

Original Article

Association between quality of life and anxiety, depression, physical activity and physical performance in maintenance hemodialysis patients

Yi-Nan Li ^{a,b}, Bryan Shapiro ^a, Jun Chul Kim ^{a,c}, Min Zhang ^{a,d}, Janos Porszasz ^e,
Rachelle Bross ^{f,g}, Usama Feroze ^h, Rajeev Upreti ⁱ, David Martin ^{j,n},
Kamyar Kalantar-Zadeh ^{g,k,l}, Joel David Kopple ^{a,l,m,*}

^a Division of Nephrology and Hypertension, Los Angeles Biomedical Research Institute at Harbor – UCLA Medical Center, Torrance, CA 90502, USA

^b Department of Nephrology, The First Affiliated Hospital of Xiamen University, Xiamen, Fujian 361003, China

^c Division of Nephrology, CHA Gumi Medical Center, CHA University, Kyungsangbuk-do 730728, South Korea

^d Division of Nephrology, Tianjin Union Medical Center, Tianjin 300121, China

^e Rehabilitation Clinical Trials Center, Division of Respiratory & Critical Care Physiology & Medicine, Los Angeles Biomedical Research Institute at Harbor – UCLA Medical Center, Torrance, CA 90502, USA

^f UCLA Clinical and Translational Science Institute, Los Angeles Biomedical Research Institute at Harbor – UCLA Medical Center, Torrance, CA 90502, USA

^g Harold Simmons Center for Kidney Disease Research and Epidemiology, Los Angeles Biomedical Research Institute at Harbor – UCLA Medical Center, Torrance, CA 90502, USA

^h George Washington University/Inova Fairfax Hospital Psychosomatic Fellowship Program, Washington, DC 20052, USA

ⁱ Max Super Specialty Hospital, New Delhi, Delhi 110092, India

^j Division of Psychology, Department of Psychiatry, Harbor – UCLA Medical Center, Torrance, CA 90502, USA

^k Division of Nephrology and Hypertension, University of California at Irvine, Irvine, CA 92697, USA

^l UCLA Fielding School of Public Health, Los Angeles, CA 90095, USA

^m David Geffen School of Medicine at UCLA, Los Angeles, CA 90502, USA

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Abstract

Objective: Maintenance hemodialysis (MHD) patients often have impaired quality of life (QOL), anxiety, depression, and reduced daily physical activity (DPA) and physical performance. The contributions of these latter factors to reduced QOL in MHD are poorly understood. We examined the association of QOL with anxiety, depression, DPA, and physical performance.

* Corresponding author. Los Angeles Biomedical Research Institute, Harbor – UCLA Medical Center, 1124 West Carson Street, Torrance, CA 90502, USA.

E-mail address: jkopple@labiomed.org (J.D. Kopple).

ⁿ Current address: AIDS, American Psychological Association, Washington, DC 20052, US.

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Methods: Seventy-two relatively healthy adult MHD patients, vintage ≥ 6 months, and 39 normals of similar age range and gender distribution were studied. QOL was assessed using the Kidney Disease Quality of Life-Short Form (KDQOL-SF). Anxiety and depression were each evaluated with two questionnaires. DPA and physical performance were assessed with a physical activity monitor, Human Activity Profile, and 6-minute walk, sit-to-stand, and stair-climbing tests.

Results: Most KDQOL components were reduced in MHD patients versus normals. KDQOL components in patients were commonly inversely correlated with measures of anxiety and depression ($P < 0.05$) and were more reduced in patients with both anxiety and depression. KDQOL was often impaired in patients with either anxiety or depression. However, most KDQOL scores did not differ between patients and normals without anxiety or depression. DPA, Human Activity Profile, and physical performance often correlated with KDQOL scores in adjusted models, but after further adjustment for anxiety and depression, DPA, Human Activity Profile, and physical performance correlated less frequently with KDQOL scores. This reduction in significant correlations after adjustment for anxiety and depression was particularly pronounced for the association between KDQOL and DPA.

Conclusion: In relatively healthy MHD patients, KDQOL scores are usually decreased in those with anxiety and/or depression but are usually normal in those without anxiety or depression. Lower DPA in MHD patients with reduced KDQOL scores often appears to be associated with anxiety and depression. The relationship between QOL and physical performance appears to be less influenced by anxiety and/or depression. These data suggest that treatment of anxiety and depression in MHD patients may improve their QOL, DPA, and possibly physical performance.

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Keywords: Quality of life; Anxiety; Depression; Kidney disease; Kidney failure

Introduction

Maintenance hemodialysis (MHD) patients frequently experience reduced quality of life (QOL) and have decreased daily physical activity (DPA) and physical performance.^{1–4} Many reports indicate that anxiety and/or depression are associated with a reduction in their QOL and with reduced DPA and physical performance.^{3,5–9} An important question is whether the direct relation between QOL scores and DPA and physical performance may be mediated by anxiety or depression in MHD patients. This question may have important clinical implications, because reduced DPA and physical performance as well as depression are associated with increased hospitalizations and enhanced mortality rates.^{10–15} As part of ongoing studies of the effects of altered physical capacity in MHD patients, we conducted a cross-sectional study of the frequency and severity of impaired QOL scores and their relationship with DPA and physical performance. We assessed the extent to which anxiety and depression in MHD patients may account for both their impaired QOL and to the interaction of DPA and physical performance with QOL. A cohort of relatively healthy MHD patients was selected for study in order to minimize the confounding effects of comorbid conditions, which occur commonly in these individuals and can lower their QOL.

