

## Original Article

# Association of Osteosarcopenia with Functional Outcomes in Older Adult Patients Undergoing Rehabilitation

Ryo Mannen<sup>1,2</sup>, Keisuke Maeda<sup>3,4</sup>, Tatsuro Inoue<sup>3,5</sup>, Akio Shimizu<sup>6,7</sup><sup>1</sup>Department of Nutritional Management, Faculty of Nutritional Science, Sagami Women's University, Sagami-hara, Kanagawa, Japan;<sup>2</sup>Graduate School of Integrated Pharmaceutical and Nutritional Sciences, University of Shizuoka, Shizuoka City, Shizuoka, Japan;<sup>3</sup>Department of Geriatric Medicine, Hospital, National Center for Geriatrics and Gerontology, Obu, Aichi, Japan;<sup>4</sup>Nutrition Therapy Support Center, Aichi Medical University Hospital, Nagakute, Aichi, Japan;<sup>5</sup>Department of Physical Therapy, Niigata University of Health and Welfare, Niigata City, Niigata, Japan;<sup>6</sup>Department of Rehabilitation Medicine, Mie University Graduate School of Medicine, Tsu, Mie, Japan;<sup>7</sup>Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University, Nagakute, Aichi, Japan

## Abstract

**Objectives:** Osteosarcopenia is characterized by the coexistence of sarcopenia and osteoporosis. This comorbid condition is thought to negatively affect functional outcomes. In this study, we investigated the negative impact of osteosarcopenia on the functional outcomes of older patients undergoing rehabilitation. **Methods:** This single-center retrospective cohort study was conducted at Hamamatsu City Rehabilitation Hospital in Japan and included 184 participants  $\geq 65$  years. Functional outcomes were assessed using the functional independence measure (FIM), the minimum clinically important difference (MCID) achieved on the FIM, and home discharge. Multiple linear and logistic regression analyses were conducted to assess the independent association of osteosarcopenia with FIM score at discharge and the FIM MCID. Additionally, the association between osteosarcopenia and home discharge was examined. **Results:** Osteosarcopenia was present in 30.4% of participants. Osteosarcopenia did not reach a statistically significant association with FIM at discharge (95% confidence interval [CI]:  $-2.518-8.489$ ;  $\beta$ , 0.058), FIM MCID (odds ratio [OR]: 1.919; 95% CI: 0.698–5.277), or discharge to home (OR: 0.525; 95% CI: 0.126–2.189). **Conclusions:** Osteosarcopenia was prevalent among older patients undergoing rehabilitation, but its association with functional outcomes at discharge did not reach statistical significance. Intensive rehabilitation may have masked its adverse effects, warranting further longitudinal studies.

**Keywords:** Aging, Frail elderly, Functional status, Rehabilitation, Sarcopenia

## Introduction

In recent years, many countries have seen an increase in the number of older people, and geriatric syndromes have become a significant concern. Geriatric syndromes refer to health issues and symptoms specific to older adults and are caused by multiple factors that may affect their daily lives. Geriatric syndromes include osteoporosis and sarcopenia. In osteoporosis, bone mineral density (BMD) progressively declines with age<sup>1</sup>, which results in an increased risk of fragility fractures<sup>2</sup>. Furthermore, postmenopausal women are at a higher risk of developing osteoporosis owing to decreased estrogen secretion<sup>3</sup>.

*The authors have no conflict of interest.*

**Corresponding author:** Ryo Mannen, PhD, Department of Nutritional Management, Faculty of Nutritional Science, Sagami Women's University, 2-1-1 Bunkyo, Minami-ku, Sagami-hara, Kanagawa 252-0383, Japan

**E-mail:** r-mannen@star.sagami-wu.ac.jp

**ORCID:** 0009-0007-7476-5726

**Edited by:** Yannis Dionyssiotis

**Accepted** 1 April 2026

Sarcopenia has been recognized as an independent disease, and is characterized by decreased muscle mass, strength, and physical function<sup>4</sup>. Both osteoporosis and sarcopenia increase the risk of falls, fractures, and functional impairment<sup>5</sup>. Therefore, prevention, early detection, and intervention are important for maintaining independence in activities of daily living (ADL) in older adults.

Osteosarcopenia occurs when osteoporosis and sarcopenia are present simultaneously<sup>6</sup>. This disease has been linked to several other conditions, including depression, malnutrition, peptic ulcers, inflammatory arthritis, and mobility limitations<sup>7</sup>. Studies indicate that osteosarcopenia prevalence varies from 1.5%–64.3%, and increases with advanced age, reaching 17.8% in individuals <80 years and 24.8% in those aged ≥80 years<sup>8</sup>. The prevalence of osteosarcopenia is significantly higher in females (19.4%) than in males (15.3%), and hospital in-patients (24.7%) than in community-dwelling older adults (12.9%)<sup>8</sup>. Osteosarcopenia has also been shown to be associated with the incidence of disability in community-dwelling older adults<sup>9</sup>. Considering these findings, osteosarcopenia may require greater prevention, early detection, and intervention strategies than either disease alone.

Osteoporosis and sarcopenia are reportedly associated with functional outcomes<sup>1,10</sup>. Therefore, osteosarcopenia, combining both diseases, has the potential to exert a more significant adverse effect on functional outcomes than either disease alone. Previous studies have reported that osteosarcopenia is associated not only with adverse outcomes in community-dwelling older adults but also with outcomes such as fractures, falls, and mortality in hospitalized patients<sup>9,11</sup>. In older patients admitted to rehabilitation wards after fractures, the degree of functional recovery at discharge and the possibility of returning home are often key clinical considerations; however, to our knowledge, no studies have examined whether osteosarcopenia affects functional recovery in this rehabilitation population, particularly when assessed using functional status measures such as the functional independence measure (FIM)<sup>12</sup>. Furthermore, some studies suggest that osteosarcopenia does not necessarily increase the risk of fractures or falls<sup>11</sup>. Whether it exerts a synergistic effect on functional outcomes remains unclear. Considering the high prevalence of osteosarcopenia in hospitalized patients, the identification of its outcomes in rehabilitation patients hospitalized for fractures and other diseases may assist with determining the prognosis in this population. Therefore, in the current study, we aimed to investigate the negative effects of osteosarcopenia on the functional outcomes of older patients undergoing rehabilitation.

