two hundred and seventeen pairs whose recipient age at transplantation $\geq$18 years from 1996 to 2006 were included in the analysis. Clinically treated and biopsy-proven acute rejection in posttransplant one year were considered as acute rejection (AR) group (n=43).
Results: There was no significant difference in distribution of donor's and recipient's polymorphisms between AR group and non-AR group. In haplotype analysis, frequencies of recipient's selectin haplotypes in AR group and non-AR group were AC:AT:GC = 41:16:27 and 146:93:97, respectively. And carriers of recipient's selectin AT haplotype have borderline-lower risk of AR (OR 0.505, [95% CI, 0.250-1.022]; p=0.055). In a multivariable analysis with recipient age, gender of recipient/donor, HLA mismatch, donor age at nephrectomy, and donor relation as covariates, adjusted odds ratio for AR was 0.49 (95% CI, 0.211-0.997; p=0.049).
Conclusions: Our data suggest the possible role of selectin in kidney transplantation, particularly for the occurrence of acute rejection. To clarify the role of the analysed polymorphisms for long-term survival, larger studies in the future are needed.

MP469 PROSPECTIVE STUDY OF MICROCHIMERISM IN RENAL ALLOGRAFT RECIPIENTS: ASSOCIATION BETWEEN HLA DR MATCHING, MICROCHIMERISM AND ACUTE REJECTION

Gholamreza Pourmand, Mohsen Taherimahmoudi, Abdolrasoul Mehrsai, Mohamadreza Nikoobakht, Alireza Shahnazari. *Urology Research Center, Tehran, Iran*

Introduction and Aims: The presence of donor-derived hematopoietic cells in blood and various tissues of the organ recipients, termed allogeneic microchimerism, has been considered to play and essential role in establishment of organ acceptance. In this study, we prospectively determined the presence of peripheral blood microchimerism (PBM) in 20 male-to-female renal allograft recipients up to 30 months post-transplantation.
Methods: Recipients were categorized according to the pattern of microchimerism into microchimeric and nonmicrochimeric groups, and then state of human leukocyte antigens (HLA) Class II (DR/DQ) matching, episodes of acute rejection, age at transplantation, renal function, and history of blood transfusion were compared. DNA was extracted from donor, pre-transplant, and post-transplant (1 wk; 1, 3, 6, 12, 18, 24, and 30 months) peripheral blood samples. We analyzed PBM using nested polymerase chain reaction (PCR) amplification specific for the SRY region of the Y chromosome with a sensitivity up to 1:1000000.
Results: Microchimerism was detected in 13 (65%) of 20 recipients at various intervals. The highest frequency of microchimerism was at 1 wk (55%). Among microchimeric recipients, none were positive on all post-transplant analyses. Interestingly, nomicrochimeric cases were negative throughout the study. The three recipients with an episode of acute rejection during the first week after transplantation were all in the nonmicrichimeric group with completely mismatched HLA-DR antigens. HLA-DR incompatibility was significantly lower (t-test, $p<0.05$) in microchimeric cases (1.0+0.58) than in nonmicrochimeric ones (1.9+0.38). But regarding HLA-DQ and other clinical parameters mentioned above, significant difference was not observed. We propose that there is an association between HLA-DR matching, microchimerism and acute graft rejection in our recipients.
Conclusions: Our study demonstrates that, with routine immunosuppressive protocols, higher compatibility of HLA-DR antigens facilitates microchimerism induction. Then, development of new stronger immunosuppressive protocols (including conditioning) or augmentation of chimeric state (by donor specific bone marrow infusion), especially in completely mismatched HLA-DR renal allograft recipients, may be useful for graft acceptance.

MP470 COMPARISON OF FOUR COMMONLY USED IMMUNOSUPPRESSANTS ON ENDOTHELIAL FUNCTION

Cecilia M. Shing[1], Robert G. Fasset[2], Lindasy Brown[3], Louise A. Lexis[4], Jeff S. Coombes[2,5]. *[1]School of Human Life Sciences, University of Tasmania, Launceston, Tasmania, Australia; [2]Renal Research Tasmania, Launceston General Hospital, Launceston, Tasmania, Australia; [3]Biomedical Sciences School, University of Queensland, Brisbane, Queensland, Australia; [4]School of Biomedical Sciences, Victoria University, Melbourne, Victoria, Australia; [5]School of Human Movement Studies, University of Queensland, Brisbane, Queensland, Australia*

Introduction and Aims: Endothelial dysfunction is an early marker of atherosclerosis following renal transplant and immunosuppressive therapy has been implicated in this process. The aim of this investigation was to compare the effect of four commonly used immunosuppressants on endothelial and smooth muscle function in rats.
Methods: Cyclosporine A (CSA) [10 $mg \cdot kg^{-1} \cdot day^{-1}$ (low dose) and 25 $mg \cdot kg^{-1} \cdot day^{-1}$ (high dose)], sirolimus (0.4 $mg \cdot kg^{-1} \cdot day^{-1}$), tacrolimus (1.0 $mg \cdot kg^{-1} \cdot day^{-1}$), everolimus (2.5 $mg \cdot kg^{-1} \cdot day^{-1}$) and respective vehicles were administered to eight week old male Wistar rats for 10 consecutive days. Aortic vascular function was assessed *in vitro*. Smooth muscle contraction (isometric tension) was assessed by exposing rings to increasing concentrations of noradrenaline (NA). Acetylcholine (ACh) and sodium nitroprusside (SNP) were added to aortic rings pre-contracted with NA to assess endothelial-dependent and endothelial-independent relaxation, respectively.
Results: Maximal contraction in response to NA was significantly reduced with low (-40.2±7.4%; mean ± SE) and high dose (-46.3±11.6%) CSA

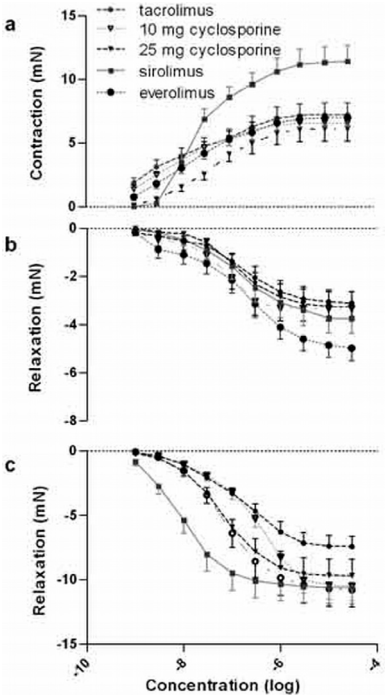


Figure 1

and everolimus (-32.1±12.6%) when compared to sirolimus (Figure 1a). Maximal relaxation in response to ACh was significantly reduced with low (-66.3±34.8%) and high dose (-101±43.3%) CSA and tacrolimus (-13±21.6%) when compared to everolimus (Figure 2b). Tacrolimus significantly reduced SNP-induced relaxation when compared to low CSA (59.8±20%), everolimus (73±31.3%) and sirolimus (62.8±25%), but not high dose CSA (Figure 3c). Sirolimus significantly enhanced relaxation in response to SNP (3nM to 30nM) when compared to low and high CSA, everolimus and tacrolimus.

Conclusions: Administration of sirolimus was associated with the least impairment of smooth muscle contraction. All immunosupressants studied impaired endothelial-dependent relaxation, but everolimus produced the least dysfunction. Tacrolimus was associated with the greatest impairment of endothelial-independent relaxation. Calcineurin and mTOR inhibitors exert different effects on vascular function. Since impaired endothelial-dependent relaxation is a predictor of future cardiovascular pathology, everolimus may prove less damaging than sirolimus, CSA or tacrolimus. However, before recommendations may be made, the implications of impaired endothelium-independent relaxation and smooth muscle contraction for the development of cardiovascular pathology require further investigation.

MP471 MODULATION OF ALPHA-INTERFERON SYNTHESIS BY ASPIRATION BIOPSY CULTURES BY ANTI-IL-2αCHAIN RECEPTOR ANTIBODY THERAPY

Gerardo Oliveira[1], Paula Xavier[2], Susana Norton[1], Carla Araujo[1], Sergio Gaiao[1], Manuel Pestana[1]. *[1]Unidade de Investigaçao e Desenvolvimento de Nefrologia, Faculdade de Medicina da Universidade do Porto, Porto, Portugal; [2]Centro de Histocompatibilidade do Norte, CHN, Porto, Portugal*

Introduction and Aims: Previously we described a significant down-regulation of Toll-like receptors-4 and -9 expression in fine-needle aspiration biopsy (FNAB) samples of kidney transplants (Tx) treated with anti-IL-2α-chain receptor antibody (IL-2RAb). Also, we have already reported that FNAB samples cultures from acutely rejecting Tx synthesize significantly higher amounts of interferon-α (IFN) as compared to stable Tx. We studied the influence of different immunosuppressive regimens upon IFN synthesis by FNAB cultures.

Methods: Tx from cadaver donors were treated from the outset with three regimens: group I: CsA/MMF/Pred (n=28); group II: thymoglobuline/CsA/MMF/Pred (n=9), group III:IL-2RAb/CsA/MMF/Pred (n=18). Every Tx remained rejection-free for the first six months. FNAB were done on day seven post-surgery and the samples were cultured in RPMI with autologous serum and rIL-2 at 10 U/ml for 48h. At the end supernatants were collected and kept at -70°C until testing. IFN was measured by ELISA kits from R&D.

Results: No significant differences were found for donor-recipient demographic pairs between the three groups with the exception that all from group II were second Tx. No significant differences were observed for serum creatinine beteween groups on day seven. Tx from group II did not commence CsA by day 7 while CsA blood levels were significantly lower among III as compared to I (p=0.02). IFN (pg/ml) - I: 7.9±9.9; II: 37.6±40; III: 5.5±2.6. III was significantly lower than II ($p<0.02$) and close to significantly lower than I (p=0.059) while II was higher than I (p=0.09).

Conclusions: Therapy with IL-2RAb is associated with down-regulation of IFN synthesis, this is significant when compared to thymoglobulin and close to significant when compared to current triple therapy. Together with our previous findings on TLR expression this suggest that one of the main actions of IL-2Rab might be through modulation of innate immune response with lower priming of antigen-presenting cells. IFN output by FNAB cultures may also come from NK cells suggesting a lower activation with IL-2RAb. The values observed with thymoglobulin were not anticipated but it is known that during the first doses there is a moderate surge of cytokine release wich may explain our observations. Also, we acknowledge that thymoglobulin patients were not receiving CsA on the day of sampling which would suggest that CsA might modulate IFN too and that this down-regulation is further deepened by IL-2RAb. This hypothesis may be tested with a comparison with Tx not treated with cacineurin inhibitors from the outset but we do not follow such strategy in our unit. As IFN may constitue one of the links between innate and adaptive immune response we surmise that our findings on IFN are of clinical relevance.

MP472 ★ SIGNS OF CELLULAR SENESCENCE IN CYCLOSPORINE A AND TACROLIMUS TREATED RENAL TUBULE CELLS

Christian Koppelstaetter[1], Georg Kern[1], Paul Jennings[2], Maria Schaumeier[1], Gert Mayer[1]. *[1]Division of Nephrology, Innsbruck Medical University, Innsbruck, Austria; [2]Department of Physiology, Innsbruck Medical University, Innsbruck, Austria*

Introduction and Aims: The nephrotoxic potential of the calcineurin inhibitors (CNI) Cyclosporine A (CsA) and Tacrolimus (FK506) is well recognized. Chronic CNI nephropathy and renal organ ageing share some clinical features, such as renal fibrosis and tubular atrophy, allowing to speculate that CNI may exert some of their deleterious effects via induction of a stress induced phenotype. Recently we could show that CsA induces common pathways of cellular senescence in renal proximal tubule cells by inducing the production of H_2O_2.

Methods: We compared dose dependent (0, 0.25, 0.5, 1, 2, 5, 10 and 20μM) effects of CsA and FK506 in the human renal proximal tubule cells. Telomere length (determined by real time PCR), DNA synthesis (by BrdU incorporation), cell viability (by Resazurin conversion) and H_2O_2 production (by Amplex Red) were evaluated in HK-2 cells exposed to CsA and FK506 for 24 hours.

Results: Hydrogenperoxide production was induced by both calcineurin inhibitors, although CsA lead to a more significant increase of H_2O_2 than FK506. At non cytotoxic concentrations (assessed by resazurin conversion) there was a significant and dose dependent decrease in BrdU-incorporation with CsA ($P<0.05$) which was not observed following FK506 exposure. At a dose of 10 M Cyclosporine lead to a reduction of telomere length of 14% (P=0.063) compared to 6% in FK506 treated samples (P=0.067).

Conclusions: In summary, renal tubule cells exposed to CsA and FK506 show effects which are also seen in cellular senescence. Even though CsA and FK506 possess the same downstream pathways their effect on viability and proliferation on renal cells are significantly different. Compared to CsA FK506 shows less telomere reduction, less production of H_2O_2 and no significant inhibition of DNA-synthesis resulting in a less altered proliferation grade in cells treated with FK506.

MP473 DONOR RISK FACTORS FOR DELAYED GRAFT FUNCTION (DGF) IN CADAVERIC RENAL TRANSPLANTATION (rTx)

Roberta Giraudi[1], Monica Meucci[5], Fabrizio Fop[1], Paola Magistroni[2], Riccardo Bosco[3], Ernesto Turello[4], Raffaella Giacometti[2], Stefano Roggero[2], Piero Stratta[4], Giuseppe Paolo Segoloni[1], Antonio Amoroso[2]. *[1]S.C. Nephrology, Dialysis and Transplantation, San Giovanni Hospital, Torino, Italy; [2]S.C. Transplant Immunology Service, San Giovanni Hospital, Torino, Italy; [3]S.C. Nephrology and Transplantation, Piemonte Orientale University, Novara, Italy; [4]Procurement Regional Coordination, San Giovanni Hospital, Torino, Italy; [5]S.C. Intensive Care Unite, Valle d'Aosta Hospital, Aosta, Italy*

Introduction and Aims: Delayed graft function (DGF), defined as the need of dialysis within one week following rTx, is a common post-transplant complication. The usual rate of DGF is 10% to 40% and depends on many variables.
The purpose of this study is to evaluate donor risk factors for DGF, to determine which therapeutic strategies are correct to prevent DGF in the setting of donor management and to evaluated some pre-transplant recipient risk factors.
Methods: In this retrospective study, all primary deceased donor, between January 2000 and December 2006, were identified in the database of the Regional Transplantation Centre of Piemonte and Valle d'Aosta. We analyzed 562 consecutive donors from 32 Intensive Care Units (ICU) and 1073 renal recipients transplanted in the two rTx Centres.
Regarding donors, DGF was compared with age, sex, cause of death, body max index (BMI), history of hypertension and diabetes, renal function, days in ICU, blood pressure, hypotensive period, cardiac resuscitation, use of catecholamine, cold ischemia time (CIT) and renal biopsy, for donors over 50 yrs. In recipients, DGF was compared with age, sex, BMI, current and historical panel reactive antibodies (PRA%), previuos transplants, patient hospitalization.
Results: The incidence of DGF is 30%, being a significant factor in long-term patient and graft survival ($p<0,005$). Predictive donor factors are: age ($60,3\pm13,1$ ys in DGF transplants vs $46,8\pm18,2$ ys in no-DGF transplants, $p<0,05$), cause of death (cerebrovascular accident vs trauma, $p<0,05$), history of hypertension (58% vs 29%, $p<0,05$), renal function evaluated with Cockcroft formula ($84,4\pm37,6$ vs $99,1\pm39,5$, $p<0,05$) and with renal biopsy ($2,4\pm1,1$ mean score vs $2,2\pm1,2$, $p<0,05$), BMI in female gender ($27,2\pm5$ vs $23,3\pm3,7$, $p<0,05$). Donor employment of catecholamines results in less incidence of DGF ($p<0,05$)
As in literature, prolonged CIT is associated with increased DGF: $19,4\pm4,9$ hours in DGF transplants vs $18,1\pm5,2$ in non-DGF transplants, $p<0,05$.
In recipients the occurrence of DGF is associated with age ($54,1\pm10,7$ ys in DGF recipients vs $48,5\pm12,9$ ys in no DGF recipients), BMI in female gender ($24,1\pm3,9$ vs $22,4\pm3,6$), current and historical PRA% ($15,3\pm24,9$% vs $11,8\pm23,2$%/$5,8\pm17,1$% vs $3,2\pm12,0$%), previous transplants, prolonged patient hospitalization ($31,8\pm30,6$ vs $19,2\pm30,6$, $p>0,05$).
Conclusions: DGF remains a common complication in rTx and is important because it increases risk of graft loss and patient survival; in order to reduce incidence is mandatory a close cooperation between all the specialists involved in the multidisciplinary process of organ donation, in particular between anesthetists, immunologists, surgeons and nephrologists.

