Determinants of outcome dialysis
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Chapter 5

Quality of life

Abstract

**Background and purpose.** Information on the longitudinal quality of life (QL) of patients treated by different dialysis modalities is lacking. Therefore, we performed a prospective cohort study on the QL over time in hemo (HD)- and peritoneal dialysis (PD) patients.

**Methods.** New chronic dialysis patients from 13 Dutch dialysis centers were consecutively included. The patients’ self-assessment of QL was measured with the SF-36 form at 3, 6, 12, and 18 months after the start of dialysis treatment.

**Results.** Out of 230 patients who completed the QL questionnaire at least once, 139 patients stayed on their initial dialysis modality, 26 patients switched dialysis modality, 35 patients were transplanted, 28 patients died and two patients had recovery of renal function. The QL of patients who died during the study period was considerably worse at baseline and worsened at a faster rate than in the other patient groups. In patients who stayed on their initial dialysis modality, the physical QL decreased over time, whereas the mental QL tended to remain stable. After adjustment for the initial value of QL and comorbidity, a consistently favorable effect of HD on physical QL over time was found compared with PD, whereas mental QL values remained similar. Parameters of adequacy of dialysis were not associated with QL over time.

**Conclusion.** This prospective cohort study shows that physical QL over time in HD patients is better than in PD patients.
Introduction

Studies on the outcome of dialysis over time have mainly focused on mortality. These studies suggest that younger patients as well as those with less comorbidity, a better nutritional status, and a greater small solute removal tend to live longer. Results on which dialysis modality provides the highest survival rate are conflicting.

Currently, there is general consensus that in addition to survival, the quality of the remaining life is a highly relevant patient outcome in the evaluation of treatment. According to The World Health Organization, health is defined as ‘a state of complete physical, psychological and social well-being and not merely the absence of disease or infirmity’. Consistent with this definition, a comprehensive assessment of quality of life (QL) should cover at least the patient’s functioning and well-being in the physical, psychological and social domains.

With a few exceptions, information from the literature on QL of dialysis patients is derived from cross-sectional studies. These few longitudinal studies examined only hemodialysis (HD) patients or compared QL before and after kidney transplantation. Moreover, the interpretation of these studies is limited because of small sample sizes, and no or insufficient adjustment for case mix. Consequently, no information is available on the long-term QL of patients treated by different dialysis modalities.

Against this background, the objective of our multicenter study was to assess the QL of a cohort of new chronic HD and peritoneal dialysis (PD) patients at 3, 6, 12 and 18 months after the start of dialysis with an established QL tool.

Methods

Study population

End-stage renal disease (ESRD) patients older than 18 years starting chronic dialysis who had never received renal replacement therapy in the past and who had survived the first three months on dialysis were eligible for the study. From 13 Dutch dialysis centers we included consecutive patients who started dialysis between October 1, 1993 and April 1, 1995 after their informed consent was obtained. These patients were participating in the Netherlands Cooperative Study on the Adequacy of Dialysis, phase 1 (NECOSAD-1). Dialysis treatment was prescribed by the individual patient’s physician.

Data collection

At baseline, that is, three months after the start of dialysis, information was collected on demography, underlying kidney disease, comorbid status, nutritional...
status, hemoglobin, use of erythropoietin (EPO), residual renal function, and dialysis adequacy. The QL was assessed at baseline and at 6, 12, and 18 months after the initiation of chronic dialysis treatment.

The underlying kidney disease was classified according to the codes of the European Dialysis and Transplant Association-European Renal Association Registry. Comorbidity was defined in terms of presence of conditions not directly related to the uremic state, either at the start of dialysis or in the medical history. Next, every patient was assigned a low, medium or high death risk index based on comorbidity and to a lesser extent advanced age. This classification was described by Khan et al. The low-risk group in this classification comprised patients less than 70 years old with no comorbid illness; the medium-risk group included patients between 70 and 80 years of age and patients less than 80 years of age with one or more of the following diseases: angina, myocardial infarction, cardiac failure, chronic obstructive airways disease, pulmonary fibrosis, or liver diseases (cirrhosis, chronic hepatitis), peripheral vascular and cerebrovascular disease, and patients less than 70 years of age with diabetes mellitus. The high-risk group comprised patients more than 80 years of age, patients of any age with two or more organ dysfunctions in addition to ESRD, and patients of any age with visceral malignancy. In addition, patients were classified according to the presence or absence of diabetes mellitus and cardiovascular conditions (angina pectoris, myocardial infarction, class III to IV congestive heart failure or peripheral vascular disease).

