

# Impact of Sarcopenia on the Hip Fracture Treatment Outcomes: A Single-institution Case-control Study

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## Research Article

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# Abstract

**Background:** Although sarcopenia has been known as a risk factor for hip fractures, only a few reports have described the impact of sarcopenia on hip fracture treatment outcomes. The current study therefore sought to investigate the effect of sarcopenia on treatment outcomes of patients with hip fractures.

**Methods:** This case–control study involved 337 patients (67 males and 270 females) with hip fractures aged  $\geq$  years (mean age:  $84.1 \pm 7.1$  years) who underwent surgery from January 2013 to June 2019. The mean follow-up period was 17.1 (1–60) months. All patients were assessed for sarcopenia using dual-energy X-ray absorptiometry upon hospitalization. Treatment outcomes and one-year mortality rates were compared between patients with and without sarcopenia. Furthermore, we determined whether sarcopenia was a risk factor for one-year mortality in hip fracture patients using a Cox proportional hazards model.

**Results:** The prevalence of sarcopenia in patients with hip fracture was 231 (68.5%). Those with sarcopenia had a lower Barthel index ( $P < 0.0001$ ) and hospital discharge rate ( $P = 0.035$ ). Cox proportional hazards regression analysis adjusted for age and sex found that sarcopenia was a risk factor for one-year mortality (hazard ratio, 3.173, 95% confidence interval, 1.095–9.199,  $P = 0.033$ ).

**Conclusions:** Patients with hip fracture who had sarcopenia had a lower Barthel index, lower hospital discharge rate, and higher one-year mortality. Moreover, sarcopenia was identified as a risk factor for one-year mortality among those with hip fractures. The aforementioned findings may help clinicians better manage those with hip fracture.

## Background

Age-related loss of muscle mass, called sarcopenia, a term proposed by Rosenberg et al. in 1989 (1), has been recognized as an independent condition by the International Classification of Disease, Tenth Revision (2). Sarcopenia can be attributed to aging, undernutrition, disuse, and inflammation, resulting in functional decline, loss of independence, and early mortality among elderly individuals (3). Sarcopenia has been identified as a risk factor for falls among elderly individuals, while patients with sarcopenia suffer from increased incidences of fractures (4,5). Indeed, Hida et al. reported that sarcopenia was a risk factor for hip fractures (6), which also affect activities of daily living and mortality among elderly individuals. Another study found that half of the patients with hip fractures ultimately develop permanent disability and mobility and are at high risk of institutionalization (7). Mortality rates among those suffering from hip fractures had been reported to exceed 10% (8,9), with increases rates observed within the first year after injury (10,11). The correlation between muscle mass and bone mass has been well known, with combined cases of sarcopenia and osteoporosis being common (12). However, little is known regarding the impact of sarcopenia on hip fracture treatment (13–15). Therefore, the current study aimed to investigate the characteristics of patients with sarcopenia and determine the impact of sarcopenia on hip fracture treatment outcomes.

