Applied nutritional investigation

Associations among Geriatric Nutrition Risk Index, bone mineral density, body composition and handgrip strength in patients receiving hemodialysis

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ABSTRACT

Objectives: Malnutrition occurs as a complication of hemodialysis (HD) and has been identified as a risk factor for osteoporosis, sarcopenia, and low physical performance. The aim of this study was to assess the associations among nutrition, bone mineral density (BMD), body composition, and handgrip strength (HGS) in patients receiving HD.
Methods: We enrolled 164 patients receiving HD who have undergone the dual energy x-ray absorptiometry (DXA) examination, categorized according to baseline Geriatric Nutritional Risk Index (GNRI) values calculated by serum albumin levels and body weight index. GNRI was used to evaluate nutritional status, and DXA to investigate BMD and body composition. Additionally, HGS test was performed. Multiple stepwise linear regression analysis was used to identify the factors associated with BMD, T-score, and HGS.
Results: Compared with patients with tertile 1 of GNRI, those with tertile 3 of GNRI tend to have higher lumbar spine BMD and T-score, higher femoral neck BMD, higher total hip BMD, higher left distal mid-third radius BMD and T-score, higher fat mass index, higher android-to-gynoid ratio, higher lean mass index, and higher HGS. An increase in GNRI tertile was associated with an increase of BMD and a decrease of osteoporosis prevalence. The GNRI was positively correlated with BMD and T-score, body composition, and HGS. Low lean mass index and high parathyroid hormone were significantly associated with low BMD and T-score. Additionally, high GNRI and high left distal mid-third radius BMD were significantly associated with high HGS.
Conclusions: The present study demonstrated that good nutrition, indicated as high GNRI, resulted in higher BMD and T-score, lean mass index, and HGS in patients receiving HD. Using GNRI to evaluate nutritional status and using DXA to investigate BMD and body composition in patients receiving HD is important to bone health and physical performance.

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Introduction

Nutrition is an important issue for patients receiving hemodialysis (HD). Malnutrition is closely associated with major adverse clinical outcomes and can result in increased rates of hospitalization and mortality [1]. Several tools have been developed to assess malnutrition status, including the Mini Nutritional Assessment-Short Form [2], nutrition risk score [3], Malnutrition Universal Screening Tool [4], Malnutrition Screening Tool [5], and Geriatric Nutritional Risk Index (GNRI) [6]. Among them, the GNRI, which considers serum albumin and body mass index (BMI), was originally developed as a simple tool to assess the nutritional risk of elderly hospitalized patients [6]. Several studies have reported that the GNRI can predict all-cause [7,8] and cardiovascular

mortality [9] in patients receiving chronic dialysis. Additionally, the GNRI was recently correlated with progression to dialysis in patients with chronic kidney disease (CKD) not yet receiving dialysis [10].

Low bone mineral density (BMD) is common in patients with end-stage renal disease (ESRD), and it can be used to predict outcomes. In addition, CKD-mineral and bone disorder (MBD) has been reported to contribute to low BMD in patients with ESRD [11]. CKD and HD increase the risk for bone loss and fractures, both of which are associated with a reduced quality of life [12]. Sarcopenia is characterized by a reduction in muscle mass and limited mobility and function, and it is also an important comorbidity in patients receiving HD [13]. Moreover, osteoporosis and sarcopenia have both been reported to increase the risk for hospitalization and mortality [12,13]. In addition to being an important complication in patients undergoing HD [14], malnutrition is an important risk factor for osteoporosis and sarcopenia in these patients [15]. A positive association has been reported between lean body mass (LBM) and BMD in patients undergoing HD [16], although other studies have not found this association [17,18]. Thus, the association between BMD and body composition remains unclear in patients with ESRD.

Patients undergoing HD have been shown to experience a rapid decline in muscle mass, which can then result in a reduced physical performance compared with healthy individuals. Previous studies have reported prevalence rates of sarcopenia ranging from 3.6% to 31.5% in patients receiving HD [19–21]. Therefore, accurately measuring muscle mass would seem to be important to predict low physical performance in these patients. However, previous studies have reported conflicting results regarding the association between physical performance and muscle mass [22,23].

