

# Daily physical activity and physical function in adult maintenance hemodialysis patients

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## Abstract

**Background** Maintenance hemodialysis (MHD) patients reportedly display reduced daily physical activity (DPA) and physical performance. Low daily physical activity and decreased physical performance are each associated with worse outcomes in chronic kidney disease patients. Although daily physical activity and physical performance might be expected to be related, few studies have examined such relationships in MHD patients, and methods for examining daily physical activity often utilized questionnaires rather than activity monitors. We hypothesized that daily physical activity and physical performance are reduced and correlated with each other even in relatively healthier MHD patients.

**Methods** Daily physical activity, 6-min walk distance (6-MWT), sit-to-stand, and stair-climbing tests were measured in 72 MHD patients (32 % diabetics) with limited comorbidities and 39 normal adults of similar age and gender mix. Daily physical activity was examined by a physical activity monitor. The human activity profile was also employed.

**Results** Daily physical activity with the activity monitor, time-averaged over 7 days, and all three physical performance tests were impaired in MHD patients, to about 60–70 % of normal values ( $p < 0.0001$  for each measurement). Human activity profile scores were also impaired ( $p < 0.0001$ ). MHD patients spent more time sleeping or in marked physical inactivity ( $p < 0.0001$ ) and less time in  $\geq$  moderate activity ( $p < 0.0001$ ).

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These findings persisted when comparisons to normals were restricted to men or women separately. After adjustment, daily physical activity correlated with 6-MWT but not the two other physical performance tests. Human activity profile scores correlated more closely with all three performance tests than did DPA.

**Conclusions** Even in relatively healthy MHD patients, daily physical activity and physical performance are substantially impaired and correlated. Whether training that increases daily physical activity or physical performance will improve clinical outcome in MHD patients needs to be examined.

**Keywords** Chronic kidney disease · Kidney failure · Physical performance · Exercise · Exercise capacity

Daily physical activity is reportedly decreased in maintenance hemodialysis (MHD) patients [1–3]. Most of these investigations employed self-reported questionnaires [1, 2, 4–6], although some studies used activity-measuring instruments that directly measure daily physical activity [7, 8]. These latter studies were usually conducted in small groups [7, 9] or for less than 7 days [9, 10].

Cardiopulmonary exercise capacity, muscle strength, and physical performance (PP) are commonly impaired in MHD patients [11, 12], but relationships of daily physical activity to physical performance are not well-defined. We know of only one study that examined the relationship of daily physical activity to physical performance in MHD patients [13]. Reduced daily physical activity and physical performance are also clinically relevant because they are associated with increased hospitalization rates [14], cardiovascular mortality [2, 15], and all-cause mortality [2, 15, 16] in different patient groups. The relationship of kidney failure to daily physical activity and physical performance is complicated because MHD patients may be physically disabled due to strokes, limb amputations, or other comorbidities. Several studies examined daily physical activity or physical performance in MHD patients who used walking-assistive devices (e.g., canes or walkers) [13, 17]. Thus, it is difficult to ascertain the contribution of comorbidities rather than kidney failure and its treatment per se to MHD patients' daily physical activity and physical performance. The present study was conducted to examine daily physical activity and physical performance in a comparatively large number of relatively healthy MHD patients who had low degrees of comorbidity and to assess whether relationships exist between their daily physical activity and physical performance. Daily physical activity was assessed by an accelerometer. Healthy adults of similar age and gender distribution served as controls.

## 1 Methods

### 1.1 Study participants

Inclusion criteria for MHD patients were as follows: (1) age,  $\geq 18$  years; (2) MHD vintage,  $\geq 6$  months; (3) MHD treatment, thrice weekly; (4) no hospitalizations during the previous 3 months, except for vascular access repair; (5) no amputations or prostheses in lower extremities; (6) able to ambulate and ability to complete all study protocol tests and wear the physical activity monitor for 10 days; and (7) good compliance to study protocol. Exclusion criteria included the following: (1) any acute infectious or other inflammatory illnesses, (2) active cancer except basal cell carcinoma, (3) myocardial infarction or angina pectoris within the past 12 months, and (4) current heart or lung failure or severe liver disease.

All but four 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. In order to increase the number of diabetic MHD patients, four MHD patients with diabetic nephropathy who satisfied the entry criteria were recruited from two additional DaVita chronic dialysis centers. 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. Normal controls were recruited from the South Bay area of Los Angeles County through their church affiliation. To our knowledge, no normal volunteers engaged in regular sports activities. The authors certify that they comply with the ethical guidelines for authorship and publishing of the *Journal of Cachexia, Sarcopenia and Muscle*. This study was approved by the IRB of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center. All subjects gave informed written consent.

## 2 Measurements

### 2.1 Clinical characteristics

Clinical and demographic data including the Charlson Comorbidity Index, using the original scoring system [18], were recorded for each patient; scores for age and severe renal failure were included in the Charlson Comorbidity Index [19]. MHD patients underwent blood and serum measurements, described in Tables 1 and 2, which were performed in the DaVita central laboratory (DeLand, Florida). Blood was obtained immediately before a routine mid-week hemodialysis. Blood test results for MHD patients presented here were