## Materials and Methods

### *Study design and participants*

We conducted a single-center retrospective cohort study at Hamamatsu City Rehabilitation Hospital. We included patients aged ≥65 years with hip, kneecap, or vertebral compression fractures who required rehabilitation. In the Japanese healthcare system, patients typically transition from acute care to convalescent rehabilitation. In this study, the hip fracture category included intertrochanteric fractures and cases after total hip arthroplasty (THA), and the kneecap fracture category included cases after total knee arthroplasty (TKA). Vertebral compression fractures comprised fractures of the thoracic and lumbar vertebrae. The Japanese medical insurance system provides rehabilitation units for individuals who have experienced stroke, musculoskeletal disease, and hospital-associated deconditioning. This study included patients admitted to the rehabilitation units between June 2019 and July 2021. We included patients who required rehabilitation for functional decline following fractures, regardless of the injury mechanism. Fractures were not categorized as fragility or traumatic in this study. Exclusion criteria were incomplete data, the presence of a pacemaker, and in-hospital mortality. Approval for this study was obtained from the Ethics Committee of Hamamatsu City Rehabilitation Hospital (approval number: 21-82). Informed consent was waived by the Ethics Committee due to the retrospective design of the study. Consequently, an opt-out approach was adopted, whereby information regarding the study was disclosed on the hospital's official website and notice boards. Participants were provided with the opportunity to decline participation in accordance with the procedures described in these announcements prior to data anonymization.

### *Functional outcomes*

The main outcomes were the FIM<sup>12</sup> score at discharge and the minimum clinically important difference (MCID) achieved in the FIM. The FIM evaluates activities of daily living through motor and cognitive functions. The total score ranges from 18 to 126 points, where higher scores reflect greater independence in daily activities. The FIM MCID was defined as an improvement of at least 22 points in the FIM score compared to a previous report<sup>13</sup>. The secondary outcome was the home discharge rate.

### *Definition and diagnosis of osteosarcopenia, osteoporosis, and sarcopenia*

The patients were classified into four groups: osteosarcopenia, osteoporosis only, sarcopenia only, and neither osteoporosis nor sarcopenia (normal). Patients with osteosarcopenia were defined as those with both sarcopenia and osteoporosis. The criteria from

the Asian Working Group for Sarcopenia (AWGS) 2019<sup>14</sup> were used to diagnose sarcopenia in patients with decreased muscle mass and strength. However, although walking speed and five times sit-to-stand tests are part of the AWGS 2019 diagnostic criteria, they could not be performed in all patients in this study because of fractures and pain. Muscle mass was assessed using the skeletal muscle mass index (SMI), which was obtained by summing the muscle masses of both the upper and lower limbs measured using bioelectrical impedance analysis (BIA) (InBody S10; InBody Japan, Tokyo, Japan) to calculate the appendicular skeletal muscle (ASM) and then dividing by the square of the height (m). Decreased muscle mass was defined as an SMI value <7.00 kg/m<sup>2</sup> for men and <5.70 kg/m<sup>2</sup> for women. Handgrip strength was assessed to measure muscle strength. Decreased muscle strength was defined as handgrip strength <28.0 kg and <18.0 kg for men and women, respectively. Handgrip strength measurements were performed using the hand dynamometer (MG-4800; CHARDER Electronic, Taichung, Taiwan) while participants were seated on a chair or bed with elbows flexed at 90°. Measurements were taken twice for each hand, and the highest value was used for analysis. The BMD of the femur and/or lumbar spine was measured using dual-energy X-ray absorptiometry (DXA) (Figa, GE Healthcare, USA). Femoral BMD was measured at the femoral neck, and lumbar spine BMD was measured at the posteroanterior lumbar spine (L1–L4) and calculated as the mean of L1–L4. Exclusion of vertebrae with compression fractures or severe deformities was not performed because detailed information on individual vertebrae was not consistently available in this retrospective study. Osteoporosis was defined using the World Health Organization (WHO) criteria of BMD T-score of  $\leq -2.5$  SD<sup>15</sup>. We used an accurately obtained BMD of the femur or lumbar spine given that metal objects may be present inside the patients' bodies, influencing the readout. Given that all participants were Japanese, we also assessed osteoporosis using the Japanese Osteoporosis Society (JOS) criteria<sup>16</sup>. The JOS criteria use population specific cutoffs for Japanese individuals and may yield diagnoses that do not fully coincide with the WHO definition. To evaluate the impact of potential nondifferential misclassification due to definitional differences, we evaluated the associations with functional outcomes using the JOS criteria. The cutoff value according to the JOS criteria was a femoral BMD of  $\leq 0.751$  g/cm<sup>2</sup>, or a lumbar spine BMD of  $\leq 0.954$  g/cm<sup>2</sup>.

### **Patient characteristics**

Data on patient characteristics were obtained from medical records. They included age, sex, number of days from disease onset to admission to a rehabilitation unit, body mass index (BMI), fracture type, comorbidities,

nutritional status, swallowing ability, and cognitive function. Comorbidities were assessed using the Charlson Comorbidity Index (CCI)<sup>17,18</sup>, which is a predictor of poor prognosis. Nutritional status was evaluated by a registered dietitian through the mini nutritional assessment tool short form (MNA-SF), with higher scores indicating better nutritional status<sup>19</sup>. Swallowing ability was assessed by a speech–language therapist using the food intake level scale (FILS)<sup>20</sup>. The FILS is an ordinal scale scored on a 1–10 point scale, with a focus on daily consumption, where a higher score indicates better swallowing ability. Cognitive function was assessed using the mini-mental state examination (MMSE), where lower scores indicate lower cognitive function.

### **Sample size calculation**

Based on a previous study<sup>21</sup>, we hypothesized that the FIM MCID achievement rates for patients without sarcopenia undergoing rehabilitation would be approximately 60%. No data were available on previous FIM MCID achievements in patients with osteosarcopenia. However, clinical observations suggested that patients with osteosarcopenia may achieve approximately half the FIM MCID compared to the control group. Therefore, we set the target achievement rate at 40% for patients with osteosarcopenia. We expected that 148 patients would be needed to detect this difference, at  $\alpha = 0.05$  and power = 0.9.

### **Statistical Analysis**

Each variable was expressed as the number (%), mean, and median [IQR]. To compare the four independent groups, one-way analysis of variance (ANOVA) was used for parametric data and the Kruskal–Wallis test was used for non-parametric data. To examine the independent relationship between osteosarcopenia and discharge FIM scores, we employed multiple linear regression analysis. We also analyzed the association between osteosarcopenia and the achievement of the FIM MCID using multivariate logistic regression analysis. The association between osteosarcopenia and home discharge was evaluated using multivariate logistic regression analysis. Model 1 classified participants into four groups: normal, osteoporosis only, sarcopenia only, and osteosarcopenia. To further enhance the statistical power, Model 2 analyzed participants in three groups: normal, others (osteoporosis or sarcopenia only), and osteosarcopenia. Model 3 analyzed participants in two groups: osteosarcopenia and others. Covariates for multivariate regression and sensitivity analyses were selected based on their potential impact on functional outcomes and included age, sex, fracture type, onset, CCI, MNA-SF, FIM at admission, FILS at admission, and MMSE.

