Association between fatigue and sarcopenia in middle-aged Korean cancer survivors: A cross-sectional study

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Research article

Keywords: Cancer survivors, sarcopenia, fatigue, quality of life

Posted Date: April 3rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-19208/v1

Abstract

Background Fatigue is a common and distressing symptom of cancer survivors, negatively affecting health-related quality of life. We evaluated the relation between fatigue and low relative skeletal muscle mass in middle-aged cancer survivors.

Methods Study participants were 693 Korean cancer survivors aged 40-64 years, who was recruited between September 2014-February 2017 from a cancer survivorship clinic of a university-affiliated hospital. We measured appendicular skeletal muscle mass of study participants with bioelectrical impedance analysis and collected selected variables through a self-administered questionnaire and medical record review. Fatigue was evaluated by a 9-item fatigue severity scale (FSS) which was validated in previous studies. Sarcopenia was defined by appendicular skeletal muscle index cut-off values stratified by sex (< 7.0kg/m2 for males, <5.7kg/m2 for females). Severe fatigue was defined as high FSS score (≥36). The association between sarcopenia and fatigue was assessed using multiple logistic regression analysis.

Results Overall, 18.6% of study participants were sarcopenic, 15.0% for males and 20.3% for females. Total scores of FSS (29.3 vs, 23.5, P = 0.034) and prevalence of severe fatigue (FSS≥36) (39.4% vs. 19.3%, P = 0.012) were higher in the sarcopenia group compared with the non-sarcopenia group, distinctively in male cancer survivors. Even after adjusting for selected covariates including cancer related factors and lifestyle factors, sarcopenia was significantly associated with severe fatigue in male survivors (Odd ratio [OR]: 5.36, 95% CI: 1.47, 19.54) and pre-menopausal females (OR: 2.33, 95% CI: 1.06, 5.13). However, the significant association was not found for post-menopausal females (OR: 2.28, 95% CI: 0.77, 6.79).

resConclusion Sarcopenia was positively associated with severe fatigue of middle-aged cancer survivors, independent of cancer related factors and lifestyle factors.

Background

Early diagnosis of cancer and the development of effective cancer treatment have significantly improved survival rate of cancer patients, incurring continuously growing numbers of cancer survivors globally. Middle-aged cancer survivors account for nearly 50% of the total cancer survivors [1, 2]. With increasing elapsed time after cancer treatment, other health problems became more crucial than the cancer, which may be more distinct for younger cancer survivors whose remaining life expectancy would be adequately lengthy.

Fatigue is a common and distressing symptom of cancer survivors and may negatively affect health-related quality of life of cancer survivors even until several years after completing primary treatment [3–6]. The National Comprehensive Cancer Network (NCCN) suggested that all cancer patients should be screened for fatigue when they visit a clinic and should receive further evaluation and intervention if the degree of fatigue is moderate to severe [7]. However, risk factors of fatigue in cancer patients remain unclear, despite several studies that have investigated etiology of fatigue in cancer patients [5, 8–11].

Low skeletal muscle mass has been suggested to be associated with higher overall mortality, breast-cancer-specific mortality [12] and higher risk of cardiovascular disease [13] in cancer survivors. Additionally, skeletal muscle mass has been suggested as a factor related to fatigue in cancer patients, although findings on the association between skeletal muscle mass and fatigue have been inconsistent between studies. Some studies have shown strong association between low skeletal muscle mass and fatigue [14, 15], whereas other studies have not found any association [6, 16, 17]. Interestingly, studies that found no association between skeletal muscle mass and fatigue were mostly conducted on elderly people or female cancer patients [6, 16, 17]. However, the association between skeletal muscle mass and fatigue among middle-aged cancer survivors remains unclear. In particular, the middle-aged cancer survivors are the most productive age group in society and they are most likely to return to work after cancer treatment. Thus, it is crucial to identify factors associated with fatigue of middle-aged cancer survivors.

Thus, we conducted a cross-sectional study to investigate the association between low relative skeletal muscle mass and fatigue in middle-aged cancer survivors between the ages of 40 and 64.

Methods

Study participants

Study participants were 693 middle-aged (40–64) male and female cancer survivors who underwent measurement of body composition including skeletal muscle mass with bioelectrical impedance analysis (BIA). They were recruited September 2014-February 2017 when they visited a cancer survivorship clinic of a university-affiliated hospital for evaluating long-term health problems and routine surveillance.

