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Association Between Length of Stay in the Intensive Care Unit and Sarcopenia Among Hemiplegic Stroke Patients

Aeri Jang, MD[1], Chang Hoon Bae, MD[1], Soo Jeong Han, MD, PhD[1,2], Hasuk Bae, MD, PhD[1,2]

[1]Department of Rehabilitation Medicine, Ewha Womans University Mokdong Hospital, Seoul;
[2]Department of Rehabilitation Medicine, Ewha Womans University College of Medicine, Seoul, Korea

Objective To discuss the association between the length of stay at the intensive care unit (ICU) and sarcopenia among hemiplegic stroke patients.

Methods This study evaluated 66 hemiplegic stroke patients with history of ICU admission using handgrip strength and bioelectrical impedance analysis to obtain height-adjusted appendicular skeletal muscle mass. The diagnosis of sarcopenia was made according to the muscle mass based on the Asian Working Group for Sarcopenia. The patients were divided into sarcopenic and non-sarcopenic groups. The two groups were statistically analyzed, and the significant factors with differences were studied. A multivariate logistic regression analysis was performed to examine the association between length of stay in the ICU and sarcopenia, after adjusting for potential confounders.

Results Among 66 hemiplegic patients with an ICU admission history, 12 patients were diagnosed with sarcopenia. Sarcopenia patients showed lower scores on the Korean version of the Modified Barthel Index and the Korean version of the Mini-Mental State Examination. Additionally, patients with sarcopenia had a longer length of stay in the ICU, and univariate and multivariate analyses confirmed that the ICU length of stay was significantly related to sarcopenia (adjusted odds ratio=1.187; 95% confidence interval, 1.019–1.382; p=0.028).

Conclusion The length of stay in the ICU was significantly associated with sarcopenia in hemiplegic stroke patients.

Keywords Sarcopenia, Stroke, Intensive care units, Length of stay, Bioelectrical impedance analysis

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Corresponding author: Hasuk Bae
Department of Rehabilitation Medicine, Ewha Womans University Mokdong Hospital, 1071 Anyangcheon-ro, Yangcheon-gu, Seoul 07985, Korea. Tel: +82-2-2650-5035, Fax: +82-2-2650-5145, E-mail: acebhs@ewha.ac.kr
ORCID: Aeri Jang (https://orcid.org/0000-0003-2156-8255); Chang Hoon Bae (https://orcid.org/0000-0003-0677-4261); Soo Jeong Han (https://orcid.org/0000-0002-5685-0384); Hasuk Bae (https://orcid.org/0000-0003-0508-3696).

INTRODUCTION

Sarcopenia refers to the loss of skeletal muscle mass (SMM) and it is known to be affected by various factors such as age, sex, disuse, nutritional status, comorbidities, inflammation, and insulin resistance [1-3]. The loss of muscle mass causes major changes in muscle strength and function [4]; thus, sarcopenia is known to be a risk factor for mobility impairment, disability, loss of independence, hospitalization, and death [5].

Post-stroke hemiplegic patients experience various complications such as disability, muscle wasting, dysphagia, and cognitive impairment. Sarcopenia is a common secondary complication in hemiplegic patients, and multiple factors such as age and poor nutrition are potential risk factors of the secondary sarcopenia [6]. The mechanism of muscle change after a stroke is not clearly understood, but multiple factors, such as disuse, denervation, inflammation, remodeling, and spasticity, are known to be involved in the mechanism [7].

It is previously known that admission to the intensive care unit (ICU) among hemiplegic patients increases the mortality rate and affects the functional outcome afterward [8]. Immobility is one of the main causes of skeletal muscle wasting [9]; thus, it can be expected that the severity of SMM loss is related to the immobilization period. In this study, we hypothesize that the ICU length of stay is associated with sarcopenia in hemiplegic stroke patients.

