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Role of sarcopenia risk in predicting COVID-19 severity and length of hospital stay in older adults: a prospective cohort study

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Abstract

Sarcopenia is more common in the elderly and causes adverse outcomes with increased morbidity and mortality. This prospective cohort study assessed the association of sarcopenia risk with the severity of COVID-19 at the time of admission and during hospitalisation and the length of hospital stay. Two hundred patients (aged ≥ 60 years) who were hospitalised for COVID-19 were enrolled using consecutive sampling between 29 December 2020 and 20 May 2021. The sarcopenia score of the patients was assessed using the Strength, Assistance in walking, Rising from a chair, Climbing stairs, and Falls questionnaire. The severity of COVID-19 was determined using the modified National Early Warning Score (m-NEWS) system for 2019 n-CoV-infected patients at admission (T1), day three (T2) and at discharge (T3). Data were analysed using SPSS, version 22 and STATA, version 14. Of the 165 patients included, thirty four (20·6 %) were at risk of sarcopenia. The length of hospital stay was slightly longer in patients with sarcopenia risk, but the difference was not significant ($P = 0·600$). The adjusted OR of respiratory rate (RR) > 20 /min at T1 for the sarcopenia risk group was 6·7-times higher than that for the non-sarcopenic group ($P = 0·002$). According to generalised estimating equations, after adjusting for confounding factors, the m-NEWS score was 5·6 units higher in patients at risk of sarcopenia ($P < 0·001$). Sarcopenia risk could exacerbate COVID-19 severity and increase RR at admission, as well as the need for oxygen therapy at discharge.

Key words: **Sarcopenia: SARC-F questionnaire: COVID-19: National early warning score: Respiratory rate**

Coronavirus disease 2019 (COVID-19) has been a public health emergency since March 2020[1]. This severe acute respiratory syndrome coronavirus 2 has infected over 480 million individuals and caused more than 6 million deaths worldwide[2]. The common symptoms of COVID-19 are fever, fatigue, headache, diarrhoea, anorexia and loss of taste and smell, as well as respiratory symptoms such as cough and shortness of breath. Moreover, interstitial pneumonia may result in acute respiratory distress syndrome with subsequent sepsis-induced coagulopathy and multiple organ dysfunction[3,4]. Adherence to safety measures and strengthening the immune system are important approaches for protecting individuals against COVID-19 until approved pharmacological therapies and vaccines become globally available[3,5].

The overall prevalence and number of severe cases of COVID-19 are higher among older individuals[6]. Factors such as sarcopenia, chronic diseases and nutritional inadequacy, which are more prevalent in older adults, can adversely affect the immune system and physiological function[6–8].

Particularly, sarcopenia is a progressive, generalised skeletal muscle disorder defined by the loss of muscle mass, physical performance and strength[9,10]. Risk factors for this disorder include ageing, nutritional deficiency, chronic diseases, physical inactivity, anxiety and very low 25-hydroxyvitamin D levels[11]. The prevalence of sarcopenia in the elderly ranges from 9·9 to 40·4 %, according to a systematic review[12]. This prevalence's range depend on factors such as the reference used for its definition, age, gender and ethnicity[11,13]. Specifically, different definitions of sarcopenia do not necessarily measure the same underlying variables; thus, even within the same population, sarcopenia estimation can vary depending on the definition[14]. In addition, sarcopenia is more prevalent among non-Asian

Abbreviations: COVID-19, coronavirus disease 2019; m-NEWS, modified National Early Warning Score; RR, respiratory rate; SARC-F, Strength, Assistance in walking, Rising from a chair, Climbing stairs, and Falls.

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individuals[15], men older than 80 years and women younger than 70 years[16].

Nutritional status, sarcopenia and the immune system are strongly related to each other. Nutritional deficiency exacerbates sarcopenia and as a result will weaken the immune system[17]. In COVID-19 patients, sarcopenia can cause deterioration of respiratory system function by weakening the muscles involved in respiration. Moreover, it can increase the risk of aspiration because of its negative impact on the muscles involved in swallowing[11,18]. On the other hand, a combination of obesity and sarcopenia can result in a state called sarcopenic obesity, in which there is a reduction in muscle mass in addition to an elevation in fat mass[19]. Studies have shown that the prevalence of systemic inflammation and oxidative stress is higher in sarcopenic obesity than in sarcopenia alone and can result in the deterioration of immune system function[20].

