Original Article

Association between bone mineral density, muscle volume, walking ability, and geriatric nutritional risk index in hemodialysis patients

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Background and Objectives: Hemodialysis patients are at risk for bone loss and sarcopenia, characterized by reduced muscle mass and limited mobility/function. Osteoporosis and sarcopenia both increase the risk of hospitalization and death in affected individuals. Malnutrition also occurs as a complication of hemodialysis and has been identified as a risk factor for osteoporosis and sarcopenia. In this study, we examined the relationship between osteoporosis, muscle volume, walking ability, and malnutrition in hemodialysis patients. **Methods and Study Design:** Forty-five hemodialysis patients were evaluated. Bone mineral density (BMD) and muscle volume were measured by dual-energy X-ray absorptiometry. Muscle volume and strength were evaluated using lean mass index (LMI), handgrip strength, and walking ability. The time required for a patient to walk 10 meters was measured to evaluate walking ability. The geriatric nutritional risk index (GNRI) was used to assess malnutrition. **Results:** Multiple linear regression analysis showed that older age, female sex, lower LMI, and higher total type I procollagen N-terminal propeptide were correlated with lower BMD of lumbar spine. Higher age and lower LMI were correlated with lower BMD of the femoral neck. Female sex and lower GNRI were correlated with lower LMI. Longer duration of hemodialysis was correlated with lower walking ability. **Conclusions:** Our findings suggest that muscle preservation is required to maintain both lumbar spine and femoral neck BMD. Similarly, nutritional management is necessary to maintain BMD via preservation of muscle volume. Complementary nutritional therapies are needed to improve osteoporosis and sarcopenia in high-risk hemodialysis patients.

Key Words: hemodialysis, lean mass index (LMI), geriatric nutritional risk index (GNRI), bone mineral density (BMD), sarcopenia

INTRODUCTION

Chronic kidney disease and hemodialysis increase the risk of bone loss and fracture, which are associated with a reduction in quality of life.[1] Sarcopenia, characterized by reduced muscle mass and limited mobility/function, is also an important comorbidity in hemodialysis patients.[2] Osteoporosis and sarcopenia increase the risk of hospitalization and mortality.[1,2] Malnutrition is one of the vital complications in patients undergoing hemodialysis.[3,4] In addition, malnutrition is an important risk factor for osteoporosis and sarcopenia in hemodialysis patients.[5,6] In this study, we used geriatric nutritional risk index (GNRI) as a tool to assess nutritional status.[7] We examined the risk factors for bone loss, reduction of muscle volume, and walking ability. Multivariable regression analysis was performed to evaluate the correlations between BMD, muscle volume, GNRI, and walking ability in hemodialysis patients.

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METHODS

Participants

We prospectively studied 45 patients who underwent hemodialysis for renal failure at a single institution (Ikeda hospital, Kagoshima, Japan) from 2016. Muscle volume and strength were evaluated using lean mass index (LMI), handgrip strength, and walking speed. Handgrip was measured using the Glip-D (provided by Takei Scientific Instruments Co. Ltd, Niigata, Japan). We diagnosed vertebral fracture with X-rays of the entire spine in the standing position. We evaluated the patients' age, sex, and duration of hemodialysis. Body weight was measured to the nearest 0.1 kg using digital scales with participants clothed in a disposable light paper gown and not wearing shoes. Body weight was measured just after hemodialysis. Height (cm) was measured to the nearest millimeter without shoes using DC-250 (Tanita Co. Ltd, Tokyo, Japan). We measured blood levels of tartrate-resistant acid phosphatase-5b (TRACP5b), total type I procollagen N-terminal propeptide (total P1NP), undercaroxylated osteocalcin (ucOC), serum amyloid A protein (SAA), cystatin C, 1,25(OH)2D3, and intact parathyroid hormone (intact PTH).

Inclusion criteria are following: age≥18 years; those on maintenance hemodialysis for longer than 6 months. Exclusion criteria is following: expected survival time less than 1 year; a confirmed diagnosis of malignancy; failure to walk 10 meters, such as patients with a history of cardiovascular failure, amputation surgery, or severe peripheral angiopathy; unwillingness to participate in this study.

Ethics approval and consent to participate

This research protocol was approved by Ikeda Hospital (Approval No. 270701). This study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000. All patients gave their written informed consent for participation in this clinical study.