MATERIALS AND METHODS

Subjects

The study evaluated post-stroke hemiplegic patients with a history of ICU admission between April 2017 and April 2020 at Ewha Womans University Mokdong Hospital. The hemiplegic patients, who had been referred to the Department of Rehabilitation Medicine, were retrospectively evaluated based on the initial evaluation data within a week after the transfer. The eligible patients were divided into two groups, sarcopenic and non-sarcopenic, and multiple factors, including the length of stay in the ICU, were analyzed to evaluate the relationship with sarcopenia in hemiplegic stroke patients. Then, the effect of sarcopenia on the patients' functional outcome level, whether the patient was able to participate in ambulatory activities, was studied.

The inclusion criteria were: (1) the first stroke patients; (2) above or equal to 60 years of age; (3) unilateral brain lesion confirmed by radiologic evidence; (4) patients diagnosed with post-stroke unilateral hemiplegia; (5) the Korean version of the Mini-Mental State Examination (MMSE-K) score higher than or equal to 10; and (6) a history of ICU admission before the transfer to the Department of Rehabilitation Medicine. The exclusion criteria were as follows: (1) history of a previous stroke; (2) bilateral brain lesions; (3) patients with previously diagnosed musculoskeletal disease causing weakness or muscle atrophy or both; and (4) presence of edematous lesions in the extremities. Patients with impaired cognition (MMSE-K <10) were excluded from the study because the handgrip strength test in severely demented patients might not be accurate due to poor cooperation.

The study was retrospectively carried out after the protocol approval from the Institutional Review Board of Ewha Womans University Mokdong Hospital (IRB No. 2020-04-026-001).

Methods

Data collection

A total of 66 post-stroke hemiplegic patients (35 males, 31 females) were included in the study. The patients' age, sex, stroke type (hemorrhagic or ischemic), hemiplegic side, Glasgow Coma Scale (GCS) score at the time of admission, height (cm), body weight (kg), appendicular skeletal muscle mass (ASMM, kg), the Korean version of the Modified Barthel Index (K-MBI), ICU length of stay and hospital stay (day), MMSE-K, handgrip strength of the non-hemiplegic side (kg), and height-adjusted ASMM (kg/m^2) were analyzed. Height and weight were used to obtain body mass index (BMI; calculated as weight in kilograms divided by height in meters squared). In addition, the ambulatory status at the time of transfer to the Department of Rehabilitation Medicine was used for functional evaluation; the ambulatory group included all the patients who were able to walk independently or ambulate with assistance.

Assessment of sarcopenia

The European Working Group on Sarcopenia in Older People (EWGSOP) is one of the widely used guidelines for the clinical definition of sarcopenia. However, the

EWGSOP definition has a cutoff value based on the European population [3], which might not accurately represent ethnic differences. Therefore, we used the guidelines developed by the Asian Working Group for Sarcopenia (AWGS), which includes differences arising from Asian anthropometric, cultural, and lifestyle-related issues, to diagnose sarcopenia [3,10].

According to the newly updated AWGS guideline in 2019 [10], the diagnosis of sarcopenia is made when the following two conditions are present: (1) confirmed low muscle mass and (2) low muscle strength or low physical performance. We retrospectively reviewed the muscle strength at the time of the transfer and grouped the patients with low muscle strength a “possible sarcopenia” group. Bioelectrical impedance analysis (BIA) tests were carried out to confirm the diagnosis, and height-adjusted ASMM was used to measure muscle quantity.

Muscle strength was tested using the Hydraulic Hand Dynamometer (model SH5001; SAEHAN Corp., Changwon, Korea). In order to increase the accuracy of the test results, the patients with minimal cooperation (MMSE-K <10) were excluded. Both hemiplegic and non-hemiplegic side handgrip strength was measured in a sitting position with shoulder adduction and elbow flexion (90°), based on the recommendations of the American Society of Hand Therapists [11]. The measurements were made by a skilled occupational therapist.

According to the AWGS guideline, “possible sarcopenia” can be diagnosed in patients with a handgrip strength of non-hemiplegic side less than 28 kg in males and 18 kg in females [10]. Among the 66 patients included in the study, 38 patients were “possible sarcopenia” patients (18 males, 20 females).

