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ORIGINAL RESEARCH

Comparison of Body Composition, Strength, and Physical Performance Measurements Between Healthy Participants and Hemodialysis Patients

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Purpose: This study evaluated the difference in physical performance tests, strength, and total and regional mass using a comprehensive dataset between maintenance hemodialysis (HD) patients and a healthy population.

Patients and Methods: A total of 84 HD patients were enrolled. We selected 42 healthy participants (HPs) age- and sex-matched to the 84 HD patients as controls. Collected data were sex, age, body mass index (BMI), laboratory findings, total and regional measurements for lean mass or fat mass, thigh muscle area (TMA), handgrip strength, and physical performance measurements.

Results: There were no significant differences in BMI, total lean mass, or total fat mass including regional fat mass between the two groups. Lean leg mass and TMA were greater in HPs than in HD patients. All measurements of physical performance, including handgrip strength, were better in HPs than in HD patients. A multivariate analysis of lean leg mass, TMA, and physical performance measures had similar results to the same data studied with a univariate analysis.

Conclusion: We demonstrated that HD patients had decreased physical performance and strength compared to HPs. The difference in leg muscle mass was most prominent among the total and regional body compositions between HPs and HD patients.

Keywords: body composition, hemodialysis, physical performance, strength

Introduction

Hemodialysis (HD) is the most common modality among three renal replacement therapies, which are HD, peritoneal dialysis, and kidney transplantation. As HD-related technology has advanced, short-term mortality in HD patients has decreased. However, long-term survivors can be prone to chronic complications due to the non-removal of uremic toxins or dialysis-associated effects. Malnutrition is one of the most common complications in HD patients.[1] It is associated with a decrease in muscle mass, physical performance, and strength, which results in frailty or disability in HD patients. Various methods are commonly used for objective muscle mass measurements. These include dual-energy X-ray absorptiometry (DEXA) evaluation, bioimpedance analysis (BIA), computed tomography (CT), or equations on creatinine kinetics.[2] However, there is no gold standard for estimating muscle mass.

Understanding changes in body composition in stable HD patients can be useful to screen for malnourishment-related complications during chronic HD. Previous

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studies have evaluated changes in body compositions using longitudinal data sets—most of these used baseline values at the initiation of dialysis or total mass.[3–7] However, the value at the initiation of dialysis may be inappropriate to identify effects of chronic HD because initial HD patients are more likely to be of hypervolemic status and malnourished because of the retained uremic toxin before sufficient dialysis.[8] In addition, the total mass may not be more sensitive than regional values for predicting pathologic changes. To overcome these limitations, we compared stable maintenance HD patients to an age- and sex-matched healthy population without other comorbidities using comprehensive data. These data included regional mass (such as appendicular, arms, and legs lean mass, as well as thigh muscle area). This study evaluated the differences in physical performance tests, strength, and total and regional mass using a comprehensive data set between stable maintenance HD patients and a healthy population.

Patients and Methods

Study Population

The institutional review board of the CHA Gumi Medical Center (No. 12-07) approved this study, which was performed in a tertiary medical center between September 2012 and March 2015. It was a cross-sectional study based on the analysis of an existing data set.[9] This study was conducted in accordance with the Declaration of Helsinki. We included all patients undergoing HD aged ≥20 years, with a duration of dialysis ≥6 months, ability to ambulate without an assistive device, ability to communicate with the interviewer, and no hospitalization within the three months before enrolment. None of the patients were on opioids, antihistamines, or antidepressants, which are associated with decreased physical activity and cognitive function. A total of 84 HD patients were enrolled. We selected 42 healthy participants (HPs) age- and sex-matched to the 84 HD patients for healthy controls. All HPs did not have comorbidities, such as diabetes mellitus (DM) or hypertension and were not on any medications. Informed consent was obtained before enrollment.

Baseline Variables

Collected baseline data for both two groups were sex, age, and hemoglobin (g/dL), C-reactive protein (CRP, mg/dL), blood urea nitrogen (mg/dL), creatinine (mg/dL), 25-hydroxy (25-OH) vitamin D (ng/mL), and albumin (g/dL) levels. The presence of DM, dialysis vintage, Charlson comorbidity index score and single-pool Kt/Vurea (spKt/Vurea) were evaluated for HD patients. Laboratory analyses were performed prior to the HD sessions and were repeated three times in the following three weeks for HD patients. The mean of the three values was considered for each variable. DM was defined as a patient-reported history or a medical record of a DM diagnosis or anti-DM medication. The Charlson comorbidity index score and spKt/Vurea were calculated using the previously described methods.[10,11] All HD patients underwent three HD sessions per week. All measurements, including body composition measurements and physical performance tests, were performed on the day after the midweek HD session.