## Methods

This case-control study involved 337 patients with hip fracture aged  $\geq 65$  years (66 males, 271 females) with a mean age of  $84.1 \pm 7.1$  (65–102) years who underwent surgery from January 2013 to June 2019. The mean follow-up period was  $17.1 \pm 14.5$  (1–60) months. All patients were measured for skeletal muscle mass index (SMI) and bone mineral density using dual-energy X-ray absorptiometry (Lunar iDXA; GE Healthcare, Tokyo, Japan) upon hospitalization. To avoid measurement errors in muscle mass and bone mineral density, 44 patients who had undergone orthopedic surgery with metal implants were excluded. Moreover, skeletal muscle mass could not be assessed in 45 patients (Figure 1). Sarcopenia was defined as the loss of appendicular skeletal muscle mass (ASM) (i.e., skeletal muscle mass in the arms and legs), with the SMI being calculated as  $ASM/height^2$  ( $kg/m^2$ ) according to the consensus of the Asian Working Group for Sarcopenia criteria (male,  $<7.00 kg/m^2$ ; female,  $<5.40 kg/m^2$ ) (16). Walking speed could not be measured due to the presence of fractures, while grip strength could not be measured due to the inability of maintaining a standing or sitting position, an intravenous catheter in the dominant hand, and cognitive impairment in half of the patients. Given that many of the patients sustained fractures due to falls, we concluded that impaired physical function was the primary etiology. Therefore, sarcopenia was diagnosed using only SMI values. Osteoporosis was defined as a T score of  $\leq -2.5$  standard deviations in the femoral neck without fracture. Hip fractures were classified as a femoral neck or trochanteric fractures. Characteristics and treatment outcomes were compared between both patients with and without sarcopenia. Nutritional status was assessed using the geriatric nutritional risk index (GNRI) (17), which was calculated using the following formula:  $14.89 \times \text{serum albumin (g/dL)} \boxtimes 41.7 \times [\text{body weight (kg)}/\text{ideal body weight (kg)}]$ . The ideal body weight was defined as that which resulted in a body mass index (BMI) of 22. GNRI was classified into the following four grades of nutrition-related risk:  $<82$ , major risk;  $82$  to  $<92$ , moderate risk;  $92$  to  $\leq 98$ , low risk; and  $>98$ , no risk. Treatment outcomes were assessed using hospital stay, hospital mortality, the Barthel index (18) at discharge, home discharge rate, and one-year mortality. Statistical analyses consisted of Student's t-test for continuous variables, the Mann-Whitney U test for non-continuous variables, and the Pearson Chi-Square test for categorical variables. A multivariate logistic regression model was used to calculate adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for factors related to sarcopenia. Kaplan-Meier survival curves for those with and without sarcopenia were prepared, and log-rank tests were performed. Furthermore, Cox proportional hazards analysis adjusted for age and sex was performed to calculate adjusted hazard ratios (HRs) with 95% CIs for one-year mortality. All statistical analyses were performed using IBM SPSS v.23.0 for Windows (IBM Institute, Inc., Cary, NC, USA), with  $P < 0.05$  indicating statistical significance. This study was approved by National Center for Geriatrics and Gerontology review board and all experiments were performed in accordance with the ethical standards laid down in the amended Declaration of Helsinki. This study was conducted with the ethics committee of National Center for Geriatrics and Gerontology (approval number: No. 1124). Informed consent was obtained from all individual participants included in the study.

## Results

The prevalence of sarcopenia among patients with hip fracture was 68.5%. With regard to patient characteristics, those with sarcopenia were predominantly male, had more femoral neck fractures, and had lower BMI, Barthel index, and GNRI than those without sarcopenia. ( $P < 0.0001$ ,  $P = 0.006$ ,  $P < 0.0001$ ,  $P = 0.019$ ,  $P < 0.0001$ , respectively) (Table 1). Multivariate logistic regression analysis was performed to determine factors associated with sarcopenia, excluding SMI as an explanatory variable. Accordingly, male sex, low BMI, low GNRI, femoral neck fractures were associated with sarcopenia (OR 9.166, 95% CI 3.193–26.315,  $P < 0.0001$ ; OR 0.719, 95% CI 0.622–0.830,  $P < 0.0001$ ; OR 0.952, 95% CI 0.910–0.996,  $P = 0.019$ ; OR 2.112, 95% CI 1.113–4.006,  $P = 0.022$ , respectively) (Table 2). Patients with sarcopenia had a lower Barthel index ( $P < 0.0001$ ) and hospital discharge rate ( $P = 0.035$ ) than those without sarcopenia (Table 3). Figure 2 shows the Kaplan–Meier survival curves for one-year mortality for those with and without sarcopenia, with the former having a higher one-year mortality than the latter ( $P = 0.011$ ).

Furthermore, Cox proportional hazards regression analysis adjusted for age and sex revealed that sarcopenia was a risk factor for one-year mortality (HR 3.173, 95% CI 1.095–9.199,  $P = 0.033$ ) (Table 4).