The nutritional status was assessed by the body mass index, percentage of lean body mass, serum albumin, and an estimation of dietary protein intake. The percentage of lean body mass was estimated by anthropometry from the sum of thickness of the triceps, biceps, subscapular, and suprailliac skinfolds, by the method of Durnin and Womersley. Because skin turgor and hydration may affect subcutaneous skinfold thicknesses, measurements in HD patients were made after dialysis when the patient was at dry weight. The dietary protein intake was assessed as protein catabolic rate [PCR; in HD: PCR (g/24hr) = 9.35 * urea generation rate (mg/min) + 0.294 * urea distribution volume (l); in PD: PCR (g/24hr) = 19 + 0.2134 * urea appearance (mmol/24hr)]\textsuperscript{15,16} normalized to actual body weight (nPCR). The urea distribution volume (V) was determined by the formulae of Watson et al.\textsuperscript{17} Subsequently, anthropometric parameters and serum albumin were combined to a malnutrition index, corrected for age, sex, height and frame size, similar to the index described by Harty et al.,\textsuperscript{18} but without the use of subjective global assessment. A score of 11 or higher was defined as severe malnutrition.

Renal function was estimated as the residual glomerular filtration rate (rGFR), renal Kt/V\textsubscript{urea}, and renal creatinine clearance. The rGFR was defined as the mean renal clearance of urea and creatinine.

The total removal of waste products (renal and dialysis) was measured as clearance estimated by total weekly Kt/V\textsubscript{urea} and total weekly urea appearance in
Quality of life

HD and PD patients. In PD patients, the total weekly creatinine clearance and the total weekly creatinine appearance were calculated. HD $Kt/V_{\text{urea}}$ was estimated using a second-generation Daugirdas formula.\textsuperscript{19} Peritoneal $Kt/V_{\text{urea}}$ and creatinine clearance were calculated from a 24-hour dialysate collection.

The HD patients collected all urine during an interdialytic interval. Blood samples were taken before and after the dialysis session preceding the interval and at the end of this interval. The PD patients collected 24-hour urine and dialysate. A blood sample was taken immediately after the collection period.

The patients' perception of their level of QL was assessed with the 36-item MOS-Short Form Health Survey Questionnaire (SF-36\textsuperscript{TM}).\textsuperscript{20} The SF-36 is a generic multidimensional instrument consisting of eight multi-item scales representing physical functioning, social functioning, role-limitations caused by physical problems, role-limitations caused by emotional problems, mental health, vitality, bodily pain, and general health perceptions. The scale scores were transformed to a 0 to 100 scale, with a higher score indicating a better QL. Subsequently, the scale scores were standardized to the scale scores of an age-matched general Dutch population sample ($n=775$, age range 45 to 74; 66% male).\textsuperscript{21} Finally, the physical and mental components of the eight scales were combined into a physical (PCS) and mental (MCS) component summary score.\textsuperscript{22} The PCS primarily reflects the dimensions physical functioning, role limitations caused by physical health problems, pain, and general health perceptions. The MCS reflects primarily mental health, role limitations caused by emotional problems, social functioning, and vitality. A linear T-score transformation was used so that both PCS and MCS had a mean of 50 and a standard deviation of 10 in the general population sample. The reliability and validity of the SF-36 has been extensively supported in various demographic and patient populations, including ESRD patients.\textsuperscript{20,23-25} In our population, internal consistency coefficients (Chronbach alphas) of the SF-36 scales ranged between 0.73 and 0.93.

