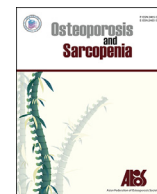




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## Original article

## Daily activity relates to not only femoral bone mineral density, but also hip structural analysis parameters: A cross-sectional observational study



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## ABSTRACT

**Objectives:** Physical activity to maintain bone mass and strength is important for hip fracture prevention. We aim to investigate the relationship between physical performance/activity status and bone mineral density (BMD)/hip structural analysis (HSA) parameters among postmenopausal women in Japan.

**Methods:** Sixty-two postmenopausal women diagnosed with osteoporosis (mean age:  $72.61 \pm 7.43$  years) were enrolled in this cross-sectional observational study. They were evaluated for BMD and HSA in the proximal femur by dual-energy X-ray absorptiometry and underwent several physical performance tests, the Geriatric Locomotive Function Scale of 25 questions (GLFS-25). Principal component analysis (PCA) was used to summarize data on the BMD/HSA parameters. Partial correlation analysis, multiple regression analysis, and structural equation modeling (SEM) were performed to investigate the relationship between physical performance/activity status and BMD/HSA parameters of the proximal femur. **Results:** In a partial correlation analysis adjusted for age and body mass index (BMI), GLFS-25 scores were correlated with HSA parameter ( $|r| = 0.260\text{--}0.396$ ,  $P < 0.05$ ). Principal component 1 (PC1) calculated by PCA was interpreted as more reflective of bone strength based on the value of BMD/HSA parameters. The SEM results showed that the model created by the 3 questions (Q13, brisk walking; Q15, keep walking without rest; Q20, load-bearing tasks and housework) of the GLFS-25 had the best fit and was associated with the PC1 score ( $\beta = -0.444$ ,  $P = 0.001$ ).

**Conclusions:** The GLFS-25 score was associated with the BMD/HSA parameter, which may reflect the bone strength of the proximal femur as calculated by PCA.

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## 1. Introduction

Hip fractures based on osteoporosis are a major cause of morbidity and mortality [1]. The mortality rate for hip fracture is as high as 30% 1 year after the occurrence of a fracture [2]. With an aging population, hip fracture is expected to affect up to 6.3 million people worldwide after 2050 [3]. Therefore, efforts to prevent

osteoporosis and subsequent hip fracture are extremely important.

Physical activity to maintain bone mass and strength is important for fracture prevention. Many studies have shown that physical activity has a positive effect on femoral bone mineral density (BMD) [4–6]. However, to perform physical activity, the locomotive system, including muscles, joints, cartilage, bones, the spine, intervertebral discs, and nerves, need to function properly. The Japanese Orthopaedic Association has proposed the term “locomotive syndrome” due to a disorder of the locomotive organs [7]. Recent studies have shown an interrelationship between several diseases, such as osteoporosis, locomotive syndrome, frailty, and sarcopenia, in the elderly population [8–10]. These musculoskeletal comorbidities may further exacerbate a decline in physical activity. Therefore, early detection of musculoskeletal problems and appropriate intervention may prevent fractures.

The majority of studies focusing on physical activity have used only BMD assessed by dual-energy X-ray absorptiometry (DXA). Generally, DXA is difficult to assess separately for trabecular and cortical bones [11]. Recently, it was demonstrated that the strength of the proximal femur associated with hip fracture impacted cortical bone more than the trabecular bone [12,13]. Hip structural analysis (HSA) has been incorporated into DXA, which enables cortical and mechanical analyses of the proximal femur [14]. Kaptege et al discovered through HSA that older women with hip fractures had thinner cortical bone width and lower fracture strength in the proximal femur [15]. If the relationship between physical performance/physical activity and cortical bone parameters of the proximal femur was clarified, specific strategies for maintaining cortical bone health could be developed.

Furthermore, bone strength is determined by BMD (~70%) and bone quality (~30%). Bone structure parameters calculated by HSA are encompassed in bone quality. Considering these factors, information from HSA in addition to BMD may reflect more information about an individual's bone strength than BMD alone.

No study has examined the relationship between physical performance/activity status and parameters calculated using HSA in postmenopausal women in Japan. In addition, no study has investigated the relationship between the BMD/HSA parameters, which reflect bone strength more than BMD alone, and physical performance/activity status. This study aims to investigate the relationship between physical performance/physical activity status and the BMD/HSA parameters among postmenopausal women in Japan. Identifying these relationships may reveal physical issues that impact proximal femoral bone strength and cortical bone fragility.

