

*Original Article*

## **Risks and complications in 160 living kidney donors who underwent nephroureterectomy**

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### **Abstract**

**Background.** The rate of living donor renal transplantations has increased. However, in view of the possible complications, the question as to whether the condition of the recipient justifies operation of the donor still remains unanswered. The present retrospective study evaluates the perioperative and post-operative risks and complications for the donor at a single major transplantation centre.

**Methods.** From 1994 to 2001, 160 live donor nephroureterectomies were performed. The median age of living donors was 51 years (range 21–77 years); 19 patients were older than 61 years. After confirming blood group compatibility and negative cross-match, donors underwent an extensive medical and psychological examination. Comorbidities and anatomical features of the donor were evaluated and the impact they may have on the outcome was determined. The nephroureterectomies were performed transperitoneally, with the right kidney being preferred. Pre-operative, intraoperative and post-operative complications were documented. Serum creatinine levels as well as new-onset proteinuria or hypertension were used as criteria for assessing long-term renal function.

**Results.** Complications were observed in 41 donors: 35 were minor and six were major (splenectomy; revisions due to liver bleeding, incarcerated umbilical hernia or infected pancreatic pseudocyst; pneumothorax; and acute renal failure). No patient died. Multiple arteries (14 patients), significant renal artery stenosis (two patients) and additional risk factors (e.g. increased age and previous operations) did not affect the

complication rate. In the post-operative follow-up period of 0.5–62 months (mean: 38 months), renal function remained stable in all donors.

**Conclusions.** Living donor nephrectomy appears to be a safe intervention in specialized centres, where it entails a low morbidity for the donor. Even in high-risk donors, long-term complications were not observed.

**Keywords:** complications; living donor nephrectomy; living donor renal transplantation; nephroureterectomy

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### **Introduction**

Living donor renal transplantation has become increasingly common in Germany. Nevertheless, the operations on healthy persons continue to be controversial in professional and public debates. The undisputed medical benefit for the recipient can only be justified when freedom of choice and optimal protection for the donor in respect of morbidity and mortality can be assured. Large-scale multicentre studies [1], detailed surveys of the literature [2] as well as progress reports of various centers have shown that short-term and long-term outcomes after living donor renal transplantation are favourable for the donor [3–6]. Although cases of hypertension and proteinuria have been reported, the numbers are small and the patients can usually be controlled by conservative measures [5–9]. Recent data from Sweden even found renal donors to have a higher life expectancy compared with the rest of the population [10], most likely due to the selection of especially healthy persons as living donors. However, it is crucial that life expectancy of renal donors does not seem to be reduced compared with age-matched groups. Despite these promising data,

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unilateral nephroureterectomy in living donors does entail risks [11]. To ensure safety and freedom of choice, the German transplant law requires both donor and recipient to be fully informed about the procedure, long-term outcome and possible perioperative and post-operative risks and complications. In order to make a qualified decision, the donor and recipient should have the right to request information about the experience and results of the transplant centre performing the operation.

The present study reviews possible pre-operative problems and the management of perioperative and post-operative complications of live donor nephrectomy at a single major transplantation centre.

## Subjects and methods

### Patients

From October 1994 to October 2001, 160 healthy donors underwent a unilateral nephroureterectomy for related and non-related transplantation. Potential donors <18 years were excluded. After confirmation of blood group compatibility and negative cross-match, the donors underwent an intensive medical and urological examination. Coronary artery disease was usually considered to be an exclusion criterion, whereas mild hypertension (controlled with a single oral medication) was not. An angiography was performed in all donors prior to the operation to document the condition and number of renal arteries. The finding of multiple arteries of the donor kidney was not regarded as an exclusion criterion, but the kidney with fewer arteries was selected preferentially for donation. Human lymphocyte antigen typing was performed for all potential donors. After confirmation of their medical suitability, donor and recipient were seen by a psychologist to ensure that the decision to donate a kidney was voluntary and that their relationship was emotional and close. All donors participated in the Munich Prospective Study concerning the expected life-changes shortly before and factual changes 1 year after transplantation, with strict psychological care/evaluation prior to and after transplantation that was conducted by the Department of Psychology.

### Donor characteristics and selection of donor organs

The median age of living donors was 51 years (range 21–77 years), with the majority of donors being between 31 and 60 years old. Nineteen patients were older than 61 years. The ratio of male to female donors was 1:2. Renal function was normal in all patients (Table 1).