Information about the sarcopenia effect on the severity of COVID-19 is rare and controversial. In a previous study on hospitalised COVID-19 patients, with a median age of 62 years, sarcopenia was associated with a longer hospital stay. The authors assessed the severity of the disease using the National Early Warning Score system at baseline and found a significant difference between sarcopenic and non-sarcopenic groups[21]. The National Early Warning Score is a system for scoring the physiological measurements that enable the early detection of clinical deterioration[22]. However, another study reported no significant difference between patients with low and normal skeletal muscle index in terms of mortality, admission to the intensive care unit and the National Early Warning Score at baseline (median age, 51 years)[23].

It is clear that prevention, early diagnosis and treatment of sarcopenia are important for the management of COVID-19 and other acute respiratory diseases[18]. Therefore, the present study assessed the potential effect of sarcopenia risk on the severity of COVID-19 at admission and during hospitalisation in a large sample of older patients.

Materials and methods

Study population

This prospective cohort study was performed at the Nikan Hospital in Tehran, Iran, which is a referral centre for COVID-19. All subjects were patients aged 60 years or older, admitted to the hospital between 29 December 2020 and 20 May 2021, with a confirmed diagnosis of COVID-19 according to the Centers for Disease Control and Prevention guidelines. The COVID-19 test used was real-time PCR for nasopharyngeal and oropharyngeal samples. Those who had a history of hepatic and end-stage renal disease, as well those undergoing dialysis, were not included. The participants were enrolled using consecutive sampling.

Sample size calculation was performed according to Fleiss' odds-based sample size calculation method[24]. Ratio (unexposed/exposed), percent outcome in unexposed group and OR were used. Based on the results of Yao Ma *et al.*[25], who reported that among their initial population of 114 patients, twenty-six out of thirty-eight subjects with risk of sarcopenia and seventeen out of seventy-six patients without risk of sarcopenia (according to Strength, Assistance in walking, Rising from a chair, Climbing stairs, and Falls (SARF-C)) were diagnosed with severe COVID-19, the current study obtained a population of 164 patients to reach the two-sided confidence level of 95 % at a power of 90 %. Because of the high likelihood of dropouts from this study of elderly patients with COVID-19, we considered a 20 % dropout rate and obtained 200 initial participants. The Epi Info™, version 7.2.5.0 (STATCALC), was used to calculate the sample size.

Sarcopenia screening

For all subjects, the SARC-F questionnaire was used for screening sarcopenia (online Supplementary Table S1)[26]. This questionnaire contains five questions that evaluate risk of sarcopenia. Out of a total possible score of 10, a score ≥ 4 indicates a risk of sarcopenia[27]. Because COVID-19 safety precautions encourage decreased contact between patients and researchers, we did not complete the SARC-F questionnaire during hospital stay. After discharge, the subjects were contacted and the SARC-F questionnaire was completed. The participants were asked to complete questionnaire based on their pre-COVID-19 condition.

Baseline characteristics

The baseline demographic characteristics, comorbidities and laboratory results, which were recorded during the first 24 h after admission, were extracted from the patients' electronic records in accordance with pandemic health protocols and to minimise physical contact with patients. Demographic characteristics encompassed age, sex, marital status and education. Comorbidities included diabetes mellitus, hypertension, CVD, chronic kidney disease, respiratory disease, cancer and chronic digestive problems, which result in a decrease of nutrient intake or absorption, as well as surgeries that may cause weight reduction and the use of immunosuppressants.

The blood chemistry reported: leucocytes, lymphocytes, neutrophils, platelets and erythrocytes counts, as well as the Hb concentration, prothrombin tprothrombin time me, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, creatine phosphokinase and ferritin levels. Fasting blood samples (5 cc) were collected from the anterior arm veins of the patients, centrifuged and their serum samples were isolated. Complete blood count was performed using a cell counter (Nihdon Kohden Celltac E). Prothrombin time was estimated by coagulation method (clot) using the appropriate kit (Thermo Fisher Scientific). Serum levels of aspartate aminotransferase and alanine aminotransferase were determined using the appropriate kit with International Federation of Clinical Chemistry (IFCC/UV) method (Ziest Chem; Iran). Serum level of alkaline phosphatase was determined using the appropriate kit with color spectrometric spectrophotometry method (Pars Lab). Serum creatine phosphokinase activity was detected using an auto-analyser (Biorex fars; Iran). Serum ferritin levels were determined by ELISA using a human ferritin enzyme immunoassay test kit (Immunobiological Laboratories; Germany).

