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Factors associated with health-related quality of life among hemodialysis patients in the DOPPS

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Abstract
Objective To identify modifiable factors associated with health-related quality of life (HRQOL) among chronic hemodialysis patients.
Methods Analysis of baseline data of 9,526 hemodialysis patients from seven countries enrolled in phase I of the Dialysis Outcomes and Practice Patterns Study (DOPPS). Using the Kidney Disease Quality of Life Short Form (KDQOL-SF^{TM}), we determined scores for 8 generic scale summaries derived from these scales, i.e., the physical component summary [PCS] and mental component summary [MCS], and 11 kidney disease-targeted scales. Regression models were used to adjust for differences in comorbidities and sociodemographic and treatment factors. The Benjamini–Hochberg procedure was used to correct *P*-values for multiple comparisons.
Results Unemployment and psychiatric disease were independently and significantly associated with lower scores for all generic and several kidney disease-targeted HRQOL measures. Several other comorbidities, lower educational level, lower income, and hypoalbuminemia were also independently and significantly associated with lower scores of PCS and/or MCS and several generic and kidney disease-targeted scales. Hemodialysis by catheter was associated with significantly lower PCS scores, partially explained by the correlation with covariates.
Conclusion Associations of poorer HRQOL with preventable or controllable factors support a greater focus on psychosocial and medical interventions to improve the well-being of hemodialysis patients.

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Abbreviation List

HRQOL	Health-related quality of life
DOPPS	Dialysis Outcomes and Practice Patterns Study
KDQOL-SF	Kidney Disease Quality of Life Short Form
PCS	Physical Component Summaries
MCS	Mental Component Summaries
ESRD	End-stage renal disease
SF-36	Short-Form Health Survey
SBP	Systolic blood pressure
NPCR	Normalized protein catabolic rate
BMI	Body Mass Index
ADIFS	Adjusted difference in score
eKt/V	Equilibrated Kt/V (dialysis dose)

Introduction

Advances in chronic hemodialysis have improved survival of end-stage renal disease (ESRD) patients [39]. To optimize dialysis therapy, however, the health-related quality of life (HRQOL) of hemodialysis patients also needs to be improved. To improve the HRQOL of these patients, it is important to identify factors that contribute to their poor quality of life [7, 15, 31, 33, 35].

Several instruments have been developed to assess HRQOL [13, 32, 36]. Some of these instruments are generic while others are specific for patients with certain diseases. One of the most used generic HRQOL instruments is the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) [23, 24, 26, 36, 37]. The SF-36 assesses eight generic scales of HRQOL. Two composite measures, the physical component summary (PCS) and the mental component summary (MCS), are derived from the eight scales. Previous studies have shown that hemodialysis patients with lower scores in each one of eight scales and the summary components of the SF-36 were at higher risk of death and hospitalization [7, 21]. The Kidney Disease Quality of Life Short Form (KDQOL-SF^{TM}) was developed to take into account particular concerns of patients with kidney diseases and ESRD. This HRQOL instrument combines the 36 generic items of the SF-36 with 43 kidney disease-targeted items. Eleven scales are defined from the kidney disease-targeted items, resulting in a total of 19 scales (i.e., eight generic and eleven targeted to patients with kidney disease and treated by dialysis) [12]. We have shown that hemodialysis patients with lower scores in several of the kidney disease-targeted scales were also at higher risk of death and hospitalization [19, 22]. These findings call attention to the importance of studies in the hemodialysis population aimed at identifying patient characteristics and modifiable factors related to poor HRQOL. This should help direct early preventive interventions to improve outcomes for ESRD patients treated with hemodialysis.

We assessed HRQOL scores by using the KDQOL-SF in a large, multinational sample of hemodialysis patients from the Dialysis Outcomes and Practice Patterns Study (DOPPS). The main objective was to identify patient characteristics and potentially modifiable factors associated with summary measures of HRQOL (i.e., PCS and MCS) and assess the influence of comorbidities and other covariates on the association. To better understand findings for PCS and MCS, we also studied factors independently associated with the eight generic scales and the eleven kidney disease-related scales of HRQOL from the KDQOL-SF version 1.3.

Methods

Study sample

The present analysis was based on baseline data from phase I of the DOPPS, an international, prospective, observational study of hemodialysis practice patterns and associated outcomes [11, 40]. A total of 17,034 hemodialysis patients were enrolled in DOPPS I. The present analysis was based on data from 9,526 patients from 143 facilities (3,962 patients) in the United States, 101 facilities (3,371 patients) in Europe (France, Germany, Italy, Spain, and the United Kingdom), and 65 facilities (2,193 patients) in Japan. These 9,526 patients provided HRQOL data no more than 60 days from the completion of a medical questionnaire that contained the patient's characteristics. This reduced the probability of important changes in patient characteristics from the time of completion of the medical questionnaire and the time of collection of HRQOL data. Random sampling was performed at both the facility and patient levels. In the United States, 161 dialysis facilities were selected by random sampling from 2,894 facilities. In Europe, the sample was composed of 20 facilities from each of five participating countries. In Japan, 66 dialysis facilities were enrolled from a list of 2,653 facilities. Within each European country and

Japan, the sampling was proportionately stratified by geographic region and facility type (e.g., hospital, satellite, private, free-standing). Within each participating facility in the United States, Japan, and European countries, the census listing was used to select a random sample of 20–40 patients, varying according to facility size. For more detail on these methods please see the citation by Young et al. [40]. Data collection began in 1996 in the United States, 1998 in Europe, and 1999 in Japan. Patients were replaced on an ongoing basis as they left participating facilities for reasons of death, transplantation, change in treatment modality, withdrawal from dialysis, recovery of renal function, or transfer to another facility. This increased the sample size and percent of newer incident patients in the study. This also helped ensure a steady sample size during the study.