Methods

Study methods have been described in detail previously^{2,4} and are summarized here.

Study design and participants

Inclusion criteria included the following: (1) age, ≥ 18 years; (2) no hospitalizations during the previous 3 months, except for vascular access repair; (3) no amputations or prostheses in lower extremities; (4) able to ambulate and ability to complete all study protocol tests; and (5) likelihood of good compliance to the protocol. Exclusion criteria included the following: (1) acute infectious or other inflammatory illnesses; (2) current heart failure, lung failure, severe liver disease, or active cancer except basal cell carcinoma; and (3) myocardial infarction or angina pectoris within the past 12 months. Almost all MHD patients were recruited from two DaVita Corporation-owned chronic dialysis centers in the South Bay area of Los Angeles County. At the time of study, these two centers were treating 335 MHD patients. Normal controls were of similar age range and gender distribution and had no known acute or chronic systemic illnesses or disorders of the extremities that could impede mobility or other physical activities. The normal controls denied participating in regular sports activities.

This was a cross-sectional, non-interventional study. All participants made one visit to the Outpatient Clinical Translational Research Center (for hemodialysis patients, on the day after a hemodialysis treatment) where they underwent a 6-minute walk test (6-MWT), and sit-to-stand and stair-climbing tests, and filled out questionnaires. Collection and processing of blood specimens have been described previously.⁴ The study was approved by the institutional review boards of the Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center. All participants signed informed consent statements.

QOL assessment

QOL was assessed in MHD patients and normal controls using the Kidney Disease and Quality of Life-Short Form (KDQOL-SF) (KDQOL Working Group, RAND Corporation, Santa Monica, CA, USA).¹⁶ The questionnaire consists of the generic 36-Item Short Form Health Survey (SF-36) as well as 11 multi-item scales focusing on quality of life issues specific to patients with kidney disease (end-stage renal disease (ESRD)-targeted areas).^{17,18} Thirty-five items of the SF-36 are organized into 8 quality of life dimensions. One item, self-reported health transition, is not considered relevant to these 8 dimensions. The SF-36 produces 2 summary measures of physical and mental health: the physical health composite score and mental health composite score.¹⁹ There are 11 items comprising the ESRD-targeted areas of the KDQOL. KDQOL scales are assessed quantitatively—a score between 0 and 100 is calculated with higher scores reflecting better health and well-being. In MHD patients, the KDQOL was administered on the same day as the physical performance tests after completion of these physical performance tests.

Anxiety and depression questionnaires

Participants completed the Beck Anxiety Inventory (BAI), the Beck Depression Inventory (BDI)-II, and the Hospital Anxiety and Depression Scale (HADS-anxiety and HADS-depression).²⁰ The BAI is a 21-item self-report inventory for assessing severity of clinical anxiety. Respondents rate each item on a 4-point scale ranging from 0 (“Not at all”) to 3 (“I could barely stand it”) with regard to their anxiety-related symptoms during the past week. The BAI is scored by summing the severity ratings across all 21

items; total scores can range from 0 to 63. Scores are considered to indicate the following: 0–7, minimal anxiety; 8–15, mild anxiety; 16–25, moderate anxiety; 26–63, severe anxiety. Similarly, the BDI is a 21-item inventory to measure severity of depressive symptoms.²¹ All items are rated from 0 to 3, and respondents are asked to rate their depressive symptoms during the previous two weeks. The BDI total scores can range from 0 to 63. BDI scores are considered to indicate the following: 0–13, minimal depression; 14–19, mild depression; 20–28, moderate depression; 29–63, severe depression. The HADS-anxiety and HADS-depression were also used to assess symptoms of anxiety and depression.²² This questionnaire comprises 14 items divided into two parts for rating anxiety and depression. Each item has a 4-response category range from 0 to 3. The scale ranges from 0 to 21 for both depression and anxiety. For both anxiety and depression scores, 0–7 is considered normal, 8–10 borderline abnormal, and 11–21 abnormal.²²

DPA

DPA was assessed with a physical activity monitor (Actigraph GT3X+ Activity Monitor®, Actigraph, Fort Walton Beach, FL, USA) that was strapped to the lateral side of the pelvis on the non-dominant side of the hips.⁴ The activity monitor was worn continuously for 10 days, including nights, except when participants took baths, showered, or swam. Physical activity levels were calculated during the last 7 full days of activity. The average daily vector magnitude for DPA was calculated as the square root of the sum of the squares of the movement readings from each of the three dimensional axes. We classified activity level as sleep or marked physical inactivity (i.e., vector magnitude of 0–500), light physical activity (vector magnitude of 501–2689), and moderate or greater physical activity (vector magnitude ≥ 2690).^{4,23}

All participants completed the Human Activity Profile questionnaire, in which the person describes how frequently he/she performs physical activities requiring various amounts of energy expenditure and intensities of physical performance.²⁴ The Human Activity Profile is calculated as a maximum activity score which indicates the value of the highest oxygen-demanding activity for each type of activity listed in the questionnaire that the subject states that he/she still performs. The Human Activity Profile adjusted activity score is the respondent's maximum

activity score minus the number of activities that the person indicates that he/she can no longer perform. These scores are considered to estimate, respectively, their highest level of energy expenditure (the maximum activity score) and average level of energy expenditure (the adjusted activity score).⁴