Associations between nutritional status and bone mass have been reported in various populations, such as individuals with chronic obstructive pulmonary disease [24], ESRD [25–27], non-alcoholic fatty liver disease [28], rheumatoid arthritis [29], and cardiovascular disease [30]. Additionally, wasting of skeletal muscles is a well-known consequence of malnutrition, a common problem in hospitalized patients [31–33]. Nutritional status has been reported to be important regarding functional status as assessed by muscle strength and activities of daily living (ADLs) in geriatric institutionalized and cardiac patients [34,35]. Accordingly, the aim of this study was to assess associations among GNRI, BMD, body composition, and handgrip strength (HGS) in patients receiving HD.

Participants and methods

Study patients and design

We enrolled 178 patients with ESRD undergoing maintenance HD three times a week for >3 mo at a dialysis clinic of a regional hospital in Taiwan in June 2017. We excluded patients who refused to undergo dual energy x-ray absorptiometry (DXA) examinations (n = 6); had bilateral below-the-knee amputations (n = 3); and had been hospitalized or received antibiotic treatment in the previous 4 wk (n = 5). The remaining 164 patients were included. This study was approved by the Institutional Review Board of Kaohsiung Medical University Hospital, and all of the patients provided written informed consent. The methods were carried out in accordance with the approved guidelines.

Calculation of the GNRI

Based on the original nutritional risk index for elderly individuals [6], the GNRI was calculated according to baseline serum albumin level and body weight as follows:

$$GNRI = [14.89 \times albumin\ (g/dL)] + [41.7 \times (body\ weight/ideal\ body\ weight)].$$

If the patient's body weight exceeded the ideal body weight (IBW), body weight/IBW was set to 1. The IBW in the present study was defined as the value calculated from the height and a BMI of 22 kg/m^2 [36].

BMD and body composition measurements

DXA was used to assess body composition with a Horizon Wi DXA system (Hologic, Waltham, MA, USA). BMD (g/cm^2) was assessed at the lumbar spine (L2–L4), femoral neck, total hip and left distal mid-third radius. All scans and calculations were performed by one radiologic technologist to minimize variations in the measurements. Mean values of bone, fat, and lean mass were evaluated from whole body measurements using BMD and lean mass index (lean mass/height^2) [37]. T-scores were used to compare the patients with healthy individuals matched by sex with peak bone mass according to the manufacturer's instructions. The T-score is defined as follows [38]:

$$(individual's\ BMD - young\ adult\ mean\ BMD)/SD\ of\ the\ young\ adult\ normal\ population.$$

A T-score above −1.0 was defined as normal BMD, osteopenia between −1.0 and −2.5, and osteoporosis was defined as a T-score less than −2.5.

Anthropometric measurements

Anthropometric measurements were performed at three different sites (mid-upper arm circumference, forearm circumference, triceps skinfold thickness [TSFT]) using Harpenden (West Sussex, UK) skinfold calipers. The mean of three measurements for each anthropometric measurement was used for analysis. The anthropometric measurements were performed before the dialysis session.

Assessment of handgrip strength

Each participant performed an HGS test. Three trials were performed on each hand using a manual hydraulic dynamometer (Jamar Hydraulic Hand Dynamometer; Sammons Preston, Chicago, IL, USA) set at the second grip position [39]. Average HGS was calculated as the average value in the right hand plus that in the left hand divided by 2 [39].

Collection of demographic, medical, and laboratory data

All demographic information and relevant medical histories of the participants, including age, sex, and a history of diabetes were recorded from their medical records. BMI was calculated as body weight in kilograms divided by height in meters squared. Blood samples were obtained from the patients after fasting for 12 h within 1 mo of enrollment and analyzed using an autoanalyzer (Roche Diagnostics GmbH, D-68298 Mannheim COBAS Integra 400). Serum intact parathyroid hormone (PTH) concentration was evaluated using a commercially available two-sided immunoradiometric assay (The CIS bio international is located in Saclay, France). Vitamin D was analyzed using chemiluminescent immunoassay by autoanalyzer (Roche COBAS e 411).