Furthermore, regarding the diagnostic criteria for osteoporosis, the WHO definition may not fully reflect Japanese population characteristics and may underestimate its prevalence in this cohort. To address the

	Normal	Osteoporosis only	Sarcopenia only	Osteosarcopenia	p-value
n (%)	46 (25.0)	16 (8.7)	66 (35.9)	56 (30.4)	
Age, years, mean (SD)	79.5 (7.2)	80.7 (8.3)	83.4 (7.3)	85.1 (7.3)	0.001
Sex, n (%)					
- Male	10 (21.7)	0 (0.0)	28 (42.4)	9 (16.1)	<0.001
- Female	36 (78.3)	16 (100.0)	38 (57.6)	47 (83.9)	
BMI, kg/m <sup>2</sup> , mean (SD)	22.9 (4.0)	20.5 (2.7)	20.9 (2.9)	18.8 (2.9)	<0.001
SMI, kg/m <sup>2</sup> , mean (SD)	6.0 (0.9)	5.7 (1.2)	5.1 (0.9)	4.3 (0.8)	<0.001
Handgrip strength, kg, mean (SD)	22.0 (7.5)	19.8 (3.0)	15.4 (6.5)	13.0 (5.0)	<0.001
BMD, g/cm <sup>2</sup> , mean (SD)					
- Femoral neck (n = 172)	0.674 (0.123)	0.512 (0.144)	0.643 (0.120)	0.519 (0.100)	<0.001
- Lumbar spine (n = 12)	1.084 (0.156)	0.739 (0.105)	0.993 (0.161)	0.677 (0.099)	<0.001
Fracture type, n (%)					
- Hip fracture	36 (78.3)	14 (87.5)	50 (75.8)	41 (73.2)	0.001
- Kneecap fracture	7 (15.2)	0 (0.0)	1 (1.5)	0 (0.0)	
- Vertebral compression fracture	3 (6.5)	2 (12.5)	15 (22.7)	15 (26.8)	
Onset at admission, day, median [IQR]	19.0 [15.2, 24.0]	18.0 [14.8, 25.8]	21.0 [16.2, 27.8]	20.0 [16.0, 28.2]	0.565
CCI, score, median [IQR]	1 [0, 1]	0 [0, 1]	1 [0, 2]	1 [0, 1]	0.164
MNA-SF, score, median [IQR]	9.0 [7.0, 10.0]	8.0 [7.0, 10.0]	7.0 [4.0, 9.0]	6.0 [4.0, 7.0]	<0.001
FIM at admission, score, median [IQR]	92 [83, 99]	93 [76, 107]	79 [64, 89]	74 [62, 86]	<0.001
FILS at admission, score, median [IQR]	9 [8, 9]	9 [8, 9]	8 [8, 9]	8 [8, 9]	0.005
MMSE at admission, score, median [IQR]	26 [23, 29]	25 [23, 29]	23 [16, 27]	22 [19, 27]	0.017

Abbreviations: SD: Standard deviation, IQR: Interquartile range, BMI: Body mass index, SMI: Skeletal muscle mass index, BMD: Bone mineral density, CCI: Charlson comorbidity index, MNA-SF: Mini nutritional assessment short form, FIM: Functional independence measure, FILS: Food intake level scale, MMSE: Mini mental state examination.

**Table 1.** Patient characteristics upon admission.

possibility that definitional discrepancies could obscure consistent associations with outcomes, we additionally analyzed the data using the JOS criteria derived from Japanese populations. This approach allowed us to assess the robustness of our findings regarding the association between osteosarcopenia and functional outcomes.

Osteoporosis is known to have a higher prevalence in female<sup>22</sup>. Furthermore, hip fractures have been shown to have a negative association with ADL<sup>23</sup>. Based on this, we also conducted analyses exclusively on female participants and patients with hip fractures to examine whether these states influenced the outcomes. Statistical analyses were performed using R version 3.4.0 (The R Foundation for Statistical Computing, Vienna, Austria). The statistical

significance level was set at  $P < 0.05$  to determine significant differences.

## Results

Tables 1 and 2 show the patient characteristics at admission and discharge. We investigated data from 198 older adult patients aged  $\geq 65$  years who were admitted to rehabilitation units. Fourteen patients were excluded due to missing data (four patients), use of a pacemaker (seven patients), or death during hospitalization (three patients). Finally, 184 (25.5% male, 74.5% female) patients were included in the analysis. The mean age was  $82.7 \pm 7.6$  years, and the mean BMI was  $20.7 \pm 3.5$  kg/m<sup>2</sup>. Sixteen patients (8.7%) had osteoporosis, 66 (35.9%) had

	Normal	Osteoporosis only	Sarcopenia only	Osteosarcopenia	p-value
Length of stay, d, median [IQR]	40.0 [29.2, 51.0]	41.5 [32.8, 54.2]	46.0 [35.0, 56.0]	41.5 [33.0, 56.0]	0.377
FIM at discharge, score, median [IQR]	113 [102, 119]	117 [100, 121]	102 [76, 114]	100 [82, 110]	0.001
FILS at discharge, score, median [IQR]	9.0 [8.0, 9.0]	9.0 [8.8, 9.0]	8.0 [8.0, 9.0]	8.0 [8.0, 9.0]	0.004
<b>Discharge outcome, n (%)</b>					
- Others	4 (8.7)	2 (12.5)	17 (25.8)	18 (32.1)	0.025
- Home	42 (91.3)	14 (87.5)	49 (74.2)	38 (67.9)	
<b>Achieved the FIM MCID, n (%)</b>					
- No improvement	31 (67.4)	9 (56.2)	35 (53.0)	30 (53.6)	0.436
- Improvement	15 (32.6)	7 (43.8)	31 (47.0)	26 (46.4)	

Abbreviations: IQR: Interquartile range, FIM: Functional independence measure, FILS: Food intake level scale, MCID: Minimum clinically important difference.

**Table 2.** Patient characteristics upon discharge.

sarcopenia, and 56 (30.4%) had osteosarcopenia. Most patients with osteosarcopenia were female and had a femoral neck bone density of  $0.519 \pm 0.100$  g/cm<sup>2</sup> and a lumbar spine bone density of  $0.677 \pm 0.099$  g/cm<sup>2</sup>. The average length of stay was 42.5 days, which did not reach significance in the univariate analysis. The FIM at discharge reached significance in the univariate analysis and was the lowest in the osteosarcopenia group.

