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## Relation Between Anxiety, Depression and Physical Activity and Performance in Maintenance Hemodialysis Patients

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### Abstract

**Objective**—Maintenance hemodialysis (MHD) patients have a high prevalence of anxiety and depression and decreased daily physical activity (DPA) and exercise capacity. Since affective disorders may affect DPA and physical performance, we investigated possible relationships between anxiety or depression and DPA and physical performance in relatively healthy MHD patients

**Design**—Cross-sectional cohort study

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**Setting**—UCLA Clinical and Translational Science Institute (CTSI) at Harbor-UCLA Medical Center

**Subjects**—72 relatively healthy MHD patients and 39 normal adults

**Intervention**—DPA was measured for seven days with an Actigraph Activity Monitor®. Physical performance was assessed using 6-minute walk (6-MWT), sit-to-stand (STS) and stair climbing tests. Subjects completed the Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (HADS)

**Main Outcome Measure**—Physical activity counts (expressed as vector magnitude), performance in 6-MWT, STS, and stair-climbing tests, and BAI, BDI and HADS scores

**Results**—Anxiety and depression by BAI and BDI were identified in 43% and 33% of MHD patients and 2.5% and 5% of normals ( $p < 0.0001$  for each comparison). MHD patients without anxiety or depression had decreased DPA and physical performance compared to normals, indicating that MHD patients have reduced DPA and physical performance independent of anxiety or depression. MHD patients with both anxiety and depression generally had the most impaired DPA and physical performance. Higher BAI and BDI scores were each associated with impaired physical performance. In fully-adjusted analyses, the average DPA in MHD patients was negatively correlated with the BDI ( $r = -0.33$ ,  $p = 0.01$ ) but not with the BAI. DPA on the day of hemodialysis ( $p = 0.01$ ), day after dialysis ( $p = 0.03$ ), and day two after dialysis ( $p = 0.03$ ) each correlated negatively with degree of depression by BDI. MHD patients displayed negative correlations between BAI and 6-MWT ( $p = 0.03$ ) and between BAI and STS ( $p = 0.04$ )

**Conclusions**—In relatively healthy adult MHD patients, anxiety and depression are common and are associated with impaired physical performance. There was a trend towards stronger negative associations between BDI scores and DPA than between BAI scores and DPA.

### Keywords

Hemodialysis; Physical performance; Daily physical activity; Anxiety; Depression; Protein-energy wasting

## INTRODUCTION

Daily physical activity (DPA) and physical performance are frequently diminished in maintenance hemodialysis (MHD) patients.<sup>1–3</sup> Most studies have not attempted to differentiate the effects of comorbid illnesses on DPA and physical performance in these patients. Anxiety and depression occur commonly in MHD patients.<sup>4–7</sup> Little is known about the relationship between the DPA, physical performance and symptoms of anxiety and depression in these individuals. We conducted this study to examine the association between anxiety, depression and DPA and physical performance in relatively healthy MHD patients. Clinically stable MHD patients underwent a cross-sectional study of the relationship between the presence and severity of anxiety or depression and their DPA and physical performance. This investigation was carried out as part of a long term effort to examine factors that may predispose to anxiety and depression and low levels of physical activity in MHD patients and interventions that might improve these conditions.

## METHODS

### Study population

Most of the methods employed in this study have been described in more detail previously.<sup>8</sup> Clinically stable MHD patients and sedentary normal adults of similar age range, gender distribution and educational levels were studied. Inclusion criteria included ages 18 years or older, no hospitalizations for the previous three months, except for vascular access repair in MHD patients, no amputations or prostheses in lower extremities, able to ambulate and ability to complete all study protocol tests, able to read in English or Spanish and, for MHD patients, MHD treatment thrice-weekly for at least six months. Exclusion criteria included acute infectious or other inflammatory illnesses, active cancer except for basal cell carcinoma, documented myocardial infarction or angina pectoris within the past 12 months, current heart or lung failure or severe liver disease, evidence for noncompliance or inability to give informed consent.

Normal controls had no known acute or chronic systemic illnesses or disorders of extremities that would impede motility or other physical activity. Very few normal subjects engaged in regular sports activities, the study was approved by the institutional review boards of Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center (HUMC), and all participants signed informed consent statements.

