Effects of sarcopenia on changes in prevalence of patients with depressive mood during hospitalization in geriatric rehabilitation

Running Title  Sarcopenia and depressive mood in rehabilitation

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CONFLICT OF INTEREST

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None.
Effects of sarcopenia on changes in the prevalence of patients with depressive mood during inpatient geriatric rehabilitation

ABSTRACT

Background: The effect of sarcopenia on depressive mood during geriatric rehabilitation remains unclear. This study investigated the potential influence of sarcopenia on depressive mood among geriatric patients in a rehabilitation setting.

Methods: This observational cohort study enrolled 204 patients aged ≥65 years (mean: 78.8±7.6 years, 45.1% women) admitted to a rehabilitation unit between April 2020 and July 2021. Sarcopenia was diagnosed based on the Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment (AWGS2019) criteria, which include low handgrip strength and muscle mass. Depressive mood was defined as a 15-item Geriatric Depression Scale score of ≥6 points. We applied logistic regression models to examine the influence of sarcopenia on depressive mood at discharge.

Results: We observed sarcopenia in 58.3% of patients. The logistic regression model showed that sarcopenia negatively influenced depressive mood at discharge (odds ratio, 5.460; 95% confidence interval, 2.344–13.415). Of the 68 patients without depressive mood at admission, those with sarcopenia (n=31) had a significantly higher incidence of depressive mood at discharge compared with patients without sarcopenia (n=37) (41.9% vs. 16.2%, p=0.037).

Conclusion: Sarcopenia at admission negatively affected depressive mood at discharge from geriatric rehabilitation. Thus, early and routine assessment of sarcopenia is vital for patients undergoing geriatric rehabilitation.

Key Words: sarcopenia, functional status, aging, rehabilitation, frail elderly
INTRODUCTION

Sarcopenia and depressive mood are common geriatric syndromes that frequently co-occur and have a pronounced effect on geriatric health, especially in rehabilitative settings. Sarcopenia, a progressive skeletal muscle disorder characterized by reduced muscle function and muscle mass \(^1\), affects approximately 50% of patients undergoing rehabilitation \(^2, 3\). In this setting, sarcopenia significantly impedes functional recovery \(^2, 4\). Similarly, a depressive mood adversely affects rehabilitation outcomes, compromising patient compliance among older adults undergoing rehabilitation \(^5\). Therefore, the concurrent presentation of these conditions poses a significant challenge for functional recovery.

While previous cross-sectional studies have reported an association between sarcopenia and depressive mood in older adults \(^6, 7\), few have examined the effect of sarcopenia on depressive mood during hospitalization. Sarcopenia is negatively associated with functional outcomes \(^2, 4, 8\) and disability \(^1\). Additionally, depressive mood is exacerbated by functional disability \(^9\). Therefore, sarcopenia may negatively affect depressive mood.

Despite the known relationship between sarcopenia and depressive mood, our understanding of the potential negative effects of sarcopenia on depressive mood during the recovery phase of geriatric rehabilitation remains limited. Existing research has mainly focused on cross-sectional analyses without considering temporal changes in these conditions \(^6, 7\). Therefore, longitudinal studies are urgently needed.

This prospective observational study aimed to fill this research gap by exploring the potential influence of sarcopenia on depressive mood in patients undergoing geriatric rehabilitation.

METHODS

1. Study design and participants

This prospective observational cohort study enrolled individuals aged $\geq65$ years who were admitted to a rehabilitation unit under the jurisdiction of the Japanese medical insurance scheme. In this scheme, patients with stroke, musculoskeletal diseases, or hospital-associated deconditioning are eligible for the post-acute phase \(^9, 10\). Patient care is provided by an interdisciplinary team comprising medical practitioners, nurses, physiotherapists, occupational therapists, and registered dietitians to reinstate patient activities of daily living (ADLs) that deteriorate during the acute phase. The attending physician and the therapist in charge sequentially modified the rehabilitation program for each patient according to the disease severity and symptoms. This study included 243 patients admitted between April 1, 2020, and July 31, 2021. We excluded patients who did not consent to participate, those who did not complete the 15-item Geriatric
Depression Scale (GDS-15)\(^1\), and those who were transferred due to deteriorating health conditions.

2. Ethical considerations

The Ethics Committee of XXX Hospital approved this study (No. 21-82), which was conducted in accordance with the tenets of the Declaration of Helsinki. We included the participants in the study after verbally informing them of the study objectives and obtaining their consent.