### Donor nephroureterectomy, perfusion and preparation of the donor organ

At the beginning of our living donor renal transplantation programme, the donor operation generally preceded the operation on the recipient. Later on, both operations were carried out simultaneously. For the first seven patients (done by the same surgeon, N.S.), a flank incision was chosen

**Table 1.** Donor characteristics ( $n = 160$ )

	Patients ( $n$ )
Age (years)	
18–20	0
21–30	11
31–40	27
41–50	36
51–60	67
61–70	14
71–80	5
Sex	
Male	62
Female	98
Donor kidney	
Left	56
Right	104
Creatinine (mean $\pm$ SD)	
Pre-operative	0.88 $\pm$ 0.12 mg/dl
Post-operative <sup>a</sup>	1.45 $\pm$ 0.52 mg/dl

<sup>a</sup>One patient with acute renal failure (creatinine maximum: 6.42 mg/dl) is included.

for the nephroureterectomy, whereas the following 153 operations (done by the same surgeon, J.T.) were performed transperitoneally with the patient in an overextended supine position.

After the kidney of the non-heparinized donor was removed, the organ was handed to a second team immediately starting the arterial gravitational perfusion with cold Euro-Collins solution (0–4°C) (warm ischaemia: 0.5–1.5 min).

Routine placement of intraperitoneal and subcutaneous wound drainage was discontinued in the last series of 47 patients. The right kidney was usually preferred, unless contraindicated by vascular or other anatomy. The average duration of operation was 2.45 h (range 2–4 h). The mean post-operative stay was 8 days (SD  $\pm$  2 days).

### Renal function measurements

For each patient, serum creatinine and 24 h urine creatinine clearance values were obtained at baseline. To assess total renal plasma flow as well as its relative distribution between the two kidneys, renal scans using mercaptoacetyl triglycine as radiolabelling agent were taken in all patients. Additionally, inulin clearances were tested for clarification if necessary. Furthermore, every patient was tested for microalbuminuria (three times). Patients suspected of having renal disease or decreased renal function as determined by repeatedly increased threshold values in either of the tests or by confirmed microalbuminuria were excluded from donor nephrectomy. Patients were checked for diabetes mellitus by oral glucose challenge. Virological workup included hepatitis A, B, and C, HIV, HHV-8, CMV and EBV.

Post-operatively, serum creatinine values were determined daily until discharge. Later on, however, patients could be persuaded to come in for routine serum creatinine checks only with difficulty, so those values are few. In theory, 24 h creatinine clearances, 24 h blood pressure measurement, microalbuminuria testing and renal scans were to be repeated annually, but we were able to obtain creatinine clearances on a regular basis only in a minority of donors.

## Results

### *Perioperative and post-operative complications*

None of the donors died. To date, all donors examined have fully recovered. Major complications were observed in six patients (3.8%) (Table 2). Splenectomy, secondary liver haemorrhage requiring immediate revision and pancreatic pseudocyst with consecutive infection developing after injury to the pancreas were all due to severe adhesions. An incarcerated umbilical hernia occurred shortly after nephroureterectomy and was repaired without complications. A transient acute renal failure episode involving the non-transplanted kidney in one donor caused an increase of serum creatinine up to 6.42 mg%, which normalized spontaneously. A post-operative pneumothorax, probably due to central vein catheter, required thoracic drainage and healed without sequelae.

There were several minor complications. Ten donors experienced an intraoperative haemorrhage of neighbouring organs, including the spleen, pancreas and/or adrenal glands. All these episodes could be successfully stopped at the time of operation. One of the donors suffered severe intra-operative bleeding. The post-operative diagnostic workup revealed severe bleeding diathesis caused by factor XII deficiency (16% of the standard).

Of note, the nephroureterectomy was discontinued intraoperatively in three further patients. A 35-year-old donor (excessive tobacco consumption of 20–40 cigarettes per day) developed severe bronchospasm during induction of anaesthesia. A 62-year-old donor suffered an acute cardiac arrest after entering the abdominal cavity. The kidney of a 31-year-old donor revealed a suspicious 2 mm capsular spot after exposure. Intraoperative biopsy showed a primary chromophil

renal cell carcinoma (pT1, G1). Because of its size, it was impossible to detect the tumor pre-operatively either by sonography or by helicoidal computerized tomography (CT) scan. Post-operative tumour staging (e.g. helicoidal abdominal CT scan) showed no signs of metastases. In all three patients, no late sequelae of these complications have been noted in the interim.