Figure 1 shows the results of multivariate linear regression analysis of the effect of osteosarcopenia on FIM scores at discharge. Regardless of the osteoporosis diagnostic criteria used, osteoporosis (95% confidence interval [CI]:  $-8.515$ – $5.655$ ;  $\beta$ ,  $-0.017$ ,  $P = 0.691$ ), sarcopenia (95% CI:  $-1.440$ – $8.590$ ;  $\beta$ ,  $0.073$ ,  $P = 0.161$ ), and osteosarcopenia (95% CI:  $-2.518$ – $8.489$ ;  $\beta$ ,  $0.058$ ,  $P = 0.286$ ) did not reach a statistically significant association with FIM at discharge. In Models 2 and 3, which used different group classifications, osteosarcopenia still did not reach statistical significance in relation to FIM.

Figure 2 shows the results of the multiple logistic regression analysis that investigated the association between osteosarcopenia and achievement rates of the FIM MCID. Regardless of the osteoporosis diagnostic criteria used, the results did not reach a statistically significant association between the FIM MCID and osteoporosis (odds ratio [OR]: 1.142; 95% CI: 0.321–4.061;  $P = 0.838$ ), sarcopenia (OR: 1.974; 95% CI: 0.780–4.994;  $P = 0.151$ ), or osteosarcopenia (OR: 1.919; 95% CI: 0.698–5.277;  $P = 0.206$ ). In Models 2 and 3, which used different group classifications, osteosarcopenia still did not reach statistical significance in relation to FIM MCID.

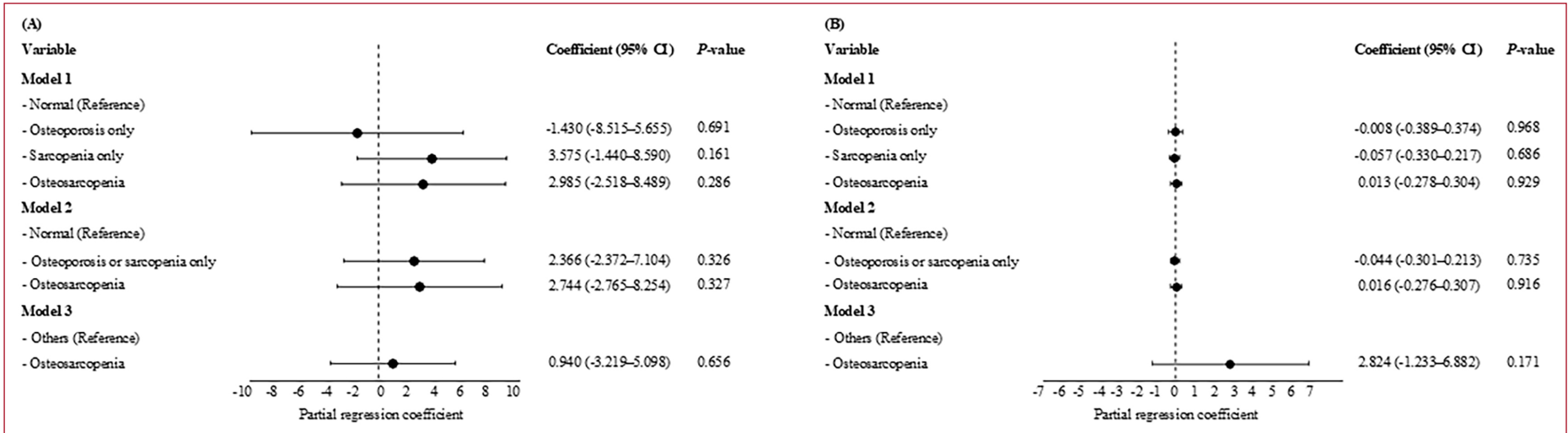
Figure 3 shows the results of multiple logistic regression analysis of the association between osteosarcopenia and home discharge. Regardless of the osteoporosis diagnostic criteria used, the results did not reach a statistically significant association between home discharge and osteoporosis (OR: 0.693; 95% CI: 0.081–5.904;  $P = 0.738$ ), sarcopenia (OR: 0.565; 95% CI: 0.142–2.243;  $P = 0.417$ ), or osteosarcopenia (OR: 0.525; 95% CI: 0.126–2.189;  $P = 0.376$ ). In Models 2 and 3, which used different group classifications, osteosarcopenia still did not reach statistical significance in relation to home discharge.

Similarly, in analyses conducted exclusively on female participants and patients with hip fractures, osteosarcopenia did not reach a statistically significant association with FIM, FIM MCID, or home discharge (Supplementary Figures 1 and 2).

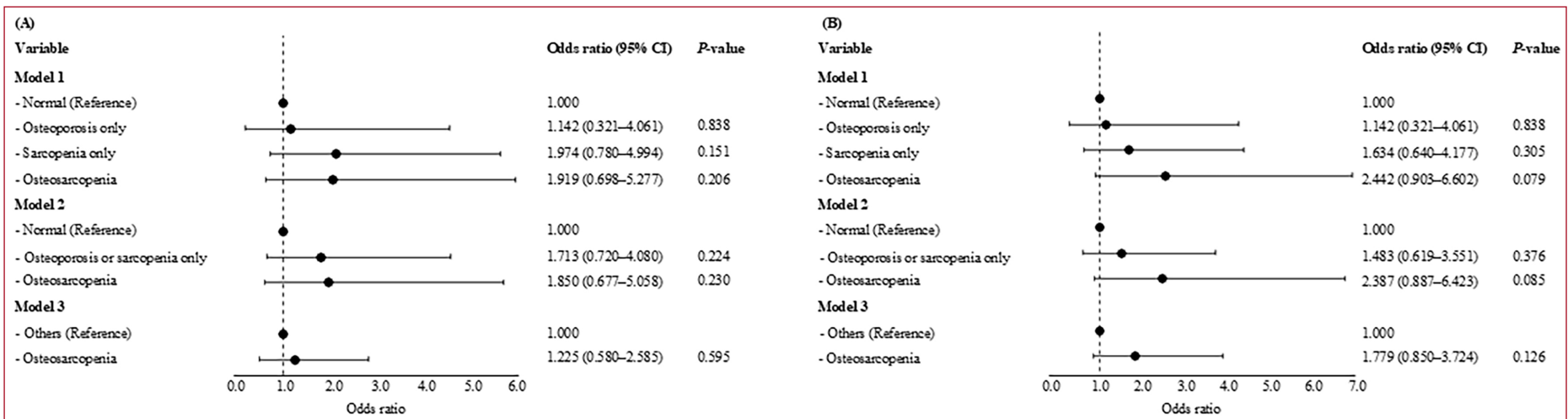
## Discussion

In this study, we investigated the negative impact of osteosarcopenia on the functional outcomes of older patients undergoing rehabilitation. Our results did not reach a statistically significant association between osteosarcopenia, improved functional outcomes, and home discharge.

