The association between health-related quality of life and mortality among hemodialysis patients

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Key words: *hemodialysis; health related quality of life; SF-36; mortality.*

Summary. *Introduction. Mortality rates for patients undergoing maintenance hemodialysis remain high. Published data regarding association between health-related quality of life (HRQOL) and mortality among hemodialysis patients are inconsistent. Very few data are published on the change in HRQOL over time as a predictor of mortality. The aim of this study was to assess whether HRQOL and change of it over time could be considered an independent predictor of mortality in hemodialysis patients.*

Material and methods. This prospective observational study enrolled 183 patients undergoing maintenance hemodialysis. HRQOL was measured annually 2004–2008 using a generic Short Form 36 questionnaire. Physical component summary (PSC) and mental component summary (MSC) scores were calculated. The change of the patient's HRQOL over time was calculated as a difference between SF-36 scores of the first and the last HRQOL measurements.

Results. The median follow-up was 48 months (range, 1–72 months). Cutoff values for HRQOL predicting mortality for PSC score was ≥35 and for MSC score was ≥45. In the model adjusted for age, sex, dialysis months, creatinine, albumin and hemoglobin levels, mortality risk decreased by 0.96 (95% CI, 0.95–0.99) for 1-point increase in the baseline PSC score and decreased by 0.97 (95% CI, 0.95–0.98) for 1-point increase in the baseline MSC score. A 1-point decline in the PSC score (relative risk, 1.11; 95% CI, 1.008–1.221) and MSC score (relative risk, 1.07; 95% CI, 1.002–1.149) over the period of follow-up were associated with a significant additional increase in mortality.

Conclusions. Both baseline HRQOL and decline of HRQOL are independent predictors of mortality in hemodialysis patients.

Introduction

Hemodialysis is a life-saving treatment for the patients with end-stage renal disease. Whereas patient survival has traditionally been the main indicator of treatment success, the role of evaluating the patient's subjective experience is being increasingly recognized. Measurement of health-related quality of life (HRQOL) shows the impact of illness on the patient's physical, physiological, and social functioning. HRQOL may be affected by several factors, including the clinical manifestations of disease, the side effects of treatment, the quality of the social relationships of a patient (1).

Despite technological advances in hemodialysis over the past decades, overall mortality rates for patients undergoing maintenance hemodialysis are strikingly high (2, 3). There are some predictors of mortality established in this population, such as serum albumin, hemoglobin, comorbidity, but other potentially modifiable predictors of mortality are need to be identified (4, 5). A question rises about the possible prognostic role of HRQOL for survival. There are data demonstrating that HRQOL predicts outcomes among hemodialysis patients, although not all studies have confirmed these results (6–11). To our knowledge, only few published studies have examined changes in HRQOL over time as a predictor of mortality (3). The aim of our study was to assess whether health-related quality of life and change of it over time could be considered an independent predictor of mortality in hemodialysis patients.

Material and methods

A prospective observational study enrolled patients undergoing maintenance hemodialysis (MH) at the Hospital of Kaunas University of Medicine. Data

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collection began in January 2004 and ended in January 2008. The data regarding health-related quality of life, laboratory values, treatment factors were collected once per year, so part of the patients were evaluated more than one time during this study. Outcome data on survival were collected from beginning of the study to the end of follow-up in January 2010.

Health-related quality of life was measured through a validated Lithuanian version of the generic Short Form 36 (SF-36) questionnaire. It consists of 36 questions, 35 of which are compressed into eight scales: 1) physical functioning scale that captures abilities to deal with the physical requirement of life, such as walking and flexibility; 2) role-physical evaluates the extent to which physical capabilities limit activity; 3) bodily pain scale evaluates the perceived amount of pain experienced during the previous 4 weeks; 4) general health scale evaluates general health in terms of personal perception; 5) vitality scale evaluates feelings of energy and fatigue; 6) social functioning scale evaluates how physical health and emotional problems interfered with social interactions during the previous 4 weeks; 7) role-emotional reflects the extent to which emotional factors interfere with activities; 8) mental health evaluates feelings of anxiety and depression. All eight scales are assessed quantitatively and scores between 0 and 100 are calculated, with a higher score indicating better health status. The scales of SF-36 are summarized into two dimensions: physical health component summary (PSC) and mental health component summary (MCS). All patients were instructed to complete the questionnaire on their own between hemodialysis sessions. Assistance with survey completion was offered, if necessary.

