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Incidence and risk factors of sarcopenia in hospitalized survivors of COVID-19; a retrospective cohort study

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Abstract

Introduction: Among the persistent conditions affecting patients in the post-acute COVID-19 period, sarcopenia is increasingly emphasized. In this study, we aimed to determine the incidence of sarcopenia and to reveal the risk factors predicting it in hospitalized survivors of COVID-19.

Methodology: This is a retrospective cohort study conducted between December 2021 and May 2022 in the post-COVID follow-up center of a tertiary hospital in Turkey. One hundred and sixty-eight patients who were hospitalized because of COVID-19 and discharged were included in the study. The SARC-F scale was applied to determine the risk of sarcopenia in the participants. Twelve patients with a SARC-F score ≥ 4 before COVID-19 were excluded from the study. The medical records of the remaining 156 participants were reviewed, and their demographic characteristics, COVID-19 disease data, hemogram, and CRP parameters were also noted.

Results: Sarcopenia risk was detected in 17 (10.9%) patients whose median age was higher than the others. Increased risk for sarcopenia was higher in women, lack of education, use of assisted respirators at home, having a psychiatric illness, losing > 10% weight during the hospitalization, and being treated in the intensive care unit. Multiple regression analysis showed that female gender (OR: 8.04 [1.51-42.76]), having a psychiatric illness (OR: 13.23 [2.12-82.51]), and losing > 10% weight during hospitalization (OR: 18.46 [2.57-132.72]) predicted the sarcopenia risk.

Conclusions: Sarcopenia should be closely monitored in patients with cases of severe inflammatory effect, inadequate food intake, and diminished physical activity such as hospitalized survivors of COVID-19.

Key words: COVID-19; malnutrition; preventive medicine; sarcopenia.

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Introduction

Sarcopenia is a progressive and generalized skeletal muscle disorder characterized by loss of muscle mass and function, and failure to provide appropriate care and treatment imposes high personal, social, and economic burdens [1]. Although it has been shown that the prevalence of sarcopenia in the community is approximately 10%, this increases to 40% in nursing home residents and 69% in rehabilitation patients after acute inpatient treatment [2-4]. Sarcopenia may develop because of aging with no other specific cause, or it may occur secondary to a systemic disease, especially a disease that can start inflammatory processes or cause a sedentary life, diminished physical activity, and prolonged hospitalization [1,5,6]. Malnutrition, hypoxia, decreased neuronal stimulation, or corticosteroid use are thought to cause sarcopenia [7]. It is associated with cognitive impairment and inflamed postoperative complications [8-10]. Sarcopenia increases all-cause mortality risk, as well as increases falls and fractures [11,12].

There is a bidirectional interaction between COVID-19 and sarcopenia. Longer hospital stays and higher mortality rates have been reported in patients with sarcopenia at the onset of COVID-19 [13]. Numerous patients suffer from new-onset sarcopenia during the post-acute COVID-19 period [14-16]. The severe inflammation induced by COVID-19 produces a catabolic state that affects the quantity, structure, and function of skeletal muscles, resulting in acute sarcopenia [17]. Symptoms such as loss of appetite, anosmia and dysgeusia can lead to inadequate food intake and exacerbation of catabolism [18]. In addition, long-term bed rest and diminished physical activity, hypoxia, and medically induced hypercortisolemia also contribute to the process [19-20].

"The International COVID-19 Airways Diseases Group" states sarcopenia to be considered a research

topic in their proposal to understand the long-term sequelae of COVID-19 [21]. In the current study, we aimed to determine the incidence of sarcopenia, reveal the risk factors predicting it, and take action for high-risk groups to prevent sarcopenia in hospitalized survivors of COVID-19.

Methodology

This is a single-center retrospective cohort study conducted between December 2021 and May 2022 in the post-COVID follow-up center of Trabzon Kanuni Traning and Research Hospital, that served as a reference center during the COVID-19 pandemic in Turkey. The study was approved by the Trabzon Kanuni Training and Research Hospital, Clinical Research Ethics Committee (11.04.2022, 2022/28). Written informed consent was obtained from the participants.

Patients who have been hospitalized because of COVID-19 are routinely called to post-COVID follow-up center at the 1st, 3rd, 6th, 12th, 18th, and 24th months after discharge. The health status of each patient was evaluated in the follow-ups by performing physical examinations, scales, and medical tests determined by the Ministry of Health, Republic of Turkey. The sample of the study comprised 168 patients who volunteered to participate after the mentioned routine evaluation was completed in this center.