Data analysis

Patients were classified in the following categories: (1) patients who started and stayed on HD throughout follow-up, (2) patients who started and stayed on PD throughout follow-up, (3) patients who switched their dialysis modality one time or more, (4) patients who were transplanted, and (5) patients who died. Patients who switched their dialysis modality and died later on were classified as deceased ($N=5$); patients who switched from one dialysis modality to the other and later underwent transplantation were classified as transplanted ($N=1$).

Differences in baseline characteristics between groups were analyzed with one-way analysis of variance in the case of continuous variables and with chi-square tests for categorical variables.

Repeated-measures analysis of variance was used to establish changes in the QL
over time (time effect), differences in the QL between treatment groups (treatment effect), and the interaction between changes in the QL by time and treatment group (time by treatment effect). To take possible QL differences into account that may have selected for the choice of dialysis modality, the baseline QL was included as a covariate. In addition, the results were adjusted for the possible confounding effects of age, gender, clinical characteristics, nutritional status and adequacy of dialysis. All factors that were univariately associated with a P-value ≤ 0.20 were taken into account as covariates in the analysis of variance. As parameters of dialysis dose are not equally calculated for HD and PD patients, these variables were analyzed separately for HD and PD patients. Based on these models, mean effects with their 95% confidence intervals (95% CI) were calculated.

To study the influence of selective drop-out, the repeated-measures analysis of variance was repeated on an intention-to-treat basis, that is, according to the initial dialysis modality irrespective of modality switches, transplantation, and death during follow-up.

The descriptive analyses were carried out using SPSS for Windows 8.0 software (SPSS Inc., Chicago, IL, USA). The repeated-measures analysis of variance was performed with the mixed procedure of SAS for Windows 6.12 statistical software (SAS Institute Inc., Cary, NC, USA). The mixed procedure fits mixed linear models, that is, models with both fixed and random effects. A mixed model is a generalization of the standard linear model, the generalization being an ability to analyze data with several sources of variation instead of just one.

Results

Baseline characteristics of patients

Out of 250 included patients, 230 patients (121 HD, 109 PD) completed the QL questionnaire at least once. Reasons for nonresponse and characteristics of nonresponders have been described previously. Two patients whose renal function recovered were excluded from this analysis. From the remaining 228 patients (119 HD and 109 PD) 139 patients stayed on their initial dialysis modality (84 HD and 55 PD) and 26 (5 HD and 21 PD) patients switched dialysis modality. Thirty-five (15 HD and 20 PD) patients were transplanted, and 28 (15 HD and 13 PD) patients died during the 15 months of follow-up. Reasons for a switch from PD to HD were mainly peritonitis (N=11), catheter problems (N=2), other medical reasons (N=5), a combination of anorexia and behavioral problems (N=1), low IQ (N=1) and the patient’s own choice (N=1). The five HD patients switched to PD because of shunt problems (N=3), inability to endure the HD procedure (N=1), and the patient’s own choice (N=1).

Baseline characteristics of these patients are presented in Table 1, which shows
that the transplanted patients were younger and less ill, whereas the deceased patients were older and most severely ill. Significant differences were found between the five groups with respect to age, Khan's comorbidity-age index, cardiovascular comorbidity, diabetes mellitus, body mass index, albumin, hemoglobin, use of EPO and the renal creatinine appearance rate (all P<0.05).

The baseline physical and mental QL of all patient groups was significantly lower than the corresponding values of an age-matched general population sample. The QL of stay-on-PD and transplanted patients was more or less similar, followed by, in rank order of decreasing QL, stay-on-HD, dialysis switchers, and deceased patients. Only the differences in physical QL between stay-on-PD and transplanted patients on the one side and deceased patients on the other side were significant (P=0.001).

**Quality of life over time**

In Figure 1, the physical and mental QL during follow-up is displayed for all patients according to their stay on mode of renal replacement therapy. Because follow-up was discontinued after transplantation, no QL assessment can be given at 18 months in the subgroup of patients who were transplanted during the study period.

