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Egypt J Radiol Nucl Med (2024) 55:63
https://doi.org/10.1186/s43055-024-01232-z

Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH Open Access

Association between thoracic density and area with COVID-19 outcomes

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Abstract

Background The relationship between sarcopenia and the consequences of COVID-19 is not yet fully understood. It is noteworthy that information about muscle status can be easily retrieved by segmenting specific regions of skeletal muscles on CT scans. Our aim in this study was to investigate the relationship between sarcopenia and the consequences of COVID-19.

Methods In this analytical cross-sectional study, 338 patients with COVID-19 who had a positive PCR test for COVID-19 and underwent chest CT scan in Loghman-e-Hakim Hospital from July to September 2021 were evaluated. Age, sex, background diseases, mechanical ventilation, duration of hospitalization, as well as lab tests, ICU admission and mortality were extracted from patient records. The severity of COVID-19 disease and the area and density of paraspinal muscles at the level of T5 and T12 vertebrae were evaluated through chest CT scans.

Results Length of stay had significant relationship with T5 density (1.15 (< 0.001)) and T12 density (1.24 (< 0.001). The mean of T12 area (3.35 ($P = 0.005$) and T12 density 4.59 ($P = 0.012$) were significantly lower in ICU admitted. There was a significant relationship between mortality and age, cardiovascular disorders, COPD, underlying disease, length of stay, WBC and lymphocyte levels, as well as the severity of the disease.

Conclusions Based on the results of this study, we can infer that the use of CT scan in patients with COVID-19 and the determination of muscle area and density can predict the consequences of COVID-19, such as a longer duration of hospitalization, the need for admission to the ICU, and mortality.

Keywords Sarcopenia, COVID-19 disease, Area and density of paraspinal muscles, T5 and T12 vertebrae

Background

The COVID-19 disease is caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was first identified in Wuhan, China, in December 2019 [41]. Every day, people around the world are getting infected with this virus. According to various studies, many comorbidities have been identified that increase the probability of the disease progressing to a severe type, such as chronic obstructive respiratory disease (COPD), cardiovascular disease (CVD), obesity, and other conditions that suppress the immune system [19, 22–27], Obesity, diabetes mellitus (DM), and high blood pressure are among the comorbidities seen in hospitalized patients following COVID-19 [21, 52].

Identifying these factors can be beneficial for disease risk assessment and balancing hospital resources. Correlations have been seen between obesity and poor infection recovery outcomes in patients admitted to the intensive care unit (ICU), especially when sarcopenia is seen in association with overweight [13, 31, 34]. Obese patients have a higher risk of hospital and ICU admission, mechanical ventilation, and death [30, 48]. It has

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been shown that, in addition to weight, muscle volume reduction, especially in the chest, is associated with poor outcomes in the management of Covid-19 infection [17]. Sarcopenia is an age-related clinical syndrome characterized by progressive loss of skeletal muscle mass and strength [12].

Sarcopenia can be a cause for different courses of the Covid-19 disease between patients or a symptom of other diseases that lead to different courses of the disease. The relationship between sarcopenia and the consequences of Covid-19 is not yet fully understood [43]. It is noteworthy that information about muscle status can be easily retrieved by segmenting specific regions of skeletal muscles [3, 8, 18, 46]. Our aim in this study was to investigate the relationship between sarcopenia and the consequences of Covid-19 disease in patients with Covid-19 admitted to Loghman-e-Hakim Hospital from July to September 2021.

Methods

This study was conducted using a cross-sectional analytical method on patients with COVID-19 who were admitted to Loghman-e-Hakim Hospital from July to September 2021. Patients who were admitted to the hospital with a positive polymerase chain reaction (PCR) test for COVID-19 and underwent a chest CT scan in the first 24 h of admission, were included in the study. Patients with underlying neurological diseases, malignancies, and those under the age of 18 were excluded from the study.

While the COVID-19 disease outbreak took place in Iran, our tertiary referral center, encountered daily rises in the number of chest CT scan requests. A remarkable number of cases were younger than 40 years old and according to the Iranian Radiology Society (ISR) consensus [38], we applied a low-dose chest CT protocol mainly adjusted from lung cancer screening CT protocol [10]. Therefore, patients presenting in earlier days, underwent standard-dose CT scan; whereas, more recent cases underwent the low-dose protocol. Scanning parameters are presented in Table 1. Images were obtained with one of two CT scanners (Activion 16, Toshiba, Japan and Somatom scope power 16, Siemens Healthineers, Germany). The CT scan results were instantly transferred to picture archiving and communication system (PACS). Preliminary reports where available within 2 h.

