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Quality-of-Life and Mortality in Hemodialysis Patients: Roles of Race and Nutritional Status

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Summary

Background and objectives Maintenance hemodialysis (MHD) patients often have protein-energy wasting, poor health-related quality of life (QoL), and high premature death rates, whereas African-American MHD patients have greater survival than non-African-American patients. We hypothesized that poor QoL scores and their nutritional correlates have a bearing on racial survival disparities of MHD patients.

Design, setting, participants, & measurements We examined associations between baseline self-administered SF36 questionnaire–derived QoL scores with nutritional markers by multivariate linear regression and with survival by Cox models and cubic splines in the 6-year cohort of 705 MHD patients, including 223 African Americans.

Results Worse SF36 mental and physical health scores were associated with lower serum albumin and creatinine levels but higher total body fat percentage. Spline analyses confirmed mortality predictability of worse QoL, with an almost strictly linear association for mental health score in African Americans, although the race–QoL interaction was not statistically significant. In fully adjusted analyses, the mental health score showed a more robust and linear association with mortality than the physical health score in all MHD patients and both races: death hazard ratios for (95% confidence interval) each 10 unit lower mental health score were 1.12 (1.05–1.19) and 1.10 (1.03–1.18) for all and African American patients, respectively.

Conclusions MHD patients with higher percentage body fat or lower serum albumin or creatinine concentration perceive a poorer QoL. Poor mental health in all and poor physical health in non-African American patients correlate with mortality. Improving QoL by interventions that can improve the nutritional status without increasing body fat warrants clinical trials.

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Introduction

Monitoring patient-reported outcomes (PROs) including self-reported mental and functional health of individuals with chronic disease states is important for assuring optimal disease management and patient satisfaction (1). The subjective or self-reported state of well being, as it relates to the health condition, also known as "health related quality of life" (QoL), is a core PRO measure in individuals with advanced chronic kidney disease (CKD) including those with ESRD (1). QoL may also serve as a prognostic measure and predictor for such other outcomes as survival (2–5). Chronic illnesses are often associated with poor QoL (6). Patients undergoing chronic dialysis treatment have a poorer QoL compared with the general population (7). Improving QoL and other PROs in the dialysis patient population has evolved as a goal for renal replacement therapy (1). Poor mental health, which may also be manifested as depression, is highly prevalent in CKD patients and is an independent risk factor for higher mortality in dialysis patients (8–10). Worse QoL may also be reported by the patient as poor physical health (11). Indeed the two main QoL domains or dimensions, *i.e.*, mental health and physical health scores, correlate with other PROs and survival (12–15). In dialysis patients, QoL scores also correlate with measures of nutritional status, which *per se* are strong predictors of longevity in this patient population (16,17). In particular, biochemical parameters such as serum albumin and body composition measures may be related to QoL (18–20).

Major racial and ethnic disparities including in perceived QoL are among important and unresolved issues that may influence outcomes in dialysis patients (21–23). Approximately one third of the 400,000 U.S. dialysis patients are African Americans, although they comprise only 14% of the U.S. general population (24,25). The treated ESRD rate for African Americans is one of the highest in the world. Nonetheless, African American and Hispanic patients with ESRD

have consistently greater survival over the past several decades than non-Hispanic whites, with a death rate of 187 and 180 per 1000 patient-years at risk, respectively, compared with 207 per 1000 patient-years at risk for the entire U.S. dialysis population (24,25). The causes of these disparities remain largely unknown. In a recent survey, Streja *et al.* (26) showed that survival advantages of African American and Hispanic dialysis patients may be related to differences in nutritional and inflammatory status. Better QoL was reported in African-American maintenance hemodialysis (MHD) patients than the non-African American counterparts (27). The interplay between QoL, nutritional status, race, and clinical outcomes has not been well studied.

The SF36 is a validated self-administered questionnaire to assess QoL in MHD patients (28) both as a stand alone tool and as a component of the Kidney Disease Quality of Life survey instrument (29). In this study, we used the SF36 to assess the two main QoL dimensions (mental health and physical health) in a group of MHD patients who were then followed for up to 6 years. We hypothesized that, irrespective of race or nutritional status, mental health and physical health are independently associated with subsequent survival in these patients.

Materials and Methods

Patient Population

We studied MHD patients who participated in the Nutritional and Inflammatory Evaluation in Dialysis (NIED) Study (30). The original patient cohort was derived from a pool of >3000 MHD outpatients over 5 years in eight DaVita chronic dialysis facilities in the South Bay area of Los Angeles (see the NIED Study website at www.NIED-Study.org for more details and previous publications (31–33). Inclusion criteria were outpatients who had been undergoing MHD treatment for at least 8 weeks, were 18 years of age or older, and signed the Institutional Review Board–approved consent form. From October 1, 2001 through September 30, 2007, 893 MHD patients signed the informed consent form and underwent the periodic evaluations of the NIED Study. For this study, data including SF36 were available for 705 MHD patients. A modified version of the Charlson comorbidity index (*i.e.,* without the age and kidney disease components) was used to assess the severity of comorbidities (34,35).

SF36 QoL Scoring System

The SF36 questionnaire has two main dimensions (mental health and physical health) and eight scales or components, *i.e.,* physical function, role physical, body pain, vitality, general health, mental health (not to be confused with the dimension under the same designation), role mental, and social function. The first five of these scales comprise physical health, whereas the last five of these scales constitute the mental health dimension. The scales vitality and general health are part of both the mental health and physical health dimensions. Each of the eight scales is rated 1 to 5, which contribute to the scoring of these scales (see Appendix for more details). The SF36 scores of each of the two dimensions are based on mathematical averaging of the scores of five scales (28,36).

Anthropometric Measures

Body weight assessment and anthropometric measurements were performed while patients underwent a hemodialysis treatment or within 5 to 20 minutes after termination of the treatment. Biceps skinfold and triceps skinfold thicknesses were measured with a conventional skinfold caliper using standard techniques as described previously (37,38).

Near Infra-Red Interactance

To estimate the percentage of body fat and fat-free body mass, near infra-red (NIR) interactance was measured at the same time as the anthropometric measurements (39). A commercial NIR sensor with a coefficient of variation of 0.5% for total body fat measurement (portable Futrex 6100) was used. NIR measurements were performed by placing, for several seconds on the upper aspect of the arm without a vascular access, a Futrex sensor and entering the required data (date of birth, gender, weight, and height) of each patient (33).

Laboratory Tests

All routine laboratory measurements were performed by DaVita Laboratories (Deland, FL) using automated methods. Serum high-sensitivity C-reactive protein (CRP) was measured by a turbidometric immunoassay (40,41). IL6 and TNFα were measured with immunoassay kits (42–44). CRP, TNFα, and IL6 were measured in the General Clinical Research Center Laboratories of Harbor-UCLA Medical Center. Serum prealbumin was measured using immunoprecipitin analysis. Plasma total homocysteine concentrations were determined by HPLC in the Harbor-UCLA Clinical Laboratories.

Statistical Analyses

Pearson's correlation coefficient (r) was used for analyses of linear associations. Multivariate regression analyses and analyses of covariance were performed to obtain adjusted P values controlled for case-mix and other covariates. Restricted cubic spline graphs were used as exploratory data analysis strategies to show systematic relations between SF36 and mortality (45). Thereafter, to calculate hazard ratios (HRs) of death, we used Cox proportional hazard models after controlling for relevant covariates. Plots of log [−log (survival rate)] against log (survival time) were performed to establish the validity of the proportionality assumption.

Case-mix and comorbidity covariates included gender, age, African-American race, diabetes mellitus, and dialysis vintage. The malnutrition-inflammation complex syndrome (MICS) variables included values for albumin, creatinine, hemoglobin, total iron-binding capacity, normalized protein nitrogen appearance, lymphocyte percentage, and body mass index. Inflammatory markers in fully adjusted Cox models included serum CRP, TNFα, and IL6. Descriptive and multivariate statistics were carried out with the statistical software STATA version 11.0 (STATA, College Station, TX).