The physical QL of patients who died during the study period was considerably worse at baseline and worsened at a faster rate before dying than in the other patient groups. Transplanted patients started off at the same level as stay-on-PD patients, but improved with time, whereas the stay-on-PD patients worsened with time. The physical QL of patients who changed their initial dialysis modality was similar to the QL of stay-on-HD patients during the first year of dialysis treatment but decreased faster afterwards (Figure 1).

The initial value of mental QL in the patients who died before the end of the study period was considerably lower than the stay-on-dialysis and transplanted patients and deteriorated rapidly with time. Patients who switched from dialysis modality also reported a lower mental QL at baseline but showed an inconsistent pattern of change during follow-up. The mental QL over time of patients who were transplanted during the study period was similar to the stay-on-PD patients. Mental QL scores of both stay-on-dialysis and transplanted patients were closer to the general population norm than their physical QL scores.

Statistical analysis of the QL over time was restricted to the stay-on-HD and PD patients, because of the small number of patients and the high drop-out rate in the other categories.

**Physical QL over time: stay-on-HD versus stay-on-PD patients**

Overall, a statistically significant decline in the physical QL over time was observed (18 vs. 3 months, -1.9 points; 95% CI, -3.3 to -0.5, P=0.02; Figure 1). This
Table 1. Baseline characteristics: demography, primary kidney disease, comorbidty, nutritional status, hemoglobin, and use of EPO (mean (SD) or %).

<table>
<thead>
<tr>
<th></th>
<th>Stay-on-HD (n=84)</th>
<th>Stay-on-PD (n=55)</th>
<th>Dialysis switchers (n=26)</th>
<th>Transplanted (n=35)</th>
<th>Deceased (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60 (15)</td>
<td>52 (14)</td>
<td>51 (14)</td>
<td>45 (13)</td>
<td>67 (10)</td>
</tr>
<tr>
<td>Male</td>
<td>55%</td>
<td>69%</td>
<td>58%</td>
<td>57%</td>
<td>64%</td>
</tr>
<tr>
<td>Primary kidney disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12%</td>
<td>18%</td>
<td>8%</td>
<td>3%</td>
<td>29%</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>12%</td>
<td>16%</td>
<td>12%</td>
<td>23%</td>
<td>4%</td>
</tr>
<tr>
<td>Vascular</td>
<td>27%</td>
<td>24%</td>
<td>19%</td>
<td>20%</td>
<td>29%</td>
</tr>
<tr>
<td>Other</td>
<td>49%</td>
<td>42%</td>
<td>62%</td>
<td>54%</td>
<td>39%</td>
</tr>
<tr>
<td>Medium and high comorbidity-age index (Khan index)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular comorbidity%</td>
<td>33%</td>
<td>22%</td>
<td>35%</td>
<td>6%</td>
<td>43%</td>
</tr>
<tr>
<td>Diabetes mellitus%</td>
<td>17%</td>
<td>22%</td>
<td>8%</td>
<td>6%</td>
<td>32%</td>
</tr>
<tr>
<td>Percentage lean body mass</td>
<td>73.2 (9.1)</td>
<td>77.0 (7.7)</td>
<td>78.0 (9.3)</td>
<td>76.3 (6.9)</td>
<td>73.0 (7.8)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.7 (4.7)</td>
<td>23.3 (3.3)</td>
<td>22.2 (3.9)</td>
<td>22.6 (2.9)</td>
<td>24.6 (4.1)</td>
</tr>
<tr>
<td>Severe malnutrition (Harris index)</td>
<td>12%</td>
<td>16%</td>
<td>31%</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>Protein catabolic rate (g/kg/day)</td>
<td>1.0 (0.3)</td>
<td>1.3 (0.3)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>39.5 (4.2)</td>
<td>37.5 (5.7)</td>
<td>35.7 (6.3)</td>
<td>37.2 (4.5)</td>
<td>35.1 (5.4)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.2 (1.2)</td>
<td>11.4 (1.5)</td>
<td>10.4 (1.8)</td>
<td>10.6 (1.2)</td>
<td>10.1 (1.5)</td>
</tr>
<tr>
<td>Use of erythropoietin%</td>
<td>87%</td>
<td>64%</td>
<td>73%</td>
<td>66%</td>
<td>79%</td>
</tr>
</tbody>
</table>

