

# Fatigue and primary sarcopenia in geriatric patients

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## SUMMARY

**OBJECTIVE:** This study aimed to investigate the frequency of fatigue in geriatric patients with primary sarcopenia and to evaluate the relationship between fatigue and symptoms such as depression and sleepiness.

**METHODS:** This case-control study was conducted between December 2020 and August 2021 in the geriatrics outpatient clinic of Istanbul University-Cerrahpasa. The European Working Group on Sarcopenia in Older People 2 criteria were considered for the diagnosis of sarcopenia. Demographic data, accompanying chronic diseases, comprehensive geriatric assessments, and laboratory values of the patients were noted. Scales used to assess fatigue in all participants include Fatigue Assessment Scale, Fatigue Severity Scale, and Fatigue Impact Scale and associated symptoms include Geriatric Depression Scale and Epworth Sleepiness Scale.

**RESULTS:** The mean (standard deviation) age was 75.3 (7.1) for 51 primary sarcopenia (38 female) patients and 73.5 (5.8) for 51 control (37 female) patients. There was no significant difference between the two groups in terms of gender and age ( $p=0.822$ ,  $p=0.171$ ). The prevalence of hypertension was higher, and the level of education was lower in the sarcopenic group than in the nonsarcopenic group ( $p=0.017$ ,  $p=0.013$ ). Fatigue Assessment Scale, Fatigue Severity Scale, Fatigue Impact Scale total, Fatigue Impact Scale cognitive, Fatigue Impact Scale physical, and Fatigue Impact Scale social questionnaire scores were significantly higher in the sarcopenic group (all  $p<0.001$ ). The Geriatric Depression Scale score was statistically higher in the sarcopenic group; however, there was no significant difference in the Epworth Sleepiness Scale score between the two groups ( $p=0.014$ ,  $p=0.072$ ). Multivariate analysis was performed on education level, hypertension, fatigue questionnaires, and Geriatric Depression Scale, which were found to be significant in the univariate logistic regression analysis. In the multivariate logistic regression analysis, only the Fatigue Impact Scale total was determined to be associated with sarcopenia [odds ratio 1.161, 95% confidence interval (1.084–1.242)].

**CONCLUSION:** In primary sarcopenia, there is mental and social fatigue as well as physical fatigue. Therefore, the prevention and treatment of sarcopenia in geriatric patients is important.

**KEYWORDS:** Sarcopenia. Fatigue. Depression. Sleepiness.

## INTRODUCTION

With advancing age, various degrees of loss in body functions occur. Muscle loss in the elderly is one of the most important natural processes. The third decade for muscle mass was accepted as the turning point, and 27 years was indicated as the threshold at which skeletal mass began to be negatively correlated with age among both men and women<sup>1</sup>. The European Working Group on Sarcopenia in Older People (EWGSOP) updated the 2010 sarcopenia definition in 2019. According to the decisions taken in EWGSOP2, the primary parameter of sarcopenia is low muscle strength. Sarcopenia is probable when low muscle strength is detected. By adding “low muscle mass” to this, the diagnosis of “sarcopenia” is made<sup>2</sup>. Sarcopenia can cause an increase in the risk of falls and fractures due to falls, deterioration in activities of daily living, movement disorders, increased hospitalization, decreased quality of life, and even death. As can be seen, sarcopenia is associated with many adverse conditions in the elderly and can be considered a marker of frailty<sup>3,4</sup>.

Fatigue can be defined as “an overwhelming, debilitating, and persistent feeling of burnout that reduces the person’s ability to perform activities of daily living, including working effectively and performing customary family and social duties”<sup>5</sup>. The 50% concordance in idiopathic chronic fatigue in monozygotic twins suggests that both genetic and environmental factors are important in the pathogenesis<sup>6</sup>. Fatigue is common, with a rate of approximately 20% in the general population<sup>7</sup>. Researchers have investigated the relationship between fatigue and many diseases and revealed that this rate increases up to 50% in cancer, chronic infections, autoimmune, and neurological diseases in which the immune system is affected<sup>8</sup>. The geriatric population is at higher risk of fatigue due to both physiological changes and comorbid conditions.

This study aimed to investigate the frequency of fatigue in geriatric patients with primary sarcopenia and to evaluate the relationship between fatigue and symptoms such as depression and sleepiness in these patients.

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## METHOD

This prospective, case-control study was conducted between December 2020 and August 2021 in the geriatrics outpatient clinic of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty. The Ethics Committee of the Cerrahpasa Medical Faculty approved the study protocol (09.09.2020-117341) and written informed consent for study participation was obtained from all participants.