The data, including age, dialysis months, adequacy of dialysis (as measured by urea reduction ratio, Kt/V), hematological and biochemical parameters, time of death, were obtained from medical records. The protocol was approved by the local Research Ethics Committee.

Survival analysis was performed to test hypothesis of an association between SF-36 scores and mortality. Cox proportional hazard models were used to calculate hazard ratios of death and their 95% confidence intervals (CI) both in unadjusted and adjusted analyses. Log-rank tests were used to compare the Kaplan-Meier estimates of event rates between several groups. The time of origin was the date of first evaluation of HRQOL. The event defined was death whereas those cases alive at the end of follow-up were censored at the last observation. Cutoff values were detected using area under the receiver operating characteristic (ROC) curves.

Mortality data were used as a dichotomized outcome. Age, hemoglobin, albumin, C-reactive protein (CRP), Kt/V, creatinine, dialysis months, SF-36 scores were classified as continuous variables whereas gender was classified as a categorical variable. For continuous variables, the mean and standard deviation were calculated. For categorical variables, the proportion of individuals who were in each category was examined.

The change of HRQOL over time was calculated as a difference between SF-36 scores of the first and last HRQOL measurements. The positive value shows a decline in HRQOL and negative value means an improvement in HRQOL. Logistic regression was used to estimate an association between change of HRQOL over time and mortality.

The *t* test (if there was a normal distribution of variables) and nonparametric Mann-Whitney rank sum test (if variable distribution was not normal) were used for group mean comparisons between surviving and deceased patients.

Statistical significance was established for *P* values below 0.05. All analyses were performed using the SPSS 15.0 statistical software.

Results

In total, 229 eligible patients on maintenance hemodialysis were contacted. Of these, 202 individuals were enrolled: 27 patients were excluded because they refused to complete questionnaire (22 patients) or were mentally impaired or did not understand Lithuanian language (5 patients). Out of the 202 patients enrolled, only 189 provided complete data from all SF-36 dimensions (13 patients left several questions unanswered). In 6 cases, the exact information on survival or time of death was missing. This left a total of 183 patients whose data were entered into the final analysis.

The mean age of the patients was 56.7±15.9 years, 103 (56.3%) were men, the mean PSC score was 40.6±18.9, and the mean MSC score was 48.9±19.7. The median follow-up was 48 months (range, 1–72 months).

A total of 68 (37.2%) patients died and 115 (62.8%) were alive at the end of follow-up. Table 1 compares characteristics of deceased and surviving patients at the time of first evaluation of HRQOL. Comparison of two major dimensions of the SF-36 showed that the PSC score and the MSC score were significantly higher in surviving patients (45.7±16.6 and 53.6±17.1) when compared with that of deceased patients