* a, b, c: Initial dialysis mode: *: 5 HD, 21 PD; b: 15 HD, 20 PD; c: 15 HD, 13 PD; all modality changes, transplantations and deaths took place within the study period; d: mean values can not be calculated in dialysis switchers, transplanted and deceased patients due to the mixed composition of these groups with respect to dialysis mode; e: significant differences between groups (P<0.05).
Table 1. Continued.

<table>
<thead>
<tr>
<th></th>
<th>Stay-on-HD (n=84)</th>
<th>Stay-on-PD (n=55)</th>
<th>Dialysis switchers&lt;sup&gt;a&lt;/sup&gt; (n=26)</th>
<th>Transplanted&lt;sup&gt;b&lt;/sup&gt; (n=35)</th>
<th>Deceased&lt;sup&gt;c&lt;/sup&gt; (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual GFR (ml/min/1.73m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>2.8 (2.1)</td>
<td>3.1 (2.3)</td>
<td>2.8 (2.3)</td>
<td>4.0 (3.0)</td>
<td>3.0 (2.2)</td>
</tr>
<tr>
<td>Kt/V&lt;sub&gt;urea&lt;/sub&gt; (/week)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3.4 (1.0)</td>
<td>2.1 (0.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>0.5 (0.4)</td>
<td>0.6 (0.5)</td>
<td>0.5 (0.4)</td>
<td>0.8 (0.6)</td>
<td>0.6 (0.5)</td>
</tr>
<tr>
<td>Creatinine clearance (l/wk/1.73m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>84 (30)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>36 (30)</td>
<td>41 (32)</td>
<td>35 (31)</td>
<td>53 (39)</td>
<td>37 (30)</td>
</tr>
<tr>
<td>Urea appearance (mmol/wk/1.73m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2140 (628)</td>
<td>1770 (545)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>377 (320)</td>
<td>478 (408)</td>
<td>411 (385)</td>
<td>580 (406)</td>
<td>399 (303)</td>
</tr>
<tr>
<td>Creatinine appearance (mmol/wk/1.73m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>22.8 (14.1)</td>
<td>30.6 (19.9)</td>
<td>25.6 (23.7)</td>
<td>36.2 (22.3)</td>
<td>21.3 (13.8)</td>
</tr>
<tr>
<td>Physical summary QL score</td>
<td>40.7 (8.8)</td>
<td>43.6 (7.3)</td>
<td>41.0 (9.3)</td>
<td>44.2 (8.2)</td>
<td>36.4 (9.7)</td>
</tr>
<tr>
<td>Mental summary QL score</td>
<td>44.9 (11.9)</td>
<td>46.1 (7.5)</td>
<td>40.4 (12.5)</td>
<td>46.4 (10.5)</td>
<td>40.1 (11.8)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Initial dialysis mode: 5 HD, 21 PD; 15 HD, 20 PD; 15 HD 13 PD; all modality changes, transplantations and deaths took place within the study period; <sup>b</sup> mean values can not be calculated in dialysis switchers, transplanted and deceased patients due to the mixed composition of these groups with respect to dialysis mode; <sup>c</sup> significant differences between groups (P<0.05).
Figure 1. Change over time in physical and mental summary quality of life (QL) according to the stay on mode of renal replacement therapy (means ± standard errors). QL values are normalized to a general population mean of 50 and a standard deviation of 10 (that is, a T-score metric, as discussed in the Methods section).
decline tended to be more pronounced in PD compared to HD patients (time-treatment interaction effect, \( P = 0.06 \)). When a correction was applied for differences in the baseline physical QL, a significant treatment effect was found: Patients on HD did better compared to PD with a mean difference over time of 2.3 points (95% CI, 0.3 to 4.3, \( P = 0.03 \)). This adjustment for the baseline QL value did not change the time effect, whereas the borderline significant time-treatment interaction effect disappeared. These effects remained stable after additional correction for other baseline characteristics that were univariately related (\( P \leq 0.20 \)) to the physical QL over time (age, comorbidity-age index, diabetes mellitus, hemoglobin, and albumin; Figure 2). Only the comorbidity-age index contributed significantly to this model: patients with a medium or high comorbidity-age index were consistently more impaired compared with patients with a low comorbidity-age index (mean difference over time, -2.7 points; 95% CI, -4.7 to -0.6, \( P = 0.01 \)).