Results

The mean age ± SD of the 705 MHD patients was 53.5 ± 14.7 years; 47% of patients were women, 32% were Afri-

can-American (n = 223), and 55% were diabetic. The mean dialysis vintage was 30 ± 32 months (median: 19 months; interquartile range: 7 to 44 months). Tables 1 and 2 show the values of relevant demographic and clinical variables according to the quartiles of SF36 mental and physical health dimensions, respectively. The proportions of women and diabetics were lower in the fourth quartile of the SF36 dimensions. In addition to diabetes mellitus, Charlson morbidity scores, triceps skinfolds, and NIR body fat percentages showed decreasing trends across improving mental and physical health score quartiles. Among laboratory measures, serum albumin and creatinine levels increased across increasing quartiles of SF36 scores.

Table 3 shows the correlation coefficients between mental and physical health scores and relevant variables. The two SF36 dimensions were positively correlated with serum albumin and creatinine concentrations and negatively with total body fat percentage. Figures 1–3 show serum albumin and creatinine concentrations

Table 1. Baseline demographic, clinical, and laboratory values in the cohort and according to quartiles of SF36 Mental Health Dimension in 705 maintenance hemodialysis patients

	Quartile 1 (worse scores) (n = 177) (1 to <37.2)	Quartile 2 (n = 176) (37.3 to <51.3)	Quartile 3 (n = 177) (51.4 to >69.4)	Quartile 4 (best scores) (n = 175) (69.5 to 100)	P for Trend
Demographic					
age (years)	55.2 ± 13.2	53.6 ± 14.4	52.51 ± 15.1	52.7 ± 16	0.08
women (%)	100 (56%)	87 (49%)	80 (45%)	65 (37%)	<0.001
marital status (% married)	62 (44%)	59 (46%)	62 (46%)	65 (46%)	0.78
race (% African American)	65 (37%)	45 (26%)	58 (33%)	55 (31%)	0.58
insurance (% Medicare)	63 (59%)	61 (53%)	55 (49%)	59 (43%)	0.01
diabetes mellitus (%)	110 (64%)	100 (58%)	93 (54%)	80 (46%)	0.001
Charlson comorbidity score	2.14 ± 1.70	2.01 ± 1.62	1.70 ± 1.55	1.65 ± 1.63	<0.001
crude mortality (%)	82 (46%)	75 (43%)	61 (34%)	56 (32%)	0.002
Body composition					
body mass index (kg/m^2)	26.6 ± 6.0	26.7 ± 6.5	26.0 ± 5.8	26.0 ± 5.4	0.20
triceps skinfold (mm)	18.8 ± 10.2	18.0 ± 9.5	16.6 ± 9.3	16.3 ± 9.0	0.004
midarm muscle circumference (cm)	31.6 ± 6.1	31.8 ± 6.0	31.1 ± 6.2	31.1 ± 4.9	0.34
NIR measured body fat (%)	47.8 ± 27.1	47.4 ± 29.3	42.2 ± 25.5	41.3 ± 24.8	0.008
Hemodialysis treatment					
dialysis vintage (month)	28.8 ± 31.6	25.9 ± 28.2	32.0 ± 37.3	31.7 ± 31.5	0.23
dialysis dose (Kt/V single pool)	1.61 ± 0.31	1.62 ± 0.30	1.59 ± 0.26	1.62 ± 0.28	0.91
nPNA (nPCR; g/kg/d)	1.03 ± 0.24	1.11 ± 0.25	1.07 ± 0.23	1.06 ± 0.22	0.73
erythropoietin dose (1000 U/wk)	15.6 ± 14.5	12.9 ± 94.4	14.0 ± 12.0	12.3 ± 84.4	0.02
active vitamin D dose (ug/mo)	41 ± 34	39 ± 28	40 ± 32	44 ± 42	0.41
Biochemical measurements					
serum albumin (g/dl)	3.83 ± 0.38	3.89 ± 0.34	3.90 ± 0.37	3.97 ± 0.34	<0.001
prealbumin (mg/dl)	27.4 ± 8.9	29.3 ± 10.07	29.5 ± 9.26	28.15 ± 9.2	0.76
creatinine (mg/dl)	9.58 ± 2.9	9.94 ± 2.9	10.46 ± 3.0	10.95 ± 3.3	<0.001
TIBC (mg/dl)	207 ± 38	209 ± 37	207 ± 39	209 ± 38	0.79
calcium (mg/dl)	9.34 ± 0.72	9.34 ± 0.63	9.39 ± 0.74	9.38 ± 0.61	0.46
iron saturation ratio	31.9 ± 11.6	32.5 ± 11.2	31.6 ± 10.8	32.2 ± 10.7	0.99
phosphorus (mg/dl)	5.7 ± 1.5	5.7 ± 1.3	6.0 ± 1.4	5.7 ± 1.4	0.43
ferritin (ng/ml)	593 ± 425	614 ± 422	534 ± 358	558 ± 428	0.18
total homocysteine (μmol/L)	21.6 ± 9.5	22.8 ± 9.8	25.0 ± 13.1	24.6 ± 9.7	0.002
C-reactive protein (mg/L)	6.3 ± 6.3	5.1 ± 4.7	5.1 ± 5.5	6.0 ± 7.6	0.63
IL6 (pg/ml)	18.4 ± 54.8	13.6 ± 36.4	20.7 ± 68.6	14.0 ± 24.0	0.67
TNF (pg/ml)	8.5 ± 12.0	9.7 ± 13.4	8.3 ± 7.9	7.9 ± 9.7	0.34
white blood cells	7.1 ± 1.9	7.2 ± 1.7	7.2 ± 1.7	7.0 ± 2.0	0.93
lymphocytes	22.9 ± 8.1	22.2 ± 7.3	22.7 ± 7.5	23.1 ± 7.1	0.63
blood hemoglobin (g/dl)	12.1 ± 1.0	12.1 ± 0.9	12.0 ± 0.9	12.1 ± 0.9	0.77

Values expressed as mean ± SD or percent. Albumin in g/dl may be converted to g/L by multiplying by 10; creatinine in mg/dl to μmol/L by multiplying by 88.4; calcium in mg/dl to mmol/L by multiplying by 0.2495; phosphorus in mg/dl to mmol/L by multiplying by 0.3229. Ferritin levels expressed in ng/ml and μg/L are equivalent. White blood cell count in 103/μl and 109/L is equivalent. P for dialysis dose (vintage), ferritin level, vitamin D dose, CRP level, IL6 levels, and TNF level are based on logarithmic values of these measures. nPNA, normalized protein nitrogen appearance; nPCR, normalized protein catabolic rate; TIBC, total iron binding capacity.

Table 2. Baseline demographic, clinical, and laboratory values in the cohort and according to quartiles of SF36 Physical Health Dimension in 703 maintenance hemodialysis patients