## 2. Methods

### 2.1. Subjects

This cross-sectional observational study was approved by the author's affiliate Institutional Review Board (IRB approval numbers: 19-015 Hiroshima International University and 2019-1 Shimura Hospital). The study participants were patients who visited the osteoporosis outpatient clinic of our hospital from April 2019 to June 2020. The subjects of our study were postmenopausal women with osteoporosis aged  $\geq 60$  years. All subjects had no history of osteoporosis treatment and were able to walk without a walking aid. The exclusion criteria for our study were the same criteria used in our previous studies [16] and a history of hip fracture. All subjects underwent blood and bone assessments for osteoporosis treatment. Informed consent was obtained from all subjects prior to the start of the study, and physical performance tests were conducted.

### 2.2. Blood tests

Since previous studies have shown a relationship between nutrition and osteoporosis [17], we used total protein, albumin, and estimated glomerular filtration rate values in our analysis. The bone metabolic status of the subjects was assessed with type I procollagen N-terminal propeptide (electrochemiluminescence immunoassay, BML, Tokyo, Japan), and tartrate-resistant acid phosphatase 5b (EIA, BML, Tokyo, Japan).

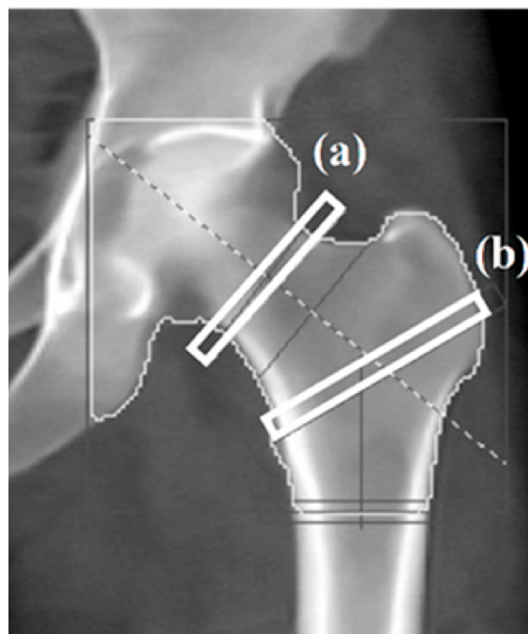
### 2.3. Radiographic assessment

Radiography of the thoracic and lumbar spines were obtained. Vertebral fractures at T4 to L4 were measured independently by 3 researchers. Vertebral fractures were defined according to the report by Genant et al. [18].

### 2.4. DXA

BMD of the proximal femur and lumbar spine were assessed by DXA (Hologic, Bedford, MA, USA). The subjects were diagnosed with osteoporosis based on the percentage young adult mean value measured by DXA. In 4 patients who underwent balloon kyphoplasty at the lumbar vertebrae, BMD of the normal lumbar vertebrae was assessed.

On the basis of the DXA data, the HSA of the proximal femur was assessed. Subperiosteal width (SubPeriWidth), estimated endosteal width (EndoCortWidth), and cortical thickness were calculated as cortical bone parameters. Similarly, the cross-sectional area (CSA), the cross-sectional moment of inertia (CSMI), the section modulus (Z), and the buckling ratio (BR) were calculated as strength parameters [19,20]. Parameters calculated in the narrow neck region (NN) and intertrochanter region (IT) were used in the analysis (Fig. 1).



**Fig. 1.** Calculated region of the hip structural analysis parameters used in this study. Parameters calculated in the narrow neck region (NN) and intertrochanter region (IT) were used in the analysis.

(a); Narrow neck region, (b); Intertrochanter region.

### 2.5. Physical performance evaluations

For physical performance evaluation, grip strength, one-leg standing time, standing test, and two-step test were performed. Each subject was provided a full explanation and movement practice before the test. The subject was provided a break between each test. The physical performance test, excluding the stand-up test, was conducted twice. The highest score was used in the analysis. The details of each physical performance test are described below. A digital grip strength meter (TKK-5401, Niigata, Japan) was used to measure the maximum grip strength of the dominant hand. One-leg standing time was performed with the eyes open and measured up to 120 seconds. In this study, the nondominant leg was raised, and standing time on the dominant leg was used in the analysis. The stand-up and two-step tests were performed on the basis of the methods previously reported by Ishibashi et al [21]. Stand-up scores of 0–8 are allocated to the successful performance of subjects. Higher scores show better ability. In the two-step test, the two-step value of the distance traveled divided by the individual's height was used in the analysis.