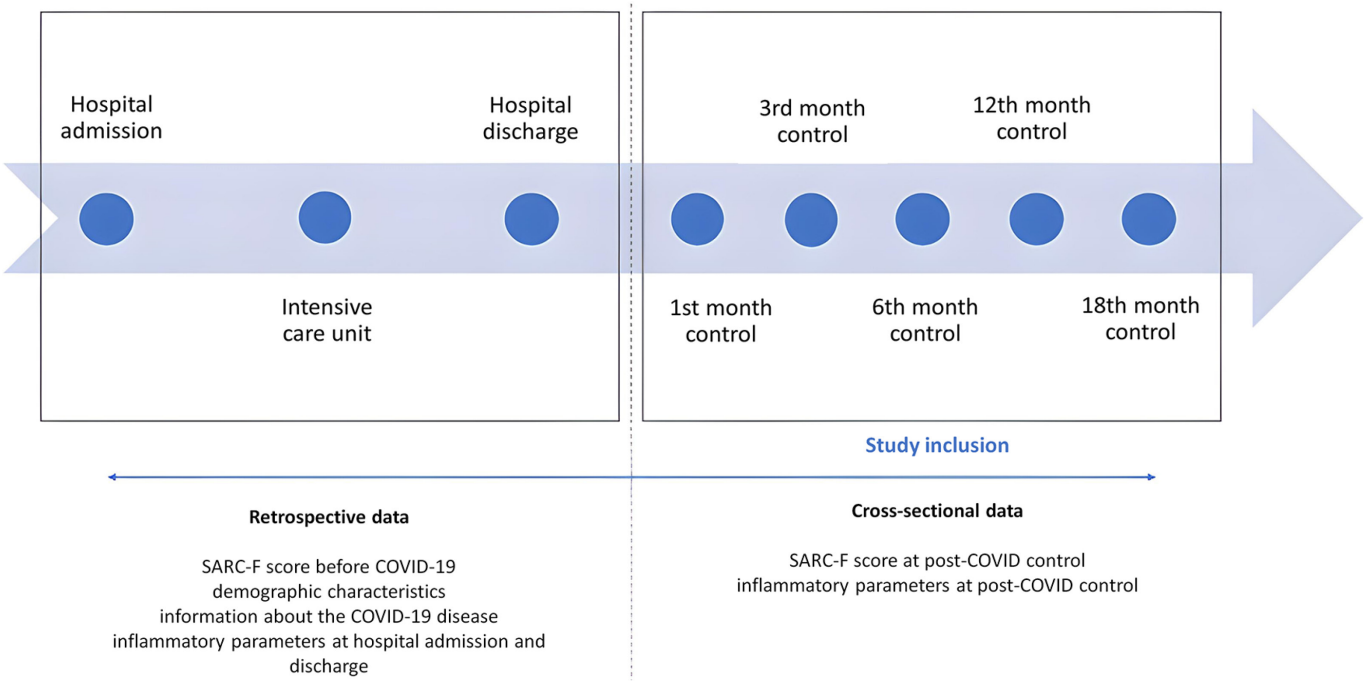
The SARC-F sarcopenia scale was administered to the participants, and they were asked to be evaluated separately, considering both before the disease and at the time of administration. Twelve patients with a SARC-F score ≥ 4 before COVID-19 were excluded from the study. The medical records of the remaining 156 participants were reviewed by the researchers, and their demographic characteristics, COVID-19 disease data, hemogram, and CRP parameters were also noted (Figure 1).

Sarcopenia risk was assessed using the SARC-F scale. This scale, which comprises five components: strength, assistance walking, rising from a chair, climbing stairs, and falling, was developed as a rapid screening test for the diagnosis of sarcopenia [22]. SARC-F items reflect health status changes associated with the consequences of sarcopenia. If the score is ≥ 4, the risk of sarcopenia is considered to be present. It has been reported that the Turkish version of the scale is valid and reliable [23].

Demographic characteristics of the participants, including age, gender, educational status, marital status, employment status, smoking history, presence of any allergy, use of assisted respirators at home, chronic diseases, and psychiatric illnesses, as well as the time elapsed after discharge, weight loss during the hospital stay and COVID-19 vaccines administered before getting ill and vaccine types were scanned from electronic patient records. Length of stay in the hospital was calculated as service, intensive care unit, and total.