**Table 1** Characteristics of study participants

| Characteristic                            | MHD patients<br><i>N</i> =72 | Normal controls<br><i>N</i> =39 | <i>p</i> Value |
|---|------------------------------|---------------------------------|----------------|
| Age (years)                               | 52.3±12.9                    | 51.0±12.7                       | 0.570          |
| Gender (M/F)                              | 49/23                        | 23/16                           | 0.391          |
| Male (%)                                  | 68                           | 59                              |                |
| DM/non-DM                                 | 23/49                        |                                 |                |
| Dialysis vintage (months)                 | 53.9±45.0<br>47.8 (51.4)     |                                 |                |
| Race (%)                                  |                              |                                 | 0.423          |
| African American                          | 29 (40 %)                    | 8 (21 %)                        |                |
| Asian                                     | 22 (31 %)                    | 19 (49 %)                       |                |
| Caucasian                                 | 5 (6.9 %)                    | 4 (10 %)                        |                |
| Hispanic                                  | 15 (21 %)                    | 8 (21 %)                        |                |
| Pacific Islander                          | 1 (1.4 %)                    | 0                               |                |
| Education levels (%)                      |                              |                                 | 0.056          |
| Below high school graduate                | 14 (19 %)                    | 2 (5.1 %)                       |                |
| High school graduate                      | 25 (35 %)                    | 14 (36 %)                       |                |
| ≤2 years of college                       |                              |                                 |                |
| ≥2 years of college                       | 33 (46 %)                    | 23 (59 %)                       |                |
| Charlson comorbidity index                | 5.7±2.7                      | —                               |                |
| Weight (kg)                               | 78.9±21.5<br>76.4 (25.6)     | 74.8±14.5<br>77.0 (18.9)        | 0.237          |
| Body mass index (kg/m <sup>2</sup> )      | 27.8±5.8<br>26.2 (7.6)       | 27.0±3.9<br>27.0 (5.9)          | 0.388          |
| Lean body mass (kg)                       | 54.0±15.4<br>51.5 (17.7)     | 51.4±11.3<br>49.1 (15.9)        | 0.315          |
| Lean body mass index (kg/m <sup>2</sup> ) | 18.9±3.4<br>18.3 (3.0)       | 18.4±2.7<br>18.2 (3.2)          | 0.472          |
| Body fat (%)                              | 28.3±8.5<br>26.8 (11)        | 27.9±8.1<br>25.8 (14)           | 0.786          |
| Serum albumin (g/dL)                      | 4.1±0.3                      | 4.1±0.2                         | 0.606          |
| Serum creatinine (mg/dL)                  | 10.5±4.3<br>9.8 (3.8)        | 0.84±0.2                        | <0.0001        |
| <i>nPNA</i> (g protein/kg/day)            | 1.10±0.26                    |                                 |                |
| Sp Kt/Vurea                               | 1.72±0.40                    |                                 |                |
| Serum TIBC (ug/mL)                        | 240.6±40.1                   |                                 |                |
| Serum ferritin (ng/mL)                    | 453.2±313.2                  |                                 |                |
| Hemoglobin (g/dL)                         | 11.2±0.8<br>11.2 (0.9)       | 13.8±1.3<br>14 (2.1)            | <0.0001        |
| Serum calcium (mg/dL)                     | 9.0±0.7                      |                                 |                |
| Serum phosphorus (mg/dL)                  | 5.3±1.4                      |                                 |                |
| Serum PTH (pg/mL)                         | 480±277<br>456 (305)         |                                 |                |
| Serum bicarbonate (mEq/L)                 | 24.5±2.6                     |                                 |                |

Data expressed as mean±standard deviation. Non-normally distributed data are expressed as median values with the interquartile range (IQR, i.e., the arithmetic difference between the 25th percentile value and the 75th percentile value) shown in parentheses

*nPNA* normalized protein nitrogen appearance, also referred to as protein catabolic rate; *TIBC* total iron binding capacity; *PTH* parathyroid hormone

values obtained monthly and averaged over the 3 months immediately prior to obtaining the other study measurements. Normal controls had blood drawn for a CBC and serum creatinine and albumin which were measured in the Harbor-UCLA Medical Center clinical laboratory.

Normal volunteers who had abnormal test results were excluded from the study. Only one normal was excluded, and that was because the daily physical activity measurements from his ActiGraph (see below) were not available.

**Table 2** Physical activity and physical performance; MHD patients vs. normal controls

|  | MHD patients<br><i>N</i> =72   | Normal controls<br><i>N</i> =39 | <i>p</i> Value |
|--|--------------------------------|---------------------------------|----------------|
| Human activity profile                             |                                |                                 |                |
| Maximum activity score                             | 82.5 (13.5)                    | 92 (5)                          | <0.0001        |
| Adjusted activity score                            | 72 (22)                        | 89 (5)                          | <0.0001        |
| Time spent by monitor readings (%)                 |                                |                                 |                |
| Sleep or marked physical inactivity                | 81.9±5.8                       | 72.8±6.0                        | <0.0001        |
| Light activity                                     | 14.4±4.4                       | 20.0±4.5                        | <0.0001        |
| ≥ Moderate activity                                | 3.7±2.1                        | 7.2±3.0                         | <0.0001        |
| Average daily physical activity (vector magnitude) |                                |                                 |                |
| Daily physical activity (mean of 7 days)           | 395,727 (222,350)              | 636,112 (243,634)               | <0.0001        |
| Day of HD  | 327,250 (188,085)              |                                 |                |
| 1-day-post-HD                                      | 442,720 (246,824) <sup>a</sup> |                                 |                |
| 2-days-post HD                                     | 393,353 (275,123) <sup>b</sup> |                                 |                |
| 6-min walk distance (meters)                       | 441.3±121.9                    | 617.6±63.2                      | <0.0001        |
| Sit-to-stand test (no. cycles in 30 s)             | 15.9±5.3                       | 26.2±5.4                        | <0.0001        |
| Stair-climbing test (seconds per 22 stairs)        | 15.8±11.0                      | 9.8±1.1                         | <0.0001        |

Data expressed as mean±standard deviation. Non-normally distributed data are expressed as median values with the interquartile range (IQR, i.e., the arithmetic difference between the 25th percentile value and the 75th percentile value) shown in parentheses

<sup>a</sup> 1-day-post-HD vs day of HD  
*p*=0.018

<sup>b</sup> 2-days-post-HD vs day of HD  
*p*=0.057; 1-day-post-HD vs 2-days-post-HD *p*=0.441

## 2.2 Body composition studies

MHD patients and normal subjects visited the HUMC Clinical and Translational Research Center in the morning after fasting for at least eight hours. MHD patients visited the Clinical and Translational Research Center one day after a hemodialysis treatment. Height, body weight, and body mass index (BMI, body weight (kilograms) divided by body height (squared meters)) were measured. 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 (Hologic; model DXA Discovery A; Bedford, MA.)