### *Vascular anomalies of the donor organ*

Arterial vascular conditions were regular in 144 donors, but 16 patients (10%) presented with arterial vascular anomalies (Table 3). The most frequent form of vessel reconstruction consisted of joining at least two arteries by means of the 'common channel technique'. When a third artery was present, a separate anastomosis was performed.

In two pre-operatively hypertensive donors, a significant renal artery stenosis was found by angiography (Figure 1 left) and in one of these cases, an additional pole artery was detected. In both patients, the stenosing parts were excised during the *ex vivo* preparation and the vessels anastomosed with the arteries of the recipient (Figure 1 right). Both donors were normotensive after the operation.

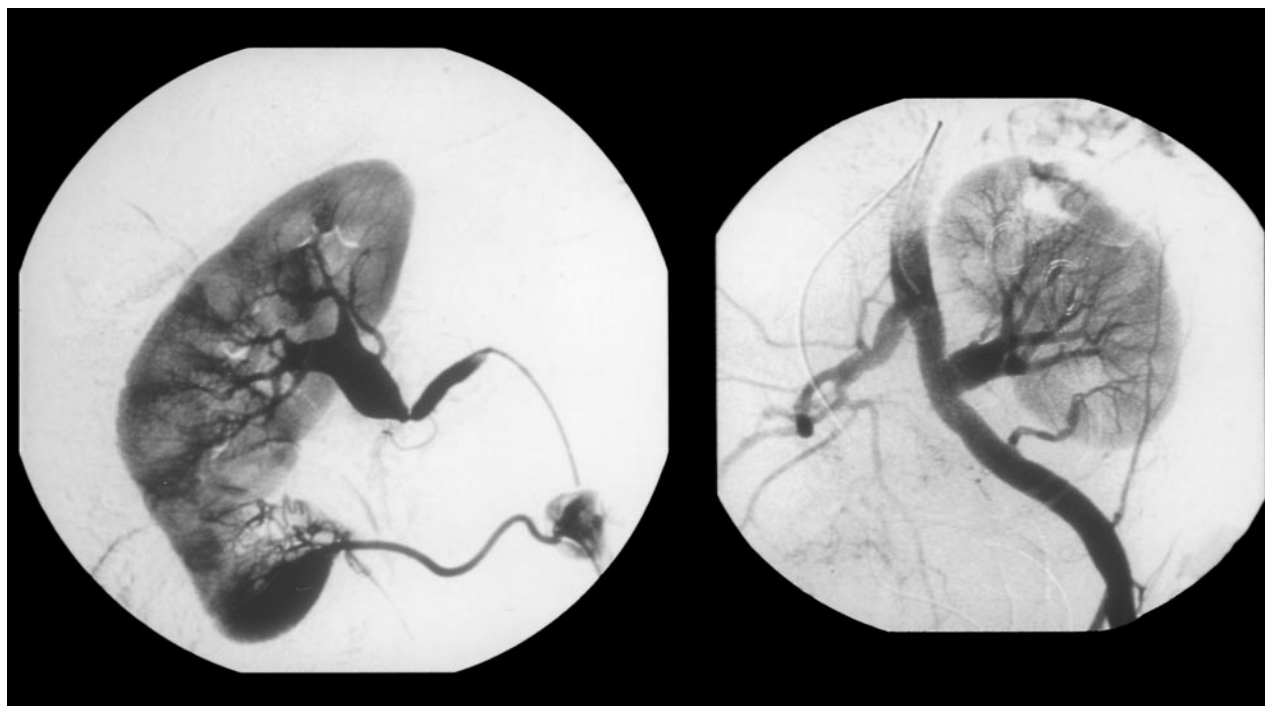
**Table 3.** Renal arteries in 160 related live kidney donors

	Patients ( <i>n</i> )
Normal	144
Two arteries	9
Three arteries	4
Pole artery in main artery	1
Renal artery stenosis (1 × additional pole artery)	2