Statistical analysis

Descriptive statistics were given as percentages, means ± SD, or medians (25th-75th percentile) for HD duration, triacylglycerols (TGs), and PTH. One-way analysis of variance followed by a Bonferroni post hoc test was used to compare variables among the study groups. Pearson's correlation analysis was used to evaluate associations among DXA parameters, body composition, anthropometric measurement, HGS, and the GNRI. Multiple stepwise linear regression analysis was used to identify the factors associated with BMD, T-score, and HGS adjusting for age, sex, a history of diabetes, log-transformed duration of HD, GNRI, total body fat, android-to-gynoid ratio, lean mass index, log-transformed TGs, total cholesterol (TC), hemoglobin (Hb), calcium-phosphorous product, uric acid, log-transformed PTH, vitamin D, mid-upper arm circumference, forearm circumference, and TSFT. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS version 19 (SPSS Inc. Chicago, IL, USA).

Results

We enrolled 164 patients undergoing HD (54.9% men and 45.1% women) with a mean age of 60.1 ± 10.6 y. Table 1 shows comparisons of the characteristics among the patients classified by GNRI tertiles with cutoff values of <96.8, 96.8 to 100.8, and ≥100.8, respectively. The mean GNRI values of the tertiles were 93.4 ± 3, 98.8 ± 1.2, and 103.1 ± 1.8, respectively. Compared with patients in tertile 1, those in tertile 3 tended to be younger, predominantly male, and had higher BMI, lumbar spine BMD and T-score, femoral neck BMD, total hip BMD, left distal mid-third radius BMD and T-score, fat mass index, android-to-gynoid ratio, lean mass index, albumin, Hb, mid-upper arm circumference, forearm circumference, HGS, and Karnofsky score.

Table 1
Comparison of baseline characteristics among chronic HD patients stratified by the tertiles of GNRI

Characteristics	All patients (N = 164)	GNRI tertile 1 (n = 54)	GNRI tertile 2 (n = 56)	GNRI tertile 3 (n = 54)	P-value
Age (y)	60.1 ± 10.6	62.7 ± 11.8	60.8 ± 9	56.9 ± 10.3*	0.014
Men (%)	54.9	38.9	51.8	74.1*,†	0.001
Diabetes (%)	51.8	44.4	57.1	53.7	0.389
Duration of HD (y)	6.87 (3.30–13.13)	8.92 (4.26–15.38)	7.07 (3.17–12.27)	5.12 (2.75–11.07)	0.093
GNRI (score)	98.4 ± 4.5	93.4 ± 3	98.8 ± 1.2*	103.1 ± 1.8*,†	<0.001
BMI (kg/m^2)	23.9 ± 4	21.6 ± 3.5	24.4 ± 3.4*	25.8 ± 3.9*	<0.001
DXA parameters					
Lumbar spine BMD (g/cm^3)	0.92 ± 0.18	0.87 ± 0.17	0.92 ± 0.19	0.98 ± 0.17*	0.006
T-score	−1.21 ± 1.69	−1.67 ± 1.59	−1.28 ± 1.73	−0.65 ± 1.63*	0.017
Femoral neck BMD (g/cm^3)	0.61 ± 0.14	0.58 ± 0.15	0.60 ± 0.13	0.65 ± 0.12*	0.020
T-score	−2.29 ± 1.18	−2.53 ± 1.24	−2.34 ± 1.17	−1.95 ± 1.06	0.059
Total hip BMD (g/cm^3)	0.73 ± 0.16	0.69 ± 0.16	0.73 ± 0.16	0.78 ± 0.15*	0.009
T-score	−1.79 ± 1.28	−2.07 ± 1.35	−1.79 ± 1.24	−1.47 ± 1.20	0.080
Left distal mid-third radius BMD (g/cm^3)	0.63 ± 0.12	0.59 ± 0.10	0.63 ± 0.11*	0.67 ± 0.12*,†	0.001
T-score	−1.26 ± 1.92	−1.82 ± 1.65	−1.24 ± 1.83	−0.67 ± 2.15*	0.016
Body composition					
Total body fat (%)	32.9 ± 7.1	32.3 ± 7.4	33.9 ± 6.7	32.3 ± 7.1	0.413
Fat mass index (kg/m^2)	7.8 ± 2.6	7 ± 2.5	8.1 ± 2.4	8.3 ± 2.9*	0.016
Android/gynoid ratio	1.1 ± 0.2	1 ± 0.2	1.1 ± 0.2*	1.2 ± 0.2*	<0.001
Lean mass index (kg/m^2)	14.8 ± 2.1	13.4 ± 1.6	14.9 ± 1.9*	16 ± 1.8*,†	<0.001
Laboratory parameters					
Albumin (g/dL)	3.9 ± 0.3	3.7 ± 0.3	3.9 ± 0.1*	4.1 ± 0.1*,†	<0.001
Hemoglobin (g/dL)	10.3 ± 1.3	10.1 ± 1.4	10.3 ± 1.3	10.7 ± 1.2*	0.032
Total cholesterol (mg/dL)	172.2 ± 42.6	163.5 ± 38.8	179.6 ± 44.9	173.1 ± 43	0.138
Triacylglycerols (mg/dL)	111 (82.3–164.8)	95.5 (70.5–130.3)	115.5 (83.5–194.8)	134 (96.8–183.3)	0.052
CaXP product (mg^2/dL^2)	42.6 ± 18.8	39.5 ± 7.9	45.4 ± 29.2	42.8 ± 11.3	0.253
Uric acid (mg/dL)	7.3 ± 1.5	7.1 ± 1.3	7.5 ± 1.5	7.4 ± 1.6	0.470
PTH (pg/mL)	301.1 (159.4–507.7)	290.7 (158.7–467.4)	288.7 (131.8–521.3)	321.8 (178.9–581)	0.420
Vitamin D (nmol/L)	27.6 ± 9.6	27.8 ± 8.5	26.5 ± 8.7	28.4 ± 11.6	0.576
Anthropometric measurement					
Mid-upper arm circumference (cm)	28 ± 3.9	26 ± 3.3	28.7 ± 4*	29.3 ± 3.6*	<0.001
Forearm circumference (cm)	25.3 ± 1.6	25 ± 1.4	25.1 ± 1.6	25.8 ± 1.8*	0.014
Triceps skinfold thickness (cm)	17 ± 7.5	15.2 ± 6.3	18 ± 7.6	17.8 ± 8.2	0.093
Handgrip strength (kg)	19.6 ± 7.9	16.5 ± 6.4	18.8 ± 6.9	23.6 ± 6.6*,†	<0.001
Charlson Comorbidity Index	5.5 ± 2.2	5.7 ± 2.3	5.8 ± 2.1	4.9 ± 2	0.060
Karnofsky score	87 ± 15.1	83 ± 17.1	86.8 ± 14.7	91.3 ± 12.1*	0.015