The Geriatric Locomotive Function Scale of 25 questions (GLFS-25) was used to investigate the physical and activity status of the subjects. Each question has 5 alternatives scored from 0 to 4 from better to worse, and total scores between 0 and 100 are calculated for 25 questions. Previous studies reported a cutoff value of 16 for GLFS-25 [22]. On the basis of the cutoff value, a GLFS-25 score  $\geq 16$  was considered locomotive dysfunction.

### 2.6. Statistical analysis

Initially, the Shapiro–Wilk test confirmed the normality of the demographic data, blood data, physical performance data, and DXA parameters.

Partial correlation analysis (adjusted for age and BMI) was used to examine the relationship between biological data, physical performance data, and DXA parameters. We performed a power analysis (effect size 0.5, significance level 5%) to determine the power of the partial correlation analysis in the 62 subjects who participated in our study. The effect size was in accordance with

previous studies [23]. The power analysis showed that the calculated power was 0.988.

In this study, multiple regression analysis was performed to determine the physical performance data associated with BMD/HSA parameters. The independent variable was input using the forced entry method. We performed principal component analysis (PCA) on the BMD and HSA parameters of the proximal femur to determine the dependent variables for multiple regression analysis. PCA can extract important information from many variables in a dataset and summarize that information into a small number of principal components (PCs) [24]. According to previous reports, it is recommended to have at least twice as many subjects as variables used in the PCA [25]. In our study, 3 PCs reflecting information on the BMD and HSA parameters were calculated. Among the PCs calculated by PCA, PC1—which explained most of the variation in the BMD and HSA parameters—was considered the parameter that may be most reflective of bone strength. The score of each PC calculated using PCA was used as the dependent variable for multiple regression analysis. Multicollinearity was confirmed using the variance inflation factor. It has been reported that the minimum number of subjects required to perform a multiple regression analysis is 10 times the number of independent variables used [26]. There were 62 subjects in this study, so a maximum of 6 independent variables were available.

In addition, this study used structural equation modeling (SEM) to investigate the questionnaire items of the GLFS-25 that are related to PCs. The fit of the model was assessed using the chi-square statistic, root mean square error of approximation (RMSEA), goodness-of-fit index (GFI), adjusted goodness-of-fit index (AGFI), comparative fit index (CFI), and Akaike's information criterion (AIC). We evaluated the goodness-of-fit according to the following criteria, as in previous studies [27]: chi-square values greater than 0.05, RMSEA of less than 0.05, GFI, AGFI, and CFI, with a value above 0.90, indicating a good fit.

We considered a P-value  $< 0.05$  to be significant. PCA and multiple regression analyses were performed in SPSS (version 27, IBM Corp., Armonk, NY, USA). SEM was performed using HAD (version 17, Kansei Gakuin University, Hyogo, Japan). R version 2.8.1 (R Foundation for Statistical Computing, Vienna, Austria, <http://www.R-project.org/>) was used for other statistical analyses.

**Table 1**  
Characteristics of the subjects (n = 62).

Variable	Value (mean $\pm$ SD)	Range (minimum–maximum)
Age, yr	72.6 $\pm$ 7.4	60–87
Height, cm	151.2 $\pm$ 5.8	139.6–163.5
Weight, kg	49.2 $\pm$ 6.8	33.5–65.0
BMI, kg/m <sup>2</sup>	21.5 $\pm$ 2.8	17.0–28.6
Total protein, g/dL	7.0 $\pm$ 0.5	5.9–8.3
Albumin, g/dL	4.2 $\pm$ 0.3	3.5–4.7
eGFR, mL/min	65.2 $\pm$ 16.4	29.5–105.3
TRACP-5b, mU/dL	283.3 $\pm$ 112.8	116.0–583.0
P1NP, $\mu$ g/L	32.2 $\pm$ 16.7	11.7–76.8
T-score, SD		
Femur neck	–3.0 $\pm$ 0.8	–4.6 to –0.5
Total hip	–2.4 $\pm$ 0.9	–4.3 to –0.5
Lumbar spine	–2.6 $\pm$ 1.1	–4.8 to 1.2
Handgrip strength, kg	23.6 $\pm$ 3.8	13.7–30.7
One-leg standing time, s	65.7 $\pm$ 45.6	2.3–120.0
Stand-up test score	2.6 $\pm$ 1.2	0–5
Two-step test score	1.2 $\pm$ 0.2	0.7–1.5
GLFS-25 score	11.5 $\pm$ 11.0	0–47
GLFS-25 score $\geq 16$ , n (%)	15 (24.2)	–
History of diagnosed vertebral fracture, n (%)	20 (32.3)	–