Assessment of Body Composition and Strength

Body mass index (BMI, kg/m^2) was calculated as body weight divided by the height in meters squared. Lean mass (kg), fat mass (kg), and total bone mineral density (BMD, g/cm^2) were evaluated using whole-body DEXA (GE Medical Systems Lunar, Madison, WI, USA). Total lean mass was defined as the total body measurement, and appendicular lean mass (ALM) was calculated as the sum of the upper and lower extremities. Lean arm and leg masses were calculated using the sum of both upper and lower extremities, respectively. Total and regional measurements of fat mass were calculated using the same definitions used for lean mass.

The thigh muscle area (TMA, cm^2), visceral fat area (VFA, cm^2), and subcutaneous fat area (SFA, cm^2) were evaluated using CT obtained using a 320-slice CT scanner (Aquilion ONE; Toshiba Medical Systems Corp., Tokyo, Japan). For TMA, an axial image was obtained at the midpoint of a line extending from the superior border of the patella to the greater trochanter (3 mm thickness, five slices). For VFA and SFA, a transverse image was obtained between the L3 and L4 vertebral bodies.[12] The images were analyzed using analysis software (ImageJ 1.45S; National Institutes of Health, Bethesda, MD, USA).

Volume status was evaluated based on the edema index measured using multifrequency BIA (InBody, Seoul, Korea). The edema index was defined as the ratio of extracellular water to total body water and measured at 30 minutes or more after the end of the midweek HD session. Hand-grip strength (HGS) was measured in all patients. Each patient performed three trials with their dominant hand using a manual hydraulic dynamometer (Jamar® Hydraulic hand dynamometer; Sammons Preston, Chicago, IL, USA). The highest value among the three trials was selected.

Assessment of Physical Performance

Measurements for physical performance were performed as previously described.[9] Briefly, gait speed (GS, m/s) was calculated using the 4-meter static walking test.[13] For the sit-to-stand test performed five times test (5STS), each patient was seated on a chair with their arms crossed and hands touching their shoulders.[14] The patients were asked to stand up and sit down five times as quickly as possible, and the time taken in seconds was recorded. For the sit-to-stand 30-s test (STS30), patients were seated on a chair with their arms crossed and hands touching their shoulders. Scores were defined as the number of times a patient could stand up in 30 s without using their arms for support.[15] For the 6-minute walk test (6-MWT, m), patients were asked to walk at their usual pace for 6 min, and the distance covered was recorded in meters.[16] For the timed up-and-go test (TUG, s), the patients were instructed to stand up from an arm chair, walk 3 m, turn around, return to the chair, and sit down.[17] The time in seconds was recorded. The Short Physical Performance Battery test (SPPB) was calculated using GS, 5STS, 6-MWT, and the balance test, with a score between 0 and 12.[18]

Statistical Analysis

The data were analysed using IBM SPSS Statistics version 25 (SPSS Inc., Chicago, IL, USA). Our study retrospectively evaluated an existing data set. Therefore, our study sample size was not planned using a determination or power calculation. Categorical variables are expressed as counts (percentages). The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test. Continuous variables with normal distribution are expressed as mean ± standard deviation and were compared using Student's *t*-test. Those data with non-normal distributions are expressed as the median (interquartile range) and were compared using the Mann–Whitney *U*-test. The correlation between two continuous variables was assessed using Pearson's or partial correlation analyses. Multivariate analysis was performed using an analysis of covariance and adjusted for age, sex, and BMI. In addition, we performed subgroup analyses according to age or sex. The level of statistical significance was set at $P < 0.05$.

Results

The mean age of HPs and HD patients was 55.6 ± 16.1 and 56.5 ± 11.9 years, respectively (Table 1). The proportion of men and women was similar in the two groups. The hemoglobin, serum albumin, and 25-OH vitamin D levels were significantly higher in HPs than in HD patients. C-reactive protein, blood urea nitrogen, and creatinine levels were lower in HPs than in HD patients.