At study entry, a medical questionnaire completed by a study coordinator in the dialysis unit provided information regarding baseline patient characteristics. The questionnaires were translated from American English to French, German, Italian, Japanese, Spanish, and Queen's English. In each country the translated questionnaires were reviewed for meaning and context by nephrologists and pre-tested in dialysis centers not selected for the study. The KDQOL-SF^{TM} version 1.3 was used to assess HRQOL. The items that form the generic core of KDQOL-SF version 1.3 are those developed for SF-36 version 1. The patient responses to the KDQOL-SF were used to calculate the two generic summary scores (i.e., MCS and PCS) of the SF-36**,** which are derived from the eight scales of the SF-36: physical functioning, role-physical, bodily pain, general health, vitality (energy/fatigue), social functioning, mental health (emotional well-being), and role-emotion [37]. The MCS and PCS scores were calculated by using the scoring algorithms proposed by Ware et al. [37]. This approach is based on z-score transformation using means and standard deviations of each SF-36 scale score of the general United States population. The range of scores in our sample for PCS was 6.7–65.5 and for MCS was 7.8–73.5. The eleven scales derived from the kidney disease-targeted items are: (1) symptoms/problems, (2) effects of kidney disease on daily life, (3) burden of kidney disease, (4) work status, (5) cognitive function, (6) quality of social interaction, (7) sexual function, (8) sleep, (9) social support, (10) dialysis staff encouragement and (11) patient satisfaction. The specific questions that contributed to the eight generic SF-36 scales and to the eleven kidney disease-targeted subscales are presented in the Appendix and can also be found at http://gim.med.ucla.edu/kdqol/downloads/download.html.

Statistical methods

Linear mixed models were used to compare scores of HRQOL measures between groups of patients with different characteristics. Twenty-one separate models were developed, each using a different HRQOL measure as the dependent variable (MCS, PCS, eight SF-36 subscales, and 11 KDQOL subscales). The facility (dialysis centre) was modeled as a random effect. To estimate adjusted differences in scores (ADIFS), we used regression models which included the following covariates: age, gender, length of time on dialysis, body mass index (BMI) by Kg/m^2, country of dialysis treatment, yearly household income, education, occupational status, living status, marital status, epoetin use, dialysis dose (equilibrated Kt/V [eKt/V]) [6], type of vascular access, serum albumin, serum creatinine, serum phosphorus, hemoglobin, predialysis systolic blood pressure (SBP), normalized protein catabolic rate (nPCR) in g/Kg/day, and 15 comorbidities. These models took into account facility clustering, as patients treated in the same unit tend to be more similar to each other in several aspects than patients treated in different units. To permit estimation of the score of a HRQOL measure for a patient with a specific combination of characteristics, we defined an arbitrary reference group (the intercept of the regression model) as patients of average age (59.5 years), male gender, unmarried, with income >$10,000, education ≥ college, employed, living with family/friends, serum albumin ≥3.5 g/dl, hemoglobin ≥11 g/dl, eKt/V ≥ 1.2, vascular access by fistula or graft, predialysis SBP ≥ 110 mm Hg, BMI ≥ 20, and no comorbidity (Tables 3 and 4). Missing data were handled through the use of indicator variables that were coded as 1 or 0 to indicate the presence or absence information. Missing values occurred less than 5% of the time for all variables, except sexual function, which was missing 56% of the time, partly because only patients who had sexual activity in the previous four weeks were asked to respond to questions about sexual function. The Benjamini–Hochberg procedure was used to estimate *P*-values corrected for multiple comparisons (*P*-corrected) [3]. Four sets of *P*-values were adjusted for multiple comparisons: all coefficients for the PCS model (23), all coefficients for the MCS model (23), all coefficients for all SF-36 subscale models (23 × 8), and all coefficients for all kidney disease-related subscale models (23 × 11). A *P*-corrected-value of <0.05 was considered statistically significant. Because of concerns that the effect of age on scales related to mental health domains of HRQOL is non-linear, we developed additional models to test the quadratic effect of the coefficient of

age on the scores of MCS, mental health, role emotional, and social function scales. All statistical analyses were performed using SAS software, version 9.1 (SAS Institute, Cary NC) [34].

Results

Baseline characteristics of the 9,526 patients who responded to the KDQOL questions no more than 60 days from the completion of a medical questionnaire are shown in Table 1. The mean age was 59.5 ± 14.8 years, 58% were male, and 50% were on dialysis for at least 1.5 years.

Table 1 Baseline Characteristics of the Patients (n = 9,526)

Measure	Mean (SD) or %
Mean age (years)	59.5 (14.8)
Age groups (%)	
18–29	3.5
30–49	21.6
50–59	20.9
60–69	25.2
≥70	28.8
Male (%)	58.5
Median years on dialysis	1.5
Mean body mass index (Kg/m^2)	23.8 (5.3)
Country (%)	
France	8.4
Germany	6.9
Italy	7.3
Japan	23.0
Spain	7.1
United Kingdom	5.8
United States	41.6
Yearly household income (%)	
<$5,000	12.0
$5,000–$10,000	26.3
$10,001–$20,000	27.6
$20,000–$40,000	21.8
$40,000–$75,000	8.2
>$75,000	4.1
Education (%)	
High school or less	79.1
Attended college	20.9
Occupational status (%)	
Employed	20.5
Retired	37.7
Disabled	16.2
Unemployed	8.5
Homemaker, never employed	17.1
Living status (%)	
Live alone	14.5
Live with family/friends	82.3
Live in nursing home	3.0
Homeless/prisoner	0.2
Marital status (%)	
Single	15.9
Married	60.5
Widowed	13.8
Divorced/Separated	8.7
Unknown	1.1
Treatment factors	
Mean Epoetin (U/kg/wk)	135 (131)
Mean eKt/V	1.32(0.29)
Mean Predialysis SBP (mmHg)	150 (25)
Mean nPCR (g/Kg/day)	1.04(0.25)
*Laboratory variables**	
Albumin g/dl	3.7 (0.5)
Creatinine mg/dl	9.5 (3.3)
Phosphorus mg/dl	5.7 (1.8)
Hemoglobin g/dl	10.2 (1.7)
Comorbidities (%)	
Coronary heart disease	33.8
Congestive heart failure	28.4
Other cardiac disorders	30.4
Hypertension	75.5
Cerebrovascular disease	13.5
Peripheral vasculopathy	19.9
Diabetes mellitus	33.3
Lung disease	9.0
Cancer, excluding skin	9.1
HIV/AIDS	0.7
Gastrointestinal bleeding	5.8
Neurologic disease	6.1
Psychiatric disease	18.2
Recurrent cellulitis	5.9
Type of vascular access (%)	
Fistula	47.4
Graft	27.8
Permanent catheter	13.1
Temporary catheter	11.7