Table 1. Characteristics of 183 patients on maintenance hemodialysis by survival

Characteristic	All patients n=183	Surviving patients n=115	Deceased patients n=68	P^a
SF-36 score				
Physical functioning	46.9±28.3	54.5±25.8	33.9±27.8	<0.001
Role-physical	26.9±35.9	33.0±37.1	16.54±31.3	<0.01
Bodily pain	52.3±29.0	58.2±27.1	42.2±29.5	<0.001
General health	32.5±15.5	34.2±15.1	29.8±16.0	0.032
Vitality	45.4±21.5	49.7±19.5	38.2±22.9	<0.001
Social functioning	65.6±24.6	69.8±22.2	58.5±27.0	<0.01
Role-emotional	43.9±43.2	54.5±42.2	25.9±39.0	<0.001
Mental health	57.4±21.7	60.4±19.9	52.5±23.8	0.022
PSC	40.6±18.9	45.7±16.6	31.9±19.5	<0.001
MSC	48.9±19.7	53.6±17.1	40.97±21.2	<0.001
Change in PSC	0.64 ± 19.7*	–7.1±15.5**	15.8±18.5***	<0.001
Change in MSC	–0.39±19.8*	–7.7±15.3**	14±19.9***	<0.001
Age, years	56.7±15.9	51.1±16.2	64.3±11.0	<0.001
Gender, men, %	56.3	56.5	55.9	0.53
Hemoglobin, g/L	100.2±11.5	101.0±10.3	99.2±12.8	0.36
Albumin, g/L	38.8±3.5	39.7±3.07	37.9±3.67	<0.01
CRP, mg/L	10.3±14.0	7.0±4.5	13.8±19.0	0.20
Creatinine, μmol/L	843.5±240.9	878.6±270.0	797.39±189.2	0.042
Kt/V	1.3±0.21	1.25±0.2	1.29±0.21	0.22
Dialysis months	28.8±23.2	27.7±23.2	30.2±23.2	0.52

PSC, physical health component summary; MCS, mental health component summary.
*n=80; **n=53; ***n=27.
[a]Comparing the groups of surviving and deceased patients.

(31.9±19.5 and 40.97±21.2) (P<0.001). The same significant differences among all eight scales of SF-36 were found. Surviving patients were younger; they had significantly higher serum albumin and creatinine levels as compared with the deceased patients.

Cutoff values for HRQOL predicting mortality were calculated: cutoff value for PSC score was ≥35 and cutoff value for MSC score was ≥45. Figs. 1 and compare survival rates between patients groups with PSC and MSC above and below the cutoff value. Lower MSC and PSC were associated with significantly worse survival in the unadjusted analysis.

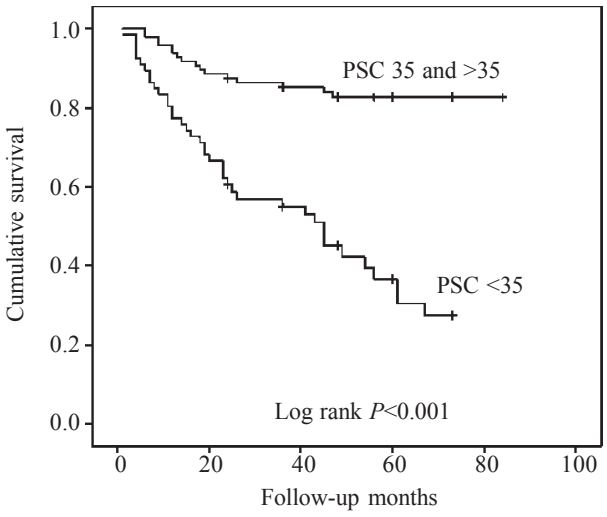

Fig. 1. Kaplan-Meier survival curves for different baseline physical health component summary (PSC) groups

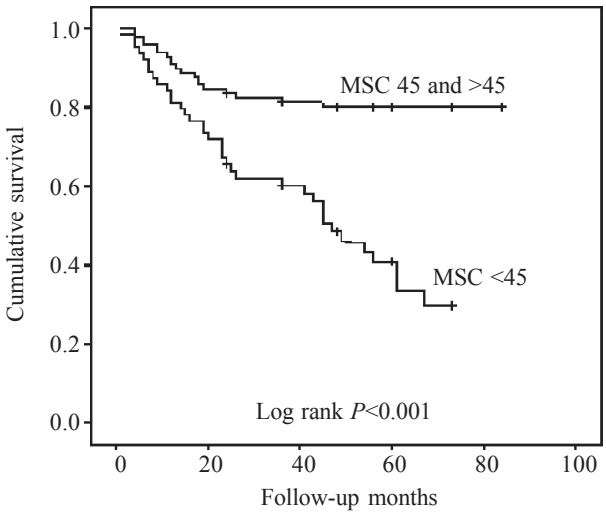

Fig. 2. Kaplan-Meier survival curves for different baseline mental health component summary (MSC) groups

