



Published in final edited form as:

J Ren Nutr. 2015 March ; 25(2): 217–222. doi:10.1053/j.jrn.2014.10.017.

FACTORS AFFECTING DAILY PHYSICAL ACTIVITY AND PHYSICAL PERFORMANCE IN MAINTENANCE DIALYSIS PATIENTS

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Abstract

Background—Maintenance hemodialysis (MHD) patients display reduced daily physical activity (DPA) and physical performance (PP). Previous studies did not differentiate the effects of kidney failure and MHD treatments from comorbidities as causes for reduced DPA and PP. In relatively healthy MHD patients and normal adults, we evaluated DPA and PP and examined relationships between DPA and PP and possible associations between anxiety or depression and DPA and PP.

Methods—DPA, 6-minute walk distance (6-MWD), sit-to-stand (STS) and stair-climbing tests were measured in 72 MHD patients (40% diabetics) with limited comorbidities and 39 normal adults of similar age and gender mix. Anxiety and depression were measured by the Beck anxiety and depression inventories.

Results—DPA, time-averaged over seven days, and all three PP tests were impaired in MHD patients, to about 60–70% of normal values ($p < 0.0001$ for each measurement). MHD patients spent more time sleeping or physically inactive ($p < 0.0001$) and less time in moderate activity ($p < 0.0001$). Adjusted DPA correlated with 6-MWD but not STS or stair-climbing. Anxiety and depression were identified in 43% and 33% of MHD patients and 2.5% and 5.1% of normal ($p < 0.0001$ for each comparison). Most of the reduction in DPA and PP tests were observed in MHD patients without anxiety or depression. However, MHD patients with both anxiety and depression generally had the most impaired DPA and PP. In MHD patients, higher adjusted anxiety scores were correlated with impaired 6-MWD and STS, whereas adjusted average DPA was negatively correlated with depression ($r = -0.33$, $p = 0.006$) but not anxiety. DPA on the hemodialysis day ($p = 0.01$), day after dialysis ($p = 0.03$), and day-2 after dialysis ($p = 0.03$) each correlated negatively with degree of depression but not with anxiety. MHD patients displayed negative adjusted correlations between anxiety and 6-MWD ($p = 0.03$) and STS ($p = 0.04$).

Conclusions—In relatively healthy MHD patients, DPA and PP are substantially impaired and correlated with each other, even in patients without evidence for anxiety or depression. Anxiety and depression are common in MHD patients and are associated with further impairment in DPA and PP.

Keywords

hemodialysis; physical activity; depression; anxiety

Maintenance hemodialysis (MHD) patients are reported to have reduced daily physical activity (DPA) and physical performance (PP) (1,2). This is a source of concern because low DPA and decreased PP are each associated with worse outcomes in MHD patients (3–5). The factors that are associated or predispose to low DPA and PP are not well understood. Studies generally evaluated cohorts of MHD patients that included individuals who could have debilitating comorbid conditions, and the extent to which kidney failure or dialysis treatment per se cause reduced DPA and PP is unclear. We examined factors that might cause reduced DPA and PP in MHD patients. Specifically, we investigated whether DPA and PP are reduced in MHD patients who are relatively healthy and largely free of debilitating comorbid conditions. In addition, since DPA may be affected by physical capacity, we examined whether there is an association between DPA and PP, at least in these relatively healthy MHD patients. Finally, since anxiety and depression occur commonly in MHD patients and are frequently associated with altered DPA or physical function in the general population, particularly in elderly people, we evaluated whether these two affective disorders are also associated with DPA and PP in our MHD patients.