Table 1 Baseline Characteristics

	HPs (n = 42)	HD Patients (n = 84)	*P*-value
Age (years)	55.6 ± 16.1	56.5 ± 11.9	0.714
Sex (men)	21 (50%)	44 (52.4%)	0.801
Diabetes mellitus	–	44 (52.4%)	–
Dialysis vintage (years)	–	2.9 (4.9)	–
CCI score	–	6 (3)	–
Hemoglobin (mg/dL)	14.2 ± 1.8	11.0 ± 0.6	<0.001
Albumin (g/dL)	4.4 ± 0.3	3.8 ± 0.3	<0.001
C-reactive protein (mg/dL)	0.09 (0.15)	0.20 (0.40)	<0.001
Blood urea nitrogen (mg/dL)	14.6 ± 3.6	59.4 ± 14.7	<0.001
Creatinine (mg/dL)	0.8 ± 0.2	10.3 ± 2.6	<0.001
25-hydroxy vitamin D (ng/mL)	15.6 (13.0)	10.2 (6.5)	<0.001
spKt/Vurea	–	1.4 ± 0.3	–

Notes: Data are expressed as mean ± standard deviation for variables with normal distribution and median (interquartile range) for variables with non-normal distribution. *P*-values were tested using Student's *t*-test for variables with normal distribution and Mann–Whitney *U*-test for variables with non-normal distribution.
Abbreviations: HPs, healthy participants; HD, hemodialysis; CCI, Charlson comorbidity index.

Table 2 Comparison of Body Composition Between Healthy Participants and Hemodialysis Patients

	HPs	HD Patients	*P*-value
Body mass index (kg/m^2)	23.8 ± 2.9	23.7 ± 3.6	0.955
Total lean mass (kg)	43.2 ± 8.4	43.0 ± 8.1	0.921
Appendicular lean mass	18.7 ± 4.1	17.4 ± 3.8	0.074
Arms lean mass	4.8 ± 1.4	4.6 ± 1.1	0.280
Legs lean mass	14.0± 2.9	12.8 ± 2.9	0.045
Trunk lean mass	20.8 ± 3.9	22.0 ± 4.2	0.128
Total fat mass (kg)	18.2 ± 5.8	17.4 ± 7.7	0.589
Arms fat mass	1.6 ± 0.6	1.6 ± 0.9	0.991
Legs fat mass	5.3 ± 1.9	4.7 ± 2.1	0.138
Trunk fat mass	10.5 ± 3.6	10.4 ± 5.0	0.852
Sagittal abdomen diameter (cm)	20.0 ± 2.6	20.5 ± 3.1	0.417
Abdominal VFA (cm^2)	106 (106)	145 (81)	0.282
Abdominal SFA (cm^2)	138 ± 53	128 ± 71	0.407
Total BMD (g/cm^2)	1.12 ± 0.11	1.06 ± 0.13	0.018
Arms BMD	0.96 ± 0.16	0.85 ± 0.16	<0.001
Legs BMD	1.19 ± 0.15	1.11 ± 0.18	0.010
Spine BMD	1.02 ± 0.14	1.03 ± 0.16	0.828
Pelvis BMD	1.06 ± 0.11	0.97 ± 0.14	0.001
Edema index	0.345 ± 0.010	0.355 ± 0.015	<0.001
Thigh muscle area (cm^2)	109 ± 26	97 ± 23	0.010
Intramuscular fat area (cm^2)	4.6 ± 2.8	5.5 ± 4.8	0.232
Thigh SFA (cm^2)	51.5 ± 24.9	50.2 ± 28.5	0.804

Notes: Data are expressed as mean ± standard deviation for variables with normal distribution and median (interquartile range) for variables with non-normal distribution. *P*-values were tested using Student's *t*-test for variables with normal distribution and Mann–Whitney *U*-test for variables with non-normal distribution.
Abbreviations: HPs, healthy participants; HD, hemodialysis; VFA, visceral fat area; SFA, subcutaneous fat area; BMD, bone mineral density.

There were no significant differences in BMI, total lean mass, or total fat mass including regional fat mass between the two groups (Table 2). Abdominal VFA and SFA did not differ between the two groups. BMD measurements were higher in HPs than in HD patients. The edema index was greater in HD patients than in HPs. Lean leg masses and TMA were greater in HPs than in HD patients. However, there was no significant difference in fat distribution between the two groups. All physical performance measurements, including HGS, GS, 5STS, STS30, 6MWT, TUG, and SPPB, were better in HPs than in HD patients (Table 3).