Physical performance tests

The three physical performance tests were conducted in the following order: 6-MWT, sit-to-stand, and stair-climbing test. The 6-MWT measured the distance (meters) that participants walked back and forth along an 80-foot (24.4 m) horizontal corridor during a 6-min period of time while they were repetitively encouraged to walk fast. Study participants could slow down, rest, or even stop walking if they wished, but the 6-min timer was kept running. In the sit-to-stand test, participants rose from a fully seated position to full standing and then returned to the starting fully seated position as frequently as possible, with encouragement, during a 30s period. This test measured the number of sit-to-stand cycles completed in 30 s. The stair-climbing test measured the time (seconds) for participants to climb 22 steps as fast as possible, again with encouragement, without running, jumping, or skipping steps. The 6-MWT was performed once, the sit-to-stand and stair-climbing tests were each performed twice at 5-min intervals, and the better of the two scores was selected for analysis. Participants underwent these physical performance tests after they received a detailed explanation and demonstration of each test by a trained examiner.

Statistical analyses

Statistical analyses were performed using STATA 12 statistical software (StataCorp LP, College Station, TX, USA). Variables were expressed as mean \pm standard deviation (SD) and were compared between MHD and normal control group by a Student's *t*-test for independent samples. Categorical variables of \geq three groups were compared using a one-way analysis of variance (ANOVA). Comparisons within multiple groups were made using a Tukey's honest significant difference test for pairwise comparisons. Comparisons between two groups were made using a 2-tailed *t*-test. Four covariates were adjusted for in case-mix analyses: age, gender, presence of diabetes mellitus, and dialysis vintage. In some cases, analyses were further adjusted

for anxiety and depression status. A *P*-value of <0.05 was considered to indicate statistical significance.

Results

Participant characteristics

MHD patients were 52 ± 13 years, 32% female, and 40% diabetic, with a dialysis vintage of 54 ± 45 months. Normal controls were 51 ± 13 years and 41% female. Seven MHD patients had a history of depression, and there was no history of schizophrenia in either group. The racial/ethnic distribution was similar in both groups, but there was a trend for the MHD patients to have less formal schooling. Body mass index in MHD patients was (27.8 ± 5.8) kg/m² and did not differ significantly from normal controls ((27.0 ± 3.9) kg/m²). Serum albumin in both groups was 4.1 g/dl. Blood hemoglobin in MHD patients was (11.2 ± 0.8) g/dl and (13.8 ± 1.3) g/dl in normal controls, and serum creatinine was (10.5 ± 4.3) mg/dl predialysis in MHD patients as compared to (0.8 ± 0.2) g/dl in normals. The Charlson comorbidity score was 1.7 ± 1.1 in normal controls and 5.7 ± 2.7 in MHD patients. This number includes two points for kidney failure in each MHD patient plus two additional points for MHD patients who have diabetes mellitus.^{25,26} Comparisons between these 72 MHD patients and 39 normal controls have been described in greater detail in previous reports.^{2,4}

Several measurements of DPA, assessed by the Actigraph[®] and Human Activity Profile maximum activity score (MAS), and adjusted activity score (AAS), and the 6-MWT, sit-to-stand, and stair-climbing test results were reduced in MHD patients as compared to normal controls ($P < 0.0001$ for each comparison).⁴ BAI, BDI, and HADS scores indicated increased frequency and severity of anxiety and depression in MHD patients.²

KDQOL scores

The KDQOL SF-36 component scores were significantly lower ($P < 0.05$) in MHD patients as compared to normal controls, except for two components—emotional well-being and mental health composite score, which did not differ between the two groups (Table 1). The KDQOL ESRD-targeted component scores were also significantly lower in MHD patients, except for quality of social interaction and social support (Table 1).

Table 1
KDQOL component scores in MHD patients (versus normal controls) and their correlations with anxiety and depression scores.