* These findings represent an unweighted summary across countries

** Values are predialysis at study start

SBP = systolic blood pressure, nPCR = normalized protein catabolic rate, HIV = seropositive for the human immunodeficiency virus

Summary measures

Table 2 shows the unadjusted scores for the two generic SF-36 summary measures (i.e., PCS and MCS) and Table 3 shows differences in the scores of PCS and MCS, adjusted for the variables listed in Table 1. The bold numbers in Tables 2 and 3 represent the differences that remained statistically significant (P-corrected < 0.05) after correcting for multiple comparisons.

Physical component summary (PCS)

The mean unadjusted PCS scores decreased steadily from younger to older groups (Table 2). Significantly

Table 2 Scores of the summary measures* of health-related quality of life by selected patient characteristics

Characteristics	Levels	PCS	MCS
Age **	18–29***	43.3 ± 9.4	44.8 ± 11.5
	30–49	**39.5 ± 10.5** [c]	44.8 ± 11.8
	50–59	**36.7 ± 10.6** [c]	45.1 ± 11.8
	60–69	**34.2 ± 10.4** [c]	44.5 ± 12.1
	≥70	**32.3 ± 10.0** [c]	44.7 ± 11.8
Sex	Male (ref)	**36.6 ± 10.7** [c]	44.4 ± 12.0
	Female	34.4 ± 10.8	45.0 ± 11.8 [a]
Marital status	Married (ref)	35.9 ± 10.6	44.5 ± 11.8
	Not married	35.4 ± 10.9 [a]	45.0 ± 11.9
Yearly income	≥$10,000 (ref)	35.9 ± 10.8	45.3 ± 11.8
	<$10,000	35.2 ± 10.6 [b]	**43.4 ± 12.0**[c]
Education	Attended college (ref)	36.3 ± 10.8	46.9 ± 11.5
	High school or less	35.5 ± 10.8 [a]	**44.3 ± 11.9** [c]
Occupation status	Employed (ref)	42.6 ± 9.4	46.6 ± 11.3
	Unemployed	**34.5 ± 10.5** [c]	**44.1 ± 11.9** [c]
Living status	Living w/family or friends (ref)	35.9 ± 10.8	44.8 ± 11.8
	Living alone	35.7 ± 10.8	44.5 ± 12.1
	Living in nursing home	**30.0 ± 9.3** [c]	45.1 ± 13.1
	Homeless/prisoner	36.6 ± 11.8	43.6 ± 12.2
Serum Albumin (g/dL)	≥3.5 (ref)	36.5 ± 10.7	44.8 ± 11.7
	<3.5	**32.4 ± 10.4** [c]	44.4 ± 12.4
Hemoglobin (g/dL)	≥11 (ref)	35.6 ± 10.9	45.0 ± 11.8
	9–11	36.1 ± 10.7	44.8 ± 11.9
	<9	36.3 ± 10.6 [a]	44.0 ± 11.8 [b]
Equilibrated Kt/V	≥1.2 (ref)	35.4 ± 10.7	44.8 ± 11.9
	<1.2	**37.3 ± 10.8** [c]	44.6 ± 11.7
Vascular access	Fistula or graft (ref)	36.7 ± 10.7	44.7 ± 11.7
	Catheter	**32.0 ± 10.3** [c]	44.9 ± 12.3
Predialysis SBP(mm Hg)	>140	36.1 ± 10.7	44.9 ± 11.8
	140–110 (ref)	35.6 ± 11.0	44.6 ± 11.8
	<110	**33.1 ± 10.9** [c]	44.4 ± 12.9
Body mass index (Kg/m^2)****	≥20 (ref)	35.3 ± 10.7	45.0 ± 11.9
	<20	**37.3 ± 10.8** [c]	**43.8 ± 11.8** [c]
Comorbidities	Absence (ref)	41.3 ± 9.8	46.1 ± 11.4
	Cerebrovascular/neurologic	**31.2 ± 10.2** [c]	**43.6 ± 11.8** [c]
	Cardiac disease	**33.2 ± 10.4** [c]	44.5 ± 11.9
	Peripheral vasculopathy	**30.6 ± 9.9** [c]	44.0 ± 12.4 [b]
	Diabetes	**32.5 ± 10.2** [c]	44.7 ± 12.8
	Lung disease	**30.5 ± 10.3** [c]	**43.4 ± 12.0** [c]
	Cancer, excluding skin	**33.2 ± 10.2** [c]	45.1 ± 12.3
	Psychiatric disease	**32.6 ± 10.3** [c]	**40.5 ± 12.4** [c]

Bold numbers call attention to statistically significant differences ($P < 0.05$) after correction for multiple comparisons by Hochberg

[a] $0.01 \le P \le 0.05$, [b] $0.001 \le P < 0.01$, [c] $P < 0.001$

* PCS = physical component summary, MCS = mental component summary

** ref = referent category for statistical comparisons

*** The estimated unadjusted reduction in scores per 5 year was 1.05 ($P < 0.0001$) for PCS and only 0.01 ($P = 0.8012$) for MCS

**** In an analysis restricted to patients treated in Europe and the United States, the means of the PCS scores were found to be similar between patients with BMI < 20 Kg/m2 (PCS score = 34.3 ± 10.5) and ≥20 Kg/m^2 (PCS score = 34.2 ± 11.1). Also in this analysis restricted to Europe and the United States the PCS scores were similar across hemoglobin levels: 34.1 ± 10.4, 33.8 ± 10.6 and 34.8 ± 10.9 for hemoglobin <9, 9–11 and ≥11 g/dl, respectively

lower unadjusted PCS scores were observed (Table 2) for females, unemployed patients, those living in nursing homes, patients with serum albumin <3.5 g/dl, those with predialysis SBP < 110 mm Hg versus SBP of 110–140, and patients with catheters as vascular access for hemodialysis. In the whole sample, the unadjusted PCS score was significantly lower for patients with BMI ≥ 20 Kg/m^2 than in patients with BMI < 20 Kg/m^2. In an analysis restricted to patients treated in Europe and the United States, however, the means of the PCS scores were found to be similar between patients with BMI < 20 Kg/m^2 and ≥20 Kg/m^2. The inverse association between age and PCS scores remained significant even after adjustments for