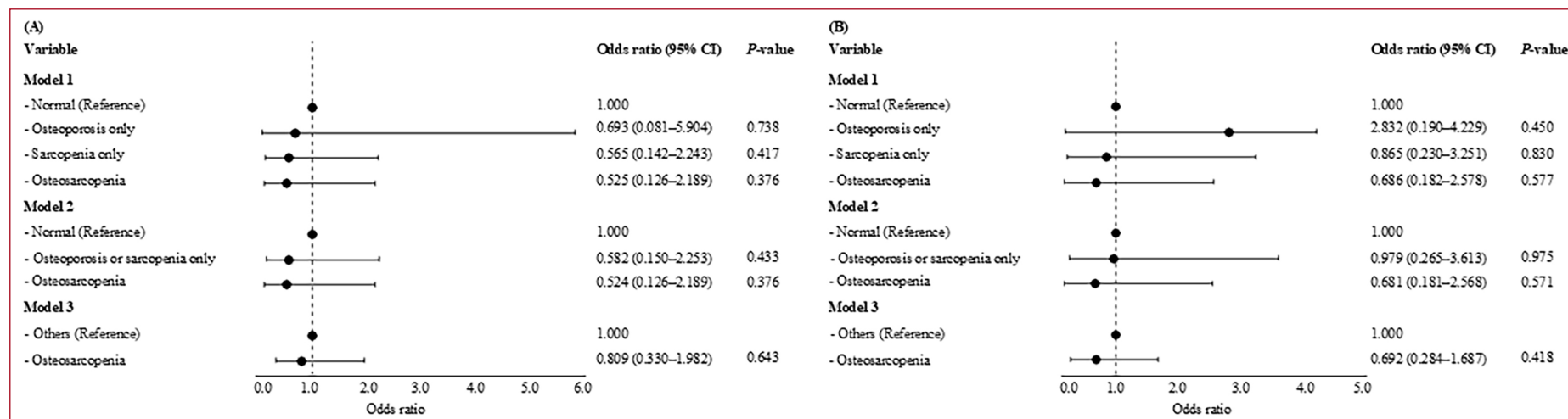
One potential reason that osteosarcopenia did not reach a significant association with functional outcomes might be insufficient statistical power. An association between osteosarcopenia and functional disability in community-dwelling older adults has been previously reported<sup>4</sup>. In this study, the univariate analysis showed a statistically significant difference in FIM at discharge, with



**Figure 1.** Multiple regression analysis of osteosarcopenia for FIM at discharge. (A) represents the group diagnosed with osteoporosis according to the WHO criteria, and (B) represents the group diagnosed according to the JOS criteria. Model 1 analyzed the four groups: normal, osteoporosis only, sarcopenia only, and osteosarcopenia. Model 2 increased statistical power by analyzing three groups: normal, others (osteoporosis or sarcopenia only), and osteosarcopenia. Model 3 further increased statistical power by analyzing two groups: others and osteosarcopenia.



**Figure 2.** Logistic regression analysis for FIM MCID. (A) represents the group diagnosed with osteoporosis according to the WHO criteria, and (B) represents the group diagnosed according to the JOS criteria. Model 1 analyzed the four groups: normal, osteoporosis only, sarcopenia only, and osteosarcopenia. Model 2 increased statistical power by analyzing three groups: normal, others (osteoporosis or sarcopenia only), and osteosarcopenia. Model 3 further increased statistical power by analyzing two groups: others and osteosarcopenia.



**Figure 3.** Logistic regression analysis for home discharge. (A) represents the group diagnosed with osteoporosis according to the WHO criteria, and (B) represents the group diagnosed according to the JOS criteria. Model 1 analyzed the four groups: normal, osteoporosis only, sarcopenia only, and osteosarcopenia. Model 2 increased statistical power by analyzing three groups: normal, others (osteoporosis or sarcopenia only), and osteosarcopenia. Model 3 further increased statistical power by analyzing two groups: others and osteosarcopenia.

osteosarcopenia having the lowest value. However, in the multivariate analysis, the association did not reach statistical significance. We estimated the required sample size to ensure adequate statistical power to reject the null hypothesis. Although the overall sample met the required size, dividing participants into four groups likely reduced statistical power. In the multivariable analyses, the 95% confidence intervals were wide across all groups, strongly suggesting limited power. In addition, heteroscedasticity may have influenced the estimates.

We also thought that differences in the study population may have influenced the association between osteosarcopenia and functional outcomes. Community-dwelling older adults usually have better motor function and ADL than hospitalized patients. Among community-dwelling older adults, the prevalence of osteosarcopenia has been reported to be low<sup>24</sup>. Those with osteosarcopenia tend to be substantially more frail than their community counterparts, which likely makes between-group differences in outcomes easier to detect. By contrast, our study population comprised patients who required rehabilitation therapy after fracture. As suggested by Japanese health statistics indicating that approximately 80% of patients with hip fracture require convalescent rehabilitation<sup>25</sup>, our study population was likely already relatively

homogeneously frail, irrespective of osteosarcopenia status. Therefore, the additional adverse effect of osteosarcopenia on functional outcomes may have been difficult to detect in our study. More importantly, the rehabilitation intervention itself may have acted as an effect modifier, mitigating the potential negative impact of osteosarcopenia. All patients in this study received specialized rehabilitation, and this intensive intervention may have uniformly promoted functional recovery, potentially masking any adverse prognostic effect of osteosarcopenia on functional outcomes.

Additionally, incomplete assessment of potential risk factors may have influenced our findings. For example, biomarkers have been reported to influence functional outcomes<sup>26</sup>. Additionally, potential risk factors reflecting patient severity, such as fracture severity and prior fracture history, may also have acted as confounders. These are not only important risk factors for osteoporosis but also factors that directly impede recovery during rehabilitation<sup>27,28</sup>. In this study, we could not adjust for these confounding factors, which may have obscured the true impact of osteosarcopenia. Furthermore, the definition of osteoporosis could also influence interpretation. We defined osteoporosis solely by DXA T-scores. However, current

clinical definitions diagnose osteoporosis based on either a T-score threshold or the presence of fragility fractures<sup>29</sup>. Failing to identify prior fragility fractures may have resulted in inadequate risk stratification. This potential misclassification could have artificially inflated the frailty within the control group, thereby attenuating or diluting the observed differences from the osteosarcopenia group.

Osteosarcopenia did not reach a statistically significant association with home discharge. Sarcopenia is reportedly an impediment to home discharge<sup>30</sup>. Yoshimura et al. reported that the mean age of older adult inpatients undergoing the same rehabilitation was  $74.9 \pm 13.2$  years<sup>30</sup>. In contrast, the target population of this study was older, with a mean age of  $82.7 \pm 7.6$  years. The older the patient, the more common the functional and cognitive decline. Therefore, the target population may have affected the results of this study.

