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Relationship between locomotive syndrome and sarcopenia in patients with cancer: a prospective cohort study

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Abstract

Background

Locomotive syndrome (LS) and sarcopenia are both associated with impaired mobility; however, their relationship in patients with cancer remains unclear. This study aimed to clarify the relationship between severe LS and sarcopenia and its individual components in patients with cancer.

Methods

This prospective cohort study included patients hospitalized for cancer treatment who were prescribed rehabilitation at two university hospitals. LS and sarcopenia were assessed at baseline and at the six-month follow-up. LS stage 3 was defined as severe LS. Sarcopenia was diagnosed according to the Asian Working Group for Sarcopenia criteria based on gait speed, grip strength, and skeletal muscle mass index. The association between severe LS and sarcopenia was analyzed using Fisher's exact test. Gait speed, grip strength, and skeletal muscle mass index were compared between patients with and without severe LS using Welch's t-test.

Results

A total of 114 patients were included in the analysis (mean age, 68.1 ± 12.6 years; 64 men and 50 women). At baseline, 26 patients had severe LS and 11 had sarcopenia. Severe LS was not significantly associated with sarcopenia (4/26 [15.4%] vs. 7/88 [8.0%], $p = 0.27$). Patients with severe LS had lower gait speed (80.5 ± 20.1 vs. 103.8 ± 18.8 cm/s, $p < 0.01$) and grip strength (22.7 ± 8.4 vs. 26.8 ± 7.4 kg, $p = 0.03$), whereas skeletal muscle mass index did not differ significantly between the groups (7.6 ± 1.5 vs. 7.4 ± 1.3 kg/m², $p = 0.60$). At six months, 31 patients had severe LS and 11 had sarcopenia. The association between severe LS and sarcopenia remained non-significant (6/31 [19.4%] vs. 5/83 [6.0%], $p = 0.07$). Patients with severe LS continued to have lower gait speed (77.5 ± 21.6 vs. 105.4 ± 20.0 cm/s, $p < 0.01$) and grip strength (21.7 ± 7.3 vs. 27.9 ± 6.8 kg, $p < 0.01$), while skeletal muscle mass index remained comparable between the groups (7.0 ± 1.4 vs. 7.5 ± 1.2 kg/m², $p = 0.08$).

Conclusions

Severe LS was not significantly associated with sarcopenia at baseline or at the six-month follow-up in patients with cancer. However, patients with severe LS consistently exhibited lower gait speed and grip strength without a significant difference in skeletal muscle mass index. These findings suggest that severe LS and sarcopenia represent related but distinct aspects of physical impairment in patients with cancer, and that functional impairment associated with severe LS may occur without a concomitant reduction in skeletal muscle mass.

Introduction

Cancer has become increasingly prevalent in aging populations, and advances in cancer treatment have prolonged survival for many patients. Consequently, maintaining mobility, activities of daily living (ADL), and quality of life (QOL) has become increasingly important in cancer care. Mobility impairment in patients with cancer can result not only from the cancer itself but also from cancer treatment and coexisting musculoskeletal disorders.

Locomotive syndrome (LS), a concept proposed by the Japanese Orthopaedic Association, is characterized by impaired mobility due to dysfunction of the locomotive organs [1]. Previous studies have demonstrated a high prevalence of LS among patients with cancer [2]. The concept of “Cancer Locomo” encompasses mobility impairment associated with cancer and can be classified into three categories: locomotive dysfunction directly caused by cancer, locomotive dysfunction related to cancer treatment, and locomotive dysfunction coexisting with cancer [3]. Thus, LS may provide a framework for identifying mobility impairment arising from the diverse musculoskeletal problems encountered during cancer treatment.