## 2.3 Physical performance tests

Immediately after the body composition tests, subjects underwent three physical performance tests in the following order: 6-min walk test (6-MWT), sit-to-stand test, and stair-climbing test. The 6-MWT measured the distance (meters) that participants walked back and forth along an 80-ft (24.4 m) horizontal corridor during a 6-min period of time while they were repetitively encouraged to walk fast. Using a standard 6-MWT protocol, participants were encouraged to walk fast using the following phrases for consistency: “You’re doing well,” “Keep up the good work,” “Good work,” “You have ..... minutes to go,” and “You have only ..... minutes left.” Study subjects could slow down, rest, or even stop walking if they wished, but the 6-min timer 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 30-s

period. This test measured the number of sit-to-stand cycles completed during 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-climb 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.

## 2.4 Daily physical activity

Daily physical activity (DPA) was assessed both with a physical activity monitor (ActiGraph GT3X+ Activity Monitor®, ActiGraph, Fort Walton Beach, FL) and a questionnaire, the Human Activity Profile. All participants completed the Human Activity Profile questionnaire, which elicits a person’s description of the frequency that he/she performs physical activities requiring various amounts of energy expenditure and degrees of physical performance [20]. The human activity profile score is calculated as a maximum activity score, indicating the highest oxygen-demanding activity listed in the questionnaire that the subject indicates that he/she still performs. The human activity profile-adjusted activity score is calculated as the subject’s maximum activity score minus the number of less oxygen-demanding physical activities that the subject indicates that he/she can no longer perform. These scores, respectively, estimate the highest level of energy expenditure (the maximum activity score) and

average level of energy expenditure (the adjusted activity score) as compared to normal individuals of the same age and gender [20].

During their CTRC visit, study participants were instructed to wear an activity monitor that was strapped to the lateral side of the pelvic bone on the non-dominant side of the hips. The activity monitor (ActiGraph®) was worn continuously for 10 days, including nights, except when subjects took baths, showered, or swam. This pager-sized ambulatory accelerometer detects physical activity in three dimensions. ActiGraph's digital filtering algorithms measure the frequency and direction of movements by the subject, the orientation of the person's body (e.g., lying, sitting, standing), and the time of day and date of each movement [21]. Physical activity was calculated during the last seven full days of activity. For MHD patients, these 7 days included three hemodialysis days and four non-hemodialysis days. Thus, on one of these 7 days, daily physical activity was measured on the second day after a hemodialysis.

The average daily vector magnitude (VM) for daily physical activity 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., a VM of 0–500), light physical activity (VM of 501–2689), and moderate or greater physical activity (VM  $\geq 2,690$ ) [21]. A VM score of 0–500 was taken to indicate sleep or marked physical inactivity based upon our observations of the subjects' activities when these readings were obtained.

### 3 Statistical analyses

Statistical analyses were performed using STATA 11 statistical software (StataCorp LP College Station, TX). Continuous variables were expressed as mean  $\pm$  standard deviation (SD) and were compared between groups by independent *t* tests. Variables that were non-normally distributed as determined by the Shapiro-Wilk test of normality were reported as the median and interquartile range (IQR, i.e., the arithmetic difference between the 25th percentile value and the 75th percentile value). Categorical variables with  $\geq$  three groups were compared with one-way analysis of variance (ANOVA). Up to three covariates were adjusted for in multiple regression analyses: age, gender, and presence of diabetes mellitus. A 2-tailed *p* value of  $<0.05$  was considered statistically significant. When ANOVA was not used, no statistical adjustment was made for the number of comparisons performed.

### 4 Results

Seventy-six MHD patients and 40 normal controls were recruited and studied. Five participants were excluded

because of prosthetic leg (one MHD patient) or not wearing the activity monitor for at least 7 days (three MHD patients, one normal). We obtained sufficient data for analysis on 72 MHD patients and 39 normal controls. Their characteristics are shown in Table 1. MHD patients and normal controls were  $52.3 \pm 12.9$  (SD) (range, 24–85), and  $51.0 \pm 12.7$  (range, 20–75) years old, respectively. Dialysis vintage was  $53.9 \pm 45.0$  months. Only 31.6 % of the MHD patients had diabetes mellitus, which may reflect the fact that the inclusion/exclusion criteria selected a healthier subset of MHD patients and, hence, a disproportionately large number of diabetic patients were excluded from the study. There were no significant differences between MHD patients and normals with regard to age, weight, gender distribution, educational level, and racial/ethnic distribution. MHD patients and normals each had normal serum albumin levels, averaging 4.1 g/dL. Fat-free, edema-free (lean) body mass, and percent body fat were not different, and their BMI averaged in the overweight range (Table 1). The Charlson Comorbidity Index in the MHD patients averaged  $5.7 \pm 2.7$  (median value, 5; range of values, 2–13).