Methods

Daily physical activity (DPA) and three measures of PP, the 6-minute walk distance (6-MWD), sit-to-stand and stair-climbing tests, were measured in 72 relatively healthy MHD patients (40% diabetics) with limited comorbidities and 39 normal adults of similar age and gender mix. DPA was assessed for 10 days with a physical activity monitor (Actigraph GT3X+ Activity Monitor®) and is reported as **vector magnitude units**. Vector magnitude (VM) is calculated as the square root of the sum of the squares of the movement readings from each of the three dimensional axes of movement as determined by the Actigraph Activity Monitor® (9). Sleep or marked physical inactivity was classified as a VM of 0–500; light physical activity was classified as a VM of 501–2689, and moderate or greater physical activity as a VM \geq 2690. To allow time for adjustment to the activity monitor, the first three days of the measured DPA were deleted from analysis. The Human Activity Profile was also administered to the patients and normal subjects. Anxiety and depression were assessed by the Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (6–8). More details concerning the methods employed are described elsewhere (9,10).

Results

Some characteristics of the subjects are shown in Table 1. Among the MHD patients, dialysis vintage was $53.9 \pm$ SD 45 months; Sp Kt/V averaged 1.72 ± 0.40 ; serum bicarbonate

was 24.5 ± 2.6 mEq/L; serum phosphorus was 5.3 ± 1.4 mg/dL, and the Charlson Comorbidity Index was 5.7 ± 2.7 . 29 MHD patients (18 M/11 F) and no normal control had diabetes mellitus.

Daily physical activity (DPA), measured with the activity monitor, time-averaged over seven consecutive days, and all three physical performance (PP) tests were impaired in MHD patients, to about 60–70% of normal values ($p < 0.0001$ for each measurement) (Table 2). DPA on the day of hemodialysis, day after dialysis, and day two after dialysis were each significantly lower as compared to the normal adults. These abnormalities were observed separately in both male and female MHD patients (Table 2) and in both diabetic and non-diabetic MHD patients as compared to normal adults. In comparison to the hemodialysis day, DPA was significantly greater 1-day-post-hemodialysis and borderline significantly greater 2-days-post hemodialysis (Table 2). This decreased DPA on the hemodialysis day may reflect, at least in part, the inactivity of patients on the hemodialysis day due to their need to lie or sit quietly in a reclining chair for over four hours in association with their hemodialysis procedure, in addition to their waiting time to start hemodialysis and to their commute to and from the hemodialysis center. There was no significant difference in the DPA between 1-day- and 2-days-post-hemodialysis.

DPA was not different in male vs. female MHD patients or normal men vs. women (Table 2). However, 6-MWD was significantly greater and stair-climbing times were significantly longer in male vs. female MHD patients, and sit-to-stand cycles were significantly greater in normal men vs. normal women (Table 2). Human activity profile scores were also impaired in MHD patients as compared to the normal adults ($p < 0.0001$). MHD patients spent more time sleeping or in marked physical inactivity ($p < 0.0001$) and less time in moderate activity ($p < 0.0001$). After adjustment for age, gender and diabetes, DPA correlated with 6-MWD but not the two other PP tests. Human activity profile scores correlated more closely with all three performance tests than did DPA.

Anxiety and depression, determined by the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI), were present in 43% and 33% of MHD patients and in 2.5% and 5.1% of normals (MHD patients vs. normals: BAI, $p < 0.0001$; BDI, $p = 0.0003$). MHD patients with both anxiety and depression generally had the most impaired DPA and PP (Tables 3 and 4). Higher BAI and BDI scores were each associated with impaired PP. In MHD patients, higher anxiety scores, adjusted for age, gender and diabetes, but not depression scores, were correlated with impaired 6-MWD and STS. In analyses adjusted for age, gender and diabetes, the 7-day average DPA in MHD patients was negatively correlated with the BDI scores ($r = -0.33$, $p = 0.006$) but not with the BAI scores. In these adjusted analyses, DPA also correlated negatively with the degree of depression by BDI, but not BAI, on the day of hemodialysis ($p = 0.01$), day after dialysis ($p = 0.03$), and day two after dialysis ($p = 0.03$). MHD patients displayed negative correlations between BAI and both 6-MWD ($p = 0.028$) and sit-to-stand tests ($p = 0.035$), but there were no significant correlations between BDI scores and PP tests. However, MHD patients without anxiety or depression also had substantially decreased DPA and PP as compared to normals (Tables 3 and 4). Indeed, most of the reduction in DPA and PP in MHD patients was also observed in those patients who did not have either anxiety or depression; the DPA and PP test scores of MHD patients with

or without anxiety and/or depression were much closer to each other than the DPA or PP scores of any of these groups were to the normal adults.