Demographic information of patients, including age, sex, and underlying diseases such as DM, CVD, respiratory disease (asthma and COPD), chronic kidney disease (CKD), immune system deficiency, mechanical ventilation, the hospitalization time, as well as laboratory tests including white blood cell (WBC) and lymphocytes count, ICU admission, and mortality, was extracted from patient records. Additionally, the severity of COVID-19 disease and the area and density of paraspinal muscles at the level of T5 and T12 vertebrae (Figs. 1, 2, 3, 4) were evaluated by two experienced radiologists through observation and evaluation of chest CT scans of patients. In case of disagreement, a third person with more experience made the decision.

The severity of COVID-19 disease was quantitatively classified as follows: [4]

Illness severity: Score 1: No ground glass or consolidation/ Score 2: The presence of ground glass opacities

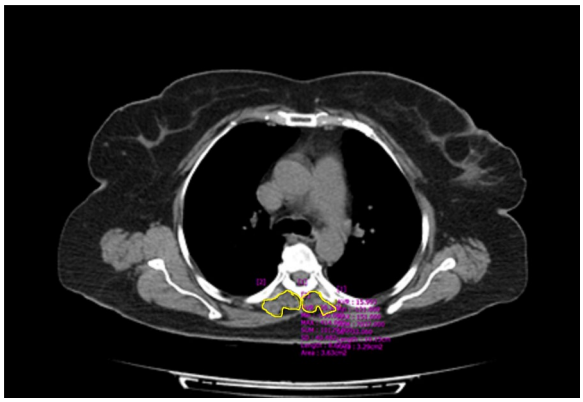

Fig. 1 Paraspinal muscles area at T5 level

Table 1 Standard-Dose and Low-Dose CT Protocols

Vendor	Activion 16, Canon		Somatom 16, Siemens	
Protocol	**Low-dose**	**Standard-dose**	**Low-dose**	**Standard-dose**
Scan type	Helical	Helical	Spiral	Spiral
Rotation time, s	0.75	0.75	0.6	0.6
Detector configuration, mm	16 × 1.0	16 × 1.0	16 × 1.2	16 × 1.2
Pitch	Fast (1.438)	Standard (0.938)	1.5	1
kV	120	120	110	130
mA/reference mA	30	80–500	20	110
Sure exposure/CARE dose	ON	ON	ON	ON