Values in the table are shown as mean  $\pm$  standard deviation (SD) or n (%). BMI, body mass index; eGFR, estimated glomerular filtration rate; TRACP-5b, tartrate-resistant acid phosphatase 5b; P1NP, procollagen type I N-terminal propeptide; GLFS-25, Geriatric Locomotive Function Scale of 25 questions.

### 3. Results

#### 3.1. Characteristics of the subjects

Sixty-two postmenopausal women who satisfied the inclusion criteria of our study were included in the study. Table 1 shows the information of the subjects. The mean age of the subjects was  $72.6 \pm 7.4$  years.

#### 3.2. Partial correlation analysis (adjusted for age and BMI)

Table 2 shows the results of partial correlation analysis. Handgrip strength showed a significant correlation with CSMI and Z in the NN. The stand-up test score showed a significant correlation between total hip BMD and BR in the IT. The GLFS-25 score showed a significant correlation with many BMD and HSA parameters such as CT, CSA, and BR ( $|r| = 0.287\text{--}0.447$ ,  $P < 0.05$ ).

In contrast, the one-leg standing time and two-step test score did not show a significant correlation with any of the parameters.

#### 3.3. PCA

The results of the PCA are shown in Table 3. The PC loading of PC1 was high in the neck and total hip BMD and HSA parameters, excluding SubPeriWidth and EndoCortWidth in the NN and IT. PC1 could explain 54.581% of the BMD/HSA parameters of the neck and total hip. We interpreted the total explained variance explained by PC1 as indicating that PC1 may be a more reflective measure of bone strength. The PC loading of PC2 showed high SubPeriWidth, EndoCortWidth, and CSMI in the NN. In PC3, the information of SubPeriWidth and EndoCortWidth in the IT was reflected.

#### 3.4. Multiple regression analysis

Table 4 shows the results of the multiple regression analysis using the forced entry method. The independent variables used in this analysis were those that were evaluated for multicollinearity and showed significant correlations with BMD or HSA parameters in partial correlation analysis. PC1 score was used as the dependent variable in multiple regression analysis. As a result, GLFS-25 (standardized  $\beta = -0.340$ ,  $P = 0.017$ ) was selected as the independent variable. However, when PC2 and PC3 were used as dependent variables, there was no independent variable to explain the dependent variables.

#### 3.5. SEM

Standard regression coefficients that did not show a significant association were removed, and a final model was created based on the GFI (Fig. 2). The  $\chi^2$  value of the final model was 0.714 ( $P = 0.700$ ). The other indices of goodness-of-fit were CFI = 1.000, GFI = 0.994, AGFI = 0.971, RMSEA = 0.000, and AIC = 16.714. Latent variables used in this study are shown as the daily activity in the ellipses in Fig. 1. The latent variables and the 3 variables (Q13, brisk walking ( $\beta = 0.668$ ,  $P < 0.001$ ); Q15, keep walking without rest ( $\beta = 0.700$ ,  $P < 0.001$ ); Q20, load-bearing tasks and housework ( $\beta = 0.543$ ,  $P < 0.001$ )) all showed significant associations. Moreover, the daily activity parameter, which represents the latent variable, was significantly related to the PC1 score ( $\beta = -0.444$ ,  $P = 0.001$ ).