### Study design

This was a cross-sectional, non-interventional study. All participants made one visit to the Outpatient Clinical Translational Research Center (CTRC) at HUMC. MHD patients visited the CTRC the day after a hemodialysis treatment. Participants underwent body composition studies and then performed a 6-minute walk test (6-MWT), sit-to-stand (STS) test and stair-climbing test and filled out the questionnaires. In MHD patients, blood was obtained immediately before a routine mid-week hemodialysis, and measurements were performed in the DaVita central laboratory (DeLand, Florida). The blood test results for MHD patients were the values obtained monthly and averaged over the three months prior to obtaining the other study measurements. On the day of their CTRC visit, normal controls had blood drawn for a CBC and serum creatinine and albumin which were measured in the HUMC clinical laboratory. Blood pressure and respiratory and cardiac rates were measured before the physical performance tests were performed. No subject had obvious edema at the time of study. Lean body mass, fat mass and bone mass were measured by dual energy X-ray absorptiometry (DEXA, Hologic; model DXA Discovery A; Bedford, MA). Study participants were then instructed to wear the activity monitor (see below) continuously for 10 days except when showering, bathing or swimming. For all subjects, efforts were made to keep the following factors associated with the testing sessions constant: time of day, staff members administering the various tests, and location where tests were performed.

### Clinical Characteristics

The measured clinical characteristics of the patients included age, racial/ethnic/gender, educational level, diabetes, dialysis vintage. Data regarding patient's clinical history were

obtained by patient interviews and chart reviews. The methods for conducting other measurements have been described previously.<sup>8</sup>

### **Anxiety and Depression Questionnaires**

Subjects completed the Beck Anxiety Inventory (BAI) and Beck Depression Inventory-II (BDI), and the Hospital Anxiety and Depression Scale (HADS-A and HADS-D). The BAI is a 21-item self-report inventory for assessing severity of clinical anxiety<sup>9</sup>. Subjects 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 0–63. Scores were classified as follows: of 0–7, no anxiety; 8–15, mild anxiety; 16–25, moderate anxiety; 26–63, severe anxiety. The BDI is a 21-item inventory to measure severity of depressive symptoms.<sup>10</sup> All items are rated from 0–3, and respondents are asked to rate their depressive symptoms during the previous two weeks. The BDI is also scored by summing the severity ratings across all 21 items, and again, total scores can range from 0–63. BDI scores were classified as follows: 0–13, no depression; 14–19, mild depression; 20–28, moderate depression; 29–63, severe depression. The HADS-A and HADS-B are also used to assess symptoms of anxiety and depression.<sup>11</sup> This questionnaire comprises 14 items divided into two parts for rating of depression and anxiety. 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.<sup>11</sup>

### **Physical Performance**

Immediately after completing the body composition tests, study subjects underwent three physical performance tests, as previously described in more detail.<sup>8</sup> Tests were performed in the following order: 6-minute walk test (6-MWT), sit-to-stand (STS) test and stair-climbing test. The 6-MWT measured the distance (in meters) that participants walked back and forth, with encouragement, along an 80-foot (24.4 meters) flat surface corridor during a 6-minute period of time.<sup>8</sup> Study subjects could slow down if they desired, but the 6-minute timer kept running. No subject stopped walking during the 6-MWT.

For the STS test, participants were required to rise from a fully seated position to a full standing position and then return to the starting fully seated position as many times as possible, with encouragement, during a 30 second period.<sup>8</sup> Participants sat in the middle of a standard straight-back chair with arms, with their feet flat on the floor and with their arms crossed at the wrists and held against the chest. (Seat height = 44.5 cm/17.5 inches; seat wide = 44.5 cm/17.5 inches). The score is given as the number of sit-to-stand cycles completed during the 30 seconds. The stair-climbing time was measured on a staircase with a banister on the right side consisting of 22 steps. Participants were encouraged to climb the stairs as fast as possible without running, jumping or skipping steps, and were allowed to use the banister for balance if necessary. The stair climbing time was the number of seconds taken to climb 22 steps.<sup>8</sup> The 6-MWT was done once; the sit-to-stand and stair climbing tests were each performed twice at 5-minute intervals, and the better of each of the two

scores was selected for analysis. Participants underwent these three tests after they received a detailed explanation and demonstration of the test by a trained examiner.

### Daily Physical Activity

During the CTSC visit, study participants were instructed to wear an activity monitor that was strapped over the lateral side of the pelvic bone on the non-dominant side of the hips.<sup>8</sup> The activity monitor (Actigraph GT3X+ Activity Monitor®, Actigraph, Fort Walton Beach, FL) was worn continuously for 10 days except when subjects took baths, showered or swam. This pager-sized device measures the frequency and direction of movements by the subject, the orientation of the person's body (e.g., lying, sitting or standing), and the time of day and date of each movement. Physical activity was calculated during the last 7 full days of activity. The average daily vector magnitude (VM) 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 over 7 days. We classified activity level as sleep or marked physical inactivity (VM of 0–500), light physical activity (VM of 501–2689), moderate or greater physical activity (VM of 2690).<sup>8,12</sup>