The Institutional Review Board (IRB) of the Samsung Medical Center approved the study protocol (IRB File Number: SMC 2013-07-133). Informed consent was obtained from all individual participants included in this study.

Study variables

Sarcopenia (low relative skeletal muscle mass) assessment

We defined relatively low skeletal muscle mass (sarcopenia) for this study according to the diagnostic algorithm proposed by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) and Asian Working Group for Sarcopenia (AWGS), because the algorithm has been widely used in clinical and research settings, especially for Asians [17–19]. Previously, given that sarcopenia is a phenomenon closely related to aging, sarcopenia was a concept applied only to older people and the diagnostic criteria for sarcopenia included low muscle strength, low muscle quantity or quality, and low physical performance in elderly people. However, the most recently proposed diagnostic algorithm by EWGSOP2 removed the age criteria for sarcopenia definition, accepting that sarcopenia could begin earlier in life regardless of age [18, 20, 21].

Appendicular skeletal muscle mass (ASMM) is a key measurement for ascertaining the presence of sarcopenia. EWGSOP2 recommends the dual X-ray absorptiometry (DXA), computed tomography (CT), magnetic resonance imaging (MRI) and bioimpedance analysis (BIA) to evaluate muscle mass for sarcopenia research [18]. Although the DXA may be a more widely used instrument for muscle mass measurement, using the DXA in primary care clinic is difficult, costly, not portable, and has radiation exposure risk [22]. Conversely, BIA is more suitable for primary care clinics because it is portable, free of charge at the hospital in South Korea, fast processing, non-invasiveness, radiation-free, and was validated in previous studies for sarcopenia assessment [19, 23]. Thus, we assessed ASMM for this study via BIA with a body composition analyzer (InBody 720; Biospace) and calculated height-adjusted Appendicular muscle mass index (AMMI) to estimate skeletal muscle mass by dividing appendicular skeletal muscle mass with height squared (kg/m^2). Then, we used the AWGS cutoff values sarcopenia, which were 7.0 kg/m^2 for males and 5.7 kg/m^2 for females [19].

Fatigue assessment

Fatigue was evaluated in all participants using the fatigue severity scale (FSS), which was validated after the Korean translation in previous studies [24, 25]. The FSS is a nine-item self-administered questionnaire assessing subjective status during the previous one week and each item is assessed by a seven-point Likert scale, ranging between 1 (strongly disagree) and 7 (strongly agree) [26]. The FSS score is calculated by totaling the scores of all nine items. Higher scores suggest a greater level of fatigue and a total score of 36 or higher indicates severe fatigue [27, 28]. We classified study participants into two groups using the cut-off value of FSS score for the severe fatigue (≥ 36 or < 36).

Other variables

We collected data on demographic and socioeconomic characteristics, health behavioral factors, and history of comorbid chronic diseases of study participants using a self-administered questionnaire. If necessary, a trained research assistant compensated for incompletely answered questions with in-person interviews. Information on cancer site, stage (I, II, III, or IV) and all types of treatments (operation, chemotherapy, or radiotherapy) were collected by reviewing participants’ medical records. We classified cancer treatment modality into four groups: operation only, chemotherapy with or without operation, radiotherapy with or without operation, and combined chemotherapy and radiotherapy with or without operation. We measured weight and height using a standardized scale and a stadiometer to the nearest 0.1 kg and 0.1 cm, respectively. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). We classified BMI into four levels (underweight; <18.5, normal; 18.5–22.9, overweight; 23-24.9, and obese; ≥ 25). We classified exercise into two groups, depending on whether or not participants exercise more than 150 minutes weekly. We classified smoking status into three groups (never smoker, past smoker, or current smoker). We collected data on alcohol use such as frequency of drinking weekly, type of liquor, and the amount of liquor consumption per occurrence. We then classified alcohol consumption into three levels (< 7 g/week, 7–97 g/week, or ≥ 98 g/week) which we calculated using the details above.