MP474 THE INFLUENCE OF CYCLOSPORINE A AND RAPAMYCIN ON APOPTOSIS OF HUMAN CD8+CD28- CELLS IN MIXED LYMPHOCYTE CULTURE (MLC)

Anna Korecka[1], Janusz Wyzgal[2], Grazyna Korczak-Kowalska[1,2]. *[1]Departament of Immunology, Faculty of Biology, Warsaw University, Warsaw, Poland; [2]Transplantation Institute, The Medical University of Warsaw, Warsaw, Poland*

Introduction and Aims: Cyclosporine A (CsA) and rapamycin (RAPA) are immunosuppressive drugs with different mechanisms of action. Previous studies report that CsA inhibits apoptosis whereas RAPA induces apoptosis of lymphocytes. Apoptosis of alloreactive lymphocytes is essential to initiate of transplant tolerance. The maintenance of tolerance requires the presence of regulatory cells. Induction of apoptosis by immunosuppressive drugs can be favourable to transplant tolerance in case of apoptosis of alloreactive cells, but apoptosis of regulatory cells is undesirable. The aim of this study was to evaluate the influence of cyclosporine A and rapamycin on apoptosis of human CD8+CD28- regulatory cells in Mixed Lymphocyte Culture (MLC).
Methods: Peripheral Blood Mononuclear Cells (PBMCs) were obtained from healthy volunteers and were cultured in MLC with or without CsA (200ng/ml/10^6cells) or RAPA (20ng/ml/10^6cells). After six days the level of apoptosis was determined (annexin V, propidium iodide, anty-CD8 and anty-CD28 mAbs).
Results: Drugs had the influence of cell cultures and proliferation of lymphocytes were decreased over twofold. We observed that CsA decreased and RAPA increased apoptosis of PBMCs but there was a change of only a few percent towards over a dozen percent apoptotic cells in control cultures. Apoptosis of CD8+ population and CD8+CD28- subpopulation gained a few percent. CsA slightly decreased the level of apoptotic cells in CD8+ population but RAPA didn't induce apoptosis of CD8+ cells. Drugs seems to have no influence on apoptosis of CD8+CD28- cells.
Conclusions: We used therapeutic concentration of drugs that are enough to decrease proliferation of alloreactive cells. It is possible that bigger concentrations of CsA and RAPA have greater influence on the apoptosis of PBMCs. The level of apoptosis observed in CD8+CD28- cells was very low. These cells can be resistant on apoptosis and drugs can have no effect of their apoptosis. It is possible that although examined immunosuppressive drugs affect the apoptosis of cells in MLC generally, they doesn't interfere with generation of regulatory cells and with obtaining of transplant tolerance.

MP475 SOLUBLE CD30 (sCD30) IN ACUTE REJECTION OF RENAL ALLOGRAFTS: A SYSTEMATIC STUDY IN PATIENTS WITH SERIAL PROTOCOL BIOPSIES

Sabine Niescken[1], Michael Mengel[2], Mario Schiffer[1], Heike Luehrs[1], Irina Scheffner[1], Hermann Haller[1], Wilfried Gwinner[1]. *[1]Nephrology, Medical School Hannover, Hannover, Germany; [2]Pathology, Medical School Hannover, Hannover, Germany*

Introduction and Aims: Soluble CD30 (sCD30) has been implicated in acute rejection of renal allografts and in long-term graft survival; however, the exact role of this molecule is uncertain. Aim of this longitudinal study was to examine sCD30 serum and urine levels in patients who never had experienced acute allograft rejection compared to patients with a single acute rejection episode.
Methods: Patients were included who had protocol biopsies available at 6 weeks, 3 and 6 months after transplantation, along with serum and urine samples at these time points. Biopsies were evaluated according to the updated Banff classification. sCD30 concentrations were determined with a commercial ELISA kit. Patients in the rejection group (n=22) had experienced acute T-cell mediated tubulointerstitial rejection at 3 months, without any additional rejection episodes at 6 weeks or 6 months, or in any additional diagnostic biopsy during the first half year after transplantation. Patients in the control group (n=37) were without acute rejection in protocol biopsies and any additional diagnostic biopsy.
Results: Serum levels of sCD30 were not different between the groups at 6 weeks post transplantation. At the time of the acute rejection episode at 3 months, sCD30 serum levels were higher by 26%, compared to the patients without rejection ($p<0.05$). At 6 months, sCD30 levels further increased by 98% in the rejection group ($p<0.05$). Serum sCD30 levels correlated weakly with urinary sCD30 concentrations. sCD30 serum levels were independent of the presence of delayed graft function, recipient and donor age and gender, number of HLA-mismatches, and of allograft function.
Conclusions: In this carefully selected patient groups, sCD30 serum levels were not predictive with regards to acute T-cell mediated rejection. Yet, higher sCD30 levels at the time of rejection and the subsequent steep rise in sCD30 indicate persistent immunological activation, which can explain the reported inferior long-term graft survival in patients with high sCD30 levels.

MP476 GENERAL PHARMACOGENETICS OF TACROLIMUS AND CYCLOSPORINE IN RENAL TRANSPLANT PATIENTS

Stepan Bandur[1], Eva Novotna[1], Petra Hribova[1], Irena Brabcova[1], Katerina Hyklova[1], Ondrej Viklicky[1,2]. *[1]Transplant Laboratory, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Department of Nephrology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic*

Introduction and Aims: Calcineurin inhibitors, tacrolimus (FK 506) and cyclosporine A (CsA), represent basic component of immunosuppressive therapy on patients after renal transplantation. These drugs are characterized by narrow therapeutic range and large interindividual variability in their pharmacokinetics with possible important clinical consequences. Both drugs are substrates for metabolizing enzyme cytochrome P450 (CYP) and for the efflux transporter P- glycoprotein (P- gp.) which influence their overall bioavailability. The single nucleotide polymorphisms (SNP) in the genes (CYP3A4, CYP3A5, MDR-1) determine enzymatic and transport activity of these proteins and are supposed to determine individual diversity of drug disposition.
Methods: We genotyped, using PCR- RFLP approach, 408 and 423 renal transplant patients, treated with cyclosporine and tacrolimus based immunosuppressive regimen respectively, for CYP3A4, CYP3A5 and MDR-1 exons 12, 21 and 26 SNPs in this study. This is the largest cohort of transplant patients genotyped for these SNPs to date. The objective was to evaluate markers of drug disposition (concentration/dose ratio, the day of achievement of target blood level and the achievement of target level within the first posttransplant week) as well as acute cellular rejection incidence and graft survival in relation to considered SNPs.
Results: In patients treated with tacrolimus, C/D ratio was significantly higher in those with CYP3A4*1/*1 genotype (lower protein expression) as compared to the *1/*1B genotype (P<0,001), similarly C/D ratio was higher in CYP3A5*3/*3 (lower protein expression) genotyped patients. Consistent correlation was found among the day of achievement of target level and the achievement of target level within first week and these polymorphisms as well. In patients group with cyclosporine based immunosuppression there was observed higher C/D ratio in CYP3A4*1/*1 genotype subjects (P<0,05). None of the MDR-1 polymorphisms was associated with considered drug bioavailability characteristics. There was not found any correlation among acute cellular rejection incidence or long term kidney graft survival and evaluated SNPs.
Conclusions: CYP3A4 and CYP3A5 gene polymorphisms significantly influence bioavailability of tacrolimus early after transplantation as well as in stable renal transplant recipients. These polymorphisms seem to be useful for more appropriate dosage of tacrolimus and may represent effective tool in personalized immunosuppressive therapy. Relationship among acute cellular rejection rate, kidney graft outcome and evaluated SNPs remain unclear.

MP477 ★ DONOR PRE-TREATMENT WITH AN HIF-PROLYLHYDROXYLASE-INHIBITOR IMPROVES FUNCTION AND INCREASES LONG-TERM GRAFT SURVIVAL IN AN ALLOGENIC RAT TRANSPLANT MODEL

Wanja M. Bernhardt[1], Uwe Gottmann[2], Fabian Doyon[2], Bjorn Buchholz[1], Valentina Campean[3], Stephen Klaus[4], Lee Flippin[4], Michael Arend[4], Carsten Willam[1], Michael S. Wiesener[1], Christina Warnecke[1], Benito Yard[2], Kai-Uwe Eckardt[1]. *[1]Med 4, Nephrology and Hypertension, University Hospital Erlangen-Nuremberg, Erlangen, Germany; [2]Nephrology, University Hospital Mannheim, Mannheim, Germany; [3]Pathology, University Hospital Erlangen-Nuremberg, Erlangen, Germany; [4]FibroGen Inc., South San Francisco, CA, USA*

Introduction and Aims: Besides immunological aspects, the long-term survival of a renal allograft depends on the initial injury caused by the sequence of cold ischemia, warm ischemia and reperfusion and is thus already determined at the time of transplantation. Hypoxia-inducible transcription factors (HIF) are essential for adaptation to low oxygen. Normoxic inactivation of HIF is regulated by oxygen-dependent hydroxylation of HIF by prolyl-hydroxylases (PHD). Pharmacological inhibition of the PHD results in HIF accumulation with subsequent activation of nephroprotective genes. We examined the effect of donor treatment with a specific inhibitor of the PHD (FG-4497) on graft-function in a rat model of allogenic kidney transplantation (KTx).
Methods: The Fisher-Lewis rat model of KTx was used. Isogenic transplantations served as controls.Orthotopic transplantation of the left donor-kidney was performed after 24h of cold storage. The right kidney was removed at the time of KTx (acute) or at day 10 (chronic). 6h prior to kidney explantation, donor animals were treated with a single dose of FG 4497 (40mg/kg i.v.) or vehicle (Veh) Recipients were followed up for 10 days (acute, n=6-8) or 24 weeks (chronic, n=13-14).
Results: Donor-preconditioning with FG 4497 resulted in HIF accumulation and induction of HIF target genes, which persisted beyond cold storage. It reduced acute renal injury (Serum creatinine FG-4497: 0.660.20 vs Veh 1.491.36; p<0.05) and improved histomorphology at 10 days. Donor-preconditioning improved long term survival of recipient animals (mortality after 24 wks: 7/13 Veh vs. 3/14 FG-4497; 0/13 of the isogenic controls; p<0.05 FG-4497 vs.Veh).
Conclusions: Pretreatment of organ donors with FG-4497 improves short- and long-term outcome after prolonged cold storage and subsequent allogeneic KTx. These findings may have significant clinical implications.

Renal transplantation – Clinical studies 2

MP478 INFLUENZA VIRUS VACCINATION IN KIDNEY TRANSPLANT RECIPIENTS: SERUM ANTIBODY RESPONSE TO DIFFERENT IMMUNOSUPRESSIVE DRUGS

Mauro J.C. Salles, Yvoty As Sens, Clarisse M. Machado, Lucy V. Boas. *Medicine, Santa Casa of Sao Paulo School of Medicine, Sao Paulo, Brazil; Instituto Medicina Tropical, Universidade de Sao Paulo, Sao Paulo, Brazil*

Introduction and Aims: Influenza vaccine response in kidney transplant recipients has shown conflicting results, which can be associated with different immunosuppressive regimens. We prospectively assessed the humoral immunity to the inactivated influenza vaccine in kidney transplant recipients.
Methods: Seventy five kidney transplant recipients with at least 6 months from transplantation received one dose of inactivated influenza vaccine 2004-2005. Anti-hemagglutinin antibody response against each strain was measured by hemagglutination inhibition test before and monthly up to 6 months after. The geometric mean titer (GMT) of each strain was calculated using the log-transformed values from all subjects: the GMT was taken as the antilog of mean of the transformed value. Logistic regression model was used to asses the impact of different immunosuppressive drugs on the vaccine response rates.
Results: One month after vaccination, 57.4% of patients acquired protective titers of antibodies to at least one vaccine strain. The GMT of H1N1 and H3N2 strains increased from 2.75 and 2.44 to 13.54 (P=0.001) and 7.30 (P<0.001), respectively. Pre and post-vaccination protection rates for H1N1 and H3N2 increased from 9.3% to 45.3% (P<0.001) and 9.3% to 33.3% (P<0.001). The H1N1 and H3N2 seroconversion rates after vaccination were 36% and 25.3%, respectively. There was no antibody response to influenza B virus. Compared to the use of azathioprine (AZA), Mycophenolate Mofetil (MMF) reduced the H1N1 [P=0.011, OR 0.26 (IC 95% 0.097-0.734)] and H3N2 [P=0.033, OR 0.30 (IC 95% 0.10-0.91)] protection rates and the seroconversion rates for the H3N2 strain [P=0.036, OR 0.26 (IC 95% 0.07-0.91)].
Conclusions: Kidney transplant recipients submitted to an anti-influenza vaccination responded with antibody production against strains H1N1 and H3N2 of influenza A virus, but not to influenza B virus. Use of MMF decreased the humoral immune response to the anti-influenza vaccine.

MP479 KIDNEY GRAFT SURVIVAL RATES DO NOT IMPROVE BY ERA: THE IMPACT OF FACTOR "AGE"

Elisabetta Bertoni, Aida Larti, Alberto Rosati, Maurizio Salvadori. *Renal Unit, Careggi University Hospital, Florence, Tuscany, Italy*

Introduction and Aims: According registry data on kidney transplantation, graft survival rate improves because of rejection rate reduction but is impaired by the increasing number of older donors and recipients. As the age of both donors and recipients dramatically increased in our country, aim of this study was to verify in our center how the graft survival rate changed by era.

Methods: We compared both the 5-year actual graft survival rate and the 5-year death censored graft survival rate of 89 recipients transplanted in 1991-1995 (period A) with 221 recipients transplanted in 1996-2000 (period B). As in period B we adopted new immunosuppressants as MMF, Neoral and IL-2R inhibitors, we expected an improvement in graft survival. The two period rejection rates and the incidence of donors and recipients > 50 years were considered. Kaplan-Meier estimates and Log-Rank test were performed by the Collaborative Transplant Study (CTS) whom our data had been regularly sent to.

Results: Period B 5-year graft survival rate was lower with respect to period A (76.3% vs 82%). The death censored graft survival rate was similar (87.1% vs 87.5%). The period B acute rejection incidence was 18% vs 40% of period A ($p<0.001$). Both overall donor and recipient age had the highest impact on 5-year graft survival rate: for donor age 21-50 yrs 86.2% vs 65.7% for donor age >50 yrs ($p<0.0001$). Similar effect was observed for recipient age: 84.1% for age 21-50 yrs vs 68% for age >50 yrs ($p= 0.0023$). In period A donors >50 yrs were 23.6% vs 50.2% in period B ($p< 0.001$). Similarly, period A recipients >50 yrs were 35.9% vs 42.9% in period B ($p<0.01$). 5-year graft survival rate of recipients with donor <50 yrs improved in period B with respect to period A (89.2% vs 87.2%). Similarly the 5-year graft survival rate of recipients <50 yrs improved (85.2% vs 81.5%). Considering the death censored 5-year graft survival rate for period B with respect to period A, we observed a significant improvement either for donors >50 yrs (82.5% vs 65.8%) and for recipients >50 yrs (90.2% vs 81.2%).

Conclusions: Kidney graft survival rate of patients transplanted in 1991-1995 was higher with respect to 1996-2000. These data disagree with the survival rates expected by the reduction of 1-year rejection rate due to new immunosuppressants. Expanded donor criteria can account for such discrepancy. Indeed in period B we had more donors and recipients over 50 years. Most of graft failure were due to death with function, but also a poorer quality of kidneys accounts for this phenomenon. Indeed looking for graft survival rate of patients under 50 yrs we observed an improvement as expected.

MP480 PHARMACOKINETICS AND PHARMACODYNAMICS OF CINACALCET IN PATIENTS WITH HYPERPARATHYROIDISM AFTER RENAL TRANSPLANTATION

Andreas L. Serra[1], Natascia Corti[2], Stefan Russmann[2], Simone Braun[1], Rudolf P. Wüthrich[1]. [1]*Clinic for Nephrology, University Hospital, Zurich, Switzerland;* [2]*Division of Clinical Pharmacology and Toxicology, University Hospital, Zurich, Switzerland*

Introduction and Aims: Persistent hyperparathyroidism (HPT) with hypercalcemia and hypophosphatemia is common after renal transplantation and adversely affects the outcome of kidney transplant recipients. Studies have shown that treatment with cinacalcet corrects hypercalcemia and lowers PTH levels in these patients. So far cinacalcet's steady-state pharmacokinetics and their correlation with pharmacodynamics (PK/PD) have only been studied in hemodialysis patients, but not in renal transplant recipients with persistent hyperparathyroidism (HPT). To gain further insight into cinacalcet's effects on calcium-phosphate homeostasis, we determined its steady-state pharmacokinetics and pharmacodynamic effects in these patients.

Methods: In a prospective, single center, open label study we examined the effect of a 2-week treatment with 30 mg and subsequent 2-week treatment with 60 mg cinacalcet daily on calcium-phosphate homeostasis over 24 hours and determined the steady-state pharmacokinetics of cinacalcet in stable renal allograft recipients. The urinary calcium excretion was determined in timed urine samples.

Results: Median $AUC_{0\text{-}24}$ was 784.8 ng*h/ml and C_{max} was 68.5 ng/ml for 60 mg cinacalcet which is higher, and oral clearance (CL/F) was 76.9 l/h which is lower in renal transplant recipients compared to previously published data of hemodialysis patients (50 mg cinacalcet $AUC_{0\text{-}24}$ 179, C_{max} 17.2, CL/F 279). We also observed a non-proportional increase of $AUC_{0\text{-}24}$ after doubling of the cinacalcet dose, whereas a proportional increase has been shown in hemodialysis patients at daily doses of up to 200 mg. The once daily administration of cinacalcet effectively and dose-dependently reduced iPTH and serum calcium. Cinacalcet and parathyroid hormone (PTH) concentrations showed an inverse correlation and were fitted to a simple E_{max} model (E_{max}=80% reduction vs. baseline, EC_{50}=13 ng/ml). The 8-hour fractional urinary excretion of calcium was increased after 60 mg cinacalcet (baseline 0.85±0.17%, 30 mg 1.53±0.35%, 60 mg 1.92±0.37%). Renal function remained stable.

Conclusions: Cinacalcet's higher and non-proportional increase of $AUC_{0\text{-}24}$ in transplant recipients compared to hemodialysis patients evokes the possibility of a pharmacokinetic interaction with concomitant cyclosporine treatment. Cinacalcet effectively corrected the biochemical abnormalities of persistent HPT. The transient calciuria could potentially favor nephrocalcinosis and reduce bone mineral density, suggesting that higher doses of cinacalcet need to be used with caution in renal transplant recipients with severe persistent hyperparathyroidism.