### 4. Discussion

There were 2 main findings of this study. The first finding was an association between GLFS-25 and BMD/HSA parameters of the

**Table 2**  
Results of age and BMI-adjusted partial correlation analysis.

Variable	DXA parameters													
	BMD						HSA							
	Femur neck		Total hip		Lumbar spine		Narrow neck region			Intertrochanter region				
	Cortical bone parameters		Strength parameters		Cortical bone parameters		Cortical bone parameters			Strength parameters				
	SubPeri Width	EndoCort Width	CT	CSA	CSMI	Z	BR	SubPeri Width	EndoCort Width	CT	CSA	CSMI	Z	BR
TP	-0.186	-0.122	-0.267*	-0.222	-0.297*	-0.294*	-0.013	0.014	0.034	-0.063	-0.120	-0.104	-0.058	-0.001
ALB	-0.038	0.024	-0.098	-0.067	-0.150	-0.130	-0.052	-0.037	-0.058	0.062	-0.072	-0.078	-0.043	-0.113
eGFR	0.086	0.027	-0.020	0.114	-0.119	-0.033	-0.203	-0.023	-0.060	0.110	0.033	0.027	0.060	-0.112
TRACP-5b	0.015	-0.008	0.214	0.039	-0.026	0.012	-0.089	0.044	0.045	-0.021	-0.009	0.105	0.116	0.007
PINP	0.047	0.005	0.253	0.062	0.034	0.035	-0.036	0.120	0.127	-0.033	0.016	0.107	0.098	0.055
Handgrip strength	0.141	0.240	-0.174	0.248	0.295*	0.260*	0.038	0.134	0.082	0.177	0.230	0.201	0.159	-0.179
One-leg standing time	0.127	0.241	-0.102	0.14	0.079	0.096	-0.089	-0.110	-0.152	0.148	0.137	0.041	0.114	-0.236
Stand-up test score	0.193	0.320*	0.182	0.027	0.081	0.126	-0.174	0.050	-0.032	0.250	0.149	0.117	0.190	-0.290*
Two-step test score	0.017	0.103	-0.194	-0.049	-0.045	0.007	-0.113	0.052	0.027	0.084	0.008	0.009	0.046	-0.182
GLFS-25 score	-0.370**	-0.447**	-0.227	0.176	-0.308*	-0.191	0.396**	0.114	0.200	-0.287*	-0.210	-0.042	-0.160	0.371**

All analyses were adjusted for age and BMI.

\* $P < 0.05$ , \*\* $P < 0.01$ .

The numbers in the table indicate  $r$  (partial correlation coefficient).

TP, total protein; ALB, albumin; eGFR, estimated glomerular filtration rate; TRACP-5b, tartrate-resistant acid phosphatase 5b; PINP, procollagen type I N-terminal propeptide; GLFS-25, Geriatric Locomotive Function Scale of 25 questions; DXA, dual-energy X-ray absorptiometry; BMD, bone mineral density; HSA, Hip Structural Analysis; SubPeriWidth, subperiosteal width; EndoCortWidth, estimated endosteal width; CT, cortical thickness; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; Z, section modulus; BR, buckling ratio.

**Table 3**  
Principal component analysis for BMD and HSA parameters.

Variable		Principal component			
		1	2	3	
DXA parameters	BMD	<b>0.940</b>	-0.142	0.000	
		<b>0.941</b>	-0.093	-0.157	
HSA	Neck	0.045	<b>0.958</b>	-0.243	
	Total hip	-0.100	<b>0.955</b>	-0.240	
	Narrow neck	Cortical bone parameters	SubPeriWidth	<b>0.889</b>	-0.288
			EndoCortWidth	<b>0.930</b>	0.040
			CT	<b>0.889</b>	0.040
		Strength parameters	CSA	<b>0.930</b>	-0.068
			CSMI	<b>0.579</b>	<b>0.725</b>
			Z	<b>0.772</b>	0.486
	Intertrochanter	Cortical bone parameters	BR	-0.687	0.640
			SubPeriWidth	0.024	0.413
			EndoCortWidth	-0.269	0.446
		Strength parameters	CT	<b>0.902</b>	-0.136
CSA			<b>0.955</b>	0.067	
CSMI			<b>0.776</b>	0.324	
	Z	<b>0.850</b>	0.153		
	BR	<b>-0.876</b>	0.242		
	Eigen value	8.733	3.726	2.099	
	Total explained variance (%)	54.581	23.289	13.121	

The principal component load is shown in this table.

Principal component loadings > 0.7 are in bold.

DXA, dual-energy X-ray absorptiometry; BMD, bone mineral density; HSA, Hip Structural Analysis; SubPeriWidth, subperiosteal width; EndoCortWidth, estimated endosteal width; CT, cortical thickness; CSA, cross-sectional area; CSMI, cross-sectional moment of inertia; Z, section modulus; BR, buckling ratio.