**Table 2.** Perioperative and post-operative complications after 160 related live donor nephroureterectomies (*n* = 41)

	Minor complications <i>n</i> (%)	Major complications <i>n</i> (%)	Minor and major complications in patients > 61 years <i>n</i> (%)
UTI ( <i>Escherichia coli</i> )	16 (10%)		5 (3.1%)
Unknown fever (antibiotics)	7 (4.4%)		2 (1.3%)
Splenic haemorrhages	5 (3.1%)		1 (0.6%)
Blood transfusion	5 (3.1%)		2 (1.3%)
Pneumonia	4 (2.5%)		1 (0.6%)
AG haemorrhages	3 (1.9%)		0
Severe scar pain	2 (1.3%)		0
Pleural effusion	2 (1.3%)		0
Slight pulmonary oedema (1 day)	2 (1.3%)		1 (0.6%)
Pancreatic haemorrhage	2 (1.3%)		0
Wound infection	1 (0.6%)		0
Splenectomy		1 (0.6%)	0
Liver bleeding (2nd OP)		1 (0.6%)	0
IUH (2nd OP)		1 (0.6%)	1 (0.6%)
PP + infection (2nd OP)		1 (0.6%)	1 (0.6%)
Pneumothorax		1 (0.6%)	0
ARF (transient)		1 (0.6%)	0
Total	49 (21.9%)	6 (3.8%)	

AG, adrenal gland; ARF, acute renal failure; IUH, incarcerated umbilical hernia; OP, operation; PP, pancreatic pseudocyst.



**Fig. 1.** (Left) Lower pole artery and significant renal artery stenosis of a right donor kidney caused by renal hypertension. (Right) Sufficient anastomosis of both arteries after transplantation into the left fossa iliaca. Note two JJ catheters with which the double ureter was stented. Both donor and recipient were normotensive after operation.

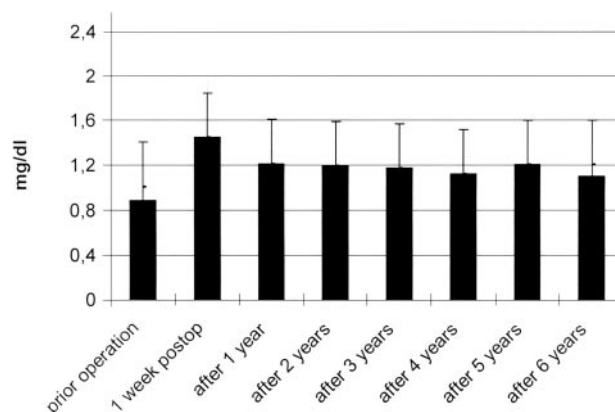
#### *Additional operations*

For two donors, additional operations prior to nephroureterectomy were necessary. In one case, a cholecystectomy was performed due to symptomatic cholelithiasis and gallbladder hydrops. In the other, a contralateral adrenalectomy was performed to remove a benign adenoma of the adrenal cortex. Neither perioperative nor post-operative complications were observed.

#### *Post-operative kidney function*

**Hypertension.** Blood pressure after donor nephrectomy was monitored by 24 h blood pressure measurement (mean minimum value: 100/65 mmHg; mean maximum value: 125/80 mmHg; mean day-time value: 125/80 mmHg; mean night-time value: 110/60 mmHg). Seven out of 100 (7%) patients (age >60 years), from whom data were available from 24 h blood pressure measurements, suffered from mild hypertension (mean: 145/95 mmHg) and were treated successfully with a single oral antihypertensive medication, mostly  $\beta$ -blockers (mean: 130/80 mmHg). However, in five out of seven patients, mild hypertension (controlled with a single oral medication) had been noted prior to the operation. Severe hypertension was not encountered.

**Proteinuria.** A one-plus positive urine dipstick was found in six out of 110 (6%) patients tested. In eight patients (five out of these were >60 years), 24 h urine collection showed non-significant proteinuria (micro-



**Fig. 2.** Renal function measured by serum creatinine (prior to the operation  $n=160$ , 1 week post-operation  $n=160$ , after 1 year  $n=135$ , after 2 years  $n=128$ , after 3 years  $n=122$ , after 4 years  $n=115$ , after 5 years  $n=108$  and after 6 years  $n=102$ ).

albuminuria) with 55–110 mg/24 h. Severe proteinuria was not seen in any case.

**Renal function (Figure 2).** Renal function was normal in all patients prior to the operation (mean serum creatinine: 0.88 mg/dl). Post-operatively, serum creatinine peaked at 1.45 mg/dl in the first week and then fell to 1.2 mg/dl. This value remained stable within the observation period. Renal function with one kidney returned to 73% of the initial values with two kidneys. Nevertheless, serum creatinine was >1.2 mg/dl (maximum: 1.8 mg/dl) in 30% of the patients, but has not deteriorated further in recent years.