KDQOL components	MHD patients (n = 72)	Normal controls (n = 39)	Correlations with KDQOL in MHD patients			
			BAI (n = 72)	BDI (n = 72)	HADS-Anxiety (n = 72)	HADS-Depression (n = 72)
ESRD-targeted areas						
Symptom problem list	79.9 ± 16.3 ^a	95.8 ± 4.4	-0.59 ^{b,c} (-0.56 ^c)	-0.47 ^c (-0.42 ^c)	-0.46 ^c (-0.42 ^c)	-0.41 ^c (-0.40 ^c)
Effects of kidney disease	65.0 ± 25.9	–	-0.35 ^c (-0.35 ^c)	-0.67 ^c (-0.58 ^c)	-0.46 ^c (-0.42 ^c)	-0.54 ^c (-0.52 ^c)
Burden of kidney disease	43.2 ± 27.6	–	-0.22 (-0.21)	-0.48 ^c (-0.41 ^c)	-0.44 ^c (-0.45 ^c)	-0.59 ^c (-0.58 ^c)
Work status	30.6 ± 38.0 ^a	82.1 ± 26.9	-0.08 (-0.01)	-0.21 (-0.14)	-0.18 (-0.10)	0.03 (0.06)
Cognitive function	82.2 ± 18.2 ^a	91.3 ± 10.7	-0.38 ^c (-0.33 ^c)	-0.48 ^c (-0.39 ^c)	-0.57 ^c (-0.52 ^c)	-0.55 ^c (-0.54 ^c)
Quality of social interaction	82.1 ± 18.2	87.9 ± 11.7	-0.27 ^d (-0.24 ^d)	-0.40 ^c (-0.32 ^c)	-0.45 ^c (-0.39 ^c)	-0.37 ^c (-0.34 ^c)
Sexual function ^e	77.9 ± 29.3 ^a	95.3 ± 10.3	-0.03 (-0.19)	-0.62 ^c (-0.59 ^c)	-0.32 (-0.36)	-0.42 ^d (-0.38)
Sleep	60.6 ± 21.9 ^a	78.3 ± 13.8	-0.56 ^c (-0.58 ^c)	-0.59 ^c (-0.60 ^c)	-0.46 ^c (-0.48 ^c)	-0.35 ^c (-0.33 ^c)
Social support	81.5 ± 26.5	86.9 ± 14.3	-0.28 ^d (-0.32 ^c)	-0.46 ^c (-0.51 ^c)	-0.31 ^c (-0.34 ^c)	-0.35 ^c (-0.35 ^c)
Dialysis staff encouragement	76.2 ± 23.4	–	-0.25 ^d (-0.22)	-0.34 ^c (-0.33 ^c)	-0.20 (-0.15)	-0.26 ^d (-0.27 ^d)
Patient satisfaction	73.8 ± 23.4	–	-0.24 ^d (-0.24 ^d)	-0.35 ^c (-0.35 ^c)	-0.33 (-0.33 ^c)	-0.35 ^c (-0.35 ^c)
SF-36 composite scores						
Physical health composite score	40.4 ± 9.5 ^a	53.0 ± 4.8	-0.42 ^c (-0.40 ^c)	-0.30 ^d (-0.22)	-0.29 ^d (-0.28 ^d)	-0.27 ^d (-0.26 ^d)
Mental health composite score	50.6 ± 10.2	53.7 ± 6.9	-0.37 ^c (-0.34 ^c)	-0.60 ^c (-0.58 ^c)	-0.62 ^c (-0.62 ^c)	-0.56 ^c (-0.56 ^c)
Role physical	44.8 ± 43.2 ^a	90.4 ± 23.4	-0.20 (-0.18)	-0.29 ^d (-0.22)	-0.24 ^d (-0.21)	-0.28 ^d (-0.25 ^d)
Pain	74.4 ± 26.6 ^f	86.0 ± 20.7	-0.48 ^c (-0.44 ^c)	-0.30 ^d (-0.22)	-0.35 ^c (-0.30 ^c)	-0.19 (-0.16)
General health	51.3 ± 20.6 ^a	75.6 ± 15.9	-0.34 ^c (-0.28 ^d)	-0.54 ^c (-0.48 ^c)	-0.48 ^c (-0.45 ^c)	-0.41 ^c (-0.39 ^c)
Emotional well-being	79.1 ± 17.5	82.6 ± 15.9	-0.46 ^c (-0.42 ^c)	-0.69 ^c (-0.66 ^c)	-0.67 ^c (-0.64 ^c)	-0.64 ^c (-0.64 ^c)
Role emotional	70.8 ± 41.8 ^a	93.2 ± 21.9	-0.20 (-0.18)	-0.39 ^c (-0.33 ^c)	-0.39 ^c (-0.37 ^c)	-0.37 ^c (-0.34 ^c)
Social function	71.9 ± 24.7 ^a	91.0 ± 12.5	-0.47 ^c (-0.44 ^c)	-0.57 ^c (-0.56 ^c)	-0.60 ^c (-0.59 ^c)	-0.57 ^c (-0.57 ^c)
Energy/fatigue	56.7 ± 22.2 ^a	74.4 ± 14.3	-0.47 ^c (-0.45 ^c)	-0.53 ^c (-0.51 ^c)	-0.50 ^c (-0.50 ^c)	-0.54 ^c (-0.54 ^c)

Data are presented as mean ± standard deviation.

KDQOL: Kidney Disease and Quality of Life; MHD: maintenance hemodialysis; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; HADS: Hospital Anxiety and Depression Scale; ESRD: end-stage renal disease; SF-36: 36-Item Short Form Health Survey.

^a $P < 0.01$ vs. normal controls as compared by a student's t -test for independent samples.

^bCorrelation coefficients not in parentheses are unadjusted. Correlation coefficients in parentheses are adjusted for age, gender, presence of diabetes mellitus, and dialysis vintage.

^c $P < 0.01$, ^d $0.01 \leq P < 0.05$ in correlations between KDQOL component score and anxiety or depression score in MHD patients.

^e $n = 30$ and $n = 24$ respondents for sexual function component in MHD patients and normal controls, respectively.

^f $0.01 \leq P < 0.05$ vs. normal controls as compared by a student's t -test for independent samples.

Association of anxiety and depression scores with KDQOL

The BAI, BDI, HADS-anxiety, and HADS-depression scores were significantly and inversely correlated with almost every KDQOL, ESRD and SF-36 component score in both unadjusted and case-mix adjusted analyses (Table 1). As an example, the scores from the above anxiety and depression questionnaires were inversely correlated ($P < 0.05$) with the physical health composite score and mental health composite score, where a lower physical health composite score or mental health composite score indicated a poorer quality of life score. The only exception was the correlation of the BDI score with the physical health composite score which was significant in unadjusted models but significant only at $0.05 < P < 0.10$ with case-mix adjustment (Table 1).