Compared with normals, MHD patients had significantly worse scores in all measures of daily physical activity (Table 2). The 7-day mean daily physical activity of MHD patients, measured by the ActiGraph activity monitor and expressed as the VM, averaged 60.8 % of the daily physical activity of normals. MHD patients, in comparison to normals, showed a significantly greater percent of their time in sleep or marked physical inactivity and a significantly smaller percent of their time performing either light daily activity or moderate or greater daily activity. Daily physical activity in the MHD patients varied according to their hemodialysis (HD) schedule (Table 2). Daily physical activity was significantly lower on the day of HD (day 0) than on the day following dialysis (1-day-post-HD). Daily physical activity 2-days-post-HD tended to be greater than daily physical activity on the day of HD and less than daily physical activity on day-1-post-HD but was not statistically different from either of these days. On each of these 3 days of the HD schedule, daily physical activity was significantly lower than the daily physical activity of the normals.

Both human activity profile scores, the maximal activity score and adjusted activity score, were reduced (Table 2). The 6-MWT, sit-to-stand, and stair-climbing measurements in MHD patients were 71.5, 60.7, and 161.2 %, respectively, of the values obtained from normal controls ( $p < 0.001$  for each comparison, Table 2). The reduced distance walked during the 6-MWT occurred even though no patient stopped walking.

In either MHD patients and normal adults, the daily physical activity, human activity profile Maximum Activity Score and Adjusted Activity Score values were not significantly different in women as compared to men (Table 3). In MHD patients, the

**Table 3** Physical activity and physical performance by gender group

|  | MHD patients<br>N=72 |                   | MHD: male vs. female |  | Normal controls<br>N=39 |                   | Normals: male<br>vs. female |  | Males: MHD<br>vs. normals |  | Females: MHD<br>vs. normals |  |
|--|----------------------|-------------------|----------------------|--|-------------------------|-------------------|-----------------------------|--|---------------------------|--|-----------------------------|--|
|  | Males<br>N=49        | Females<br>N=23   | p                    |  | Males<br>N=23           | Females<br>N=16   | p                           |  | p                         |  | p                           |  |
| Age (years)  | 51.8±13.0            | 53.8±13.0         | 0.545                |  | 51.3±14.7               | 50.6±9.5          | 0.868                       |  | 0.884                     |  | 0.407                       |  |
| Vintage (months)                                   | 46.9 (46.7)          | 51.4 (72.4)       | 0.018                |  | —                       | —                 | —                           |  | —                         |  | —                           |  |
| Physical activity                                  |                      |                   |                      |  |                         |                   |                             |  |                           |  |                             |  |
| Human activity profile                             |                      |                   |                      |  |                         |                   |                             |  |                           |  |                             |  |
| Maximum activity score                             | 84 (10)              | 82 (18)           | 0.155                |  | 92 (5)                  | 89.5 (4)          | 0.472                       |  | <0.0001                   |  | <0.0001                     |  |
| Adjusted activity score                            | 76 (21)              | 69 (26)           | 0.319                |  | 91 (4)                  | 88 (4)            | 0.285                       |  | <0.0001                   |  | <0.0001                     |  |
| Time spent by monitor (%)                          |                      |                   |                      |  |                         |                   |                             |  |                           |  |                             |  |
| Sleep or inactive                                  | 82.0±5.8             | 81.7±6.0          | 0.840                |  | 72.9±6.1                | 72.7±6.0          | 0.920                       |  | <0.0001                   |  | <0.0001                     |  |
| Light activity                                     | 14.2±4.4             | 14.9±4.5          | 0.534                |  | 19.3±4.3                | 21.0 ±4.6         | 0.245                       |  | <0.0001                   |  | 0.0002                      |  |
| ≥ Moderate activity                                | 3.8±2.0              | 3.3±2.2           | 0.341                |  | 7.8±3.3                 | 6.4±2.3           | 0.151                       |  | <0.0001                   |  | <0.0001                     |  |
| Average daily physical activity (vector magnitude) | 421,539 (260,044)    | 365,050 (184,522) | 0.398                |  | 644,556 (305,427)       | 596,642 (244,376) | 0.435                       |  | <0.0001                   |  | <0.0001                     |  |
| Daily physical activity (mean of 7 days)           |                      |                   |                      |  |                         |                   |                             |  |                           |  |                             |  |
| Day of HD  | 324,559 (203,547)    | 329,942 (135,789) | 0.315                |  | —                       | —                 | —                           |  | —                         |  | —                           |  |
| 1-day-post-HD                                      | 443,085 (261,536)    | 442,355 (211,902) | 0.438                |  | —                       | —                 | —                           |  | —                         |  | —                           |  |
| 2-days-post HD                                     | 398,185 (268,775)    | 360,273 (273,908) | 0.887                |  | —                       | —                 | —                           |  | —                         |  | —                           |  |
| Physical performance                               |                      |                   |                      |  |                         |                   |                             |  |                           |  |                             |  |
| 6-min walk distance (meters)                       | 467.6±98.9           | 385.3±147.6       | 0.007                |  | 632.9±60.7              | 595.5±61.9        | 0.068                       |  | <0.0001                   |  | <0.0001                     |  |
| Sit-to-stand test (cycles per 30 s)                | 16.5±5.6             | 14.7±4.2          | 0.175                |  | 28.1±3.9                | 23.6±6.3          | 0.009                       |  | <0.0001                   |  | <0.0001                     |  |
| Stair-climbing test (seconds per 22 stairs)        | 13.5±5.0             | 20.8±17.2         | 0.008                |  | 9.6±1.2                 | 10.2±1.0          | 0.109                       |  | <0.0001                   |  | 0.008                       |  |

Data expressed as mean±standard deviation. Non-normally distributed data are expressed as median values with the interquartile range (IQR. i.e., the arithmetic difference between the 25th percentile value and the 75th percentile value) shown in parentheses



6-MWT and the stair-climbing speed were significantly reduced in women. In normal adults, performance in the sit-to-stand test was significantly lower in women than in men. Moreover, male and female MHD patients, analyzed separately, each displayed significantly lower daily physical activity and human activity profile maximum activity and adjusted activity scores and reductions in all three physical performance tests as compared to normal men and women, respectively.