Analysis of the four individual scales that compose the physical QL summary score indicated that the time effect was concentrated in the physical functioning scale (18 vs. 6 months, -6.7 points; 95% CI, -10.2 to -3.2, \( P = 0.001 \)) and somewhat less in the general health perceptions scale (18 vs. 6 months, -4.9 points; 95% CI, -8.2 to -0.5, \( P = 0.02 \)), whereas the treatment effect was concentrated in the bodily pain dimension (PD vs. HD: -7.8 points, 95% CI: -14.9 to -0.7, \( P = 0.03 \)). No time-treatment interaction effects were observed for the individual subdimensions (further details of the individual SF-36 scales over time are shown in Table 2).

**Mental QL over time: stay-on-HD versus stay-on-PD patients**

No overall significant decline in the mental QL over time could be demonstrated, although there appeared to be a slight decline in PD toward the end of follow-up (Figure 1). There was no significant difference in the mental QL between HD and PD, and this result did not change after correction for the baseline mental QL. An additional correction for other baseline characteristics that were univariately related (\( P \leq 0.20 \)) to mental QL over time (comorbidity-age index, cardiovascular comorbidity, residual GFR, renal urea appearance, renal creatinine appearance, and the renal \( \text{Kt/V}_{\text{area}} \)) did not change these results either (Figure 2). Only cardiovascular comorbidity contributed significantly to this model. Patients with cardiovascular comorbidity had a lower mental QL (mean difference over time, -3.0 points; 95% CI, -5.7 to -0.3, \( P = 0.03 \)).

Although no time effect was observed in the mental QL summary score, an inspection of the composing scales revealed a significant time effect in the social functioning and vitality scale. Both QL subdimensions showed a deterioration with time (social functioning 18 vs. 6 months, -5.2 points, 95% CI, -9.3 to -1.1, \( P = 0.047 \); vitality -4.3 points, 95% CI, -7.5 to -1.2, \( P = 0.03 \)) (Table 2). Neither a treatment nor a treatment-time interaction effect was observed in any of the mental subdimensions (further details of the individual SF-36 scales over time are shown...
Figure 2. Change over time in physical and mental summary quality of life (QL) of the stay-on-HD and the stay-on-PD patients adjusted for the baseline value of QL and comorbid status (means ± standard errors). QL values are normalized to a general population mean of 50 and a standard deviation of 10 (that is, a T-score metric, as discussed in the Methods section).
Table 2. Adjusted mean (standard error) of the individual SF-36 scales over time by dialysis modality.

<table>
<thead>
<tr>
<th>SF-36™ scale</th>
<th>Stay-on-HD months</th>
<th>Stay-on-PD months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td><strong>Physical QL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning&lt;sup&gt;b&lt;/sup&gt;</td>
<td>59.4 (1.9)</td>
<td>55.5 (2.0)</td>
</tr>
<tr>
<td>Role functioning - physical</td>
<td>38.4 (4.3)</td>
<td>38.3 (4.5)</td>
</tr>
<tr>
<td>Bodily pain&lt;sup&gt;c&lt;/sup&gt;</td>
<td>71.9 (2.8)</td>
<td>71.4 (2.9)</td>
</tr>
<tr>
<td>General health perceptions&lt;sup&gt;b&lt;/sup&gt;</td>
<td>45.8 (1.8)</td>
<td>44.4 (1.9)</td>
</tr>
<tr>
<td><strong>Mental QL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental health</td>
<td>69.5 (1.8)</td>
<td>68.9 (1.9)</td>
</tr>
<tr>
<td>Role functioning - emotional</td>
<td>57.4 (4.7)</td>
<td>57.2 (4.9)</td>
</tr>
<tr>
<td>Social functioning&lt;sup&gt;b&lt;/sup&gt;</td>
<td>71.5 (2.6)</td>
<td>67.5 (2.6)</td>
</tr>
<tr>
<td>Vitality&lt;sup&gt;b&lt;/sup&gt;</td>
<td>51.8 (1.9)</td>
<td>50.5 (2.0)</td>
</tr>
</tbody>
</table>