All participants completed the Human Activity Profile (HAP) which is a questionnaire that is considered to be an indicator of capacity to expend energy and a person's physical performance level.<sup>13</sup> The HAP is composed of 94 activity items ranked in ascending order of level of physical activity from the least oxygen demanding activity, 1 = getting in and out of chairs or bed, to the maximum oxygen consuming activity, 94 = running or jogging 3 miles in 30 minutes or less.<sup>8</sup> Respondents may check off only one of three available answers for each activity item, assuming that they had the opportunity or need to perform that activity: "still doing this activity", "have stopped doing this activity," or "never did this activity". The respondent did not have to actually perform these activities in their daily living. The HAP is calculated as a maximum activity score (MAS) and an adjusted activity score (AAS). The MAS indicates the highest oxygen-demanding activity in the questionnaire that the subject indicates that he/she still performs. The AAS is calculated as the subject's MAS minus the number of less oxygen demanding physical activities that the subject indicates that he/she can no longer perform. The MAS is an estimate of the respondent's highest level of energy expenditure in comparison to normal individuals of the same age and gender. The AAS is an estimate of the subjects' average level of energy expenditure as compared to normal individuals of the same age and gender.

### Data Analyses

Statistical analyses were performed using STATA 11 statistical software (StataCorp LP College Station, TX). Continuous variables were expressed as mean±standard deviation (SD). Comparisons between three or more numerical or categorical groups were conducted by a one-way analysis of variance (ANOVA) or chi-square test. Persons who met the threshold for anxiety diagnosis by either BAI or HADS-anxiety scores and/or met the criteria for depression diagnosis by either BDI or HADS-depression scores, were considered to have, respectively, anxiety or depression. Subjects were subsequently divided into four categories: those displaying neither anxiety nor depression (A–D–), those displaying anxiety and depression (A+D+), those displaying anxiety but not depression (A+D–), and those

displaying depression but not anxiety (A–D+). Correlations of variables pertaining to physical activity, physical performance, and anxiety and depression status in MHD patients and normal controls were performed by regression analysis. Multiple regression analyses were performed to adjust for covariates when indicated. In regression analyses, adjustments were made for up to three covariates: age, gender, presence of diabetes mellitus, blood hemoglobin, and dialysis vintage. In all analyses, a 2-tailed P value <0.05 was considered to indicate statistical significance. In statistical comparisons where ANOVA was not used, no adjustment was made for the number of comparisons performed. When the ANOVA test was statistically significant, a Tukey's honestly significant difference (HSD) test was used to make pairwise comparisons among MHD patients.

## RESULTS

Seventy-two MHD patients and 39 normal adult controls were studied. Twenty-nine MHD patients had diabetes mellitus. Demographic and clinical characteristics are shown in Table 1 or were published previously.<sup>8</sup> Age, gender, body mass index and lean body mass (Table 1) and racial, ethnic distribution and educational level of the MHD patients were not different from the normal controls.<sup>8</sup> Mean serum albumin concentrations were similar to the normals and within the healthy range for normal people. The Charlson comorbidity index (CCI) of the MHD patients was similar to values in other reports of MHD patients and can be considered to be in or close to the healthier range.<sup>8</sup>

Anxiety and depression scores in the participants are shown in Table 2. Mean scores were significantly greater in MHD patients than in normals, indicating more frequent and severe anxiety and depression in the former group. This was observed whether the testing was performed by the BAI, BDI, HADS-A or HADS-D. There was also a much greater percentage of MHD patients who had mild or more severe anxiety or depression (Table 2), regardless of which test was employed to assess anxiety or depression (Table 2). Only 10% of MHD patients showed anxiety with the HADS-A scale, whereas 43% of patients displayed anxiety with the BAI questionnaire. Among the normal subjects, only one or two individuals showed evidence for mild or more severe anxiety or depression as evidenced by the BAI and BDI, whereas normal participants did not display anxiety or depression by the HADS-A or HADS-D scales.

Diabetic MHD patients displayed significantly greater anxiety and depression scores than non-diabetic MHD patients as determined by the BAI, BDI and HADS-A scales, but not by the HADS-D scale (Table 3). In unadjusted correlational analyses in the MHD patients, neither dialysis vintage nor blood hemoglobin correlated with anxiety or depression as measured by either the Beck or HADS scales (data not shown). Also in unadjusted analyses, body mass index correlated with BAI scores ( $r=0.30$ ,  $p=0.01$ ) but not with BDI. Lean body mass did not correlate with either BAI or BDI scores. However, of the 72 MHD patients, body mass index was <22 kg/m<sup>2</sup> in only 10 patients and 35 kg/m<sup>2</sup> in 7 patients. Hence, the sample size could be considered too small for careful analyses of the relation of body mass index or lean body mass to anxiety and depression. MHD patients older than the mean and median age ( 52 years old), as compared to younger MHD patients (<52 years), did not have significantly greater anxiety and depression scores as assessed by all four scales (Table

4). A greater proportion of diabetic MHD patients had anxiety but no depression than had neither anxiety nor depression (Table 5).