	Quartile 1 (worse scores) (n = 177) (1 to <28.4)	Quartile 2 (n = 176) (28.4 to <43.6)	Quartile 3 (n = 176) (43.8 to <62.2)	Quartile 4 (best scores) (n = 174) (62.2 to 100)	P for Trend
Demographic					
age (years)	56.9 ± 12.6	55.0 ± 14.2	51.8 ± 14.5	50.0 ± 16.4	<0.001
women (%)	95 (54%)	86 (49%)	87 (49%)	63 (36%)	0.002
marital status (% married)	55 (41%)	70 (51%)	67 (49%)	55 (41%)	0.85
race (% African American)	64 (37%)	52 (30%)	56 (32%)	52 (30%)	0.27
insurance (% Medicare)	70 (62%)	61 (53%)	54 (52%)	54 (39%)	<0.001
diabetes mellitus (%)	122 (70%)	103 (59%)	89 (52%)	67 (39%)	<0.001
Charlson comorbidity score	2.3 ± 1.70	2.15 ± 1.58	1.61 ± 1.53	1.44 ± 1.58	<0.001
crude mortality (%)	89 (51%)	75 (43%)	56 (32%)	54 (31%)	<0.001
Body composition					
body mass index (kg/m^2)	27.2 ± 6.5	26.4 ± 6.2	26.4 ± 5.2	25.4 ± 6.1	0.012
triceps skinfold (mm)	19.2 ± 10.1	17.5 ± 9.6	17.6 ± 9.1	15.6 ± 9.5	<0.001
midarm muscle circumference (cm)	32.3 ± 6.3	31.1 ± 6.1	31.3 ± 5.0	30.6 ± 5.6	0.016
NIR measured body fat (%)	50.0 ± 28.6	45.5 ± 26.9	44.9 ± 22.6	37.8 ± 27.3	<0.001
Hemodialysis treatment					
dialysis vintage (month)	28.8 ± 31.6	25.9 ± 28.2	31.9 ± 37.3	31.7 ± 31.3	0.013
dialysis dose (Kt/V single pool)	1.58 ± 0.32	1.64 ± 0.32	1.61 ± 0.28	1.62 ± 0.28	0.41
nPNA (nPCR; g/kg/d)	1.05 ± 0.24	1.07 ± 0.24	1.08 ± 0.24	1.07 ± 0.22	0.44
erythropoietin dose (1000 U/wk)	15.6 ± 13.8	14.0 ± 12.2	12.9 ± 91	12.4 ± 96.6	0.005
active vitamin D dose (ug/mo)	38 ± 26	44 ± 37	41 ± 42	41 ± 30	0.56
Biochemical measurements					
serum albumin (g/dl)	3.81 ± 0.34	3.84 ± 0.38	3.96 ± 0.34	3.99 ± 0.35	<0.001
prealbumin (mg/dl)	27.4 ± 8.9	28.2 ± 9.4	29.4 ± 9.79	29.19 ± 9.5	0.05
creatinine (mg/dl)	9.2 ± 2.9	9.9 ± 3.1	10.6 ± 3.1	11.3 ± 3.4	<0.001
TIBC (mg/dl)	210 ± 40	209 ± 42	207 ± 39	206 ± 38	0.30
calcium (mg/dl)	9.33 ± 0.70	9.33 ± 0.75	9.40 ± 0.63	9.40 ± 0.62	0.26
iron saturation ratio	30.0 ± 9.55	33.3 ± 11.3	32.6 ± 11.8	33.2 ± 11.1	0.002
phosphorus (mg/dl)	5.71 ± 1.54	5.70 ± 1.26	5.78 ± 1.55	5.89 ± 1.43	0.21
ferritin (ng/ml)	583 ± 435	599 ± 430	577 ± 398	542 ± 438	0.32
total homocysteine (μmol/L)	22.8 ± 11.9	23.5 ± 11.9	24.1 ± 10.1	24.0 ± 9.5	0.28
C-reactive protein (mg/L)	6.8 ± 6.0	5.8 ± 5.9	4.4 ± 4.7	5.8 ± 7.6	0.05
IL6 (pg/ml)	17.9 ± 44.9	19.2 ± 64.0	18.2 ± 59.7	13.9 ± 21.9	0.40
TNF (pg/ml)	8.8 ± 12.2	8.0 ± 10.5	9.5 ± 10.6	8.6 ± 11.3	0.85
white blood cells	7.3 ± 1.9	7.2 ± 1.9	7.2 ± 1.9	6.8 ± 1.9	0.02
lymphocytes	21.4 ± 8.2	23.1 ± 8.1	23.5 ± 7.4	22.9 ± 7.2	0.06
blood hemoglobin (g/dl)	12.1 ± 1.0	12.1 ± 1.0	12.2 ± 0.9	12.1 ± 0.9	0.68

Values expressed as mean ± SD or percent. Albumin in g/dl may be converted to g/L by multiplying by 10; creatinine in mg/dl to μmol/L by multiplying by 88.4; calcium in mg/dl to mmol/L by multiplying by 0.2495; phosphorus in mg/dl to mmol/L by multiplying by 0.3229. Ferritin levels expressed in ng/ml and μg/L are equivalent. White blood cell count in 103/μl and 109/L is equivalent. P for dialysis dose (vintage), ferritin level, vitamin D dose, CRP level, IL6 levels, and TNF level are based on logarithmic values of these measures. nPNA, normalized protein nitrogen appearance; nPCR, normalized protein catabolic rate; TIBC, total iron binding capacity.

and the NIR measured total body fat percentage, respectively, across the quartiles of the two dimensions and eight scales of the SF36 in all 705 MHD patients. The two nutritional biomarkers were incrementally higher across higher QoL score quartiles, whereas body fat exhibited an opposite trend.

During the follow-up period of up to 6 years, 274 (39%) patients died, 92 (11%) underwent transplantation, and 147 (18%) left the cohort. Table 4 shows the HR of mortality across quartiles of mental and physical health. The death HR increased across worsening QoL scores even after extensive multivariate adjustment for demographics and measures of nutrition and inflammation including several inflammatory markers and cytokines. Figure 4 shows the cubic splines of the mortality predictabilities of mental and physical health scores. A linear trend toward increased death risk with worse mental health score was observed in the entire cohort. Figures 5 and 6 show the cubic splines in African-American and other MHD patients separately. The Cox

Table 3. Unadjusted and case-mix adjusted correlation coefficients *r* for the SF36 Physical and Mental Health Dimensions against pertinent clinical, laboratory, and demographic values

SF36 Dimensions	Physical Health		Mental Health	
	Unadjusted *r*	Adjusted *r*[a]	Unadjusted *r*	Adjusted *r*[a]
Age	**−0.20** (<0.001)	**−0.11** (0.005)	**−0.07** (0.06)	−0.02 (0.65)
NIR total body fat %	**−0.18** (<0.001)	**−0.08** (0.03)	**−0.12** (0.002)	−0.06 (0.11)
Kt/V (single pool)	0.03 (0.34)	0.05 (0.16)	0.03 (0.38)	0.06 (0.12)
Dialysis vintage month	**0.08** (0.02)	−0.03 (0.38)	0.04 (0.23)	−0.02 (0.59)
Body mass index	**−0.10** (0.006)	−0.06 (0.11)	−0.07 (0.07)	−0.05 (0.23)
Triceps skinfold	**−0.14** (0.000)	**−0.08** (0.04)	**−0.11** (0.004)	−0.06 (0.13)
MAMC	**0.08** (0.02)	0.06 (0.14)	0.05 (0.21)	0.03 (0.42)
Erythropoeitin dose	**−0.10** (0.01)	**−0.11** (0.01)	**−0.10** (0.01)	**−0.10** (0.02)
Serum albumin	**0.21** (0.000)	**0.13** (0.001)	**0.14** (0.000)	**0.10** (0.009)
Creatinine	**0.25** (0.000)	**0.13** (0.000)	**0.16** (<0.001)	**0.10** (0.01)
Intact PTH	0.01 (0.80)	−0.04 (0.29)	−0.01 (0.96)	−0.02 (0.62)
Hemoglobin	0.01 (0.78)	0.02 (0.60)	0.01 (0.97)	0.01 (0.90)
Ferritin	−0.04 (0.29)	−0.04 (0.30)	−0.04 (0.27)	−0.05 (0.24)
TIBC	−0.02 (0.53)	−0.02 (0.67)	0.01 (0.78)	0.02 (0.66)
Iron saturation	**0.13**[b] (0.001)	**0.08** (0.03)	0.03 (0.41)	0.009 (0.82)
Prealbumin	**0.09** (0.03)	0.03 (0.50)	0.06 (0.16)	0.02 (0.57)
CRP[c]	**−0.13** (0.001)	**−0.10** (0.007)	−0.06 (0.13)	−0.05 (0.19)
IL6[c]	−0.07 (0.06)	−0.04 (0.30)	−0.03 (0.42)	−0.02 (0.58)
TNFα[c]	0.04 (0.23)	0.03 (0.37)	0.04 (0.34)	0.03 (0.44)

P values are in parentheses.
[a]Case-Mix adjusted correlation coefficients (controlled for age, race, gender, diabetes, log of vintage). MACM, mid-arm circumference muscle; intact PTH, parathyroid hormone; TIBC, total iron binding capacity.
[b]Values with significant *P* value are highlighted in bold.
[c]Logarithmic values were studied.

regression estimated HRs of death for the aforementioned linear mortality predictabilities of the two dimensions and eight scales are listed in Table 5 for the entire cohort and by race. In the fully adjusted models, for each 10- unit drop in the mental and physical health scores, the death HRs (and 95% confidence intervals) were 1.12 (1.05 to 1.19) and 1.08 (1.02 to 1.15), respectively ($P < 0.001$).