Sarcopenia is characterized by loss of skeletal muscle mass accompanied by reduced muscle strength and/or physical performance and represents another important cause of functional impairment in patients with cancer. Sarcopenia has been associated with adverse clinical outcomes in patients with cancer and may be influenced by multiple factors related to cancer and its treatment [4–6]. Although both LS and sarcopenia are associated with impaired physical function, they represent different concepts and are assessed using different criteria. Previous research has examined the relationship among LS, sarcopenia, and frailty in the general older population [7]; however, the relationship between LS and sarcopenia in patients with cancer remains unclear.

Therefore, this prospective cohort study aimed to clarify the relationship between severe LS and sarcopenia in patients with cancer at baseline and at the six-month follow-up. We also aimed to clarify the differences in the individual components of sarcopenia, including gait speed, grip strength, and skeletal muscle mass index, between patients with and without severe LS.

Methods

Study Design and Setting

This prospective cohort study was conducted at two university-affiliated hospitals in Japan between April 2020 and March 2021. Participants were prospectively enrolled during hospitalization and underwent assessments at baseline and at the six-month follow-up. The study protocol was approved by the institutional review boards of both participating institutions, and written informed consent was obtained from all participants before enrollment.

Participants

Consecutive adult patients who were hospitalized for cancer treatment and prescribed rehabilitation by their attending physicians during the study period were eligible for inclusion. The inclusion criteria were a diagnosis of a malignant tumor, hospitalization for cancer treatment, and referral for rehabilitation during hospitalization. Patients with missing LS and/or sarcopenia status at baseline were excluded. For the longitudinal analysis, participants with both LS and sarcopenia status available at the six-month follow-up were included.

Assessment of Locomotive Syndrome and Sarcopenia

LS was assessed using the Locomotive Syndrome Risk Test proposed by the Japanese Orthopaedic Association, consisting of the Stand-Up Test, Two-Step Test, and 25-question Geriatric Locomotive Function Scale (GLFS-25) [8]. Based on the results of these tests, participants were classified into LS stages 0, 1, 2, or 3, with LS stage 3 defined as severe LS. LS was assessed at baseline and at the six-month follow-up.

Sarcopenia was diagnosed according to the Asian Working Group for Sarcopenia (AWGS) criteria [9]. Muscle strength was assessed by handgrip strength, physical performance by habitual gait speed, and skeletal muscle mass by bioelectrical impedance analysis using an InBody body composition analyzer (InBody Japan Inc., Tokyo, Japan). Skeletal muscle mass index (SMI) was expressed in kg/m².

Low muscle strength was defined as handgrip strength <26 kg in men and <18 kg in women, low physical performance as habitual gait speed <80 cm/s, and low skeletal muscle mass as an SMI <7.0 kg/m² in men and <5.7 kg/m² in women. Sarcopenia was defined as low skeletal muscle mass accompanied by either low muscle strength or low physical performance according to the AWGS criteria. Sarcopenia was assessed at baseline and at the six-month follow-up.

Outcomes

Baseline demographic and clinical characteristics, including age, sex, body mass index (BMI), and cancer type, were collected from medical records. Cancer type was classified according to the primary cancer site.

The primary outcome was the association between severe LS and sarcopenia at baseline and at the six-month follow-up. Secondary outcomes were differences in the individual components of sarcopenia, including gait speed, grip strength, and SMI, between participants with and without severe LS at each time point.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as number and percentage. The association between severe LS and sarcopenia at baseline and at the six-month follow-up was analyzed using Fisher's exact test because of the small number of participants with sarcopenia. Gait speed, grip strength, and SMI were compared between participants with and

without severe LS using Welch's t-test. All statistical tests were two-sided, and a p value <0.05 was considered statistically significant. Participants with missing data for individual variables were excluded only from the corresponding analysis. Multivariable analysis was not performed because of the small number of participants with sarcopenia. All statistical analyses were performed using JMP Pro 17 (SAS Institute Inc., Cary, NC, USA).

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by both participating institutions' review boards. The patients and/or their families were informed that data from the case would be collected, analyzed, and submitted for publication, and written consent for their participation was obtained.