## Discussion

Potential risks of living donor kidney transplantation continue to be the main topic of every public and professional discussion in this field and have to be addressed when obtaining informed consent from the donor and the recipient. The risks associated with donating a kidney are doubtless smaller than those entailed in paragliding or mountaineering. Nevertheless, complications do occur and can be as harmless as a urinary tract infection (UTI) or as dramatic as an intraoperative cardiac arrest.

In response to the questions and concerns of the donor in the setting of pre-operative counselling, we propose a grading system of possible risks and complications under the following six headings.

### **Minor and frequent complications after nephroureterectomy (e.g. minor intraoperative haemorrhages, wound healing problems, UTIs and scar pain)**

The first category of risks comprises complications that are completely reversible after conservative intervention. Their total of 21.9% in our study is representative and comparable with series of other centres [6]. In other series [3], only severe or major complications are documented, so that the overall complication rate seems to be lower compared with that in our study in which all, including minor, complications are reported. Minor complications occurred in 0.6–10% of patients, which is very low compared with other urological operations and is in some cases lower than data published to date [5,12]. Yet, even in cases with minor problems, preventative measures are necessary, as the patient with factor XII deficiency shows. Despite thorough pre-operative evaluation, not all possible problems can be precluded. Consequently, careful post-operative care is crucial.

Minor complications also include ongoing late wound and scar pain. Current studies show evidence that extraperitoneal standard access of flank incision, especially when combined with a rib excision for better access, may be the reason [13,14]. In a prospective randomized study of 104 living donors, the flank incision was compared with a transabdominal ventral access [15]. No significant differences with regard to cold ischaemia, duration of operation, etc. were found. The rate of minor complications in the flank incision group was 17%, vs 11% for the transabdominal incision. Additionally, the transabdominal approach allows better access to the renal vessels. Therefore, our group switched to the abdominal access after seven patients. So far, we have not experienced any additional risks in terms of incidental splenectomy [13], post-operative intestinal obstruction or bowel adhesion [16]. However, it remains an open question as to whether major complications, such as liver or pancreas injury, could have been avoided by a classical flank incision.

Laparoscopic live donor nephrectomy has been performed in many specialized centres worldwide. In the mean time, there are several techniques for laparoscopic kidney resection, including the transperitoneal or retroperitoneal, strictly laparoscopic or hand-assisted approach. Laparoscopic procedures seem to have some advantages, e.g. with regard to the rates of complication or the short hospital stay, and the preliminary results concerning graft function are encouraging. However, long-term data are not available at present. The authors have extensive experience and have followed up a large patient group since 1994. The complication rate in this special patient group (e.g. many old patients, multiple vessels and pre-operative risks) was low and the hospital stay was not much longer compared with laparoscopic operations. Further studies are necessary to determine whether long-term follow-up for the recipients and the donors is favourable when comparing laparoscopic procedures with conventional techniques [17]. Routine placement of intraperitoneal and subcutaneous wound drainage was discontinued in the last series of 47 patients in order to reduce post-operative pain and infection. Seven patients developed unexplained fever that subsided after empirical antibiotic treatment. Despite intensive diagnostic investigations, no cause could be found. Eight patients experienced less significant pulmonary complications, including pleural effusions and mild pulmonary oedema, probably caused by fluid overload in the recovery area.

### **Severe, rare complications and complications which might be expected when a nephroureterectomy is carried out under difficult conditions (e.g. intraoperative injuries of neighbouring organs, such as those due to substantial intra-abdominal synechia)**

This category comprises three cases. One is a case of splenectomy together with removal of the left kidney and the second is a case in which surgical revision became necessary due to post-operative haemorrhage of the liver following right nephrectomy. In the third case, surgical revision was necessary due to the development of a pancreatic pseudocyst with subsequent infection after injury of the pancreas. This was caused by severe adhesions between the pancreas and kidney, probably due to pancreatitis that had not been detected pre-operatively. After appropriate treatment, all patients remained stable and without complications during follow-up. In addition, 10 patients experienced less critical complications consisting of intraoperative haemorrhages of the neighbouring organs, including the spleen, pancreas and/or suprarenal glands, all of which could be successfully stopped. All these patients had more or less severe intra-abdominal adhesions.