ASMM was obtained by a trained medical doctor using a BIA system (Inbody S10; InBody Corp., Seoul, Korea). The patients’ body composition was evaluated in a supine position using the BIA system. The system was capable of analyzing segmental soft lean mass (SLM) in the upper and lower limbs of each side. SLM (kg) is the summation of body water, protein, and non-osseous minerals (fat and minerals in bones are excluded); thus, SLM is mostly composed of muscle mass, and it can be interpreted to represent the SMM within extremities. The ASMM can be calculated by summating the SLM from the bilateral upper and lower extremities, and adjustment was made based on the patient’s height [12,13].

The AWGS cutoff point for height-adjusted ASMM was <7.0 kg/m^2 for males and <5.7 kg/m^2 for females, and those below the cutoff points were diagnosed with confirmed sarcopenia. Among the 38 “possible sarcopenia” patients, 12 patients (5 males, 7 females) were diagnosed with sarcopenia.

Statistical analysis

Continuous variables with normal distribution are presented as mean±standard deviation; those without normal distribution are presented with median and interquartile range (IQR; 25–75 percentile). Categorical variables are shown as numbers and percentages. In order to analyze the mean difference, continuous variables were compared using Student t-test and Mann-Whitney U-test. Categorical variables were analyzed using the chi-square test for intergroup differences.

The major risk factors of sarcopenia were analyzed using logistic regression. In order to control for confounding effects among the variables, socio-demographic variables such as age, sex, and statistically significant variables obtained from univariate analysis were analyzed using multivariate logistic regression; the factors did not show multicollinearity. Furthermore, the functional ambulatory status of the sarcopenia and non-sarcopenia groups was evaluated. In this study, a p-value of less than 0.05 was considered statistically significant, and statistical analyses were performed using SPSS Statistics for Windows (version 26; IBM Corp., Armonk, NY, USA).

RESULTS

Among the patient pool, 66 patients (35 males, 31 females) were selected via inclusion and exclusion criteria. Among these 66 patients, there were 22 hemorrhagic patients and 44 ischemic patients; 19 patients had right hemiplegia, and 47 patients had left hemiplegia.

According to the diagnostic criteria defined by the AWGS guidelines, the patients with low muscle strength and low muscle mass were selected; with further study, patients confirmed to have sarcopenia were 12 (18.18%), and 54 (81.82%) had non-sarcopenia.

Factors associated with sarcopenia

Table 1 shows a summary of the general characteristics between the sarcopenia and non-sarcopenia groups.

Table 1. Comparison of characteristics between sarcopenic and non-sarcopenic groups among stroke patients (n=66)

Variable	Sarcopenia	Non-sarcopenia	p-value
Number of patients	12 (18.18)	54 (81.82)	
Age (yr)	76.50±7.66	73.02±8.15	0.181
Sex			0.383
Male	5 (14.29)	30 (85.71)	
Female	7 (22.58)	24 (77.42)	
Stroke type			0.086
Hemorrhagic	7 (31.82)	15 (68.18)	
Ischemic	5 (11.36)	39 (88.64)	
Hemiplegic side			0.305
Right	2 (10.53)	17 (89.47)	
Left	10 (21.28)	37 (78.72)	
Glasgow Coma Scale	13.50 (12.50–14.50)	14.00 (13.00–15.00)	0.261
Height (cm)	159.92±9.75	161.06±7.51	0.652
Body weight (kg)	52.48±7.18	60.00±9.69	0.014*
BMI (kg/m^2)	20.57±2.68	23.11±3.29	0.015*
K-MBI	34.58±17.47	50.22±22.65	0.028*
ICU length of stay (day)	9.50 (6.00–25.50)	6.00 (5.00–8.00)	0.019*
Hospital stay (day)	50.50 (46.50–61.00)	33.50 (26.00–45.00)	<0.001*
MMSE-K	15.50 (14.00–18.00)	22.50 (18.00–26.00)	0.002*
Handgrip strength (kg)	13.18±6.40	22.09±9.26	0.002*
ASMM (kg/m^2)			
Height-adjusted ASMM	5.81±0.64	7.79±1.47	<0.001*
ASMM of non-hemiplegic limbs	7.49±1.74	10.10±2.40	0.001*
ASMM of hemiplegic limbs	7.56±1.67	10.00±2.25	0.001*