Table 3 Adjusted* differences in scores (ADIFS) of the generic SF-36® scales of quality of life by patient characteristics

	Physical component summary (PCS)	Mental component summary (MCS)	Physical functioning	Role physical	Bodily pain	General health	Vitality	Social functioning	Role emotional	Mental health
Intercept[A] (Referent patient)	38.3	51.0	56.1	50.5	69.2	50.2	52.7	74.1	69.3	75.7
Age (per 5 year older)	**–0.7**[c]	+0.1	**–2.6**[c]	**–1.7**[c]	**–0.4**[c]	+0.1	**–0.7**[c]	**–0.4**[c]	**–1.5**[c]	+0.2
Female (vs. male)	**–1.5**[c]	–0.4	**–5.9**[c]	+0.1	**–3.9**[c]	–0.8	**–2.3**[c]	–0.5	–0.5	–2.6 [b]
Married (vs. not married)	+0.1	–0.5	+1.1	–1.2	–0.9	–0.4	–0.6	–1.1	+0.2	–1.3 [a]
Yearly Income $<10,000 (vs. ≥$10,000)	–0.3	**–1.1**[c]	–1.2	–1.5	–1.9 [a]	–0.7	–0.6	–1.1	**–4.7**[c]	**–2.0**[c]
High school or less (vs. attended college)	–0.6[a]	**–1.6**[c]	**–3.3**[c]	–1.8	**–3.6**[c]	–2.1 [b]	–1.8 [a]	–0.7	**–7.1**[c]	**–4.0**[c]
Unemployed (vs. employed)	**–2.7**[c]	**–2.1**[c]	**–7.1**[c]	**–11.2**[c]	**–5.3**[c]	**–4.2**[c]	**–4.2**[c]	**–4.2**[c]	**–11.4**[c]	**–3.4**[c]
Living status (vs. living with family/friends)										
Living alone	+0.9 [b]	–0.6	+2.6 [b]	+1.0	–0.3	+0.7	+0.3	+1.0 [a]	0.0	-1.2
Living in nursing home	–0.3	+1.8 [a]	**–8.3** [c]	+8.7 [b]	+3.2	+1.1	+2.4	+1.9	+8.3 [b]	+0.5
Homeless/prisoner	+1.4	–0.1	–0.7	+1.5	+4.1	+1.9	+1.6	+3.8	–6.8	+2.9
Serum albumin < 3.5 g/dL(vs. ≥3.5 g/dl)	**–1.5**[c]	–0.8 [b]	**–4.0** [c]	**–4.6**[c]	**–3.0**[c]	**–1.9**[c]	**–2.2**[c]	**–3.3**[c]	–3.4 [b]	–1.8 [b]
Hemoglobin (vs ≥ 11 g/dL)										
<9 g/dl	–0.8	–0.7 [a]	–0.8	**–6.3**[c]	–1.2	–0.4	–1.0	–2.2 [a]	–4.0 [a]	–0.8
9–11 g/dl	–0.4	–0.1	–0.4	**–3.6** [c]	+0.1	–0.1	+0.3	–0.8	–2.3	+0.7
eKt/V < 1.2 (vs. ≥1.2)	+0.6	–0.2	+1.5	–0.6	+2.0 [a]	+0.9	+0.7	–0.6	–0.3	+0.3
Access by Catheter (vs. Fistula or graft)	–0.8 [a]	–0.1	–1.4	–3.8 [a]	–0.7	–0.8	–1.1	–2.8 [b]	0.0	+0.2
Predialysis SBP < 110 (vs. ≥110 mm Hg)	–1.1	+0.6	–4.6 [b]	+1.6	–1.6	–2.3	–1.0	–0.1	+1.3	–0.5
Body Mass Index < 20 (vs. ≥20 Kg/m^2)	–0.2	–0.5	–1.2	+0.5	–0.5	–0.6	–0.7	**–2.8**[c]	+0.3	–0.7
Comorbidity (yes vs no)										
Cerebrovascular / neurologic disease	**–2.0**[c]	–0.9 [a]	**–7.2**[c]	–4.2 [b]	–2.2 [a]	**–3.1**[c]	**–3.5**[c]	**–4.7**[c]	–3.4 [a]	–2.1 [b]
Cardiac disease	**–1.6**[c]	–0.2	**–4.0**[c]	–2.3 [a]	**–4.0**[c]	**–2.5**[c]	**–2.2**[c]	–1.1	–1.4	–1.2 [a]
Peripheral vasculopathy	**–2.9**[c]	–0.1	**–8.4**[c]	–4.3 [b]	**–5.9**[c]	**–3.0**[c]	**–3.3**[c]	**–3.8**[c]	–1.0	–1.8 [b]
Diabetes	**–1.7**[c]	–0.7 [a]	**–6.7**[c]	**–4.0**[c]	–1.0	**–3.3**[c]	**–2.5**[c]	–2.1 [b]	**–4.5**[c]	–1.8 [b]
Lung disease	**–1.9**[c]	–1.1 [a]	**–5.0**[c]	–2.9	–2.9 [a]	**–4.6**[c]	**–3.9**[c]	–3.0 [a]	–1.9	–2.6 [b]
Cancer, excluding skin	–0.8 [a]	+0.1	–1.7	–3.6	–0.2	–1.5	–1.1	–1.8	–0.6	+0.3
Psychiatric disease	**–1.4**[c]	**–5.6**[c]	**–5.0**[c]	**–6.6**[c]	**–7.0**[c]	**–5.9**[c]	**–7.7**[c]	**–10.5**[c]	**–11.8**[c]	**–10.5**[c]