Serious complications can be inevitable, especially in cases of serious adhesions. Therefore, relevant information regarding the potential donors' previous

operations is crucial. The higher surgical risks in respect of unexpected intra-abdominal adhesions should be discussed with the potential donors. The informed consent should state whether the planned donor nephroureterectomy should be cancelled intraoperatively if risks are greater than anticipated.

### **Severe, rare and non-predictable complications before, during or after the nephroureterectomy (e.g. intraoperative acute cardiac arrest)**

This category of risks comprises three cases: a temporary cardiac arrest, a heavy bronchial spasm after initiating anesthesia and a post-operative acute renal failure. Extensive post-operative assessment of the pulmonological, cardiological, nephrological or urological systems was unable to explain these incidents. Creatinine normalized spontaneously over time after the operation. All three patients are meanwhile recovered and free of symptoms.

The lesson learned from this category is that even healthy potential donors in whom a thorough pre-operative medical examination is unremarkable must be informed about such rare but life-threatening complications [18]. The likelihood of unexpectedly finding a malignant tumour (e.g. renal cell carcinoma) as well as the very unlikely possibility of death from the consequences of the operation should be discussed.

### **Severe, predictable complications after nephroureterectomy due to increased clinical risks known pre-operatively (e.g. post-operative pneumonia due to advanced age and obesity)**

Our experience with donors from this category has shown that they can be operated on without an increased rate of complications when intensified perioperative measurements are taken [19]. The easiest way of reducing risks and complications is to exclude patients with known risk factors, a policy applied by many transplantation centres. The decision, however, becomes more difficult when the donor is highly motivated. In one case, a 65-year-old patient, in excellent mental condition is resolved to sacrifice a kidney for his diseased wife, despite being told that there is a 30–50% probability of myocardial infarction resulting from coronary heart disease. The conflict between self-determination of the patient and the doctor's sense of responsibility has to be addressed by a multidisciplinary team, including psychologists and anaesthesiologists. With regard to the future development of living donor renal transplantation, the following question arises: Which criteria, especially considering the progress of intensive care, are to be considered if one is going to accept donors with predictably raised risks?

### **Risks arising from the donor organ**

Vessel anomalies (e.g. multiple renal arteries and renal artery stenosis) can technically jeopardize the successful transplantation of the donor organ on the part of the recipient, explaining why some transplantation centers refuse to transplant kidneys with multiple arteries [6,20]. In our experience multiple arteries are not a contraindication for live donor nephrectomy if carefully evaluated and monitored post-operatively. The refusal to perform a donor nephrectomy is especially difficult to accept for highly motivated donors. After all, multiple blood vessels supplying the kidneys are to be expected in 25–40% of potential donors. For the patients reported in our series who had multiple renal arteries on both sides, the kidney with the smaller number of arteries was chosen for transplantation. Additionally, the pre-operatively diagnosed single artery supply was found intraoperatively to be a duplicated artery supply in four patients and the pre-operatively diagnosed duplicated artery turned out to be a triple artery supply in two additional patients. In these cases, the transabdominal access proved to be especially opportune. As a result of the technical difficulties and the increased perioperative care of donors with multiple arteries, the transplantation of these organs should be reserved to centres with greater experience. Although we had 19 patients > 61 years old, we detected no increased complication rate in this subgroup (Table 2).

### **Long-term donor evaluation**

Donation had no significant long-term effect in the majority of our donors. In the post-operative follow-up period of 0.5–62 months (mean: 38 months), the long-term renal function remained stable in all donors. Although other authors have reported an increased incidence of hypertension and proteinuria combined with living donor nephrectomy, in our series the incidence of these complications was very low and occurred mainly in the older donors. This phenomenon may be equally prevalent in the normal population. Rehabilitation of all donors was good to excellent. After the very brief hospitalization, ~95% of all donors could go back to work or could perform their daily chores within 4 weeks.

### **Conclusions**

Living donor transplantation entails a calculable risk for the donor. Compared with other operations, it also has a very low morbidity and mortality. In spite of additional risk factors (e.g. advanced age, difficult vessel conditions and necessary secondary operations), the rate of complications in our patients was not higher than reported in other publications. Nevertheless, living donor renal transplantation is not without

risk and even life-threatening complications may occur. Therefore, a complete and carefully performed medical examination of the donor as well as strict and responsible judgement of indications are mandatory. Last but not least, donors need to be informed about all possible risks of this elective operation.

*Conflict of interest statement.* None declared.

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