BMD, bone mineral density; CaXP product, calcium x phosphorus product; DXA, dual-energy x-ray absorptiometry; GNRI, Geriatric Nutrition Risk Index; HD, hemodialysis; PTH, parathyroid hormone.
*$P < 0.05$ in comparison of those with GNRI tertile 1.
†$P < 0.05$ in comparison of those with GNRI tertile 2.

Figure 1 shows the distribution of normal BMD (T-score $\geq −1.0$), osteopenia (T-score $−1.0$ to $−2.5$) and osteoporosis (T-score $< −2.5$) stratified by the tertiles of GNRI. There was a significant trend of a stepwise increase in normal BMD and a decrease in osteoporosis corresponding to an increase in GNRI tertile at each site ($P = 0.009$ for trend at the lumbar spine; $P_{trend} = 0.014$ at the femoral neck; $P_{trend} = 0.044$ at the total hip; and $P_{trend} = 0.041$ at the left distal mid-third radius).

*Correlation between GNRI and DXA parameters, body composition, anthropometric measurement, and HGS*

The GNRI was positively correlated with lumbar spine BMD ($r = 0.198$, $P = 0.012$), lumbar spine T-score ($r = 0.175$, $P = 0.040$), femoral neck BMD ($r = 0.254$, $P = 0.001$), femoral T-score ($r = 0.245$, $P = 0.003$), total hip BMD ($r = 0.292$, $P < 0.001$), total hip T-score ($r = 0.255$, $P = 0.002$), left distal mid-third radius BMD ($r = 0.288$, $P < 0.001$), left distal mid-third radius T-score ($r = 0.250$, $P = 0.003$), fat mass index ($r = 0.218$, $P = 0.005$), android-to-gynoid ratio ($r = 0.405$, $P < 0.001$), lean mass index ($r = 0.539$, $P < 0.001$), mid-upper arm circumference ($r = 0.337$, $P < 0.001$), forearm circumference ($r = 0.189$, $P = 0.016$), TSFT ($r = 0.178$, $P = 0.024$), and HGS ($r = 0.398$, $P < 0.001$). However, the GNRI was not correlated with total body fat ($r = 0.023$, $P = 0.766$).