## Discussion

Given that sarcopenia promotes functional decline, loss of independence, and earlier mortality among elderly individuals (3), screening for patients with sarcopenia is imperative. The present study found that 68.5% of the included patients with hip fracture had sarcopenia (91.0% in males and 63.1% in females) and that male sex, underweight, undernutrition, and femoral neck fractures were associated with sarcopenia. Several studies have reported a higher prevalence of sarcopenia in men with hip fractures (6,19). Considering that males have more muscle mass than females, they may be more susceptible to the effects of age-related loss of muscle mass.

Underweight and undernutrition have been known risk factors for sarcopenia (3,20). Furthermore, while the type of hip fracture has been associated with age, sex, and bone mineral density (21–23), no study has yet investigated the relationship between the type of hip fracture and sarcopenia. Moreover, sarcopenia can be a negative prognostic predictor for patients with cancer (24). However, little is known regarding the impact of sarcopenia on hip fracture management. Previous studies have reported that sarcopenia promotes poor functional outcomes after surgery and increases the risk of five-year mortality in patients with hip fractures (13–15). Indeed, the present study found that patients with sarcopenia had a lower Barthel index, lower hospital discharge rate, and higher one-year mortality rate, which remains consistent with those presented in previous studies. These findings can potentially help clinicians make better treatment decisions and provide more information regarding surgical management to the patients and their families.

Our study found that the type of hip fracture was related to sarcopenia. Notably, one study showed that patients with trochanteric fractures had lower bone mineral densities than those with femoral neck fractures (23), while another found a correlation between muscle mass and bone mass (12). Therefore, we expected higher rates of trochanteric fractures among the sarcopenia group. However, the sarcopenia

group had higher rates of femoral neck fractures than trochanteric fractures. Only a few studies have investigated the relationship between body composition and type of hip fracture. Among them, Di Monaco et al. reported that patients with femoral neck fractures had higher body fat mass than those with trochanteric fractures (25). The difference between femoral neck and trochanteric fractures lies within muscle attachment considering that the magnitude of the reaction force applied to the bone caused by muscle contractions may affect the type of fracture. Nonetheless, further studies are needed to determine the relationship between muscle mass and type of hip fracture.

No consensus has been established regarding the treatment for low muscle mass. However, studies have shown that the combination of exercise training and nutritional supplementation can effectively improve muscle mass (26). Exercise training, even at low intensity, has been shown to reduce mortality among elderly individuals (27). As such, patients with hip fractures should continue to exercise as much as possible after discharge. While no therapeutic agents are currently available for the treatment of low muscle mass, drugs utilized for the treatment of osteoporosis, such as alendronate and alfacalcidol, have been reported to have positive effects on muscle volume (28,29). However, given that these studies were conducted in the general population, it remains unclear whether similar results would be obtained in patients with hip fractures. Furthermore, gaining muscle mass does not prevent aging-related loss of muscle strength (30). Bimagrumab (BYM338; Novartis), a fully human monoclonal antibody that prevents ligand binding and promotes differentiation of human myoblasts (31), has shown promising results in the treatment of sarcopenia. Studies have shown that although bimagrumab promoted greater muscle mass compared to placebo, no improvements in physical function were noted (32). Further studies are therefore needed to develop an effective drug for the treatment of sarcopenia.

The presented study has several limitations worth noting. First, walking speed and grip strength could not be measured given the difficulty of evaluating physical function in patients during the acute phase of fractures. Although the diagnosis of sarcopenia requires assessing walking speed and grip strength, the current diagnostic criteria are controversial given that they exclude patients with locomotor disease (e.g., osteoarthritis, osteoporosis, and lumbar spinal stenosis). Sakai et al. reported that sarcopenia among elderly patients with locomotor disease (osteoarthritis, spondylosis, and osteoporosis) should be evaluated using muscle mass alone without physical performance (33). Considering that most cases of fractures in elderly individuals are caused by falls and that most patients with hip fractures have osteoporosis, it may be reasonable to conclude that patients with hip fractures have impaired physical function. Second, the current study did not assess comorbidities (e.g., cancer, cardiac diseases, endocrine diseases, and neurological disease). Given that some patients had dementia or no relatives, a common occurrence in actual clinical practice, accurate medical histories could not be obtained. These comorbidities may have affected the treatment outcomes. However, given that these comorbidities also affect muscle mass loss (secondary sarcopenia), the diagnosis of sarcopenia may help assess the severity of these comorbidities.