Menopausal status of female participants was categorized into two groups (pre-menopausal or post-menopausal). Marital status had two groups (living with spouse or partner, or not). We categorized education into three levels (middle school or below, high school, or college or above). Comorbid chronic diseases included the following diseases that were known to be highly related to fatigue: diabetes, cerebrovascular disease, cardiovascular disease, chronic liver disease, anemia, thyroid disease, chronic renal disease, and chronic respiratory disease. Study participants were classified into three groups by the total number of comorbid diseases (0,1, or ≥ 2).

Statistical analysis

Characteristics of study participants according to the presence of sarcopenia were compared using the Student's t test or Chi-squared test. We evaluated the association between sarcopenia and fatigue using three logistic regression models. At first, we conducted age-adjusted logistic regression analysis. Then, we did further adjustment for cancer related factors. Finally, obesity, lifestyle factors, and educational level were additionally adjusted.

All statistical analyses were performed using SPSS version 25.0 (IBM Corp. in Armonk, NY.). A two-sided p-value of less than 0.05 was statistically significant in all analyses.

Results

Overall, 18.6% of study participants were sarcopenic: 15.0% among males and 20.3% among females.

Table 1 shows the characteristics of study participants according to the presence of sarcopenia. There was no significant difference in mean age according to the sarcopenic status in males and females. The mean height and weight were relatively low in the sarcopenic group ($p < 0.001$). Sarcopenia tended to be more prevalent with decreasing BMI level in both sexes ($p < 0.001$). The presence of sarcopenia was not different by smoking status, exercise, alcohol consumption, marital status, education level, and menopausal status in females. The clinical characteristics of participants such as cancer type, cancer stage, cancer treatment modality, and number of comorbidities were also not significantly different between the sarcopenic and non-sarcopenic groups.

Table 2 and Figure 1 show the distribution of FSS according to the presence of sarcopenia. The total scores of FSS of the sarcopenic group were significantly higher compared with that of the non-sarcopenic group, only in male cancer survivors (29.3 vs, 23.5, $p = 0.034$) (Figure 1). Severe fatigue (FSS≥36) was more prevalent among the sarcopenic group than among the non-sarcopenic group, which was also distinct only in male survivors (39.4% vs. 19.3%, $p = 0.012$). The mean score of each FSS item tended to be higher in the sarcopenic group than in the non-sarcopenic group, although statistically significant difference was shown for only a few items.

Table 3 shows the association between sarcopenia and severe fatigue. In the age-adjusted logistic regression model, cancer survivors with sarcopenia had significantly higher risk of severe fatigue (odds ratio [OR] 1.71, 95% confidence interval [CI] 1.14, 2.58), which was evident in males (OR 2.97, 95% CI 1.31, 6.72) but not in females (OR 1.39, 95% CI 0.86, 2.23) regardless of menopausal status. With further adjustment for lifestyle factors and educational level, sarcopenia was significantly associated with severe fatigue in male survivors (OR 5.36, 95% CI: 1.47, 19.54) as well as in female pre-menopausal survivors (OR: 2.33, 95% CI: 1.06, 5.13). However, significant association was not found for postmenopausal females (OR: 2.28, 95% CI: 0.77, 6.79).

Discussion

To the best of our knowledge, this study is the first to evaluate the association between sarcopenia and fatigue in middle-aged Asian cancer survivors, and we found sarcopenia was associated with severe fatigue, especially in male survivors and pre-menopausal female survivors.

A Japanese study, of which more than 75% of the subjects were female, found no relation between muscle strength and fatigue in comparisons of cancer survivors and healthy participants [6]. A cross-sectional study of Latin Americans including mainly elder people (mean age was 76 for the sarcopenic participants and 70 for the participants without sarcopenia) also concluded that sarcopenia and fatigue were not associated [17]. In a cross-sectional study of European advanced cancer patients (mean age 64), there was no significant association between higher muscle mass and lower fatigue levels in females [16].

However, some studies have shown strong association between low skeletal muscle mass and fatigue, similarly to the findings of this study. A study on Norwegian cancer patients (mean age 65) with advanced (stage IIIB-IV) non-small cell lung cancer, low skeletal muscle index (SMI) was significantly associated with high fatigue in the male cancer patients [14]. A cross-sectional study of Chinese cancer patients (older than age 18) also found that cancer-related fatigue increased dramatically when sarcopenia was severe [15]. These two studies included advanced cancer patients over stage III and skeletal muscle mass was measured by CT scan.