Mental health scores remained robust predictors of survival in both African-American and other races, whereas physical health and the eight scales did not show statistically significant associations with death. In 223 African-American MHD patients, each 10-unit drop in the mental health score was associated with a 10% increase in death risk, *i.e.*, a death HR of 1.10 (1.03 to 1.18; $P < 0.001$). The spline analyses in Figure 5 confirmed the substantially more linear and incremental associations of mental health score with mortality in African Americans. An increasing trend of mortality was associated with lower scores on mental and physical health dimensions of SF36, and it was robust even after controlling for case-mix and other nutritional and inflammatory measures. There was a 62 and 45% higher chance of death in patients with the lowest (*versus* highest) score quartile of mental and physical health of SF36, respectively. Each 10-unit decrease in each of the two dimensions and eight subscales of the SF36 score

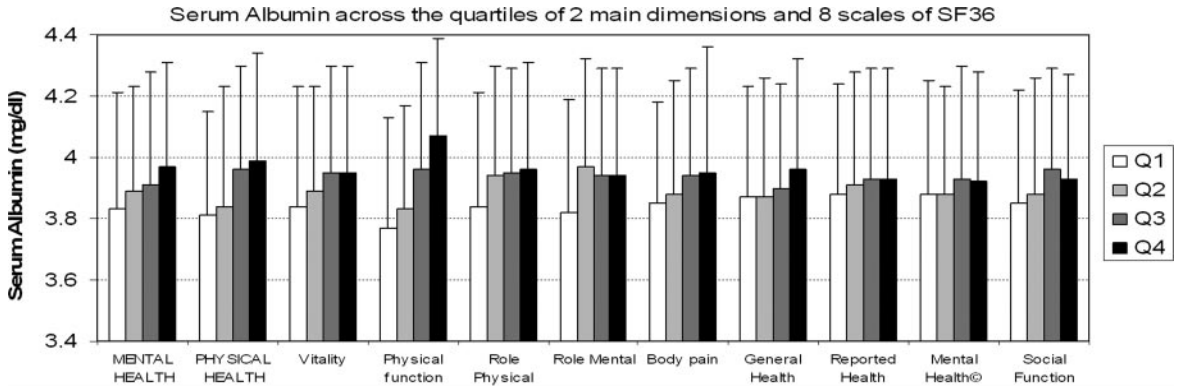

Figure 1. | **Serum albumin level across four quartiles of the two dimensions and eight scales of SF36 (error bars indicate SD).** SF36 consists of two main dimensions, mental health and physical health, and each dimension consists of five subscales. 1) Mental Health consists of role mental, mental health, social function, vitality, and general health). 2) Physical health consists of physical function, role physical, body pain, vitality, and general health. Detail in appendix.

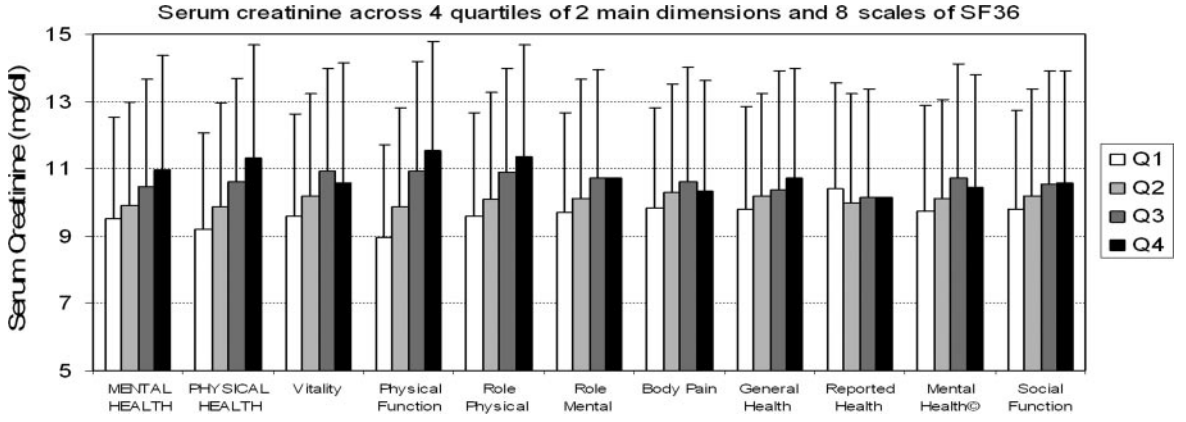

Figure 2. | **Serum creatinine level across the four quartiles of the two dimensions and eight scales of SF36 (error bars indicate SD).** SF36 consists of two main dimensions, mental health and physical health, and each dimension consists of five subscales. 1) Mental Health consists of role mental, mental health, social function, vitality, and general health). 2) Physical health consists of physical function, role physical, body pain, vitality, and general health. Detail in appendix.

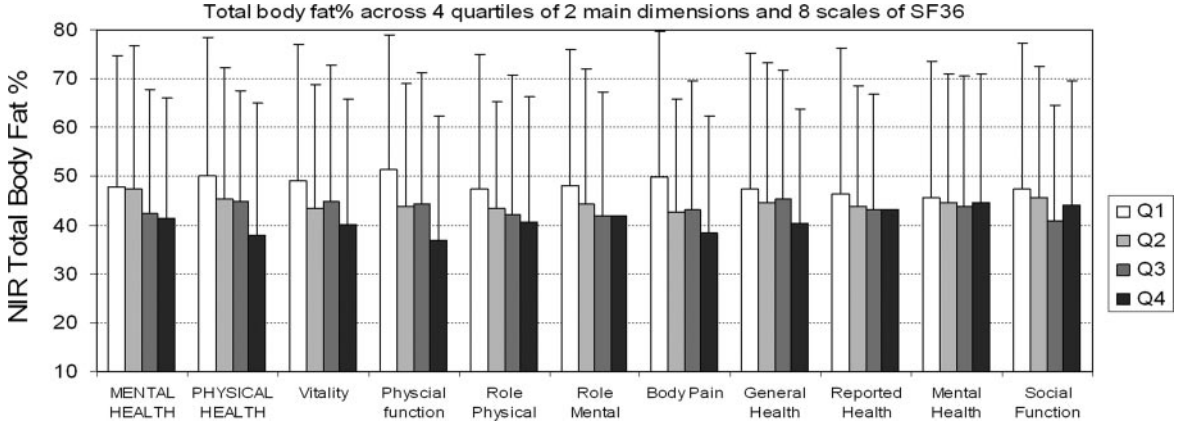

Figure 3. | **Total body fat percentage (assessed by NIR) across the four quartiles of the two dimensions and eight scales of SF36 (error bars indicate SD).** SF36 consists of two main dimensions, mental health and physical health, and each dimension consists of five subscales. 1) Mental Health consists of role mental, mental health, social function, vitality, and general health). 2) Physical health consists of physical function, role physical, body pain, vitality, and general health. Detail in appendix.