Weekly averaged daily physical activity was negatively associated with age in MHD patients in unadjusted analyses (Fig. 1a), as reported by Johansen et al. [22], and after adjustment for gender and diabetes mellitus ( $r=-0.342$ ,  $p<0.004$ ). In normal controls, weekly averaged daily physical activity was not correlated with age, whether unadjusted (Fig. 1b) or adjusted for gender ( $r=-0.224$ ,  $p=0.177$ ). Daily physical activity correlated directly with MHD vintage in unadjusted analyses (Fig. 2) and with adjustment for age and gender or age, gender, and diabetes (Table 4). In unadjusted analyses, weekly averaged daily physical activity correlated with 6-MWT (Fig. 2), sit-to-stand, and stair-climbing time in MHD patients. In MHD patients, DPA correlated only with 6-MWT but not with sit-to-stand or stair-climbing after adjustment for age and gender or age, gender, and diabetes (Table 4). In normal subjects in unadjusted analyses, daily physical activity correlated directly with the 6-MWT ( $r=0.345$ ,  $p=0.032$ ) but not with adjustment for age and gender. In normals, daily physical activity did not correlate with either sit-to-stand or stair-climbing measurements in either unadjusted or adjusted analyses. As might be expected, in both unadjusted and adjusted analyses, averaged weekly daily physical activity was significantly associated with the daily physical activity analyzed for each day of the HD cycle as well as for percent time in sleep or marked physical inactivity or in moderate or greater physical activity (Table 4).

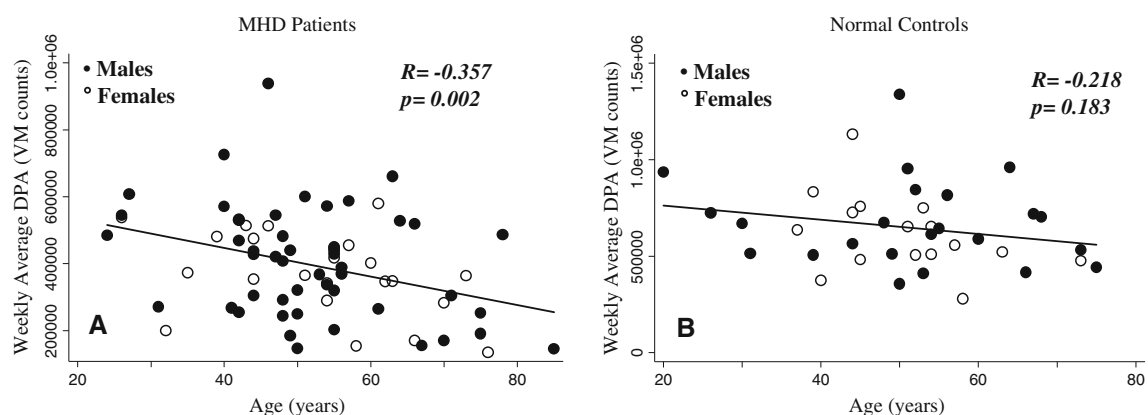
Average weekly daily physical activity was significantly associated with the maximum activity and adjusted activity scores of the human activity profile in unadjusted analyses but not when the analyses were adjusted for age and gender or age, gender, and diabetes. Interestingly, the maximum activity

scores and the adjusted activity human activity profile scores each strongly correlated with 6-MWT and sit-to-stand and stair-climbing tests in both unadjusted and the age, gender, and diabetes adjusted analyses (Table 4, Figs. 3 and 4).