Several studies have reported that exercise could reduce fatigue of cancer patients [29–31]. Studies revealed that starting exercise programs before cancer treatment can effectively reduce fatigue level as well as improve cancer treatment outcomes [31–34]. Although the underlying mechanism has not been clarified, the positive effect of exercise on the psychological status, cardiopulmonary function, and muscle system may explain the beneficial effects of exercise in cancer patients. Additionally, exercise was found to increase muscle protein synthesis, muscle mass, slow muscle depletion, and improve muscle strength [35]. Thus, it could be possible that sarcopenic persons less involved in physical exercise are less likely to take an advantage of exercise-related health benefits, which may result in higher prevalence of fatigue among them. In this study, although statistical significance was lacking, survivors with sarcopenia tended to be less involved with an adequate level of exercise. Interestingly this study found that significant inverse association between sarcopenia and fatigue persists even after adjusting for the exercise level. Although further study is necessary, this finding may suggest a biological mechanism directly underlying the association between sarcopenia and fatigue.

In a review of 28 studies published January 1950-March, 2014, the prevalence of sarcopenia in cancer patients was 14%-78.7% [36]. In the past, the diagnosis of sarcopenia had been applicable only for the elderly, thus, studies on sarcopenia had been conducted mostly in the elderly population [16, 17]. The prevalence of sarcopenia among cancer survivors has been reported to widely vary. The various sarcopenia prevalence between studies may be attributable to the diverse demographic characteristics of the study population such as age and sex. However, the new revised definition of sarcopenia suggests that sarcopenia begins earlier in life regardless of age [18]. Afterwards, several studies have investigated the prevalence and related factors of sarcopenia of the middle-aged population [37, 38].

In this study of middle-aged cancer survivors, the prevalence of sarcopenia was 15% in males and 20% in females, which was much lower than the prevalence observed in other Korean studies (34% in males and 33% in females) [39]. We think that this discrepancy might be caused by the different age distribution between the two Korean cancer survivor studies.

The prevalence of fatigue has also been known to vary by the influence of several factors. A study reported that approximately 45% of cancer survivors experienced fatigue during cancer treatment and was reduced to approximately 29% after the completion of cancer treatment [3]. The prevalence of fatigue after the completion of cancer treatment in the previous study is similar to the fatigue prevalence observed in this study. Female cancer patients are more likely to report fatigue than male patients, consistent with the finding of this study that fatigue prevalence was lower in male cancer survivors (22%) than that in female cancer survivors (32%). Cancer type may also affect fatigue levels. Breast and colorectal cancer survivors were known to complain more about fatigue than prostate cancer survivors [11]. In a Korean study, the prevalence of fatigue was 66% in disease-free breast cancer survivors [40]. Fatigue prevalence tended to be especially higher when cancer patients had received additional treatment such as radiation therapy, chemotherapy, or hormone therapy compared to when they had received surgical treatment only. The study conducted only for breast cancer survivors showed that the cancer stage was associated with fatigue [41]. The relatively low prevalence of fatigue shown in our study compared to the prevalence in previous studies may be because cancer survivors with an early stage of cancer (Stage I) accounted for more than 50% of the participants in our study.

The present study has limitations to be considered. First, study participants were recruited from a survivorship clinic of an academic hospital in Korea, which may limit generalization of study findings to all cancer survivors. Second, this study could not apply comprehensive sarcopenia which includes muscle strength and physical performance level because of the lack of data. We identified a sarcopenic person based on skeletal muscle mass for this study, given that loss of muscle mass may well reflect deteriorating physical function [35]. Third, we measured fatigue level using the FSS which is a reliable and validated tool for assessing fatigue in the general population [24, 25], instead of the Brief Fatigue

Inventory (BFI) which may be more commonly used for cancer survivors [42]. Fourth, the innate problem of cross-sectional design of this study made it difficult to clearly understand the cause-effect relationship between sarcopenia and fatigue.

Conclusion

In conclusion, sarcopenia of cancer survivors was found to be closely associated with severe fatigue independent of cancer related factors and lifestyle factors. We found sarcopenia was associated with severe fatigue, especially in male survivors and pre-menopausal female survivors. In particular, our study includes early stage cancer (Stage I) survivors, who accounted for more than 50% of the participants, and large numbers of younger cancer survivors. Also, our study found that significant inverse association between sarcopenia and fatigue persists even after adjusting for the exercise level. This finding suggests that sarcopenia may be a risk factor for fatigue in cancer survivors.