Abbreviations are: QL, quality of life; HD, hemodialysis; PD, peritoneal dialysis. <sup>a</sup> Adjusted for baseline QL and comorbidity (Khan's risk index in case of the physical QL scales and cardiovascular comorbidity in case of the mental QL scales); <sup>b</sup> significant time effect (P<0.05); <sup>c</sup> significant treatment effect (P<0.05).
in Table 2).

**Intention-to-treat analysis**

Additionally, we assessed the change over time in physical and mental summary QL with an intention-to-treat approach. Regarding the physical QL, a significant decline in course of time was observed (18 vs 3 months, -2.0; 95%CI, -3.2 to -0.8, \( P<0.01 \)). No statistically significant treatment effect nor a different change pattern over time was observed between HD and PD patients. After adjustment for baseline differences in physical QL and comorbid status (comorbidity-age index) the physical QL of HD patients was still favorable to that of PD patients (HD vs. PD 1.6; 95% CI, 0.04 to 3.2, \( P=0.04 \)), whereas the time effect remained unchanged (18 vs. 6 months, -2.0; 95%CI, -3.2 to -0.8, \( P<0.01 \); Figure 3).

No change over time in the mental summary QL was observed for both treatment groups. HD patients reported a consistently lower mental QL at all time points compared with PD patients (HD vs. PD -2.6; 95% CI, -5.0 to -0.2, \( P=0.03 \)). However, after correction for baseline differences in mental summary QL and cardiovascular comorbidity this treatment effect disappeared (Figure 3).

**Discussion**

This study explored the relationship between dialysis modality and the physical and mental QL during the first 18 months of renal replacement therapy. In line with findings in other dialysis patients, the mental QL appeared closer to normal than the physical QL. In patients who stayed on their initial dialysis modality, physical QL decreased over time, whereas the mental QL tended to remain stable. After adjustment for the initial value of QL, there appeared to be a consistently favorable effect of HD on the physical QL over time compared with PD, whereas the mental QL remained similar. A correction for other significant baseline characteristics did not change the observed time and treatment effects. It implies that a HD patient will rate his/her physical QL more favorably during the first 18 months of dialysis compared with a PD patient who has a similar clinical status and physical QL at the start of dialysis treatment.

As we were especially interested in the mid-term effects of HD and PD on QL, we initially studied only those patients who stayed on their initial dialysis modality throughout the study period. This may have slightly biased the estimated effects, as only therapy survivors were analyzed. However, when we repeated the analysis for any patient who started chronic HD or PD irrespective of stay on that modality (that is, intention-to-treat analysis) virtually similar time, treatment and treatment-time interaction effects were observed for both the physical and mental QL.

An analysis of the scales that primarily compose the physical summary QL
Figure 3. Change over time in physical and mental summary quality of life (QL) according to the initial dialysis modality (i.e., intention-to-treat analysis) adjusted for the baseline value of QL and comorbid status (means ± standard errors). QL values are normalized to a general population mean of 50 and a standard deviation of 10 (that is, a T-score metric, as discussed in the Methods section).
score indicated that the time effect was concentrated in the physical functioning (limitations in physical activities) and somewhat less in the general health perceptions dimension (personal evaluations of health), whereas the treatment effect was concentrated in the bodily pain dimension (intensity of pain and effect of pain on normal activities). The permanent physical burden of PD compared to the intermittent character of HD and peritonitis may be alternate explanations for the higher pain perception of PD patients. A potential superiority of HD regarding dialysis adequacy was not supported by the present adequacy parameters studied: In both HD and PD, none of the estimates of the adequacy of dialysis was associated with the physical QL.

