Health-Related Quality of Life, Treatment Efficacy, and Hemodialysis Patient Outcome

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CLINICAL STUDY

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The aim of the study was to examine the influence of improved treatment of hemodialysis (HD) patients on their health-related quality of life (HrQoL) and to assess the predictive value of HrQoL dimensions on patient outcome. The prospective cohort study involved 102 HD patients, and their clinical and laboratory parameters and HD adequacy indices were followed from 2001 to 2007. HrQoL was measured using KDQOL-SF Version 1.3 in 2001, 2004, and 2007. During a six-year period, quality of HD and anemia treatment improved and resulted in significant increase of mean Kt/V (1.2–1.56) and hemoglobin levels (86.5–115.6 g/L). All four HrQoL dimensions (i.e., physical, mental health, kidney disease target issues, and patient satisfaction) remained unchanged, but significant improvement in several HrQoL physical health domains and the effects of kidney disease domain was found. Mortality rate decreased from 18.6% to 7.14% per year. Age was associated positively, but kidney disease target issue score negatively, with patient death. Improved HD adequacy and anemia treatment in HD patients were followed with maintenance of all four HrQoL dimensions unchanged over six years. Moreover, an improvement in several physical health domains and the effects of kidney disease domain was found. Age and kidney disease target issue appeared as significant predictors of patients' death.

Keywords health-related quality of life, hemodialysis adequacy, hemodialysis patients' outcome

INTRODUCTION

Advances in the treatment of end-stage renal disease (ESRD) patients contributed to improvement of their survival, but their health-related quality of life (HrQoL) was still much lower than for the general population.[1,2] Therefore, improvement of HrQoL is one of the main goals of ESRD patient treatment. Some valid and reliable instruments for assessment of HrQoL of this population have been developed, but the Kidney Disease and Quality of Life—Short Form (KDQOL-SF™) was the most frequently used instrument in the last decade. In several single-center and multicenter studies that used this instrument, HrQoL of patients on different dialysis modalities was assessed,[3,4] factors associated with different domains of HrQoL were analyzed,[3,5,6] and the association of HrQoL and patient outcome was evaluated.[3,4,7] Most of these studies were cross-sectional, and only a few of the longitudinal studies examined whether the improvement of ESRD patient treatment had an influence on their HrQoL.

In all hemodialysis centers in our country, including our institute, the treatment of hemodialysis (HD) patients has been improving from 2001. That stimulated us to undertake a prospective study with the aim of examining whether the better treatment of HD patients had any influence on their HrQoL, and to assess the predictive value of HrQoL dimensions on HD patient outcome.

MATERIALS AND METHODS

The prospective cohort study involved 102 (86.4%) patients selected from the population of 118 patients maintained by HD at the Institute of Urology and Nephrology, Clinical Center of Serbia. Patients who refused or were unable to fill in the questionnaire for HrQoL measurement and those less than three months on HD were excluded from the study. The causes of ESRD were polycystic kidney disease (n = 19), chronic glomerulonephritis (n = 18), rapidoprogressive glomerulonephritis (n = 5), nephrosclerosis (n = 13), chronic pyelonephritis (n = 9), systemic disease (n = 12), diabetic nephropathy (n = 5),

Balkan endemic nephropathy (n = 2), other (n = 17), and unknown (n = 2).

Informed consent was obtained from each patient.

Patients selected were followed over six years from April 2001. All patients were dialyzed thrice weekly for 4–5 hours with a bicarbonate-based solution. Until the end of 2000, the type of dialyzers used depended more on the possibility of their purchase than on medical indications because of the generally poor financial situation in the health centers. Near the end of 2001, the supply of dialyzers improved, and dialyzers with higher surface area became available, which enabled improvement of HD adequacy. Also, in 2001, only 25 patients (24.5%) received human recombinant erythropoietin (EPO), but from the beginning of 2003, EPO could be used according to Anemia European guidelines,[8] so 70–74% of the patients were supplemented with EPO.