To reveal the inflammation status in the participants, blood tests performed at the time of

Figure 1. Study flow diagram.



hospitalization, discharge, and post-COVID follow-up were reviewed. Among these tests, CRP and hemogram parameters of WBC, Neutrophil, Lymphocyte and Platelet counts and MPV were recorded. Neutrophil/Lymphocyte ratio (NLR), Platelet/Lymphocyte (PLR) ratio and MPV/Lymphocyte ratio (MPVLR) were calculated and involved in the study.

Statistical analyzes were performed using SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were made. The distribution of numerical variables was tested for normality using the Kolmogorov-Smirnov test. Mann-Whitney U test and Spearman test were used for comparison of numerical variables. The Chi-square test was used to compare categorical variables. Categorical variables were expressed as frequency (percentage) and numerical variables were expressed as median [interquartile range (IQR)]. Multivariate logistic regression analysis was performed to predict the risk of sarcopenia including statistically significant variables. A p value < 0.05 was considered significant.

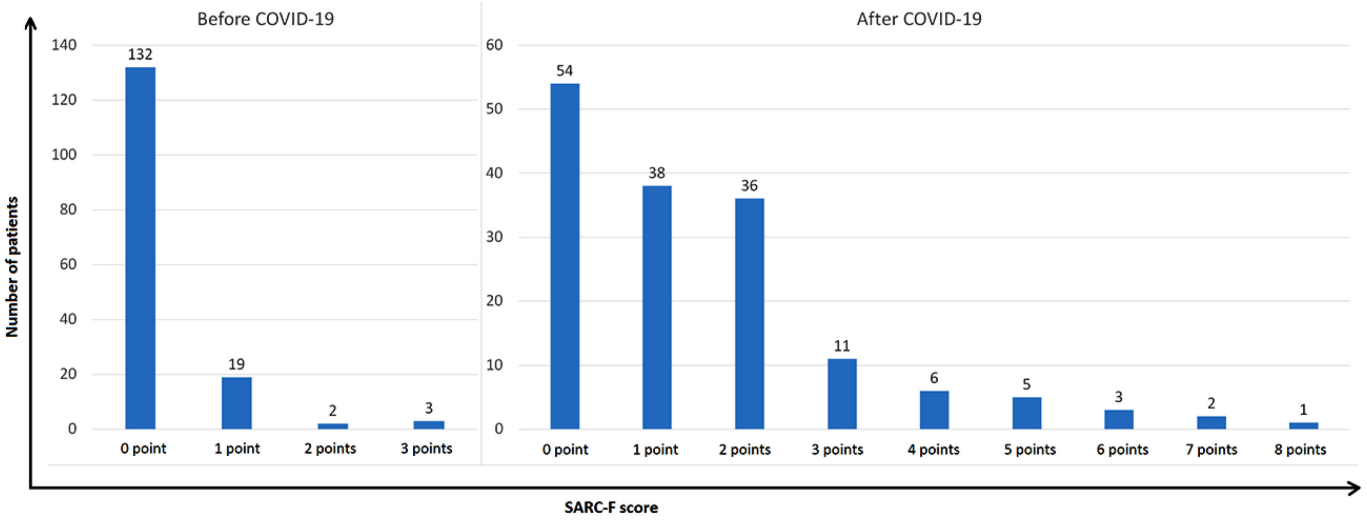
Results

The median age of 156 participants who were determined to have no signs of sarcopenia prior to contracting COVID-19 was 55 [IQR:22]. While 118 (75.6) of the participants were those who attended for the 1-3 months follow-up, 38 (24.4) were 6 months or more ago from discharge. Eighty-nine (57.1) of the participants were treated in the intensive care unit for at least 1 day with a median of 5 [IQR:6] days. The median length of hospital stay for all participants was 13 [IQR:13] days.

Table 1. Participants' demographic characteristics and information about the COVID-19 disease.

Characteristics	n (%)
Gender	
Female	64 (41.0)
Male	92 (59.0)
Educational status	
Uneducated	21 (14.0)
At least primary school graduate	129 (86.0)
Marital status	
Single	35 (23.3)
Married	115 (76.7)
Employment status	
Worker	59 (39.3)
Unemployed	91 (60.7)
Smoking status	
Current smoker	4 (2.7)
Former smoker	37 (24.8)
Non-smokers	108 (72.5)
Presence of any allergy	
Yes	19 (12.8)
No	130 (87.2)
Use of assisted respirators at home	
Yes	6 (4.0)
No	145 (96.0)
Chronic disease	
Yes	76 (48.7)
Hypertension	49 (31.4)
Diabetes Mellitus	29 (18.6)
Lung disease	15 (9.6)
Thyroid disease	14 (9.0)
Cardiovascular disease	9 (5.8)
Neurological disease	5 (3.2)
Rheumatic disease	4 (2.6)
No	80 (51.3)
Psychiatric illness	
Yes	11 (7.1)
No	145 (92.9)
Weight loss during hospitalization	
≤10%	92 (64.3)
>10%	51 (35.7)
At least two doses of COVID-19 vaccine	
Yes	65 (42.8)
Inactivated virus vaccine	55 (36.2)
mRNA vaccine	10 (6.6)
No	87 (57.2)