### Study population and setting

A total of 102 patients, 51 patients with primary sarcopenia and 51 controls, who applied to our geriatrics outpatient clinic, were included in this study. Demographic data, accompanying chronic diseases, and laboratory values of the patients were noted. In addition, comprehensive geriatric evaluations of the patients were performed.

Patients with probable secondary sarcopenia (being bed-bound, advanced organ failure, malignancy, malnutrition, HIV infection, rheumatoid arthritis, malabsorption, and steroid use) and active infection were excluded from the study. Dementia was excluded as it may make it difficult to cooperate to the questionnaires. Due to the effect of depression on fatigue, patients who were already diagnosed with depression or who were diagnosed with depression during our clinical evaluation were not included in the study.

### Sarcopenia diagnosis

The EWGSOP2 criteria were considered for the diagnosis of sarcopenia and cutoff values<sup>2</sup>. For the diagnosis of sarcopenia, a handgrip strength test is performed initially. If low muscle strength is detected, it is considered “probable sarcopenia.” Afterward, muscle mass is measured, and in case of low muscle mass, it is considered “sarcopenia.” If low muscle strength and slowed walking speed are added to muscle mass, it is defined as “severe sarcopenia.” For a positive handgrip strength test, the cutoff value was accepted as 27 kg for men and 16 kg for women. Bioelectrical impedance analyzer device (Tanita Body Composition Analyzer® TBF-300 model, Tanita Co., Tokyo, Japan) was used to measure skeletal muscle mass index (SMMI) in kg/m<sup>2</sup> after 12 h of fasting and its cutoff value was <7.0 kg/m<sup>2</sup> in males and <5.5 kg/m<sup>2</sup> in females. The cutoff value of the gait speed was accepted as ≤0.8 m/s<sup>2</sup>.

### Fatigue Questionnaires and Geriatric Assessment

**Fatigue Severity Scale (FSS):** It is a nine-item questionnaire. By evaluating the last week's process, the participant is asked nine questions. As an answer, the participant is asked to give a score between 1 and 7 for each item: 1 signifies strong discord,

and 7 signifies strong harmony. The total score is divided by 9, and if it is ≥, the participant is considered to have fatigue. The FSS was developed by Krupp et al. and the Turkish validation was performed by Gencay-Can and Can<sup>9,10</sup>.

**Fatigue Impact Scale (FIS):** It determines the physical, cognitive, and social effects of fatigue in the last month. It consists of 40 questions in total: cognitive effects are evaluated with 10 questions, social effects are evaluated with 10 questions, and psychosocial effects are evaluated with 20 questions. Each question is read to the participants and asked to give the most suitable value between 0 (no problem) and 3 (very big problem). Each field is evaluated separately. The FIS was first developed by Fisk et al. in 1994, and its Turkish validation was done by Armutlu et al.<sup>11,12</sup>.

**Fatigue Assessment Scale (FAS):** FAS, consisting of a total of 10 questions, 5 of which are about physical fatigue and 5 about mental fatigue, was designed by De Vries et al.<sup>13</sup>. Each option is read to the participants and asked to answer each question on a scale of 1–5, with 1 indicating never and 5 always. The total score ranges from 10 to 50. A score between 22 and 50 indicates fatigue.

**Epworth Sleepiness Scale (ESS):** This scale consists of eight questions developed to determine daytime sleepiness<sup>14</sup>. A Turkish validity and reliability study was also conducted<sup>15</sup>. Considering the last month, the probability of napping is questioned in a total of eight different daily situations. Each condition is read to the patient individually and asked to give a value between 0 (I never sleep) and 3 (I probably sleep). The value given to each state is summed up numerically, the maximum score is 24, and the higher score indicates more daytime sleepiness. Value of >10 is considered abnormally increased daytime sleepiness.

**Geriatric Depression Scale (GDS):** It was developed by Yesavage et al.<sup>16</sup>. The Turkish validation of the short form of the GDS was performed by Durmaz et al.<sup>17</sup>. The participant is asked 15 questions to be answered as yes or no. The numerical value given to each question is summed up; a maximum of 15 points can be obtained, and the higher the scale score, the higher the depressive state. Value of ≥5 is considered increased depressive mood.