A one-way ANOVA compared KDQOL scores among MHD patients who exhibited anxiety, depression, both anxiety and depression, or neither anxiety nor depression, as determined by their BAI and BDI scores (Table 2). The diagnosis of anxiety was made when their BAI score was ≥ 8 , and the diagnosis of depression was made when their BDI score was ≥ 14 . Analyses were adjusted for age, gender, diabetes, and dialysis vintage. MHD patients without either anxiety or depression had significantly higher (more normal) scores for many KDQOL and SF-36 components than MHD patients with both anxiety and depression (Table 2). Patients without anxiety or depression not uncommonly had significantly higher KDQOL or SF-36 scores as compared to patients with either anxiety or depression. The MHD patients with both anxiety and depression commonly had lower scores than any of the other three groups of patients. Significantly lower scores in patients

Table 2
KDQOL component scores according to anxiety and depression status in MHD patients and normal controls.

Items	MHD patients A–D–	MHD patients A+D–	MHD patients A–D+	MHD patients A+D+	<i>P</i> -value among MHD patients ^a	Normal controls A–D–
<i>n</i> (male/female)	30 (18/12)	14 (8/6)	11 (10/1)	17 (13/4)	0.182	36 (20/16)
Age, years	50.3 ± 13.8	54.5 ± 10.4	52.8 ± 12.6	53.6 ± 14.0	0.726	50.3 ± 12.6
Diabetic, %	23	50	36	35	0.037	0
ESRD-targeted areas						
Effects of kidney disease	76.4 ± 20.9 ^b	75.7 ± 17.7 ^c	58.2 ± 28.5	40.3 ± 20.1 ^{b,c}	0.002	
Burden of kidney disease	54.7 ± 28.5 ^{b,c}	50.0 ± 21.9	27.3 ± 19.0 ^b	27.6 ± 24.0 ^c	0.025	
Dialysis staff encouragement	80.0 ± 22.2	85.7 ± 20.7	80.7 ± 18.8	58.7 ± 22.9	0.090	
Patient satisfaction	79.4 ± 17.3	80.9 ± 23.5	77.3 ± 27.2	55.9 ± 22.8	0.570	
Symptom problem list	89.5 ± 9.6 ^{b,c}	74.1 ± 10.3 ^b	87.7 ± 9.8 ^d	62.5 ± 17.3 ^{c,d}	0.003	96.3 ± 4.1
Work status	35.0 ± 43.8	21.4 ± 32.3	31.8 ± 40.5	29.4 ± 30.9	0.963	81.9 ± 27.1 ^e
Cognitive function	93.6 ± 10.0 ^{b,c,d}	78.6 ± 15.5 ^b	75.8 ± 24.5 ^c	69.4 ± 16.3 ^d	0.015	92.2 ± 10.1
Quality of social interaction	89.6 ± 12.2	81.9 ± 18.6	83.0 ± 19.4	68.6 ± 19.8	0.361	88.1 ± 11.1
Sexual function ^f	89.3 ± 18.3	79.7 ± 24.9	50.0 ± 57.7	62.5 ± 10.2	0.090	95.5 ± 10.6
Sleep	72.3 ± 17.3 ^b	63.0 ± 10.7 ^c	62.7 ± 22.9 ^d	36.5 ± 16.5 ^{b,c,d}	0.002	79.0 ± 13.8
Social support	85.6 ± 23.9	94.1 ± 15.4	80.4 ± 26.7	64.8 ± 31.2	0.064	86.7 ± 14.7
Overall health	68.3 ± 18.2 ^b	67.1 ± 19.0	60.9 ± 23.9	50.0 ± 10.0 ^b	0.022	81.1 ± 12.6
SF-36 composite scores						
Physical health composite score	43.6 ± 8.6	38.4 ± 7.3	44.6 ± 10.2	33.7 ± 8.8	0.308	53.3 ± 4.8 ^e
Mental health composite score	56.6 ± 5.5 ^{b,c}	50.6 ± 7.1 ^d	45.7 ± 10.5 ^b	43.4 ± 12.4 ^{c,d}	0.008	53.9 ± 6.8
Role physical	61.7 ± 40.3	44.6 ± 42.9	38.6 ± 49.2	19.1 ± 32.5	0.535	91.0 ± 23.3
Pain	85.7 ± 17.3	63.4 ± 18.6	83.9 ± 29.8	57.4 ± 32.4	0.228	86.0 ± 20.7
General health	56.3 ± 20.0	57.9 ± 15.5	55.0 ± 19.4	34.7 ± 18.3	0.140	76.5 ± 15.5 ^e
Emotional well-being	89.1 ± 8.8 ^{b,c}	80.9 ± 11.7 ^d	78.5 ± 16.0 ^{b,d}	60.6 ± 20.0 ^{c,d}	0.001	83.3 ± 15.5
Role emotional	91.1 ± 26.2	66.7 ± 45.3	42.4 ± 44.9	56.9 ± 45.3	0.968	92.6 ± 22.7
Social function	85.4 ± 20.8 ^{b,c}	66.1 ± 13.4 ^b	69.3 ± 28.2	54.4 ± 24.2 ^c	0.004	91.7 ± 12.0
Energy/fatigue	68.0 ± 19.7 ^b	54.6 ± 14.2 ^c	62.3 ± 21.8 ^d	35.3 ± 16.5 ^{b,c,d}	0.014	74.6 ± 14.5

Data are presented as mean ± standard deviation.