Figure 2. Distribution of SARC-F score among participants before and after COVID-19.



Participants demographic characteristics and COVID-19 disease data are shown in Table 1.

While the SARC-F scores of the participants increased by a median of 1 [IQR:2] point at the time of administration compared to pre-COVID-19, sarcopenia risk was detected in 17 (10.9) patients (Figure 2).

The median age of the patients with sarcopenia was higher than the others (65 [IQR:19] vs. 54 [IQR:23], p = 0.023), and there was also a positive correlation between age and the increase in the SARC-F score (r = 0.161, p = 0,045). Increased risk for sarcopenia was higher in women, lack of education, use of assisted respirators at home, having a psychiatric illness, losing over 10% weight during the hospitalization, and being treated in the intensive care unit. Comparison of the sarcopenia risk and the difference in the SARC-F scale according to participants' demographic characteristics and the COVID-19 disease data is shown in Table 2.

There were correlations between the WBC, lymphocyte and MPVLR detected in the post-COVID follow-up and the increase in the SARC-F score (r = 0.164, p = 0.041, r = 0.208, p = 0.009, r = -0.244, p = 0.002, respectively). No statistically significant relationship was found between other inflammatory parameters at hospital admission, discharge, and post-COVID follow-up, and the risk of sarcopenia or an increase in the SARC-F score.

Multiple regression analysis showed that female sexuality (OR: 8.04 [1.51 - 42.76]), having a psychiatric illness (OR: 13.23 [2.12 - 82.51]), and losing > 10% weight during hospitalization (OR: 18.46 [2.57 - 132.72]) were independent risk factors for sarcopenia.

Discussion

As a result of our study, it was determined that the sarcopenia risk occurs in one out of every 10 hospitalized survivors of COVID-19 patients who were

Table 2. Comparison of the sarcopenia risk and the difference in the SARC-F scale according to participants' demographic characteristics and information about the COVID-19 disease.

Characteristics	Sarcopenia risk	*p* value	Difference in the SARC-F	*p* value
Age (years)	65 [19]	0.023	0.161*	0.045
Gender		0.035		0.379
Female	11 (17.2)		1 [2]	
Male	6 (6.5)		1 [2]	
Educational status		<0,001		0.026
Uneducated	8 (38.1)		2 [4]	
At least primary school graduate	9 (7.0)		1 [2]	
Marital status		1		0.658
Single	4 (11.4)		1 [2]	
Married	13 (11.3)		1 [2]	
Employment status		0.157		0.888
Worker	4 (6.8)		1 [2]	
Unemployed	13 (14.3)		1 [2]	
Presence of any allergy		1		0.780
Yes	2 (10.5)		1 [2]	
No	15 (11.5)		1 [2]	
Use of assisted respirators at home		0.019		0.035
Yes	3 (50.0)		1 [2]	
No	14 (9.7)		3.5 [6]	
Chronic disease		0.377		0.823
Yes	10 (13.2)		1 [2]	
No	7 (8.8)		1 [2]	
Psychiatric illness		0.020		0.124
Yes	4 (36.4)		2 [3]	
No	13 (9.0)		1 [2]	
Time elapsed after discharge		0.367		0.038
1-3 months	11 (9.3)		1 [2]	
≥6 months	6 (15.8)		1.5 [3]	
Weight loss during hospitalization		0.003		0.001
≤10%	5 (5.4)		1 [1]	
>10%	11 (21.6)		1 [3]	
At least two doses of COVID-19 vaccine		0.368		0.241
Yes	9 (13.8)		1 [2]	
No	8 (9.2)		1 [2]	
Intensive care unit treatment		0.026		<0,001
Yes	14 (15.7)		1 [2]	
No	3 (4.5)		0 [1]	
Length of stay in intensive care unit (days)	7 [8]	0.067	0,085*	0,427
Total length of stay in the hospital (days)	23.5 [18]	0.107	0,269*	0,001