MP481 HLA MATCHING IS ASSOCIATED WITH BETTER OUTCOME AFTER RENAL TRANSPLANTATION IN EUROTRANSPLANT SENIOR PROGRAM

Nikolina Basic-Jukic[1], Petar Kes[1], Ljubica Bubic-Filipi[1], Josip Pasini[2]. [1]*Department of Dialysis, University Hospital Zagreb, Zagreb, Croatia;* [2]*Department of Urology, University Hospital Zagreb, Zagreb, Croatia*

Introduction and Aims: In 1999 Eurotransplant (ET) has launched "senior" program which allocates kidneys from elderly donors to the patients who are older than 65 years. It is targeted to increase the number of renal transplantations. It allocates kidneys based on age, ABO-type compatibility, and negative crossmatch, without donor HLA-typing. Croatia has introduced its own "senior" program based on ET allocation scheme, but with HLA matching.

Methods: All patients who underwent first renal transplantation at the age of 65 years or older were identified and followed-up prospectively. Their HLA matching, cold ischemia time, renal function, immunosuppressive protocol, surgical and medical complications, and duration of hospitalization were recorded.

Results: Until the December 2007, 22 elderly patients received an allograft from donors who were older than 60 years. Only patients with follow-up of at least 12 months, patients who lost their graft or patients who died after transplantation were included in investigation. Eighteen patients fulfill the criteria. There were 7 female and 11 male patients, with the mean age at transplantation of 67 years. Mean donor age was 66 years. Number of HLA-MM ranged from 1 to 5, and cold-ischaemia time from 7 to 15 hours. Immunosuppressive protocol consisted of cyclosporine A, mycophenolate mofetil and steroids, with daclizumab induction in cases with more than 3 HLA mismatches because of the financial limits in the country. With the mean follow-up of 14 months, patient survival was 94.4%, and graft survival was 88.8%. One patient died after stroke and severe bleeding from the gastric ulcer. One patient lost his graft because of severe bleeding from the renal artery anastomosis. Delayed graft function (DGF), defined as the need for dialysis after transplantation, occurred in 14/18 patients. Older recipients required prolonged hospitalization for transplantation (45, range 16-131) than younger patients (32, range 14-52), ($p<0.01$). Posttransplant complications were frequent and included posttransplant diabetes mellitus in one patient, delayed wound healing in 5 patients, lymphocaele in 2 patients and development of the neoplasm of own kidney in one patient. Only one patient experienced acute rejection that was successfully treated with steroids (5.5%), compared to 35-40% of acute rejections in ET "senior" program.

Conclusions: Renal transplantation in elderly patients is associated with increased incidence of posttransplant surgical and medical complications which demand prolonged hospitalization. HLA matching is associated with significant decrease in the incidence of acute rejections with relatively short

cold ischaemia time. High incidence of DGF indicates that cyclosporin should be avoided in elderly recipients during the first posttransplant days. Our results demonstrate that excellent graft and patient survival justify transplantation in this group of patients.

MP482 THE EFFECT OF DIETARY SALT INTAKE ON BLOOD PRESSURE IN KIDNEY TRANSPLANT RECIPIENTS

Zeki Soypacaci[1], Sule Sengul[1], Emine Akal Yildiz[2], Sim Kutlay[1], Sehsuvar Erturk[1], Bulent Erbay[1], Kenan Keven[1]. [1]*Department of Nephrology, Ankara University School of Medicine, Ankara, Turkey;* [2]*Department of Nutrition and Dietetics, Hacettepe University, Schoof of Health Technology, Ankara, Turkey*

Introduction and Aims: Postransplant hypertension (HT) is a common problem in kidney recipients (KiRs). Dietary salt intake has long been recognized as a major factor affecting blood pressure such that sodium intake is a component of lifestyle modification guidelines for control of high blood pressure. The relationship between dietary salt intake and posttransplant HT has not been extensively investigated. Our aim was to evaluate the effect of dietary salt intake on blood pressure in KiRs.
Methods: We examined the relationship between dietary salt intake and blood pressure in 52 KiR with stable allograft function (after 6 months of transplantation, serum creatinine < 2mg/dl) and hypertension (on at least one antihypertensive drug and/or office blood pressure ≥120/80 mmHg). The KiRs who had been on any diuretics were not included in the study. For baseline evaluation, office blood pressure measurements and 24-hour ambulatory blood pressure monitoring (ABPM) were recorded, and daily salt intake (24-hour urinary excretion of sodium on an unrestricted diet) and urine electrolytes were measured. After baseline evaluation, low sodium diet (80 mmmol/day) was prescribed for all patients. All study parameters were repeated after 14 days on low sodium diet. Because of noncompliance to low sodium diet, 14 patienst were excluded, and the study was completed with 38 patients (F/M:12/26,cadaveric/living:18/20, transplant duration: 47±42 months, mean age: 41±11 years).
Results: Results are presented in Table 1.

Table1

Parameter	Before low Na diet	After low Na diet	P
24h-urine Na (mEq/day)	177±72	85±37	<0.001
Spot urine Na/Creatinine	0.96±0.61	0.67±0.57	<0.05
Office Systolic BP (mmHg)	132±18	123±13	<0.001
Office Diastolic BP (mmHg)	87±10	81±7	<0.001
24-h ABPM-mean Systolic BP (mmHg)	125±11	120±9	<0.001
24-h ABPM-mean DiastolicBP (mmHg)	80±8	76±6	<0.001
24h-urine Ca (mg/day)	109±83	89±73	<0.001
24h-urine Mg (mg/day)	107±44	85±45	<0.001

Na: Sodium, BP: Blood pressure, ABPM: Ambulatory Blood Pressure Monitoring, Ca: Calcium, Mg: Magnesium.

Conclusions: We conclude that dietary salt intake in KiR with HT is high, and after 14-days on low sodium diet in combination with antihypertensive treatment appears to efficiently reduce blood pressure in KiR. Both office measurements and ABPM can be used for monitoring of blood pressure in KiR. Twenty-four-hour urine sodium excretion should be regularly checked in these patients as a useful marker to test whether the patient comply with low sodium diet.

MP483 ENDOTHELIAL FACTORS FOLLOWING ISCHEMIA/REPERFUSION INJURY – THE IMPACT ON ALLOGRAFT HISTOLOGY AND FUNCTION AT 1 AND 6 MONTHS AFTER RENAL TRANSPLANTATION

Jelka Masin-Spasovska[1], Goce Spasovski[1], Sonja Dzikova[1], Ljupco Lekovski[2], Beti Dejanova[3], Vesela Maleska[3], Aleksandar Sikole[1], Zivko Popov[2], Ninoslav Ivanovski[1]. [1]*Department of Nephrology;* [2]*Department of Urology;* [3]*Department of Physiology, University Clinical Center, Skopje, Macedonia, The Former Yugoslav Republic of*

Introduction and Aims: Ischemia-reperfusion injury (IRI) is an unavoidable consequence of renal transplantation (Tx) and continues to be the leading cause of graft damage and loss. Endothelial dysfunction has been shown to be an early key event preceding IRI. The aim of our study was to evaluate the levels of vasoactive endothelial factors following IRI: endothelin (ET_1), nitric oxide (NO) and free oxygen radicals (FOR); and to estimate the post-IRI effects on allograft function and histology at 1 and 6 months after Tx.
Methods: 40 consecutive living related kidney transplant recipients were included. We analyzed the variables of ET_1, NO, FOR at various time points: before Tx, after Tx, at day 1, at 1, 2, 3 weeks and at 1 and 6 months after Tx. A surveillance protocol biopsies were performed at 1 and 6 months after Tx and blindly reviewed using Banff ' 97 criteria. Patients were divided in two groups according to the occurrence of delayed graft function (DGF) and acute rejection (AR) within the first 2 weeks after Tx: G1 (no DGF and/or AR; n=28) and G2 (with DGF and/or AR; n=12).
Results: There was no difference in the demographic data, while the groups differed significantly in the mean cold ischemic time (3.2±1.1 vs. 4.2±0.6; $p<0.01$) in G1 and G2, respectively. G2 had also significantly higher ET_1 levels after and at day 1 post Tx, higher NO levels after Tx and at day 1 post Tx [102.7±37.1 vs. 44.9±22.4 ($p<0.01$); 76.5±43.7 vs. 21.5±12.8 ($p<0.01$); 138.8±12.8 vs. 120.6±38.6 ($p<0.05$) and 74.9±20.3 vs. 50.8±19.9 ($p<0.01$)], respectively. Moreover, significantly higher levels of FOR were found in G2 when compared with G1 after Tx, at day 1, and at 1 and 2 weeks post Tx [306.3±48.2 vs. 217.6±58.3 ($p<0.01$); 336.3±112.8 vs. 154.8±61.6 ($p<0.01$); 341.3±90.3 vs. 210.6±92.8 ($p<0.01$), and 341.8±133.3 vs. 244.9±67.5 ($p<0.05$)], respectively. A significantly higher percentage of AR gr. IA, IIA and IIB was found in G2 in comparison with G1 at 1 and 6-month biopsy [75 vs. 32% ($p<0.01$) and 75 vs. 43% ($p<0.05$)], respectively. Importantly, the proportion of the increased mean CAN score (sum of scores for chronic histological changes) from 1 to the 6-month biopsy was higher in G2 [1.8±1.7 vs. 5.0±2.8; $p<0.01$; (278%)] in comparison with G1 group [2.2±1.5 vs. 4.5±2.0; $p<0.01$; (205%)]. However, the graft function in terms of calculated creatinine clearance was significantly superior in G1 compared to G2 at 1 month, while there was only a slight difference at 6 months after Tx.
Conclusions: The endothelial factors of IRI initiate an inflammatory immunological response and a subsequent occurrence of DGF/AR as reflected by the higher percentage of acute and chronic histological lesions at 1 and 6-month biopsy. Graft function was superior in the group without DGF/AR at 1 month, while it did not reach statistical significance at 6 months post Tx compared to the group with DGF/AR.

MP484 HISTOLOGICAL FINDINGS IN EARLY PROTOCOL BIOPSIES OF STABLE RENAL ALLOGRAFTS – BENEFICIAL EFFECTS OF TREATMENT OF BORDERLINE CHANGES AND SUBCLINICAL REJECTIONS

Jelka Masin-Spasovska[1], Goce Spasovski[1], Sonja Dzikova[1], Gordana Petrusevska[2], Ljupco Lekovski[3], Daniel Petrovski[3], Aleksandar Sikole[1], Zivko Popov[3], Ninoslav Ivanovski[1]. [1]*Department of Nephrology;* [2]*Department of Pathology;* [3]*Department of Urology, University Clinical Center, Skopje, Macedonia, The Former Yugoslav Republic of*

Introduction and Aims: The renal allograft biopsy plays an important role in the management of graft dysfunction. It is essential for an accurate diagnosis of rejection and may also demonstrate features of rejection which have a prognostic and therapeutic implications. The aim of the present study was to identify subclinical acute rejections (SAR) and borderline changes (BC) as well as the histological markers of chronic allograft nephropathy (CAN) among protocol biopsies performed at 1 and 6 months after living donor kidney transplantation, and to assess the possible beneficial effects of the treatment of SAR and BC found at 1-month biopsies, on the graft histology and function at 6 months.
Methods: Forty paired allograft biopsies performed at 1 and 6 months after transplantation were reviewed according to the Banff ' 97 scoring scheme. Patients were divided in two groups according to the treatment of BC and SAR found at 1-month biopsy to a group of treated and group of untreated BC and SAR. The tretment course consisted of 3 day pulses of 500 mg methylprednisolone each.
Results: The mean age of donors and recipients was 59.3±13.1 and 34.3±9.8 years, respectively. Among all biopsies only 7.5% (6/80) showed

no histopathological lesions. At first month biopsy the histology of BC was found in 32.5% and SAR in 40% of patients. At 6 months the proportion of these findings was even higher, 30% and 47.5%, respectively. The mean HI (histological index/total sum of scores for acute and chronic changes), increased significantly at 6-month biopsy 5.3±2.9 vs. 7.8±3.6 ($p<0.001$). Similarly, the mean CAN score (sum of histological markers for chronicity) of 2.1±1.5 at 1 month, increased significantly to 4.6±2.3 ($p<0.001$) at 6-month biopsy. When divided according to the treatment of BC and SAR, the group of treated BC/SAR found at 1-month biopsy had a mean HI score of 7.0±1.8, which remained almost at the same value at 6-month biopsy (7.3±2.4). On the other hand, the proportion of these changes in untreated BC/SAR group increased from 5.0±2.0 to 8.4±4.3 ($p<0001$). However, there was no significant difference in the graft function, i.e. calculated creatinine clearance at 1 and 6 months post transplantation, in both groups.
Conclusions: Based on our findings, we would suggest that 1-month protocol biopsy is a potentially useful tool, as it might detect a high incidence of BC or SAR in stable renal allografts. The presence of an untreated BC and SAR found at 1-month biopsies showed a greater susceptibility for histological deterioration on the 6-month biopsies, accelerating the process of CAN. Therefore, we would recommend a histological diagnosis of SAR and BC at 1-month after transplantation and antirejection treatment accordingly. However, it remains to be demonstrated weather the treatment of BC and SAR provides a long-term benefit on graft outcome and survival.

MP485 ADDITION OF SPIRONOLACTONE TO DUAL BLOCKADE OF RENIN ANGIOTENSIN SYSTEM (RAS) DRAMATICALLY REDUCES SEVERE PROTEINURIA IN RENAL TRANSPLANT PATIENTS: AN UNCONTROLLED PILOT STUDY AT SIX MONTHS

Eduardo Gutiérrez, Jorge González, Elisa Ramírez, Eva Mérida, José Mª Gutiérrez, Enrique Morales, Manuel Praga, Amado Andrés, José [a] Morales. *Nephrology Department, Hospital Universitario 12 de Octubre, Madrid, Spain*

Introduction and Aims: Experimental and clinical data strongly suggest that aldosterone may contribute to proteinuria and progressive renal disease. In fact, antagonist of aldosterone seems to be effective controlling proteinuria in native kidneys. However there is no information in renal transplant patients a population in whom the presence and the amount of proteinuria are risk factors for graft loss, cardiovascular disease and death.
The aim of the study was to evaluate if the addition of an antagonist of aldosterone, spironolactone, provide an additional antiproteinuric effect to the angiotensin converting enzyme inhibitor (ACEI) and angiotensin type 1 receptor antagonists (ARB).
Methods: We evaluate in 9 renal transplant patients (serum creatinine < 3 mg/dl) the six-month effects of spironolactone (25 mg/d) on severe proteinuria in spite of the treatment with ACEI (Enalapril or captopril) plus ARB (Losartan or Valsartan). Patients also received cation-exchange resins and they were carefully controlled (mainly renal function and serum potassium) in the renal transplant outpatient clinic, every week in the first month and twice a month thereafter.
Results: The most important data are showed in Table 1. The reduction in proteinuria (in seven patients more than 50%, mean 61.6%)) was early and sustained at six months with mild non-significant deterioration of renal function. Notably, nobody presented severe hyperkalemia.

Table 1

	Baseline	Month 1	Month 6
SCr (mg/dl)	1,6±0,6 (1,1-2,8)	1,6±0,5 (1-2,6)	1,7±0,5 (0,9-2,8)
MDRD-4 (ml/min)	54,6±17,4 (25,7-76,4)	52,8±15,5 (28-78,4)	47,9±15 (25-70)
Proteinuria (g/d)	4,9±1,5 (3-7,4)	3,4±1,4 (0,5-5,3)*	2,2±1,1 (0,4-3,8)**
Serum K (mEq/l)	4,6±0,4 (4-5,2)	4,7±0,7 (3,9-6,2)	5±0,9 (4-6,8)

*$p<0,05$ Baseline vs Month 1. **$p<0,05$ Baseline vs Month 6.

Conclusions: This pilot study demonstratred that Spironolactone dramatically decreased severe proteinuria in patients treated with ACEI plus ARB without significant changes on renal function or serum potassium. Therefore, it suggest that triple blockade of RAS is feasible in selected renal transplant patients to reduce proteinuria, although caution to avoid severe hyperkalemia is required. Finally, prospective and randomized studies testing the use of Spironolactone with or without ACEI/ARB after renal transplantation are mandatory.

MP486 EFFECT OF HCV VIRUS ON INSULIN RESISTANCE IN POST RENAL TRANSPLANT PATIENTS

Magdy El-Sharkawy [1], Manal Ali [2]. *[1] Nephrology, Ain-Shams University, Cairo, Egypt; [2] Clinical Pathology, Ain-Shams University, Cairo, Egypt*

Introduction and Aims: New-onset diabetes mellitus (NODM)is a common complication of kidney transplantation and is associated with increases in graft loss, morbidity and mortality.
Numerous epidemiological studies have reported a higher prevalence of type 2 diabetes mellitus (DM2) in subjects infected by
The aim of this work is to study the relation between insulin resistance and virus load in HCV +ve renal transplant patients with and without diabetes and to investigate the role of TNF-alpha.
Methods: Patients: this study included 79 patients, divided into 4 groups; Group I: 20 HCV +ve diabetic patients, Group II: included 23 HCV +ve non diabetic patients, Group III: 20 HCV –ve diabetic patients, Group IV: included 16 HCV-ve transplant patients. To all the following investigations were carried: HOMA method for insulin resistance.
Fasting serum glucose, ALT and AST, serum insulin, TNF-α measurements, anti-HCV antibodies (ELISA), and HCV RNA quantitative PCR. all HCV+ve patient had HCV before renal transplantation, and all are receiving CSA, MMF or AZA, and steroids.
Results: Showed that HOMA index was highly significantly increased in patients with HCV, HCV+DM and DM (GI, GII, GIII), compared with control (GIV) ($p<0.001$). Furthermore, patients with HCV+DM had statistically significant higher levels in HOMA index compared to those of DM alone ($p<0.001$). Serum TNF-alpha levels were also significant increased in patients with HCV and HCV + DM compared with patients with D.M alone and to control group ($p<0.001$). HCV RNA load showed a significant correlation with both HOMA index and TNF-alpha levels ($r = 0.811$ and 0.848, respectively) ($p<0.001$).
Conclusions: This study showed that HCV infection in renal transplant patients is associated with insulin resistance. And the degree of insulin resistance is directly proportional to the virus load. The mechanism of insulin resistance may be through increased TNF-alpha secretion, which showed also significant correlation with virus load.