Table 4. Death hazard ratio across the 4 quartiles of the Mental Health Dimension (upper panel) and Physical Health Dimension (lower panel) score in 705 maintenance hemodialysis patients

Mental Health Quartiles	First Quartile (n = 177)	Second Quartile (n = 176)	Third Quartile (n = 177)	Fourth Quartile (n = 175)	Trend P
Unadjusted	**1.79** (1.27 to 2.51) P = 0.001	**1.60** (1.13 to 2.26) P = 0.008	1.13 (0.79 to 1.63) P = 0.50	1.00 (Reference)	**<0.001**
Adjusted[a] (full)	**1.62** (1.12 to 2.34) P = 0.01	**1.66** (1.14 to 2.4) P = 0.008	0.99 (0.66 to 1.5) P = 0.95	1.00 (Reference)	**0.001**

Physical Health Quartiles	First Quartile (n = 176)	Second Quartile (n = 176)	Third Quartile (n = 177)	Fourth Quartile (n = 174)	Trend P
Unadjusted	**2.03** (1.44 to 2.84) P = 0.000	**1.59** (1.12 to 2.26) P = 0.009	1.05 (0.72 to 1.53) P = 0.78	1.00 (Reference)	**<0.001**
Adjusted[a] (full model)	**1.45** (1.0 to 2.1) P = 0.05	1.37 (0.93 to 2.0) P = 0.11	1.00 (0.67 to 1.5) P = 1.0	1.00 (Reference)	**0.008**

Case-mix variables includes age, gender, race/ethnicity, diabetes, and log vintage. MICS variables includes values for albumin, creatinine, hemoglobin, total iron-binding capacity, normalized protein catabolic rate, lymphocyte percentage, and body mass index. CI, confidence interval; MICs, malnutrition-inflammation-cachexia syndrome.
[a]Full model consists of case mix and MICS and logarithm of three inflammatory markers: C-reactive protein, IL6, and TNFα.

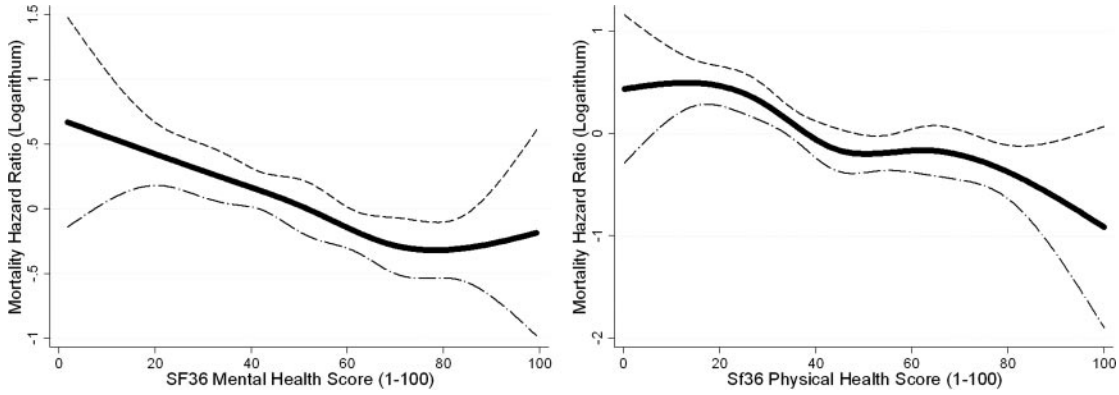

Figure 4. | Cubic spline survival analyses exhibiting the association between SF36 scores and mortality in 705 MHD patients over 6 years. (Left) Mental health score ($P < 0.001$). (Right) Physical health score ($P < 0.001$).

was associated with 8 to 15% higher mortality. However, African-American race did not exhibit a statistically significant interaction with QoL–mortality association (P for interaction terms > 0.20).

Discussion

In this prospective 6-year cohort study of 705 MHD patients including 223 African Americans, lower QoL scores derived from self-administered SF36 questionnaires were associated with higher mortality risk. Both the mental health and physical health dimensions of the SF36 showed significant associations with mortality in all MHD patients. The death predictability of the mental health scores was slightly more pronounced in African American, whereas the association of worse physical health score and death risk did not reach statistical significance in this group. Lower QoL scores not only correlated with surrogates of protein energy wasting, including lower serum albumin and creatinine levels, but also with obesity, *i.e.*, higher total body fat percentage. These findings may have important implications for the management of dialysis patients who frequently have poor health-related QoL and nutritional derangements including both protein energy wasting and obesity.

Monitoring PROs including the subjective state of well being, together known as QoL measurements, is of particular importance for CKD patients, because the physical and mental debilities experienced by CKD patients can be insidious and yet have grave consequences (1,6,9). In recent years, more attention has been drawn toward re-examining the overall role and potential application of patient self-reported states of well being and functioning by using self-administered QoL questionnaires in dialysis populations (9–12). The SF36 is one of the most commonly used PRO instruments for QoL evaluation in maintenance dialysis patients (9,10). Our study suggests that better QoL was associated with higher predialysis serum creatinine and albumin levels, which are surrogates, respectively, for larger muscle mass and/or greater meat intake, and for higher visceral protein stores. Lowrie *et al.* (46) found that

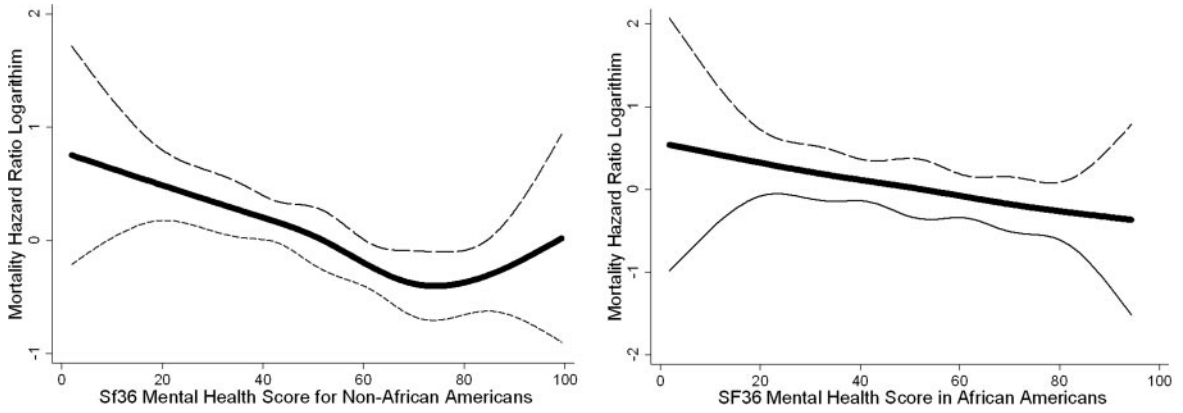

Figure 5. | **Cubic spline survival analyses exhibiting the association between SF36 mental health score and mortality over 6 years.** (Left) 482 non-African–American MHD patients ($P < 0.001$). (Right) 223 African-American MHD patients ($P < 0.001$).

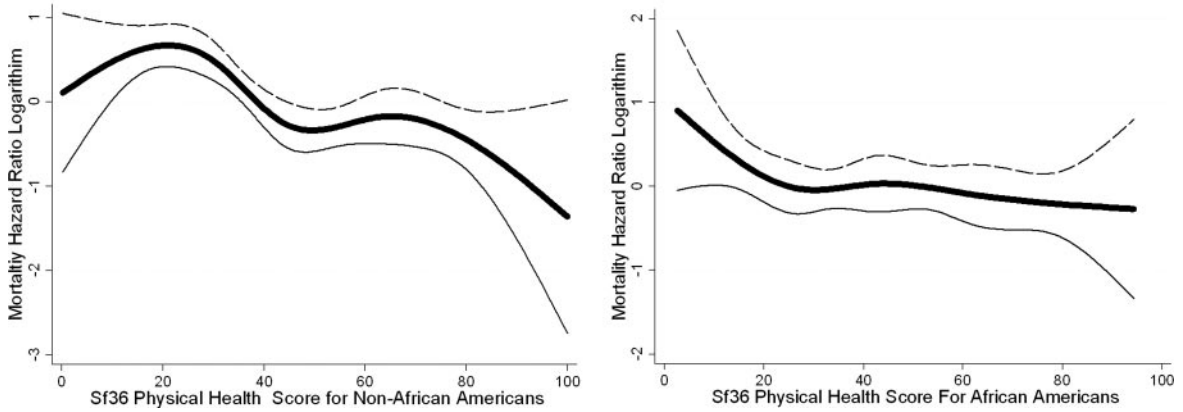

Figure 6. | **Cubic spline survival analyses exhibiting the association between SF36 physical health score and mortality over 6 years.** (Left) 482 non-African–American MHD patients ($P < 0.001$). (Right) 223 African-American MHD patients ($P > 0.20$).

the SF36 score was significantly correlated with serum albumin, creatinine, and hemoglobin. Ohri-Vachaspati and Sehgal (47) showed that inadequate protein nutrition, as reflected by low serum albumin level and low protein nitrogen appearance, was independently associated with poor QoL. The mental and physical health dimensions showed an especially strong association with the patients' protein/energy status. These nutritional markers showed a significantly positive correlation with both dimensions in both unadjusted and adjusted models. These finding are also consistent with previous reports by Lowrie *et al.* (48), Kalanar-Zadeh *et al.* (2), and Ohri-Vachaspati and Sehgal (47).