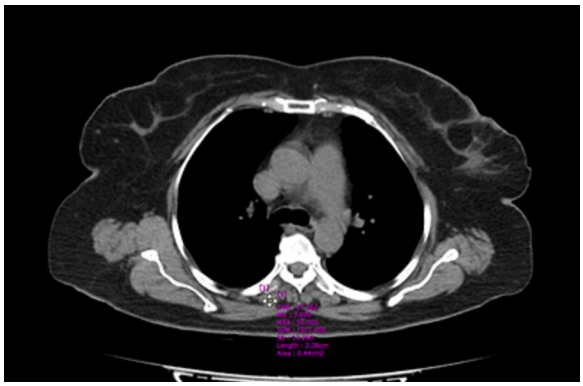

Fig. 2 Paraspinal muscles density at T5 level

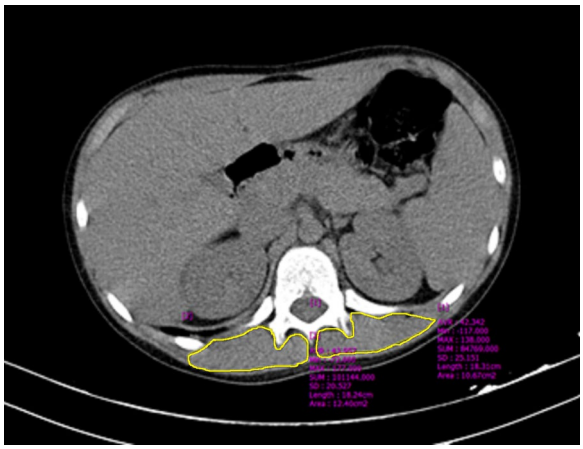

Fig. 3 Paraspinal muscles area at T12 level

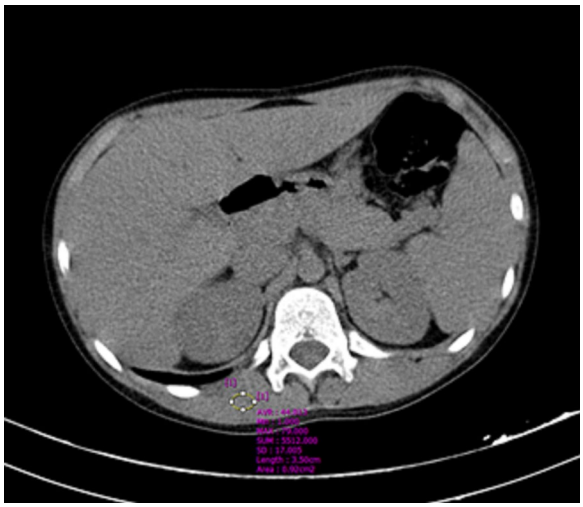

Fig. 4 Paraspinal muscles density at T12 level

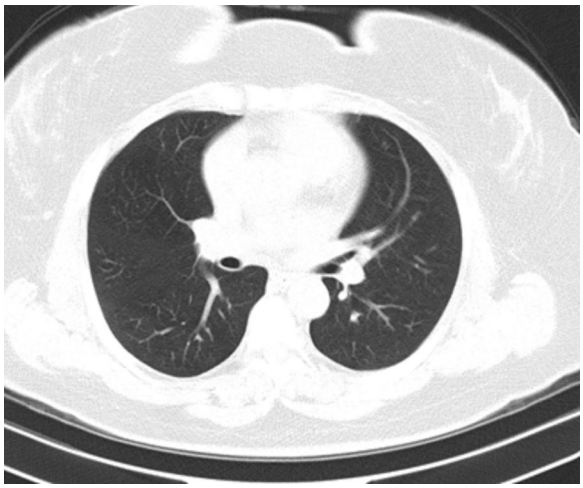

Fig. 5 COVID-19 disease severity score 1

Fig. 6 COVID-19 disease severity score 2

without consolidation Score/ 3: Simultaneous presence of ground glass opacities and consolidation/ Score 4: Presence of consolidation without ground glass opacities (Figs. 5, 6, 7, 8).

The data was analyzed using SPSS statistical analysis software. Independent sample T test, ANOVA, univariate and multivariate linear or logistic regression were used for analysis based on dependent variable. In Table 5, we ran a multiple linear regression with all of the variables (mortality, hospitalization time, ICU admission, mechanical ventilation, severity), and in Table 6, association between mortality and variables, was adjusted for T5 area and density and T12 area and density. In this study, written consent was obtained from the patients. All information was kept confidential, and all provisions of

Fig. 7 COVID-19 disease severity score 3

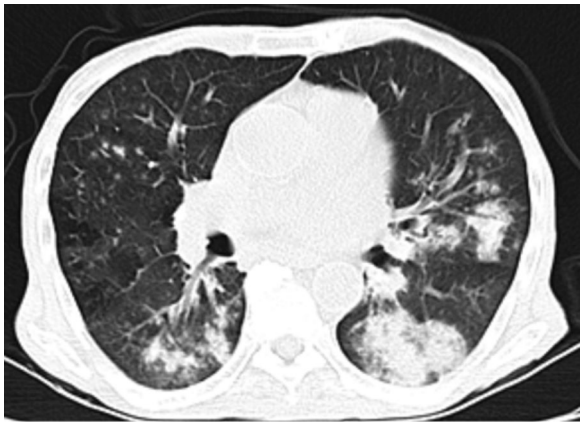

Fig. 8 COVID-19 disease severity score 4

the Declaration of Helsinki were observed at every stage of the research.

Results

In this article, which examines the relationship between sarcopenia and the consequences of Covid-19 disease, 383 patients with Covid-19 were examined, of whom 199 (52%) were men and 184 (48%) were women. The average age of these patients was 53.85 (SD = 18.61) years.

Tables 2 and 3 describe the frequency of underlying diseases and other studied variables. In order to analyze the data, the distribution of quantitative variables was checked. All items except WBC had a normal distribution. Non-parametric tests were used for WBC.

The area and density of the paraspinal muscles at the level of T5 and T12 vertebrae were investigated and compared separately by demographic variables and are shown in Table 4.