HD adequacy was assessed by calculation of Kt/V, and normalized protein catabolic rate (nPCR) was determined.[9]

HrQoL was measured using the self-administered KDQOL-SF Version 1.3,[10] translated into the Serbian language (see http://gim.med.ucla.edu/kdqol/page8.htlm).

The questionnaire consists of 80 items divided into 19 domains and includes both general measures and measures specific to patients with kidney disease. The general measures are based on questions from a 36-item Short Form Health Survey (36-SF), which includes 8 domains/36 items, and specific measures are based on kidney-disease-targeted questions, which include 11 domains/43 items. One additional item is about health status compared to that of one year previous. Nineteen health-related domains are categorized in four dimensions of HrQoL as used by Bakewell et al.[3]:

1. *Physical health* is composed of measures of seven domains: physical functioning, work status, role limitation due to physical health, general health perception, pain, energy/fatigue, and social function.
2. *Mental health* comprises five domains: emotional well-being, quality of social interactions, burden of kidney disease, social support, and role limitation due to emotional problems.
3. *Kidney disease target issues*: cognitive function, symptoms/problems, effects of kidney disease, sexual function, and sleep.
4. *Patient satisfaction*: patient satisfaction and perception of dialysis staff encouragement.

The KDQOL-SF version 1.3 questionnaires were given to the patients who completed them during a dialysis session at the hospital (average 20 minutes) or at home, returning them at the next dialysis session. To make sure the patients adequately filled in the surveys, the directions were read out. Approximately 10% of the patients needed assistance from the nurses, physicians, or family members.

Body weight and height were measured, and body mass index (BMI) was calculated according to the formula: weight (kg) / height^2 (m^2).

Laboratory analyses involved the determination of peripheral blood cell counts and serum creatinine, albumin, cholesterol, and triglyceride levels measured enzymatically using automatic methods. C-reactive protein (CRP) was determined by nephelometry (normal values <5 mg/L). Predialysis and postdialysis blood samples were obtained midweek.

Clinical status, laboratory parameters, and HD adequacy were followed regularly. HrQoL was measured at the onset of the study (April 2001), in June 2004, and in April 2007. By June 2004, two patients left the cohort and 27 patients died, but 61 (83.6%) of the remaining patients completed the questionnaire. The third measurement of HrQoL comprised 55 (84.6%) of 65 patients that still were on HD in our center (note that two patients left the cohort and six patients died from 2004 to 2007).

The database includes demographic (sex, age, BW, BMI), clinical (underlying disease, BP, HD duration), HrQoL, laboratory, as well as HD adequacy.

Statistics

The data are presented as arithmetic means with standard deviation (X ± SD). Comparison between groups was made by the *t*-test or the Mann-Whitney test, as appropriate, as well as with ANOVA.

The internal consistency of QoL item scores was calculated by Cronbach's alpha, and it is generally accepted that its value should be in excess of 0.70.[11] Cronbach's alpha ranged from 0.71 to 0.91 of completed questionnaires for eight generic scales, but in three of the disease-specific scales, Cronbach's alpha was less than 0.7 (cognitive function = 0.60, quality of social interaction = 0.56, quality of social support = 0.63). After removing one item from cognitive function and quality of social interaction, Cronbach's alpha coefficients reached 0.62 and 0.68, respectively.

In order to analyze the risk of death, Kaplan-Meier curves and univariate survival analysis were obtained with the Cox proportional hazard model. The primary dependent variable was the time of death measured in months. Variables that were potential predictors of death in univariate analysis ($p < 0.01$) were tested in a multivariate Cox proportional hazard model. The calculations were made using SPSS.

RESULTS

The characteristics of 102 hemodialysis patients included in the study in April 2001 are shown in Table 1. The patients were on regular HD for 81.4 months on average, and their mean Kt/V was 1.2 and mean hemoglobin level 86.5 g/L, because only 25 of them had been treated with EPO. The mean values of four dimensions of HrQoL are also presented in Table 1.