MHD patients who had neither anxiety nor depression had significantly more impaired 6 MWT, sit-to-stand and stair climbing scores as compared to normals without anxiety or depression (Table 5). MHD patients without anxiety or depression also had lower MAS and AAS scores and less 7 day DPA than normals without anxiety or depression (Table 6). Among the MHD patients, there were associations between anxiety, depression or a combination of anxiety and depression and reduced physical activity or impaired physical performance (Tables 5 and 6). MHD patients with both anxiety and depression had longer stair climbing times than patients with neither anxiety nor depression and patients with depression but no anxiety. The MHD patients who had both anxiety and depression had lower MAS and AAS scores than MHD patients who had neither anxiety nor depression or who were without anxiety but had depression (Table 6). Those MHD patients who had anxiety without depression also had lower AAS scores than the two groups of MHD patients who did not have anxiety. There was a trend for MHD patients with both anxiety and depression to have lower DPA scores on the day of hemodialysis and the day following hemodialysis as compared to the other three groups of MHD patients (Table 6).

In unadjusted correlational analyses, age was significantly negatively correlated with the 7-day average DPA ( $p=0.002$ ), the 6-minute walk distance ( $p=0.0001$ ), sit to stand cycles ( $p=0.002$ ) and positively correlated with the stair climbing time ( $p<0.0001$ ). In unadjusted analyses, neither hemoglobin concentrations nor body mass index were significantly correlated with any of these four physical activity or performance tests. Lean body mass, in unadjusted analyses, correlated only with stair climbing time ( $p=0.026$ ) and was marginally correlated with the 6-minute walk distance ( $p=0.053$ ).

The BAI scores in MHD patients were negatively correlated, both unadjusted and after adjustment for age, gender, diabetes, blood hemoglobin, and dialysis vintage, with the 6-MWT and sit-to-stand cycles but not stair climbing time (Table 7). BDI, HADS-A and HADS-D scores, in fully-adjusted analyses, did not correlate with any of these three measures of physical performance. The BAI scores correlated, after full adjustment, with the MAS and AAS scores but not with DPA (Table 8). In unadjusted models, BDI scores correlated negatively with MAS and AAS scores and with 6-MWT, average DPA, DPA on the HD day and second day after HD, and the percent time spent sleeping or in marked physical inactivity, in light activity and in moderate or greater activity (Table 8). The BDI scores, after adjustment for age, gender and diabetes, also correlated inversely with MAS and AAS scores, average DPA, and percent time in sleep or marked physical inactivity, light activity and moderate or greater activity. DPA on the day of hemodialysis ( $r=-0.30$ ,  $p=0.01$ ), day after dialysis ( $r=-0.27$ ,  $p=0.03$ ), and day two after hemodialysis ( $r=-0.27$ ,  $p=0.03$ ) also each correlated negatively with degree of depression by BDI. But neither the DPA at these times (data not shown) nor the 7-day averaged DPA correlated with the BAI, HAD-A or HAD-D scores. The HADS-A score correlated with the MAS and AAS, whereas there was a not-significant trend ( $p=0.07$ ) for the HADS-D score to correlate only with the percent of time spent in moderate or greater physical activity (Table 8).

## DISCUSSION

Anxiety and depression occur commonly in MHD patients, with prevalence rates ranging between 30% and 60% and between 20% and 70%, respectively.<sup>4-6</sup> A recent meta-analysis of patients undergoing chronic dialysis indicated a point prevalence of depression of 22.8 percent (95% CI, 18.6-27.6%).<sup>7</sup> However, this was the point prevalence of depression when diagnosed by clinical interviews. The prevalence of depression in chronic dialysis patients when determined by a number of different self- or clinician-administered questionnaires was much higher, 39.3 percent (95% CI, 36.8-42.0). These values do not indicate the lifetime incidence or disease course incidence of depression in chronic dialysis patients, which presumably would be substantially greater. In the present study, as assessed by BAI and BDI scores, 43 percent of MHD patients displayed mild or more severe anxiety and 33 percent of patients showed mild or more severe depression, as compared to only 3 percent and 5 percent, respectively, of the normal controls (Table 2). The prevalence of anxiety and depression in MHD patients was detected less commonly by the HADS-A and HADS-D scores, suggesting that at least in our MHD patients these latter scales may be less sensitive at detecting anxiety or depression. The BAI and BDI are widely used measures of anxiety and depression.<sup>14,15</sup> The greater prevalence of anxiety and depression in diabetic as compared to non-diabetic MHD patients may reflect the greater disease burden in the former individuals.