## Conclusions

In summary, the current study identified male sex, underweight, undernutrition, and femoral neck fractures as factors associated with sarcopenia in patients with hip fracture. Moreover, among patients with hip fractures, those with sarcopenia had a lower Barthel index, lower hospital discharge rate, and higher one-year mortality compared to those without it. Furthermore, sarcopenia was identified as a risk factor for the one-year mortality among those with hip fractures. The aforementioned findings may help clinicians in the management of patients with hip fractures.

## **Declarations**

### **Ethics approval and consent to participate**

This study was approved by National Center for Geriatrics and Gerontology review board and all experiments were performed in accordance with the ethical standards laid down in the amended Declaration of Helsinki. This study was conducted with the ethics committee of National Center for Geriatrics and Gerontology (approval number: No. 1124).

### **Consent to publish**

Informed consent was obtained from all individual participants included in the study.

### **Availability of data and materials**

The datasets analyzed during the current study available from the corresponding author on reasonable request.

### **Competing Interests**

Not applicable

### **Funding**

Not applicable

### **Authors' Contributions**

Hiroki Iida carried out the studies and drafted the manuscript. Hiroki Iida prepared figures 1-2 and table 1-4. Taisuke Seki, Yoshihito Sakai, Shiro Imagama participated in its design and helped to draft the manuscript. Hiroki Iida, Yoshihito Sakai, Tsuyoshi Watanabe, Norimitsu Wakao, Hiroki Matsui recruited the participants. All authors read and approved the final manuscript.

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Not applicable

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## Tables

Table 1. Comparison of the patient characteristics for hip fracture with and without sarcopenia

variables	Sarcopenia (N=231)	without sarcopenia (N=106)	P-value
Age (years)	83.8±7.1	84.7±7.0	0.262
sex (male : female)	60:171	6:100	<0.0001
BMI(kg/∅)	19.2±2.9	22.7±3.0	<0.0001
cognitive impairment (N, %)	113, 48.9%	50, 47.2%	0.635
home residence (N, %)	158, 68.4%	73, 68.9%	0.132
Barthel index (before injury)	68.5±31.2	77.2±25.3	0.019
GNRI	89.9±9.9	99.2±8.8	<0.0001
Osteoporosis (N, %)	182, 78.8%	75, 70.8%	0.108
Femoral neck fracture (N, %)	111, 48.1%	34, 32.1%	0.006
SMI(kg/∅)	4.87±0.64	6.14±0.65	<0.0001

Values are presented as mean ± standard deviation.

BMI: body mass index.

GNRI: geriatric nutritional risk index.

SMI: skeletal mass index.

Table.2 Comparison of the treatment outcomes for hip fracture with and without sarcopenia

	sarcopenia(N=231)	without sarcopenia(N=106)	P-value
Barthel index (at discharge)	48.9±32.4	61.7±31.0	<0.001
stays at acute care institutions (days)	28.8±18.6	28.3±14.3	0.811
Home discharge(N,%)	111,48.1%	64,60.4%	0.035

Values are presented as mean  $\pm$  standard deviation.

Table 3. The logistic regression analysis for related factors of sarcopenia

variables	Odd ratio	95%CI	P-value
age	0.984	0.939-1.031	0.498
male sex	9.166	3.193-26.315	<0.0001
BMI	0.719	0.622-0.830	<0.0001
Barthel index (before injury)	0.991	0.980-1.002	0.108
GNRI	0.952	0.910-0.996	0.019
femoral neck fracture	2.112	1.113-4.006	0.022

The dependent variable was the presence of sarcopenia.