The patients were followed for the following six years. During this period, the quality of HD as well as ane-mia treatment improved and comparison of mean Kt/V and hemoglobin levels detected significant increase (see Table 2). At the same time, mean age of examined patients changed insignificantly, but the time spent on HD treatment was significantly longer for patients examined in 2004 and 2007 than in those at the outset of the study. The measurement of HrQoL was repeated every three years. Comparison of mean values of all four HrQoL dimensions revealed no differences (see Table 2).

Comparison of scores for individual health domains obtained by three repeated measurements revealed several significant differences. The scores for SF-36 domains are presented in Figure 1. In 2001, lower scores were found for all domains than in 2004 and 2007. The differences were significant between scores for physical functioning and the score for role limitation due to physical health

Table 1
Characteristics of the examined population (n = 102) at the onset of the study

Age (years)	55.4 ± 13.8 (21–82)
Gender (n, M/F)	47/55
Dialysis duration (months)	81.4 ± 55.5 (11–231)
Hemoglobin (g/L)	86.5 ± 15.6
Serum albumin (g/L)	38.8 ± 3.7
Serum total cholesterol (g/L)	4.8 ± 1.2
Serum triglycerides (g/L)	2.3 ± 1.4
Serum CRP (mg/L)	8.2 ± 9.9
Serum creatinine (umol/L)	957.9 ± 186.8
Kt/V	1.2 ± 0.22
nPCR (g/kg/day)	1.1 ± 0.27
Body mass index (kg/m^2)	22.5 ± 3.7
On treatment with EPO (n)	25
Physical health	46.1 ± 23.3
Mental health	59.5 ± 21.7
Kidney disease target issues	60.1 ± 18.3
Patient satisfaction	75.9 ± 20.0

Data are given as mean ± standard deviation.

Abbreviations: EPO = erythropoietin, CRP = C-reactive protein; Kt/V = fractional urea clearance.
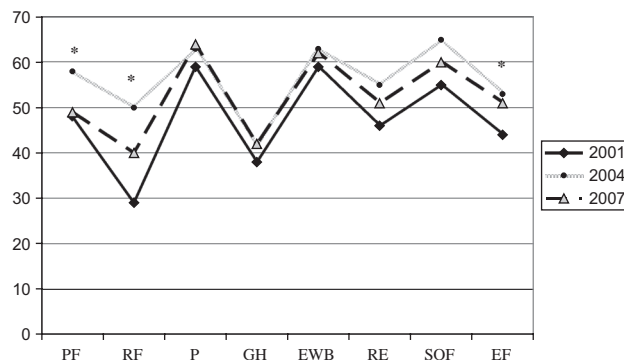
Figure 1. The scores of SF36 domains for examined patients in 2001, 2004 and 2007. *p < 0.05. Abbreviations: PF = physical functioning, RF = role limitation due to physical health, P = pain, GH = general health perception, EWB = emotional well-being, RE = role limitation due to emotional problems, SOF = social function, EF = energy/fatigue.

Table 2
Age, hemodialysis duration, serum hemoglobin concentration, dialysis adequacy, and four HrQoL dimensions patients in 2001, 2004, and 2007

Parameters	2001	2004	2007	p*
Age (years)	55.4 ± 13.8	54.3 ± 11.0	57.0 ± 13.5	ns
Hemodialysis duration (months)	81.4 ± 55.5	96.3 ± 59.4	121.4 ± 64.4	0.000
Hemoglobin (g/L)	86.5 ± 15.6	106.6 ± 18.7	115.6 ± 19.7	0.000
Kt/V	1.2 ± 0.22	1.37 ± 0.19	1.56 ± 0.22	0.000
Physical health	46.1 ± 23.3	51.3 ± 12.9	46.1 ± 15.2	ns
Mental health	59.5 ± 21.7	65.8 ± 14.7	62.4 ± 12.5	ns
Kidney disease target issues	60.1 ± 18.3	61.5 ± 17.2	65.7 ± 14.9	ns
Patient satisfaction	75.9 ± 20.0	74.0 ± 17.0	75.5 ± 20.5	ns

Data are given as mean ± standard deviation.