We hypothesized that osteosarcopenia would exhibit a negative synergistic effect, resulting in a decline in functional outcomes. A scoping review by Inoue et al.<sup>11</sup> reported that osteosarcopenia may not demonstrate a synergistic negative effect of sarcopenia and osteoporosis on fractures and falls. However, the reason for this discrepancy between the logic and results has not yet been clarified, and doing so may partially explain the results of the present study.

The target population in this study was not significantly different from that of previous studies<sup>31-33</sup>. In this study, the prevalence of osteosarcopenia was 30.4%, with males accounting for 16.1% and females accounting for 83.9%. Prevalence rates in previous studies have been in the range of 15.4%–65.7% in hospitalized patients<sup>11</sup>. Furthermore, the ratio of males to females also showed a higher proportion of females<sup>17,34,35</sup>, consistent with the results of this study. These findings suggest that the validity of the target population in this study is not a significant concern.

This study has several limitations. First, it was conducted at a single center, which may limit the generalizability of the findings. Given potential influences of patient characteristics and rehabilitation practices at our institution, our findings are not fully representative of all hospitalized older adults. Accordingly, a multicenter, large-scale observational study is needed to evaluate the true impact of osteosarcopenia. In such a study, it is essential to accurately stratify patients using more consensus-based diagnostic criteria, such as the clinical definition of osteoporosis which includes the presence of fragility fractures, and to adjust for confounders not evaluated in this study, such as prehospitalization activity levels, standardized rehabilitation intensity, and biomarkers. Second, significant differences were observed in baseline FIM scores between groups. Although we adjusted for baseline FIM scores and other severity-related factors (such as CCI, MNA-SF, FILS, and MMSE) in our analysis, more rigorous methods, such as matching, would be necessary to better control for these differences. Third, the wide 95% CI suggest that a larger sample size

may be required to detect significant differences between groups. Fourth, osteoporosis was assessed solely by DXA bone mineral density. Current definitions indicate that a diagnosis may be established by bone densitometry (WHO criteria) or by a history of fragility fractures<sup>29</sup>. Accordingly, nondifferential misclassification bias may have occurred, which could have attenuated the observed association between osteosarcopenia and functional outcomes. Finally, data on participants' prehospitalization residential status were not available. However, since all participants were transferred from acute care hospitals, their prehospitalization residential status likely had minimal impact on discharge outcomes. A similar previous study conducted on patients transferred from an acute care hospital also did not report prehospitalization residential status<sup>30</sup>.

## Conclusion

In this study, osteosarcopenia was observed in 30.4% of older patients with fractures admitted to rehabilitation units. Although the associations of osteosarcopenia with FIM at discharge, achievement of the FIM MCID, and home discharge did not reach statistical significance, intensive rehabilitation during hospitalization may have mitigated its adverse effects, thereby masking its impact on functional outcomes at discharge. Further large-scale, multicenter, longitudinal studies are warranted to clarify the long-term clinical impact of osteosarcopenia in this population.

### Ethics approval

*This study was approved by the Ethics Committee of Hamamatsu City Rehabilitation Hospital (approval number: 21-82) and was conducted in accordance with the Declaration of Helsinki (1964) and its later amendments.*

### Consent to participate

*Informed consent was waived by the Ethics Committee due to the retrospective design of the study. Consequently, an opt-out approach was adopted, whereby information regarding the study was disclosed on the hospital's official website and notice boards. Participants were provided with the opportunity to decline participation in accordance with the procedures described in these announcements prior to data anonymization.*

### Authors' contributions

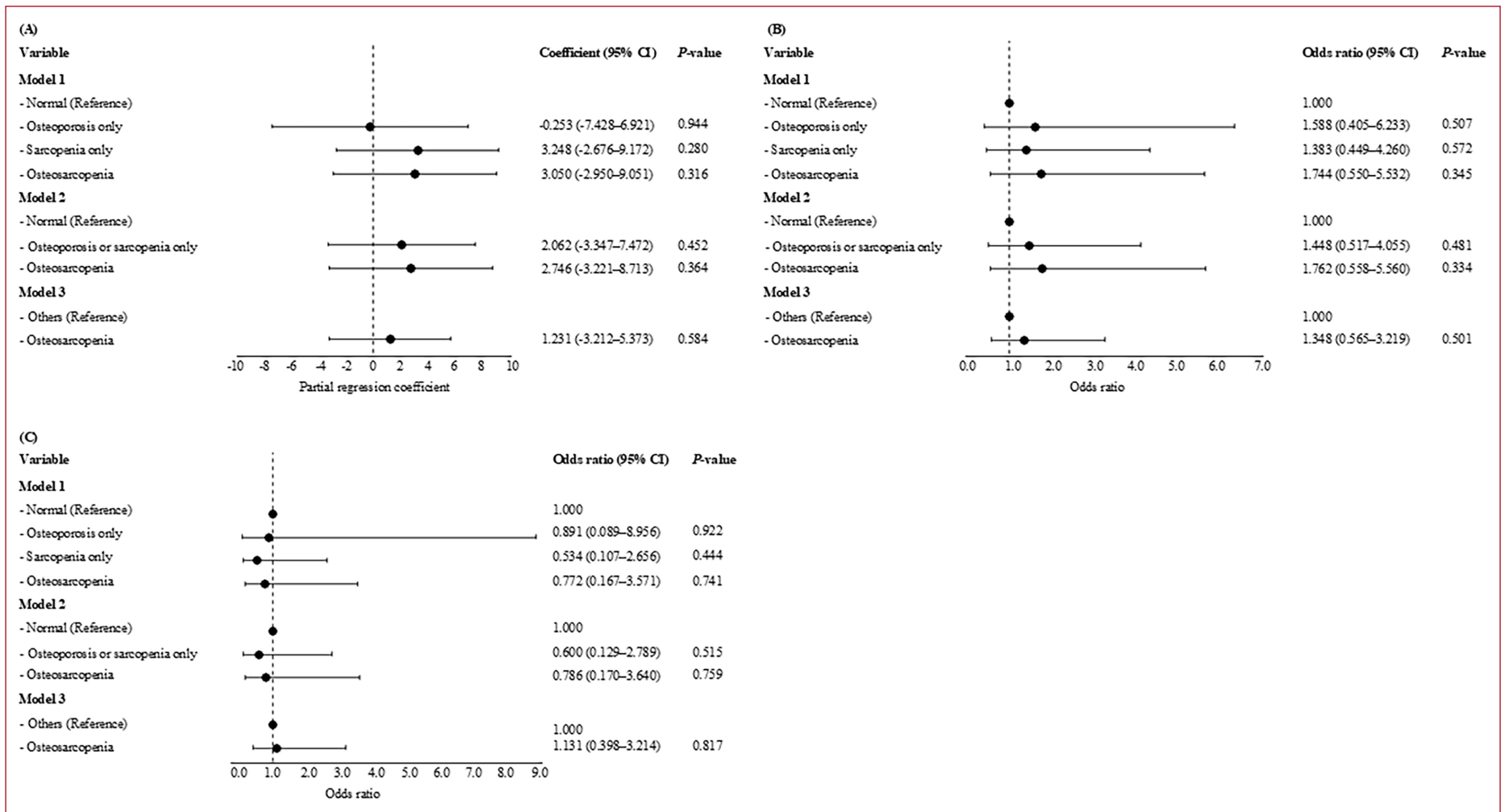
*Ryo Mannen: Writing-original draft, Conceptualization, Methodology, Formal analysis, Data curation, Project administration. Keisuke Maeda: Writing-review & editing. Tatsuro Inoue: Writing-review & editing. Akio Shimizu: Writing-review & editing, Conceptualization, Methodology, Project administration. All authors read and approved the final version of the manuscript.*