*Adjusted for all variables in Table 1

Bold numbers call attention to statistically significant differences ($P < 0.05$) after adjustments for multiple comparisons. Comorbidities were selected based on their high prevalence or severity among hemodialysis patients, by Hochberg. [a]$0.01 \le P \le 0.05$, [b]$0.001 \le P < 0.01$, [c] $P < 0.001$ before multiple comparisons

[A] Referent patient is defined as a 59.5-year-old, male, unmarried, with income >$10,000, who attended college, employed, living with family/friends, serum albumin ≥ 3.5 g/dl, hemoglobin ≥ 11 g/dl, eKt/v ≥ 1.2, vascular access by fistula or graft, BMI ≥ 20, predialysis SBP ≥ 110 mm Hg, no comorbidity

Table 4 Adjusted* differences in score (ADIFS) of the kidney disease related scales of quality of life by patient characteristics

	Symptoms / Problems	Effect of Kidney Disease on Daily Life	Burden of Kidney Disease	Work Status	Cognitive Function	Quality of Social Interaction	Sexual Function	Sleep	Social Support	Dialysis Staff Encouragement	Patient Satisfaction
Intercept[A] (Referent patient)	78.2	73.2	52.2	67.1	84.5	82.2	89.4	66.8	78.3	82.0	72.5
Age (per 5 year older)	–0.1	**+0.7** [c]	–0.2	+0.2	–0.1	**+0.8** [c]	–0.7 [b]	**+0.3** [c]	**+1.0** [c]	**+1.0** [c]	**+0.6** [c]
Female (vs. male)	**–1.5** [c]	+0.2	+0.5	–0.5	0.0	**+1.4** [c]	**+13.7** [c]	+0.8	–1.0	–0.6	–0.1
Married (vs. not married)	–0.4	**–3.5** [c]	–2.3 [b]	–2.1 [a]	–0.3	0.0	**-13.1** [c]	–1.6 [b]	+2.0 [b]	+0.8	–0.2
Yearly Income $<10,000 (vs. ≥$10,000)	**–2.0** [c]	+0.1	–0.9	**–3.4** [c]	**–1.9** [c]	**–1.6** [c]	–0.1	–1.1 [a]	–0.7	+1.0	–0.5
High school or less (vs. attended college)	**–2.3** [c]	+0.5	–1.7 [a]	**–6.6** [c]	**–3.3** [c]	–0.7	+0.2	–1.3 [a]	–0.1	**+2.8** [c]	+0.3
Unemployed (vs. employed)	**–2.7** [c]	**–3.9** [c]	**–5.4** [c]	**–44.2** [c]	**–3.1** [c]	–1.5 [a]	**–7.6** [c]	**–3.4** [c]	–1.3	+0.2	–0.7
Living status (vs. living with family/friends)											
Living alone	–1.0	–0.3	+2.5 [b]	0.0	+0.5	–0.2	–1.3	**–2.7** [c]	**–3.4** [c]	–1.3	–1.5 [a]
Living in nursing home	+1.7	+2.4	+3.6 [a]	+3.4	–2.1	–0.7	+6.3	+0.4	**–10.1** [c]	–1.1	–1.2
Homeless/prisoner	–0.2	+2.1	+2.0	–2.7	–8.3	–5.7	–2.4	–0.1	–6.0	–12.1 [a]	+2.6
Serum albumin < 3.5 g/dl (vs. ≥3.5 g/dl)	–1.4 [b]	–1.6 [b]	–0.9	–2.6 [b]	–1.4 [a]	–0.2	–3.3 [a]	–0.9	+0.2	+1.2 [a]	+1.3 [a]
Hemoglobin (vs. ≥ 11 g/dl)											
<9 g/dl	–1.3 [a]	+0.1	–0.8	–1.1	–0.4	–1.0	+0.7	–0.4	–0.1	+0.3	–0.8
9–11 g/dl	+0.2	+0.6	+0.7	–0.2	–0.1	+0.1	–0.7	+0.1	–0.8	+0.2	0.0
eKt/V < 1.2 (vs. ≥1.2)	+0.4	+0.9	+0.4	+1.5	+0.7	+0.2	+4.3 [a]	–0.1	+0.2	–0.3	+0.8
Access by catheter (vs. Fistula or graft)	0.0	-1.2	–2.8 [b]	+1.6	–0.7	–0.3	–1.1	–0.1	+0.4	–0.4	+1.4
Predialysis SBP < 110 (vs. ≥110 mm Hg)	–2.0 [a]	–3.2 [b]	–0.7	+0.7	–1.1	+0.1	–5.2	+0.1	–3.0 [a]	+0.5	–0.5
Body mass index < 20 (vs. ≥20 Kg/m^2)	0.0	-0.2	–0.5	+1.0	–1.6 [b]	–0.4	+1.4	+0.7	–1.5 [a]	–1.2 [a]	–0.4
Comorbidity (yes vs. no)											
Cerebrovascular/ neurologic disease	–0.5	–1.0	–1.0	**–4.0** [c]	**–4.5** [c]	–1.3 [a]	–2.6	+0.7	–2.7 [b]	–0.7	+0.2
Cardiac disease	**–2.2** [c]	–1.7 [b]	–1.5 [a]	–2.2 [b]	**–1.8** [c]	–0.8	–3.1 [b]	**–2.4** [c]	–0.8	–0.2	+0.3
Peripheral vasculopathy	**–2.4** [c]	**–3.6** [c]	–1.8 [a]	–1.8 [a]	+0.1	+0.1	–4.5 [b]	–1.8 [b]	–0.8	–0.4	–1.3 [a]
Diabetes	–1.1 [a]	**–2.1** [c]	**–2.5** [c]	**–3.7** [c]	–1.1 [a]	–1.3 [b]	**–6.4** [c]	–1.6 [b]	–1.2	+0.9	+0.2
Lung disease	**–3.5** [c]	–2.1 [a]	**–5.2** [c]	0.0	+0.4	–1.6 [a]	–1.2	–2.6 [b]	–1.3	–0.1	+1.1
Cancer, excluding skin	+0.3	–1.3	+0.7	–2.4 [a]	+1.0	–0.9	–3.0	0.0	-0.2	–0.9	–0.5
Psychiatric disease	**–6.1** [c]	**–7.2** [c]	**–8.8** [c]	**–3.9** [c]	**–7.6** [c]	**–6.9** [c]	**–5.5** [c]	**–6.1** [c]	**–6.3** [c]	**–2.3** [c]	–2.4 [a]