Discussion

The results of these studies indicate that even in relatively healthy MHD patients, daily physical activity (DPA) and physical performance (PP) are substantially impaired and tend to correlate with each other. These disorders are clinically relevant because they are associated with increased morbidity, lower survival rates and probably impaired quality of life in MHD patients (3–5). It is not known what maneuvers might increase DPA or PP in these patients. Whether physical training will improve DPA, PP or clinical outcomes in MHD patients needs to be examined. Moreover, it has not been demonstrated that improving DPA or PP will improve clinical outcomes, and we believe that this is also a question that requires further research.

Our findings indicate that depression and anxiety are common in MHD patients. This has been reported previously (11,12), and it is noteworthy that even in our relatively healthy MHD patients the prevalence of these disorders is at least as high as is described in previous publications (11,12). It is to be emphasized that even in our relatively healthy patients who did not show evidence for anxiety or depression, both DPA and PP were substantially reduced as compared to our normal adults. Nonetheless, our results also indicate that depression in particular is correlated with further reductions in DPA and that anxiety in particular is correlated with a further decrease in PP tests. Anxiety and particularly depression have been associated with reduced physical activity in other population groups (13–15). These observations raise the question as to whether, in at least some MHD patients, treatment of anxiety or depression will improve DPA or PP.

Depression and possibly anxiety are associated with low quality of life and increased morbidity and mortality in MHD patients (16,17), as well as in people without kidney failure (18,19). 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 (20,21). These same factors may account for the reduced DPA and PP in anxious or depressed MHD patients. There are complex neurobiochemical and immunological changes and altered physical fitness associated with anxiety and depression that might also account for reduced DPA and PP in MHD patients (22–27). Thus it is possible, but not proven, that treatment of anxiety and depression might improve DP and PP. It should be emphasized, however, that even in our MHD patients who had neither anxiety nor depression, there were major reductions in DPA and PP in comparison to the normal adults. A limitation of the subgroup analyses in this study was the relatively small sample size of the patients.

Can increased physical activity or regular exercise reduce anxiety or depression? In people without kidney failure, exercise often appears to be an effective treatment for anxiety and possibly depression (22, 24, 28–32). Since anxiety and depression are common in MHD patients and are associated with reduced quality of life and increased morbidity and

mortality (16–19), these considerations provide a strong rationale for clinical trials to assess whether 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 |
| Body Mass Index (kg/m ²) | 27.8 ± 5.8 | 27.0 ± 3.9 | 0.388 |
| Body Fat † (%) | 28.3 ± 8.5 | 27.9 ± 8 | 0.786 |
| Lean Body Mass (kg) | 54 ± 15.4 | 51.4 ± 11.3 | 0.315 |
| Serum albumin (g/dL) | 4.1±0.3 | 4.1±0.2 | 0.606 |
| Hemoglobin (g/dL) | 11.2 ± 0.8 | 13.8±1.3* | < 0.0001 |

* Data with units are given as the mean ± standard deviation. Numbers in parentheses indicate range of values.

† 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.

Table adapted from Zhang et Al (10).