Abbreviations

FSS: Fatigue severity scale; OR: Odds ratio; NCCN: National Comprehensive Cancer Network; BIA: Bioelectrical impedance analysis; EWGSOP2: European Working Group on Sarcopenia in Older People 2; AWGS: Asian Working Group for Sarcopenia; ASMM: Appendicular skeletal muscle mass; DXA: Dual X-ray absorptiometry; CT: Computed tomography; MRI: Magnetic resonance imaging; AMMI: Appendicular muscle mass index; BMI: Body mass index; CI: Confidence interval; SMI: Skeletal muscle index; BFI: Brief Fatigue Inventory

Declarations

Ethics approval and consent to participate

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the Samsung Medical Center approved the study protocol (IRB File Number: SMC 2013-07-133). Informed consent was obtained from all individual participants included in this study.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to information that could compromise research participant privacy or consent.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by a grant (1720270) of the National R&D Program for Cancer Control funded by the Ministry of Health & Welfare, Republic of Korea. The funding source had no involvement in the study design, data collection, data analysis, or data interpretation of this study.

Authors' contributions

SS and YMS designed the study and selected the study methodology. JS, JEL, DWS, JL, JHH, BLC and YMS collected the data. SS, IYC and YMS performed the statistical analysis and wrote the manuscript. SS and YMS analyzed and interpreted the data. SS, IYC and YMS edited the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We thank the National Research and Development Program for Cancer Control and Ministry of Health & Welfare for their funding, and the participants of the study for their cooperation.

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Tables

Table 1 Characteristics of study subjects according to the presence of sarcopenia, cancer survivors age 40-64

	Males (n = 220)			Females (n = 473)		
	Non-sarcopenic (n = 187)	Sarcopenic (n = 33)	P value*	Non-Sarcopenic (n = 377)	Sarcopenic (n = 96)	P value*
Age, years	55.6±6.4	56.0±6.8	0.743	54.0±6.3	54.0±6.1	0.964
Height, cm	169.0±6.0	164.2±5.6	<.001	158.2±5.2	155.4±4.7	<.001
Weight, kg	67.7±9.3	55.5±7.6	<.001	58.3±8.6	47.4±4.3	<.001
Body mass index, kg/m^2	23.7±2.8	20.6±2.9	<.001	23.3±3.3	19.6±1.8	<.001
Underweight (<18.5)	3 (25.0)	9 (75.0)	<.001	14 (22.2)	28 (66.7)	<.001
Normal (18.5-22.9)	79 (79.8)	20 (20.2)		176 (73.3)	64 (26.7)	
Overweight (23-24.9)	45 (95.7)	2 (4.3)		91 (96.8)	3 (3.2)	
Obese (≥25)	60 (96.8)	2 (3.2)		96 (99.0)	1 (1.0)	
ASMM(kg)						
Total	22.7±2.8	17.5±2.0	<.001	16.1±1.9	12.8±1.2	<.001
Upper extremities	6.0±0.9	4.5±0.6	<.001	3.9±0.6	2.9±0.3	<.001
Lower extremities	16.7±2.0	13.0±1.5	<.001	12.2±1.4	9.9±1.0	<.001
ASMI(kg/m^2)	7.9±0.7	6.5±0.5	<.001	6.4±0.5	5.3±0.3	<.001
Lean mass (kg)	53.5±5.6	43.0±3.1	<.001	39.9±3.8	33.5±2.2	<.001
Exercise			0.474			0.452
≥150 minutes/week	95 (88.0)	13 (12.0)		155 (82.0)	34 (18.0)	
< 150 minutes/week	57 (82.6)	12 (17.4)		121 (76.6)	37 (23.4)	
Smoking status			0.071			0.242
Never smoker	24 (70.6)	10 (29.4)		346 (78.8)	93 (21.2)	
Past smoker	140 (87.5)	20 (12.5)		26 (89.7)	3 (10.3)	
Current smoker	19 (90.5)	2 (9.5)		5 (100.0)	0 (0.0)	
Not stated	4 (80.0)	1 (20.0)		-	-	
Alcohol consumption			0.188			0.898
< 7g/week	99 (81.1)	23 (18.9)		315 (79.3)	82 (20.7)	
7-97g/week	46 (88.5)	6 (11.5)		54 (81.8)	12 (18.2)	
≥98g/week	42 (91.3)	4 (8.7)		8 (80.0)	2 (20.0)	
Menopausal status						0.850
Yes	-	-		157 (79.3)	41 (20.7)	
No	-	-		220 (80.0)	55 (20.0)	
Marital status			0.377			0.617
Live together	168 (86.2)	27 (13.8)		309 (80.5)	75 (19.5)	
Single	14 (77.8)	4 (22.2)		59 (75.6)	19 (24.4)	
Not stated	0 (0.0)	0 (0.0)		9 (81.8)	2 (18.2)	
Education level			0.779			0.154
Middle school or below	11 (91.7)	1 (8.3)		21 (95.5)	1 (4.5)	
High school	68 (87.2)	10 (12.8)		168 (80.4)	41 (19.6)	
College or above	94 (83.2)	19 (16.8)		160 (76.6)	49 (23.4)	
Not stated	14 (82.4)	3 (17.6)		28 (84.8)	5 (15.2)	