*Adjusted for all variables in Table 1

Bold numbers call attention to statistically significant differences ($P < 0.05$) after adjustments for multiple comparisons. Comorbidities were selected based on their high prevalence or severity among hemodialysis patients, by Hochberg. [a]$0.01 \le P \le 0.05$, [b]$0.001 \le P < 0.01$, [c] $P < 0.001$ before multiple comparisons

[A]Referent patient is defined as a 59.5-year-old, male, unmarried, with income >$10,000, who attended college, employed, living with family/friends, serum albumin ≥ 3.5 g/dl, hemoglobin ≥ 11 g/dl, eKt/v ≥ 1.2, vascular access by fistula or graft, BMI ≥ 20, predialysis SBP ≥ 110 mm Hg, no comorbidity

covariates and multiple comparisons (Table 3). Except for non-skin cancer, the differences in PCS scores by comorbidity status remained statistically significant (*P*-corrected < 0.05) after adjustments for covariates; for PCS the significant adjusted difference in scores varied from –1.4 for psychiatric disease to –2.9 for peripheral vasculopathy (Table 3). After adjustments for covariates (Table 3), significantly lower scores were observed for females, those who had not attended college, the unemployed, and hypoalbuminemic patients (serum albumin <3.5 g/dl).

Mental component summary (MCS)

Significantly (*P*-corrected < 0.05) lower unadjusted MSC scores were observed for patients with yearly income <$10,000, those who had not attended college, the unemployed, patients with BMI < 20 Kg/m^2, and those with cerebrovascular/neurologic disease, lung disease, or psychiatric disease (Table 2). After adjustments for covariates (Table 3), significantly (*P*-corrected < 0.05) lower scores in MCS were observed for patients with yearly income <$10,000 (ADIFS = –2.0), those who had not attended college (ADIFS = –4.0), and patients with psychiatric disease (ADIFS = –10.5). Older age was not significantly associated with reduced scores in MCS. The quadratic effect of the coefficient of age on the MCS scores were also not statistically significant (*P* > 0.05).

Adjusted differences in the eight generic scales by patient characteristics (Table 3)

Comparisons by demographic and socioeconomic variables

Except for mental health and general health, older ages were associated with significantly (*P*-corrected <0.05) lower adjusted scores for all SF-36 scales. The quadratic effect of the coefficients of age on the scores of mental health, role emotional, and social function scales was not significant (*P* > 0.05). Females had significantly lower scores than males in physical functioning, bodily pain, and vitality.

Being unemployed (compared with employed) was independently and significantly (*P*-corrected <0.05) associated with lower scores in all eight SF-36 scales, with larger differences being observed for role-emotional and role-physical. Patients who had not attended college and those with yearly income <$10,000 had lower adjusted scores for both role-emotional and mental health. Patients who had not attended college also had lower adjusted scores for physical functioning and bodily pain.

Comparisons by laboratory/treatment variables, BMI, predialysis SBP, and comorbidities

Patients with serum albumin <3.5 g/dl had significantly (*P*-corrected < 0.05) lower scores in physical functioning, role-physical, bodily pain, general health, vitality, and social functioning. There was a significantly lower adjusted score in role-physical among patients with hemoglobin <9.0 g/dl compared with hemoglobin ≥11.0 g/dl (ADIFS = –6.3). After corrections for multiple comparisons, lower BMI was only significantly associated with lower scores in social function and no significant association with generic scales of HRQOL was observed for predialysis SBP, type of vascular access, and dialysis dose.

Psychiatric diseases were independently and significantly associated with lower scores in all eight SF-36 scales. Except for non-skin cancer, all the other comorbidities were also associated with lower scores for several generic scales of HRQOL.

Adjusted differences in the kidney disease-related scales by patient characteristics (Table 4)

Comparisons by demographic and socioeconomic variables

Older ages were associated with significantly (*P*-corrected < 0.05) higher adjusted scores of several kidney-disease-related scales. Females had significantly (*P*-corrected < 0.05) lower scores than males in symptoms/problems but higher scores for quality of social interaction and sexual function. Married patients had significantly (*P*-corrected < 0.05) lower scores for sexual function and effects of kidney disease on daily life.

Unemployment was independently and significantly (*P*-corrected < 0.05) associated with lower scores of several kidney disease-related scales. Significantly lower scores in kidney disease-related scales were also observed for patients who had not attended college, had lower incomes, or were living alone or in nursing homes.

Comparisons by laboratory/treatment variables, BMI, predialysis SBP, and comorbidities

After corrections for multiple comparisons, patients with psychiatric disease remained associated with

lower scores for ten of the eleven kidney disease-related scales of HRQOL. Except for non-skin cancer, all the other comorbidities were significantly associated with lower scores for at least two kidney disease-related scales. Serum albumin, hemoglobin, dialysis dose by eKt/V, type of vascular access, predialysis SBP, and BMI were not significantly (P-corrected > 0.05) associated with adjusted differences in any kidney disease related-scale after correcting the P-values for multiple comparisons.

Discussion

In the present study, several characteristics of hemodialysis patients were found to be associated with differences in scores of both generic and kidney disease-related components of HRQOL. Some characteristics observed as associated with lower scores in the physical or mental components of HRQOL are potentially modifiable by social or medical interventions such as unemployment, lower income, living in nursing homes, hypoalbuminemia, use of catheter as vascular access for hemodialysis, and the presence of comorbidities.