Determinants of BMD in the study patients

Table 2 shows the determinants of BMD using multivariate stepwise linear regression analysis after adjusting for age, sex, a history of diabetes, log-transformed duration of HD, GNRI, total body fat, android-to-gynoid ratio, lean mass index, log-transformed TGs, TC, Hb, calcium-phosphorous product, uric acid, log-transformed PTH, vitamin D, mid-upper arm circumference, forearm circumference, and TSFT. PTH was negatively lumbar spine BMD, whereas lean mass index and forearm circumference were positively correlated with lumbar spine BMD. Age and PTH were negatively correlated with femoral neck BMD, whereas lean mass index, forearm circumference, and TSFT were positively correlated with femoral neck BMD. Age and PTH were negatively correlated with total hip BMD, whereas lean mass index was positively correlated with total hip BMD. Age, HD duration, and TC were negatively correlated with left distal mid-third radius BMD, whereas sex (male versus female) and lean mass index were positively correlated with left distal mid-third radius BMD.

Determinants of T-score in the study patients

Table 3 shows the determinants of T-score using multivariate forward linear regression analysis after adjusting for demographic,
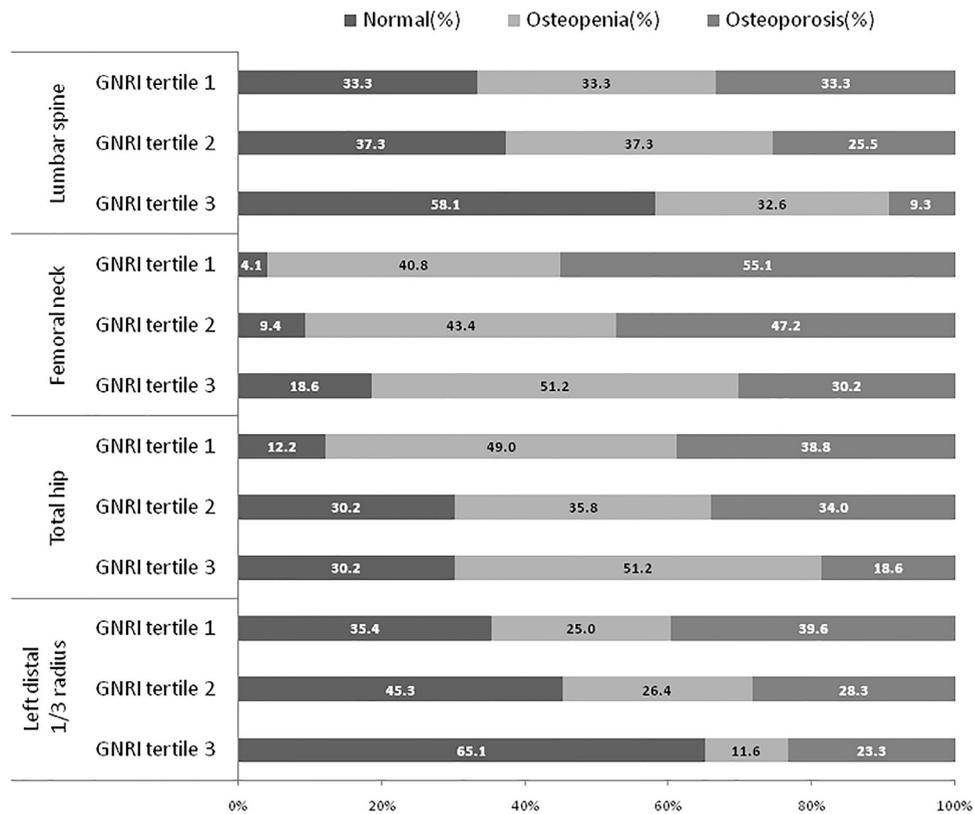
Fig. 1. The distribution of normal BMD (T-score ≥ −1), osteopenia (T-score −1 to −2.5), and osteoporosis (T-score < −2.5) stratified by the tertiles of GNRI. There was a significant trend for a stepwise increase in normal BMD and a decrease in osteoporosis corresponding to the increase in GNRI tertile in each site. BMD, bone mineral density; GNRI, Geriatric Nutrition Risk Index.