Cancer type			0.174			0.113
Stomach	122 (87.8)	17 (12.2)		83 (69.7)	36 (30.3)	
Breast	2 (100.0)	0 (0.0)		186 (82.3)	40 (17.7)	
Lung	28 (82.4)	6 (17.6)		25 (80.6)	6 (19.4)	
Thyroid	3 (60.0)	2 (40.0)		40 (90.9)	4 (9.1)	
Colorectal	8 (100.0)	0 (0.0)		9 (69.2)	4 (30.8)	
Liver	4 (80.0)	1 (20.0)		2 (100.0)	0 (0.0)	
Prostate	3 (60.0)	2 (40.0)		-	-	
Cervical	-	-		9 (90.0)	1 (10.0)	
Others	(77.3)	5 (22.7)		23 (79.3)	6 (20.7)	
Cancer Stage			0.073			0.129
I	111 (89.5)	13 (10.5)		189 (76.2)	59 (23.8)	
II	26 (68.4)	12 (31.6)		93 (83.0)	19 (17.0)	
III-IV	39 (86.7)	6 (13.3)		61 (79.2)	16 (20.8)	
Not reported	11 (84.6)	2 (15.4)		34 (94.4)	2 (5.6)	
Cancer treatment			0.908			0.734
Operation only	99 (85.3)	17 (14.7)		130 (77.4)	38 (22.6)	
Chemotherapy ± operation	29 (82.9)	6 (17.1)		69 (79.3)	18 (20.7)	
Radiotherapy ± operation	7 (87.5)	1 (12.5)		48 (84.2)	9 (15.8)	
Chemotherapy + radiotherapy ± operation	40 (83.3)	8 (16.7)		117 (81.8)	26 (18.2)	
Not reported	12 (92.3)	1 (7.7)		13 (72.2)	5 (27.8)	
Number of comorbidities			0.303			0.415
0	102 (84.3)	19 (15.7)		222 (81.6)	50 (18.4)	
1	52 (85.2)	9 (14.8)		101 (78.3)	28 (21.7)	
≥2	33 (86.8)	5 (13.2)		54 (75.0)	18 (25.0)	

N number, *ASMM* appendicular skeletal muscle mass, *AMMI*(ASMM/height^2) appendicular muscle mass index

Data were presented as mean ± standard deviation for continuous variables or number (%) for categorical variables.

Sarcopenia was defined according to appendicular muscle mass index cut-off values stratified by sex (< 7.0kg/m^2 for men, <5.7kg/m^2 for women).

* The *P* values were estimated by the Student's t test, and Chi-square test or Fisher's exact test for examining differences between sarcopenic survivors and non-sarcopenic survivors.