*r value; Data are given as median [interquartile range] or n (%).

predicted to have no risk of sarcopenia before the disease. Studies are reporting varied results owing to the evaluation method of sarcopenia, the time of evaluation, and the characteristics of the researched population. A study conducted in Italy reported the prevalence of sarcopenia as 19.5% in which the hand grip strength was evaluated for the diagnosis of sarcopenia, and patients with an average recovery time of 3 months from COVID-19 disease were included [16]. Another study in which the SARC-F scale was used, the risk of sarcopenia was found in one-fifth of the patients in the 1st month post-COVID, whereas the frequency of hospitalized patients only in the intensive care unit was reported approximately 90% immediately after discharge [24-25]. In our study, lower rates about sarcopenia seem to have been determined according to these reported findings. First, we only tried to identify the newly emerging sarcopenia risk and the factors that may affect it and evaluated the incidence. When we calculate the prevalence with our data, this rate is 17%. In addition, that half of the participants did not receive intensive care treatment may suggest that this group had a relatively mild disease and reduced the frequency of sarcopenia. Eventually, only three of the patients who did not receive intensive care treatment were at risk of sarcopenia.

We determined female gender as a risk factor for sarcopenia risk. Testosterone hormone in men has a protective influence in terms of muscle metabolism may have led to this result [26,27]. In addition, studies report that post-acute COVID symptoms are more common in women [28-30]. It is also known that mortality because of COVID-19 is higher in men [31]. The higher survival rate of women among severely ill patients, who are more likely to develop sarcopenia afterwards, may have suggested that women are at greater risk of sarcopenia. The other parameter predicting the risk of sarcopenia was >10% weight loss during the disease. Numerous studies in the literature reporting the strong relationship between malnutrition and sarcopenia make this result understandable [3,32-34]. Finally, we found that having any psychiatric illness before COVID-19 increased the risk of sarcopenia. Various studies have reported that depression is associated with sarcopenia [35,36]. This can be explained by the fact that this patient group is malnourished during and after the disease process and has a lower motivation in terms of rehabilitation, as well as the possibility of creating false positives by giving relatively more negative answers to SARC-F scale questions.

Although we observed a correlation between some inflammatory parameters and the change in SARC-F score, none of the inflammatory parameters at disease onset, discharge, or post-COVID follow-up predicted the sarcopenia risk. Although this result is surprising to us, should not be mistaken. It is clear that inflammation both directly increases muscle catabolism and leads to malnutrition, paving the way for the development of sarcopenia [37-40]. That the entire population included in our study was exposed to high levels of inflammation because of COVID-19 may have caused no statistical difference.

"European Working Group on Sarcopenia in Older People" defines sarcopenia lasting ≥ 6 months as chronic sarcopenia [1]. In our study, the risk of sarcopenia was observed at a rate of 15.8% in those who were survived from COVID-19 for ≥ 6 months. Among the patients included in the study, the longest period after discharge was 18 months after the disease, and the number of these was limited. It makes difficult to comment on the persistence of sarcopenia. However, to reveal this combat long time follow-ups in patients under risk could be an issue of future studies.

Although the SARC-F scale is very successful in indicating the sarcopenia risk, the diagnosis of sarcopenia is made by demonstrating low muscle mass and low muscle strength [1]. Further studies in which these parameters will be evaluated with objective measurements will contribute to the subject. Because of the retrospective nature of the study, the presence of sarcopenia before COVID-19 in the participants was tried to be determined with the SARC-F scale applied at the time of post- COVID follow-up. Recall factor limited our study nevertheless we think it did not have a significant impact on our findings. However, a scale applied at the admission to the hospital would have produced more accurate results about patients. Finally, patients who were called after discharge and came for follow-up were included in our study. We do not know whether the patients who did not come for control did not apply because they felt healthy or too bad to come to the hospital. This may have overestimated or underestimated the incidence of sarcopenia.

Conclusions

Our study showed that a significant proportion of hospitalized survivors of COVID-19 patients without any previous signs of sarcopenia are at risk for sarcopenia. It would be reasonable to monitor sarcopenia and take precautions by providing appropriate interventions, in cases where severe inflammatory effect is observed and patients' food

intake and movements are restricted, such as COVID-19, especially in women and those with psychiatric diseases. Governments should take into consideration of stakeholders' advices in terms of sarcopenia management by supplying standardized devices on diagnosis and providing rehabilitation services in population under risk.

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