Table 3 Comparison of Strength and Physical Performance Between HPs and HD Patients

	HPs	HD Patients	*P*-value
HGS (kg)	30.0 (19.3)	26.0 (9.8)	<0.001
GS (m/s)	1.08 ± 0.18	0.92 ± 0.20	<0.001
5STS (s)	5.3 (2.3)	7.8 (3.4)	<0.001
STS30	25.0 ± 6.9	17.8 ± 5.7	<0.001
6MWT (m)	569 (119)	479 (142)	<0.001
TUG	5.6 (1.3)	6.7 (2.9)	<0.001
SPPB	12.0 (0)	11.5 (2.0)	<0.001

Notes: Data are expressed as mean ± standard deviation for variables with normal distribution and median (interquartile range) for variables with non-normal distribution. *P*-values were tested using Student's *t*-test for variables with normal distribution and Mann–Whitney *U*-test for variables with non-normal distribution.
Abbreviations: HPs, healthy participants; HD, hemodialysis; HGS, handgrip strength; GS, gait speed; 5STS, five times sit-to-stand test; STS30, sit-to-stand for 30-s test; 6-MWT, 6-minute walk test; TUG, timed up-and-go test; SPPB, short physical performance battery.

Multivariate analysis of lean leg mass, TMA, and physical performance measures had similar results to those obtained from the univariate analysis (Supplementary Table 1). For HGS, ALM had the highest correlation coefficients in HPs in two correlation analyses (Supplementary Table 2). Statistical significance in two correlation analyses was maintained in TMA and lean arm masses in HD patients. Significant correlations were not obtained for GS in HPs, but the partial correlation was positive with some lean mass indicators. TMA and some lean mass indicators significantly correlated in HD patients, but partial correlation showed a positive association with TMA alone. Two correlation analyses between TMA and STS30 or 6MWT were greater in HD patients than in HPs. The TMA was inversely associated with TUG in both groups, but a partial correlation showed that the association was sustained in HD patients alone. The partial correlation showed an inverse association of SPPB with TMA in HD patients alone.

We performed subgroup analyses according to age or sex. The numbers of male and female patients were 21 and 21 in HPs, and 44 and 40 in HD patients, respectively. Patients who were <65 or ≥65 years old were 33 and 9 in HPs, and 61 and 23 in HD patients, respectively. First, we compared body composition measurements or physical performance tests between HPs and HD patients according to sex or age group (Supplementary Tables 3 and 4). The differences in muscle mass measurements between HPs and HD patients were maintained in males or those aged ≥65 years. The difference in BMD between the two groups was maintained in females or those aged <65 years. The difference in physical performance tests between the two groups was maintained in most subgroups. There was no significant difference in the edema index between the two groups in those aged ≥65 years. Second, we performed correlation analyses between muscle mass measurements and physical performance tests according to sex or age group (Supplementary Table 5). In HPs, HGS was associated with most muscle mass regardless of age or sex. HPs aged <65 years showed similar trends in STS30, TUG, or 6MWT compared with those using total HPs. In HD patients, results using the total cohort showed the highest correlation for TMA, and the trend was similar in patients aged <65 years or of the male sex.

Discussion

First, we evaluated total and regional muscle mass measurements between patients on maintenance HD with age- and sex-matched HPs. Total, arms, trunk lean masses, and ALM did not differ between the two groups, and leg lean mass was greater in HPs than in HD patients. A decrease in leg lean mass mainly caused the lower ALM in HD patients. In addition, we evaluated CT measurements of characteristics of leg lean mass, which showed that the difference between the two groups existed in the muscle mass but not in fat mass, including the intramuscular and subcutaneous fat. Consequently, the lower physical performance and strength in HD patients were more associated with decreased muscle mass than a fatty change in the muscle. Maintenance dialysis patients were prone to insulin resistance and chronic inflammation, which decreased muscle mass.[19] The merged effect for these factors may be presented as a non-difference in fat mass and a significant decrease in muscle mass, especially leg muscle mass, relative to those in HPs. The multivariate analyses of these differences showed similar trends to the results from the univariate analysis.