Table 2 Distribution of fatigue severity scale according to the presence of sarcopenia

	Males ($n = 220$)			Females ($n = 473$)		
	Non-sarcopenic ($n = 187$)	Sarcopenic ($n = 33$)	*P* value*	Non-sarcopenic ($n = 377$)	Sarcopenic ($n = 96$)	*P* value*
Fatigue severity scale						
Total	23.5±14.1	29.3±16.4	0.034	27.8±15.5	30.5±15.2	0.128
Significant Fatigue (FSS≥36), No. (%)	36 (19.3)	13 (39.4)	0.012	115 (30.5)	36 (37.5)	0.118
Score of each FSS item (0-7)						
My motivation is lower when I am fatigued	3.0±2.0	3.4±1.9	0.225	3.5±2.2	4.1±2.2	0.032
Exercise brings on my fatigue	3.0±1.9	3.5±1.9	0.174	3.3±2.0	3.5±2.0	0.319
I am easily fatigued	3.1±2.0	3.7±2.2	0.137	3.8±2.1	4.1±2.0	0.215
Fatigue interferes with my physical functioning	2.8±1.8	3.4±2.1	0.074	3.4±2.1	3.6±2.0	0.407
Fatigue causes frequent problems for me	2.3±1.6	3.0±2.1	0.087	2.8±1.9	3.0±2.0	0.399
My fatigue prevents sustained physical functioning	2.4±1.7	3.1±2.0	0.025	2.8±1.9	3.1±2.0	0.121
Fatigue interferes with performing certain duties and responsibilities	2.2±1.7	3.0±2.1	0.056	2.5±1.8	2.8±1.9	0.215
Fatigue is among my three most disabling symptoms	2.6±1.8	3.5±2.2	0.066	3.2±2.2	3.6±2.0	0.175
Fatigue interferes with my work, family, or social life	2.3±1.6	3.2±2.1	0.019	2.7±1.9	2.9±1.8	0.313

N number, *ASMM* appendicular skeletal muscle mass, *AMMI*(ASMM/height^2) appendicular muscle mass index, *FSS* fatigue severity scale

Data were presented as mean ± standard deviation or number of subjects (%).

Sarcopenia was defined by appendicular muscle mass index cut-off values stratified by sex (< 7.0kg/m^2 for men, <5.7kg/m^2 for women).

The FSS is a 9-item self-report questionnaire. Each item is rated on a seven-point score response and respondents choose a score between 1 (no impairment at all) and 7 (severe impairment) corresponding to their perceived impairment. Higher scores reflect greater impairment.

* The *P* values were estimated by the Student's t test, and Chi-square test or Fisher's exact test for examining differences between sarcopenic survivors and non-sarcopenic survivors.

Table 3 Association between sarcopenic and significant fatigue (FSS≥36)

		Age-adjusted		Model 1		Model 2	
		OR (95% CI)*	*P* value*	OR (95% CI)*	*P* value*	OR (95% CI)*	*P* value*
Overall (*n* = 693)	No sarcopenia	1.00		1.00		1.00	
	Sarcopenia	1.71 (1.14, 2.58)	0.01	1.87 (1.22, 2.86)	0.004	2.05 (1.24, 3.38)	0.005
Men (*n* = 220)	No sarcopenia	1.00		1.00		1.00	
	Sarcopenia	2.97 (1.31, 6.72)	0.009	4.31 (1.64, 11.30)	0.003	5.36 (1.47, 19.54)	0.011
Women (*n* = 473)	No sarcopenia	1.00		1.00		1.00	
	Sarcopenia	1.39 (0.86, 2.23)	0.179	1.58 (0.95, 2.62)	0.077	1.87 (1.04, 3.36)	0.036
Premenopause	No sarcopenia	1.00		1.00		1.00	
(*n* = 275)	Sarcopenia	1.55 (0.85, 2.85)	0.156	1.82 (0.94, 3.53)	0.078	2.33 (1.06, 5.13)	0.036
Postmenopause	No sarcopenia	1.00		1.00		1.00	
(*n* = 198)	Sarcopenia	1.20 (0.55, 2.63)	0.649	1.56 (0.65, 3.71)	0.32	2.28 (0.77, 6.79)	0.138

FSS fatigue severity scale, *N* number, *OR(95% CI)* odds ratio (95% confidence interval), *ASMM* appendicular skeletal muscle mass, *AMMI*(ASMM/height^2) appendicular muscle mass index

Sarcopenia was defined by appendicular muscle mass index cut-off values stratified by sex (< 7.0kg/m^2 for men, <5.7kg/m^2 for women).