Anthropometric assessments

A trained nutritionist measured weight, height BMI of all participants at the time of admission. If the patient was able to stand, the weight was measured using a Seca digital scale (model 813) with an accuracy of 100 g (bearing capacity of up to 200 kg). The participants were barefoot and wore the least possible clothing when weighed. The standing height without shoes was assessed using a tape measure mounted on the wall with a precision of 0·1 cm. The weights of patients who were unable to stand (n 10) were estimated using the mid-arm circumference as weight (kg) = 4 × (mid-arm circumference (cm))–50[28]. For individuals with spinal deformation (n 5), the knee height was used to estimate height. For males, this was predicted as height (cm) = 62·913 + (2·077 × knee height (cm)), and for females, it was predicted as height (cm) = 76·362 + (1·76 × knee height (cm))[29]. BMI was calculated as weight (kg)/height^2 (m^2).

Malnutrition screening

Nutrition risk screening 2002 was used to screen for malnutrition[30]. This screening tool has two steps. The initial step consists of four yes/no questions. If the subjects answered yes to any of the questions in the primary step, they moved to the second step. A score of ≥ three out of the maximum of seven points indicated that the subject was nutritionally at risk[31]. This screening was completed at the time of admission.

COVID-19 clinical presentation

COVID-19 severity was determined with the modified National Early Warning Score (m-NEWS) for 2019 n-CoV-infected patients[32] (online Supplementary Table S2). Clinical presentation of COVID-19 signs, including systolic blood pressure (mmHg), respiratory rate (RR; per min), pulse rate (per min), body temperature (T; °C), consciousness, oxygen saturation (%) and O_2 therapy requirement, was measured at three times: at admission (T1), three days after admission (T2) and at discharge (T3). The length of hospital stay, COVID-19 symptoms at admission (cough, dyspnoea, fever, digestive disorders, anorexia and headache) and presence of pulmonary involvement as determined by lung computed tomography were recorded. Chest computed tomography was obtained within 24 h of admission.

Ethical approval and patient consents

The study protocol was approved by the Research and Technology Deputy of Shahid Beheshti University of Medical Sciences (research number: 25392) and the Ethics Committee of Shahid Beheshti University of Medical Sciences (ethics code: IR.SBMU.NNFTRI.REC.1399.060) on 27 December 2020. Before data collection, implementation methods and study objectives were explained to the patients, and all participants signed informed consent forms.

Statistical analysis

All data collected were analysed using Statistical Package Software for Social Science, version 22 (SPSS) and STATA, version 14. Data distribution normality was assessed using the Kolmogorov–Smirnov test. Quantitative variables were described as mean and standard deviation (SD). Qualitative variables were described as percentages. Participants at risk of sarcopenia were compared with non-sarcopenic participants using independent samples t test for quantitative variables and Pearson's χ^2 test or Fisher's exact test for qualitative variables with a continuity correction for 2 × 2 tables.

Binary logistic regression was used to associate having a systolic blood pressure ≥ 130 mmHg, an RR > 20 /min[33], a pulse rate > 100 /min[34], a body temperature ≥ 38°C, a O_2 saturation < 94 %[35] and the need for oxygen therapy, with the presence or absence of sarcopenia. Repeated measures ANOVA was used to evaluate changes in the m-NEWS score in the risk of sarcopenia and non-sarcopenic groups. Generalised estimating equations were used to determine the multiplicity of these changes between sarcopenia and the m-NEWS score at different times after controlling for the effect of confounding variables (P < 0·200 in the univariate test). Generalised estimating equations were calculated using STATA software. Two-tailed tests were performed, and statistical significance was set at P < 0·050.

Results

Of the 200 eligible older people originally included in our study, five participants required haemodialysis due to COVID-19 complications, twenty-three participants did not cooperate in filling out the SARC-F questionnaire and seven patients died. Thus, the results were obtained from the remaining 165 participants with COVID-19 (Fig. 1). The mean (SD) age of 165 participants was 69·0 (SD 7·6) years (median: 68; minimum (min): 60; maximum (max): 95). The mean (SD) weight and

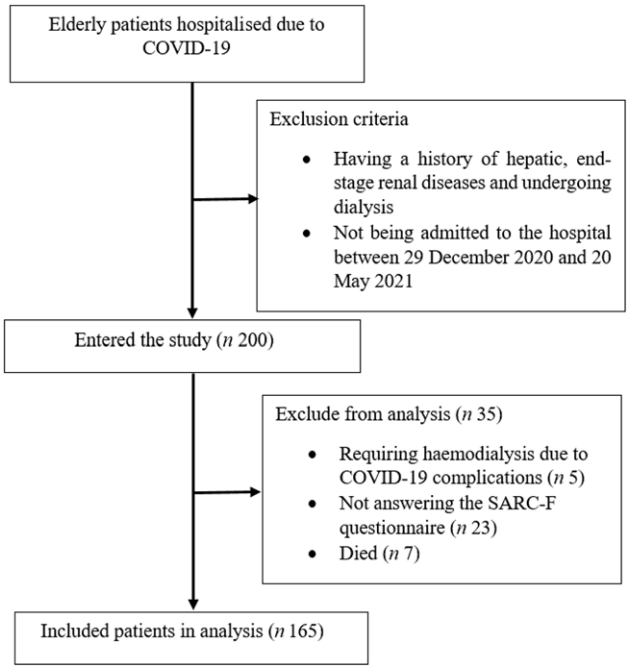

Fig. 1. Flow diagram of the participants.