Dual energy X-ray absorptiometry measurements

Body composition was measured via dual energy X-ray absorptiometry (DXA) using the Horizon Wi DXA system (Hologic, Waltham, MA, USA). Bone mineral density (BMD) (g/cm^2) was evaluated in the lumbar spine (L2-L4) and femoral neck. The scanning of patients and calculation of data were performed by one radiologic technologist to minimize variations in measurement. From whole body measurements, mean values for bone, fat, and lean mass were evaluated using BMD and lean mass index (LMI; LM/height^2).[8]

Geriatric nutritional risk index

The GNRI was calculated with a modification of the nutritional risk index (NRI) for elderly patients.9 GNRI was derived from serum albumin and body weight using the following formula:

GNRI = [1.489 × albumin (g/L)] + [41.7 × (body weight / ideal body weight)]

Body weight or ideal body weight were set to 1 when the patient's body weight exceeded the ideal body weight. The ideal body weight was defined as a BMI of 22.[7,10]

Table 1. Demographic data†

Patients characteristics	n=45
Age	63 (57-68)
Female sex	25 (55.6%)
Duration of hemodialysis (months)	63 (35-123)
Vertebral fracture	5 (11.1%)
GNRI	94.3 (92.3-98.3)
Albumin (g/dL)	3.7 (3.4-3.9)
Body weight (kg)	55.7 (47.3-61)
The ratio of body weight to ideal body weight	1.02 (0.92-1.11)
Lumbar spine BMD (g/cm^2)	0.87 (0.76-1.01)
T-scores (lumber spine BMD)	-1.5 (-2.1- -0.3)
Femoral neck BMD (g/cm^2)	0.60 (0.50-0.68)
T-scores (femoral neck BMD)	-2.0 (-2.7- -1.3)
LMI (kg/m^2)	14.6 (13.6-15.9)
Hand grip (kg)	23.3 (18.6-32.1)
10m gait time (sec)	6.3 (5.7-7.3)
Total P1NP (ng/mL)	241 (132-340)
TRACP 5b (mU/dL)	528 (322-756)
SAA (μg/mL)	7.7 (3.5-14.0)
PTH intact (pg/mL)	101 (55.0-184)
B2MG (mg/L)	27.8 (25.0-29.9)
Cystatin C (mg/L)	6.3 (5.6-6.7)
1a 25 (OH)$_2$ vit D (pg/mL)	15.0 (11.0-23.0)
uc OC (ng/mL)	45.9 (25.0-79.9)

GNRI: Geriatric Nutritional Risk Index; BMD: bone mineral density; LMI: lean mass index; P1NP: N-terminal propeptide of type I procollagen; TRACP 5b: Tartrate-resistant Acid Phosphatase 5b; SAA: serum amyloid A; PTH: parathormone; B2MG: β2-microglobulin; uc OC: undercarboxylated osteocalcin.

†Data are presented as number (%); or median (range 25% quartile-75% quartile).

Walking ability

Maximum walking speed along a 10-meter walkway was measured to assess patients' walking ability. The time (in seconds) required for patients to walk 10 meters was recorded.

Statistical analysis

Multiple linear regression analysis and multivariable stepwise binomial logistic regression analysis were performed to correlate demographic data with the response variable. Because of the relatively small number of patients and the large number of confounding factors, we applied a stepwise variable selection method to identify significant factors, as previously described.[11] Analysis was performed using BellCurve for Excel (Social Survey Research Information Co., Ltd., Tokyo, Japan).

RESULTS

Risk factors for lower BMD in the lumbar spine and femoral neck

The demographic and clinical characteristics of the 45 patients who underwent DXA scanning of the lumbar spine and femoral neck are shown in Table 1. BMD of the lumbar spine and femoral neck, LMI, GNRI, the number of vertebral fractures, and walking ability were evaluated. We performed multiple linear regression analysis to define risk factors for numerically lower BMD. Multiple linear regression analysis showed that older age, female sex, lower LMI, and higher total P1NP were correlated

Table 2. Risk factors for low BMD

Variables	Partial regression coefficient	Standardized partial regression coefficient	*p* value†
Lumbar spine			
Coefficient of determination R^2: 0.571			
Age	-0.006	-0.341	0.005
Female sex	-0.116	-0.305	0.045
Lean mass index (kg/m^2)	0.042	0.424	0.003
Hand grip (kg)	-0.005	-0.228	0.155
Total P1NP (ng/mL)	-0.0003	-0.235	0.044
Femoral neck			
Coefficient of determination R^2: 0.625			
Age	-0.004	-0.306	0.017
Female sex	-0.056	-0.203	0.077
Lean mass index (kg/m^2)	0.030	0.418	<0.001
TRACP 5b (mU/dL)	-0.0001	-0.156	0.177
B2MG	-0.003	-0.1968	0.122

P1NP: N-terminal propeptide of type I procollagen; GNRI: Geriatric Nutritional Risk Index; TRACP 5b: Tartrate-resistant Acid Phosphatase 5b; B2MG: β2-microglobulin.
†*p* value is for partial regression coefficient.