Table 2 Frequency percentage of underlying diseases and other variables among the studied population

	Yes	No
DM	94 (24.5%)	289 (75.5%)
CVD	136 (35.5%)	274 (64.5%)
COPD	42 (11%)	341 (89%)
CKD	20 (5.2%)	363 (94.8%)
Immunodeficiency	13 (3.4%)	370 (96.6%)
ICU admission	161 (42%)	222 (58%)
Need for mechanical ventilation	85 (22.2%)	265 (69.2%)
Mortality	85 (22.2%)	298 (77.8%)

Table 3 The frequency of the disease of Covid-19

Disease severity	Frequency	Percentage
Score 1	42	11%
Score 2	192	50.1%
Score 3	128	33.4%
Score 4	21	5.5%

In order to predict the consequences of disease and mortality based on sarcopenia criteria, linear regression and logistic regression models were used, respectively, and the results are shown in Tables 5 and 6.

Table 5 shows the association between the studied variables and the outcome, including T5 muscular area, T5 muscular density, T12 muscular area and T12 muscular density, which are shown both in Unadjusted and Adjusted analysis. About the association between mortality with muscle loss, we showed mass of muscle was losses Compared with patients who were alive, we saw same results in T5 area and density and T12 area and density. All outcomes in the unadjusted analysis were significant, but in the adjusted state for the variables shown in Table 6, it can be said that the longer the length of stay in the hospital, the average T5 muscular density and T12 muscular density decrease by 1.15 and 1.24 units, respectively. This amount was statistically significant ($P < 0.001$). It can also be said that the average T12 area and T12 density were significantly lower in people admitted to the ICU (3.35 ($P = 0.005$) and 4.59 ($P = 0.012$) units, respectively).

Considering that the association of mortality with mechanical ventilation and ICU admission was not precise and was overestimated, we did not include these two variables in the model.

Table 6 shows the association of mortality with the studied variables, including age, sex, DM,

Table 4 The mean of the T5 and T12 muscular surface and density according to demographic and clinical patient's information

Variable	T5 muscular area	T5 muscular den	T12 muscular area	T12 muscular den
Sex	15.71 ± 5.90	27.62 ± 13.28	20.55 ± 7.17	35.70 ± 11.37
Male (N = 199)	14.23 ± 5.61	25.24 ± 14.30	18.85 ± 7.33	34.58 ± 12.51
Female (N = 184)	*P* = 0.012	*P* = 0.093	*P* = 0.023	*P* = 0.363
Age	12.69 ± 5.34	15.02 ± 9.09	16.73 ± 6.13	23.18 ± 11.80
> = 65 (N = 111)	15.94 ± 5.73	31.16 ± 12.64	20.96 ± 7.37	40.05 ± 7.83
< 65 (N = 272)	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
DM	12.87 ± 3.82	21.17 ± 12.64	19.17 ± 6.22	31.54 ± 12.27
YES (94)	15.69 ± 6.17	28.20 ± 13.76	19.92 ± 7.60	36.34 ± 11.59
NO (289)	*P* < 0.001	*P* < 0.001	*P* = 0.342	*P* = 0.001
CVD	13.19 ± 5.42	20.02 ± 12.35	17.62 ± 6.22	28.03 ± 11.39
YES (136)	15.99 ± 5.78	30.03 ± 13.03	20.89 ± 7.58	39.09 ± 10.30
NO (247)	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
COPD	14.72 ± 6.27	23.68 ± 18.90	18.05 ± 7.57	26.32 ± 16.33
YES (42)	15.03 ± 5.75	26.82 ± 13.05	19.94 ± 7.23	36.25 ± 10.81
NO (341)	*P* = 0.763	*P* = 0.301	*P* = 0.132	*P* < 0.001
CKD	14.30 ± 5.44	27.29 ± 10.44	19.43 ± 4.05	34.33 ± 9.25
YES (20)	15.03 ± 5.83	26.43 ± 13.99	19.75 ± 7.43	35.21 ± 12.07
NO (363)	*P* = 0.567	*P* = 0.729	*P* = 0.750	*P* = 0.690
Immunodeficiency disease	14.00 ± 5.45	37.83 ± 15.07	18.24 ± 6.30	37.34 ± 14.54
YES (13)	15.03 ± 5.82	26.08 ± 13.62	19.78 ± 7.32	35.09 ± 11.84
NO (370)	*P* = 0.514	*P* = 0.016	*P* = 0.402	*P* = 0.591
Underlying disease	13.55 ± 5.27	22.21 ± 14.12	18.19 ± 6.39	30.28 ± 12.49
YES (202)	16.61 ± 5.95	31.24 ± 11.79	21.45 ± 7.84	40.61 ± 8.43
NO (181)	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
ICU add	13.15 ± 5.93	21.22 ± 13.87	16.77 ± 6.80	30.49 ± 13.48
YES (161)	16.33 ± 5.33	30.29 ± 12.48	21.88 ± 6.88	38.55 ± 9.32
NO (222)	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
Mechanical ventilation	12.49 ± 5.46	21.46 ± 14.29	16.37 ± 7.10	30.65 ± 14.74
YES (118)	16.11 ± 5.61	28.71 ± 13.01	21.23 ± 6.87	37.17 ± 9.82
NO (265)	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
Mortality	12.09 ± 4.95	21.00 ± 14.16	16.27 ± 7.15	30.57 ± 15.02
YES (85)	15.82 ± 5.77	28.04 ± 13.33	20.72 ± 7.03	36.47 ± 10.55
NO (298)	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
Severity	17.17 ± 6.37	31.25 ± 10.28	23.36 ± 6.36	38.73 ± 11.10
1 (42)	14.84 ± 5.86	26.76 ± 14.34	19.85 ± 7.52	35.86 ± 11.11
2 (192)	14.64 ± 5.63	25.44 ± 13.57	18.45 ± 7.02	33.15 ± 12.97
3 (128)	14.24 ± 4.36	20.67 ± 14.31	19.17 ± 6.31	33.87 ± 12.63
4 (21)	*P* = 0.076	*P* = 0.023	*P* = 0.002	*P* = 0.039
		P = 0.004*		*P* = 0.008*
Hos-time	r = −0.198	r = −0.405	r = −0.260	r = −0.467
	P < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
Lymph	r = −0.039	r = 0.006	r = 0.123	r = 0.255
	P = 0.443	*P* = 0.900	*P* = 0.016	*P* < 0.001
WBC	r = 0.076	r = 0.010	r = 0.014	r = −0.115
	P = 0.137	*P* = 0.844	*P* = 0.780	*P* = 0.025