Table 1. Baseline characteristics of COVID-19 participants

	All (*n* 165)		Groups: Sarcopenia risk (*n* 34)		Groups: Non-Sarcopenic (*n* 131)		
Qualitative variables	*n*	%	*n*	%	*n*	%	*P*
Sex							
Female	73	44·2	23	67·6	50	38·2	0·002*
Male	92	55·8	11	32·4	81	61·8	
Marital status							
Single	6	3·6	3	8·8	3	2·3	0·103†
Married	159	96·4	31	91·2	128	97·7	
Comorbidities (yes)							
Diabetes mellitus	70	42·4	12	35·3	58	44·3	0·345*
Hypertension	75	45·5	19	55·9	56	42·7	0·171*
CVD	64	38·8	18	52·9	46	35·1	0·057*
Chronic kidney disease	6	3·6	2	5·9	4	3·1	0·604†
Respiratory disease	8	4·8	1	2·9	7	5·3	>0·99†
Cancer	17	10·3	2	5·9	15	11·5	0·529†
Chronic digestive problem	87	52·7	24	70·6	63	48·1	0·019*
Surgery	10	6·1	2	5·9	8	6·1	>0·99†
Malnutrition (yes)	7	4·2	2	5·9	5	3·8	0·629†
Quantitative variables	Mean	SD	Mean	SD	Mean	SD	*P*‡
Age (years)	69·0	7·6	75·1	9·0	67·5	6·4	<0·001
BMI (kg/m^2)	27·9	4·6	28·4	4·7	27·8	4·6	0·483
Laboratory results at admission							
WBC count (μl/10^3)	6·9	3·2	8·0	3·5	6·6	3·1	0·022
Lymphocyte count (%)	19·3	9·3	20·8	9·7	18·9	9·2	0·295
Neutrophil count (%)	73·5	11·3	71·3	11·6	74·1	11·2	0·203
PLT (μl/10^3)	215·2	90·9	245·3	113·2	207·4	82·8	0·032
Erythrocytes count (μl/10^6)	4·9	0·9	4·6	0·6	4·9	0·9	0·056
Hb (g/dl)	12·8	1·6	12·3	1·4	12·9	1·6	0·027
PT (second)	13·9	2·3	14·4	3·4	13·8	1·9	0·188
AST (IU/l)	40·1	31·6	34·6	14·9	41·6	34·6	0·264
ALT (IU/l)	31·4	19·8	28·0	13·2	32·2	21·2	0·283
ALP (IU/l)	158·0	67·6	171·6	94·1	154·5	58·8	0·202
CPK (U/l)	151·1	148·9	109·9	86·3	162·2	160·2	0·105
Ferritin (ng/ml)	547·4	417·7	374·5	309·8	584·7	429·4	0·005

PLT, platelet; PT, prothrombin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; CPK, creatine phosphokinase.
* Obtained from χ^2.
† Obtained from Fisher's exact test.
‡ Obtained from independent samples *t* test.

BMI of participants were 79·0 (SD 13·8) kg and 27·9 (SD 4·6) kg/m^2, respectively.

Using the SARC-F, 131 participants (79·4 %) were non-sarcopenic and thirty-four participants (20·6 %) were at risk of sarcopenia. Table 1 shows the baseline characteristics of at risk of sarcopenia compared with non-sarcopenic participants. The sarcopenia risk group was significantly older than the non-sarcopenic group (75·1 (SD 9·0) *v.* 67·5 (SD 6·4) years, $P < 0·001$) and had a greater proportion of females (23 (67·6 %) *v.* 50 (38·2 %) in the non-sarcopenic group, $P = 0·002$). Also, it was found that 70·6 % of participants who were at risk of sarcopenia had chronic digestive problems (chronic nausea, vomiting, chewing disorders such as needing dentures, dysphagia, peptic ulcer, bloating, constipation and diarrhoea), while 48·1 % of the non-sarcopenic group had such conditions ($P = 0·019$). No statistically significant differences were observed between groups in terms of malnutrition, BMI or other demographic values and past medical history characteristics.