3. Patient characteristics

We collected data on the patients’ demographic, nutritional, and functional characteristics. Demographic details such as sex, age, and number of days between the onset of the primary disease and admission to the rehabilitation unit, along with the Charlson Comorbidity Index (CCI)\(^12\), were included. The CCI is a weighted index that incorporates 19 conditions associated with poor prognosis. The nutritional data included Malnutrition Universal Screening Tool (MUST) scores. Body mass index (BMI; kg/m\(^2\)) was calculated as the weight (kg) divided by the square of the height (m). The MUST score, which ranges from 0 to 6, includes components such as BMI, percentage of body weight loss, and the presence of acute illness affecting dietary intake\(^13\). We considered patients with MUST scores ≥2 to be at risk of malnutrition. Functional and cognitive assessments were conducted using the Functional Independence Measure (FIM), Food Intake Level Scale (FILS), and Mini-Mental State Examination (MMSE). Physical or occupational therapists administered the FIM, a measure of ADLs\(^14\). The FIM includes motor and cognitive domains, with scores ranging from 18 to 126. The FILS, a measure of swallowing function\(^15\), was evaluated by speech-language therapists and rates swallowing function from level 1 (only oral care; no swallowing training) to level 10 (no dietary restrictions; the patient consumes three oral meals daily). The MMSE\(^16\) is a measure of cognitive function whose scores range from 0 to 30 and is evaluated by occupational therapists.

4. Definition of sarcopenia

We used the Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment (AWGS2019) criteria\(^17\) to identify sarcopenia. According to these criteria, sarcopenia was diagnosed when low handgrip strength and reduced muscle mass were evident. The handgrip strength of the left and right hands was measured using a digital Jamar-type handheld dynamometer (G-4800; CHARDER Electronic, Taichung, Taiwan) within 3 days of admission. The participants were asked to exert maximum isometric effort on the dynamometer while seated with their elbows bent at 90°. Measurements were obtained twice, and the highest value was used in the analysis. Low handgrip strength was defined as <18 kg for women and <28 kg for men\(^17\). Skeletal muscle mass was evaluated by calculating the skeletal muscle mass index (SMI), which represents appendicular skeletal muscle mass (kg) derived from bioelectrical impedance analysis (BIA) divided by height in meters squared. BIA measurements were acquired with the
participants in the supine position within 3 days of admission, following rest, and before lunch. Reduced muscle mass was defined as SMI $<5.70$ kg/m$^2$ in women and $<7.00$ kg/m$^2$ in men$^{17}$. 

5. Outcomes

The primary outcome was the prevalence of depressive mood at discharge. The secondary outcome was the incidence of depressive mood in patients without depressive mood at admission. A registered dietitian obtained the GDS-15 scores at admission and discharge by interviewing the patients. The GDS-15 includes 15 items, each scored either 0 or 1, culminating in a total summed score ranging from 0 to 15$^{11}$. This study defined a depressive mood as a GDS-15 score of $\geq 6$, based on previous studies$^{6,18}$. 

6. Sample size calculation

A previous study suggested that sarcopenia can result in an approximately three-fold increase in the prevalence of depressive mood$^{19}$. However, data regarding the prevalence of depressive mood at discharge in patients diagnosed with sarcopenia are currently unavailable. Notably, depressive mood was observed in approximately 15% of the patients without sarcopenia$^{19}$. Hence, we assumed that 50% of the patients with sarcopenia would present with a depressive mood at discharge. An estimated sample size of 50 patients per group would be required to detect this difference, assuming a significance level ($\alpha$) of 0.01 and a power of 0.9. We performed the sample size calculations using R version 4.0.3 (R Project for Statistical Computing, Vienna, Austria).

7. Statistical analysis

The participants’ baseline characteristics, categorized based on the presence or absence of sarcopenia, are presented as means and standard deviations for continuous variables, median and interquartile ranges for ordinal variables, and counts and percentages for categorical variables. To compare the characteristics of the sarcopenia and non-sarcopenia groups, we employed the t-test for continuous variables, the Mann-Whitney U test for ordinal variables, and the chi-squared test for categorical variables. We used a multivariable logistic regression model to ascertain the effect of sarcopenia on depressive mood (GDS-15 $\geq 6$ points) at discharge. Additionally, as a sensitivity analysis, we investigated whether sarcopenia was associated with the incidence of depressive mood during hospitalization in patients without depressive mood at admission (GDS-15 score $<6$). We selected covariates based on directed acyclic graphs. The covariates in the multivariate model included age, sex, primary disease, CCI, days from onset to admission, MUST, FILS, FIM, MMSE, and GDS-15 scores at admission. We conducted statistical analyses using R version 4.0.3. Statistical significance was set at $p<0.05$.

RESULTS
During the observation period, 33 patients who failed to complete the GDS-15 questionnaire and six patients who required transfer due to deteriorating health conditions were excluded from the study. Consequently, the analysis included 204 patients (mean age: 78.8±7.6 y, 45.1% women).

**Table 1** summarizes the baseline patient characteristics. The patients in the sarcopenia group were significantly older (81.5±6.9 y vs. 75.0±7.0 y, p<0.001) and exhibited a significant reduction in functional status, as evidenced by lower total FIM and FILS scores, compared with those in the non-sarcopenia group (both p<0.001). Moreover, the sarcopenia group demonstrated significantly higher GDS-15 scores [7 (5–9) vs. 6 (3–9), p=0.003] and a greater prevalence of depressive mood (73.9% vs. 56.5%, p=0.014) than the non-sarcopenia group.

Of the 68 patients without depressive mood at admission, the sarcopenia group (n=31) showed a significantly higher incidence of depressive mood at discharge than the non-sarcopenia group (n=37) (41.9% vs. 16.2%, p=0.037) (Figure 1).