Using Cox proportional hazard models, HRQOL was found to be significantly associated with the risk of death. As shown in Table 2, the unadjusted mortality risk decreased by 0.96 per one-point increase in the HRQOL PSC score and decreased by 0.97 for one-point increase in the MSC score. In the model adjusted for age, sex, dialysis months, creatinine, albumin, and hemoglobin, mortality risk decreased by 0.96 for each point increase in the PSC score and decreased by 0.97 for each point increase in the MSC score. Among the laboratory values, serum albumin showed a strong association with prospective mortality: relative risk of death was 0.87 to 0.88 for each 1 g/L increase depending on Cox regression analysis model (Table 3). Age also was significantly associated with dialysis mortality, showing a relative risk of death of 1.05 for each year of age.

The separate survival analyses of each single SF-36 scale showed that every scale was a prognostic factor for mortality in the unadjusted analysis, whereas in the adjusted analyses, all scales, except general health scale, were also independent predictors of mortality (Table 2).

During our study, 80 patients completed SF-36 questionnaire more than one time (2, 3, or 4 times) and change in HRQOL for these patients was calculated. Among these individuals, the mean PSC score change was 0.64±19.7 (range, –46 to 56) and the mean MSC score change was –0.39±19.8 (range, –38 to 52). A 1-point decline in the PSC score was associated with a significant additional increase in the relative risk for mortality by 1.11 (95% CI, 1.008–1.221; *P*=0.033) after adjusting for baseline PSC score, gender, baseline age, serum albumin, hemoglobin, and creatinine. Similar associations between 1-point decline in MSC and increase in mortality were observed (relative risk, 1.07; 95% CI, 1.002–1.149; *P*=0.044).

Discussion

According to our data, a decline in two main dimensions of HRQOL (physical and mental health component summaries) over time was associated with an additional increase in mortality risk. A similar association was reported by Knight at al. (3). They examined the association between a 6-month decline in the SF-36 PSC and MSC scores and subsequent mortality and found that 10-point decline in the PSC and MSC scores were significantly associated with increased mortality.

In this study, we found that scores of the SF-36, a self-administered questionnaire used to assess

Table 2. Relative risks of death per 1-point higher HRQOL according to the Cox regression analysis

SF-36 domain	Unadjusted RR of death (95% CI)	*P*	Adjusted* RR of death (95% CI) of death (95% CI)	*P*
Physical functioning	0.97 (0.96–0.98)	<0.001	0.98 (0.97–0.99)	<0.01
Role-physical	0.98 (0.97–0.995)	<0.01	0.989 (0.98–1.00)	0.043
Bodily pain	0.98 (0.97–0.99)	<0.001	0.98 (0.97–0.995)	<0.01
General health	0.97 (0.95–0.99)	<0.01	0.99 (0.97–1.014)	0.42
Vitality	0.97 (0.96–0.987)	<0.001	0.98 (0.97–0.99)	0.025
Social functioning	0.98 (0.97–0.99)	<0.01	0.98 (0.96–0.99)	<0.01
Role-emotional	0.98 (0.979–0.99)	<0.001	0.991 (0.98–0.998)	0.019
Mental health	0.98 (0.97–0.995)	<0.01	0.98 (0.98–0.997)	<0.01
PSC	0.96 (0.94–0.97)	<0.001	0.96 (0.95–0.99)	<0.01
MSC	0.97 (0.95–0.98)	<0.001	0.97 (0.95–0.98)	<0.01

*Adjusted for age, gender, dialysis months, albumin, creatinine, hemoglobin.
PSC, physical health component summary; MCS, mental health component summary.