KDQOL: Kidney Disease and Quality of Life; MHD: maintenance hemodialysis; ESRD: end-stage renal disease; SF-36: 36-Item Short Form Health Survey. A–D– means the subjects displaying neither anxiety nor depression, A+D+ means those displaying anxiety and depression, A⁺D– means those displaying anxiety but not depression, and A–D+ means those displaying depression but not anxiety.

^aANOVA analyses comparing different MHD patient groups according to anxiety and depression status adjusted for age, gender, presence of diabetes, and dialysis vintage.

^{b,c,d}Pairwise comparisons (adjusted for age, gender, presence of diabetes, and dialysis vintage). Significantly different from values in other columns with the same superscript ($P < 0.05$), as determined by a Tukey's honest significant difference test for pairwise comparisons.

^eSignificantly different ($P < 0.05$) from MHD A–D– patients as determined by 2-tailed *t*-test adjusted for age, gender, and presence of diabetes.

^f $n = 14$, $n = 8$, $n = 4$, $n = 4$, and $n = 22$ respondents for sexual function in MHD A–D–, A+D–, A–D+, A+D+ patients and A–D– normal controls, respectively.

with both anxiety and depression were particularly common for effects of kidney disease, symptom/problem list, sleep, emotional well-being, energy/fatigue, and mental health composite score. The MHD patients who had neither anxiety nor depression displayed KDQOL scores that were rather similar to the normal controls who did not have anxiety or depression (Table 2); the scores of these MHD patients were significantly below normal scores only for work status, general health, and physical health composite score ($P < 0.05$).

Association of physical activity with KDQOL score

The 7-day average DPA levels in MHD patients, measured by the Actigraph[®] accelerometer, usually did

not correlate significantly with KDQOL ESRD-targeted or SF-36 scores after correlations were adjusted for age, gender, diabetes, or dialysis vintage (Table 3). Moreover, the associations that were statistically significant mostly became insignificant after further adjustment for the anxiety and depression scores, although the trends in the associations often persisted. In the fully adjusted model, only 7-day average DPA and the percent time spent in ≥ moderate physical activity correlated with the role-physical subscale; only percent time in moderate or greater physical activity correlated with physical health composite score, and percent time in sleep or marked inactivity correlated with dialysis staff encouragement and patient satisfaction (Table 3).

Table 3

Correlations between KDQOL components and daily physical activity measured by Actigraph[®] accelerometer and Human Activity Profile scores in MHD patients ($n = 72$).

KDQOL components	Actigraph [®] 7-day average DPA	Actigraph [®] Percent time in moderate or greater physical activity	Actigraph [®] Percent time in sleep or marked inactivity	Human Activity Profile Maximum activity score	Human Activity Profile Adjusted activity score
ESRD-targeted areas			Correlation Coefficients		
Symptom-problem list	0.07 (−0.05) ^a	0.14 (0.02)	−0.11 (0.00)	0.23 (0.12)	0.35 ^b (0.27 ^c)
Effects of kidney disease	0.12 (0.01)	0.15 (0.04)	−0.16 (−0.05)	0.25 ^c (0.14)	0.23 (0.13)
Burden of kidney disease	0.00 (−0.09)	0.08 (−0.01)	−0.01 (0.09)	0.16 (0.07)	0.15 (0.06)
Work status	0.14 (0.15)	0.16 (0.18)	−0.04 (−0.05)	0.06 (0.07)	0.20 (0.22)
Cognitive function	0.14 (0.04)	0.30 (0.22)	−0.14 (−0.05)	0.24 ^c (0.15)	0.25 ^c (0.17)
Quality of social interaction	0.09 (0.02)	0.13 (0.05)	−0.16 (−0.09)	0.04 (−0.05)	−0.04 (−0.14)
Sexual function ^d	−0.11 (−0.08)	−0.02 (−0.03)	0.16 (0.14)	0.14 (0.13)	0.23 (0.18)
Sleep	0.09 (−0.04)	0.10 (−0.04)	−0.16 (−0.04)	0.26 ^c (0.14)	0.21 (0.08)
Social support	0.26 ^c (0.21)	0.25 ^c (0.20)	−0.29 ^c (−0.24)	0.20 (0.13)	0.12 (0.05)
Dialysis staff encouragement	0.23 (0.17)	0.22 (0.15)	−0.30 ^c (−0.24 ^c)	0.16 (0.08)	0.13 (0.05)
Patient satisfaction	0.29 ^c (0.23)	0.27 ^c (0.21)	−0.37 ^b (−0.32 ^b)	0.21 (0.13)	0.15 (0.07)
SF-36 composite scores					
Physical health composite score	0.23 (0.19)	0.29 ^c (0.24 ^c)	−0.27 ^c (−0.23)	0.34 ^b (0.30 ^c)	0.46 ^b (0.42 ^b)
Mental health composite score	0.07 (−0.05)	0.18 (0.07)	−0.02 (0.12)	0.32 ^b (0.23)	0.30 ^c (0.21)
Role physical	0.34 ^b (0.29 ^c)	0.32 ^b (0.27 ^c)	−0.27 ^c (−0.22)	0.28 ^c (0.22)	0.36 ^b (0.31 ^c)
Pain	0.06 (0.00)	0.14 (0.08)	−0.15 (−0.09)	0.21 (0.15)	0.27 ^c (0.22)
General health	0.09 (0.03)	0.14 (0.07)	−0.13 (−0.07)	0.31 ^c (0.25 ^c)	0.34 ^b (0.29 ^c)
Emotional well-being	0.25 ^c (0.15)	0.27 ^c (0.17)	−0.24 ^c (−0.14)	0.40 ^b (0.33 ^b)	0.36 ^b (0.29 ^c)
Role emotional	0.16 (0.10)	0.26 ^c (0.20)	−0.08 (−0.01)	0.18 (0.11)	0.24 ^c (0.17)
Social function	0.05 (−0.05)	0.22 (0.13)	−0.07 (0.04)	0.23 (0.13)	0.27 ^c (0.19)
Energy/fatigue	0.19 (0.10)	0.24 (0.15)	−0.21 (−0.11)	0.43 ^b (0.37 ^b)	0.47 ^b (0.41 ^b)