Results

Participant Characteristics

A total of 294 participants were enrolled in the study. Of these, 33 were excluded because of missing baseline LS and/or sarcopenia status, leaving 261 participants with both LS and sarcopenia status available at baseline. Among these, 147 were not included in the six-month follow-up dataset: 45 were alive but could not complete the LS and/or sarcopenia assessment, 94 had no follow-up visit, and eight died within six months. Consequently, 114 participants had both LS and sarcopenia status available at the six-month follow-up and were included in the longitudinal analysis (Fig. 1).

Among the 114 participants included in the longitudinal analysis, the mean age was 68.1 ± 12.6 years, and 64 (56.1%) were men and 50 (43.9%) were women. The mean body mass index was 23.7 ± 4.3 kg/m². Breast cancer was the most common cancer type (20.2%), followed by prostate cancer (15.8%), gastric cancer (14.9%), and bladder cancer (12.3%). Baseline demographic characteristics are summarized in Table 1.

Distribution of LS and Sarcopenia

Among the 114 participants included in the longitudinal analysis, 26 (22.8%) had severe LS (stage 3) at baseline, whereas 88 (77.2%) had LS stages 0–2. At the six-month follow-up, 31 participants (27.2%) had severe LS and 83 (72.8%) had LS stages 0–2 (Fig. 2).

Sarcopenia was present in 11 participants (9.6%) at baseline and 11 (9.6%) at the six-month follow-up (Fig. 3).

Association Between Severe LS and Sarcopenia

At baseline, sarcopenia was present in 4 of 26 participants (15.4%) with severe LS and in 7 of 88 participants (8.0%) without severe LS. There was no significant association between severe LS and

sarcopenia (Fisher's exact test, p = 0.27) (Table 2).

At the six-month follow-up, sarcopenia was present in 6 of 31 participants (19.4%) with severe LS and in 5 of 83 participants (6.0%) without severe LS. The association between severe LS and sarcopenia was not statistically significant (Fisher's exact test, p = 0.07) (Table 3).

Comparison of the Individual Components of Sarcopenia

At baseline, participants with severe LS had a significantly lower gait speed than those without severe LS (80.5 ± 20.1 vs. 103.8 ± 18.8 cm/s, p < 0.01) and lower grip strength (22.7 ± 8.4 vs. 26.8 ± 7.4 kg, p = 0.03). SMI did not differ significantly between the groups (7.6 ± 1.5 vs. 7.4 ± 1.3 kg/m², p = 0.60) (Table 4).

At the six-month follow-up, participants with severe LS continued to have a significantly lower gait speed (77.5 ± 21.6 vs. 105.4 ± 20.0 cm/s, p < 0.01) and lower grip strength (21.7 ± 7.3 vs. 27.9 ± 6.8 kg, p < 0.01) than those without severe LS. SMI did not differ significantly between the groups (7.0 ± 1.4 vs. 7.5 ± 1.2 kg/m², p = 0.08) (Table 5).

Discussion

The present prospective cohort study clarified the relationship between severe LS and sarcopenia in patients with cancer who completed assessments at baseline and at the six-month follow-up. Severe LS was not significantly associated with sarcopenia at either time point. However, patients with severe LS had significantly lower gait speed and grip strength than those without severe LS at both baseline and the six-month follow-up, whereas SMI did not differ significantly between the groups. These findings suggest that severe LS and sarcopenia capture different aspects of physical impairment in patients with cancer and that severe LS may be characterized predominantly by impaired physical performance and muscle strength rather than reduced skeletal muscle mass.

LS and sarcopenia are both associated with impaired physical function, but their underlying concepts and diagnostic frameworks differ. LS encompasses mobility impairment caused by dysfunction of the locomotive organs [1], whereas sarcopenia is defined on the basis of reduced skeletal muscle mass in combination with reduced muscle strength and/or physical performance [9]. Cancer Locomo further encompasses mobility impairment arising from cancer itself, cancer treatment, and pre-existing or coexisting locomotive disorders [3]. Consequently, mobility impairment in patients with cancer may arise through mechanisms that are not necessarily accompanied by a reduction in skeletal muscle mass. The absence of a significant association between severe LS and sarcopenia in the present study supports the view that these conditions should not be considered interchangeable in patients with cancer.