Table 2
Determinants of BMD using multivariate forward linear regression analysis

BMD	Multivariate (forward)	
	Unstandardized coefficient β (95% CI)	P-value
Lumbar spine BMD		
PTH (log per 1 pg/mL)	−0.096 (−0.16 to −0.136)	0.002
Lean mass index (per 1 kg/m²)	0.027 (0.014−0.039)	<0.001
Forearm circumference (per 1 cm)	0.036 (0.020−0.052)	<0.001
Femoral neck BMD		
Age (per 1 y)	−0.004 (−0.006 to −0.003)	<0.001
PTH (log per 1 pg/mL)	−0.105 (−0.148 to −0.062)	<0.001
Lean mass index (per 1 kg/m²)	0.011 (0.002−0.021)	0.023
Forearm circumference (per 1 cm)	0.020 (0.008−0.032)	0.001
Triceps skinfold thickness (per 1 cm)	0.003 (0−0.005)	0.020
Total hip BMD		
Age (per 1 y)	−0.003 (−0.005 to −0.002)	<0.001
PTH (log per 1 pg/mL)	−0.124 (−0.174 to −0.074)	<0.001
Lean mass index (per 1 kg/m²)	0.033 (0.023−0.042)	<0.001
Left distal mid-third radius BMD		
Age (per 1 year)	−0.002 (−0.003 to 0)	0.001
Sex (male vs female)	0.080 (0.048−0.112)	0.048
HD duration (log per 1 y)	−0.060 (−0.091 to −0.028)	<0.001
Lean mass index (per 1 kg/m²)	0.014 (0.006−0.022)	0.001
Total cholesterol (per 10 mg/dL)	−0.004 (−0.007 to 0)	0.023

BMD, bone mineral density; CaXP product, calcium x phosphorus product; DXA, dual-energy x-ray absorptiometry; GNRI, Geriatric Nutrition Risk Index; HD, hemodialysis; PTH, parathyroid hormone.
Adjusting for age, sex, a history of diabetes, log-transformed duration of HD, GNRI, total body fat, android/gynoid ratio, lean mass index, log-transformed triacylglycerols, total cholesterol, hemoglobin, calcium-phosphorous product, uric acid, log-transformed PTH, vitamin D, midupper arm circumference, forearm circumference and triceps skinfold thickness.

Table 3
Determinants of T-score using multivariate forward linear regression analysis

T-score	Multivariate (forward)	
	Unstandardized coefficient β (95% CI)	P-value
Lumbar spine T-score		
PTH (log per 1 pg/mL)	−0.901 (−1.509 to −0.294)	0.004
Lean mass index (per 1 kg/m²)	0.267 (0.137−0.398)	<0.001
Forearm circumference (per 1 cm)	0.350 (0.193−0.506)	<0.001
Femoral neck T-score		
Age (per 1 y)	−0.033 (−0.051 to −0.016)	<0.001
PTH (log per 1 pg/mL)	−1.002 (−1.416 to −0.587)	<0.001
Lean mass index (per 1 kg/m²)	0.116 (0.022−0.210)	0.016
Forearm circumference (per 1 cm)	0.182 (0.072−0.292)	0.001
Triceps skinfold thickness (per 1 cm)	0.026 (0.004−0.049)	0.020
Total hip T-score		
Age (per 1 y)	−0.030 (−0.049 to −0.011)	0.003
PTH (log per 1 pg/mL)	−0.910 (−1.365 to −0.454)	<0.001
Lean mass index (per 1 kg/m²)	0.193 (0.090−0.296)	<0.001
Forearm circumference (per 1 cm)	0.155 (0.034−0.276)	0.013
Triceps skinfold thickness (per 1 cm)	0.025 (0−0.049)	0.048
Left distal mid-third radius T-score		
Sex (male vs female)	1.635 (1.063−2.207)	<0.001
HD duration (log per 1 y)	−0.957 (−1.602 to −0.313)	0.004
Lean mass index (per 1 kg/m²)	0.194 (0.040−0.347)	0.014
PTH (log per 1 pg/mL)	−0.703 (−1.349 to −0.057)	0.033