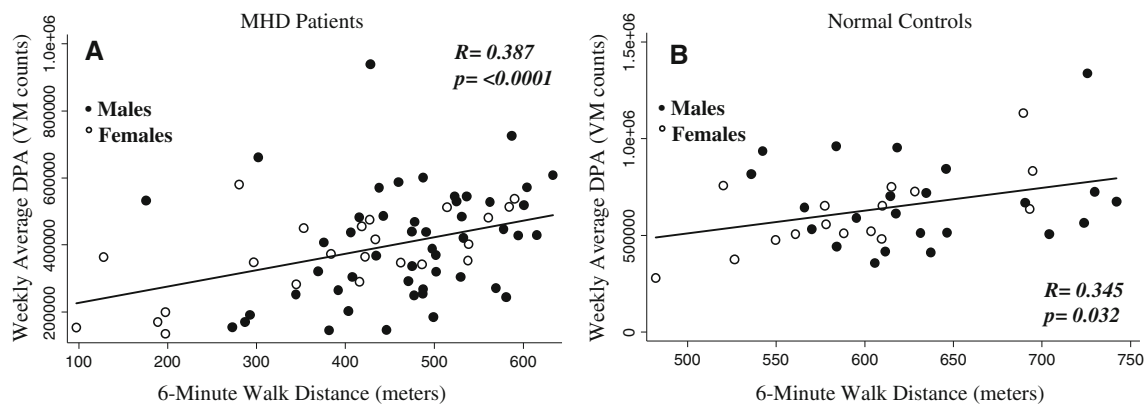
## 5 Discussion

This study indicates that daily physical activity of MHD patients, measured by the activity monitor and physical performance were substantially reduced compared with normal adults. Our accelerometer measured daily physical activity and the three physical performance tests appear to be reliable and reproducible [21, 23]. The 6-MWT and sit-to-stand test rather objectively monitor progress after exercise training in MHD patients [23]. However, after adjustment for age, gender, and diabetes, our study demonstrated a significant association only between daily physical activity and 6-MWT but not sit-to-stand or stair-climbing (Table 4). Maximum activity and adjusted activity human activity profile scores correlated with daily physical activity in unadjusted but not adjusted analyses. However, the human activity profile maximum activity and adjusted activity scores were highly significantly correlated, both before and after adjustment, with each of the three physical performance tests (Table 4, Figs. 3 and 4). These findings support the contention that the human activity profile gives a more reliable assessment of physical performance or exercise capability than it does of daily physical activity [20, 24].

The rather weak correlation between daily physical activity, determined by the activity monitor, and the physical performance tests is consistent with other studies in older men ( $\geq 65$  years old) [25], and suggest that factors in addition to physical capability also play a role in determining daily physical activity. The fact that the MHD patients in this study were a relatively healthy subgroup and that more severely debilitated MHD patients were excluded from study may also explain the rather weak correlations between daily physical activity and physical performance that were observed in the



**Fig. 1** Unadjusted correlation between weekly averaged daily physical activity (DPA) and age in MHD patients (a) and normal controls (b)



**Fig. 2** Unadjusted correlation between weekly averaged daily physical activity (DPA) and 6-min walk test in MHD patients (a) and normal controls (b)

present study; i.e., if the ranges of daily physical activity and physical performance scores among the MHD patients were greater, the correlations between these two variables might have been more statistically significant.

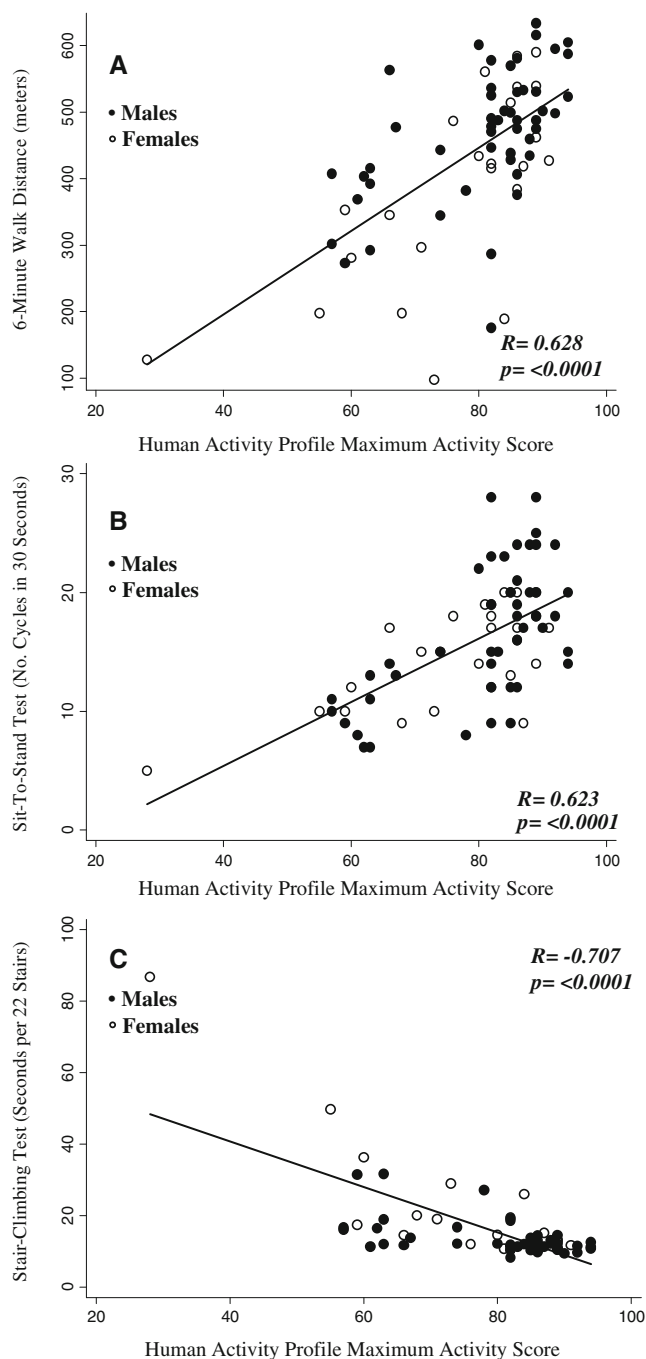
Physical inactivity and increased time at bed rest are commonly observed in MHD patients [7, 10, 26]. Decreased physical activity can lead to detrimental effects on the heart and musculoskeletal system, result in profound reductions in

physical work capacity, and aggravate such comorbid states in dialysis patients as cardiac dysfunction, skeletal muscle wasting, glucose intolerance, and reduced bone density [26]. High daily physical activity levels are associated with beneficial clinical traits in both chronic kidney disease patients and the general population. Higher usual physical activity levels, determined by questionnaires are associated with better nutritional status [5, 6], less inflammation [6], and an increased