An important finding of the present study was the consistent difference in the functional components of sarcopenia according to LS severity. Patients with severe LS had lower gait speed and grip strength at both baseline and six months, whereas no significant difference in SMI was observed at either time

point. Mobility impairment in patients with cancer is multifactorial and may be influenced by the cancer itself, treatment-related toxicity, disuse, neuropathy, systemic inflammation, and other factors [10, 11]. Therefore, impaired mobility may become apparent through reductions in physical performance and muscle strength even when skeletal muscle mass is relatively preserved. These findings also suggest that assessment of skeletal muscle mass alone may not adequately reflect the functional impairment experienced by patients with Cancer Locomo.

The prevalence of sarcopenia was relatively low in the present cohort, with 11 of 114 participants meeting the diagnostic criteria at baseline and 11 at the six-month follow-up. In contrast, severe LS was present in 26 participants at baseline and 31 at six months. Although the proportion of patients with sarcopenia was numerically higher among those with severe LS at both time points, the associations did not reach statistical significance. In particular, the difference at six months (19.4% vs. 6.0%) should be interpreted cautiously because of the small number of participants with sarcopenia. These findings indicate that severe mobility impairment does not necessarily correspond to a diagnosis of sarcopenia and highlight the importance of assessing both locomotive function and sarcopenia-related parameters when characterizing physical impairment in patients with cancer.

These findings may have implications for supportive cancer care. Mobility impairment can affect independence and the ability to continue cancer treatment, and rehabilitation interventions targeting mobility have an important role in the multidisciplinary management of patients with cancer [11–13]. Assessment of LS may provide information on functional limitations that is not captured by skeletal muscle mass alone. In clinical practice, combining assessment of locomotive function with measures of muscle strength, physical performance, and skeletal muscle mass may therefore provide a more comprehensive understanding of physical impairment in patients with cancer. Maintaining mobility is particularly important as the population of older adults living with and beyond cancer continues to increase [14–16].

This study has several limitations. First, the number of participants included in the longitudinal analysis was relatively small, particularly the number with sarcopenia, which limited statistical power and precluded multivariable analysis. Second, substantial attrition occurred during the six-month follow-up. Among participants with both LS and sarcopenia status available at baseline, some were unable to complete the LS and/or sarcopenia assessment despite being alive, some did not attend a follow-up visit, and others died within six months. Because the present analysis was restricted to participants with both LS and sarcopenia status available at six months, selection bias cannot be excluded. Third, the study included only hospitalized patients with cancer who were prescribed rehabilitation, which may limit the generalizability of the findings to the broader population of patients with cancer. Fourth, the study population included heterogeneous cancer types, and differences in cancer stage, treatment, and disease status may have affected physical function and muscle mass. Fifth, skeletal muscle mass was measured using bioelectrical impedance analysis, which may be influenced by hydration status and other clinical conditions. Finally, the six-month follow-up period may have been insufficient to capture longer-term changes in LS and sarcopenia. Larger prospective studies with longer follow-up are needed

to further clarify the relationship between LS, sarcopenia, and their individual components in patients with cancer.

In conclusion, severe LS was not significantly associated with sarcopenia at baseline or at the six-month follow-up in patients with cancer. Nevertheless, patients with severe LS consistently had lower gait speed and grip strength, whereas SMI did not differ significantly according to severe LS status. These findings suggest that severe LS and sarcopenia reflect distinct but overlapping aspects of physical impairment and that functional impairment associated with severe LS may be present even in the absence of reduced skeletal muscle mass. Comprehensive assessment of locomotive function, muscle strength, physical performance, and skeletal muscle mass may therefore be useful for characterizing physical impairment in patients with cancer.