Baseline characteristics also include the results of the laboratory tests performed within 24 h of admission are presented in Table 1. The mean leucocytes count and platelets in the sarcopenia risk group were significantly higher than in the non-sarcopenic group (leucocytes count: 8·0 (SD 3·5) *v.* 6·6 (SD 3·1) μl/10^3, $P = 0·022$; platelets: 245·3 (SD 113·2) *v.* 207·4 (SD 82·8) μl/10^3, $P = 0·032$), whereas the mean Hb concentration in the sarcopenia risk group was significantly lower than in the non-sarcopenic group (12·3 (SD 1·4) *v.* 12·9 (SD 1·6) g/dl, $P = 0·027$). As well, the mean serum ferritin was lower in the sarcopenia risk group (374·5 (SD 309·8) *v.* 584·7 (SD 429·4) ng/ml, $P = 0·005$). No statistically significant differences were observed between groups for the other studied blood tests.

Table 2 shows COVID-19 clinical presentation of the participants. Before adjusting for confounding factors at the three studied time points, all COVID-19 participants at risk of sarcopenia required oxygen therapy at T1 ($P = 0·025$). Approximately, 61·8 % of the participants at risk of sarcopenia and 38·9 % of the non-sarcopenic group required oxygen therapy at T3 ($P = 0·004$). Also, the mean RR at T1 in the sarcopenia risk group was significantly higher than in the non-sarcopenic group (20·4 (SD 3·1) *v.* 19·1 (SD 2·3) /min, $P = 0·034$).

Table 2. COVID-19 clinical presentation in participants

	All (*n* 165)		Groups				
			Sarcopenia risk (*n* 34)		Non-Sarcopenic (*n* 131)		
Qualitative variables	*n*	%	*n*	%	*n*	%	*P*
Admission							
O_2 therapy (yes)	148	89·7	34	100	114	87·0	0·025*
Pulmonary involvement detected by lung CT (yes)	144	87·3	32	94·1	112	85·5	0·252*
Three days after admission							
O_2 therapy (yes)	122	73·9	27	79·4	95	72·5	0·153†
Discharge							
O_2 therapy (yes)	72	43·6	21	61·8	51	38·9	0·004†
Quantitative variables	Mean	SD	Mean	SD	Mean	SD	*P*‡
Admission							
SBP (mmHg)	125·2	15·5	129·4	17·6	124·1	14·8	0·076
RR (/min)	19·4	2·5	20·4	3·1	19·1	2·3	0·034
PR (/min)	82·9	12·2	85·6	10·8	82·2	12·5	0·152
T (°C)	36·9	0·4	36·8	0·3	36·9	0·4	0·502
O_2 saturation (%)	90·8	4·9	90·4	3·6	90·9	5·2	0·550
Three days after admission							
SBP (mmHg)	115·0	14·6	114·4	15·6	115·2	14·5	0·788
RR (/min)	18·5	2·7	18·8	2·9	18·4	2·6	0·395
PR (/min)	76·8	13·6	80·4	19·8	75·9	11·5	0·111
T (°C)	36·6	0·4	36·6	0·4	36·6	0·4	0·736
O_2 saturation (%)	94·8	2·4	95·1	1·7	94·7	2·6	0·484
Discharge							
SBP (mmHg)	112·0	9·6	112·2	6·9	111·9	10·2	0·900
RR (/min)	17·8	1·4	17·6	1·3	17·8	1·4	0·481
PR (/min)	74·4	10·6	75·0	11·6	74·2	10·4	0·738
T (°C)	36·5	0·3	36·5	0·4	36·5	0·3	0·443
O_2 saturation (%)	95·7	2·3	95·8	1·8	95·7	2·5	0·911
Length of hospital stay (days)	9·9	4·1	10·3	4·1	9·9	4·1	0·600

CT, computerised tomography; SBP, systolic blood pressure; RR, respiratory rate, PR, pulse rate, T, body temperature.
* Obtained from Fisher's exact test.
† Obtained from χ^2.
‡ Obtained from independent samples *t* test.

Table 3. COVID-19 symptoms in participants at admission

	All (*n* 165)		Groups				
			Sarcopenia risk (*n* 34)		Non-Sarcopenic (*n* 131)		
Symptoms	*n*	%	*n*	%	*n*	%	*P*
Cough	106	64·6	20	60·6	86	65·6	0·588*
Dyspnoea	151	91·5	31	91·6	120	91·2	>0·99†
Fever	111	67·7	23	69·7	88	67·2	0·782*
Digestive disorders	49	29·9	12	36·4	37	28·2	0·362*
Anorexia	96	58·5	22	66·7	74	56·5	0·289*
Headache	53	32·3	14	42·4	39	29·8	0·165*

* Obtained from χ^2.
† Obtained from Fisher's exact test.