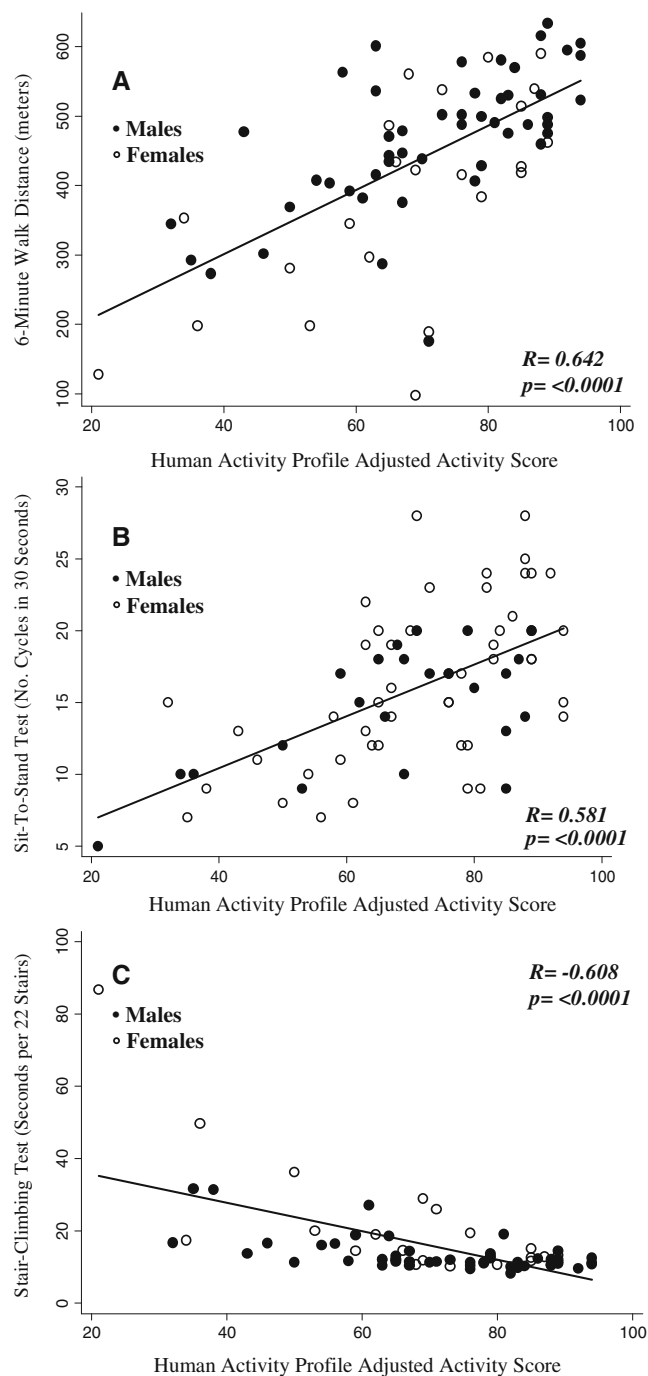
**Table 4** Correlations in MHD patients with weekly averaged accelerometer-measured daily physical activity and with the human activity profile (HAP) with no adjustments and with adjustment for covariates

|  | Unadjusted |                | Age, gender adjusted |                | Age, gender, diabetes adjusted |                |
|--|------------|----------------|----------------------|----------------|--------------------------------|----------------|
|  | <i>R</i>   | <i>p</i> Value | <i>R</i>             | <i>p</i> Value | <i>R</i>                       | <i>p</i> Value |
| Correlations with accelerometer-measured daily physical activity |            |                |                      |                |                                |                |
| Vintage (months)   | 0.266      | 0.024          | 0.252                | 0.035          | 0.257                          | 0.033          |
| Human activity profile   |            |                |                      |                |                                |                |
| Maximum activity score   | 0.277      | 0.019          | 0.102                | 0.403          | 0.101                          | 0.410          |
| Adjusted activity score  | 0.366      | 0.002          | 0.206                | 0.087          | 0.207                          | 0.087          |
| Time spent by monitor readings (%)                               |            |                |                      |                |                                |                |
| Sleep or marked physical inactivity                              | −0.868     | <0.0001        | −0.881               | <0.0001        | −0.885                         | <0.0001        |
| Light activity   | 0.745      | <0.0001        | 0.794                | <0.0001        | 0.796                          | <0.0001        |
| ≥ Moderate activity  | 0.843      | <0.0001        | 0.816                | <0.0001        | 0.820                          | <0.0001        |
| Day of HD  |            |                |                      |                |                                |                |
| 1-day-post-HD  | 0.898      | <0.0001        | 0.881                | <0.0001        | 0.881                          | <0.0001        |
| 2-days-post-HD   | 0.948      | <0.0001        | 0.942                | <0.0001        | 0.942                          | <0.0001        |
| 6-min walk distance (meters)                                     | 0.815      | <0.0001        | 0.819                | <0.0001        | 0.819                          | <0.0001        |
| Sit-to-stand test (no. cycles in 30 s)                           | 0.387      | <0.0001        | 0.258                | 0.031          | 0.263                          | 0.029          |
| Sit-to-stand test (no. cycles in 30 s)                           | 0.268      | 0.023          | 0.148                | 0.221          | 0.148                          | 0.226          |
| Stair-climbing test (seconds per 22 stairs)                      | −0.283     | 0.016          | −0.112               | 0.358          | −0.111                         | 0.363          |
| Correlations with human activity profile                         |            |                |                      |                |                                |                |
| Maximum activity score vs.                                       |            |                |                      |                |                                |                |
| 6-min walk distance (meters)                                     | 0.628      | <0.0001        | 0.496                | <0.0001        | 0.480                          | <0.0001        |
| Sit-to-stand test (no. cycles in 30 s)                           | 0.623      | <0.0001        | 0.534                | <0.0001        | 0.533                          | <0.0001        |
| Stair-climbing test (seconds per 22 stairs)                      | −0.707     | <0.0001        | −0.595               | <0.0001        | −0.584                         | <0.0001        |
| Adjusted activity score vs.                                      |            |                |                      |                |                                |                |
| 6-min walk distance (meters)                                     | 0.642      | <0.0001        | 0.523                | <0.0001        | 0.504                          | <0.0001        |
| Sit-to-stand test (no. cycles in 30 s)                           | 0.581      | <0.0001        | 0.481                | <0.0001        | 0.479                          | <0.0001        |
| Stair-climbing test (seconds per 22 stairs)                      | −0.608     | <0.0001        | −0.454               | <0.0001        | −0.437                         | <0.0002        |





