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. 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. 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.

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.” The 50% concordance in idiopathic chronic fatigue in monozygotic twins suggests that both genetic and environmental factors are important in the pathogenesis. Fatigue is common, with a rate of approximately 20% in the general population. 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. 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.
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. 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/m² after 12 h of fasting and its cutoff value was <7.0 kg/m² in males and <5.5 kg/m² in females. The cutoff value of the gait speed was accepted as ≤0.8 m/s².

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 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 ≥10 is considered abnormally increased daytime sleepiness.

Geriatric Depression Scale (GDS): It was developed by Yesavage et al. The Turkish validation of the short form of the GDS was performed by Durmaz et al. Each question 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.

Mini-Mental State Examination (MMSE): The MMSE used to screen for cognitive disorders was designed by Folstein et al. Turkish validation of the MMSE was performed by Güngen et al. 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 ≤17 points is considered malnutrition.

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 ≥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 | 75.3 (7.1) | 73.5 (5.8) | 0.171 |
| Education (elementary/high school) | 46/5 | 36/15 | 0.013 |
| Body mass index | 28.2 (5.2) | 28.7 (4.8) | 0.604 |
| Hypertension | 47 (92%) | 38 (74%) | 0.017 |
| 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.

**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)                | 0.017   |
| SARC-F                         | 4.0 (2.3)              | 1.5 (1.5)                 | <0.001  |
| Grip strength (kg)             | 15.6 (4.8)             | 24.9 (8.2)                | <0.001  |
| Skeletal muscle mass index (kg/m²) | 6.1 (0.5)          | 6.7 (0.7)                 | <0.001  |
| Gait speed (m/s)               | 0.7 (0.2)              | 0.9 (0.3)                 | <0.001  |
| Fatigue Assessment Scale       | 28.2 (6.6)             | 23.1 (5.6)                | <0.001  |
| Fatigue Severity Scale         | 4.5 (1.7)              | 2.9 (1.6)                 | <0.001  |
| Fatigue Impact Scale total     | 89.1 (21.6)            | 59.8 (13.8)               | <0.001  |
| FIS cognitive                  | 20.0 (5.7)             | 14.3 (4.4)                | <0.001  |
| FIS physical                   | 24.8 (6.5)             | 16.1 (5.4)                | <0.001  |
| FIS social                     | 59.8 (13.8)            | 44.3 (13.2)               | <0.001  |
| Epworth Sleepiness Scale       | 5.0 (3.9)              | 3.7 (3.3)                 | 0.072   |
| Geriatric Depression Scale     | 3.9 (2.7)              | 2.6 (2.4)                 | 0.014   |

SMMI: skeletal muscle mass index. Data are shown as mean (standard deviation). 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 fatigue21. 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 fatigue22. 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 diseases23. Since sarcopenia is an inflammatory condition, pro-inflammatory cytokines involved in the pathogenesis of sarcopenia may cause fatigue24.

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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