* The relation between covid-19 severity and score with T5 density, T12 density

cardiovascular disorders, COPD, CKD, immunodeficiency, underlying disease, the hospitalization time, WBC and lymphocyte count, as well as the severity of the disease. It is shown in four modes: Unadjusted mode and then Adjusted mode for T5 muscular area and T5 muscular density, and T12 muscular area and T12 muscular density.

Based on the results shown in the Unadjusted mode, there was a significant association between mortality and age, cardiovascular disorders, COPD, underlying disease, the hospitalization time, WBC and lymphocyte counts, as well as the severity of the disease.

Discussion

The aim of the present study was to investigate whether sarcopenia can predict the consequences of COVID-19 disease, such as a longer hospitalization time, the need for ICU admission, intubation, and mortality related to

Table 5 Linear regression model analysis for T5 and T12 muscular area and density

	T5 area, coefficient (95% CI)		T5 density, coefficient (95% CI)		T12 area, coefficient (95% CI)		T12 density, coefficient (95% CI)	
	Unadjusted	**Adjusted***	**Unadjusted**	**Adjusted***	**Unadjusted**	**Adjusted***	**Unadjusted**	**Adjusted***
mortality	−3.73 (−5.09 to −2.37), $P<0.001$	−1.44 (−3.68–0.80) $P=0.207$	−7.03 (−10.30 to −3.76) $P<0.001$	−1.66 (−6.71–3.39) $P=0.51$	−4.44 (−6.15 to −2.74) $P<0.001$	−0.32 (−3.07–2.42) $P=0.818$	−5.90 (−8.73 to −3.08) $P<0.001$	−0.37 (−4.61–3.87) $P=0.864$
Hos-time	−0.297 (−0.44 to −0.14) $P<0.001$	−0.103 (−0.27–0.06) $P=0.235$	−1.44 (−1.77 to −1.11) $P<0.001$	−1.15 (−1.54 to −0.77) $P<0.001$	−0.49 (−0.67 to −0.30) $P<0.001$	−0.19 (−0.40–0.01) $P=0.070$	−1.44 (−1.71 to −1.16) $P<0.001$	−1.24 (−1.56 to −0.92) $P<0.001$
ICU-add	−3.182 (−4.32 to −2.04) $P<0.001$	−1.055 (−2.95–0.84) $P=0.274$	−9.07 (−11.74 to −6.41) $P<0.001$	−6.07 (−10.34 to −1.80) $P=0.005$	−5.11 (−6.50 to −3.71) $P<0.001$	−3.35 (−5.68 to −1.03) $P=0.005$	−8.05 (−10.34 to −5.76) $P<0.001$	−4.59 (−8.17 to −1.00) $P=0.012$
Mech-vent	−3.617 (−4.82 to −2.40) $P<0.001$	−1.295 (−3.84–1.25) $P=0.319$	−7.25 (−10.17 to −4.33) $P<0.001$	3.73 (−2.01–9.49) $P=0.20$	−4.86 (−6.37 to −3.35) $P<0.001$	−0.80 (−3.94–2.32) $P=0.613$	−6.52 (−9.03 to −4.00) $P<0.001$	2.40 (−2.43 to 7.22) $P=0.329$