MP487 EXCHANGE LIVING-DONOR KIDNEY TRANSPLANTATION: ITS MERIT AND LIMITATION

Yu Seun Kim [1], Byung Jun So [2], Hee Chun Yu [3], Kyu Ha Hyu [1], Myoung Soo Kim [1]. *[1] Surgery, Yonsei University Medical Center, Seoul, Korea; [2] Surgery, Wonkang University Hospital, Iksan, Korea; [3] Surgery, Chonbuk University Hospital, Jeonju, Korea*

Introduction and Aims: The shortage of donor organs is one of the major barriers to transplantation worldwide, and especially in countries where cadaveric organ donations are limited. An exchange donor (swap) program between two families was launched in Korea in 1991. After the success of direct donor exchanges, we have developed the swap-around program by enrolling many kinds of unrelated donors. We report here on our results of exchange living-donor kidney transplants.
Methods: From September 1995 to September 2006, we performed 1,163 kidney transplants. The living-unrelated donors (LURDs) were composed of 129 exchange donors and 269 non-exchange donors. We compared the results of exchange donor transplants with non-exchange donor kidney transplants.
Results: Compared with the non-exchange group, exchange group spent a lot of time on pretransplant dialysis until transplantation. And the proportion of preemptive kidney transplant was extremely lower in the exchange group (3.9%) than in the non-exchange group (14.1%) (p=0.005). In exchange group, blood O type kidneys were restrictively allocated to blood O type recipients (78.9%) compared to non-exchange donor group (54.4%) (p=0.007). Therefore the proportion of ABO identical matching transplantation of the exchange donor group was significantly higher than that of the non-exchange donor group (87.6% versus 75.1%) (p=0.004). The overall 10-year graft survival rate (86.3%) for exchange donor kidney

transplants was comparable to that for non-exchange donor (82.3%) and one-haplomatch (81.2%) kidney transplants (p=0.2994) (Fig.). The incidence of acute rejection was similar between the exchange (32.0%) and non-exchange (29.3%) donor groups. In multivariate survival analysis, the donor type (exchange versus non-exchange) did not impact on the graft survival rate.

Conclusions: We can expect excellent clinical results by the exchange living-donor kidney transplant program as an option to reduce the donor organ shortage. But the exchange program has a considerable limitation in blood O type recipients.

MP488 IS CYSTATIN C MORE SENSITIVE THAN CREATININE IN DETECTING EARLY CHRONIC ALLOGRAFT NEPHROPATHY?

Fernanda Ortiz[1], Aimo Harmoinen[2], Timo Paavonen[3], Petri Koskinen[1], Eero Honkanen[1]. *[1]Department of Nephrology, Helsinki University Central Hospital, Helsinki, Finland; [2]Department of Chemistry, Savonlinna Central Hospital, Savonlinna, Finland; [3]Department of Pathology, Tampere University Central Hospital, Tampere, Finland*

Introduction and Aims: Cystatin C (CyC) has been suggested as a more accurate indicator of renal function than creatinine (Crea).CyC performance against graft histopathology has not been investigated.

Our aim was to compare CyC and Crea-based methods as predictors of chronic allograft damage index (CADI)

Methods: 105 protocol biopsies obtained at 6 mo post-transplantation were classified with Banff'97 and CADI. CyC and Crea were measured concomitantly. Histology was correlated to CyC, Crea, their reciprocals, CyC-estimated GFR (Larsson), Cockroft&Gault (C&G) and abbreviated MDRD using Kendall's tau. The area under ROC curve (ROC-auc), sensitivity/specificity, positive and negative predictive values were calculated at CADI cut-off of 2.

Results: Mild histological changes were best revealed by Crea, although with modest sensitivity/specificity. A Crea threshold of 111 umol/L distinguished 74% of the patients with CADI>2 and excluded this condition in 66%. For Crea, ROC-auc was 0.72 (p<0.001). Crea and 1/Crea correlated best to CADI, chronic allograft nephropathy, chronic inflammation, tubular atrophy, vascular changes and glomerulopathy. Neither C&G nor MDRD improved Crea performance alone. CyC and Larsson formula performed the same (ROC-auc 0.67). A CyC threshold of 1.12 mg/L distinguished 69% of the patients with CADI>2 and excluded it in 60%. Significant tau correlation was found between CyC, 1/CyC and Larsson with CADI, chronic inflammation, tubular atrophy and chronic vascular changes.

Conclusions: CyC, 1/CyC and Larsson-estimated GFR did not offer significant advantages over Crea in predicting mild histological allograft changes. Protocol biopsy provides information that cannot be sensitively predicted by biochemical measurements used in clinical practice.

MP489 HIGHER, ALTHOUGH STABILIZED SERUM CREATININE AT THREE MONTHS AFTER KIDNEY TRANSPLANTATION MAY BE SUSPICIOUS OF SUBCLINICAL ACUTE REJECTION

Ivo Matl[1], Eva Honsova[2], Petra Hribova[3], Irena Brabcova[3], Vera Lanska[4], Ondrej Viklicky[1]. *[1]Department of Nephrology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Department of Pathology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [3]Transplantation Laboratory, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [4]Department of Statistics, Institute for Clinical and Experimental Medicine, Prague, Czech Republic*

Introduction and Aims: The primary aim of the study was to detect subclinical acute rejection (SAR) in protocol biopsy at three months after kidney transplantation, and search for possible clinical and laboratory associations.

Methods: Protocol biopsy was carried out in 257 patients (160 men, 97 women, mean age 51.8±12.4 years) with stabilized graft function at mean 95.0±10.8 days after renal transplantation (24 from living donor, 30 second or third transplants). Panel reactive antibodies (PRA) ≥50% were in 30 patients (pts) (11,9%). Immunosuppressive treatment was triple drug therapy based on either cyclosporine A (47 pts) or tacrolimus (190 pts), or sirolimus/everolimus (20pts) along with mycophenolate mofetil, and with induction therapy in living donor transplant recipients, repeated transplantations, and in recipients with high PRA.

Results: In 133 pts (51.7%), morphological finding was normal, subclinical acute rejection (SAR) was found in 17 pts (6.6%), borderline changes (BL) in 15 pts (5.8%), chronic allograft nephropathy (CAN) in 25 pts (9.7%). Three samples were non-representative, in remaining 64 pts, "other changes" (tubular, toxic, vascular, etc.) were found. Acute rejections before biopsy were significantly more frequent (p<0.001) in pts with SAR+ BL, as compared to pts with normal findings or pts with "other changes". In pts with SAR+BL, the mean serum creatinine was 168,4±76,6 umol/L, and glomerular filtration rate calculated by MDRD was 0.69±0.2 mL/s. Both values were significantly different (p<0.01) from those in pts with normal finding: 127,7±27,8 umol/L and 0,86±0,19 ml/s respectively. Using the ROC curve analysis, the cut-off point for serum kreatinine 170 umol/L was found to discriminate normal findings from SAR+BL (odds ratio 16,3 with CI 5,6-47.9). Prevalence of SAR+BL was similar in pts treated with regimen based on cyclosporine (12,7%) or tacrolimus (12,8%).

Conclusions: This study confirms relationship between early posttransplant acute rejections and SAR+BL. Pts with serum kreatinine ≥170 umol/L, despite stabilized graft function at 3 months after transplantation, were found to be at risk for SAR+BL

Supported by Internal Grant Agency from the Czech Ministry of Health No. NR8897-4.

MP490 REDUCED ELIMINATION OF CYCLOSPORINE A IN ELDERLY (>65) KIDNEY TRANSPLANT RECIPIENTS

Pål Falck[1], Anders Åsberg[1], Karen-Therese Byberg[1], Jan Leo E. Reubseat[2], Karsten Midtvedt[3]. *[1]Department of Pharmaceutical Biosciences, School of Pharmacy, University of Oslo, Oslo, Norway; [2]Department of Pharmaceutical Chemistry, School of Pharmacy, University of Oslo, Oslo, Norway; [3]Department of Medicine, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, Norway*

Introduction and Aims: The proportion of elderly renal transplant recipients is increasing. At older age many physiological functions are altered which may affect pharmacokinetics of drugs such as cyclosporine A (CsA). The current study was performed to elucidate the effect of age on CsA pharmacokinetics.

Methods: 12-hour pharmacokinetic profiles were assessed in 25 stable kidney transplant recipients during the first and second month after transplantation. The patients were divided into two groups based on age; A: 18-64 year (n=14) and B: >65 years (n=11). All patients were treated with CsA, mycophenolate and steroids and CsA doses were adjusted by C2-monitoring. Genotyping for *CYP3A5*1/*3* and *ABCB1* (C1236T, G2677T, C3435T) were performed in all patients. Pharmacokinetic parameters were estimated with a 2-compartment population model using Erlang distribution in the absorption phase (NONMEM™), and data analysed with parametric statistics (SPSS).

Results: The two groups were both within the target C2 levels (A = 1749 ±543 vs. B = 1489 ±600 μg/L, P=0.26), but group B (age>65) needed a significantly lower CsA dose (4.3 ±0.8 vs group A; 6.1 ±2.1 mg/day/kg, P=0.025) to achieve the target C2 levels. Group B had significantly lower clearance (CL/F) of CsA compared to group A (22.7 ±5.1 vs. 30.5±11.1 L/h, P=0.031). Pearson correlation coefficient revealed a significant negative relation between age and CL/F (N=25, R^2=0.18, P=0.036). Group B also tended to have longer half live (P=0.18) compared with group A, but no other pharmacokinetic parameters were different. Estimated creatinine clearance was similar in the two groups (A: 64.7 ±19.3, B: 69.6 ±17.5 mL/min). *CYP3A5*1* or *ABCB1* genotypes did not influence the pharmacokinetics.

Conclusions: Elderly patients have a significant lower elimination of CsA. They should therefore be dosed carefully to avoid side effects and be allowed longer time intervals between dose changes.

MP491 CALCINEURIN INHIBITOR INDUCED INSULIN RESITANCE FOLLOWING RENAL TRANSPLANTATION

Anders Åsberg[1], Karsten Midtvedt[2], Monica H. Voytovich[2], Pål-Dag Line[3], Janicke Narverud[2], Anna V. Reisæter[2], Lars Mørkrid[4], Trond Jenssen[2], Anders Hartmann[2]. *[1]School of Pharmacy, University of Oslo, Norway; [2]Medical Department, Rikshospitalet Medical Center, Norway; [3]Surgical Department, Rikshospitalet Medical Center, Norway; [4]Department of Clinical Chemistry, Rikshospitalet Medical Center, Norway*

Introduction and Aims: Calcineurin inhibitors (CNI) are involved in the development of post transplant diabetes mellitus (PTDM). Changes in insulin secretion and sensitivity are central mechanisms involved in the development of PTDM. In addition alterations in endothelial function seem to be involved. The present study investigated the effect of CNI s on these factors.
Methods: In a predefined sub-study of a previously published randomized trial it was aimed to compare the effect of CNI treatment (n=27) with complete CNI-avoidance (n=27) on insulin secretion and sensitivity as well as endothelial function. An oral glucose tolerance test and endothelial function investigation with laser Doppler flowmetry was performed in 44 patients, 10 weeks and 12 months following transplantation.
Results: Insulin sensitivity differed already 10 weeks posttransplant and was significantly better after 12 months in patients never treated with CNI drugs (P=0.043). Endothelial function was significantly correlated with insulin sensitivity (N=27, R2=0.22, P=0.013) at 10 weeks posttransplant, but not after 12 months (P=0.54). Insulin secretion tended to be higher in CNI treated patients both at week 10 and month 12 (P=0.068).
Conclusions: Findings in the present study indicate that long-term CNI treatment impairs insulin sensitivity which seems to be associated with impaired endothelial function. Insulin secretion tended to be increased as a reflection of the insulin resistance. These effects combined may indicate a future risk for premature cardiovascular disease in CNI treated renal transplant recipients, but this hypothesis needs further study.
Disclosure: Roche supplied the study wtih free daclizumab and a study grant.

MP492 MATRIX METALLOPROTEINASE-9 – A NEW MARKER OF CARDIOVASCULAR RISK AFTER RENAL TRANSPLANTATION?

Olga Mareckova[1], Vladimir Teplan[1], Marta Kalousova[2], Tomas Zima[2], Ondrej Viklicky[1]. *[1]Department of Nephrology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Department of Biochemistry, Medical Faculty I. Charles University, Prague, Czech Republic*

Introduction and Aims: Matrix metalloproteinases (MMPs) including pregnancy associated plasma protein-A (PAPP-A) and MMP-9 play a role in the progression of atherosclerosis. While PAPP-A has been proposed as a new predictor of cardiovascular risk after renal transplantation (RTx), MMP-9 levels after RTx have not been determined to date. Our study was designed to determine serum PAPP-A and MMP-9 after RTx and to correlate them with renal function.
Methods: Serum PAPP-A and MMP-9 were determined at 0, 6, and 12 months post-RTx in 80 pts - 49/31 M/F, age 48.7 (22-76) years and in 22 healthy controls – 10/12 M/F, age 51.0 (22-76) years. Renal function was determined as inulin clearance, serum PAPP-A and MMP-9 by ELISA.
Results: Serum PAPP-A was significantly increased at time 0 post-RTx compared with controls (24.4±12.1 vs. 9.6±1.7 mlU/l; $p<0.01$) and we noted a significant inverse correlation between inulin clearance and serum PAPP-A ($r=0.569$; $p<0.01$). Serum MMP-9 was significantly raised at 1 year post RTx as against controls: median 602 vs. 355 ng/ml; $p<0.01$. The correlation between increased MMP-9 levels and renal function was not significant.
Conclusions: The serum levels of PAPP-A are the highest prior to RTx, and their decline in the the early post-RTx period correlates with developing graft function. In contrast, serum MMP-9 increases in the late post-RTx period. Further research is needed to explain its rise, not due to a change in renal function.
Supported by Grant NR/9398-3 IGA MH Czech Republic.

MP493 ★ CLINICAL RELEVANCE OF PREFORMED HLA DONOR-SPECIFIC ANTIBODIES IN KIDNEY TRANSPLANTATION

Carmen Lefaucheur[1], Caroline Suberbielle-Boissel[2], Gary S. Hill[3], Dominique Nochy[3], Joao Andrade[2], Corinne Antoine[1], Dominique Charron[2], Denis Glotz[1]. *[1]Nephrology and Kidney Transplantation, Saint-Louis Hospital, Paris, France; [2]Immunology and Histocompatibility, Saint-Louis Hospital, Paris, France; [3]Histopathology, Georges Pompidou European Hospital, Paris, France*

Introduction and Aims: This study analyzes the influence of preformed DSA, identified by HLA-specific ELISA assays, on graft survival and evaluates the incidence of antibody-mediated rejection (AMR) in patients with and without pregraft desensitization.
Methods: To identify patients who might have preformed HLA DSA, not identified by routine lymphocytotoxicity assays, we retrospectively screened by HLA-specific ELISAs all 237 consecutive kidney transplant recipients (performed between 1998 and 2004) for the presence of DSA in historic sera and in that at the time of transplantation (D0). We analyzed the occurrence of rejection episodes and we compared the graft survival rates between the two groups: i) patients with DSA and ii) patients with no DSA.
Results: Kidney graft survival at 8 years was significantly worse in patients with DSA (n=43) than in those without DSA (n=194) (p=.03). The incidence of AMR in patients with DSA is 9-fold higher than in patients without DSA ($p<.001$) and their graft survival is significantly worse than in DSA patients without AMR and in non-DSA patients (p=.005). The prevalence for AMR in patients with DSA detected on historic serum is 32.3% in non-desensitized patients and 41.7% in desensitized patients. The risk for AMR is significantly more elevated in patients with strongly positive DSA (score 6-8) compared to those with DSA score 4 ($p<.001$), and in patients with historic DSA+/CXM+ compared to those with DSA+/CXM- (p=.01). The detection of D0 DSA in patients with prior positive DSA identified on historic sera did not confer an additional risk of humoral rejection (p=0.33). The prevalence of AMR in desensitized patients with peak DSA was not significantly different from that of non-desensitized patients (p=0.8).
Conclusions: The presence of preformed DSA is strongly associated with graft loss in kidney transplants, related to an increased risk of AMR. Our findings demonstrate the importance of detection and characterization of DSA before transplantation. Stratification of this risk could be used to determine kidney allocation and to devise specific strategies for these patients.

MP494 NOVEL METHOD OF QUANTIFICATION OF AN INTRARENAL RESISTANCE MEASURED BY DOPPLER SONOGRAPHY IN PATIENTS AFTER KIDNEY TRANSPLANTATION (KTx) WITH DISCONTINUOUS FLOW PATTERN

Aureliusz Kolonko, Jerzy Chudek, Andrzej Wiecek. *Dept. of Nephrology, Endocrinology and Metabol. Dis., Medical University of Silesia, Katowice, Poland*

Introduction and Aims: Intrarenal pulsatility (PI) and resistive (RI) indices measured by Doppler sonography are usually determined in patients after kidney transplantation in order to estimate the posttransplant interstitial oedema. However in patients with delayed graft function PI and RI values hardly predict time of acute tubular necrosis (ATN) subsiding. Therefore we propose a new method to express the value of an intrarenal resistance, based on time of blood flow during heart cycle period in segmental arteries of the renal transplant. In this study we have analyzed the correlation of this new ratio with the duration of ATN after KTx.
Methods: Doppler sonography was performed at 2^{nd}-4^{th} day after KTx in 122 patients transplanted in our center in 2006-2007 (group I). 49 of them (40%) developed ATN, defined as the need of more than one hemodialysis after KTx. In patients without continuous flow in segmental arteries we have quantified intrarenal resistance as the time during the whole heart cycle in which the flow is present. Control (historical) group consisted of 450 patients transplanted between 1998 and 2005 (group II), in which we measured PI and RI by Doppler sonography at the same timepoint. 171 of them (38%) developed ATN according to the same criteria as for group I. Patients with primary graft nonfunction were excluded from all analyses. Results are expressed as means and 95% CI.