Declarations

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy and confidentiality considerations but are available from the corresponding author on reasonable request, subject to applicable ethical and institutional requirements.

Funding

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Masahiro Hirahata, Jungo Imanishi and Hirotaka Kawano. The first draft of the manuscript was written by Masahiro Hirahata and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Teikyo University Ethical Review Board for Medical and Health Research Involving Human Subjects (No. 19-239).

Clinical Trial Registration

Not applicable. This study was a prospective observational cohort study without an assigned intervention.

Consent to Participate

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

Consent to Publish

Patients signed informed consent regarding publishing their data.

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Tables

Table 1
Baseline demographic characteristics of the study participants

Characteristic	Total (N = 114)
Age, years	68.1 ± 12.6
Sex, n (%)	
Male	64 (56.1)
Female	50 (43.9)
Body mass index, kg/m²	23.7 ± 4.3
Cancer type, n (%)	
Breast cancer	23 (20.2)
Prostate cancer	18 (15.8)
Gastric cancer	17 (14.9)
Bladder cancer	14 (12.3)
Renal cell carcinoma	10 (8.8)
Lung cancer	8 (7.0)
Hepatocellular carcinoma	6 (5.3)
Renal pelvis or ureter cancer	5 (4.4)
Esophageal cancer	3 (2.6)
Ovarian cancer	2 (1.8)
Colorectal cancer	2 (1.8)
Laryngeal cancer	1 (0.9)
Other gastrointestinal cancer	1 (0.9)
Cervical cancer	1 (0.9)
Pancreatic cancer	1 (0.9)
Bile duct cancer	1 (0.9)
Malignant lymphoma	1 (0.9)

Table 2
Association between severe LS and sarcopenia at baseline

Sarcopenia (+)	**Severe LS (+)**	**Severe LS (-)**
	4	**7**
Sarcopenia (-)	22	81
LS, locomotive syndrome		

Table 3
Association between severe LS and sarcopenia at the six-month follow-up

Sarcopenia (+)	**Severe LS (+)**	**Severe LS (-)**
	6	**5**
Sarcopenia (-)	25	78
LS, locomotive syndrome		

Table 4
Comparison of individual components comprising sarcopenia at baseline

	Severe LS (+)		**Severe LS (-)**		**p**
	Mean	**SD**	**Mean**	**SD**	
Gait speed (cm/s)	80.5	20.1	103.8	18.8	< 0.01
Grip strength (kg)	22.7	8.4	26.8	7.4	0.03
Skeletal muscle mass index (kg/m^2)	7.6	1.5	7.4	1.3	0.60
LS, locomotive syndrome, SD, standard deviation					

Table 5
Comparison of individual components comprising sarcopenia at the six-month follow-up

	Severe LS (+)		Severe LS (-)		p
	Mean	SD	Mean	SD	
Gait speed (cm/s)	77.5	21.6	105.4	20.0	< 0.01
Grip strength (kg)	21.7	7.3	27.9	6.8	< 0.01
Skeletal muscle mass index (kg/m^2)	7.0	1.4	7.5	1.2	0.08