No change over time was observed for the mental summary QL. An inspection of the individual subscales that predominantly reflect mental QL showed a significant decline with time for social functioning and vitality. This discrepancy between individual subscale scores and the calculated summary score might be a consequence of the assumptions and methods used to calculate these summary scores.\textsuperscript{28} Thus, although the use of summary scores has the advantage to reduce the number of statistical comparisons and thereby the role of chance in testing hypotheses, relevant subscale-time or subscale-treatment interactions may be missed. Therefore, we suggest that it is useful not only to focus on the summary QL but also to inspect individual subscales, keeping in mind the statistical problem of multiple comparisons.\textsuperscript{29,30}

What is the clinical meaning of the observed differences in QL in this study? A comparison of these results with differences in QL observed in other (dialysis) populations or comparison with differences seen with therapy of proven benefit, such as EPO, may help with an interpretation. For example, the difference of 2.3 points in the physical summary QL between our HD and PD patients is approximately half of the difference in the physical summary QL observed between cancer patients and the general population of the United States.\textsuperscript{22} The difference of 7.8 points in bodily pain between our HD and PD patients is similar to the difference in bodily pain observed in type II diabetes patients compared with general population norms.\textsuperscript{20} The deterioration in physical functioning of 6.7 points in our population is approximately twice the magnitude of change in physical functioning observed in a before-and-after EPO study among HD patients.\textsuperscript{27} In the latter study, a change of approximately nine points in vitality and eight points in social functioning was seen, compared with a decrement of approximately four points in vitality and five points in social functioning in our population during follow-up.

In our study, we also examined the effect of baseline patient characteristics and adequacy of dialysis on the QL over time. Comorbidity was the only variable associated with QL over time. A higher comorbidity-age index according to Khan et al.\textsuperscript{2} correlated with a more impaired physical QL over time. Recently, it has been
demonstrated that this index provided the greatest discrimination between patient groups at risk for mortality when compared with an index that combined the effect of age and diabetes or an index based on the number of comorbid conditions. Our study shows that this Khan comorbidity-age index is also valuable to identify patients at risk for poor physical QL over time. The mental QL was associated with the presence of cardiovascular comorbidity but not with the Khan index.

None of these parameters of adequacy of dialysis were associated with QL over time. This supports the absence of an association of adequacy of dialysis with QL that we observed in our previous report. Also, DeOreo et al. did not find an association between $Kt/V_{\text{urea}}$ and physical QL in a sample of approximately 1000 prevalent patients, whereas a statistically significant though very small association between $Kt/V_{\text{urea}}$ and mental summary QL was seen: $Kt/V_{\text{urea}}$ explained 0.5% of the observed variation in the mental summary QL. The fact that in clinical practice the dose of dialysis is often based on patient reports of physical well-being may have obscured a potential relationship. On the other hand, the fact that only baseline values of adequacy of dialysis were considered or that the effect was too small to be detected in our study may also have influenced these results.

Our results demonstrated that the physical and mental QL of the deceased patients at the time of start of dialysis was already considerably worse than that of the other patient groups and deteriorated more rapidly over time time. This finding is in line with the results of DeOreo et al., who reported that the predictive power of self-reported functional status data for mortality is similar to parameters of dialysis and nutritional adequacy. Therefore, both studies make it likely that the SF-36 is a useful screening tool to identify those patients who have a high risk of death.

Our study presents evidence that the physical QL deteriorates during the first 18 months in both HD and PD, and that physical QL of PD patients compares unfavorably to HD patients throughout time. The mental QL remained stable over time and did not differ between both dialysis modes. However, before final conclusions can be drawn, these results will have to be confirmed in a randomized clinical trial. Currently, we conclude from this prospective cohort study that physical QL over time in HD patients is better than in PD patients.

References

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Chapter 5