The presence of sarcopenia was attributed a value of 1, the absence of sarcopenia was attributed a value of 0.

The male sex was attributed a value of 1, the female sex was attributed a value of 0.

Femoral neck fracture was attributed a value of 1, trochanteric fracture was attributed a value of 0.

BMI: body mass index.

GNRI: geriatric nutritional risk index.

OR: odds ratio

CI: confidence interval

Table. Cox proportional hazards analysis adjusted for age and sex for one-year mortality of sarcopenia

variables	HR	95% CI	P-value
age	1.047	0.995-1.103	0.076
male sex	2.055	0.997-4.235	0.057
sarcopenia	3.173	1.095-9.199	0.033

Death within one-year was attributed a value of 1, survival after one-year was attributed a value of 0.

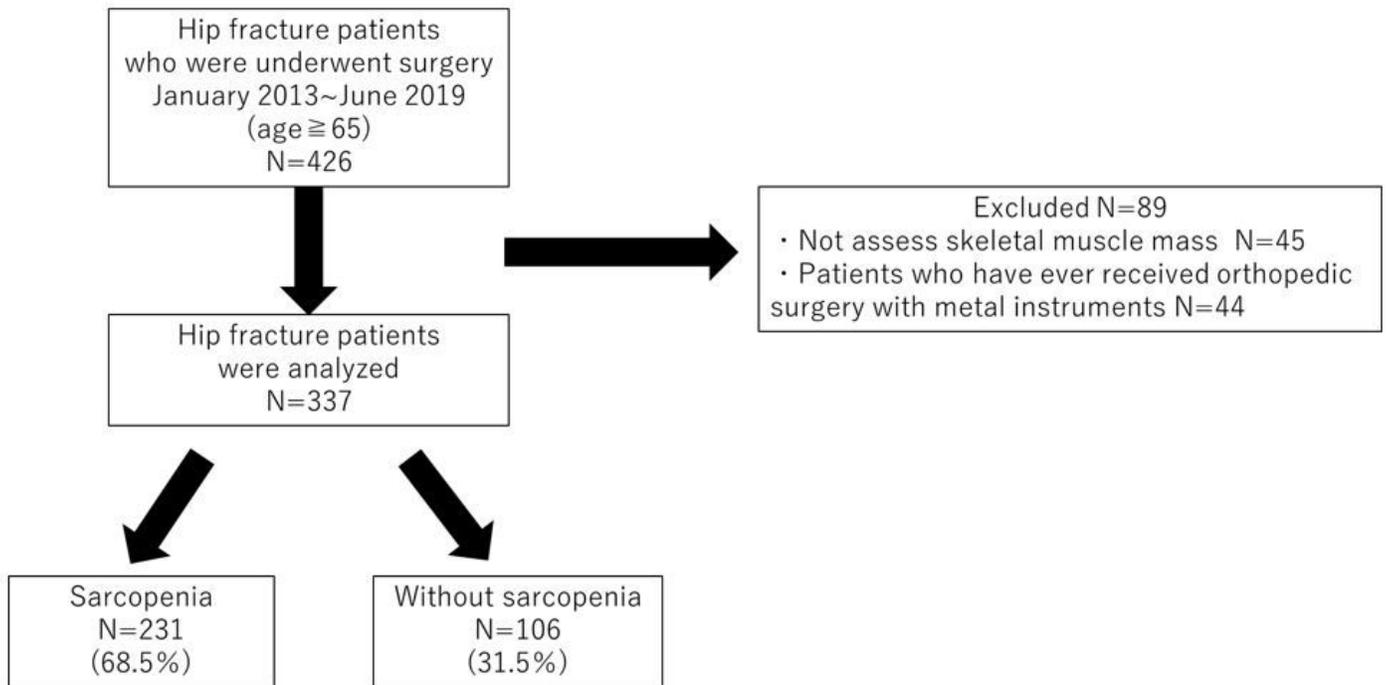
The male sex was attributed a value of 1, the female sex was attributed a value of 0.