BMD, bone mineral density; CaXP product, calcium x phosphorus product; DXA, dual-energy x-ray absorptiometry; GNRI, Geriatric Nutrition Risk Index; HD, hemodialysis; PTH, parathyroid hormone.
Adjusting for age, sex, a history of diabetes, log-transformed duration of HD, GNRI, total body fat, android/gynoid ratio, lean mass index, log-transformed triacylglycerols, total cholesterol, hemoglobin, calcium-phosphorous product, uric acid, log-transformed PTH, vitamin D, mid-upper arm circumference, forearm circumference and triceps skinfold thickness.

clinical, biochemical, and anthropometric factors. PTH was negatively correlated with lumbar spine T-score, whereas lean mass index and forearm circumference were positively correlated with lumbar spine T-score. Age and PTH were negatively correlated with femoral neck T-score, whereas lean mass index, forearm circumference, and TSFT were positively correlated with femoral neck T-score. Age and PTH were negatively correlated with total hip T-score, whereas lean mass index, forearm circumference, and TSFT were positively correlated with total hip T-score. HD duration and PTH were negatively correlated with left distal mid-third radius T-score, whereas sex (male versus female), and lean mass index were positively correlated with left distal mid-third radius T-score.

Determinants of handgrip strength in the study patients

Table 4 shows the determinants of HGS using multivariate forward linear regression analysis after adjusting for age, sex, a history of diabetes, log-transformed duration of HD, GNRI, left distal mid-third radius BMD, total body fat, android-to-gynoid ratio, lean mass index, log-transformed TGs, TC, Hb, calcium-phosphorous product, uric acid, log-transformed PTH, vitamin D, mid-upper arm circumference, forearm circumference, and TSFT. Age and a history of diabetes were negatively correlated with HGS, whereas male sex, GNRI, left distal mid-third 3 radius BMD, and forearm circumference were positively correlated with HGS.

Discussion

This study investigated associations among GNRI, BMD, body composition, and HGS in HD patients. We found that good nutrition, as indicated by a high GNRI, was associated with a higher BMD and T-score, higher lean mass index, and higher HGS. Additionally, a low lean mass index and high PTH were associated with low BMD and T-score. Moreover, the patients with a high GNRI and large left distal mid-third 3 radius BMD had high HGS.

Protein malnutrition and wasting are common problems in patients receiving HD [1], for which possible contributing causes include inadequate nutrient intake, acidemia, hormonal dysregulation, sustained inflammation, and alterations in bowel flora [40], all of which can increase morbidity and mortality. Thus, nutritional evaluation is the first and most critical step to detect malnutrition in patients receiving HD. In the present study, the patients with a

Table 4
Determinants of handgrip strength using multivariate forward linear regression analysis

Handgrip strength	Multivariate (forward)	
	Unstandardized coefficient β (95% CI)	P-value
Age (per 1 y)	−0.241 (−0.328 to −0.153)	<0.001
Sex (male vs female)	3.280 (1.040–5.520)	0.004
Diabetes	−3.482 (−5.262 to −1.702)	<0.001
GNRI (per 1 score)	0.351 (0.143–0.558)	0.001
Left distal mid-third radius BMD (per 1 g/cm³)	10.391 (0.712–20.071)	0.036
Forearm circumference (per 1 cm)	1.137 (0.482–1.792)	0.001

BMD, bone mineral density; CaXP product, calcium x phosphorus product; DXA, dual-energy x-ray absorptiometry; GNRI, Geriatric Nutrition Risk Index; HD, hemodialysis; PTH, parathyroid hormone.
Adjusting for age, sex, a history of diabetes, log-transformed duration of HD, GNRI, left distal mid-third radius BMD, total body fat, android/gynoid ratio, lean mass index, log-transformed triacylglycerols, total cholesterol, hemoglobin, calcium-phosphorous product, uric acid, log-transformed PTH, vitamin D, midupper arm circumference, forearm circumference and triceps skinfold thickness.

high GNRI had high BMD and low prevalence of osteoporosis, which is consistent with previous studies [25–27].