HD patients had worse physical performance and strength in the upper and lower extremities than those in HPs despite the decrease in mass in the leg muscles alone. This difference may be associated with muscle dysfunction, such as altered neuromuscular or mitochondrial function and overestimation of the muscle mass due to volume overload. Uremic conditions can lead to neuromuscular or mitochondrial dysfunction; however, this change cannot be detected using CT or DEXA measurements. Although our data did not evaluate these indicators, HD patients who underwent maintenance HD for several years may be already prone to these pathologies despite having similar arm muscle mass. The edema index in our study was higher in HD patients than in HPs. Volume overload is associated with the overestimation of muscle mass, consisting of a higher amount of water than fat. Considering the overestimated muscle mass in HD patients, the proportion of edema-free muscle in the arm muscle mass may be greater in HPs than in HD patients.

In HPs, HGS was associated with most muscle mass indices in two correlation analyses. Although correlations with these were lower in HD patients, the association between arms lean mass or TMA and HGS was relatively sustained in HD patients in both correlations. Pearson's correlation showed a stronger association between TMA or most lean masses and GS in HD patients. However, a partial correlation for GS showed a difference between HPs and HD patients in index with a significant association (lean masses in HPs and TMA in HD patients). A non-association between lean masses and GS in HD patients may be an inherent limitation of DEXA in estimating muscle mass in HD patients. For STS30 and 6MWT, the correlation between variables and some muscle mass indices was higher in HD patients than in HPs. The favourable association in HD patients may be associated with large differences or intervals for each value within this group. TMA generally showed favorable associations with most physical performance measurements among muscle mass indices in HD patients.

We performed subgroup analyses for matching age and sex. The difference in muscle mass measurements between HPs and HD patients was obtained in males and elderly participants, and in females, or those aged <65 years for BMD. These data may be useful to identify vulnerable groups among dialysis patients. Male sex with relatively large muscle mass and elderly patients who easily affected by chronic disease would be associated with a difference in muscle mass between HPs and HD patients. A decrease in BMD with dialysis may be more prevalent in female or young patients than males or elderly patients. The lack of a difference in the edema index between HPs and HD patients among the elderly may be more associated with a larger fat mass than muscle mass. Therefore, the association between TMA and physical performance was relatively lower in elderly HD patients than in young HD patients. According to various subpopulations, further studies are needed to identify differences in body compositions or associations between muscle mass measurements and physical performance tests.

The association between 5STS and TMA or other muscle mass measurements was weak in HD patients than that in other physical performance tests. A significant correlation between 5STS and TMA was not obtained in the Pearson's correlation analysis, but a partial correlation, when adjusted for age, sex, and BMI, showed an inverse association between 5STS and TMA. Subgroup analysis showed an inverse association between two variables in males or those aged <65 years. This shows that a non-statistical significance from the total cohort would be influenced by confounding factors, such as age or sex.

In our study, the fat mass did not differ between the two groups. A previous study showed that fat mass increases during the first three years of dialysis, but the value decreases after these first three years.[20] The lack of a difference in fat mass may be associated with the dialysis vintage; in our cohort, participants' dialysis vintage tended to be in the decreasing period after the time where increasing fat masses is typically seen. A shorter vintage may be associated with greater fat masses in HD patients, and HD patients with longer vintages lead to lower fat mass. Although a statistical significance was not obtained for total fat mass, trends were observed for an increase in VFA and decrease in SFA in HD patients. In addition, in our data, BMD was steadily lower in HD patients than in HPs. The lower BMD in HD patients is well known and can be caused by an increase in the parathyroid hormone and a decrease in 25-(OH) vitamin D levels.

Our study has limitations, including its single-center design and a small number of patients. Some of our data were from a cohort analyzed in a previous study.[9] The weak statistical significance for some variables may be associated with the small sample size. Second, we did not perform a longitudinal evaluation, which would be more valuable when comparing the two groups. Third, we did not perform multivariate analyses adjusting for sufficient confounding factors due to the limited sample size. A prospective longitudinal study including many patients is needed to overcome these limitations.

Conclusion

The present study demonstrated that HD patients had decreased physical performance and strength than HPs. The difference in the leg muscle mass was the most prominent difference among the total and regional body compositions between HPs and HD patients. Before the decrease in total muscle mass in stable HD patients, regional muscle mass measurements, such as TMA, may be more sensitive indicators for predicting a decrease in physical performance or strength than total measurements.

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Disclosure

The authors report no conflict of interest in this work.

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