**Fig. 3** Unadjusted correlations between the human activity profile maximum activity score and 6-min walk test (a), sit-to-stand test (b), and stair-climbing test (c) in MHD patients



**Fig. 4** Unadjusted correlations between the human activity profile-adjusted activity score and 6-min walk test (a), sit-to-stand test (b), and stair-climbing test (c) in MHD patients

employment rate in incident dialysis patients [27]. Increased physical activity in MHD patients is associated with less sleep disturbances [28, 29], and improved nutritional status and body composition [5, 8, 30, 31]. The amount of time spent in increased physical activity was significantly associated with greater walking ability, improved physical fitness, and better

quality of life in MHD patients [32]. As with our findings, in older men, usual physical activity correlated with exercise capacity [33]. By contrast, low daily physical activity is associated with increased hospitalizations and mortality in MHD patients [4, 15, 34, 35], greater mortality in stage 2–4 chronic kidney disease patients [36, 37], increased risk of

cardiovascular and all-cause mortality in renal transplant recipients [2], increased cancer-related mortality and all-cause mortality in cancer patients [38, 39], and increased mortality in older people [40].

While the association between physical performance and morbidity or mortality outcomes has not been directly investigated in MHD patients, several studies have used the SF-36 questionnaire Physical Component Score as a proxy for physical performance. The Physical Component Score is based largely on questionnaire items determining the extent to which patients are “limited” in performing common physical tasks of varying difficulty. In two studies, MHD patients with low Physical Component Scores had greater hospitalization or mortality risks [14, 41]. Johansen et al. reported that lower adjusted human activity profile maximum activity and adjusted activity scores were associated with increased mortality in 1,054 ambulatory MHD patients [42].

Our findings of reduced daily physical activity and physical performance may be particularly relevant because we studied an apparently healthier subgroup of MHD patients. This would suggest that renal failure and possibly, treatment regimens for renal failure per se may reduce daily physical activity and physical performance. Evidence that we studied healthier MHD patients includes the following: (1) Our inclusion/exclusion criteria precluded many comorbid conditions and stipulated that patients were not recently hospitalized, except for vascular access repair, and were able to perform the 6-MWT. (2) The patients’ serum albumin averaged 4.1 g/dL, which was the same as our normal control values and substantially higher than is reported in large epidemiological studies of MHD patients [43]. (3) Their BMI, LBM, percent body fat, and body weight were within the healthy range (Table 1). (4) Patients’ normalized protein nitrogen appearance (nPNA) was  $1.10 \pm 0.26$  g protein/kg/day, which is greater than that reported for most MHD patients [27–29]. nPNA somewhat underestimates the daily dietary protein intake [44], and this value is only slightly lower or not different from protein intake recommended for MHD patients by K/DOQI and other expert workgroups [45, 46]. Moreover, MHD patients who describe good appetite demonstrate less inflammation and greater survival [47]. (5) The mean Charlson Comorbidity Index value of the 72 MHD patients was  $5.7 \pm 2.7$  with a median value of 5, which is not high for dialysis patients [19, 48, 49]. (6) Daily physical activity and physical performance in our non-diabetic MHD patients, when analyzed separately, are still substantially and significantly decreased compared to normal adults (unpublished data).

This study does not indicate whether low daily physical activity and reduced physical performance in our MHD patients were causally related to each other. Moreover, it does not indicate whether increasing DPA will improve physical performance or whether greater exercise training to increase physical

performance will enhance DPA. It would not be unlikely that low daily physical activity and reduced physical performance may each contribute to the other disorder in MHD patients.

This study has several limitations; first, the activity monitor was worn on the hip, which might limit its ability to detect upper body movements. Second, the sampling of different racial and ethnic groups was limited, and this study was focused on relatively healthy non-diabetic and diabetic MHD patients. Among the strengths of this study, very few other studies have examined relationships between daily physical activity and physical performance in MHD patients. This study is one of the few that used an instrument to measure daily activity. Our sample size of MHD patients was rather large. Since relatively healthy MHD patients were studied, we were able, to some extent, to separate the effects of end-stage kidney disease and MHD treatment on daily physical activity and physical performance from other common comorbid conditions that afflict MHD patients, such as protein-energy wasting, severe heart disease, strokes, amputations, or emotional depression.

In summary, this study confirms and extends previous findings of major reductions in daily physical activity and physical performance in MHD patients. In MHD patients, increased physical activity and physical performance, usually determined by questionnaires, are associated with improved outcomes [2, 6, 8, 14, 15]. Since physical performance is associated with daily physical activity and can be improved with exercise training in MHD patients [50–52], exercise might also improve daily physical activity. Research is clearly indicated to examine how to best increase physical performance and daily physical activity in MHD patients and to ascertain whether such strategies will improve their clinical outcomes.

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**Conflict of interest** Jun Chul Kim, Bryan Shapiro, Min Zhang, Yanan Li, Janos Porszasz, Rachelle Bross, Usama Feroze, Rajeev Upreti, Kamyar Kalantar-Zadeh, and Joel Kopple declare that they have no conflict of interest.

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