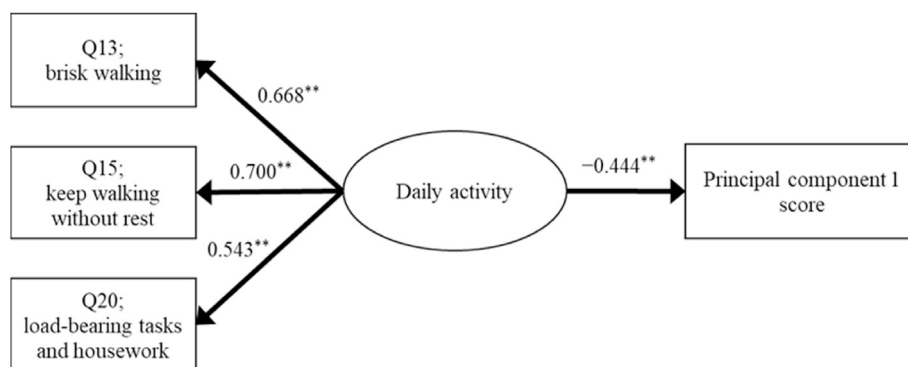
**Table 4**  
Results of multiple regression analysis.

Dependent variable: principal component 1 score				
Variable	Standardized β	SE	T-value	P-value
Handgrip strength	0.162	0.033	1.280	0.206
Stand-up test score	0.038	0.119	0.266	0.791
Total protein	-0.135	0.263	-1.131	0.263
GLFS-25 score	-0.340	0.013	-2.451	<b>0.017*</b>

Forced entry method; R<sup>2</sup> = 0.203, adjusted R<sup>2</sup> = 0.147.

\*P < 0.05.

GLFS-25, Geriatric Locomotive Function Scale of 25 questions; SE, standard error.



**Fig. 2.** Final model created by structural equation modeling  
The numbers on the arrows represent the standardized regression coefficients.

The ellipse indicates a latent variable.

χ<sup>2</sup> = 0.714, CFI = 1.000, GFI = 0.994, AGFI = 0.971, RMSEA = 0.000, AIC = 16.714. \*\*P < 0.01

CFI, comparative fit index; GFI, goodness-of-fit index; AGFI, adjusted goodness-of-fit index; RMSEA, root mean square error of approximation; AIC, Akaike's information criterion.

proximal femur. The second finding was associated with the BMD/HSA parameters of the proximal femur in the 3 questionnaires of the GLFS-25 (Q13, brisk walking; Q15, keep walking without rest; Q20, load-bearing tasks and housework).

As a first step, we performed a partial correlation analysis adjusted for age and BMI. The results showed that GLFS-25 significantly correlated with many of the BMD/HSA parameters (|r

| = 0.287–0.447, P < 0.05). In addition, multiple regression analysis also showed a relationship between GLFS-25 and PC1, which may better reflect bone strength of the proximal femur as calculated by PCA (β = -0.340, P = 0.017). Alternatively, physical functions such as grip strength and the stand-up test were not associated with PC1 in the multiple regression analysis. The relationship between various physical function tests and BMD has long been investigated.

For example, one-leg standing time [28] and grip strength [29] have been reported to be related to the BMD of the proximal femur. However, to the best of our knowledge, no studies have investigated the relationship between physical function tests and HSA parameters. Additionally, this is the first study to examine the relationship between synthetic parameters calculated by PCA, which may be more reflective of bone strength and physical function.

Fracture is a complex multifactorial event, and recent studies have shown major limitations of BMD-based criteria for fracture risk evaluation [30]. Therefore, fracture risk assessment tools that provide structural and geometric information, such as the HSA, are clinically important. In light of these considerations, the use of the BMD/HSA composite parameter calculated by PCA in this study may be important in that it reflects more information relate bone strength than BMD alone. Our results suggest that regardless of age, musculoskeletal problems, and problems with activities of daily living as assessed by the GLFS-25 are related to poor HSA parameters as well as BMD. In other words, the use of the GLFS-25, a simple tool for assessing locomotive syndrome, may be useful for evaluating the bone strength of the proximal femur.