Table 3. Relative risk of death according to the Cox regression analysis models for SF-36 dimensions and other variables

Variable	RR of death (95% CI)	*P*	Variable	RR of death (95% CI)	*P*
PSC	0.97 (0.95–0.99)	<0.01	MSC	0.98 (0.96–0.992)	<0.01
Age	1.05 (1.02–1.08)	<0.01	Age	1.05 (1.03–1.08)	<0.001
Gender	0.74 (0.40–1.4)	0.36	Gender	0.75 (0.40–1.41)	0.37
Albumin	0.88 (0.78–0.98)	0.018	Albumin	0.87 (0.78–0.97)	0.012
Creatinine	1.00 (0.998–1.001)	0.76	Creatinine	1.00 (0.99–1.001)	0.95
Hemoglobin	1.023 (0.99–1.06)	0.19	Hemoglobin	1.02 (0.99–1.06)	0.20

PSC, physical health component summary; MCS, mental health component summary.

HRQOL, had a significant association with prospective mortality in patients on maintenance hemodialysis. Lower HRQOL scores, showing worse quality of life, were significantly associated with a higher risk of death. These associations remained statistically significant after adjustment for several risk factors of death, including serum albumin concentration, age, hemoglobin, and other.

Similar to our findings concerning mortality, other studies found that the self-reported quality-of-life score was independently predictive for mortality. Data analysis of the Dialysis Outcomes and Practice Patterns Study (DOPPS) revealed that lower scores for major components of HRQOL (both physical and mental health) were strongly associated with a higher risk of death and hospitalization in hemodialysis patients, independent of a series of demographic and comorbid factors. This study enrolled more than 17 000 patients from the United States, Europe, and Japan (8). Other study of 1000 patients at three dialysis centers in the United States reported an association between lower scores in the physical component of quality of life and higher risk of death at least until the next 24 months. In this study, SF-36 physical health dimension score below the median value was twice as likely to be associated with mortality (6). A large study, involving 5256 patients in the United States and Europe, presented evidence that the mental components of quality of life predict death even after taking into account serum albumin concentration and several other risk factors (12). Lowrie et al. found a similar association between both physical and mental health dimensions of the SF-36 and dialysis mortality (13).

However, data on self-reported mental health and hemodialysis mortality are inconclusive. DeOreo in a previously mentioned study (6) found no significant association between a mental health component summary score and mortality. Mercus et al. (9), in a relatively small study (189 patients), found no association between a mental health component summary score of 30 or higher and a composite measure of poor outcome, but the composite measure did not include mortality. We found that mental health was associated with mortality similar to or even greater than physical health.

The reason that poor self-reported mental health is associated with increased mortality in hemodialysis population is unknown. Some potential mechanisms for this association have been proposed. Deficits in cognition caused by depression may result in diminished adaptive skills in the face of illness, and affective symptoms associated with depression may discourage friends and family members from providing needed assistance (14). Biological mechanism has been also proposed, for example, psychological stress has been associated with impaired wound healing and increased cardiac ischemia (15, 16). It is very important that low self-reported mental health may be amenable to treatment. Individuals on chronic peritoneal dialysis showed an improvement in the Beck Depression Inventory scores with antidepressant therapy (17). Exercise training in individuals on hemodialysis has also been shown to improve the Beck Depression Inventory scores. Identification and treatment of individuals with low MSC scores and confirmed depression may improve morbidity and improve adherence with medical therapy (18).

The mechanism of how physical HRQOL component influences mortality is probably very complex. The SF-36 physical health component summary score has been validated compared with objective measurements of physical function in individuals on hemodialysis. Painter et al. (19) compared objective physical performance in individuals with a low or higher PSC score and found that the group with high PSC scores scored higher on all physical function measurements, including gait speed and time from sit-to-stand. That means that in patients undergoing hemodialysis, the PSC score provides a rough approximation of objective physical function. Physical function may also be a marker of disease severity (20). There are no trials in individuals undergoing hemodialysis showing decreased mortality with improvement in physical function, but there is evidence that physical function can be improved through exercise training and physical rehabilitation (21).