LS, locomotive syndrome, SD, standard deviation

Figures

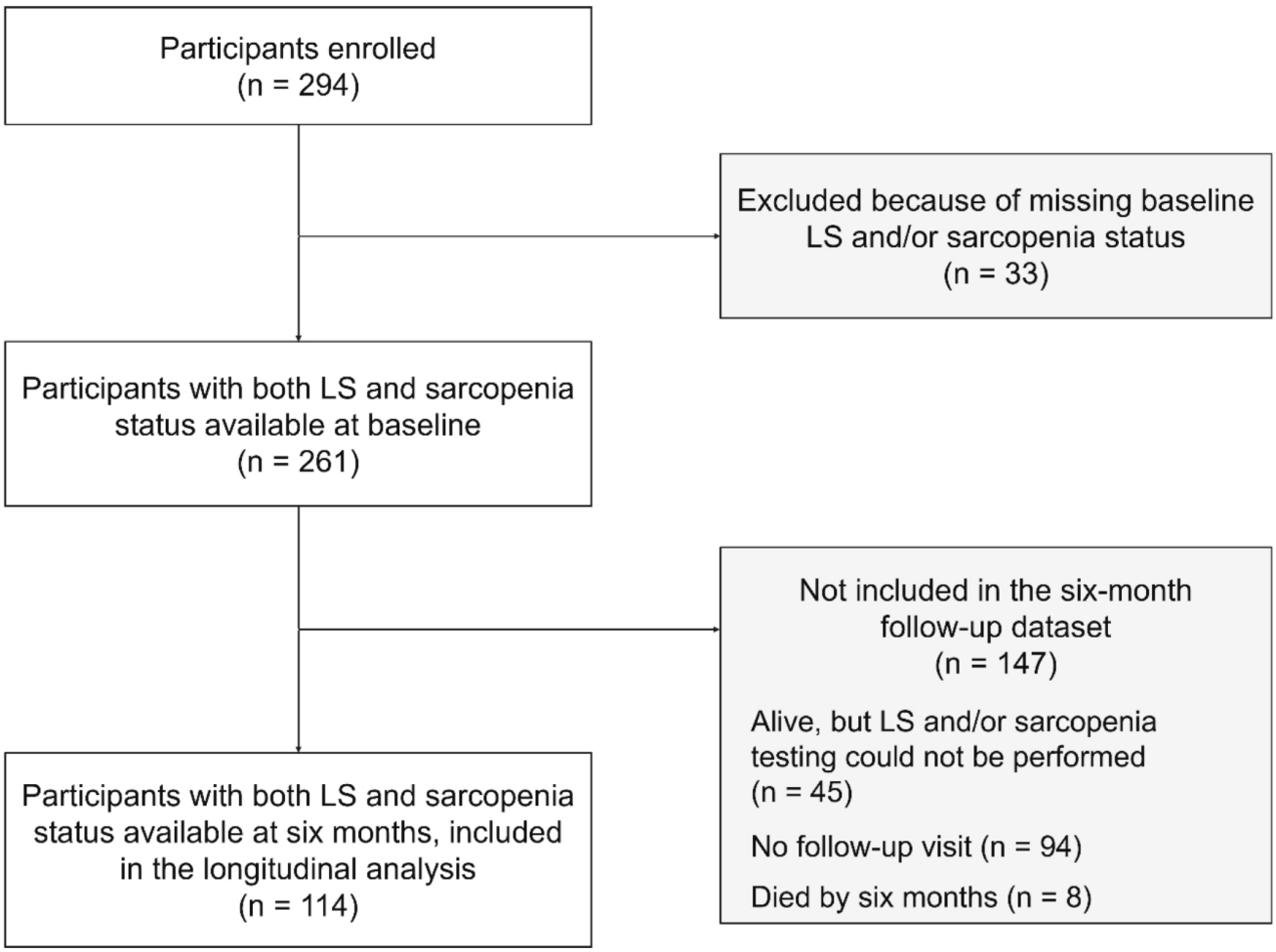


Figure 1

Participant flow from enrollment to the six-month follow-up. Of 294 enrolled participants, 261 had both locomotive syndrome (LS) and sarcopenia status available at baseline. Among these, 147 were not included in the six-month follow-up dataset because testing could not be performed despite survival (n = 45), no follow-up visit occurred (n = 94), or death occurred by six months (n = 8). The remaining 114 participants had both statuses available at six months and were included in the longitudinal analysis.