**Mini-Mental State Examination (MMSE):** The MMSE used to screen for cognitive disorders was designed by Folstein et al.<sup>18</sup>. Turkish validation of the MMSE was performed by Güngen et al.<sup>19</sup>. In the MMSE, the participant is asked to answer questions about orientation, recording memory, attention-calculation, recall, and language. It is evaluated out of a total of 30 points. Score of <24 points is considered decreased cognitive function.

Mini Nutritional Assessment (MNA): This test was developed in the 1990s and is approved for use in hospitals, clinics, and nursing homes in the geriatric population aged 65 years and above. In the first part of the MNA form, there are six questions evaluating food consumption, weight loss, mobility, stress or acute illness, the presence of neuropsychological problems, and body mass index. In the second part of the MNA form, questions about dietary habits, medical history, drug use, and subjective evaluation of health are asked, and anthropometric measurements are recorded. The highest score is 30; score of  $\leq 17$  points is considered malnutrition<sup>20</sup>.

### Statistical analysis

Pearson's chi-square test and Fisher's exact test were used to compare categorical variables. The Student's t-test was used to compare numerical variables. Spearman's correlation analysis was used to evaluate the relationship between sarcopenia, fatigue questionnaires, and comprehensive geriatric assessment tests. In the study, FAS, FSS, FIS total, GDS, hypertension, and level of education were analyzed first with the univariate logistic regression (LR) method and then variables that were found to be significant were analyzed with the stepwise multivariate LR method. The results were evaluated at 95% confidence interval and  $p < 0.05$  significance level. The IBM SPSS-20 (Statistical Package for Social Sciences, Chicago, IL, USA) package program was used for statistical analysis.

## RESULTS

Of the 51 patients with sarcopenia, 38 were female and the mean (standard deviation) age was 75.3 (7.1) years, while in the control group with 51 patients, 37 were female and the mean (standard deviation) age was 73.5 (5.8) years. There was no significant difference between the two groups in terms of gender and age ( $p=0.822$ ,  $p=0.171$ ). When compared in terms of education level, the rate of being a high school graduate was statistically significantly lower in the sarcopenia group ( $p=0.013$ ). Of the chronic diseases, only hypertension was seen statistically significantly more frequent in sarcopenic patients than in non-sarcopenic patients ( $p=0.017$ ). When the laboratory levels were examined, no significant difference was found between the two groups in terms of hemoglobin, TSH, hemoglobin A1c, and 25-hydroxyvitamin D levels ( $p=0.061$ ,  $p=0.906$ ,  $p=0.133$ , and  $p=0.113$ , respectively). Details of patients' demographic data and chronic diseases are given in Table 1.

The FAS, FSS, FIS total, FIS cognitive, FIS physical, and FIS social questionnaire scores were statistically significantly higher in the sarcopenic group (all  $p < 0.001$ ). When we accept that  $>22$  points have fatigue according to the FAS questionnaire, 44 patients in the sarcopenia group and 26 patients in the control group had fatigue ( $p < 0.001$ ). Considering  $\geq 4$  points having fatigue according to the FSS questionnaire, 32 patients in the sarcopenia group and 12 patients in the control group had fatigue ( $p < 0.001$ ). While the GDS score was statistically higher in the sarcopenic group, there was

**Table 1.** Demographic data and chronic diseases of patients.

	With sarcopenia	Without sarcopenia	p-value
Number of patients	51	51	
Gender (female/male)	38/13	37/14	0.822
Age <sup>*</sup>	75.3 (7.1)	73.5 (5.8)	0.171
Education (elementary/high school)	46/5	36/15	<b>0.013</b>
Body mass index <sup>*</sup>	28.2 (5.2)	28.7 (4.8)	0.604
Hypertension	47 (92%)	38 (74%)	<b>0.017</b>
Diabetes mellitus	20 (39%)	16 (31%)	0.407
Heart failure	5 (9%)	1 (2%)	0.205
Osteoporosis	8 (16%)	4 (8%)	0.219
Hypothyroidism	9 (18%)	9 (18%)	1.000
Asthma	3 (6%)	2 (4%)	0.647
Hyperlipidemia	8 (16%)	13 (25%)	0.221
Chronic obstructive pulmonary disease	5 (10%)	5 (10%)	0.184
Chronic kidney disease	4 (8%)	4 (8%)	1.000
Benign prostatic hyperplasia	7 (14%)	3 (6%)	0.183

Data are shown as mean (standard deviation). Statistically significant p-values are indicated as bold.

no significant difference in the ESS score between the two groups ( $p=0.014$  and  $p=0.072$ ). Muscle strength, muscle mass, and walking speed were lower in the sarcopenia group (all  $p<0.001$ ). The details of the comprehensive geriatric evaluation and fatigue questionnaire results of the sarcopenia and control group are given in Table 2. Fatigue survey results of the sarcopenia group and control group are shown in Figure 1. GDS and ESS results of the sarcopenia group and control group are shown in Figure 2.