In this study, we did not find any association of QoL with inflammatory markers. Patients who were old or diabetic or who had higher comorbidity or higher body fat reported lower mental and physical health scores. SF36 had a significant negative correlation with the percentage of body fat, as measured by NIR technology, indicating that obese MHD outpatients tended to perceive a worse QoL. Triceps skinfold measurement, another surrogate of body fat, was also negatively correlated with the scores. Our study suggests that worse QoL was associated with obesity. Although obesity is associated with deleterious outcomes in the general population, in MHD patients, the association between body mass index and mortality appears in the opposite direction, a phenomenon known as "obesity paradox" or "reverse epidemiology" (33,49–51). Although this may be regarded as a contradiction to the assumed association between a poor nutritional state and lower SF36 score, being overweight is not the same as being well nourished. Goller *et al.* (52) observed that overweight dialysis patients had lower SF36 scores and were more impaired in physical functioning. If the association between obesity and poorer QoL in ESRD patients can be further verified, the SF36 may be one of the few reliable tools to detect higher-risk patients with poor clinical outcomes among those patients who are usually considered as being "not-malnourished" by nutritional assessment.

Similar to our results, previous studies found that the self-reported QoL score was independently predictive of mortality in the elderly individuals. DeOreo (4) recently reported that a SF36-associated physical health dimension score below the median value in MHD patients was twice as likely to be associated with mortality and 1.5 times as likely with hospitalization. Lowrie *et al.* (5) found a similar association between both physical and mental health dimensions of the SF36 and dialysis mortality In this study,

Table 5. Death hazard ratios of each 10 unit decrement in the score of the SF36 two dimensions and eight components in up to 705 maintenance hemodialysis patients

	All Patients (n = 705)		African Americans (n = 223)		Non–African Americans (n = 482)	
	Unadjusted	Fully Adjusted[a]	Unadjusted	Fully Adjusted[a]	Unadjusted	Fully Adjusted[a]
SF36 dimensions						
mental health	1.13 (1.06 to 1.20)***	1.12 (1.05 to 1.19)***	1.10* (1.00 to 1.21)	1.10 (1.03 to 1.18)***	1.14 (1.06 to 1.24)***	1.16 (1.07 to 1.26)***
physical health	1.15 (1.09 to 1.22)***	1.08 (1.02 to 1.15)*	1.07 (0.98 to 1.17)	1.04 (0.94 to 1.14)	1.20 (1.11 to 1.29)***	1.11 (1.03 to 1.21)**
SF36 components						
vitality	1.16 (1.06 to 1.18)***	1.09 (1.03 to 1.16)**	1.04 (0.95 to 1.13)	1.03 (0.93 to 1.13)	1.16 (1.08 to 1.24)***	1.13 (1.04 to 1.22)**
role physical	1.03 (1.0 to 1.06)	1.00 (0.97 to 1.03)	1.00 (0.96 to 1.05)	1.00 (0.95 to 1.05)	1.04 (1.0 to 1.08)	1.01 (0.97 to 1.06)
physical function	1.16 (1.11 to 1.21)***	1.07 (1.01 to 1.13)*	1.11 (1.03 to 1.18)**	1.04 (0.95 to 1.12)	1.21 (1.14 to 1.27)***	1.08 (1.01 to 1.15)*
body pain	1.07 (1.03 to 1.12)*	1.05 (1.0 to 1.09)*	1.01 (0.95 to 1.08)	1.03 (0.96 to 1.10)	1.10 (1.05 to 1.16)***	1.07 (1.0 to 1.13)*
general health	1.08 (1.01 to 1.44)**	1.08 (1.01 to 1.15)*	1.1 (1.00 to 1.22)	1.07 (0.97 to 1.19)	1.07 (1.00 to 1.15)	1.08 (1.0 to 1.17)
role mental	1.05 (1.02 to 1.08)**	1.03 (1.0 to 1.07)*	1.04 (1.0 to 1.09)	1.04 (0.99 to 1.10)	1.04 (1.00 to 1.08)	1.05 (1.01 to 1.09)*
social function	1.09 (1.05 to 1.14)***	1.08 (1.03 to 1.13)**	1.07 (1.00 to 1.14)	1.08 (1.00 to 1.16)	1.1 (1.04 to 1.17)**	1.11 (1.04 to 1.17)**
mental health	1.04 (0.98 to 1.10)	1.08 (1.07 to 1.15)*	1.07 (0.97 to 1.18)	1.11 (1.00 to 1.24)	1.04 (0.97 to 1.11)	1.08 (1.00 to 1.16)*

MICS variables includes values for albumin, creatinine, hemoglobin, total iron-binding capacity, normalized protein catabolic rate, lymphocyte percentage, and body mass index. Full model consists of case mix and MICS and logarithm of three inflammatory markers: CRP, IL6, and TNFα. CI, confidence interval; MICS, malnutrition-inflammation-cachexia syndrome.
[a]Case-mix variables includes age, gender, race/ethnicity, diabetes, and log vintage.
* if $P < 0.05$ but >0.01 **if $P < 0.01$ but >0.001 ***if $P < 0.001$.

we showed that the mental health dimension displayed a stronger association with mortality among MHD patients. Mental health in the fully adjusted model was the strongest predictor of death. The cubic spline analyses (Figures 4 and 5) for the fully controlled Cox models, which included adjustment for proinflammatory cytokines, showed that the death risk increased almost linearly with lower scores, in particular with the mental health score. This finding is in accordance with a report by McCellan *et al.* (53), who found that mortality is independently affected by QoL and functional status in dialysis patients. Contrary to the study by Kalantar-Zadeh *et al.* (2), we found significant associations for physical health dimensions with mortality in this study. These differences may be related to a different examined population. A strong association of depression with higher mortality in dialysis patients has been documented by Kimmel *et al.* (10,54) and Hedayati *et al.* (55). Our findings are consistent with the observation that CKD patients who have a lower perception of their well being have higher mortality.

The racial and ethnic disparities of CKD have been extensively reported in the United States (56). Whereas overall long-term survival in MHD patients is dreadfully low (23,57), there exists a racial survival paradox, in that African American dialysis patients have a greater survival than whites (58) This is despite the evidence that minority MHD patients are more likely to have such poor survival indicators as hypoalbuminemia and anemia or limited pre-ESRD care (58). Similarly, for the healthier MHD patients on transplant wait lists, the annual mortality rate is higher for non-Hispanics compared with African Americans (59–61). We also evaluated racial effects in our study and found that mental health score had a robust and linear association with mortality, but physical health score did not in AAs. Our findings suggest that mental health is a stronger outcome predictor in AA MHD patients. Our findings of poor mental health score and poor clinical outcomes in AA MHD patients are consistent with a report of Fischer *et al.* (62), who found, among a cohort of 628 AAs with stages 3 to 5 CKD, a high prevalence of increased depressive affect that was infrequently treated with anti-depressants and that was associated with poorer quality of life.

A potential limitation of this study is a selection bias during enrollment. However, because mortality in our cohort was less than the base MHD population (30), it might be argued that a selection bias with such a direction would lead to a bias toward the null, so without this bias, our results may have been even stronger. Moreover, our cohort was younger and have shorter dialysis vintage than the national U.S. dialysis population. Other limitations include lack of information on dialysis access, dialysis membrane, depression treatment, and other known or unknown confounders. The strengths of our study include the sample size, which was moderately large, the comprehensive clinical and laboratory evaluations with concomitant assessment of QoL and body composition measures, and detailed evaluation of comorbid states by study physicians. Unlike previous cohorts that have been studied, ours has been extensively characterized for markers of inflammation and nutritional status, including direct total body fat measurements. The availability of these measures allowed us to assess the interaction of nutritional and inflammatory markers in this group of MHD patients. Another strength is that the subjects were selected randomly without prior knowledge of their status. Finally, the very same blood specimens that were used to measure markers of protein energy wasting were also used for the cytokines measurements.