Table 3. Risk factors for vertebral fracture

Variables	Odds ratio	*p* value
Coefficient of determination R^2: 0.451		
TRACP5b (mU/dL)	1.006 (1.001-1.011)	0.023
PTH intact (pg/mL)	0.996 (0.991-1.002)	0.211
Cystatin C (mg/L)	0.293 (0.091-0.939)	0.039

TRACP 5b: Tartrate-resistant Acid Phosphatase 5b; PTH: parathormone.

with lower BMD in the lumbar spine (Table 2). Multiple linear regression analysis showed that higher age and lower LMI were correlated with lower BMD in the femoral neck. Multivariable stepwise binomial logistic regression analysis showed that higher TRACP5b and lower cystatin C were correlated with vertebral fracture (Table 3).

Risk factors for lower LMI and walking ability

Multiple linear regression analysis showed that female sex and lower GNRI were correlated with lower LMI (Table 4). Multiple linear regression analysis showed that longer duration of hemodialysis was correlated with lower walking ability (Table 5).

DISCUSSION

It has been reported that there is a positive correlation between lean body mass and BMD in patients undergoing peritoneal dialysis.[12] Nonetheless, two papers reported that lean body mass did not correlate with BMD in dialysis patients.[13,14] Our findings suggest that lower LMI was a risk factor for lower BMD of the lumbar spine and femoral neck, which supports the correlation between lean body mass and BMD. In addition, our findings suggest that lower GNRI is a risk factor for lower LMI. These findings suggest that improvement of GNRI prevents osteoporosis via improvement of LMI. To our knowledge, this is the first report to show that GNRI correlates with BMD in hemodialysis patients. The GNRI is advocated to evaluate the risk of malnutrition-related complications in elderly patients.[9] The GNRI has been shown to be a significant predictor of mortality and healthcare costs in hemodialysis patients,[7,15-17] and thus we used GNRI in our examinations.

A few articles examined the pathogenesis of sarcopenia in hemodialysis patients. Previous reports and our findings showed that LMI, hand grip, and walking ability are significantly lower in hemodialysis patients than in healthy people in Japan.[18-20] Ren et al reported that hemodialysis duration, diabetes, and serum phosphorus level were independent risk factors for sarcopenia in hemodialysis patients.[6] Our findings showed that lower GNRI is a risk factor for lower LMI. In order to improve nutritional status in hemodialysis patients, exercise, anabolic hormones, anti-inflammatory therapies, and appetite stimulants can be considered as complementary therapies in low GNRI patients as previously reported.[21] It has been reported that significant risk factors for low walking ability in hemodialysis patients were the presence of cardiac disease, low leg strength, poor standing balance, and history of fracture.[18] Risk factors for all-cause mortality are closely associated with walking speed in hemodialysis patients.[22,23] Our findings showed that longer duration of hemodialysis is a risk factor lower walking ability. Improvement of walking ability has been reported with adequate exercise training, regardless of age and degree of deterioration.[18,24] Especially in patients with a longer duration of hemodialysis, adequate exercise training may be beneficial.

Our study had several limitations. As this study was a single-center cohort study, selection bias may have occurred. A multicenter study is necessary to confirm our findings. Because this study had a cross-sectional design, a longitudinal study should be carried out in the future to investigate changes in each factor. The number of patients

Table 4. Risk factors for low Lean Mass Index

Variables	Partial regression coefficient	Standardized partial regression coefficient	*p* value
Coefficient of determination R^2: 0.533			
Female sex	-1.515	-0.398	0.005
Duration of hemodialysis (months)	-0.004	-0.177	0.191
GNRI	0.098	0.271	0.043

GNRI: Geriatric Nutritional Risk Index.
†*p* value is for partial regression coefficient.

Table 5. Risk factors for low walking ability

Variables	Partial regression coefficient	Standardized partial regression coefficient	*p* value
Coefficient of determination R^2: 0.258			
Age	0.029	0.263	0.055
Duration of hemodialysis (months)	0.005	0.422	0.003

†*p* value is for partial regression coefficient.

and variables should be increased in future studies in order to identify important and precise risk factors.

Conclusions

Our findings suggest that muscle volume preservation is required to maintain BMD. Similarly, nutritional management is necessary to maintain muscle volume. Complementary nutritional therapies might improve the sarcopenia and osteoporosis in high-risk hemodialysis patients.

AUTHOR DISCLOSURES

The authors declare that no financial or non-financial conflict of interests exist. This work is supported by CHUGAI.

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