**Table 2** shows the results of the comparison of variables at the time of discharge. The sarcopenia group exhibited a higher GDS-15 score upon discharge than the non-sarcopenia group [8 (5–10) vs. 5 (2–7), p<0.001] and a higher prevalence of depressive mood at discharge (70.6% vs. 37.6%, p<0.001). In addition, the prevalence of depressive mood throughout hospitalization was significantly lower in the non-sarcopenia group (p=0.004).

**Figure 2** displays the findings of the multivariable logistic regression model examining the relationship between sarcopenia, its components, and depressive mood at discharge. Low muscle mass (odds ratio [OR], 2.682; 95% confidence interval [CI], 1.072–6.890; p=0.036) and low handgrip strength (OR, 3.352; 95% CI, 1.428–8.120; p<0.001), which are components of sarcopenia, were positively associated with depressive mood at discharge. Notably, sarcopenia significantly influenced depressive mood at discharge, with the highest OR (5.460; 95% CI, 2.344–13.415; p<0.001). The sensitivity analysis of patients without a depressive mood upon admission (n=68) revealed the association of sarcopenia with the incidence of depressive mood at discharge. Sarcopenia was positively associated with the incidence of depressive mood during hospitalization (OR, 5.599; 95% CI, 1.693–20.536; p<0.001).

**DISCUSSION**

In the present study, we investigated the influence of sarcopenia on depressive mood during geriatric rehabilitation and hospitalization. The results suggested that sarcopenia, along with its essential components of low muscle mass and low handgrip strength, exacerbated depressive mood at discharge. This result remained consistent even after adjusting for potential confounding factors using robust statistical methods. In addition, patients with sarcopenia had a higher incidence of depressive mood during hospitalization.
As mentioned above, sarcopenia and its key components, low muscle mass and handgrip strength, exacerbate depressive mood. Notably, sarcopenia had the most negative influence on the prevalence of depressive mood at discharge in this study. These findings suggest an intricate link between functional recovery and psychological state. Sarcopenia hinders the functional improvement of patients undergoing rehabilitation. In addition, a previous study suggested a causative relationship between physical disability and inactivity due to low muscle strength, muscle mass, and depression onset. Therefore, the targeted rehabilitation outcome may not be achieved because of inadequate functional recovery, preventing the improvement of depressive mood and worsening the patient's mental health status. The results of the present study are also consistent with the cross-sectional association of low muscle mass and low handgrip strength with depressive mood. Moreover, epidemiological studies have shown that sarcopenia and its components influence the incidence of depressive mood and anxiety, supporting our results.

Patients with sarcopenia in the present study had a higher incidence of depressive mood during hospitalization. A recent systematic review and meta-analysis indicated that exercise improves depressive mood. Notably, the population examined in our study comprised patients undergoing rehabilitation, including resistance training, to restore function. Our results suggested that sarcopenia interferes with the positive effects of exercise on mental health. Consequently, implementing early and periodic sarcopenia evaluation in geriatric patients undergoing rehabilitation is crucial. Furthermore, these findings underscore the potential necessity of exploring alternative personalized therapeutic strategies, such as pharmaceutical interventions and psychotherapy. Sarcopenia is considered a mobility phenotype associated with frailty. Attention should be paid to depression from a broader perspective in older patients requiring rehabilitation who present with frailty. Thus, comprehensive assessments, including both sarcopenia and frailty indicators, are important for better understanding and addressing the multifaceted needs of these patients.

The strength of this study is its prospective design to identify depressive mood during rehabilitation. Most previous studies exploring the relationship between sarcopenia and depressive mood in hospitalized patients have primarily utilized cross-sectional designs. In contrast, the longitudinal cohort design of our study enabled us to extend and enrich the current understanding of these associations.

This study has several limitations. First, the data were obtained from a single rehabilitation hospital, which may limit the generalizability of our findings. Second, although we accounted for numerous potential confounders, the influences of unmeasured factors associated with depressive mood, including familial relationships and the use of internal medication, cannot be eliminated and may have influenced our results. Third, the content of the rehabilitation program may have influenced the results. The rehabilitation program is a time-dependent covariate that is sequentially modified based on the disease severity and symptoms. Therefore, marginal structural models should be considered.
However, in this study, data on the detailed content of the rehabilitation programs were not collected and, thus, could not be considered in the multivariate analysis. Finally, the diagnosis of sarcopenia in this study did not meet all the criteria proposed by AWGS2019 [17]. These criteria include assessments of physical function, muscle strength, and muscle mass. However, as the study participants were older patients requiring rehabilitation, applying all criteria were difficult. Furthermore, the Global Leadership Initiative in Sarcopenia criteria consider physical function as part of the outcome [24]. Therefore, further discussion on optimal sarcopenia criteria is required.

In conclusion, the results of this study revealed that sarcopenia at admission negatively influenced depressive mood in a geriatric rehabilitation setting. These findings emphasize the need to integrate sarcopenia management into a holistic approach to improve the mental health of hospitalized older adults.