These observations are of particular concern because depression and possibly anxiety are associated with low quality of life and increased morbidity and mortality in MHD patients,<sup>16-18</sup> as well as in people without kidney failure.<sup>19-22</sup> It has been suggested that the mechanisms underlying the relationship between anxiety and depression and mortality in MHD patients include poor adherence to the prescribed dialysis treatment, hyperparathyroidism, malnutrition and chronic inflammation.<sup>23,24</sup> Anxiety and/or depression are also associated with such socio-demographic characteristics as a reduced prevalence of marriage and lower educational and socioeconomic status.<sup>25</sup> However, the complex neurobiochemical and immunological changes and physical fitness levels associated with anxiety and depression suggest that the causal relationships of these affective disorders to morbidity and mortality may be more complex.<sup>26-28</sup>

Anemia is associated with depression in chronic kidney disease and MHD patients.<sup>29-33</sup> Some studies describe a direct association between age and depression,<sup>31,34</sup> whereas, similar to the present report, other studies did not show such a relationship.<sup>33</sup> A negative association between age and depression has also been reported.<sup>35</sup> Age, but not blood hemoglobin or body mass index, was strongly correlated with DPA and the three physical performance tests. Lean body mass was significantly associated with stair climbing time and marginally with the six-minute walk distance. Due to the associations observed in the present study as well as in previous reports, many of the analyses in our study were adjusted for age, gender, presence of diabetes, blood hemoglobin and dialysis vintage.

The present study indicates that although DPA and physical performance are impaired in people undergoing MHD who do not have anxiety or depression, these emotional disorders are associated with further impairment in DPA or physical performance in MHD patients.



Studies in people without kidney failure indicate that symptoms of anxiety and depression are each associated with decreased physical activity.<sup>22,25,27,36–39</sup> People with anxiety symptoms may be particularly likely to reduce their amount of strenuous physical activity, possibly because such activity engenders many of the same physical manifestations found in anxiety reactions (e.g., air hunger, shortness of breath, rapid heart rate).<sup>27,40</sup> More intense physical activity or regular exercise are associated with less depressive or affective symptoms or anxiety in older adults<sup>38</sup> and overweight or obese individuals.<sup>37</sup> People with affective or anxiety disorders or substance abuse or dependence who exercise are more likely to have a higher health-related quality of life.<sup>36</sup> In young men and women with major depression, their pattern of symptoms appears to vary according to whether or not they are physically more active.<sup>39</sup>

The observations that anxiety and depression in both MHD patients and individuals without CKD are associated with decreased DPA and physical performance, and that the magnitude of these emotional disorders tend to be negatively correlated with their DPA and physical performance raise the question of whether physical exercise may reduce anxiety and depression. Indeed, in people without kidney failure, interventional studies clearly indicate that physical exercise regimens may decrease symptoms of anxiety and possibly depression.<sup>26,28,41–45</sup> Many types of regular exercise may reduce anxiety including walking<sup>46</sup> and yoga.<sup>47</sup> Exercise may improve symptoms of anxiety in people receiving cognitive behavioral therapy.<sup>46</sup> The effect of physical exercise on depression may be less marked and also self-limited, particularly if depressed patients are already receiving good quality care.<sup>44,48</sup>

This study has several limitations, including the cross-sectional nature of the study. Due to the relatively small sample sizes, the analyses of the subgroups as the MHD patients with anxiety and/or depression, must be considered tentative. The strengths of the study include the fact that the size of the MHD patient groups is larger than in many other studies of these individuals. There are very few published studies in MHD patients where DPA is directly measured with a mechanical activity monitor, particularly for as long as seven days. Also the three tests of physical performance are among the standard ones used.

In summary, we found that relatively healthy MHD patients without anxiety or depression have reduced DPA and physical performance. Those MHD patients with anxiety or depression display more impaired DPA and physical performance. Anxiety and depression are common in MHD patients and are associated with reduced quality of life and increased morbidity and mortality. In people without kidney failure, exercise may decrease symptoms of anxiety and depression. These observations provide a strong rationale for the institution of clinical trials to assess whether physical exercise will reduce anxiety or depression in MHD patients.

## PRACTICAL APPLICATION

In relatively healthy adult maintenance hemodialysis (MHD) patients, anxiety and depression are common and are associated with decreased daily physical activity and impaired physical performance. MHD patients who had both anxiety and depression

generally had the greatest impairment in daily physical activity and physical performance. These observations provide a strong rationale for clinical trials assessing whether regular physical exercise will reduce anxiety or depression in MHD patients.