Results: In 27 out of 47 patients with ATN the pattern of blood flow was not continuous. The mean flow time was 500 ms (250-700). There was a significant correlation between the flow time and the length of ATN defined as time to the last dialysis needed (tau -0.347, p=0.04). The similar relationship between the values of PI and RI and the lenght of ATN in the control group (II) was not significant.
Conclusions: The novel method of quantification of discontinuous flow pattern in segmental arteries of kidney graft gives a better prediction of ATN subsiding than separate PI or RI.

MP495 ★ PROTEINURIA AND SIROLIMUS: ANALYSIS OF 185 PATIENTS

Rita Birne[1], Teresa Adragao[1], Ana P. Martins[2], Augusta Gaspar[1], Patricia Branco[1], Lucia Parreira[1], Celia Nascimento[1], Jorge Dickson[1], Domingos Machado[1]. [1]*Kidney Transplant, Hospital Santa Cruz, Carnaxide, Portugal;* [2]*Pathology, Hospital Santa Cruz, Carnaxide, Portugal*

Introduction and Aims: The question of how sirolimus (SRL) therapy is connected with proteinuria remains open to discussion.
We retrospectively analysed a very large cohort of SRL-treated kidney transplant (KT) recipients and tried to understand the magnitude and predictor factors of proteinuria development and the effect of proteinuria development on graft function.
Methods: We reviewed all SRL-treated patients from our KT Department.
Results: 185 patients (pts) with 41±15 years old were submitted to SRL therapy 38,5±49,9 months after KT. Reasons for SRL immunosuppression (IMS) were neoplasia (26 pts), former IMS adverse effect (33 pts), chronic allograft nephropaty (CAN, 87 pts), delayed graft function (28 pts), SRL-based regimen (11 pts).
Mean 24 hour proteinuria increased after conversion, from 372mg at the switch to 874mg and 967mg at 3 and 6 months respectively, after SRL.
Heavy proteinuria (>1.5 g/24h) appeared in 22% of pts. Forty-three pts (23%) developed proteinuria "de novo" and in 13 pts (7%) it reached nephrotic levels. Independent predictors of nephrotic proteinuria were proteinuria before conversion (OR 3.13, p=0.013), black race (OR 12.9, p=0.006), months after KT (OR 1.02, p=0.05))and peak SRL levels (OR 1.09, p=0.047). Independent predictors of proteinuria 6 months after srl were proteinuria before conversion (B 1.32, p<0.01), months after KT (B 0.005, p=0.034), peak (B 0.046, p=0.006) and average SRL levels.
Proteinuria increase at 6 months was significantly higher in pts switched to SRL because of CAN than in the remaining groups (p=0.015). Nephrotic proteinuria de novo developed exclusively in those pts converted for CAN or for calcineurin inhibitor adverse effects.
Mean creatinine went down from 2.74±1.71 mg/dl before SRL to 2.13±1.08, 2.07±0.93 and 1.95±0.83 mg/dl at 3, 6 and 12 months, respectively, after SRL. At 12 months follow-up, kidney function improved or remained stable in 50.8% pts, worsened in 10.8% pts and the graft was lost in 11.4% pts. Independent predictors of creatinine increase or graft loss were proteinuria before conversion (OR 2.39, p=0.51), months after KT (OR 1.01, p=0.050) and increase in proteinuria after SRL (OR 10.54, p=0.004), which significance become even stronger when considering only those pts with late conversion to SRL (OR 3.20, p=0.037; OR 1.01, p=0.043; OR 7.74, p=0.019).
Conclusions: In conclusion, proteinuria can heavily increase or appear "de novo" with SRL-therapy, and independent factors observed were the already presence of proteinuria before conversion, months after KT and srl levels. Different explanations for SRL-proteinuria can be hypothesised, including, besides the interruption of a cyclosporine hemodynamic and immunomodulator effect, a possible direct effect of SRL in some susceptible cases.
The majority of the pts had good graft outcome at 12 months follow-up. Proteinuria development was the strongest predictor of graft dysfunction.

MP496 INTRAOPERATIVE AND POSTOPERATIVE RESISTANT INDICES MEASURED BY DOPPLER METHOD AS PREDICTORS OF EARLY KIDNEY ALLOGRAFT FUNCTION

Aureliusz Kolonko[1], Robert Krol[2], Jerzy Chudek[1], Jacek Ziaja[2], Lech Cierpka[2], Andrzej Wiecek[1]. [1]*Dept of Nephrology, Endocrinology and Metabol. Dis., Medical University of Silesia, Katowice, Poland;* [2]*Dept of General, Vascular and Transplant Surgery, Medical University of Silesia, Katowice, Poland*

Introduction and Aims: Kidney recipients who develop slow (SGF) or delayed graft function (DGF) present a worse long-term graft survival compared to those with immediate graft function (IGF). Early diagnosis of impaired graft function creates a potential chance of treatment modification. The aim of our prospective study was to compare the values of pulsatility (PI) and resistive indices (RI) measured both intraoperatively and postoperatively in kidney graft arteries as predictors for early graft function.
Methods: Intraoperative (before operative wound closure) transit time flowmetry and postoperative (at 2nd-4th day after kidney transplantation - KTx) Doppler ultrasound examinations were performed in 61 patients who received kidney graft supported with a single artery. Patients with episodes of acute rejection or other serious complications were excluded. IGF (n=19) was defined as serum creatinine concentration (SCr) on the 3rd day after KTx below 264 μmol/l, SGF (n=21) as SCr above 264 μmol/l and a need for maximum one dialysis, and DGF (n=21) if patient required more than one dialysis after KTx. Data are presented as means and 95% CI.
Results: In both intraoperative and postoperative measurements significantly higher values of PI and RI were observed in patients with SGF and DGF than in patients with IGF (see Table 1 below). In the second measurement the increase of PI and RI was observed independently of early graft function. The highest increases of PI and RI values were noticed in IGF group.
Conclusions: 1. High values of PI and RI measured before the end of operation and within first postoperative days comparably predict an impairment of kidney allograft function in early postoperative period. 2. The increase of both PI and RI within an early postoperative period are observed regardless of the kidney graft function.

MP497 SUCCESSFUL ABO-INCOMPATIBLE RENAL TRANSPLANTATION WITH MODEST IMMUNOSUPRESSION AND LOW MORBIDITY

Solomon Cohney[1], Masterson Rosemary[1], Walker Rowan[1], Flint Shaun[1], Francis David[1], Robertson Amanda[1], Miller Robert[1], Hogan Chris[2], Becker Gavin[1]. [1]*Nephrology, Royal Melbourne Hospital, Melbourne, Victoria, Australia;* [2]*Haematology, Royal Melbourne Hospital, Melbourne, Victoria, Australia*

Introduction and Aims: Until recently it has been standard practice to perform splenectomy and utilize higher levels of immunosuppression in recipients of ABO incompatible renal transplants (ABO Inc). This practice raises concern regarding increased risk of infective and neoplastic complications particularly in elderly recipients and those with significant co morbidity. We report a series of 26 patients, who have successfully undergone ABO Inc without splenectomy, anti-T cell antibody or pre-transplant Tacrolimus.
Methods: Between Dec 2005 & Dec 2007, 26 patients (11F; 15M) median age 37.4 years (15.3 – 73.9) have successfully undergone ABO Inc. at our institution. Pre-transplant, Saline AHG titres ranged from 1:32 to 1:64 000, (median 1:512). The blood group incompatibilities were A1 to O (n=12); A2 to O (n=3); AB to A (n=4); B to O (n=4); B to A (3). Transplantation was carried out after 1 to 2 weeks of Mycophenolate mofetil (MMF) and antibody removal (plasma exchange (n=22), and/or immunoadsorption with Glycosorb columns (n=4). Four patients received Rituximab. Post

Abstract MP496 – Table 1

	IGF		SGF		DGF	
	PI	RI	PI	RI	PI	RI
Intraoperative	0.8 (0.66-0.94)	0.53 (0.46-0.6)	1.14‡ (0.97-1.32)	0.64‡ (0.58-0.7)	1.71§ (0.85-2.57)	0.71§ (0.63-0.79)
Postoperative	1.48** (1.22-1.73)	0.68 ** (0.59-0.76)	1.66 (1.34-1.99)	0.77*†(0.71-0.82)	2.09**‡ (1.65-2.53)	0.83*‡ (0.76-0.9)

Statistical significance vs intraoperative *p<0.05; **p<0.01; statistical significance vs IGF †p<0.05; ‡p<0.01; §p<0.001.

transplantation, baseline immunosuppression consisted of Prednisolone, MMF (initial;1g b.i.d, reduced to 500 mg b.i.d by 6 weeks) & Tacrolimus targeted to trough levels:

0–2 weeks	2 weeks–month 2	month 2–3	> 3 months
10-15 ng/mL	8-12 ng/Ml	6-10 ng/mL	4-8 ng/mL

All but 1 patient received post transplant antibody depletion (plasma exchange ± immunoadsorption).

Results: At a median follow up of 8.3 months (range 0.4 - 24.2), patient and graft survival is 100%. Three patients have required treatment for antibody-mediated rejection (one due to a coexisting donor specific anti-HLA Ab) and 2 for cellular rejection. Recipient renal function (median serum creatinine 140 (80 – 240) mmol/l) is similar to donor renal function in all cases (except one with ureteric complications). Complications included transient BK viraemia (3), tissue invasive CMV disease in the setting of inadequate prophylaxis (1), urosepsis (3) and transient glucose intolerance (1).

Conclusions: We conclude that ABO Incompatible Kidney Transplantation can be performed safely without requirement for excessive immunosuppression thus significantly increasing transplant options for patients with ESKD.

MP498 EARLY ACUTE REJECTION IS A SIGNIFICANT RISK FACTOR FOR PREMATURE PATIENT DEATH IN KIDNEY TRANSPLANT RECIPIENTS OVER 60 YEARS

Kristian Heldal[1,2], Anders Hartmann[2], Torbjorn Leivestad[3], Martin Veel Svendsen[4], Bjorn Lien[5], Karsten Midtvedt[2]. *[1]Clinic of Internal Medicine, Sykehuset Telemark HF, Skien, Norway; [2]Section of Nephrology, Rikshospitalet, Oslo, Norway; [3]Institute of Immunology, Rikshospitalet, Oslo, Norway; [4]Research Unit, Sykehuset Telemark HF, Skien, Norway; [5]Department of Surgery, Rikshospitalet, Oslo, Norway*

Introduction and Aims: The number of elderly patients requiring renal replacement therapy (RRT) is markedly increasing. Elderly patients may benefit from kidney transplantation, but selecting those with the best probability to benefit is a challenge. In this study we investigated whether any variable present at transplantation or early thereafter could affect patient survival following renal transplantation.

Methods: Adult kidney transplant recipients who received their first graft between Jan 1st 1990 and Dec 31st 2005 were investigated. A validated comorbidity score was calculated (Charlson Comorbidity Index, CCI, range 1-25). The patients were grouped according to their age at grafting; Elderly (≥ 70 years), Senior (60-69 years) and Control (45-54 years). Potential covariates were analysed with respect to patient death in a univariate Cox regression model. Variables with significant impact ($P \leq 0.05$) were further analyzed in a multivariate model. Separate analyses were made in each age group.

Results: Data from 816 patients were evaluated. The following variables were included in the multivariate model: CCI, recipient age, donor age, HLA matching (no vs. any mismatch, tested separately for A, B and DR), CMV serostatus at transplantation, living donor, pre-emptive transplantation, time on dialysis prior to transplantation, delayed graft function and acute rejection episodes. Covariates with significant impact in this analysis are shown in table 1.

Table 1

Group	Variable	HR	95% CI	P-value
Elderly (≥ 70 years)	Rejection	1.880	1.313-2.691	0.001
N = 221	Time on dialysis (per month)	1.021	1.008-1.034	0.002
Senior (60-69 years)	CCI score	1.180	1.048-1.327	0.006
N = 295	Rejection	1.460	1.008-2.115	0.045
Control (45-54 years)	CCI score	1.272	1.057-1.529	0.011
N = 300	Pre-emptive transplantation	0.365	0.144-0.928	0.034
Non-elderly	CCI score	1.202	1.087-1.329	< 0.001
(Senior + Control)	Recipient age	1.072	1.050-1.095	< 0.001
N = 595	Pre-emptive transplantation	0.530	0.327-0.859	0.01

Conclusions: Early acute rejection following renal transplantation is a powerful predictor of premature death in kidney recipients over 60 years of age. This finding suggests that sufficient immunosuppression may be particularly important in recipients over 60 years. Time on dialysis but not CCI score was a significant predictor of death in recipients over 70 years.

MP499 IMMUNOSUPPRESSION WITH MYCOPHENOLATE MOFFETIL IS ASSOCIATED WITH BETTER PATIENT SURVIVAL THAN TREATMENT WITH AZATHIOPRINE IN RECIPIENTS BEYOND 70 YEARS OF AGE

Kristian Heldal[1,2], Anders Hartmann[2], Torbjorn Leivestad[3], Martin Veel Svendsen[4], Bjorn Lien[5], Karsten Midtvedt[2]. *[1]Clinic of Internal Medicine, Sykehuset Telemark HF, Skien, Norway; [2]Section of Nephrology, Rikshospitalet, Oslo, Norway; [3]Institute of Immunology, Rikshospitalet, Oslo, Norway; [4]Research Unit, Sykehuset Telemark HF, Skien, Norway; [5]Department of Surgery, Rikshospitalet, Oslo, Norway*

Introduction and Aims: Elderly kidney recipients have lower rejection rates than younger individuals and it has been argued that they may need less aggressive immunosuppressive treatment. We explored this issue in kidney recipients over 70 years of age at our centre.

Methods: Elderly kidney recipients over 70 years of age at transplantation receiving their first graft between Jan 1st 1996-Dec 31st 2005 and treated with calcineurin inhibitor, prednisolone and either azathioprine (AZA) or mycophenolate moffetil (MMF) were evaluated. Patients who were switched from AZA to MMF (or vice versa) during the first three months after transplantation were excluded leaving 149 recipients for analysis. Hazard ratio for death with AZA versus MMF was calculated in a Cox regression multivariate model adjusting for other known risk factors with significant impact in univariate analysis. These included comorbidity score, non pre-emptive transplantation, time on dialysis, deceased donor, recipient and donor age, CMV serostatus, HLA match (no vs. any mismatch, tested separately for A, B and DR), delayed graft function and acute rejection episodes. Survival analysis was done by the Kaplan Meyer method. The results were compared with 197 senior recipients 60-69 years of age from the same time period.

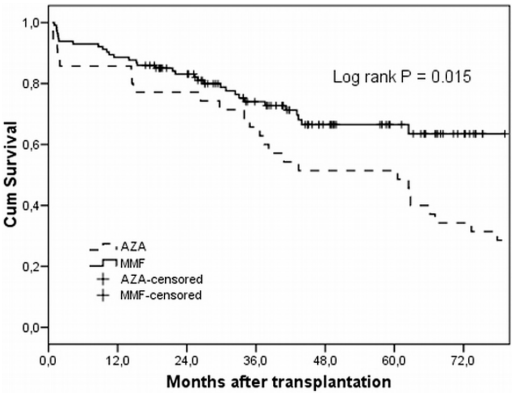


Figure 1. Elderly recipients: 70+ years.

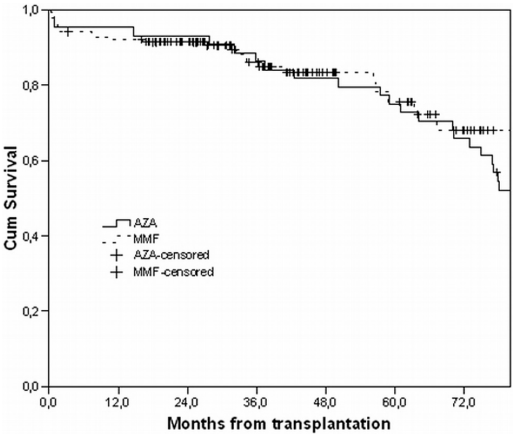


Figure 2. Senior recipients: 60–69 years.

Results: Thirty-five elderly recipients were treated with AZA, 114 received MMF. In the AZA group, 13 patients (37%) developed acute rejection during the first 3 months post transplantation opposed to 32 patients (28%) in the MMF group; ns. Elderly recipients receiving AZA had significant higher risk of death than patients receiving MMF; HR 2.04, 95% CI 1.19-3.50, P = 0.009. Five year patient survival was 51% in the AZA group compared to 67% in the MMF group. There was no difference in survival between AZA (n = 44) and MMF (n = 153) patients in the senior group. Kaplan Meyer plots of patient survival in the AZA and MMF groups are shown in Figures 1 and 2.
Conclusions: Kidney recipients over 70 years of age at transplantation receiving MMF had superior survival compared to the recipients receiving AZA. Elderly kidney recipients appear to benefit from triple immunosuppression with MMF rather than azathioprine.