The FAS, FSS, FIS total, GDS, hypertension, and education level were statistically significant in univariate LR analysis ( $p<0.001$ ,  $p<0.001$ ,  $p<0.001$ ,  $p=0.017$ ,  $p<0.001$ , and  $p=0.017$ , respectively). In the multivariate LR analysis performed on these parameters, which were significant in the univariate analysis, only the FIS total was significant [odds ratio (OR) 1.161, 95% confidence interval (CI) 1.084–1.242]. Details of the regression analysis are given in Table 3.

## DISCUSSION

To the best of our knowledge, this is the first study to evaluate the relationship between primary sarcopenia and fatigue, sleepiness, and depression. Diabetes mellitus, hypothyroidism, chronic heart failure, chronic obstructive pulmonary disease, vitamin D deficiency, or anemia can be counted as some of the secondary causes of fatigue. In this study, the fact that there was no difference between the two groups in terms of these diseases or conditions enabled us to rule out other causes of fatigue other than sarcopenia. Thus, we were able to evaluate sarcopenia as the primary cause of fatigue.

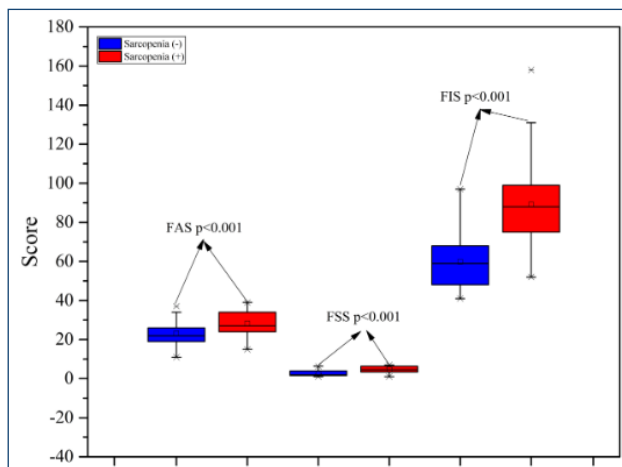


Figure 1. Fatigue survey results of sarcopenia and control groups.

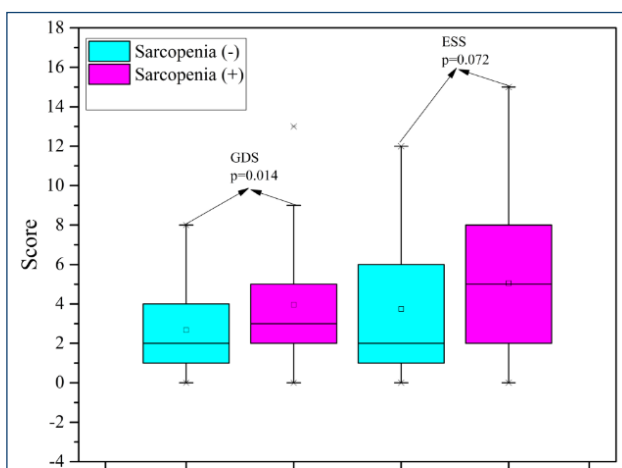


Figure 2. Geriatric Depression Scale and Epworth Sleepiness Scale results of sarcopenia and control groups.

Table 2. Comprehensive geriatric evaluation and fatigue questionnaire results of patients.

	With sarcopenia (n=51)	Without sarcopenia (n=51)	p-value
Mini-Mental State Examination	27.0 (1.8)	27.6 (1.3)	0.076
Mini Nutritional Assessment	24.6 (2.9)	26.0 (2.8)	<b>0.017</b>
SARC-F	4.0 (2.3)	1.5 (1.5)	<b>&lt;0.001</b>
Grip strength (kg)	15.6 (4.8)	24.9 (8.2)	<b>&lt;0.001</b>
Skeletal muscle mass index (kg/m <sup>2</sup> )	6.1 (0.5)	6.7 (0.7)	<b>&lt;0.001</b>
Gait speed (m/s)	0.7 (0.2)	0.9 (0.3)	<b>&lt;0.001</b>
Fatigue Assessment Scale	28.2 (6.6)	23.1 (5.6)	<b>&lt;0.001</b>
Fatigue Severity Scale	4.5 (1.7)	2.9 (1.6)	<b>&lt;0.001</b>
Fatigue Impact Scale total	89.1 (21.6)	59.8 (13.8)	<b>&lt;0.001</b>
FIS cognitive	20.0 (5.7)	14.3 (4.4)	<b>&lt;0.001</b>
FIS physical	24.8 (6.5)	16.1 (5.4)	<b>&lt;0.001</b>
FIS social	59.8 (13.8)	44.3 (13.2)	<b>&lt;0.001</b>
Epworth Sleepiness Scale	5.0 (3.9)	3.7 (3.3)	0.072
Geriatric Depression Scale	3.9 (2.7)	2.6 (2.4)	<b>0.014</b>