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**Table 1**

Clinical Characteristics of Maintenance Hemodialysis (MHD) Patients and Sedentary Normal Controls\*

Characteristics	MHD Patients	Normal Controls	P-Value
N (male/female)	72 (49/23)	39 (23/16)	--
Age (years)	52.3±12.9(24–85)	51.0±12.7(20–75)	0.611
Dialysis Vintage (months)	53.9±45 (6.2–210)	--	--
Diabetes Mellitus (male/female)	29(18/11)	0	--
Charlson comorbidity index	5.7±2.7	--	--
Body Weight (kg)	78.9 ± 21.5	74.8 ± 14.5	0.289
Body Mass Index (kg/m <sup>2</sup> )	27.8 ± 5.8	27 ± 3.9	0.388
Body Fat <sup>†</sup> (%)	28.3 ± 8.5	27.9 ± 8	0.786
Lean Body Mass (kg)	54 ± 15.4	51.4 ± 11.3	0.315
Lean body mass index (kg/ m <sup>2</sup> )	18.9 ± 3.4	18.4 ± 2.7	0.472
Serum albumin (g/dL)	4.1±0.3	4.1±0.2	0.606
Serum creatinine (mg/dL)	10.5±4.3	0.84±0.2*	< 0.0001
Hemoglobin (g/dL)	11.2 ± 0.8	13.8±1.3*	< 0.0001
nPNA <sup>††</sup> (g/kg/day)	1.10 ±0.26	--	--
Sp Kt/Vurea	1.72 ±0.4	--	--
Serum HCO <sub>3</sub> (mEq/L)	24.4±2.5	--	--
Serum phosphorus (mg/dL)	5.3±1.4	--	--

\* There were no significant differences between MHD patients and normal controls except for their prevalence of diabetes mellitus and their lower blood hemoglobin and serum creatinine concentrations (p<0.0001 for each comparison). Data are generally are given as the mean ± standard deviation. Numbers in parentheses indicate range of values

<sup>†</sup> Measured by DEXA, except for one 161 kg MHD patient who was unable to fit into the DEXA machine. His total body fat and LBM were calculated from bioelectrical impedance measurements and are included in the tables.

<sup>††</sup> nPNA, normalized protein equivalent of total nitrogen appearance (protein nitrogen appearance)

**Table 2**

Anxiety and Depression in MHD Patients and Sedentary Normal Controls

	Clinical Threshold*	MHD Patients (n=72)	Normal Controls (n=39)	P
BAI	8	8±8 (31)	2±2 (1)	<0.0001
BDI	14	11±11 (24)	4±5 (2)	0.0003
HADS-A	11	5±4(7)	2±3 (0)	<0.0001
HADS-D	11	5±4 (11)	1±2 (0)	<0.0001

Abbreviations: BAI: Beck Anxiety Inventory score; BDI: Beck Depression Inventory score; HADS-A: hospital anxiety scale; HADS-D: hospital depression scale. Data are given as mean ± SD.

\*The thresholds for diagnosing mild or more severe anxiety or depression are from Beck et al<sup>8,9</sup> and Zigmond and Snaith<sup>11</sup>. HADS score of 8–10 is considered borderline abnormal and a score ≥ 11 is abnormal<sup>11</sup>. Numbers in parentheses indicate number of patients with scores indicating mild or more severe anxiety or depression.

**Table 3**

## Anxiety and Depression in Non-Diabetic and Diabetic Maintenance Hemodialysis Patients

	Non-DM patients (n =43)	DM patients (n=29)	P
BAI	6±8 (13)	10±8 (18)	0.04
BDI	8±8 (9)	16±13 (15)	0.002
HADS-A	5±3 (2)	7±5 (5)	0.04
HADS-D	5±4 (5)	6±5 (6)	0.35

Abbreviations are defined in the legend to Table 2. Other abbreviation: DM, diabetes mellitus. Data are given as mean±standard deviation. Numbers in parentheses indicate number of patients with scores indicating mild or more severe anxiety or depression.