Among the socioeconomic factors, employment status was the one most strongly associated with HRQOL measures. It was independently associated with lower scores for all generic measures of HRQOL and several different areas of kidney disease-targeted HRQOL, such as symptom/problems, sleep, effects of kidney disease, sexual function, cognitive function, and burden of kidney disease. Similar to unemployment, lower income and lower level of education were associated with lower scores of MCS, role-emotional, and mental health. These data give support to a greater emphasis on multidisciplinary efforts to promote continuation of employment and formal education during the course of chronic kidney disease [20, 28, 30]. Besides those socioeconomic characteristics, only psychiatric disease was significantly and independently associated with lower scores in MCS and mental health after adjustments for multiple comparisons. It is also important to note the significantly lower adjusted score for effects of kidney disease on daily life and sexual function among married patients.

Type of vascular access, treatment of anemia, nutrition factors, and dialysis dose have received a great deal of attention as potential factors to improve hemodialysis outcomes [5, 15, 18, 26]. It has been shown that the use of catheters as vascular access for hemodialysis instead of AV fistulae has been associated with a higher prevalence of comorbidities, mortality risk, and rate of hospitalization [8, 29]. Late referral to nephrologists and lack of health insurance are factors associated with higher probability of initiation of hemodialysis by catheter instead of an AV fistula [1, 2]. Our analysis, without adjustment for covariates, showed that hemodialysis patients using catheters as vascular access had significantly lower scores in PCS. After adjustments for comorbidities, social variables, and other covariates, the association became weaker and not significant. Taken together these data suggest that efforts to reduce the use of catheters as vascular access in hemodialysis patients should reduce the mortality risk and improve HRQOL, particularly in the physical component of quality of life.

Correction of anemia by epoetin has been associated with improved HRQOL in dialysis patients [4]. Thus, it is plausible to expect an association between lower hemoglobin levels and poorer HRQOL. In the present study, lower hemoglobin was significantly and independently associated with lower scores in MCS, social function, and role emotional only in the analysis not corrected for multiple comparisons. In the multivariable analysis corrected for multiple comparisons, however, lower hemoglobin level was significantly associated with lower scores in role-physical, a generic HRQOL scale that assesses the extent that physical problems limit the patient's performance at work and other daily activities.

Observational studies have shown an association between higher dose of dialysis (as measured by Kt/V or urea reduction ratio) with lower mortality risk. By contrast, the HEMO Study, a major randomized clinical trial among hemodialysis patients, had not shown any benefit of dialysis dose above the average dose on survival and a small, though statistically significant, improvement in PCS [9]. In the present study, dialysis dose was not significantly associated with improvement in HRQOL scales after adjustments for covariates and corrections for multiple comparisons. In fact, a lower unadjusted score in PCS was observed among patients with higher dialysis dose as assessed by eKt/V. It is possible that the potential benefit of increasing dialysis dose in the setting of thrice-weekly hemodialysis is counterbalanced by the negative effect of post-dialysis fatigue on physical function that is apparently related to rapid removal of fluid and in some patients to a high rate of hypotensive episodes [25]. By contrast, daily hemodialysis, defined as more than five sessions per week with sessions of 2–2.5 h, is associated with less hypotensive episodes and less post-dialysis fatigue and improvements in HRQOL

[14, 38]. Thus, the benefit of daily dialysis could be, at least partially, due to less marked fluctuations in physiological and laboratory parameters. Also consistent with this possibility, the better results observed with daily, as compared with standard hemodialysis, have been observed despite the similar weekly treatment time and weekly Kt/V between the treatment modalities.

Hypoalbuminemia and lower BMI are markers of malnutrition in hemodialysis patients and have been found to be strongly related to a higher risk of mortality [16, 27]. In the present study, hypoalbuminemia was significantly (P-corrected < 0.05) and independently associated with lower scores in PCS and several generic scales of HRQOL. Hypoalbuminemia was also significantly associated with lower adjusted scores in kidney disease-targeted scales but only in the analysis not adjusted for multiple comparisons. In the unadjusted comparison using the data of the whole sample, we found a significantly lower PCS in patients with a higher BMI. Considering that patients treated in Japan have a lower mean BMI but higher mean PCS scores and the evidence that the shape of the associations of BMI with dialysis outcomes may vary by ethnicity, we performed an analysis restricted to patients treated in the United States and Europe [10, 17]. In this restricted analysis no association was observed between BMI and PCS.

Even though age and sex are not modifiable characteristics, the observed differences described between the younger and older as well as between males and females, are potentially useful to identify those who need special attention to improve HRQOL. The lack of association between MCS and age, as well as the increase with age in the scores of several scales targeted to special concerns of patients with renal failure, suggests a fair adaptation of older patients to dialysis treatment. Even though females had lower scores for several generic measures of HRQOL and symptoms/problems related to renal failure, they had higher scores for quality of social interaction and in sexual function. It is also important to note the significantly lower adjusted score for effects of kidney disease on daily life and sexual function among married patients. Health professionals who take care of hemodialysis patients should know these differences by patient characteristics to tailor interventions to meet the needs and peculiarities of each patient.

In conclusion, the present study provides insights into characteristics of hemodialysis patients that may influence measures of HRQOL. The results call attention to the potential role of psychosocial and specific medical interventions to improve the well-being of hemodialysis patients. If the relationship between poorer HRQOL and adverse outcomes is causal, then the interventions to improve HRQOL may also be effective in improving the survival of hemodialysis patients.