MP500 EDUCATION LEVEL AND PROBABILITY OF UNDERGOING RENAL TRANSPLANTATION IN A REGION OF CENTRAL ITALY

Anteo Di Napoli, Domenico Di Lallo, Lazio Dialysis Registry. *Agency Public Health Lazio*

Introduction and Aims: The rate of renal transplantation in the Lazio region of central Italy is much lower than that in northern Italian regions or other industrialised countries, such as Spain and USA. Some studies have found differences in the access to and candidacy for renal transplantation, that are associated with non-clinical factors such as sex, race, and income. Education level, as a component of socioeconomic status, may be a surrogate for other factors, related to patient's individual and social capability of being identified as a transplant candidate. The objective of this study was to evaluate the effect of level of education on access to renal transplantation among patients undergoing dialysis in the Lazio Region.
Methods: All 3677 patients aged 19–64 years, starting dialysis from 1-1-1995 to 31-12-2006, notified to Lazio Dialysis Register (RDL), were enrolled in a cohort and followed-up lasted until renal transplantation or death; then we excluded 509 subjects from analysis, because defined not clinically suitable by nephrologists. We used the Kaplan-Meier method to compare the cumulative incidences of transplantation among different educational level (elementary/junior, high school, college degree). We evaluated the effect of educational level on access to renal transplantation with a Cox multivariate regression, adjusting for age, gender, primary nephropathy, presence of diabetes, HCV status, type of dialysis, hematocrit level, serum albumin level, degree of self-sufficiency.
Results: A total of 750 patients (23.6%) underwent renal transplantation. Figure shows the higher cumulative probability of transplantation in the 12 years after the start of renal replacement therapy, for persons with higher level of education (high school or college degree) compared with elementary/junior. We found from the multivariate Cox regression analysis that education level was an independent determinant of undergoing transplantation: HR=1.63;95%CI=1.38-1.93 for patients with a high school degree and HR=1.88;95%CI=1.50-2.36, for those with a college degree, compared with patients with an elementary school/junior educational level.

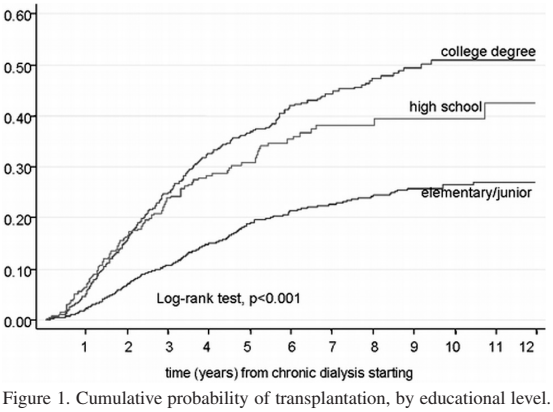


Figure 1. Cumulative probability of transplantation, by educational level.

Conclusions: Our data show that educational level plays an independent role on probability of undergoing renal transplantation, even when taking into account some important demographic, clinical, and health care setting factors. As our register does not collect information on the waiting list timing, we are not able to investigate the possible role of this factor. However, it is of extreme concern for public health policy, that in a country such as Italy, where the National Health Service provides renal transplants at no cost to the person, the absence of economic barriers does not reduce the level of discrimination in the access to a life saving treatment.

MP501 PREVALENCE AND RISK FACTORS OF ANEMIA AFTER KIDNEY TRANSPLANTATION

Roberto Marcen[1], Belen Ponte[1], Nuria Rodriguez[1], Ana Fernandez[1], Julio Pascual[1], Juan Jose VIllafruela[1], Jose Luis Teruel[1], Fernando Liano[1], Francisco Javier Burgos[2], Joaquin Ortuno[1].
[1]Nephrology, Ramon y Cajal University Hospital, Madrid, Spain; [2]Urology, Ramon y Cajal University Hospital, Madrid, Spain

Introduction and Aims: Anemia is a common complication after kidney transplantation. Its prevalence and risk factors vary among the different series. Moreover, the management of this complication has been reported many times to be inappropriate according to the recommendation given for non-transplanted patients with chronic kidney disease. The purpose of the present study was to investigate the prevalence of anemia, the risk factors associated with its development and the adequacy of its treatment in a cohort of patients with functioning grafts.
Methods: 555 patients, 328 men and 228 women with a mean age at transplant of 45.9±14.6 years were included in a cross-sectional study. Anemia was defined as a serum hemoglobin (Hb) $\leq$ 13 g/dl in men and $\leq$ 12 g/dl in women.
Results: The mean estimated glomerular filtration rate (eGFR) by the MDRD equation was 47.3±18.7 ml/min/1.73m^2, the serum Hb 13.5±1.7 g/dl, and the serum ferritin 153±185 ng/dl (41.4% <100 ng/ml). Anemia affected 157 patients (28.3%): mild 17.6%, moderate 6.7% and severe 4.0%. In the univariate analysis, Hb levels correlated with eGFR (r=0.44; p=0.000) and seroalbumin (r=0.29; p=0.000). Anemia was more common in the 179 patients on treatment with angiotensin converting enzyme inhibitors (ACEI) or with angiotensin II receptor antagonists (ARA): 38% vs 24% (p=0.001). The multivariate analysis showed the same risk factors observed in the univariate analysis. Anemia was negatively associated with eGFR (OR=0.96; CI 95% 0.94-0.97; p=0.000) and serum albumin levels (OR=0.19; CI 95% 0.09-0.50; p=0.000) but positively associated with the treatment with ACEI or ARA (OR=1.65; CI 95% 1.04-2.62; p=0.033). Anemia was not related to sex, serum ferritin levels or immunosuppressant agents. Only about 27% of anemic patients and 41% of those with Hb<11 g/dl were on treatment with erythropoiesis-stimulating agents.
Conclusions: Anemia was common after transplantation and some patients were not adequately treated. The factors associated with this complication were graft function, protein/energy malnutrition or chronic inflammation and some antihypertensive agents.

MP502 STEROID AVOIDANCE IMMUNOSUPPRESSION: LONG TERM EVALUATION IN LIVE DONOR RENAL ALLOTRANSPLANT RECIPIENTS

Ahmed Nematalla, Mohmed Bakr, Osama Gheith, Ahmed Akl, Amgad ELAgroudy, EL-Metwally ELShahawy, Mohmed Ghoneim.
Nephrology, Urology and Nephrology Center, Mansoura, Dakahleya, Egypt; Nephrology, Urology and Nephrology Center, Mansoura, Dakahleya, Egypt; Nephrology, Urology and Nephrology Center, Mansoura, Dakahleya, Egypt; Nephrology, Benha University, Benha, Kalyobeya, Egypt; Urology, Urology and Nephrology Center, Mansoura, Dakahleya, Egypt

Introduction and Aims: Steroids had the main role in renal transplantation since more than four decades.However; chronic use of steroids was associated with a lot of co- morbidities.So we aimed to assess the long term safety and efficacy of steroid free immunosupression regimen in live donor renal transplant recipients.
Methods: Ninety eight patients were randomized to receive tacrolimus (FK), mycophenolate mofetil (MMF), and basiliximab (simulect) as an induction. Steroids were given only for 3days in (49 patients, Study group)and was maintained in (49 patients, control group).Median follow up was 36 months.

Results: By the end of the third year, Patient and graft survivals were 100% in both groups. Biopsy proven acute rejection episodes were 16% in both groups.Mean serum creatinine was 1.34 mg/dl in steroid free group vs.1.33 mg/dl in the control group. Post-transplant hypertension was 4.1% vs. 14.3% respectively (p=0.08). Post-transplant D.M. was 0% vs. 26.5% respectively (p=0.0001). Post-transplant wait gain was 6% vs. 15% respectively (p=0.001). The two groups were comparable regarding cases with hepatic impairment, serious bacterial infections or malignancies (p=>0.05).
Conclusions: In cases with low immunological risk, steroid free regimen was safe and tolerable without morbidities in live donor kidney transplants, however long term use of steroids was associated with post-transplant diabetes.

MP503 INFLUENCE OF ELEVATED HOMOCYSTEIN LEVEL AND SELECTED LIPID PARAMETERS IN RENAL TRANSPLANT PATIENTS ON THE PROGRESSION OF ATHEROSCLEROTIC CHANGES ASSESSED BY INTIMA/MEDIA THICKNESS INDEX (CCA IMT)

D. Aksamit, K. Janda, E. Ignacak, E. Chowaniec, M. Kowalczyk-Michalek, B. Tabor-Ciepiela, W. Sulowicz. *Chair and Department of Nephrology, Jagiellonian University, Cracow, Poland*

Introduction and Aims: The aim of the study was to evaluate the influence of elevated homocystein level and selected lipid parameters on the progression of atherosclerotic changes in patients (pts) after renal transplantation (RTx). The study included 51 pts (17 F, 34 M) aged 15 - 62 years (median 38.1) after cadaver RTx. The mean observation period equaled 21.2 months (6 - 24 months); while total observation period was 90 person/years. Before RTx 46 pts were treated with hemodialysis, while 5 by peritoneal dialysis. Mean time on dialysis was 38.4 months (5–106). Total ischemia time ranged from 3 to 30 hours (mean 15.7). Mean HLA mismatch was 4. After RTx patients had immunosuppression: prednisone (P) + CsA + azathioprine (AZA) – 12 pts, P + CsA + mycophenolate mofetil (MMF) – 26, P + Tac + MMF – 11 and P + Tac + AZA – 2.
Methods: Homocystein level was measured using high performance liquid chromatography. Lp(a) and Apo-B levels were measured using the nephelometric method. Total cholesterol with its' HDL and LDL fractions, triglycerides and creatinine were measured by standard methods using the Hitachi 917 analyzer. Patients' blood was drawn before renal transplantation and 3, 6, 9, 12, 15, 18, 21 and 24 months after RTx. CCA-IMT was evaluated by ultrasound on 14 days, 12 and 24 months after RTx.
Results: CCA-IMT correlated significantly with homocystein levels after 12 months (R=0.53, p=0.0009) and 24 months (R=0.38, p=0.0356) post RTx. No correlation was found in the first test (before RTx) (Hcy vs. CCA–IMT; R=0.15, p=0.3417). Significant differences were found 12 and 24 months after RTx in CCA-IMT between pts with normal (≤15 umol/l) and increased (>15 umol/l) mean homocysteine concentrations, respectively: p=0.0035 and p= 0.015. Analyzing changes in CCA-IMT, significant differences were noted when comparing the CCA-IMT increment after 12 and 24 months post RTx in pts with normal (≤15 umol/l) and increased (>15 umol/l) mean homocystein concentrations, respectively: p=0.049 and p= 0.0039. No statistical differences were found between Lp(a), Apo B level (except after 9 months: R=0.15, p=0.3787) in patients having normal (≤15 umol/l) and increased (>15 umol/l) mean homocystein concentrations. Increment of CCA-IMT 12 months after RTx, significantly correlated with mean total cholesterol level (dIMT vs. chol. R=0.35, p=0.0333), but not with the HDL, LDL, Lp(a) and ApoB. Increment of CCA-IMT 24 months after RTx correlated significantly with mean level of Lp (a) (dIMT vs. Lp(a) R= -0.38, p= 0.0315), but did not correlate with the HDL, LDL and Apo B. Even though no statistical significance was noted, patients with increased total cholesterol (>5,2mmol/l) had a higher by 42% CCA-IMT when compared to remaining patients.
Conclusions: Homocystein level is an independent risk factor for atherosclerosis development in patients after RTx. After transplantation, elevated homocystein level as well as increased cholesterol and Lp (a) levels enhance progression of atherosclerotic changes evaluated by CCA-IMT.

MP504 CONVERSION FROM CYCLOSPORIN A TO TACROLIMUS DOES NOT INFLUENCE INSULIN SENSITIVITY IN KIDNEY TRANSPLANT PATIENTS DURING THREE MONTHS OBSERVATION PERIOD

Andrzej Wiecek, Maciej Bulanowski, Jerzy Chudek. *Department of Nephrology, Endocrinology and Metabolic Diseases, Medical University of Silesia, Katowice, Slask, Poland*

Introduction and Aims: Calcineurin inhibitors (Cyclosporin A- CyA and Tacrolimus- Tc) are immunosuppressive agents used in the standard triple immunosuppressive regiments in kidney transplant patients. Tc based regiments are claimed to increase the incidence of glucose metabolism disorders, partially explained by delayed and flattened secretion of insulin after meal ingestion. Only limited number of studies have analyzed changes of insulin sensitivity by metabolic clamp technique after replacement of CyA by Tc. This prospective, open study was designed to analyze insulin sensitivity in patients with normal glucose metabolism and stable kidney graft function treated with CyA and then switched to the Tc therapy.
Methods: 15 (F7/M8) non-diabetic patients after renal transplantation (BMI 26,5±0,9 kg/m^2; eGFR 37,4±4,7 ml/min, 42,1 ± 8,7 months after transplantation) receiving CyA based regiment were converted to Tc treatment. The causes of conversion were CyA side effects (hirsutismus, gingival hypertrophy, hyperlipidaemia, arterial hypertension). Insulin sensitivity was estimated using hyperinsulinemic, euglycemic clamp technique (DeFronzo *et al.* 1979) shortly before and 3 months after conversion. The doses of prednisone (8±1mg) were not modified. CyA and Tc serum concentrations were within therapeutic range (mean trough levels 148,5±11,2 ng/ml and 8,7±0,6 ng/ml respectively).
Results: Two out of 15 patients developed diabetes shortly after conversion and were excluded from further evaluation. In the remaining 13 patients the calculated insulin sensitivity index (M/I) did not change significantly (7,8 ±1,2 vs 9,0±1,2 on CyA and Tc respectively). Also body mass and eGFR did not change significantly (-0,3±0,9 kg; -1,5 ±1,3 ml/min). Moreover a strong correlation was found between changes of body mass and insulin sensitivity index (R=0,773; p=0,002).
Conclusions: Prodiabetogenic properties of tacrolimus in kidney transplant patients is not caused by its influence on insulin sensitivity.

MP505 THE INFLUENCE OF TUBULAR PHENOTYPIC CHANGES ON THE DEVELOPMENT OF DIFFUSE INTERSTITIAL FIBROSIS IN RENAL ALLOGRAFTS

Binnaz Handan Ozdemir[1], Beyhan Demirhan[1], Fatma Nurhan Ozdemir[2], Mehmet Haberal[3]. [1]*Pathology, Baskent University, Ankara, Turkey;* [2]*Nephrology;* [3]*General Surgery and Transplantation*

Introduction and Aims: It has been reported that myofibroblasts are the major cells in the development of interstitial fibrosis (IF) and therefore chronic graft dysfunction in renal allografts. In normal human kidney, tubular cells do not have myofibroblast differentiation and they don't have alpha-smooth muscle actin (alpha-SMA) expression.
Methods: In this study we aimed to show that tubular cells can undergo phenotypic changes toward myofibroblasts and induce early IF and poor graft outcome in renal allografts. The expression of alpha-SMA and the formation of vinculin and paxillin containing adhesion complexes are the primary criteria for determining the differentiation of non-muscle cells such as renal tubule cells into contractile myofibroblasts. For this reason we immunostained first year renal allograft biopsies of 74 patients with alpha-SMA, Vinculin and Paxillin primary antibodies and the expression of tubules and glomerular cells were evaluated.
Results: Myofibroblast differentiation of renal tubules (alpha-SMA, vinculin and paxillin positive tubules) was found only 30 of 74 patients. In addition glomerular cells of 36 patients showed positive alpha-SMA, vinculin and paxillin staining. The development of diffuse IF was found significantly early in cases with tubules showing myofibroblast differentiation compared to cases with tubules that did not have myofibroblast differentiation ($p<0.01$). The presence of proteinuria in first year showed significant positive correlation with the glomerular alpha-SMA, vinculin and paxillin staining ($p<0.001$). Cases whom showed tubular and glomerular alpha-SMA, vinculin and paxillin staining showed worse graft outcome compared to cases that did not show tubular and glomerular staining ($p<0.001$).

Conclusions: In conclusion our results showed that renal tubular and glomerular cells can show myofibroblastic differentiation and these cells have a role in the development of diffuse interstitial fibrosis and early proteinuria in renal allografts.

MP506 THE MANAGEMENT OF CHRONIC KIDNEY DISEASE AFTER RENAL TRANSPLANTATION. DATA FROM A SPANISH, MULTICENTER, CROSS-SECTIONAL STUDY

Roberto Marcen[1], Luis Capdevila[2], Manuel Arias[3], Ana Fernandez[1], Carmen Cantarell[2], Alberto Rodriguez[4], Carlos Gomez-Alamillo[3], Pedro Aljama[4], Joaquin Ortuno[1], Domingo Del Castillo[4]. *[1]Nephrology, Ramon y Cajal University Hosptial, Madrid, Spain; [2]Nephrology, Val D'Hebron Hospital, Barcelona, Spain; [3]Nephrology, Marques de Valcedilla Hospital, Santander, Spain; [4]Nephrology, Reina Sofia Hospital, Madrid, Spain*

Introduction and Aims: Kidney transplant recipients are considered to have chronic kidney disease (CKD) irrespective of glomerular filtration rate (GFR) or presence or absence of markers of kidney damage. The aim of the present work was to investigate the prevalence of the different stages of CKD and whether the guidelines for the general population (K/DOQI) are routinely followed in kidney transplant patients in Spain.
Methods: 2160 renal transplant recipients followed at the outpatient clinics in 4 Spanish hospitals were included in the study. There were 1376 males and 786 females, the mean age was 53.5±13.2 years and the follow-up 104±76 months. The estimated GFR (eGFR) was calculated according to the abbreviated MDRD equation and the patients were classified following the K/DOQI stages.
Results: The mean eGFR was 51.3±21.5 ml/min/1.73m^2: 87 patients (4%) were stage 1T (eGFR >90 ml/min/1.73m^2); 625 (28.9%) were stage 2T (eGFR 60-89), 1098 (50.8%) were stage 3T (eGFR 30-59); 301 (13.9%) were stage 4T (eGFR 15-30) and 49 (2.3%) were stage 5T. Anemia defined by a serum Hb < 11 g/dl was present in 11% and 43% of recipients in stages 4T and 5T, and 35% and 71% of them were on treatment with erythropoiesis-stimulating agents The iPTH levels were >110 pg/ml in 42% of patients and >300 pg/ml in 6.3%. Hypertension was quite common, 74% had an SBP >130 mmHg and 51% a DBP >80 mmHg. About 60% had serum cholesterol > 200 mg/dl despite 50% being on statins treatment. The prevalence of anemia, hyperparathyroidism, and hypertension rose with increasing CKD stage.
Conclusions: CKD defined by an eGFR < 60 ml/min/1.73 m^2 (stage 3T) was present in more than 65% at the time of the study. The prevalence of several complications increases with the progression of CKD. The control of these complications is far below targets established for nontransplant CKD patients.