**Table 4**

## Anxiety and Depression in Older and Younger Maintenance Hemodialysis Patients

	Age<52 years (n =36)	Age ≥ 52 years (n=36)	P
BAI	9±11 (17)	6±6 (13)	0.16
BDI	12±12 (13)	11±9 (11)	0.68
HADS-A	6±4 (4)	5±4 (3)	0.10
HADS-D	6±5 (5)	5±4 (6)	0.54

Age category classification was defined as relative to the mean and median age of the maintenance hemodialysis patient sample (~52 years). Abbreviations are defined in the legend to Table 2. Data are given as mean ± standard deviation. Numbers in parentheses indicate number of patients with scores indicating mild or more severe anxiety or depression



Table 5

Physical Performance According to Anxiety and Depression Status in Maintenance Hemodialysis (MHD) Patients Versus Healthy Controls

	MHD patients A-D-	MHD patients A+D-	MHD patients A-D+	MHD patients A+D+	Differences among MHD patients* p value	Normal controls A-D-
N (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
6-minute walk distance (meters)	466±119	397±116	478±124	410±122	0.013	620±65 <sup>‡</sup>
Sit-to-stand test (no. cycles in 30 seconds)	16±5	17±5	18±5	13±5	0.544	26±6 <sup>‡</sup>
Stair climbing test (seconds per 22 stairs)	14.7±7.0 <sup>d</sup>	16.2±10.0	13.1±2.7 <sup>b</sup>	19.2±18.5 <sup>a,b</sup>	<0.0001	9.7±1.1 <sup>‡</sup>

Abbreviations are as defined in Table 2. Symbols: (A<sup>-</sup>D<sup>-</sup>) subjects displaying neither anxiety nor depression, (A<sup>+</sup>D<sup>-</sup>) those displaying anxiety and depression, (A<sup>+</sup>D<sup>+</sup>) those displaying anxiety but not depression, and (A<sup>-</sup>D<sup>+</sup>) those displaying depression but not anxiety.

Data are presented as mean ± standard deviation.

\* ANOVA. Physical performance p-values adjusted for age, gender, presence of diabetes, blood hemoglobin, and dialysis vintage.

<sup>a,b</sup> Significantly different from values in other columns with the same superscript (p<0.05), as determined by a Tukey's honestly significant difference (HSD) test for pairwise comparisons (adjusted for age, gender, presence of diabetes, blood hemoglobin, and dialysis vintage).

Normal A-D- controls are significantly different from MHD A-D- patients (adjusted for age, gender, presence of diabetes, blood hemoglobin and dialysis vintage) as determined by Tukey's HSD test:

<sup>‡</sup> p<0.01.

Table 6

Daily Physical Activity According to Anxiety and Depression Status in Maintenance Hemodialysis (MHD) Patients Versus Healthy Controls

	MHD patients A-D-	MHD patients A+D-	MHD patients A-D+	MHD patients A+D+	Differences among MHD patients*	Normal controls A-D-
MAS	82±10 <sup>a</sup>	78±12	83±12 <sup>b</sup>	73±16 <sup>a,b</sup>	=0.0003	90±3 <sup>†</sup>
AAS	76±14 <sup>a,c</sup>	64±20 <sup>c</sup>	74±16 <sup>b</sup>	63±17 <sup>a,b</sup>	0.001	89±3 <sup>†</sup>
DPA- 7 day average (vector magnitude)	415881±142645	413229±195863	423944±156711	322245±124760	0.004	663304±225019 <sup>†</sup>
DPA on HD Day	372469±139164	355591±173337	380561±201589	300361±107871	0.004	--
DPA 1 day after HD	452035±177787	465143±232931	513005±248927 <sup>a</sup>	336460±142284 <sup>a</sup>	0.004	--
DPA 2 days after HD	435816±175417	433774±214628	381412±172040	364203±186121	0.152	--

Abbreviations and symbols are defined in the legends to *Tables 2* and *4*. Other abbreviations: MAS: Maximum Activity Score; AAS: Adjusted Activity Score.

\* ANOVA. P-values adjusted for age, gender, presence of diabetes, blood hemoglobin, and dialysis vintage.

<sup>a,b,c,d</sup> Significantly different from values in other columns with the same superscript (p<0.05), as determined by a Tukey's honestly significant difference (HSD) test for pairwise comparisons (adjusted for age, gender, presence of diabetes, blood hemoglobin, and dialysis vintage).

Normal A-D- controls are significantly different from MHD A-D- patients (adjusted for age, gender, presence of diabetes, blood hemoglobin and dialysis vintage) as determined by Tukey's HSD test:

<sup>†</sup> p<0.01.