In conclusion, in MHD patients, a low mental and physical health score on the self-administered SF36 QoL questionnaire was independently associated with poor survival. The mental health score *per se* was the more powerful predictor of mortality in this patient population, in whom each 10-unit lower score was associated with an approximately 12% higher death risk. A low mental health score was even more predictive of mortality among African Americans compared to whites, whereas low physical health was not. Low QoL not only correlated with low serum albumin and creatinine levels, two biochemical markers of protein energy wasting and predictors of poor survival, but also with higher total body fat percentage, which is both an obesity measure and a surrogate of more nutritional reserves and aligned with greater survival in MHD patients. These findings suggest that, despite the reported survival advantages of body fat, known as the obesity paradox, MHD patients with higher total body fat perceive a lower QoL. Hence, the survival advantages of obesity in MHD patients appears in the opposite direction to obesity–QoL relationship. Given the robust and linear association of the perceived mental health status with longevity in MHD patients, including among African Americans, clinical trials to examine the effectiveness of methods to improve QoL are warranted. Nutritional and anti-inflammatory interventions that can improve protein energy wasting and QoL without increasing body fat might be particularly indicated.

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Disclosures

K.K.Z. has been involved in studies for malnourished dialysis patients and has been partially supported by Abbott Nutrition (manufacturer of Nepri and Suplena).

References

1. Kalantar-Zadeh K, Unruh M: Health related quality of life in patients with chronic kidney disease. *Int Urol Nephrol* 37: 367–378, 2005
2. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH: Association among SF36 quality of life measures and nutrition,

hospitalization, and mortality in hemodialysis. *J Am Soc Nephrol* 12: 2797–2806, 2001
3. Mapes DL, Lopes AA, Satayathum S, McCullough KP, Goodkin DA, Locatelli F, Fukuhara S, Young EW, Kurokawa K, Saito A, Bommer J, Wolfe RA, Held PJ, Port FK: Health-related quality of life as a predictor of mortality and hospitalization: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *Kidney Int* 64: 339–349, 2003
4. DeOreo PB: Hemodialysis patient-assessed functional health status predicts continued survival, hospitalization, and dialysis-attendance compliance. *Am J Kidney Dis* 30: 204–212, 1997
5. Lowrie EG, Curtin RB, LePain N, Schatell D: Medical outcomes study short form-36: A consistent and powerful predictor of morbidity and mortality in dialysis patients. *Am J Kidney Dis* 41: 1286–1292, 2003
6. Demura S, Sato S: Relationships between depression, lifestyle and quality of life in the community dwelling elderly: A comparison between gender and age groups. *J Physiol Anthropol Appl Human Sci* 22: 159–166, 2003
7. Evans RW, Manninen DL, Garrison LP, Jr., Hart LG, Blagg CR, Gutman RA, Hull AR, Lowrie EG: The quality of life of patients with end-stage renal disease. *N Engl J Med* 312: 553–559, 1985
8. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Boyle DH, Cruz I, Umana WO, Alleyne S, Veis JH: Aspects of quality of life in hemodialysis patients. *J Am Soc Nephrol* 6: 1418–1426, 1995
9. Kimmel PL, Thamer M, Richard CM, Ray NF: Psychiatric illness in patients with end-stage renal disease. *Am J Med* 105: 214–221, 1998
10. Kimmel PL, Weihs K, Peterson RA: Survival in hemodialysis patients: The role of depression. *J Am Soc Nephrol* 4: 12–27, 1993
11. Christensen AJ, Ehlers SL: Psychological factors in end-stage renal disease: An emerging context for behavioral medicine research. *J Consult Clin Psychol* 70: 712–724, 2002
12. Valdes C, Garcia-Mendoza M, Rebollo P, Ortega T, Ortega F: Mental health at the third month of haemodialysis as a predictor of short-term survival. *Nephrol Dial Transplant* 21: 3223–3230, 2006
13. Tsai YC, Hung CC, Hwang SJ, Wang SL, Hsiao SM, Lin MY, Kung LF, Hsiao PN, Chen HC: Quality of life predicts risks of end-stage renal disease and mortality in patients with chronic kidney disease. *Nephrol Dial Transplant* 25: 1621–1626, 2010
14. Bernard SL, Kincade JE, Konrad TR, Arcury TA, Rabiner DJ, Woomert A, DeFriese GH, Ory MG: Predicting mortality from community surveys of older adults: The importance of self-rated functional ability. *J Gerontol B Psychol Sci Soc Sci* 52: S155–S163, 1997
15. Dukkipati R, Kalantar-Zadeh K, Kopple JD: Is there a role for intradialytic parenteral nutrition? A review of the evidence. *Am J Kidney Dis* 55: 352–364, 2010
16. Rambod M, Bross R, Zitterkoph J, Benner D, Pithia J, Colman S, Kovesdy CP, Kopple JD, Kalantar-Zadeh K: Association of Malnutrition-Inflammation Score with quality of life and mortality in hemodialysis patients: A 5-year prospective cohort study. *Am J Kidney Dis* 53: 298–309, 2009
17. Kalantar-Zadeh K, Streja E, Kovesdy CP, Oreopoulos A, Noori N, Jing J, Nissenson AR, Krishnan M, Kopple JD, Mehrotra R, Anker SD: The obesity paradox and mortality associated with surrogates of body size and muscle mass in patients receiving hemodialysis. *Mayo Clin Proc* 85: 991–1001, 2010
18. Feroze U, Martin D, Reina-Patton A, Kalantar-Zadeh K, Kopple JD: Mental health, depression, and anxiety in patients on maintenance dialysis. *Iran J Kidney Dis* 4: 173–180, 2010
19. Noori N, Kopple JD, Kovesdy CP, Feroze U, Sim JJ, Murali SB, Luna A, Gomez M, Luna C, Bross R, Nissenson AR, Kalantar-Zadeh K: Mid-arm muscle circumference and quality of life and survival in maintenance hemodialysis patients. *Clin J Am Soc Nephrol* 5: 2258–2268, 2010
20. Noori N, Kovesdy CP, Dukkipati R, Kim Y, Duong U, Bross R, Oreopoulos A, Luna A, Benner D, Kopple JD, Kalantar-Zadeh K: Survival predictability of lean and fat mass in men and women undergoing maintenance hemodialysis. *Am J Clin* Nutr 92: 1060–1070, 2010
21. Kalantar-Zadeh K, Golan E, Shohat T, Streja E, Norris KC, Kopple JD: Survival disparities within American and Israeli dialysis populations: Learning from similarities and distinctions across race and ethnicity. *Semin Dial* 23: 586–594, 2010
22. Agodoa L: Racial disparities in kidney health: The puzzle to solve. *Am J Kidney Dis* 40: 1337–1339, 2002
23. Agodoa L, Eggers P: Racial and ethnic disparities in end-stage kidney failure-survival paradoxes in African-Americans. *Semin Dial* 20: 577–585, 2007
24. U.S. Renal Data System: United States Renal Data System 2006 annual data report atlas of chronic kidney disease & end-stage renal disease in the United States. *Am J Kidney Dis* 49: 1–296, 2007
25. U.S. Renal Data System: Excerpts from the USRDS 2005 Annual Data Report: Atlas of end-stage renal disease in the United States. *Am J Kid Dis* 47[Suppl 1]: 1–286, 2006
26. Streja E, Kovesdy CP, Molnar MZ, Norris KC, Greenland S, Nissenson AR, Kopple JP, Kalantar-Zadeh K: Role of nutritional status and inflammation in higher survival of African American and Hispanic hemodialysis patients. *Am J Kidney Dis* , Jan 14, 2011 [Epub ahead of print]
27. Hicks LS, Cleary PD, Epstein AM, Ayanian JZ: Differences in health-related quality of life and treatment preferences among black and white patients with end-stage renal disease. *Qual Life Res* 13: 1129–1137, 2004
28. Diaz-Buxo JA, Lowrie EG, Lew NL, Zhang H, Lazarus JM: Quality-of-life evaluation using Short Form 36: Comparison in hemodialysis and peritoneal dialysis patients. *Am J Kidney Dis* 35: 293–300, 2000
29. Kutner NG: Assessing end-stage renal disease patients' functioning and well-being: Measurement approaches and implications for clinical practice. *Am J Kidney Dis* 24: 321–333, 1994
30. Colman S, Bross R, Benner D, Chow J, Braglia A, Arzaghi J, Dennis J, Martinez L, Baldo DB, Agarwal V, Trundnowski T, Zitterkoph J, Martinez B, Khawar OS, Kalantar-Zadeh K: The Nutritional and Inflammatory Evaluation in Dialysis patients (NIED) study: Overview of the NIED study and the role of dietitians. *J Ren Nutr* 15: 231–243, 2005
31. Noori N, Kalantar-Zadeh K, Kovesdy CP, Murali SB, Bross R, Nissenson AR, Kopple JD: Dietary potassium intake and mortality in long-term hemodialysis patients. *Am J Kidney Dis* 56: 338–347, 2010
32. Shantouf RS, Budoff MJ, Ahmadi N, Ghaffari A, Flores F, Gopal A, Noori N, Jing J, Kovesdy CP, Kalantar-Zadeh K: Total and individual coronary artery calcium scores as independent predictors of mortality in hemodialysis patients. *Am J Nephrol* 31: 419–425, 2010
33. Kalantar-Zadeh K, Kuwae N, Wu DY, Shantouf RS, Fouque D, Anker SD, Block G, Kopple JD: Associations of body fat and its changes over time with quality of life and prospective mortality in hemodialysis patients. *Am J Clin Nutr* 83: 202–210, 2006
34. Fried L, Bernardini J, Piraino B: Charlson comorbidity index as a predictor of outcomes in incident peritoneal dialysis patients. *Am J Kidney Dis* 37: 337–342, 2001
35. Beddhu S, Bruns FJ, Saul M, Seddon P, Zeidel ML: A simple comorbidity scale predicts clinical outcomes and costs in dialysis patients. *Am J Med* 108: 609–613, 2000
36. McHorney CA, Ware JE Jr, Raczek AE: The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 31: 247–263, 1993
37. Nelson EE, Hong CD, Pesce AL, Singh S, Pollak VE: Anthropometric norms for the dialysis population. *Am J Kidney Dis* 16: 32–37, 1990
38. Williams AJ, McArley A: Body composition, treatment time, and outcome in hemodialysis patients. *J Ren Nutr* 9: 157–162, 1999
39. Kalantar-Zadeh K, Dunne E, Nixon K, Kahn K, Lee GH, Kleiner M, Luft FC: Near infra-red interactance for nutritional