*p = ANOVA.

Abbreviations: Kt/V = fractional urea clearance, ns = non-significant.

domain in 2001 as compared to the scores obtained in 2004. Also, the score for energy/fatigue domain in 2001 was significantly lower than the scores obtained in 2004 and 2007. Figure 2 presents the kidney disease target domains for the same groups of patients. Significant differences were found only between the score for effects of kidney disease domain obtained in 2001 as compared to the scores for 2004 and 2007.

During the follow-up period, four patients left the cohort, 33 patients died, and the others are still on maintenance hemodialysis. Mortality rate decreased during the six-year period from 18.6% per the first year of the study to 7.14% per the last year of the study. The cause of death was a fatal cardiovascular event (heart failure, arrhythmia, myocardial infarction, thrombotic and hemorrhagic stroke) in 20 (60.6%), septicemia in four (12.1%), malignancy in four (12.1%), surgical complications in two (6%) patients, and unknown in three (9%) patients.

Potential predictors of mortality were selected by the univariate Cox proportional hazard model. The significant predictors were age, albumin, CRP and creatinine, as well as physical and mental health and kidney disease target issue. In the multivariate analysis, only age and kidney disease target issue score were found to be significant predictors of patients' death. Age was associated positively, but kidney disease target issue score associated negatively with patients' mortality (see Table 3).

As kidney disease target issue score was found to be a significant predictor of patients' death, the Kaplan-Meier estimate of survival in patients according to the kidney disease target issue dimension were calculated and presented in Figure 3. Patients with higher scores in this HrQoL dimension had a significantly more favorable survival rate ($p = 0.0057$).

DISCUSSION

The patients enrolled in the present study were monitored over six years, in which their treatment was improved. Namely, after severe problems in supplying hemodialysis centers with dialysis machines, dialyzers and drugs during the nineties, dialyzers with a synthetic membrane and higher surface area, and new dialysis machines and EPO became more available from the end of 2001. The main objective of the present prospective six-year study was to examine whether the improved treatment of HD patients influenced their HrQoL. Hence, enhancement of treatment was followed with the improvement of anemia and Kt/V, and HrQoL dimensions remained unchanged over all six years. The majority of previous HrQoL studies were cross-sectional, but longitudinal studies mostly followed the changes of HrQoL over time under
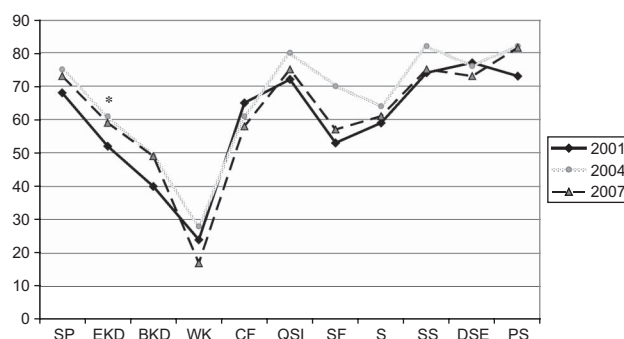
Figure 2. The scores of the kidney disease target domains for examined patients in 2001, 2004, and 2007. *$p < 0.05$. Abbreviations: SP = symptoms/problems, EKD = effects of kidney disease, BKD = burden of kidney disease, WK = work status, CF = cognitive function, QSI = quality of social interactions, S = sexual function, S = sleep, SS = social support, DSE = perception of dialysis staff encouragement, PS = patient satisfaction.