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Table 2
Physical Activity and Physical Performance in MHD Patients and Normal Controls by Gender Group

| | MHD Patients | | | | Normal Controls | | | | Males: MHD vs. Normals | | Females: MHD vs. Normals | |
|---|--------------------------------|-----------------|----------------------------|-----------------|-----------------|-------------------------|---------|---------|------------------------|--|--------------------------|---------|
| | Total* N=72 | Males N=49 | Females N=23 | Total* N=39 | Males N=23 | Females N=16 | P | P | | | | |
| <u>Physical Activity</u> | | | | | | | | | | | | |
| Human Activity Profile | | | | | | | | | | | | |
| MAS | 79.2±12.2 | 80.6 ± 10.6 | 76.2 ± 14.9 | 90.3 ± 3.4 | 90.6 ± 3.3 | 89.8 ± 3.5 | <0.0001 | <0.0001 | | | | <0.0001 |
| AAS | 70.3 ± 6.9 | 71.7 ± 16.2 | 67.4 ± 18.5 | 89.2 ± 3.7 | 89.7 ± 3.8 | 88.4 ± 3.5 | <0.0001 | <0.0001 | | | | <0.0001 |
| % time spent determined by vector magnitude | | | | | | | | | | | | |
| Sleep or inactivity | 81.9 ± 5.8 | 82.0 ± 5.8 | 81.7 ± 6.0 | 72.8 ± 6.0 | 72.9 ± 6.1 | 72.7 ± 6.0 | <0.0001 | <0.0001 | | | | <0.0001 |
| Light Activity | 14.4 ± 4.4 | 14.2 ± 4.4 | 14.9 ± 4.5 | 20.0 ± 4.5 | 19.3 ± 4.3 | 21.0 ± 4.6 | <0.0001 | <0.0001 | | | | 0.0002 |
| Moderate activity | 3.7 ± 2.1 | 3.8 ± 2.0 | 3.3 ± 2.2 | 7.2 ± 3.0 | 7.8 ± 3.3 | 6.4 ± 2.3 | <0.0001 | <0.0001 | | | | <0.0001 |
| Average weekly DPA (vector magnitude) | 395727 ± 154753 | 405129 ± 167250 | 371820 ± 124367 | 648478 ± 216519 | 671412 ± 227704 | 615512 ± 201873 | <0.0001 | <0.0001 | | | | <0.0001 |
| Day of HD | 353397 ± 150665 ^a | 365709 ± 164578 | 327170 ± 114481 | -- | -- | -- | -- | -- | | | | -- |
| 1-day-post-HD | 431351 ± 185021 ^{a,b} | 443029 ± 199943 | 406471 ± 149345 | -- | -- | -- | -- | -- | | | | -- |
| 2-days-post-HD | 407513 ± 185583 ^{a,c} | 409701 ± 191048 | 402947 ± 177700 | -- | -- | -- | -- | -- | | | | -- |
| <u>Physical Performance</u> | | | | | | | | | | | | |
| 6-MWD (meters) | 441.3 ± 121.9 | 467.6 ± 98.9 | 385.3 ± 147.6 ^d | 617.6 ± 63.2 | 632.9 ± 60.7 | 595.5 ± 61.9 | <0.0001 | <0.0001 | | | | <0.0001 |
| Sit-to-stand test (cycles per 30 seconds) | 15.9 ± 5.3 | 16.5 ± 5.6 | 14.7 ± 4.2 | 26.2 ± 5.4 | 28.1 ± 3.9 | 23.6 ± 6.3 ^d | <0.0001 | <0.0001 | | | | <0.0001 |
| Stair-climbing test (seconds per 22 stairs) | 15.8±11.0 | 13.5 ± 5.0 | 20.8 ± 17.2 ^d | 9.8 ± 1.1 | 9.6 ± 1.2 | 10.2 ± 1.0 | <0.0001 | <0.0001 | | | | 0.008 |

Data expressed as mean ± standard deviation. All statistical comparisons are unadjusted.

MAS is the Maximum Activity Score which is the highest oxygen-demanding activity that the subject indicates that he/she can perform as calculated from the Human Activity profile.