However, no statistically significant differences were observed between groups in terms of length of hospital stay. As shown in online Supplementary Table S3, two-way repeated measure ANOVA for the vital signs revealed that participants in both groups had significant decreasing trends from T1 to T3.

Table 3 shows COVID-19 symptoms in participants including cough, dyspnoea, fever, digestive disorders, anorexia and headache at admission. No significant differences were found between groups for typical COVID-19 symptoms.

We further assessed the association between vital signs, oxygen therapy and oxygen saturation with sarcopenia risk. For this purpose, we compared the OR of systolic blood pressure ≥ 130 mmHg, RR > 20 /min, pulse rate > 100 /min, body temperature ≥ 38°C, O_2 saturation < 94 % and the need for oxygen therapy for the sarcopenia risk and non-sarcopenic groups adjusted for age, sex and comorbidities (Table 4). The adjusted OR of RR > 20 /min at T1 for the sarcopenia risk group was 6·7 times higher than for the non-sarcopenia group (95 % CI 2·1, 22·0, $P = 0{\cdot}002$). The OR of the need for oxygen therapy at T3 was 5·1 times higher in participants at risk of sarcopenia than in the non-sarcopenic group (95 % CI 1·7, 15·4, $P = 0{\cdot}004$).

Finally, the m-NEWS score was assessed according to sarcopenia status. As shown in Table 5 and online Supplementary Fig. S1, regardless of the status of sarcopenia, the m-NEWS score decreased significantly over time (time effect; $P < 0{\cdot}001$). However, regardless of time, the m-NEWS score for the group at risk of sarcopenia was higher than for the non-sarcopenic group, and this difference was statistically significant (group effect; $P = 0{\cdot}002$). In the case of interaction effect, it was observed that the diminishing trend of the m-NEWS score in the sarcopenia risk and non-sarcopenic groups was similar, and this difference was not statistically significant ($P = 0{\cdot}199$).

Table 4. Association between vital signs, oxygen therapy and oxygen saturation with sarcopenia risk

	Admission			Three days after admission			Discharge		
Factors	OR	95 % CI	*P**	OR	95 % CI	*P*†	OR	95 % CI	*P*†
SBP ≥ 130 mmHg	1·4	0·6, 3·6	0·481	1·6	0·5, 5·8	0·453	< 0·001	< 0·001	>0·99
RR > 20/min	6·7	2·1, 22·0	0·002	2·1	0·5, 8·1	0·303	< 0·001	< 0·001	>0·99
PR > 100/min	2·4	0·6, 10·9	0·243	2·8	0·3, 30·5	0·400	7·9	0·2, 372·7	0·291
T ≥ 38°C	<0·001	<0·001	>0·99	Nobody	Nobody	–	Nobody	Nobody	–
O_2 saturation < 94 %	1·3	0·5, 3·5	0·674	0·8	0·2, 2·7	0·712	0·7	0·2, 3·1	0·637
Oxygen therapy needed	<0·001	<0·001	>0·99	1·5	0·3, 6·6	0·594	5·1	1·7, 15·4	0·004

SBP, systolic blood pressure; RR, respiratory rate, PR, pulse rate, T, body temperature.
As Hb could affect RR, we adjusted for Hb level at T1. However, since we measured Hb only at baseline, we did not adjust for this parameter at T2 and T3.
* Obtained from binary logistic regression, adjusted for age, sex, Hb, diabetes mellitus, hypertension, CVD, chronic kidney disease, respiratory disease, cancer, chronic digestive problem and history of surgery.
† Obtained from binary logistic regression, adjusted for age, sex, diabetes mellitus, hypertension, CVD, chronic kidney disease, respiratory disease, cancer, chronic digestive problem and history of surgery.

Table 5. Mean and SD of the modified-National Early Warning Scores (m-NEWS) at T1 to T3 follow-up times in both groups

	Groups			
	Sarcopenia risk (*n* 34)		Non-Sarcopenic (*n* 131)	
	Mean	SD	Mean	SD
m-NEWS, admission	8·0	1·7	6·3	2·5
m-NEWS, three days after admission	7·1	2·2	5·5	2·5
m-NEWS, discharge	5·5	1·6	4·3	2·5
	F statistics			*P**
Time effect	12·7			<0·001
Group effect	10·4			0·002
Interaction effect	1·6			0·199

* Obtained from two-way repeated measures ANOVA, adjusted for sex, diabetes mellitus, hypertension, CVD, chronic kidney disease, respiratory disease, cancer, chronic digestive problem and history of surgery.