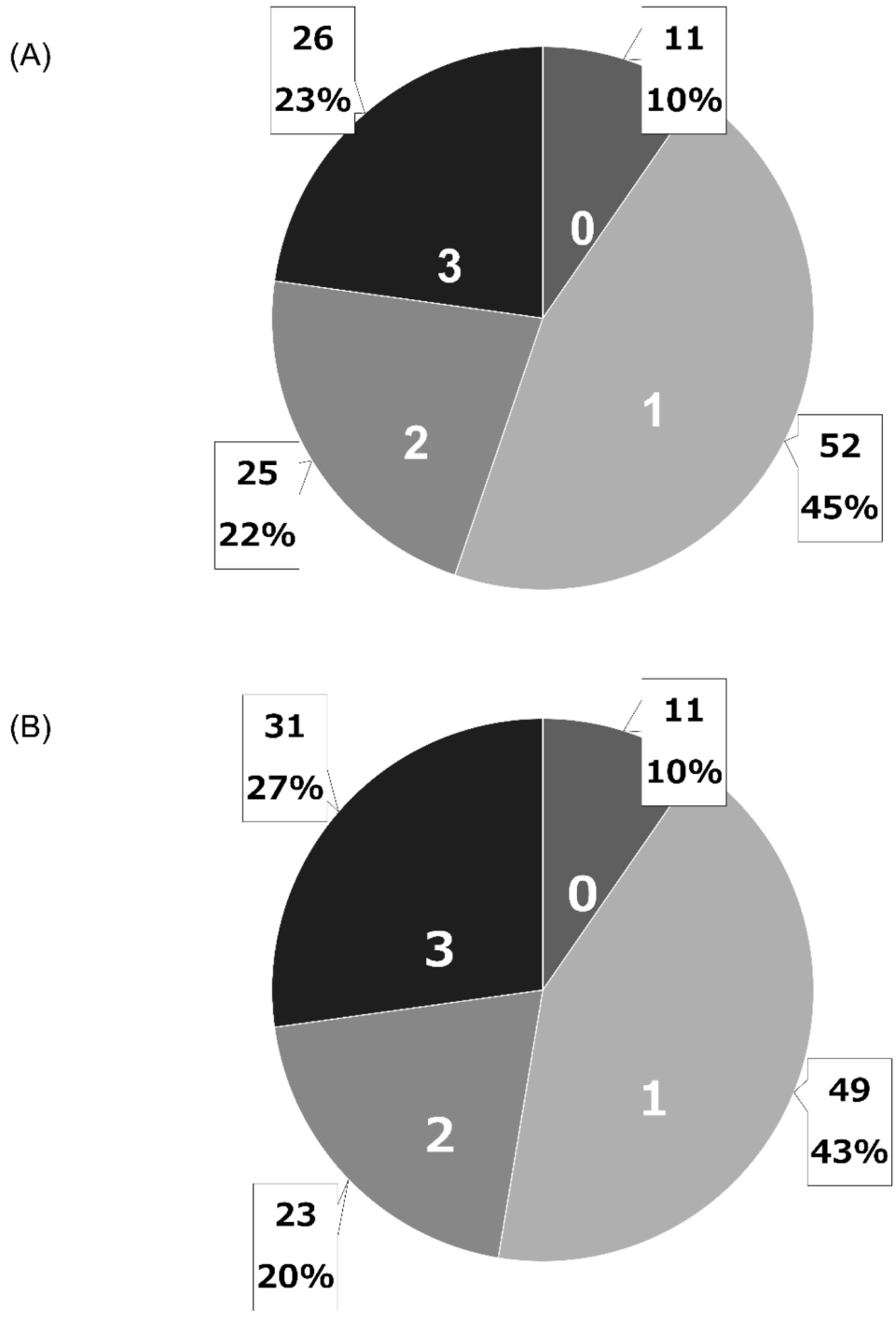


Figure 2

Distribution of locomotive syndrome stages at baseline (A) and at the six-month follow-up (B)