KDQOL: Kidney Disease and Quality of Life; MHD: maintenance hemodialysis; DPA: daily physical activity; ESRD: end-stage renal disease; SF-36: 36-Item Short Form Health Survey.

^aCorrelation coefficients are adjusted for age, gender, presence of diabetes mellitus, and dialysis vintage.

^b $P < 0.01$, ^c $0.01 \leq P < 0.05$, ^d $n = 30$ respondents for sexual function component in maintenance hemodialysis patients.

Physical activity was also assessed by the Human Activity Profile questionnaire. Maximum activity scores correlated significantly with most of the SF-36 components, and adjusted activity scores correlated with all SF-36 components in analyses adjusted for age, gender, diabetes, and vintage; there were fewer significant correlations with KDQOL ESRD-targeted components (Table 3). After further adjustment for anxiety and depression, far fewer of these associations remained significant (Table 3). Perhaps the most prominent were the persistence of the correlations between maximum and adjusted activity scores and the physical health composite score, general health, emotional well-being and energy/fatigue.

Association of physical performance with KDQOL scores

The three physical performance tests correlated with few KDQOL-ESRD and SF-36 scores after adjustment for age, gender, diabetes, and vintage (Table 4). After further adjustment for anxiety and

depression, there were substantially fewer significant associations, although again the trends in the associations persisted. The one exception was the large number of sit-to-stand scores that correlated with SF-36 scores. The fewest correlations were observed with the stair-climbing test (Table 4).

Discussion

This study confirms previous reports that decreased QOL as well as anxiety, depression, lower daily physical activity (DPA), and reduced physical performance commonly occur in MHD patients.^{1,2,4,27–29} Our study also indicates that decreased QOL, reflected by low KDQOL scores, is significantly associated with anxiety, depression, and reduced DPA and physical performance. The present study provides evidence that anxiety and depression, as measured by BAI, BDI, and HADS, are associated with a decrease in physical, mental, and ESRD-targeted elements of QOL. These findings are consistent with several previous reports of an inverse association between anxiety

Table 4
Correlations between KDQOL components and physical performance tests in MHD patients.

KDQOL components	6-Minute walk test	Sit-to-stand test	Stair climbing test
ESRD-targeted areas	Correlation	Coefficients	
Symptom-problem list	0.07 (0.01) ^a	0.35 ^b (0.31 ^c)	0.10 (0.19)
Effects of kidney disease	0.09 (0.05)	0.21 (0.14)	0.02 (0.09)
Burden of kidney disease	0.06 (0.03)	0.25 ^c (0.19)	−0.01 (0.03)
Work status	0.22 (0.23)	−0.04 (−0.04)	0.12 (0.11)
Cognitive function	0.08 (0.04)	0.11 (0.13)	−0.08 (−0.04)
Quality of social interaction	−0.18 (−0.23)	−0.14 (−0.22)	0.18 (0.24)
Sexual function ^d	−0.06 (−0.05)	0.09 (0.09)	0.20 (0.14)
Sleep	0.00 (−0.08)	0.22 (0.14)	0.03 (0.11)
Social support	0.09 (0.06)	0.11 (0.06)	0.06 (0.10)
Dialysis staff encouragement	0.30 ^c (0.29 ^c)	0.23 (0.18)	−0.04 (−0.01)
Patient satisfaction	0.26 ^c (0.24 ^c)	0.14 (0.08)	−0.28 ^c (−0.26 ^c)
SF-36 composite scores			
Physical health composite score	0.26 ^c (0.24)	0.41 ^b (0.38 ^b)	0.08 (0.11)
Mental health composite score	0.21 (0.19)	0.15 (0.07)	−0.25 ^c (−0.23)
Role physical	0.34 ^b (0.32 ^b)	0.28 ^c (0.24 ^c)	−0.09 (−0.06)
Pain	0.21 (0.19)	0.34 ^b (0.30 ^c)	0.08 (0.12)
General health	0.19 (0.17)	0.29 ^c (0.25 ^c)	−0.09 (−0.06)
Emotional well-being	0.21 (0.18)	0.30 ^c (0.24 ^c)	−0.16 (−0.12)
Role emotional	0.39 ^b (0.38 ^b)	0.10 (0.05)	−0.17 (−0.14)
Social function	0.05 (0.00)	0.17 (0.10)	0.06 (0.12)
Energy/fatigue	0.27 ^c (0.25 ^c)	0.38 ^b (0.34 ^b)	−0.13 (−0.09)

KDQOL: Kidney Disease and Quality of Life; MHD: maintenance hemodialysis; ESRD: end-stage renal disease; SF-36: 36-Item Short Form Health Survey.