### Funding

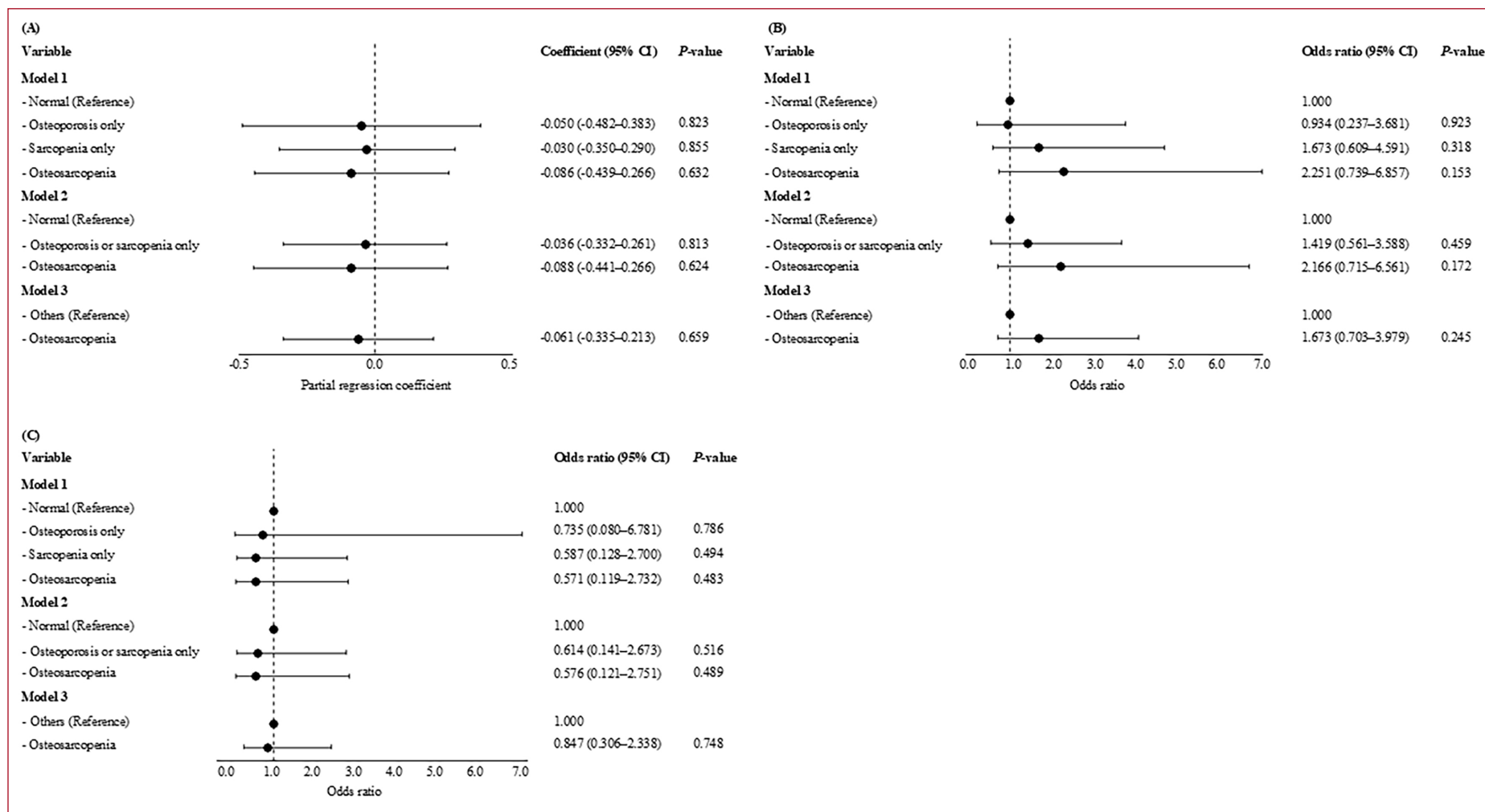
*This study was supported by The University of Nagano.*

