ORIGINAL RESEARCH

Low Physical Function in Maintenance Hemodialysis Patients Is Independent of Muscle Mass and Comorbidity

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Objectives: It is unknown whether muscle wasting accounts for impaired physical function in adults on maintenance hemodialysis (MHD).

Design: Observational study.

Setting: Outpatient dialysis units and a fall clinic.

Subjects: One hundred eight MHD and 122 elderly nonhemodialysis (non-HD) participants.

Exposure Variable: Mid-thigh muscle area was measured by magnetic resonance imaging.

Main Outcome Measure: Physical function was measured by distance walked in 6 minutes.

Results: Compared with non-HD elderly participants, MHD participants were younger (49.2 ± 15.8 vs. 75.3 ± 7.1 years; $P < .001$) and had higher mid-thigh muscle area (106.2 ± 26.8 vs. 96.1 ± 21.1 cm^2; $P = .002$). However, the distance walked in 6 minutes was lower in MHD participants (322.9 ± 110.4 vs. 409.0 ± 128.3 m; $P < .001$). In multiple regression analysis adjusted for demographics, comorbid conditions, and mid-thigh muscle area, MHD patients walked significantly less distance (−117 m; 95% confidence interval: −177 to −56 m; $P < .001$) than the non-HD elderly.

Conclusions: Even when compared with elderly non-HD participants, younger MHD participants have poorer physical function that was not explained by muscle mass or comorbid conditions. We speculate that the uremic milieu may impair muscle function independent of muscle mass. The mechanism of impaired muscle function in uremia needs to be established in future studies.

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Introduction

FRAILTY IS CLASSICALLY defined by decreased grip strength, slower walking time, exhaustion, low physical activity level, and unintentional weight loss.[1] Frailty is highly prevalent in those undergoing maintenance hemodialysis (MHD)[2] and is strongly associated with mortality and adverse health outcomes in this population.[3] Frailty is also common in older individuals experiencing age-related decrements in physical and muscle function.[1] Muscle wasting is also common in the MHD[4] and elderly populations.[5]

It is unclear whether decreased physical function in MHD patients is because of decreased muscle mass or whether uremia per se impairs muscle function. Furthermore, increased prevalence of comorbid conditions such as heart failure, peripheral vascular disease, and diabetes mellitus in the MHD population might also explain the decreased physical function in this population. Therefore, we examined the hypothesis that decreased physical function in MHD patients is largely explained by decreased muscle mass and increased comorbid conditions in the MHD population by pooling data from a dialysis cohort and a non-MHD elderly cohort.

Methods

Study Population

We combined data from a dialysis cohort and a nondialysis cohort. In both the cohorts, magnetic resonance imaging (MRI) was performed to measure mid-thigh muscle area (MTMA) and distance walked in 6 minutes (6 MW) was performed to measure physical function.

Protein Intake, Cardiovascular disease and Nutrition In stage V chronic kidney disease is a prospective observational study examining the effect of nutrient intake on vascular health, body composition, and physical functioning in adult patients (≥18 years) on MHD for at least

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3 months at the University of Utah and Vanderbilt University Medical Center (VUMC) outpatient dialysis units (NCT00566670). Exclusion criteria for the MHD cohort included patients with medical conditions with increased short-term mortality such as symptomatic heart failure, active malignancy (excluding squamous and basal cell skin cancers), and acquired immune deficiency syndrome; patients with inability to walk or those using a wheel chair; patients with contraindications to MRI such as pacemakers; and patients with atrial fibrillation which may interfere with measurement of pulse wave velocity.

The non-HD population was constituted by participants in an ongoing longitudinal study of older adults (≥65 years) at high risk of falls (NCT01080196). This ongoing study is examining the effect of a multicomponent exercise-training program on fall prevention at the University of Utah Department of Physical Therapy. Fall prevention participants were included if they were community ambulators with at least 2 comorbid health conditions and a history of at least 1 fall in the previous year. Exclusion criteria for the fall prevention cohort included dementia, progressive central nervous system disorder, myopathic or rheumatologic disease that adversely impacted muscle, and any absolute contraindications for MRI.

Data Collection

Baseline study data from both studies were used in this cross-sectional investigation. In both studies, standardized questionnaires were used to obtain demographic, medical history, medication, and socioeconomic data. Height and weight were measured following standardized protocols. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Magnetic Resonance Imaging

MRI scans of the legs were performed at both University of Utah and VUMC sites at the baseline visit. For the MHD cohort, this was on a nondialysis day. MTMA was quantified by imaging both legs in the axial plane at the midpoint of the femur. A 3-point Dixon method[6] was used to create separated fat and nonfat images, with phase unwrapping by iterative solution of the Poisson equation.[7] Percent fat volume fraction and percent nonfat volume fraction were calculated from the signal intensity of the fat and nonfat MRI images using the gradient-recalled echo signal equation and a tissue signal model.[8] Cross-sectional lean muscle area was calculated in a single axial image at the midpoint of the femur by adding the percent nonfat fraction value of each pixel over the entire leg cross-section and multiplying by pixel area.

Imaging at the University of Utah was performed on a 3 T Siemens Trio scanner (Malvern, PA). Imaging at VUMC was performed with a 3T Philips Achieva scanner (Andover, MA). Image processing, calculation of fat- and nonfat volume fraction images, and measurement of fat and muscle cross-sectional areas were performed at the University of Utah by the same observers for the dialysis and nondialysis cohorts following a standardized protocol.

Six-Minute Walk Distance

Physical function assessing locomotion was measured objectively using the 6 MW test. This test was performed per American Thoracic Society standards using a flat surface on an indoor walking course.[9] For the MHD cohort, testing was performed on nondialysis days. In all participants testing was proctored by the study coordinator. Each participant walked along the indoor course at a self-determined pace for a total of 6 minutes with a distance measuring wheel. Participants were allowed to rest briefly by leaning against the wall or sitting during the test or stop prematurely if they were unable to complete the test. There was no practice test, warm-up period, or incentive provided for performance.

Statistical Methods

Baseline characteristics of MHD and non-HD groups are presented as mean and standard deviation (SD) for continuous variables and proportions for categorical variables. Continuous variables between the subgroups were compared by t test and categorical variables by chi-square test or the Fisher exact test. To examine the relationships between MHD status with 6 MW, multivariate linear regression analyses were performed with or without adjustment for age, sex, race, smoking, alcohol, coronary artery disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease, diabetes, lung disease, and MTMA. Age ≥65 years was included as a dichotomous variable in the model because all participants are of 65 years or older in the non-HD subgroup. In addition, we related 6 MW distance with MTMA separately in MHD and non-HD subgroups in multivariate linear regression models adjusted for the aforementioned covariates. To satisfy the assumption of linear regression analyses, the independence, homoscedasticity, and normality of residuals were tested and no violations of the assumptions were found. All analyses were conducted with Stata 12 (Stata Inc, College Station, TX).

Results

The study population consisted of 108 MHD participants and 122 older (≥65 years) high fall risk participants (non-HD group). Baseline characteristics of all participants are reported in Table 1 by MHD or non-HD status. Percentages or mean (±SD) are presented. Age distributions of the MHD and non-HD participants are depicted in Figure 1. MHD participants were younger (49.2 ± 15.8 years) than non-HD participants (75.3 ± 7.1 years) ($P < .001$). Fifty-seven percent of the MHD participants and 33% of the non-HD participants were male ($P < .001$), and 62% of the MHD and 98% of the non-HD participants were Caucasian ($P < .001$).