severity	−0.797 (−1.58 to −0.01) $P=0.046$	−0.028 (−0.82–0.76) $P=0.945$	−2.73 (−4.58 to −0.88) $P=0.004$	−0.72 (−2.5–1.07) $P=0.430$	−1.60 (−2.58 to −0.63) $P=0.001$	−0.58 (−1.55–0.39) $P=0.243$	−2.18 (−3.78 to −0.58) $P=0.008$	−0.26 (−1.76–1.24) $P=0.734$

* the model was adjusted for all variables in the table

Table 6 Logistic regression model analysis for mortality

	Unadjusted	Adjusted T5 muscular area	Adjusted T5 muscular density	Adjusted T12 muscular area	Adjusted T12 muscular density
	OR (%95CI), p	**OR (%95CI), p**	**OR (%95CI), p**	**OR (%95CI), p**	**OR (%95CI), p**
Age	1.04 (1.02–1.06), $P<0.001$	1.03 (1.02–1.05), $P<0.001$	1.03 (1.02–1.05), $P<0.001$	1.03 (1.02–1.05), $P<0.001$	1.04 (1.02–1.06), $P<0.001$
sex	0.84 (0.52 to 1.37), $P=0.486$	0.68 (0.41–1.14), $P=0.142$	0.75 (0.45–1.23), $P=0.257$	0.69 (0.41–1.14), $P=0.150$	0.79 (0.48–1.30), $P=0.351$
DM	1.49 (0.87–2.54), $P=0.144$	1.56 (0.66–2.01), $P=0.605$	1.17 (0.67–2.05), $P=0.57$	1.49 (0.85–2.59), $P=0.161$	1.26 (0.72–2.18), $P=0.419$
CVD	2.40 (1.47–3.93), $P<0.001$	1.82 (1.08–3.05), $P=0.023$	1.80 (1.07–3.04), $P=0.027$	1.93 (1.16–3.21), $P=0.012$	1.74 (1.01–3.00), $P=0.045$
COPD	5.45 (2.79–10.61), $P<0.001$	6.43 (3.09–13.37), $P<0.001$	5.26 (2.61–10.58), $P<0.001$	5.34 (2.63–10.86), $P<0.001$	4.27 (2.12–8.58), $P<0.001$
CKD	0.87 (0.28–2.68), $P=0.809$	0.80 (0.25–2.55), $P=0.71$	0.93 (0.30–2.90), $P=0.902$	0.93 (0.30–2.91), $P=0.903$	0.86 (0.28–2.67), 0.793
Immun-def	1.05 (0.28–3.92), $P=0.938$	0.94 (0.24–3.65), $P=0.928$	1.67 (0.42–6.57), $P=0.464$	0.94 (0.24–3.66), $P=0.927$	1.13 (0.29–4.38), $P=0.859$
Underlying-Dis	2.64 (1.57–4.43), $P<0.001$	1.97 (1.14–3.38), $P=0.015$	2.02 (1.17–3.51), $P=0.012$	2.13 (1.25–3.65), $P=0.006$	1.96 (1.11–3.47), $P=0.020$
Hos-time	1.26 (1.18–1.35), $P<0.001$	1.21 (1.13–1.30), $P<0.001$	1.23 (1.14–1.33), $P<0.001$	1.21 (1.13–1.30), $P<0.001$	1.25 (1.15–1.35), $P<0.001$
WBC	1.05 (1.01–1.09), $P=0.013$	1.04 (1.00–1.07), $P=0.046$	1.05 (1.01–1.09), $P=0.012$	1.03 (1.00–1.07), $P=0.060$	1.04 (1.00–1.08), $P=0.024$
LYMPH	0.88 (0.85–0.92), $P<0.001$	0.88 (0.84–0.92), $P<0.001$	0.87 (0.84–0.91), $P<0.001$	0.89 (0.85–0.93), $P<0.001$	0.89 (0.85–0.93), $P<0.001$
Severity	2.39 (1.68–3.40), $P<0.001$	2.44 (1.68–3.54), $P<0.001$	2.26 (1.58–2.24), $P<0.001$	2.28 (1.57–3.30), $P<0.001$	2.29 (1.60–3.28), $P<0.001$