AAS is the Adjusted Activity Score which is the subject's MAS minus the number of less oxygen demanding physical activities that the subject indicates in the Human Activity Profile that he/she can no longer perform (See Citation 9 for further discussion of these terms).

Vector Magnitude is defined in Methods Section.

* Values for each measure of physical activity and physical performance in MHD patients are statistically different from normal controls at $p < 0.0001$.

^a Versus average weekly DPA of normal controls: $p < 0.0001$;

^b 1-day-post-HD vs day of HD: $p = 0.018$;

^c 2-days-post-HD vs day of HD: $p = 0.057$; 1-day-post-HD vs 2-days-post-HD: $p = 0.441$

^d Statistically different from the opposite gender in the same category (i.e., comparisons exclusively among MHD patients or comparisons exclusively among normal controls): $p < 0.01$

Table adapted from Kim et al (9).

Table 3

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 ^a | 78±12 | 83±12 ^b | 73±16 ^{a,b} | 0.0003 | 90±3 [†] |
| AAS | 76±14 ^{a,c} | 64±20 ^c | 74±16 ^b | 63±17 ^{a,b} | 0.001 | 89±3 [†] |
| DPA-7 day average (vector magnitude) | 41588±142645 | 413229±195863 | 423944±156711 | 322245±124760 | 0.004 | 663304±225019 [†] |
| DPA on HD Day | 372469±139164 | 355591±173337 | 380561±201589 | 300361±107871 | 0.004 | -- |
| DPA 1-day-post-HD | 452035±177787 | 465143±232931 | 513005±248927 ^a | 336460±142284 ^a | 0.004 | -- |
| DPA 2-days-post-HD | 435816±175417 | 433774±214628 | 381412±172040 | 364203±186121 | 0.152 | -- |

Symbols: (A-D-) subjects displaying neither anxiety nor depression, (A+D+) those displaying anxiety and depression, (A+D-) those displaying anxiety but not depression, and (A-D+) those displaying depression but not anxiety. Anxiety and depression status was determined by the Beck Anxiety Inventory and Beck Depression Inventory, respectively. The thresholds for diagnosing mild or more severe anxiety or depression are adapted from Beck et al (6,7).

Abbreviations: MAS: Maximum Activity Score; AAS: Adjusted Activity Score.

Data are presented as mean ± standard deviation. All statistical comparisons are adjusted for age, gender, presence of diabetes, blood hemoglobin, and dialysis vintage.

* Determined by ANOVA

^{a,b,c} 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.

[†] Normal A-D- controls are significantly different from MHD A-D- patients as determined by Tukey's HSD test; p<0.01.

Table adapted from Zhang et al (10).

Table 4

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 | 65 | 0.037 | 0 |
| 6-MWD(meters) | 466±119 | 397±116 | 478±124 | 410±122 | 0.013 | 620±65 [‡] |
| Sit-to-stand test (cycles per 30 seconds) | 16±5 | 17±5 | 18±5 | 13±5 | 0.544 | 26±6 [‡] |
| Stair climbing test (seconds per 22 stairs) | 14.7±7.0 ^a | 16.2±10.0 | 13.1±2.7 ^b | 19.2±18.5 ^{a,b} | <0.0001 | 9.7±1.1 [‡] |

Symbols are defined in the legends to Table 3.

Anxiety and depression in this table is determined by the Beck Anxiety Inventory and Beck Depression Inventory, respectively. The thresholds for diagnosing mild or more severe anxiety or depression are adapted from Beck et al (6,7).

Data are presented as mean ± standard deviation. All statistical comparisons are adjusted for age, gender, presence of diabetes, blood hemoglobin, and dialysis vintage.

* Determined by ANOVA

^{a,b} 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

[‡] Normal A-D- controls are significantly different from MHD A-D- patients as determined by Tukey's HSD test: p<0.01.

Table adapted from Zhang et al (10).