In Japan, the GLFS-25 has been used as a criteria for determining locomotive syndrome. Several studies investigating the physical performance and physical/living status of individuals presenting with locomotive syndrome as assessed by the GLFS-25 have been reported. Yoshinaga et al [31] reported that locomotive syndrome was associated with joint pain, anxiety about physical fitness in daily life, poor self-rated health, irregular eating habits, and lack of exercise. Ikemoto et al [32] reported that locomotive syndrome was associated with a decline in physical performance, such as grip strength, and increased depression. It is important to apply mechanical stress associated with physical activity to bone to maintain bone homeostasis. Considering the results of this study and previous studies, it can be said that those who experience pain in the body, decreased mobility, and anxiety in daily life may have limited physical activity, which leads to bone fragility in the proximal femur. Therefore, the use of the GLFS-25 to assess motor function and daily living conditions in postmenopausal women can lead to appropriate interventions at an early stage that reduce the risk of future fractures.

To investigate the association of each item of the GLFS-25, we used SEM. The results showed that the model created by the 3 questions ((Q13, brisk walking ( $\beta = 0.668$ ,  $P < 0.001$ ); Q15, keep walking without rest ( $\beta = 0.700$ ,  $P < 0.001$ ); Q20, load-bearing tasks and housework ( $\beta = 0.543$ ,  $P < 0.001$ )) of the GLFS-25 had the best fit and was associated with PC1 scores reflecting the bone strength for the proximal femur ( $\beta = -0.444$ ,  $P = 0.001$ ). These findings indicate that the activities of daily living that are correlated with fracture prevention have been clarified. The GLFS-25 includes 4 questions on pain, 19 questions on activities of daily living, and 2 questions on anxiety [22]. Among the 19 activities of daily living questions, brisk walking, continuous walking without rest, load-bearing tasks, and housework are activities of daily living with a slightly higher degree of difficulty. Musculoskeletal function, such as those of the lower extremities and trunk, are more important for performing these tasks. Furthermore, the presence of pain in the body can hinder the performance of these tasks. Therefore, in addition to the use of the GLFS-25, general physical function should be assessed by a medical doctor or physical therapist.

This study had some limitations. This was a cross-sectional study. Therefore, causality could not be determined, and whether improving the GLFS-25 score improves the condition of the proximal femur and decreases the risk of fracture also could not be determined. Furthermore, all the subjects in this study were postmenopausal women who visited osteoporosis outpatient clinics. Therefore, it may not be representative of the entire population. We

used PC1, a derived variable that may reflect bone strength better than BMD alone in our analysis. However, the PC score does not reflect all of the original information, and it is not possible to assess whether physical function is strongly related to either the BMD or HSA parameters. We did not study the degree of physical activity of our subjects. Therefore, differences in physical activity may affect the results. We used multivariate analyses such as PCA to investigate the relationship between the GLFS-25 and BMD/HSA parameters. We determined the minimum number of subjects required for PCA and multiple regression analysis based on past reports, but in general, multivariate analysis is a method that requires many subjects. However the number of subjects in this study ( $n = 62$ ) was small. Therefore, our results may only show trends in the GLFS-25 and BMD/HSA parameters. Future studies need to increase the number of subjects and investigate the relationship between the GLFS-25 and BMD/HSA parameters.

## 5. Conclusions

The GLFS-25 score, which reflects physical activity status, was associated with BMD/HSA parameters that may reflect more bone strength in the proximal femur as calculated by PCA. Furthermore, physical activity status as revealed by the 3 questions of the GLFS-25 (Q13, brisk walking; Q15, keep walking without rest; Q20, load-bearing tasks and housework) was associated with BMD/HSA parameters and may reflect the bone strength of the proximal femur. To reduce the risk of fracture in the future, it was considered important to evaluate the factors that are involved in problems with activities of daily living and to intervene early depending on the individual.

## CRedit author statement

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## Conflicts of interest

Nobukazu Okimoto has received consulting fees from Teijin Pharma Ltd and Asahi-Kasei Pharmaceutical Co., Ltd. Nobukazu Okimoto has received payments for lectures, such as speakers' bureau fees, from Astellas Pharma Inc.; Asahi-Kasei Pharmaceutical Co., Ltd.; Eli Lilly Japan K.K.; Chugai Pharmaceutical Co.; Amgen Astellas BioPharma K.K.; Daiichi-Sankyo Co. Ltd.; Eisai Co., Ltd.; Teijin Pharma Ltd.; Pfizer Japan Inc.; Ono Pharmaceutical Co.; and Mitsubishi-Tanabe Pharma Corp. There are no conflicts of interest for all other authors.

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