The presence of sarcopenia was attributed a value of 1, the absence of sarcopenia was attributed a value of 0.

HR: hazards ratio

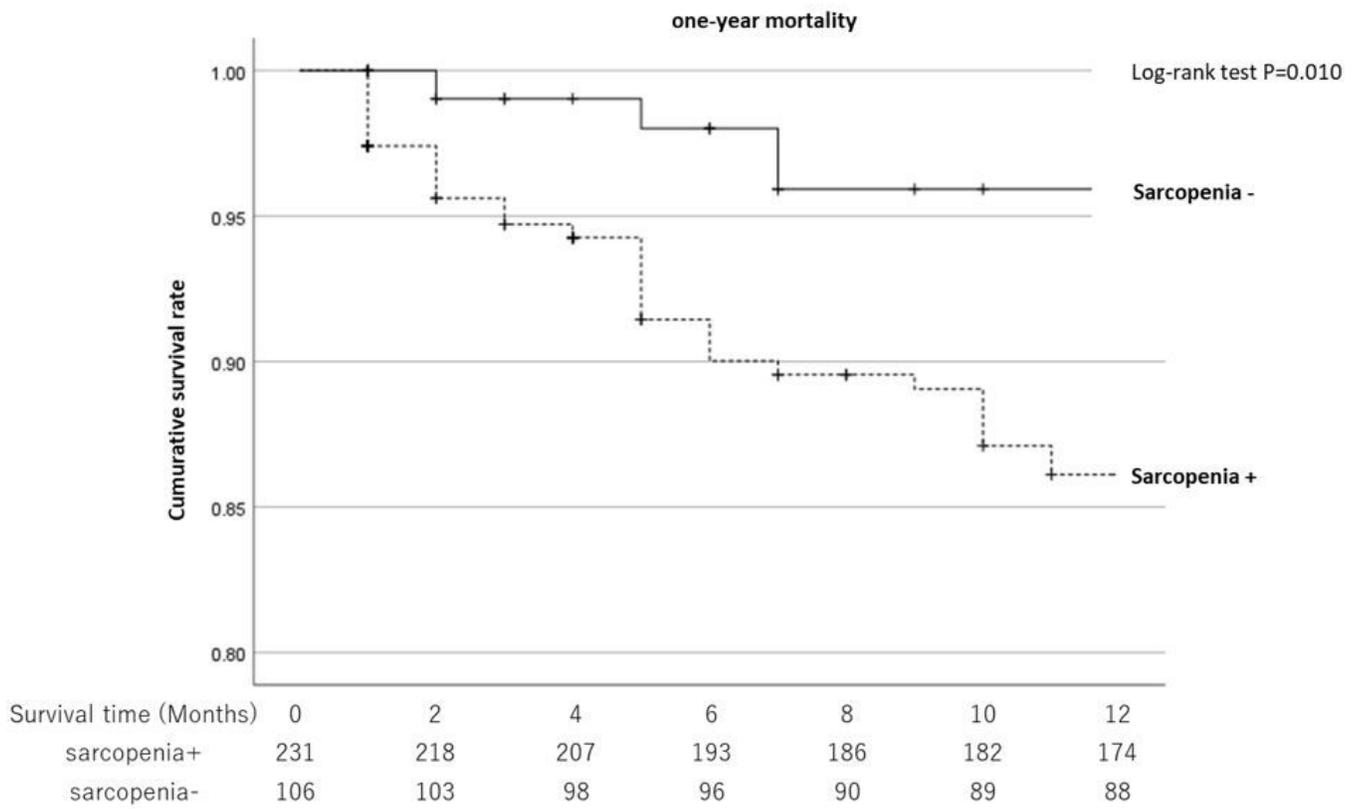
CI: confidence interval

## Figures



**Figure 1**

Flowchart showing progress through the study of the elderly patients with hip fracture.



**Figure 2**

Kaplan-Meier survival curves of one-year mortality with and without sarcopenia.