MP507 FAILURE OF RITUXIMAB RESPONSE IN TWO CASES OF RECURRENT FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS (FSGS) AFTER TRANSPLANTATION

Alessandro Amore, Licia Peruzzi, Roberta Camilla, Bruno Gianoglio, Roberto Bonaudo, Gabriella Porcellini, Rosanna Coppo. *Nephrology, Dialysis, Transplantation Unit, R. Margherita Hospital, Turin, Italy*

Introduction and Aims: FSGS is at high risk of recurrence in transplanted (Tx) kidneys. In the last years interest grew on the use of anti CD20 monoclonal antibody (rituximab) after some sporadic reports of positive results in steroid-dependent nephrotic syndrome and rare cases of recurrent FSGS.
Since mostly positive outcomes have been reported so far, a publication bias cannot be excluded at the moment.
Methods: Here we present two cases of recurrent FSGS, treated with rituximab with unsatisfactory result and persistence of nephrotic syndrome.
Results: The 1st case is a 14y old boy with FSGS progressed to ESRF at the age of 3; tx from cadaveric donor at 4. Immunesuppression was basiliximab (Bas) induction and prednisone (P), mycophenolate (Myc) and cyclosporine (Cy) association. Within 1st month after tx he had a relapse of FSGS responsive to plasmapheresis (PE, 30 sessions) and oral cyclophosphamide (CFM) with complete remission. After 6 y he had new relapse of proteinuria ($Prot_U$) and histology of FSGS recurrence, partially responsive to ACE-I. At the 10th year of tx, gradual worsening of renal function and increase of $Prot_U$ to nephrotic range were observed. The boy was switched to Tacrolimus (Tac) and 10 PE sessions were performed with limited response and $Prot_U$ reduction from 15 mg/mg$_{Cr}$ to 10 mg/mg$_{Cr}$.
Rituximab was then administered (375 mg/m^2 for 4 weekly doses) without adverse effects, but without observing significant effect. He remained persistently nephrotic and progressed to ESRF after 3 months.
The 2nd case is a 12 y old girl affected by FSGS, with negative genetic background and positive permeability factor, multidrug resistant who reached ESRF at 7y. The girl received cadaveric donor Tx at 12y after one pre-tx PE session. Immunesuppressive regimen was Bas induction, then Cy, Myc and P. PE was continued after tx for 10 sessions. Within 24h the girl displayed nephrotic $Prot_U$ and in the following days progressive oligo-anuria. Renal biopsy on day 9 showed severe acute tubular necrosis (ATN), so Cy C2 levels were kept <1200 ng/ml and dialysis was started. She was switched to Tac after 30 days. Oliguria lasted for 45 days and a 2nd biopsy confirmed ATN, without signs of rejection and no evidence of sclerosis. When diuresis increased and renal function improved until a CrCl of 35 ml/min/1.73m^2 a parallel increase of $Prot_U$ was observed until 35 mg/mg$_{Cr}$. Four Rituximab weekly doses of 375 mg/m^2 were given, observing only a very partial reduction of $Prot_U$ until 20 mg/mg$_{Cr}$. No side effects were recorded.
After one month no significant antiproteinuric response was observed and a 2nd cycle of 10 PE was performed. After one more month the girl was persistently nephrotic ($Prot_U$ 15–10mg/mg$_{Cr}$) with stable renal function (CrCl 30 ml/min/1.73m^2) and is actually kept in conservative pharmacologic treatment with Tac, Myc and P.
Conclusions: We report 2 cases of recurrent FSGS unresponsive to rituximab: a use late in the natural history in one case and a particularly multidrug resistence in the other may account for the negative results.

MP508 PREDOSE IMPDH ACTIVITY IS NOT INFLUENCED BY UNDERLYING RENAL DISEASE

Matthias Schaier[1], Dominik Scharpf[1], Christian Scholl[1], Sandra Mueller-Krebs[1], Petra Glander[2], Vedat Schwenger[1], Martin Zeier[1], Claudia Sommerer[1]. *[1]Department of Nephrology, University of Heidelberg, Heidelberg, Germany; [2]Department of Nephrology, Charite Campus Mitte, Berlin, Germany*

Introduction and Aims: The immunosuppressive activity of Mycophenolate Mofetil (MMF) is based on the reversible inhibition of inosine 5'-monophosphate dehydrogenase (IMPDH). We compared the baseline IMPDH activity of patients with autoimmune diseases and other underlying renal diseases.
Methods: For the analysis of interindividual IMPDH variability, we studied 293 Caucasian blood donors with renal diseases. IMPDH activity in peripheral mononuclear cells was measured using a non-radioactive procedure, based on the chromatographic quantification of produced xanthosine-5'-monophosphate by isocratic ion-pair reversed phase HPLC.
Results: There was no significant difference of IMPDH activity between patients with autoimmune diseases, such as systemic lupus erythematodes (n=25; 10.4±5.9 nmol/h/mg protein) and ANCA-associated vasculitis (n=92; 11.1±5.3 nmol/h/mg protein) and patients with other renal diseases (n=176; 10.8±4.3 nmol/h/mg protein). We observed a high interindividual variability in pretransplant renal patients, ranged from 1.90 to 34.82 nmol/h/mg protein. The age, body mass index, renal function and the amount of proteinuria of patients had no significant influence on IMPDH activity.
Conclusions: Our data demonstrate a high interindividual variability (non-Gaussian distribution) of predose IMPDH activity in renal patients. Underlying renal disease, age, body mass index, renal function and proteinuria had no effects on IMPDH variability. As a result of our study we confirm the need for pharmacodynamic drug monitoring to optimize MMF dosing in transplant patients.

MP509 IMPACT OF THE COMPLEMENT LECTIN PATHWAY ON CYTOMEGALOVIRUS DISEASE EARLY AFTER KIDNEY TRANSPLANTATION

Solbjorg Sagedal[1], Steffen Thiel[2], Tom E. Mollnes[3], Anders Hartmann[4]. *[1]Department of Nephrology, Ulleval University Hospital, Oslo, Norway; [2]Department of Medical Microbiology and Immunology, University of Aarhus, Aarhus, Denmark; [3]Institute of Immunology, Rikshospitalet University Hospital and Universityof Oslo, Oslo, Norway; [4]Department of Internal Medicine, Rikshospitalet University Hospital, Oslo, Norway*

Introduction and Aims: This prospective study investigated the association between pre-transplant levels of Mannose-binding lectin (MBL) plus the associated serine protease (MASP)-2 and occurrence of cytomegalovirus (CMV) infection and disease during the first 12 weeks after kidney transplantation.
Methods: Altogether 159 consecutive single kidney transplant recipients were included. The patients were screened for CMV pp65 antigenemia every second week. No CMV prophylaxis or preemptive treatment was given. MBL and MASP-2 were measured in samples taken at transplantation and 10 weeks later.
Results: CMV infection, defined as at least one positive test was found in 95 patients (59.8%). MBL and MASP-2 measured at transplantation were similar in patients with and without CMV infection. The incidence of CMV infection was also similar in 36 patients (58.3%) with pretransplant MBL level below the reference level (500 μg/L) and in patients with higher MBL levels (60.2%). CMV disease was diagnosed in 35 patients (22%), and MASP-2 levels at transplantation in the lower quartile range (<148 μg/L) was significantly associated with CMV disease during the first 12 weeks, p=0.028.

Low low levels of MBL and MASP-2 and the risk of CMV disease (n=159)

	CMV disease +	CMV disease −	p value
MBL<500 μg/L	9 (25.7%)	27 (21.8%)	0.39
MASP-2≤148 μg/L	14 (40%)	26 (21.0%)	0.028

The statistical test used is Fisher exact test.

Low MASP-2 level was tested as predictor for CMV disease when adjusting for acute rejection in a multiple proportional hazard model allowing time dependent covariates. Low MASP-2 level was found to be associated with CMV disease of borderline statistical significance (RR=1.93) (95% CI 0.98–3.81, p=0.058).

Risk factors for CMV disease during the first 12 weeks after transplantation (n=159)

	Risk ratio	95% CI	p-value
Acute rejection	2.84	1.35 - 5.97	0.006
MASP-2≤148 μg/l	1.93	0.98 - 3.81	0.058

The effects of acute rejection during the first 12 weeks and MASP-2 ≤148 μg/l at transplantation are estimated by a multiple Cox proportional hazard model which allows time dependent covariates.

MBL levels decreased significantly from transplantation to 10 weeks later, median (interquartile range) fell from 2597 μg/L (526 to 4939) to 1520 μg/L (270 to 3069) (p<0.001). In contrast MASP-2 levels increased significantly from 252 μg/L (148 to 382) to 380 μg/L (302 to 492) (p<0.001).
Conclusions: Pre-transplant MBL levels do not influence the incidence of CMV infection or disease during the first 12 weeks after kidney transplantation. However, low MASP-2 levels may have a role in the development of CMV disease.

MP510 LONG-TERM RENAL TRANSPLANT GRAFT SURVIVAL

Sola Eugenia, Cabello Mercedes, Gutierrez Cristina, Lopez Veronica, Gutierrez Elena, Sujan Seema, Burgos Dolores, Gonzalez Molina Miguel. *Nepphrology Division (Renal-Transplant Unit), University Hospital Carlos Haya, Malaga, Spain*

Introduction and Aims: Although one-year graft survival after kidney transplantation has improved, long-term improvement is less certain. This study examined the long-term results of renal graft survival.
Methods: The study included 1491 patients who received a cadaveric kidney transplant, whether a first transplant or a retransplant (excluding multiorgan transplants) from January 1985 to December 2005.
Results: Long-term GFR (aMDRD) and graft survival (Kaplan-Meier) improved significantly in the second study decade (Table), within the context of greater donor and recipient age, HLA incompatibility (2.9±1.0 vs. 3.3±0.9, p<0.0001) and donor death due to stroke. Analysis according to the four 5-year subgroups and over these same periods showed graft survival to be 70.7%, 69.3%, 75.3% and 78.8%, respectively (p<0.0001), with no differences between the first two subgroups but with differences between these and each of the last two subgroups (p<0.005). Acute rejection in 1985-95 vs. 1996-05 was 44.5% vs. 26.3% (p<0.001). Immunosuppression 1985-95: cyclosporine 99.5% and induction 9.3%; 1996-05: tacrolimus 61.2%, induction 40.3% and MMF 75.1%. Both with low-dose steroids.

Period	1985-1995 (n= 601)	1996-2005 (n=890)	p
Age R (years)	39.3±13.2	46.3±14.2	0.0001
Age D (years)	32.5±15.8	41.8±17.2	0.0001
CVA/TBI (%)	30.4/65.1	48.4/43.3	0.0001
Cold Isquemia (h)	20.2±7	15.5±5.1	0.0001
Retransplant (%)	9.5	14.1	0.008
GFR at 8 years	44.6±18.8	50.7±21.6	0.001
Graft survival 8 years	56 (%)	67 (%)	0.0001

Conclusions: Long-term graft survival after kidney transplantation did not improve over the period 1985-95 though it has improved since 1996 in the context of changes in immunosuppression, greater donor and recipient age, less HLA compatibility, and lower cold ischemia time and incidence of acute rejection.

MP511 RECURRENT IgA NEPHROPATHY IN RENAL ALLOGRAFT: A MULTICENTER REGISTRY

Rosanna Coppo, Roberta Camilla, Alessandro Amore, Licia Peruzzi, Domenico Mancuso, Antonio Amoroso, Sergio Crovella, Giuseppe Segoloni, Roberta Giraudo, Giuseppe Montagnino, Piergiorgio Messa, Chiara Venturelli, Francesco Scolari, Ciro Esposito, Antonio Dal Canton, Anna De Mauri, Giuseppe Grandaliano, Francesco Paolo Schena, Maurizio Salvadori, Elisabetta Bertoni. *Italian Multicenter Network for IgAN Recurrence, Italy*

Introduction and Aims: IgA Nephropathy (IgAN) recurs in transplanted kidney in up to two third of the cases: little is know about the clinical risk factors for recurrence. The Italian Ministry of Health granted the formation of a network of Nephrologists aimed at investigating frequency of IgAN recurrence, risk factors, effect on graft function, and strategies to limit renal trasnplant loss.
Methods: A consortium of 9 Centers of Nephrology and Immunogenetics collected retrospective data from 361 kidney transplanted patients with biopsy-proven IgAN as a cause of end-stage renal failure of native kidneys. These patients (291 males), were in median 42.8 years old (IQ 34-53) at transplantation and had a median follow-up of 20 years (IQ 16-25). Recurrence of IgAN was defined when renal biopsy of the graft showed IgAN at any time post-transplantation in subjects with hematuria and proteinuria >0.5 g/day, while non-recurrence was defined by absence of IgA deposits at a renal biopsy done less than 6 months before the serum sampling or serum creatinine <1.3 mg/dl, proteinuria <0.5 g/day and no hematuria at last follow-up.
Results: Among the patients investigated, 74 (20.5%) had biopsy-confirmed recurrent transplant IgAN after a median time of 46 months (IQ 15-79) after transplantation. The rate of recurrence was similar in both sexes (22% in males and 23% in females). No effect was found for HLA genetic background. The patients' age at diagnosis had a trend effect on the development of recurrence, mostly for patients with age < 30 years (HR 1.20 (95th CI 0.74-2.13); Log rank P=0.38). No difference in recurrence was detected in living related donors versus cadaveric donors (HR 0.68 (95th CI 0.27-1.50), P=0.86). A shorter disease duration in the native kidney from presentation to dialysis (< 1 year) was significantly associated with recurrence of IgAN in the grafted kidney (HR 2.01 (95th CI 1.09-5.51); P=0.029) and also the presence of nephrotic range proteinuria (> 3.5 g/day) during the original IgAN which led to dialysis had some effects (HR 2.06 (95th CI 0.94- 8.89); P=0.06). At COX regression analysis, the variables related to the pre-transplant IgAN history of the native kidney, which

resulted predictive of IgAN recurrence, were young age at onset (P=0.009) and nephrotic range proteinuria (P=0.013).
After renal transplantation, patients who developed proteinuria >1g/day had a significantly higher risk of recurrence of IgAN (HR 3.94 (95th CI 3.10-14.97); Log rank P>0.0001).
The presence of recurrence in the grafted kidney did not affect the kidney survival to serum creatinine levels of >2 mg/dl (HR 1.30 (95th CI 0.77 – 2.41); P:=0.28).
Conclusions: These data may be of interest in trying to assess the risk of recurrence in patients with IgAN entering the program of renal transplantation and in predicting recurrence after transplantation.

MP512 AGEs AND CARDIOVASCULAR DISEASE IN RISK RENAL TRANSPLANT PATIENTS WITH METABOLIC SYNDROME

Vladimir Teplan[1], Olga Mareckova[1], Jaroslav Racek[2], Martin Haluzik[3], Milena Stollova[1], Stefan Vitko[4]. *[1]Department of Nephrology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [2]Department of Biochemistry, Charles University, Pilsen, Czech Republic; [3]Department of Medical Faculty III, Charles University, Prague, Czech Republic; [4]Transplant Centre, Institute for Clinical and Experimental Medicine, Prague, Czech Republic*

Introduction and Aims: Advanced glycation end-product (AGEs) have been linked to endothelial dysfunction and atherosclerosis in chronic renal disease.
The aim of prospective randomized long-term study was to asses the relationship between plasma pentosidine (AGEs), asymmetric dimethylarginine (ADMA) and cardiovascular disease (CVD) in renal transplant patients (RTx) with metabolic syndrome (MS).
Methods: For a period of 36 months we monitored a total of 85RTx (M43/F42, aged 25-78 yrs, BMI≥30kg/m^2) after first cadaveric kidney transplantation (Tx) (Gr.I). MS was defined by ATP III and IDF. Control group (Gr.II.) consisted of 82 Tx pts without MS. Plasma AGEs (pentosidine) and ADMA were estimated by ELISA method. All pts were treated with tacrolimus or CyA, MMF and prednisone.
Results: During follow up, CVD related morbidity was present in 17 pts in Gr. I. (20%) and in 10 Gr.II (12.2%). Significant differences were also found in plasma (Gr. I vs. Gr. II, t-test, regression analysis): pentosidine 0.46±0.15 vs. 0.30±0.3, p<0.01, ADMA 3.68±0.56 vs. 2.4±0.41, p<0.01, proteinuria (p<0.01) mean BP (p<0.01) and inulin clearance (p<0.01).
There were significant correlation between pentosidine and BMI (r = 0.415, p<0.001), ADMA and BMI (r = 0.500, p<0.001), but negative correlation with fat adiponectin gene expression mRNA PCR (r = -0.512).
No differences were found in hs CRP, IL-6, TGFβ, TNFα and also between tacrolimus and cyclosporine A administration.
Conclusions: Metabolic syndrome after transplantation with increased AGEs, ADMA, mean BP and decreased ADPN in visceral fat was associated with higher incidence of CVD during 3 years after Tx.
The study was supported by Grant IGA NR 9398-3.