Table 3

Predictors of mortality: multivariate Cox proportional hazard model

Variable	ß	Hazard ratio (CI)	p
Age	0.061	1.063 (1.019–1.108)	0.005
Kidney disease target issues (KDI)	−0.032	0.969 (0.941–0.998)	0.034
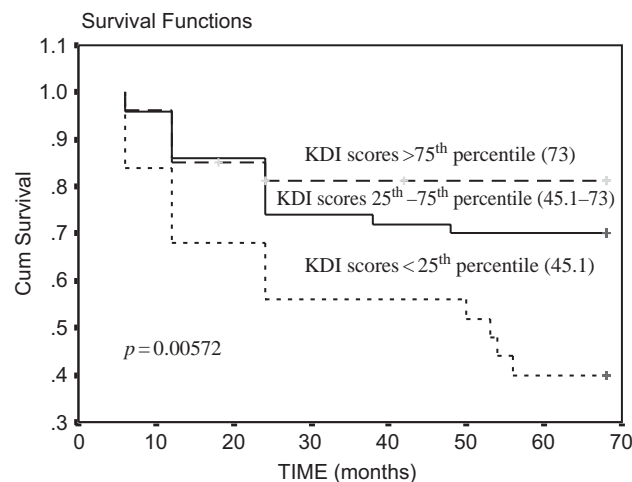
Figure 3. Kaplan-Meier estimate of survival in hemodialysis patients divided into groups in relationship to the kidney disease target issue dimension (KDI) scores.

unchanged treatment conditions. Those studies showed decline of all HrQoL dimensions over time, but significant decline was most frequently found in domains related to physical health.[3,12,13] Although the patient populations examined in those studies differed according to dialysis modalities and duration of dialysis treatment that caused some differences in the HrQoL, the loss of quality of life, especially physical health, was found in all of those populations over the follow-up period, which was up to two years. On the contrary, in our study, no significant change was found in mean values of all four HrQoL dimensions over six years. Moreover, some of the HrQoL domains increased significantly. The significant increase occurred in physical functioning and role limitation due to physical health domain in the first three-year period, but a slight decrease of these domains occurred thereafter. The score for energy/fatigue domain and for effects of kidney disease domain improved significantly between 2001 and 2004 and maintained unchanged until the end of the study. The main difference between our study and the above-mentioned studies were the improved treatment of HD patients that characterized our study. This improvement protected HD patients against the HrQoL loss in a six-year period, especially in the first three-year period.

In the literature, studies on the influence of dialysis cure upgrading on patients' HrQoL are scarce and carried out in short-term studies. Vos et al.[14] pointed out the beneficial effect of short daily home hemodialysis on HrQoL. Some authors reported a beneficial effect of anemia improvement on HrQoL,[15] while others found no association between hemoglobin and quality of life.[3] Recently, improvement of HrQoL was described in HD patients treated with human growth hormone in order to improve their nutritional status,[16] as well as in patients on frequent nocturnal HD as compared to those on conventional HD.[17] All of these studies as well as our study, in which better treatment of previously insufficiently treated patients had beneficial effect on HrQoL in long period, indicated that continuous efforts directed to the improvement of complex treatment of HD patients could lead to their better HrQoL.

One of the objectives of the present study was to analyze the predictive value of HrQoL scores. Multivariate analysis identified age as a positive predictor and kidney disease target issue score as a negative predictor of patient death. Patients with a kidney disease target issue score of more than 73 (83.6 ± 8.9) had a significantly better survival rate than patients with scores between 45.1 and 73 (59.0 ± 6.7) or less than 45.1 (36.8 ± 7.17). Using only the SF-36 Health Survey, Knight et al.[18] found that mental health and physical function were independent predictors of mortality with a significant interaction between age and physical function. Analysis of data from the DOPPS revealed that lower scores for physical, mental, and kidney disease component summary scores were strongly associated with higher risk of death, independent of a series of demographic and comorbid factors. Although the authors proposed that HrQoL scores could serve as indicators of patient outcome, the causal relationship between HrQoL and patient outcome could not be checked in this observational study.[7] Our study involved a small number of patients, but it confirmed that HrQoL, especially low kidney disease target issue score, along with age had predictive value for a poor patient outcome.

CONCLUSION

Improved HD adequacy and anemia treatment in HD patients were followed with maintenance of all four HrQoL dimensions unchanged over six years. Moreover, an improvement in several physical health domains and the effects of kidney disease domain occurred. Age and kidney disease target issue score were found as significant predictors of patients' mortality.

ACKNOWLEDGMENT

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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