Several studies have shown that albumin is one of the strongest predictors of death in dialysis patients. DOPPS data show that the PSC score lower by 10 points was associated with increased mortality risk that was similar to or even greater than the risk associated with serum albumin level lower by 1 g/dL (8). In our study, serum albumin showed a stronger association with prospective mortality than PSC and MSC score.

Our study has limitations that should be considered when interpreting the data. We had incomplete information on some potential confounders, such as education, occupational status, marital and living status, and yearly income; therefore, these variables were not included in multivariate analysis. Some published studies have shown associations between these values

and HRQOL, although there are no data showing the impact of these confounders on mortality. The other limitation is a relatively small sample size. Despite of this, the number of patients enrolled in our study was sufficient to detect association between HRQOL and mortality.

Our study additionally supports the use of health-related quality-of-life measures to identify patients who are at higher risk of death. Because this study is observational, we cannot definitely state that the association between HRQOL and the outcomes is causal. In any case, the data indicate that HRQOL can serve as a sensitive indicator of subsequent patient mortality.

Conclusions

Health-related quality of life is an independent predictor of mortality in hemodialysis patients. Change of health-related quality of life over time provides additional information predicting subsequent mortality in these patients. Future studies are needed to assess whether interventions that improve health-related quality of life also decrease the risk of death among hemodialysis patients.

Hemodialize gydomų pacientų gyvenimo kokybės ir išgyvenimo sąsaja

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Raktažodžiai: hemodializė, gyvenimo kokybė, SF-36, mirtingumas.

Santrauka. *Įvadas.* Nepaisant medicinos pažangos, nuolatine hemodialize gydomų pacientų mirtingumas išlieka didelis. Medicinos literatūroje pateikiama prieštaringų duomenų apie šių pacientų gyvenimo kokybės ir mirtingumo sąsają, o gyvenimo kokybės kitimo ir mirtingumo sąsaja yra mažai tyrinėta.

Tyrimo tikslas. Įvertinti, ar gyvenimo kokybė ir jos kitimas turi įtakos hemodialize gydomų pacientų mirtingumui.

Tyrimo medžiaga ir metodai. Išanalizuoti 183 pacientų, gydomų nuolatine hemodialize, duomenys. Perspektyviojo tyrimo metu, 2004–2008 m. laikotarpiu, gyvenimo kokybė tirta kasmet naudojant *Short Form 36* klausimyną. Apskaičiuoti fizinis (FKK) ir psichikos (PKK) gyvenimo kokybės komponentai. Gyvenimo kokybės kitimas vertintas kaip skirtumas tarp pirmo (bazinio) ir paskutinio gyvenimo kokybės tyrimų rodiklių.

Rezultatai. Vidutinė stebėsenos trukmė 48 mėn. (1–72 mėn.). Pagal ROC kreivę nustatytos kritinės gyvenimo kokybės komponentų reikšmės pacientų mirtingumui (FKK ≥35 balų, PKK ≥45 balų). Koregavus rezultatus pagal amžių, lytį, dializių trukmę, kreatinino, albumino ir hemoglobino kiekį Cox regresijos metodu, nustatyta, kad vienu balu didesnis FKK mirtingumo riziką mažino 0,96 (95% PI, 0,95–0,99), atitinkamai vienu balu didesnis PKK mirtingumo riziką mažino 0,97 (95% PI, 0,95–0,98). Gyvenimo kokybės blogėjimas stebėsenos laikotarpiu didino mirtingumo riziką: pablogėjus FKK vienu balu, mirtingumo rizika didėjo 1,11 (95% PI, 1,008–1,221); vienu balu pablogėjus PKK, mirtingumo rizika didėjo 1,07 (95% PI, 1,002–1,149).

Išvados. Gyvenimo kokybė ir gyvenimo kokybės blogėjimas yra nepriklausomi veiksniai, susiję su hemodialize gydomų pacientų mirtingumu.

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