The second important finding of this study is that a high LBM index was associated with high BMD and T-score in the patients receiving HD. Marinho et al. evaluated the association between body composition and BMD in men on HD and found that lean mass was positively associated with BMD and T-score [41]. Both lean and fat mass have been reported to be potentially important determinants of BMD [42]. However, lean mass seems to be the dominant positive predictor of BMD, and maintaining lean mass is critical to maintain bone mass [43]. A recent study showed a strong correlation between lean mass and bone geometry in athletes (high lean mass) compared with controls [44]. ESRD is associated with a rapid decline in muscle mass, leading to high mortality and poor quality of life [20,45]. Therefore, the early detection of a decline in muscle mass and accurate measurements of muscle mass are important to improve the prognosis of dialysis patients. DXA is a useful method to detect muscle mass in patients with ESRD.

The third important finding of this study is that a high PTH level was correlated with low lumbar spine BMD and T-score, low femoral neck BMD and T-score, and low total hip BMD and T-score. The onset of CKD initiates changes in bone composition and systemic mineral metabolism in addition to a loss in glomerular filtration rate (GFR). As the GFR continues to decline, the changes in mineral metabolism affect the bone microstructure through remodeling, a condition known as CKD-MBD. The Kidney Disease: Improving Global Outcomes (KDIGO) Foundation defines CKD-MBD as a wider systemic disorder of mineral and bone metabolism as a result of CKD [46]. CKD-MBD is characterized by the following:

- abnormal calcium, phosphorus, PTH, or vitamin D metabolism;
- abnormal bone turnover, mineralization, volume linear growth, or strength; and
- either vascular or extraosseous soft tissue calcifications [47].

Levels of free serum calcium decrease, and levels of serum phosphorus increase along with the decline in GFR. Subsequently, the parathyroid glands produce more PTH, which then increases urinary phosphate excretion that in turn lowers levels of serum phosphate [48]. A decrease in 1,25dihydroxyvitamin D can induce hypocalcemia, resulting in persistent PTH production, thereby leading to secondary hyperparathyroidism [49]. The accumulation of secondary hyperparathyroidism and uremic toxins then accelerates bone turnover by activating osteoclastogenesis and increasing the release of phosphate and calcium from bone [50]. High serum levels of PTH can then overwhelm indolent bone cells, leading to high bone turnover and relatively greater bone resorption than formation [48]. This may explain our finding of an association between a high PTH level and low BMD.

Another important finding of this study is that high GNRI and large left distal mid-third radius BMD were correlated with high HGS. Decreases in muscle function can be caused by various factors. Aging is commonly associated with a decline in LBM [51]. Cereda et al. [34] investigated 346 elderly long-term care residents and found that high nutritional risk (GNRI/92) was an independent predictor of functional status and mortality. Additionally, Kinugasa et al. [35] evaluated ADLs using the Barthel index in relation to functional capacity in in-patients with heart failure and found that a low nutritional level was associated with decreased ADLs after discharge from the hospital. HGS is a good predictor of overall muscle strength, a useful marker of frailty, and an important predictor of disability and mortality [52]. Purser et al. reported that poor HGS was a strong predictor of 6-mo mortality in cardiac inpatients ≥70 y of age [52]. We also found lower HGS in the patients on HD

who were at risk for poor nutrition, as indicated by a low GNRI, in the present study.

There were several limitations to this study. First, the study was cross-sectional in design, so causal relationships could not be confirmed. Second, the number of patients was relatively small. Third, patients with CKD-MBD disorder have an increased risk for fracture, cardiovascular events, and overall increased mortality. Prospective studies are warranted to address these issues. Fourth, body weight may be misleading in the presence of edema, which is common in patients receiving HD. Finally, the majority of the study patients were treated chronically with medications. For ethical reasons, we did not withdraw these medications. Hence, we could not exclude the influence of these agents on our findings.

Conclusion

Good nutrition, as indicated by a high GNRI, was associated with a higher BMD, T-score, lean mass index, and HGS in the patients on HD. Using GNRI to evaluate nutritional status and using DXA to investigate BMD and body composition in patients on HD is important to bone health and physical performance.

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