Fatigue was defined to FSS≥36.

Model 1: Adjusted for age, cancer type, and cancer treatment.

Model 2: Adjusted for age, cancer type, cancer treatment, obesity, smoking, alcohol, physical activity (≥150 minutes/week) and education level.

* Estimated by multiple logistic regression analysis.

Figures

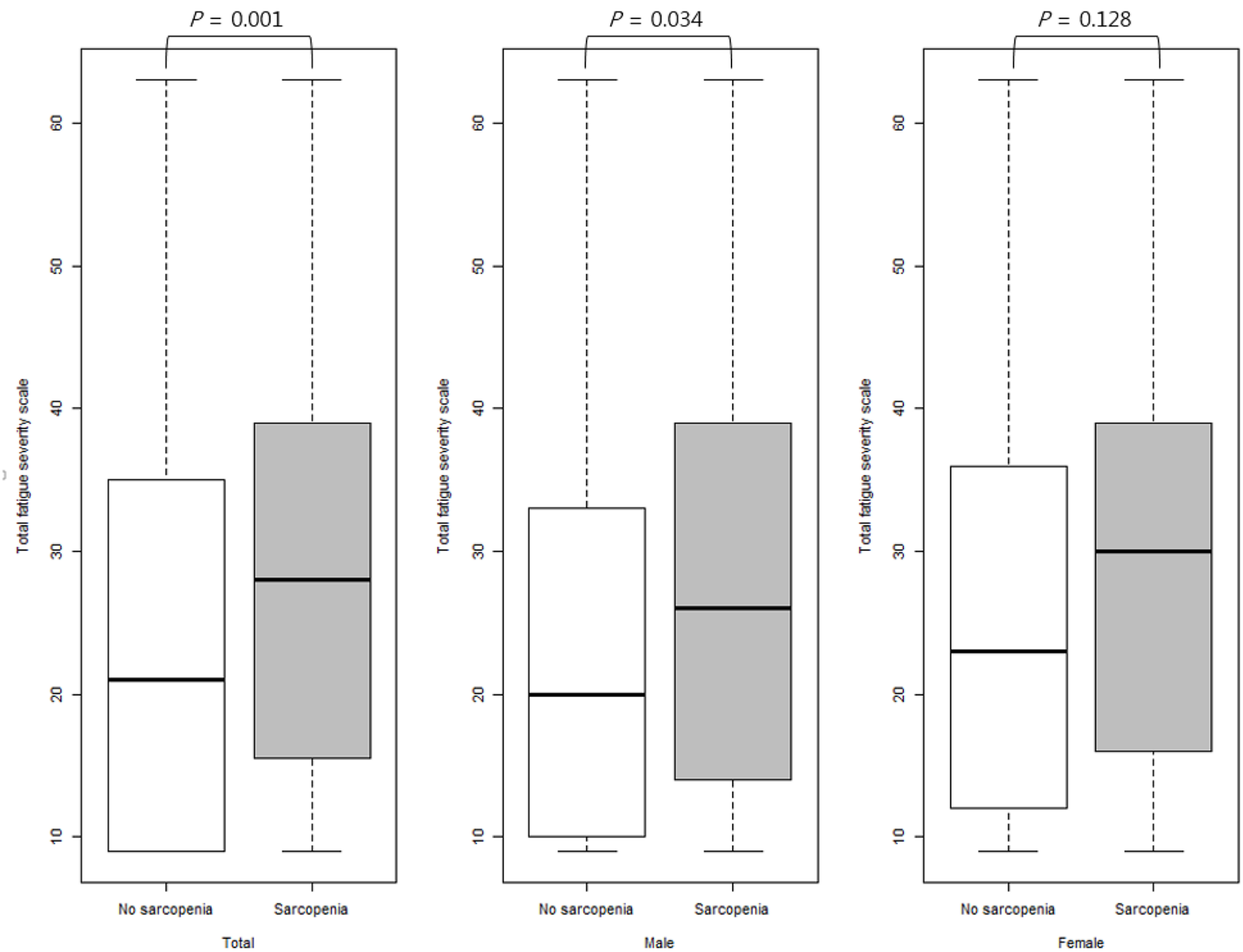

Figure 1

Distribution of total fatigue severity scale stratified by the presence of sarcopenia.