^aCorrelation coefficients are adjusted for age, gender, presence of diabetes mellitus, and dialysis vintage. Correlation coefficients in parentheses are further adjusted for anxiety and depression status.

^b $P < 0.01$, ^c $0.01 \leq P < 0.05$, ^d $n = 30$ respondents for sexual function component in maintenance hemodialysis patients.

and/or depression and QOL scores or overall perception of QOL in MHD patients.^{3,5,6}

The current study also indicates that MHD patients with both anxiety and depression display more impaired QOL scores than patients who have either anxiety or depression but not both (Table 2). The MHD patients who have either anxiety or depression, but not both, also tend to have more QOL scores that are lower than in the patients who have neither anxiety nor depression. Perhaps most strikingly, QOL scores of the patients without anxiety or depression are usually not different from normals. This finding suggests that anxiety and depression are major causes of the reduced QOL in MHD patients.

It should be remembered that the patients in this study were selected to be a relatively healthy cohort of MHD patients. Even the 23 out of 72 MHD patients who had diabetes mellitus were relatively healthy, as evidenced by their low Charlson comorbidity scores and the fact that they had to satisfy the inclusion and exclusion criteria in order to enter the study. These data are consistent with the thesis that anxiety and depression are major determinants of the QOL of relatively healthy MHD patients.

In the general adult population, there is a well-described positive correlation between DPA and health-related quality of life (HRQOL).^{30,31} Several studies have examined the relation between DPA or physical performance and QOL in MHD patients. One report from the dialysis outcomes and practice patterns study (DOPPS) found that higher levels of self-reported aerobic, but not strength-building, physical activity was positively associated with HRQOL.⁹ Almost all other reports examining the relationship between physical activity and HRQOL in MHD patients are interventional. In one study, MHD patients with low KDQOL physical health composite scores at baseline showed substantial improvement in KDQOL SF-36 component scores after 2 months of an individualized home exercise program involving strength, flexibility, and aerobic exercises.⁸ Similarly, a study of 14 Korean MHD patients reported improved QOL in these individuals after a 12-week aerobic exercise program.⁷ However, one study found no change in QOL, as determined by the KDQOL SF-36 physical health composite scores and mental health composite scores, after a 24-week intradialytic resistance training program.³²

The present study is the first to our knowledge to examine the cross-sectional associations between objectively measured DPA, using a mechanical instrument that measures physical activity, and QOL measures in MHD patients. DPA and physical performance measures correlated with several KDQOL components. These correlative relationships also often became weaker and statistically insignificant after adjustments for anxiety and depression; the exception to this being the sit-to-stand test. It is noteworthy that the Human Activity Profile scores correlated more closely with the physical performance tests than with accelerometer-measured DPA in our patients.⁴ This may reflect the more subjective nature of the Human Activity Profile, which is based upon the responder's estimates and memory.

These data support the contention that the associations between DPA and many QOL scores are mediated to a substantial degree by the presence of anxiety and depression. The foregoing considerations suggest the possibility that effective prevention or treatment of anxiety and depression in MHD patients may have major benefits for both their QOL and daily physical activity. Since depression, poor QOL scores, and low DPA are also associated with increased hospitalization and mortality rates in MHD patients,^{10–15} prevention and treatment of depression and perhaps anxiety might reduce morbidity and mortality in these individuals.

This study has several limitations. First, the sampling of different racial and ethnic groups was limited. The sample size was relatively small, although many significant associations were observed. The psychiatric evaluation was limited to anxiety and depression only, and this psychiatric assessment was restricted to the BDI, BAI, and the HADS scales. Among the strengths of this study, it is one of the few studies that have used a validated instrument to measure DPA, and DPA was measured for seven days. The fact that the MHD patients were relatively healthy facilitated our ability to separate the effects of end-stage kidney disease and MHD treatment on anxiety, depression, physical activity and performance, and quality of life from other common comorbid conditions that afflict MHD patients, such as protein-energy wasting, severe heart disease, strokes, or amputations. Finally, this study included for comparison a normal sedentary control group of similar age and gender ratio.

Conclusions

In relatively healthy MHD patients, anxiety and depression are usually associated with a lower quality

of life and to a lesser degree daily physical activity and physical performance. Among those MHD patients who do not have anxiety or depression by standard testing, quality of life scores appear to be normal. These observations suggest the possibility that treatment of anxiety and depression may improve quality of life, daily physical activity and some measures of physical performance in MHD patients.

Conflicts of interest

Joel D. Kopple serves on the Medical Advisory Board and has received consultant fees and stock from Nephroceuticals. He has received consultant fees or speaking fees from Fresenius Kabi and Chugai Pharmaceutical Co. All other authors of this manuscript declare no conflict of interest.

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