MP513 HCV INFECTION AND ACCESS TO KIDNEY TRANSPLANTATION

Anteo Di Napoli[1], Domenico Di Lallo[1], Nicola Petrosillo[2], Salvatore di Giulio[3], Lazio Dialysis Registry. *[1]Agency Public Health Lazio, Rome, Italy; [2]National Institute Infectious Diseases Spallanzani, Rome, Italy; [3]San Camillo Forlanini Nephrology Dialysis Unit, Rome, Italy*

Introduction and Aims: Several studies have investigated the effect of hepatitis C virus (HCV) Ab status on the outcomes of kidney transplantation. However, few studies have investigated the relationship between HCV infection and access to kidney transplantation. The aim of the study was to analyse the impact of HCV serologic positive test at the initiation of dialysis therapy on probability of receiving a kidney transplantation.
Methods: The source of data consisted of all 8977 patients undergoing chronic hemodialysis, notified to Lazio Dialysis Registry (RDL) from 1995 to 2006. HCV status was defined using ELISA and RIBA 3rd generation test. We conducted a retrospective cohort study to estimate the cumulative incidence of transplantation, by HCV status at the initiation of dialysis therapy, using the Kaplan-Meier method. We used a multivariate Cox model to estimate transplantation hazard ratios (HR) of HCV Ab+ compared to HCV Ab- subjects, taking into account age, sex, primary nephropathy, presence of diabetes, hematocrit level, serum albumin level, self-sufficiency degree. We excluded from the analysis 3676 subjects died during dialysis therapy without receiving a transplantation, due to competing risk.
Results: In the period 1995-2006, 7.7% of subjects undergoing chronic hemodialysis was HCV Ab+; the proportion of transplanted was higher among HCV Ab- than HCV Ab+ subjects (15.7% vs. 10.2%, p=0.005). HCV+ patients had a longer time on dialysis before a transplantation compared HCV- (mean: 39,7 vs. 31,9 months). The cumulative incidence of transplantation, by HCV status, in the period 1996-2005, is illustrated in the figure; we observed a difference between the two groups (log-rank test, p=0.001): after 5 years in dialysis [HCV- 0.20 (95%CI 0.19-0.22) vs. HCV+ 0.12 (95%CI 0.08-0.17)]; after 12 years in dialysis [HCV- 0.28 (95%CI 0.26-0.30) vs. HCV+ 0.26 (95%CI 0.16-0.41)]. We found for HCV+ subjects a lower probability to be transplanted (HR 0.61; 95%CI 0.43-0.87) and to enter in a waiting list for transplantation (HR 0.71; 95%CI 0.51-0.98) compared to HVC- subjects.

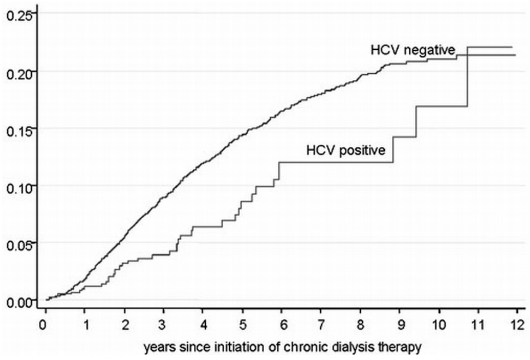


Figure 1. Cumulative incidence of transplantation, by HCV status at dialysis initiation.

Conclusions: The results of our study confirm that a subject HCV+ has lower probability of access to kidney transplantation. At present, after renal transplantation, there is no current safe and efficient therapy. Responders to pre-transplantation therapy for HCV infection show an excellent prognosis of liver function and overall outcome close to HCV-negative renal transplant recipients. Therefore, as it is known that HCV+ patients have a higher mortality in dialysis than HCV- subjects, HCV infection needs to be treated since initiation of chronic dialysis, to avoid a delay in entering in a waiting list and in receiving a kidney transplantation.

MP514 IMPACT OF BODY WEIGHT, BLOOD PRESSURE AND SERUM BIOCHEMICAL PARAMETERS ON LONGTERM RENAL TRANSPLANT OUTCOME

Alireza Hamidian Jahromi[1,2], Ghanbar-Ali Raiss-Jalali[2], Jamshid Roozbeh[2], Hamed Jalaeian[2], Ali Malek-Hosseini[2]. *[1]Oxford Transplant Unit, Churchill Hospital, Oxford, Oxfordshire, United Kingdom; [2]Organ Transplantation Unit, Shiraz University of Medical Sciences, Shiraz, Fars, Iran*

Introduction and Aims: Thanks to advancements in immunosuppression, patients are now living longer with kidney transplants, and nonimmunologic factors have become a major source of morbidity and mortality after successful kidney transplantation. In this study, we assessed the course of some non-immunologic factors (e.g. body weight, systolic/diastolic blood pressure, serum triglyceride (TG) and cholesterol) in a cohort of renal transplant recipients and evaluated their impact on long-term transplant outcome.
Methods: In a retrospective study, medical records of 100 renal transplant recipients, (65 male, 35 female) who had been transplanted in our center between February 2000 and May 2001 (more than 5 years before the time of study), were reviewed. The patient's time on dialysis before transplantation and their drug history was recorded. In all of the patients, body weight, blood pressure, serum creatinine (Cr), TG and cholesterol levels were recorded pre-transplant and 2 weeks, 1 year, 3 years and 5 years after the transplantation.

For the purpose of this study, graft dysfunction was defined as a serum Cr >2.0 mg/dl, hypertriglyceridemia as TG > 250 mg/dl, hypercholesterolemia as cholesterol >200 mg/dl and hypertension as BP>140/90 on at least two occasions or treatment with antihypertensives. Patients in hypertensive group were divided into controlled and uncontrolled hypertensive patients (BP>160/100 on at least two monthly visits). Blood chemistry values had all been measured with kinetic (UV) methods.

Results: These patients with mean age of 36.35±10.24 years (range, 16-58) were on dialysis for a mean period of 3.4±1.4 years (range, 1-7.3) before their transplantation. Development of graft dysfunction didn't show any relationship with the duration of dialysis in our patients. (P=0.71)Uncontrolled hypertensive patients had an increased risk of developing graft dysfunction in the five-year post transplant period compared to controlled hypertensive and non-hypertensive patients. (P<0.001) Patients with hypertriglyceridemia and hypercholesterolemia in the five-year post transplant period had both an increased risk of developing graft dysfunction comparing to patients with normal lipid profiles. (for both P<0.05)

A significant correlation was found between creatinine at two weeks and three years after transplantation, (r=0.398; P=0.015) as well as creatinine at three years and five years after operation (r=0.628; P=0.000). Serum Cr at two weeks post op was 1.42±0.56 mg/dl, which increased to 2.18±2.47 mg/dl at five years after transplantation. (P=0.021). Mean body weight three years and five years after transplantation was 65.25±11.63 kg and 68.05±10.62 kg, which was significantly correlated with increased risk of graft dysfunction. (P=0.01)

Conclusions: Body weight, hyperlipidemia, hypertension and specifically uncontrolled hypertension, all seemed to be risk factors for kidney graft dysfunction. Controlling these factors will be an important step towards improving graft function.

MP515 ★ OCCULT HBV INFECTION IN RENAL TRANSPLANT: A STUDY OF PREVALENCE AND INCIDENCE IN TWO TRANSPLANT CENTERS OF NORTHERN ITALY

Roberta Fenoglio[1], Marco Quaglia[1], Elisa Lazzarich[1], Elena Bruschetta[1], Cristina Cornella[1], Roberta Minisini[2], Mario Pirisi[2], Piero Stratta[1].
[1]Department of Clinical and Experimental Medicine - Nephrology, Amedeo Avogadro University, Novara, Italy; [2]Department of Clinical and Experimental Medicine - Internal Medicine, Amedeo Avogadro University, Novara, Italy

Introduction and Aims: Viral hepatitis have always been a serious problem in dialysis and renal-transplanted patients. Within this latter population HBsAg positivity is estimated to be around 10-20% and it is considered a negative prognostic factor. In the last decade there have been reports suggesting the possibility of an occult HBV, that is an infection which cannot be detected with routine serological tests. This condition is critical in transplanted patients, as immunosuppressive therapy increases host's susceptibility to infections, thus favouring HBV reactivation. Aim of the study: to assess the prevalence of occult HBV infection in patients on transplant waiting list in our Region; to identify risk factors for this condition; to quantify the incidence of post-transplant occult infection; to monitor patients who have undergone renal transplant during the study period to evaluate if immunosuppression can determine viral re-activation.

Methods: Three-hundred patients on renal transplant waiting list have been enrolled. The only exclusion criterion was HBsAg positivity. A peripheral pre-dialysis blood sample was drawn for each patient. In 47 patients who were transplanted during the observation period other blood samples were drawn at 1 month and at 6 month after transplant. Samples were analysed through nested-PCR. Positivity for occult HBV infection was defined by the presence of at least 2 out of the 4 amplified genomic regions (S, core, X, Pol). History and laboratory data were collected for each patient.

Results: Prevalence of occult HVB infection in the population on waiting list turned out to be 3.33% (10/300). Infection was significanlty more frequent in African and Asian ethnicity as compared with the Caucasic one (6,25% and 33,33% positivity vs 2,8%, respectively; p=0.001) and it was associated with anti-HCV antibodies (prevalence of anti-HCV antibodies was 10% in occult HBV negative patients vs 30% among positive patients, p=0,044) and previous liver disease (p=0.0198).

Incidence of occult infection after renal transplant turned out to be 4,44% (2 out of 44 patients who were negative at baseline observation time became positive during follow-up) whereas 3 positive patients became negative at subsequent controls.

Conclusions: Occult HBV infection prevalence is not negligible among dialysis patients, especially in the prospect of transplant related immunosuppression. Occult HBV infection is more prevalent among patients coming from countries where HBV infection is more widespread, in HCV positive patients and in those with a history of liver disease. The clinical meaning of modifications of occult HBV status in the post-transplant period is not clear yet also due to the lack of data from literature. Further studies with longer follow-up are needed to define the impact of HBV occult infection on transplant outcome and to assess the possibility or viral reactivation.

MP516 CARDIOVASCULAR EVENTS AND LIPID-TRANSFER-PROTEIN-ACTIVITY IN RENAL TRANSPLANT RECIPIENTS

Sarah Seiler[1], Axel Schlitt[2], Christof Ulrich[1], Matthias Girndt[1], Danilo Fliser[1], Gunnar H. Heine[1]. *[1]Department of Internal Medicine IV, Saarland University, Homburg, Germany; [2]Department of Internal Medicine III, Martin-Luther-University, Halle-Wittenberg, Germany*

Introduction and Aims: Patients with chronic kidney disease have a persisting higher risk of cardiovascular disease, even after succesful renal transplantation. Uremic dyslipidemia, which is characterised by low HDL-cholesterol (HDL-C) in CKD stage V patients and elevated LDL- and total cholesterol levels after renal transplantation, may contribute to this elevated cardiovascular risk. The distribution of the different lipoprotein classes is influenced by the activity of the lipid-transfer-proteins cholesteryl-ester-transfer-protein (CETP) and phospholipid-transfer-protein (PLTP). Prospective trials analysing the prognostic value of CETP- and PLTP-activity in renal transplant recipients (RTRs) are so far missing. We therefore investigated the association between lipid-transfer-protein-activity (CETP and PLTP), the rate of cardiovascular events and survival in RTRs.

Methods: CETP- and PLTP-activity were measured in 100 RTRs, 67 controls with intact renal function and 67 CKD stage V patients. We followed each patient for 3 years. After stratifying patients by median CETP- and PLTP-activity, survival curves were calculated by the Kaplan-Meier method and log-rank testing. The relationship between lipid-transfer-protein-activity and lipoprotein subclasses was assessed by Spearman's correlation coefficients. The prespecified clinical endpoints were total mortality, cardiovascular events and death of any cause.

Results: PLTP-activity did not differ between RTRs and controls with intact renal function (25.5±7.4 vs. 22.8±7.5 pmol/µl/h). Higher values were measured in CKD stage V patients (45.3±15.0 pmol/µl/h). CETP activity in RTRs and CKD stage V patients (33.4±11.4 vs. 35.1±13.7 pmol/µl/h) were reduced in comparison to CETP-activity in controls (50.2±22.8 pmol/µl/h). Furthermore in RTRs a significant inverse correlation between CETP-activity and plasma-triglycerides (r=-0.4; p<0.01) and also a positive correlation with LDL-cholesterol (r=0.2; p=0.02) could be shown. PLTP-activity was significantly positively correlated with total (r=0.3; p<0.01) and HDL-cholesterol (r=0.4; p<0.01). After a follow-up of three years there was no difference in cardiovascular event and mortality rate between RTRs with high or low CETP-activity (p=0.6), the same was true for PLTP-activity (p=0.5).

Conclusions: Uremic dyslipidemia is a complex, incompletely understood complication of chronic renal disease, which profoundly differs from dyslipidemia in the general population. We found in CKD stage V patients that CETP-activity did not change after successful renal transplantation, whereas PLTP-activity reached levels similar to our controls. However, the hypothesis that PLTP may contribute to worse outcome in CKD stage V patients was previously contradicted by our group and also in the present analysis; PLTP- and CETP-activity did not influence event-free survival in our patients and so they do not have a prognostic value in RTRs. We conclude that both CETP- and PLTP-activity are risk markers rather than risk factors in patients with renal diseases.

MP517 RENAL ALLOGRAFT FUNCTION IN ABO INCOMPATIBLE KIDNEY TRANSPLANTATION CAN BE GOOD LONG-TERM POST-TRANSPLANTATION

Atsushi Aikawa, Takeshi Kawamura, Yoshiaki Mori, Manabu Saneshige, Jiro Takasu, Yasuo Niitsu. *Nephrology, Toho University, Faculty of Medicine, Tokyo, Japan*

Introduction and Aims: The aim of this study is to evaluate long-term renal allograft function in ABO incompatible kidney transplantation (ABOINCKTx) compared with ABO compatible kidney transplantation (ABOCKTx).

Methods: Forty eight patients who had ABOINCKTx from1997 to 2004, were enrolled in this study. The blood group matchings (donor to recipient) in ABOINCKTx were 13 (A to O), 12 (B to O), 6 (AB to A), 5 (B to A), 7 (AB to B) and 5 (A to B). Immunosuppression consisted of cyclosporine or tacrolimus, and azathioprine or mycophenolate mofetile, and steroid including induction of basiliximab in 14 patients. Preconditioning such as plasmapheresis and exchange was performed to removed the anti-donor blood group antibody before Tx. Control subjects were 123 ABOCKTx recipients who had Tx in the same period. The incidence of biospy proven acute rejection was studied in both goups. The blood group antigens in renal tissues obtained by protocol allograft biopsy were stained using with the indirect immunoperuoxidase method. Graft survival rates were calculated and serum creatinine was measured sequentially in both groups.

Results: The factors of background of patients (HLA A,B, DR mismatch, age and gender of donor and recipient) in both groups were not different except the rate of the second transplantation (ABOINCKTx vs. ABOCKTx; 7/48 vs. 3/123, $p<0.008$). Donor blood group antigens were stained in any renal tissues taken by protocol biopsy. The incidence of acute rejection was higher in ABOINCKTx (22/48 vs. 20/123; $p<0.0002$). Serum creatinine levels (ABOINCKTx vs. ABOCKTx) were 1.27 ± 0.53 vs. 1.14 ± 0.54 mg/dl at 1 year ($p=0.07$), 1.36 ± 0.68 vs. 1.30 ± 1.20 mg/dl ($p=0.37$) at 3 years, 1.57 ± 0.92 vs. 1.39 ± 1.20 mg/dl ($p=0.22$) at 5 years and 1.41 ± 0.36 vs. 1.55 ± 0.79 mg/dl ($p=0.19$) at 7 years post-Tx. The 7 years graft survival rates were 95% and 94% in ABOINCKTx and ABOCKTx, respectively.

Conclusions: Renal allograft function in ABOINCKTx appeared to be good long-term post-Tx despite of long-standing expression of blood group antigens in the renal aloograft and higher rate of acute rejection.

MP518 EARLY EXPRESSION OF EPITHELIAL TO MESENCHYMAL TRANSITION MARKERS IS PREDICTIVE OF LONG-TERM RENAL GRAFT FUNCTION

Alexandre Hertig[1], Dany Anglicheau[2], Jerome Verine[3], Maxime Touzot[1], Laurent Mesnard[1], Denis Glotz[4], Nicole Brousse[5], Nicolas Pallet[2], Christophe Legendre[2], Eric Rondeau[1], Yi-Chun Xu-Dubois[1]. *[1]Urgences Nephrologiques et Transplantation Renale, APHP, Hopital Tenon, Paris, France; [2]Transplantation Renale, Hopital Necker, Paris, France; [3]Anatomo-Pathologie, Hopital Saint Louis, Paris, France; [4]Nephrologie, Hopital Saint Louis, Paris, France; [5]Anatomo-Pathologie, Hopital Necker, Paris, France*

Introduction and Aims: Epithelial to mesenchymal transition (EMT) is a potential mechanism of tissue fibrogenesis. In a previous study, we had reported that the early expression of EMT markers was associated with the progression of renal grafts towards interstitial fibrosis and tubular atrophy (IF/TA). Here, we report the long-term follow-up of this cohort, paying a special attention to the evolution of graft function.

Methods: 83 patients engrafted with a kidney from a cadaveric (n=63) or a living (n=20) donor, and in whom sequential protocol biopsies had been performed at 3 and 12 months, were included. The phenotype of epithelial cells was studied at three months according to the expression of vimentin (an intermediate filament normally expressed by fibroblast-like cells) and to the cellular localization of -catenin. Grafts in which these two markers were abnormally expressed by more than 10% of tubular cells were considered as EMT+ grafts. Serum creatinine and creatinine clearance (estimated by Gault and Cockcroft index) were collected from 12 to 24 months post-transplant and compared according to the EMT status of the graft.

Results: Multivariate analysis demonstrated that the early expression of EMT markers was an independent risk factor of the progression of graft fibrosis between 3 and 12 months. More importantly, these early phenotypic changes were associated with a progressive and sustained deterioration of the graft function: EMT+ patients had a statistically higher serum creatinine from twelve months after transplantation, and a significantly lower creatinine clearance from 18 months after transplantation (EMT+ 49.44.5 ml/min vs EMT- 61.12.3 ml/min, $p=0.01$). The difference was persistent at 24 months.

Conclusions: The expression of EMT markers by tubular epithelial cells at an early time point post-transplant (three months) is highly suggestive of an ongoing fibrogenic process, and has repercussions on the long-term graft function. Therefore, these epithelial phenotypic changes are relevant and promising biomarkers for an early detection of IF/TA.