Table 7

Correlation of Physical Performance with Anxiety and Depression Scales in Maintenance Hemodialysis Patients Unadjusted and Adjusted for Relevant Covariates

	Unadjusted		Age, gender adjusted		Fully-adjusted*	
	R	P-value	R	P-value	R	P-value
<b>Beck Anxiety Inventory Score</b>						
6-minute walk distance (meters)	-0.278	0.018	-0.294	0.014	-0.268	0.028
Sit-to-stand test (no. cycles in 30 seconds)	-0.260	0.027	-0.265	0.027	-0.258	0.035
Stair climbing test (seconds per 22 stairs)	0.109	0.363	0.095	0.436	0.052	0.677
<b>Beck Depression Inventory Score</b>						
6-minute walk distance (meters)	-0.197	0.098	-0.262	0.028	-0.192	0.120
Sit-to-stand test (no. cycles in 30 seconds)	-0.100	0.404	-0.117	0.336	-0.105	0.399
Stair climbing test (seconds per 22 stairs)	0.103	0.390	0.151	0.212	0.092	0.460
<b>HADS-Anxiety Score</b>						
6-minute walk distance (meters)	-0.136	0.254	-0.270	0.024	-0.214	0.082
Sit-to-stand test (no. cycles in 30 seconds)	-0.112	0.349	-0.190	0.116	-0.181	0.144
Stair climbing test (seconds per 22 stairs)	0.042	0.725	0.165	0.173	0.108	0.385
<b>HADS-Depression Score</b>						
6-minute walk distance (meters)	-0.096	0.425	-0.148	0.222	-0.105	0.400
Sit-to-stand test (no. cycles in 30 seconds)	-0.194	0.103	-0.225	0.061	-0.215	0.081
Stair climbing test (seconds per 22 stairs)	0.007	0.952	0.042	0.730	-0.001	0.993

\* Adjusted for age, gender, presence of diabetes, blood hemoglobin and dialysis vintage.

Table 8

Correlation of Daily Physical Activity with Anxiety and Depression Scales in Maintenance Hemodialysis Patients Unadjusted and Adjusted for Relevant Covariates

	Unadjusted		Age, gender adjusted		Fully-adjusted*	
	R	P-value	R	P-value	R	P-value
<b>Beck Anxiety Inventory Score</b>						
Maximum Activity Score (MAS)	-0.265	0.024	-0.292	0.014	-0.271	0.027
Adjusted Activity Score (AAS)	-0.268	0.023	-0.307	0.010	-0.280	0.022
DPA- 7 day average (vector magnitude)	-0.169	0.157	-0.168	0.165	-0.166	0.179
% time spent by accelerometer readings						
Sleep or marked physical inactivity	0.229	0.053	0.233	0.053	0.222	0.071
Light activity	-0.206	0.082	-0.214	0.076	-0.208	0.091
Moderate activity	-0.201	0.090	-0.206	0.087	-0.185	0.134
<b>Beck Depression Inventory Score</b>						
Maximum Activity Score (MAS)	-0.236	0.046	-0.286	0.017	-0.252	0.040
Adjusted Activity Score (AAS)	-0.277	0.018	-0.335	0.005	-0.297	0.015
DPA- 7 day average (vector magnitude)	-0.266	0.024	-0.288	0.016	-0.330	0.006
% time spent by accelerometer readings						
Sleep or marked physical inactivity	0.347	0.003	0.347	0.003	0.344	0.004
Light activity	-0.324	0.005	-0.317	0.008	-0.315	0.010
Moderate activity	-0.282	0.017	-0.311	0.009	-0.306	0.012
<b>HADS-Anxiety Inventory Score</b>						
Maximum Activity Score (MAS)	-0.211	0.075	-0.349	0.003	-0.322	0.008
Adjusted Activity Score (AAS)	-0.186	0.117	-0.327	0.006	-0.290	0.018
DPA- 7 day average (vector magnitude)	-0.024	0.839	-0.084	0.489	-0.079	0.523

	Unadjusted		Age, gender adjusted		Fully-adjusted*	
	R	P-value	R	P-value	R	P-value
% time spent by accelerometer readings						
Sleep or marked physical inactivity	0.049	0.686	0.069	0.571	0.037	0.768
Light activity	-0.003	0.977	0.003	0.998	0.029	0.815
Moderate activity	-0.128	0.294	-0.208	0.084	-0.181	0.142
<b><u>HADS-Depression Inventory Score</u></b>						
Maximum Activity Score (MAS)	-0.183	0.125	-0.231	0.054	-0.216	0.080
Adjusted Activity Score (AAS)	-0.159	0.182	-0.201	0.095	-0.182	0.140
DPA- 7 day average (vector magnitude)	-0.093	0.437	-0.107	0.377	-0.082	0.509
% time spent by accelerometer readings						
Sleep or marked physical inactivity	0.112	0.350	0.110	0.367	0.079	0.524
Light activity	-0.043	0.718	-0.035	0.777	-0.008	0.947
Moderate activity	-0.220	0.063	-0.250	0.037	-0.223	0.070

\* Adjusted for age, gender, presence of diabetes, blood hemoglobin and dialysis vintage.