SMMI: skeletal muscle mass index. Data are shown as mean (standard deviation). Statistically significant p-values are indicated as bold.

**Table 3.** Univariate and stepwise multivariate logistic regression analysis for factors associated with sarcopenia.

	Univariate LR		Multivariate LR	
	Odds ratio (95%CI)	p-value	Odds ratio (95%CI)	p-value
Fatigue Assessment Scale	1.143 (1.064–1.229)	<0.001	1.001 (0.873–1.147)	0.989
Fatigue Severity Scale	1.713 (1.334–2.200)	<0.001	0.689 (0.392–1.208)	0.193
Fatigue Impact Scale total	1.111 (1.068–1.157)	<0.001	1.161 (1.084–1.242)	<0.001
Geriatric Depression Scale	1.218 (1.035–1.434)	0.017	0.807 (0.603–1.080)	0.150
Hypertension	4.020 (1.211–13.339)	<0.001	1.826 (0.395–8.435)	0.441
Education	0.261 (0.087–0.785)	0.017	0.596 (0.107–3.327)	0.556

LR: logistic regression; CI: confidence interval. Statistically significant p-values are indicated as bold.

This study revealed that the incidence of sarcopenia decreased as the level of education increased. In fact, this result is not surprising since educated individuals pay more attention to a balanced diet and physical activities, do not delay hospital visits, and try to apply physician recommendations more carefully. Although we excluded malnutrition as the cause of secondary sarcopenia when designing the study, the MNA scores were found to be significantly lower in the sarcopenic group. This may be because the sarcopenic group might be taking foods with less protein content.

Vlietstra et al. applied the fatigue scales to 157 patients with osteoarthritis or rheumatoid arthritis, divided the patients into groups with and without sarcopenia, and found no significant difference between the groups in terms of fatigue<sup>21</sup>. In a study evaluating the relationship between sarcopenia and its components and fatigue, no significant relationship was found between sarcopenia and fatigue. However, a significant relationship was found between decreased hand grip strength and walking speed and fatigue<sup>22</sup>. In our study, however, in addition to hand grip strength and walking speed, which are the components of sarcopenia, there was also a significant relationship between sarcopenia and fatigue. The fact that the FIS total was significant in the multivariate regression analysis of our study may be due to the elaboration of fatigue as a result of the 40 questions in the FIS total.

In the literature, inflammatory immune response and pro-inflammatory cytokine levels have been associated with fatigue in various diseases<sup>23</sup>. Since sarcopenia is an inflammatory condition, pro-inflammatory cytokines involved in the pathogenesis of sarcopenia may cause fatigue<sup>24</sup>.

The limitations of our study are that it is a case-control study and the number of study participants is low.

## CONCLUSION

Fatigue is a condition with an increased frequency in sarcopenia. FIS total, FAS, and FSS fatigue scores were higher in the sarcopenic group, indicating that mental and social fatigue are present in addition to physical fatigue in sarcopenia. For this reason, protein-rich diet, adequate vitamin D intake, and physical exercise are of great importance in order to prevent sarcopenia and subsequent fatigue in geriatric patients. The biggest contribution we have made to the literature with this study is presenting the sarcopenia-fatigue relationship comprehensively by the simultaneous application of all FAS, FIS (cognitive, social, and physical), and FSS fatigue questionnaires and evaluating their relationship with ESS and GDS.

## STATEMENT OF ETHICS

The study was approved by the ethics committee of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty (09.09.2020-117341).

## AUTHORS' CONTRIBUTIONS

**VS:** Conceptualization, Formal Analysis, Investigation, Methodology. **BBK:** Data curation, Investigation, Writing – original draft. **HY:** Methodology, Supervision, Writing – review & editing.

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