Table 6. Linear mixed models examining status of sarcopenia as a predictor of COVID-19 severity

	Trimmed model				Complete model			
	β	SE	95 % CI	*P**	*β*	SE	95 % CI	*P*†
m-NEWS	1·9	0·5	0·9, 2·9	<0·001	5·6	1·2	3·3, 8·0	<0·001

m-NEWS, modified-National Early Warning Score for 2019 n-CoV patients.
* Obtained from generalised estimating equations.
† Obtained from generalised estimating equations, adjusted for age, sex, BMI, level of education, history of chronic digestive problem, CVD and hypertension, serum level of white blood cell, platelet, erythrocytes, prothrombin time, haemoglobin, creatine phosphokinase and ferritin, O_2 saturation, need for oxygen therapy, respiratory rate and pulse rate at T1.

Due to the m-NEWS score was higher in at risk of sarcopenia group, linear mixed models were used to examine the status of sarcopenia as a predictor of COVID-19 over the studied time points. As hypothesised, the models showed significant associations between sarcopenia status and the m-NEWS score in the trimmed model and in the complete model after controlling for age, sex, BMI, level of education, history of chronic digestive problems, CVD and hypertension, serum levels of leucocytes, platelets, erythrocytes, Hb, prothrombin time, creatine phosphokinase and ferritin, O_2 saturation, need for oxygen therapy, RR and pulse rate at T1. The m-NEWS score was 1·9 units higher in the group at risk of sarcopenia than in the non-sarcopenic group in the trimmed model (95 % CI: 0·9, 2·9, $P < 0·001$). The m-NEWS score was 5·6 units higher in the group at risk of sarcopenia than in the non-sarcopenic group in the complete model (95 % CI: 3·3, 8·0, $P < 0·001$) (Table 6).

Discussion

To the best of our knowledge, this is one of the first studies attempting to determine risk of sarcopenia using the SARC-F questionnaire and assessing the relationship between sarcopenia (at baseline) and the score of COVID-19 severity (m-NEWS) during a hospital stay. The validity of SARC-F has previously been confirmed by community screening sarcopenia[36,37]. During the pandemic, this questionnaire became more widely accepted as a screening test for sarcopenia due to quarantine[18,38]. In addition, as reported by previous studies, the m-NEWS system is appropriate for COVID-19 patients[22,39,40].

The current study showed that, after adjusting for confounding factors, the m-NEWS score in the group at risk of sarcopenia was 5·6-times higher than for the non-sarcopenic group. In agreement with our results, Yao Ma *et al.*[25] reported that COVID-19 participants with a greater risk of sarcopenia

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were at greater risk of severe forms of COVID-19. In this study[25], all patients were screened for sarcopenia on admission using the SARC-F scale like our study and the outcomes were assessed according to the WHO interim guidance for COVID-19.

One way to prevent COVID-19 is to quarantine and stay at home; thus, the community will face a greater prevalence of sarcopenia among the elderly caused by nutritional problems and reduced physical activity. A cohort study of older Dutch adults showed that most of them, especially those who lived alone, had difficulty obtaining food, skipped main meals, ate less than normal, and lost weight, leading to insufficient intake of energy and protein during the pandemic[41].

Protein metabolism disorders are evident in the elderly and are mainly related to an increased need for protein, inadequate food intake, decreased anabolism, elevated degradation and diminished protein synthesis due to inflammaging[42]. Ageing disturbs the balance of pro-inflammatory TNF-α, IL-1 and IL-6 with anti-inflammatory cytokines; this incites a mild inflammation, referred to as inflammaging[11,17,42]. The transcriptional activity of NF-κB also increases with ageing in a variety of tissues. NF-κB activates inflammatory cytokines, such as TNF-α, in the body[43]. Along with these inflammatory conditions, muscle proteins are broken down and their synthesis is affected, which can result in sarcopenia[11,44].

Studies have shown that, in patients with severe COVID-19, severe acute respiratory syndrome coronavirus 2 virus activates NF-κB, resulting in a cytokine storm[45]. In addition, during metabolic stress, such as in viral infections, skeletal muscles are catabolised to supply the amino acids required by the immune system, liver and gastrointestinal tract[46]. However, in sarcopenic patients, these reserves are low[11]; thus, severe COVID-19 is more probable[11]. Our results revealed that the m-NEWS scores for participants at risk of sarcopenia were greater than for non-sarcopenic participants. As anticipated, both groups showed diminishing the m-NEWS scores over time.