Values are presented as number (%) or mean±standard deviation or median (interquartile range).
BMI, body mass index; K-MBI, the Korean version of the Modified Barthel Index; ICU, intensive care unit; MMSE-K, the Korean version of the Mini-Mental State Examination; ASMM, appendicular skeletal muscle mass.
*p<0.05.

The average age for the sarcopenia group was 76.50±7.66 years, and non-sarcopenia groups were 73.02±8.15 years (p=0.181). The average body weight (52.48±7.18 vs. 60.00±9.69 kg; p=0.014) and average BMI (20.57±2.68 vs. 23.11±3.29 kg/m^2; p=0.015) were shown to be smaller in the sarcopenia group, and the differences were statistically significant. The mean score of K-MBI (34.58±17.47 vs. 50.22±22.65; p=0.028) and the median value of MMSE-K (15.50 [IQR, 14.00–18.00] vs. 22.50 [IQR, 18.00–26.00]; p=0.002) was shown to be smaller in the sarcopenia group as well; their differences were also statistically significant, which implies that the non-sarcopenic group had better ADL and cognition levels. The median length of stay in the ICU (9.50 [IQR 6.00–25.50] vs. 6.00 [IQR 5.00–8.00] days; p=0.019) and the hospital stay (50.50 [IQR 46.50–61.00] vs. 33.50 [IQR 26.00–45.00] days; p≤0.001) was greater in the sarcopenia group. Therefore, body weight, BMI, K-MBI, MMSE-K, ICU length of stay, and hospital stay showed significant differences between the two groups, whereas age, sex, height, type of stroke, GCS, and hemiplegic side were insignificant.

ICU length of stay and sarcopenia among hemiplegic stroke patients

Logistic regression analysis was performed to evaluate the major risk factors for sarcopenia among hemiplegic stroke patients. Multivariate logistic regression analyses were conducted between socio-demographic variables and the significant variables, except those variables that were closely related to the diagnosis of sarcopenia, ob-

Table 2. Unadjusted and adjusted ORs (multivariate logistic regression) for sarcopenia among hemiplegic stroke patients

Variable	Unadjusted model			Adjusted model			VIF
	OR	95% CI	p-value	AOR	95% CI	p-value	
ICU length of stay	1.159	1.048–1.281	0.004*	1.187	1.019–1.382	0.028*	1.326
Age	1.057	0.974–1.147	0.183	1.074	0.949–1.214	0.258	1.426
Sex	0.571	0.161–2.029	0.387	0.707	0.129–3.867	0.690	1.209
K-MBI	0.966	0.936–0.998	0.035*	0.984	0.946–1.024	0.436	1.191
MMSE-K	0.805	0.690–0.938	0.006*	0.824	0.666–1.021	0.077	1.212

OR, odds ratio; AOR, adjusted odds ratio; CI, confidence interval; VIF, variance inflation factor; ICU, intensive care unit; K-MBI, the Korean version of the Modified Barthel Index; MMSE-K, the Korean version of the Mini-Mental State Examination.
*p<0.05.

tained from the univariate analysis in order to control for confounding effects. The selected variables were age, sex, K-MBI, MMSE-K, ICU length of stay, and it was shown that there was no multicollinearity (variance inflation factor [VIF] <1.5).

After accounting for age, sex, K-MBI, and MMSE-K as independent variables, the ICU length of stay was significantly related to sarcopenia. In the adjusted model, the adjusted odds ratio of ICU length of stay was 1.187, with a p-value of 0.028 in the 95% confidence interval (Table 2).