## References

1. Kanis JA, Adachi JD, Cooper C, Clark P, Cummings SR, Diaz-Curiel M et al. Standardising the descriptive epidemiology of osteoporosis: recommendations from the Epidemiology and Quality of Life Working Group of IOF. *Osteoporos Int* 2013;24:2763-2764.
2. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. *Osteoporos Int* 1994;4:368-381.
3. Tella SH, Gallagher JC. Prevention and treatment of postmenopausal osteoporosis. *J Steroid Biochem Mol Biol* 2014;142:155-170.
4. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010;39:412-423.
5. López-Teros MT, Rosas-Carrasco O, Sánchez-García S, Castro-Porras L, Luna-López A, Agudelo-Botero M. The Association of Osteosarcopenia With Functional Disability in Community-Dwelling Mexican Adults 50 and Older. *Front Med (Lausanne)* 2021;8:674724.
6. Hirschfeld HP, Kinsella R, Duque G. Osteosarcopenia: where bone, muscle, and fat collide. *Osteoporos Int* 2017;28:2781-2790.
7. Huo YR, Suriyaarachchi P, Gomez F, Curcio CL, Boersma D, Muir SW et al. Phenotype of osteosarcopenia in older individuals with a history of falling. *J Am Med Dir Assoc* 2015;16:290-295.
8. Chen S, Xu X, Gong H, Chen R, Guan L, Yan X et al. Global epidemiological features and impact of osteosarcopenia: A comprehensive meta-analysis and systematic review. *J Cachexia Sarcopenia Muscle* 2023;15:8-20.
9. Inoue T, Maeda K, Satake S, Matsui Y, Arai H. Osteosarcopenia, the co-existence of osteoporosis and sarcopenia, is associated with social frailty in older adults. *Ageing Clin Exp Res* 2022;34:535-543.
10. Bertschi D, Kiss CM, Beerli N, Mauthner O, Kressig RW. Impact of sarcopenia on daily functioning: a cross-sectional study among older inpatients. *Ageing Clin Exp Res* 2022;34:2041-2046.
11. Inoue T, Maeda K, Nagano A, Shimizu A, Ueshima J, Murotani K et al. Related Factors and Clinical Outcomes of Osteosarcopenia: A Narrative Review. *Nutrients* 2021;13:291.
12. Kidd D, Stewart G, Baldry J, Johnson J, Rossiter D, Petruckevitch A et al. The Functional Independence Measure: a comparative validity and reliability study. *Disabil Rehabil* 1995;17:10-14.
13. Beninato M, Gill-Body KM, Salles S, Stark PC, Black-Schaffer RM, Stein J. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. *Arch Phys Med Rehabil* 2006;87:32-39.
14. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. *J Am Med Dir Assoc* 2020;21:300-307.
15. WHO. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 1994;843:1-129.
16. Soen S, Fukunaga M, Sugimoto T, Sone T, Fujiwara S, Endo N et al. Diagnostic criteria for primary osteoporosis: year 2012 revision. *J Bone Miner Metab* 2013;31:247-257.
17. Morley JE, Abbatecola AM, Argiles JM, Baracos V, Bauer J, Bhasin S et al. Sarcopenia with limited mobility: an international consensus. *J Am Med Dir Assoc* 2011;12:403-409.
18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-383.
19. Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Cederholm T et al. Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging* 2009;13:782-788.
20. Kunieda K, Ohno T, Fujishima I, Hojo K, Morita T. Reliability and validity of a tool to measure the severity of dysphagia: the Food Intake LEVEL Scale. *J Pain Symptom Manage* 2013;46:201-206.
21. Shimizu A, Maeda K, Ueshima J, Inoue T, Murotani K, Ohno T et al. Prevalence of sarcopenic obesity based on newly proposed diagnostic criteria and functional outcomes in older adults undergoing rehabilitation. *Mech Ageing Dev* 2022;208:111728.
22. Salari N, Ghasemi H, Mohammadi L, Behzadi MH, Rabieenia E, Shohaimi S et al. The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. *J Orthop Surg Res* 2021;16:609.
23. Dyer SM, Crotty M, Fairhall N, Magaziner J, Beaupre LA, Cameron ID et al. A critical review of the long-term disability outcomes following hip fracture. *BMC Geriatr* 2016;16:158.
24. Huang T, Li C, Chen F, Xie D, Yang C, Chen Y et al. Prevalence and risk factors of osteosarcopenia: a systematic review and meta-analysis. *BMC Geriatr* 2023;23:369.
25. Takahashi M, Iwase J, Abe M, Hashimoto N, Kosaka H, Egawa H. Insufficient Postoperative Rehabilitation in Patients with Both Proximal Femoral Fracture and Antecedent Mental Illness. *Jma j* 2020;3:265-271.
26. Inoue T, Shimizu A, Murotani K, Satake S, Matsui Y, Arai H et al. Exploring biomarkers of osteosarcopenia in older adults attending a frailty clinic. *Exp Gerontol* 2023;172:112047.
27. Kanis JA, Johnell O, De Laet C, Johansson H, Oden A, Delmas P et al. A meta-analysis of previous fracture and subsequent fracture risk. *Bone* 2004;35:375-382.
28. Phruetthiphat OA, Kanokwongnuwat W, Satravaha Y, Pinijprapa P, Chaichankul C, Gajasen P. Functional outcomes following hip fracture with concurrent vertebral fracture within a fracture liaison service. *Sci Rep* 2025;15:25417.
29. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ et al. The clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int* 2022;33:2049-2102.
30. Yoshimura Y, Wakabayashi H, Bise T, Nagano F, Shimazu S, Shiraiishi A et al. Sarcopenia is associated with worse recovery of physical function and dysphagia and a lower rate of home discharge in Japanese hospitalized adults undergoing convalescent rehabilitation. *Nutrition* 2019;61:111-118.
31. Yoo JI, Kim H, Ha YC, Kwon HB, Koo KH. Osteosarcopenia in Patients with Hip Fracture Is Related with High Mortality. *J Korean Med Sci* 2018;33:e27.
32. Di Monaco M, Castiglioni C, Bardesono F, Milano E, Massazza G. Sarcopenia, osteoporosis and the burden of prevalent vertebral fractures: a cross-sectional study of 350 women with hip fracture. *Eur J Phys Rehabil Med* 2020;56:184-190.
33. Saeki C, Oikawa T, Kanai T, Nakano M, Torisu Y, Sasaki N et al. Relationship between osteoporosis, sarcopenia, vertebral fracture, and osteosarcopenia in patients with primary biliary cholangitis. *Eur J Gastroenterol Hepatol* 2021;33:731-737.
34. Bertschi D, Kiss CM, Schoenenberger AW, Stuck AE, Kressig RW. Sarcopenia in Patients Undergoing Transcatheter Aortic Valve Implantation (TAVI): A Systematic Review of the Literature. *J Nutr Health Aging* 2021;25:64-70.
35. De Buyser SL, Petrovic M, Taes YE, Toye KR, Kaufman JM, Lapauw B et al. Validation of the FNIH sarcopenia criteria and SOF frailty index as predictors of long-term mortality in ambulatory older men. *Age Ageing* 2016;45:602-608.



**Supplementary Figure 1.** The analysis results for female subjects only are presented. (A) Multiple regression analysis of osteosarcopenia for FIM at discharge (B) Logistic regression analysis for FIM MCID (C) Logistic regression analysis for home discharge. Abbreviations: FIM: Functional independence measure, CCI: Charlson comorbidity index, MNA-SF: Mini nutritional assessment short form, FILS: Food intake level scale, MMSE: Mini mental state examination, MCID: Minimum clinically important difference.



**Supplementary Figure 2.** The analysis results for subjects with hip fractures only are presented. (A) Multiple regression analysis of osteosarcopenia for FIM at discharge (B) Logistic regression analysis for FIM MCID (C) Logistic regression analysis for home discharge. Abbreviations: FIM: Functional independence measure, CCI: Charlson comorbidity index, MNA-SF: Mini nutritional assessment short form, FILS: Food intake level scale, MMSE: Mini mental state examination, MCID: Minimum clinically important difference.