assessment of dialysis patients. *Nephrol Dial Transplant* 14: 169–175, 1999
40. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR: Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *N Engl J Med* 347: 1557–1565, 2002
41. Erbagci AB, Tarakcioglu M, Aksoy M, Kocabas R, Nacak M, Aynacioglu AS, Sivrikoz C: Diagnostic value of CRP and Lp(a) in coronary heart disease. *Acta Cardiol* 57: 197–204, 2002
42. Pecoits-Filho R, Barany P, Lindholm B, Heimburger O, Stenvinkel P: Interleukin-6 is an independent predictor of mortality in patients starting dialysis treatment. *Nephrol Dial Transplant* 17: 1684–1688, 2002
43. Stenvinkel P, Heimburger O, Jogestrand T: Elevated interleukin-6 predicts progressive carotid artery atherosclerosis in dialysis patients: association with *Chlamydia pneumoniae* seropositivity. *Am J Kidney Dis* 39: 274–282, 2002
44. Beutler B, Cerami A: The biology of cachectin/TNF: A primary mediator of host response. *Annu Rev Immunol* 7: 625–655, 1989
45. Durrleman S, Simon R: Flexible regression models with cubic splines. *Stat Med* 8: 551–561, 1989
46. Lowrie EG, Lew NL: Commonly measured laboratory variables in hemodialysis patients: Relationships among them and to death risk. *Semin Nephrol* 12: 276–283, 1992
47. Ohri-Vachaspati P, Sehgal AR: Quality of life implications of inadequate protein nutrition among hemodialysis patients. *J Ren Nutr* 9: 9–13, 1999
48. Lowrie EG, Lepain N, Lazarus JM: *Evaluation of the SF-36 Among Hemodialysis Patients*, Lexington MA, Fresenius Medical Care, 1997
49. Kalantar-Zadeh K, Kopple JD, Kilpatrick RD, McAllister CJ, Shinaberger CS, Gjertson DW, Greenland S: Association of morbid obesity and weight change over time with cardiovascular survival in hemodialysis population. *Am J Kidney Dis* 46: 489–500, 2005
50. Kovesdy CP, Anderson JE, Kalantar-Zadeh K: Paradoxical association between body mass index and mortality in men with CKD not yet on dialysis. *Am J Kidney Dis* 49:581–591, 2007
51. Leavey SF, McCullough K, Hecking E, Goodkin D, Port FK, Young EW: Body mass index and mortality in 'healthier' as compared with 'sicker' haemodialysis patients: Results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant* 16: 2386–2394, 2001
52. Goller JL, McMahon JM, Rutledge C, Walker RG, Wood SE: Dialysis adequacy and self-reported health status in a group of CAPD patients. *Adv Perit Dial* 13: 128–133, 1997
53. McClellan WM, Anson C, Birkeli K, Tuttle E: Functional status and quality of life: predictors of early mortality among patients entering treatment for end stage renal disease. *J Clin Epidemiol* 44: 83–89, 1991
54. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Alleyne S, Cruz I, Veis JH: Multiple measurements of depression predict mortality in a longitudinal study of chronic hemodialysis outpatients. *Kidney Int* 57: 2093–2098, 2000
55. Hedayati SS, Minhajuddin AT, Afshar M, Toto RD, Trivedi MH, Rush AJ: Association between major depressive episodes in patients with chronic kidney disease and initiation of dialysis, hospitalization, or death. *JAMA* 303: 1946–1953, 2010
56. Jones CA, McQuillan GM, Kusek JW, Eberhardt MS, Herman WH, Coresh J, Salive M, Jones CP, Agodoa LY: Serum creatinine levels in the US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 32: 992–999, 1998
57. Abbott KC, Reynolds JC, Trespalacios FC, Cruess D, Agodoa LY: Survival by time of day of hemodialysis: analysis of United States Renal Data System Dialysis Morbidity and Mortality Waves III/IV. *Am J Kidney Dis* 41: 796–806, 2003
58. Kalantar-Zadeh K, Kovesdy CP, Derose SF, Horwich TB, Fonarow GC: Racial and survival paradoxes in chronic kidney disease. *Nat Clin Pract Nephrol* 3: 493–506, 2007
59. Agodoa L, Norris K, Pugsley D: The disproportionate burden of kidney disease in those who can least afford it. *Kidney Int Suppl*: S1–S3, 2005
60. Kovesdy CP, Anderson JE, Derose SF, Kalantar-Zadeh K: Outcomes associated with race in males with nondialysis-dependent chronic kidney disease. *Clin J Am Soc Nephrol* 4: 973–978, 2009
61. Xue JL, Eggers PW, Agodoa LY, Foley RN, Collins AJ: Longitudinal study of racial and ethnic differences in developing end-stage renal disease among aged medicare beneficiaries. *J Am Soc Nephrol* 18: 1299–1306, 2007
62. Fischer MJ, Kimmel PL, Greene T, Gassman JJ, Wang X, Brooks DH, Charleston J, Dowie D, Thornley-Brown D, Cooper LA, Bruce MA, Kusek JW, Norris KC, Lash JP: Sociodemographic factors contribute to the depressive affect among African Americans with chronic kidney disease. *Kidney Int* 77: 1010–1019, 2010

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