Functional outcomes of sarcopenic and non-sarcopenic patients

Each patient's ambulatory status by the time of transfer to the Department of Rehabilitation Medicine was studied. The patient's condition was evaluated by medical doctors and physical therapists during rehabilitation therapy. The results showed that the sarcopenic group had a higher percentage of non-ambulatory status at transfer (Fig. 1).

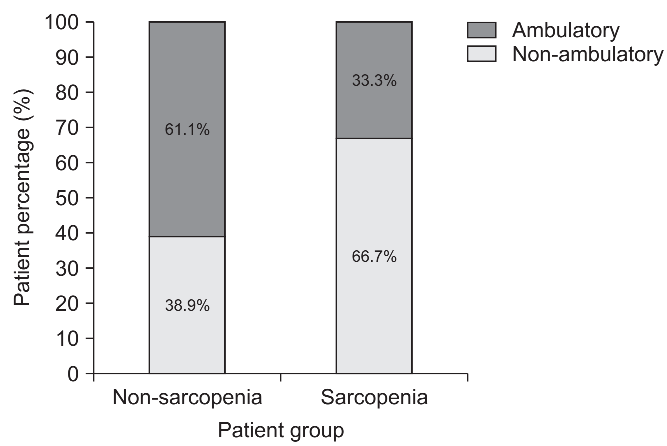

Fig. 1. Ambulatory status of sarcopenic and non-sarcopenic patient groups at the transfer.

DISCUSSION

We aimed to investigate the relationship between the ICU length of stay and sarcopenia among hemiplegic stroke patients in this study. The study showed that body weight, BMI, K-MBI, MMSE-K, ICU length of stay, and hospital stay were significantly different between the sarcopenic and non-sarcopenic patient groups; age, sex, height, stroke type, GCS, and hemiplegic side did not. In order to evaluate the relationship between ICU length of stay and sarcopenia, we conducted multivariate logistic regression analysis by controlling other variables. The analysis proved that the ICU length of stay was significantly related to sarcopenia among hemiplegic stroke patients.

A stroke damages the central nervous system's motor neurons, causing paralysis in the upper and lower extremities. Its consequences are prominent weakness and decreased physical activities [14-16]. Decreased physical activity and immobility lead to muscle weakness and atrophy [17,18]. Therefore, such consequences are generally considered to be more extreme in immobilized patient admission in the ICU [19].

There have been a few previous studies on ICU length of stay and sarcopenia. Akahoshi et al. [20] studied computed tomography (CT) imaging in 84 high-energy blunt trauma patients to evaluate the amount of skeletal muscle, proving that sarcopenia is a significant risk factor for prolonged ICU stay. The mass of skeletal muscle was estimated using skeletal muscle volume at the L3 level obtained from CT and body surface area. The study implies that there is a certain relationship between sarcopenia and prolonged ICU stay; our results showed similar findings.

Our study also found that the ASMM on the non-hemiplegic and hemiplegic sides was lower in the sarcopenia group (p>0.001) (Table 1). This finding suggests that the muscle loss observed in the sarcopenia group was not solely due to the loss of muscle in the affected hemiplegic side. This result corresponds to recent findings by Vahlberg et al. [21]; the study reported that BMI showed low total muscle mass and body fat after stroke. In addition, Chang et al. [22] reported that SMM was significantly lower in both paralytic and non-paralytic limbs in most patients with disabilities. Therefore, muscle wasting was not only caused by brain lesion-induced paralysis, but also by generalized skeletal muscle wasting in immobilized status; in other words, immobility accelerated muscle wasting in general, increasing the risk of sarcopenia.

Post-intensive care syndrome refers to the physical, cognitive, or mental impairment that occurs during ICU admission or at the point of discharge from ICU or hospital [23]. Among the numerous physical impairments, intensive care unit-acquired weakness (ICU-AW) is the acute symmetrical limb muscle weakness after admission to the ICU [9]. The pathophysiological mechanism of ICU-AW is considered to be multifactorial; a previous study suggested that microvascular ischemia, catabolism, and immobility cause skeletal muscle wasting [24]. Our study results suggest that there is a close relationship between the ICU length of stay and sarcopenia.