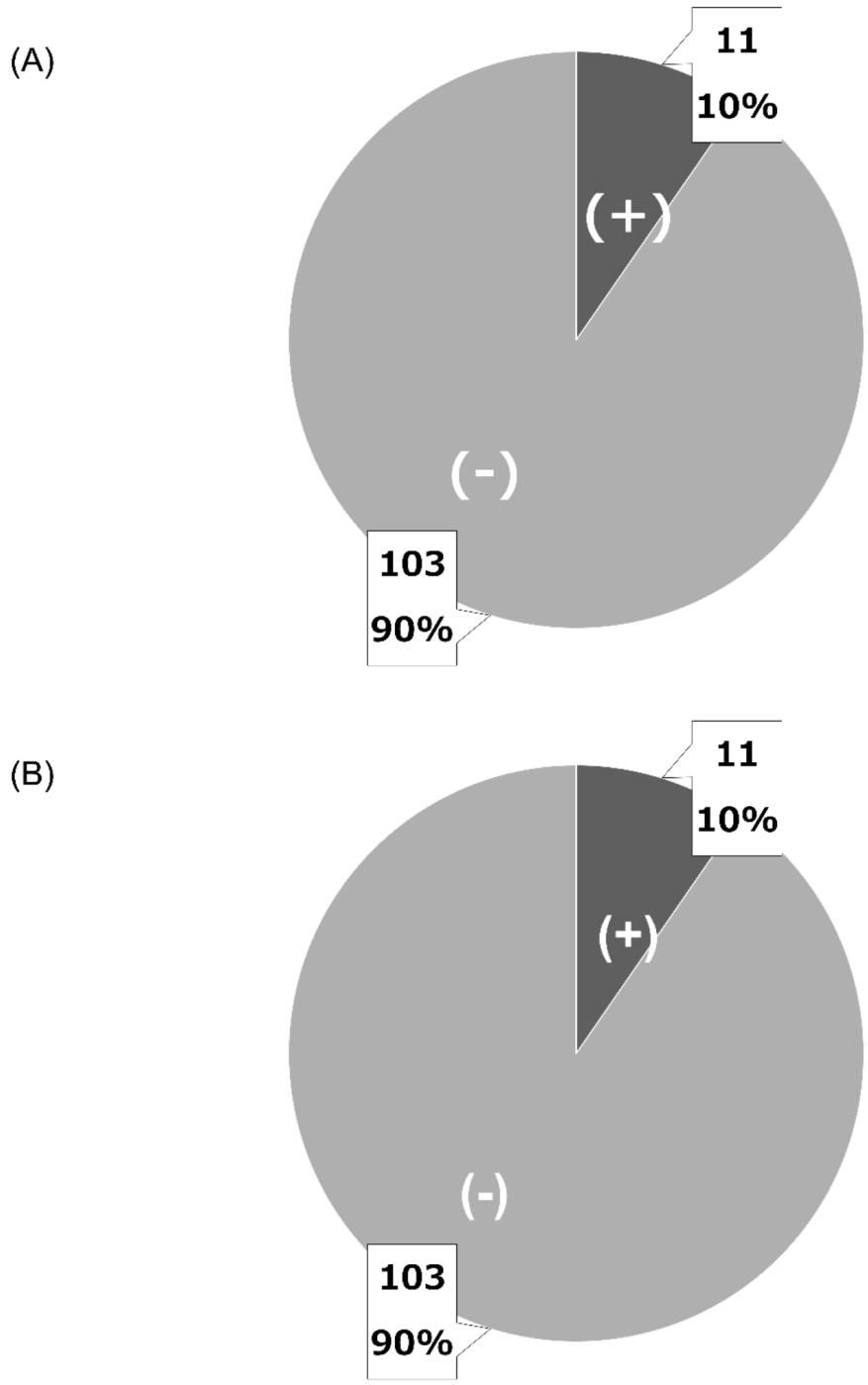


Figure 3

Sarcopenia at baseline (A) and at the six-month follow-up (B)