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Appendix

KDQOL Scales and Questions KDQOL scales and questions originally from the SF-36, version 1.0

Scale	Questions or Items
Physical functioning	The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? ***Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports***? ***Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf***? ***Lifting or carrying groceries***? ***Climbing several flights of stairs***? ***Climbing one flight of stairs***? ***Bending, kneeing or stooping***? ***Walking more than a mile***? ***Walking several blocks***? ***Walking one block***? ***Bathing or dressing yourself***? Possible responses: 1. Yes, limited a lot, 2. Yes, limited a little, 3. No, not limited at all
Role physical	During the past 4 weeks, have you had any of the following problems with your work or other regular activities as a result of your physical health? ***Cut down on the amount of time you spent on work or other activities***? ***Accomplished less than you would like***? ***Were limited in the kind of work or other activities***? ***Had difficulty performing the work or other activities (for example it took extra effort)***? Possible responses: Yes or No

Scale	Questions or Items
Bodily pain	***How much bodily pain have you had during the past 4 weeks***? Possible responses: 1. None, 2. Very mild, 3. Mild, 4. Moderate, 5. Severe, 6. Very severe ***During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)***? Possible responses: 1. Not at all, 2. A little bit, 3. Moderately, 4. Quite a bit, 5. Extremely
General health	***In general, would you say your health is***: 1. excellent, 2. very good, 3. good, 4. fair, 5. poor How true or false is each of the following four statements for you? ***I seem to get sick a little easier than other people***? ***I am as healthy as anybody I know***? ***I expect my health to get worse***? ***My health is excellent***? Possible responses: 1. Definitely true, 2. Mostly true, 3. Don't know, 4. Mostly false, 5. Definitely false
Vitality (energy/ vitality)	How much of the time during the past 4 week did you: ***feel full of pep***? ***have a lot of energy***? ***feel worn out***? ***feel tired***? Possible responses: 1. All of the time, 2. Most of the time, 3.A good bit of the time, 4. Some of the time, 5. A little of the time, 6. None of the time
Social Functioning	During the past 4 weeks how much of the time has your physical health or emotional problems interfered with your social activities? Possible responses: 1. All of the time, 2. Most of the time, 3. A good bit of the time, 4. Some of the time, 5. A little of the time, 6. None of the time ***During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups***? Possible responses: 1. Not at all, 2. Slightly, 3. Moderately, 4. Quite a bit, 5. Extremely
Role emotional	During the past 4 weeks, have you had any of the following problems with your work or other regular activities as a result of any emotional problems (such as feeling depressed or anxious)? ***Cut down on the amount of time you spent on work or other activities***; ***Cut down on the amount of time you spent on work or other activities***; ***Accomplished less than you would like***. Possible responses: yes or no.
Mental Health (emotional well-being)	How much of the time during the past 4 weeks have you: ***been a very nervous person***? ***felt so down in the dumps that nothing could cheer you up***? ***felt calm and peaceful***? ***felt downhearted and blue***? ***been a happy person***? Possible responses: 1. All of the time, 2. Most of the time, 3.A good bit of the time, 4. Some of the time, 5.A little of the time, 6. None of the time
II. KDQOL scales and questions targeted to kidney disease and dialysis patients	
Symptoms/Problems	During the past 4 weeks, to what extent were you bothered by each of the following? ***Soreness in your mouth***; ***chest pain***; ***cramps; itchy skin; dry skin; shortness of breath; faintness or dizziness; lack of appetite; washed out or drained; numbness in hands or feet; nausea or upset stomach; problems with your access site***. The questions for each of these twelve symptoms have five options of response: 1. Not at all bothered, 2. Somewhat bothered, 3. Moderately bothered, 4. Very much bothered, 5. Extremely bothered
Effect of kidney disease on daily life	How much does kidney disease bother you in each of the following areas? ***fluid restriction***; ***dietary restriction; your ability to work around the house; your ability to travel; being dependent on doctors and other medical staff; stress or worries caused by kidney disease; your sex life; your personal appearance***. The questions for each of these eight areas have five options of response: 1. Not at all bothered, 2. Somewhat bothered, 3. Moderately bothered, 4. Very much bothered, 5. Extremely bothered
Burden of kidney disease	How true or false is each of the following statements for you? *My kidney disease interferes too much with my life; Too much of my time is spent dealing with my kidney disease; I feel frustrated dealing with my kidney disease; I feel like a burden on my family.* These five questions have five options of response: 1. Definitely true, 2. Mostly true, 3. Don't know, 4. Mostly false, 5. Definitely false
Work status	***During the past 4 weeks, did you work at a paying job***? Yes or No; ***Does your health keep you from working at a paying job***? Yes or No

Scale	Questions or Items
Cognitive function	How much of the time during the past 4 weeks did you: ***react slowly to things that were said or done***? ***have difficulty concentrating or thinking***? ***become confused***? Possible responses: 1. None of the time, 2. A little of the time, 3. Some of the time, 4. A good bit of the time, 5. Most of the time, 6. All of the time.
Quality of social interaction	How much of the time during the past 4 weeks did you: isolate yourself from people around you*?* act irritable toward those around you? get along well with other people? Possible responses: 1. None of the time, 2. A little of the time, 3. Some of the time, 4. A good bit of the time, 5. Most of the time, 6. All of the time.
Sexual function	How much of a problem was each of the following in the past 4 weeks? ***enjoying sex; becoming sexually aroused.*** The questions for these aspects of sexual function have five options of response: 1. Not a problem, 2. A little problem, 3. Somewhat of a problem, 4. Very much a problem, 5. Severe problem
Sleep	On a scale from 0 (very bad) to 10 (very good), how would you rate your sleep overall? How often during the past 4 weeks did you... ***awake during the night and have trouble falling asleep again? get the amount of sleep you need? have trouble awake during the day?*** The questions for these three aspects of sleep have six options of response: 1. None of the time, 2. A little of the time, 3. Some of the time, 4. A good bit of the time, 5. Most of the time, 6. All of the time.
Social support	Concerning your family and friends, how satisfied are you: ***with the amount of time you are able to spend with your family and friends? the support you receive from your family and friends***? Possible responses: 1. Very dissatisfied, 2. Somewhat dissatisfied, 3. Somewhat satisfied, 4. Very satisfied.
Dialysis staff encouragement	How true or false is each of the following statements? ***Dialysis staff encourage me to as independent as possible***; ***dialysis staff support me in coping with my kidney disease***. Possible responses: 1. Definitely true, 2. Mostly true, 3. Don't know, 4. Mostly false, 5. Definitely false
Satisfaction with Care	Think about the care you receive for kidney dialysis. ***In terms of your satisfaction, how would you rate the friendliness and interest shown in you as a person***? Possible responses: 1. Very poor, 2. Poor, 3. Fair, 4. Good, 5. Very good, 6. Excellent, 7. The best

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