Numerous studies have suggested that physical rehabilitation during ICU admission helped improve the patient's general condition, such as muscle strength; Tipping et al. [24] reported that physical rehabilitation during ICU admission improved the patients' mobility status and muscle strength. In addition, passive stretching in the ICU can prevent muscle atrophy among patients [25]. The use of electrical muscle stimulation also proved to be efficient in preventing muscle atrophy among patients [26]. Thus, the application of physical rehabilitation in patients with prolonged ICU stay can be a preventive management strategy for lowering the risk of sarcopenia by preserving skeletal muscle mass.

When we compared the functional outcomes of the study groups with respect to the time of transfer, the non-sarcopenic group showed a higher percentage of ambulation status (Fig. 1). Similar results were reported by Hwang et al. [27], as they reported that sarcopenic patients among 230 trauma patients older than 55 years, showed poorer functional outcomes than in the non-sarcopenic group, based on the Glasgow Outcome Scale.

Our study has several limitations. One of the main limitations is that we could not establish a clear cause-and-effect relationship between ICU length of stay and sarcopenia among hemiplegic stroke patients. As described previously, our results indicated that there was a close association between them, but our cross-sectional study design could not distinguish the timely order of incidents. Therefore, we could not explain whether the patients with sarcopenia had a longer ICU length of stay or the prolonged ICU length of stay caused sarcopenia. Future studies should consider using different study designs, such as longitudinal studies, to clarify the order of incidents.

Another limitation is that we could not objectively measure physical function or physical activity of the patient at the time of the study. As mentioned above, sarcopenia can be diagnosed with low ASMM and low physical performance. Several physical performance tests can be easily performed in clinical settings, e.g., 6-m walk test, short physical performance battery, or the five times sit-to-stand test. However, many stroke patients have physical disabilities due to paralysis, balance impairment, disuse, and they often require human assistance or assistive devices for ambulation. Because of the physical limitations among stroke patients, we could not use the physical performance tests described above; instead, we studied the patients' ambulatory status at the time of transfer. Due to this limitation, we used diagnostic criteria of low ASMM and low muscle strength, excluding the physical performance of the patients. Therefore, our study might have missed sarcopenia patients with low ASMM and low physical performance. The adaptation of other evaluating tools may be considered. In 2020, Jung et al. [28] evaluated the effectiveness of ultrasound in measuring muscle thickness in the lower extremities along with other physical performance testing tools; it may be advantageous in the diagnosis and follow-up studies of sarcopenic patients.

There were several other limitations. First, we had a small number of sarcopenic patients. Second, the BIA analysis did not correctly reflect the patient's nutritional information. Proper nutritional support and routine nutrition evaluation is a major part of muscle loss prevention and the promotion of functional recovery [29,30]. Our patient pool was expected to have a good nutritional status because each in-hospital patient has undergone nutrition assessment during hospitalization. However, we could not match the patient's nutrition status by the time of the BIA evaluation, as it might have been a critical factor in the BIA evaluation results. Thus, future studies should account for the patients' nutritional status as another independent variable along with BIA evaluation.

In conclusion, ICU length of stay was significantly associated with sarcopenia in hemiplegic stroke patients. Future studies should focus on determining the cause-effect relationship and underlying mechanisms of sarcopenia. In addition, the evaluation of sarcopenia during ICU admission and the application of early rehabilitation might be beneficial in hemiplegic stroke patients.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTION

Conceptualization: Jang AR, Bae HS. Methodology: Jang AR, Han SJ, Bae HS. Formal analysis: Jang AR. Funding acquisition: Jang AR, Bae HS. Project administration: Jang AR, Han SJ, Bae HS. Visualization: Jang AR, Bae CH. Writing – original draft: Jang AR, Bae CH. Writing – review and editing: Jang AR, Bae CH, Han SJ, Bae HS. Approval of final manuscript: all authors.

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