With quarantine, staying at home causes a decline in proper physical activity, leading to muscle atrophy and a decreased muscle strength[47]. Skeletal muscles release myokines, which play a role in autocrine and endocrine signalling, in addition to muscle regeneration and haemostasis. IL-15 is a myokine that activates natural killer cells and CD8 + T lymphocytes, which play an important role in the body's defense against viruses[21]. This indicates that sarcopenia is an independent risk factor for worse outcomes of COVID-19 infection[42].

We found that participants at risk of sarcopenia had greater RR than non-sarcopenic participants at T1, independent of the confounders of age, sex, comorbidities and Hb level. Moreover, participants at risk of sarcopenia were more likely to require oxygen therapy than non-sarcopenic participants at T3 due to COVID-19, after considering confounding factors. Oxygen therapy (simple mask, reserve bag, nasal prong, etc.) followed a standardised hospital protocol in Iran. A cross-sectional study showed that sarcopenic elderly individuals had lower maximum respiratory pressure and maximum expiratory pressure than non-sarcopenic elderly individuals[48]. A decrease in the diaphragmatic muscle thickness could also explain the higher respiration rates and requirement for O_2 therapy[11].

The duration of hospital stay between the at-risk for sarcopenia and non-sarcopenic groups had no statistically significant difference. In contrast, a recent study in South Korea found that people with sarcopenia had significantly longer hospital stays than those without sarcopenia[21]. In a recent study in Turkey, adults afflicted with COVID-19 underwent CT scans of the pectoralis muscle area and their outcomes (intubation, prolonged hospital stay and death) were measured[49]. They found that pectoralis muscle area was a predictor of longer hospital stays. Increased age is considered to be a strong, independent risk factor for a prolonged hospital stay[50]. One reason for the discrepancy between these results and those of our study could be that our investigation was carried out during COVID-19 peak in Iran. As a result of overcrowding of hospitals, patients continued treatment at home as soon as they were able to be discharged from hospital and continued to recover at home, but we only took into consideration the length of the hospital stay.

The strengths of the present study are as follows. First, recruitment was performed in a referral COVID-19 hospital; thus, participants from distinct financial, cultural and societal levels willingly participated in our study. Second, sarcopenia was screened using a web-based platform that ruled out the need for an appointment after discharge that could have been difficult for elderly patients to attend. In addition, the SARC-F questionnaire was completed by an expert nutritionist.

We also had some limitations, the SARC-F questionnaire was completed based on patient recall, and we did not confirm the data by measuring skeletal muscle mass and muscle strength[51]. However, the SARC-F questionnaire has previously been validated as an effective tool for assessing sarcopenia risk[25,52]. Also, we recorded the data required to calculate the m-NEWS at T1, T2 and T3, but we only recorded laboratory results and other COVID-19 symptoms (like cough, digestive disorders, anorexia and headache) at T1. Fifteen patients were unable to stand. Therefore, we had to use estimated weight and height for these patients. We checked the effect of this discrepancy in anthropometric measurements by repeating the statistical analysis after excluding the mentioned fifteen participants, and the results did not change (data are not shown here).

COVID-19 is more easily detected and tends to be more severe in older adults. This is related to a combination of age-related immune system weaknesses and comorbid disorders[53]. Therefore, it is recommended that older adults learn ways to prevent sarcopenia through virtual education during the pandemic[20]. Adequate intake of energy, protein, Ca, vitamin D and other micronutrients, along with increased physical activity, improved sleep quality and stress management would be helpful for preventing sarcopenia[17]. The recommended protein intake is at least 1·0 to 1·2 g/kg/d in healthy older adults, 1·2 to 1·5 g/kg/d in malnourished or sarcopenic older adults afflicted with acute or chronic illness and 2·0 g/kg/d for patients afflicted with severe illness such as COVID-19[18,54]. High-quality proteins should be equally distributed across the three main meals[55]. It is also recommended that all sarcopenic patients measure their 25-hydroxyvitamin D level[56].

This study has paved the way for further research to consider the relation between sarcopenia and COVID-19. It is

also recommended to measure skeletal muscle mass and muscle strength in addition to completion of the SARC-F questionnaire, as well as to monitor the long-term effects of sarcopenia on COVID-19 complications.

Conclusion

The results of this study showed that the presence of sarcopenia exacerbated COVID-19 severity. These results suggest that patients at risk of sarcopenia had higher RR at the time of admission. Our findings are promising but should be confirmed by more long-term cohort studies to establish a possible positive relationship between sarcopenia and severe COVID-19.

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Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S000711452200215X

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