this disease. Sarcopenia is a condition of severe muscle failure that is common in the hospitalized population and is associated with an increased risk of side effects, including increased length of hospital stay and mortality [14, 28, 37, 40]. In previous studies, the relationship between sarcopenia and COVID-19 has been discussed, and the relationship between the hospitalization time and acute changes in the sarcopenia status

of the elderly has been shown [20, 45]. In studies of hospitalized patients with COVID-19 during the pandemic, biochemical evidence of muscle wasting has been reported [49], and it is thought that patients with COVID-19 are at risk of developing acute sarcopenia. This condition is characterized by a decrease in muscle mass and strength [9, 32]. These muscle changes predict poor prognosis in patients, longer hospitalization and ICU admission [1, 5, 29, 50], more ICU admissions [2], failure of extubation [29], a worse situation [7, 16, 44], and more mortality [29, 39]. The results of our study are consistent with several studies in this field that have shown the importance of sarcopenia in the adverse outcomes of patients in many diseases [6, 33, 36, 51]. Low muscle mass can affect the function of the respiratory system and the pectoralis and intercostal muscles [15, 35, 47]. Respiratory muscles, along with pharyngeal muscles, play an important role in causing coughs. Coughing itself is a defense mechanism against lung infections. Therefore, respiratory muscle disorders in patients with sarcopenia, can cause difficulties in the normal course of the cough reflex and cause failure in ventilation and acceleration of lung infections [11, 42].

If the relationship between low muscle mass and the negative consequences of COVID-19 is confirmed, the role of CT scan in diagnosis, monitoring, and prediction of prognosis will be more prominent. The strength of our study is the large sample size. One of the limitations of this study is that the evaluation is limited to hospitalized patients. Also, due to the fact that this study was a retrospective study, the patient's information was not complete, and we did not have access to some important variables such as the weight and height of some patients. Furthermore, other risk factors such as habits and lifestyle, nutrition, physical activity, etc. related to patients before contracting COVID-19 and being hospitalized are effective in changing muscle condition, which were not investigated in this study. In this study, sarcopenia was investigated based on the density and area of muscle mass, and due to the limitations of the pandemic time in hospitals, measures such as grip strength, dual-energy X-ray absorptiometry (DXA), chair stand tests, and 400-m walk tests were not performed. It is suggested that longitudinal and prospective studies be conducted, considering these variables as well as the initial muscle condition, to determine whether sarcopenia occurs before or after the infection with COVID-19.

Conclusions

Based on the results of this study, it can be inferred that the use of CT scan in patients with COVID-19 and the determination of muscle area and density can predict the consequences of the disease of COVID-19, such as a longer hospitalization, the need for ICU admission, and mortality.

Abbreviations

COVID-19	Coronavirus- 19
CT scan	Computed Tomography
ICU	Intensive Care Unit
WBC	White blood cell
SARS-CoV-2	Acute Respiratory Syndrome Coronavirus 2
COPD	Chronic Obstructive Respiratory Disease
CVD	Cardiovascular disease
DM	Diabetes mellitus
PCR	Polymerase chain reaction
CKD	Chronic kidney disease
SPSS	Statistical Package for the Social Sciences
ANOVA	Analysis of variance
SD	Standard deviation

Acknowledgements

Not applicable.

Author contributions

AA collected de data and was a major contributor in writing the manuscript. MH was in charge of the conception and design of the work, MT analyzed and interpreted the patient data, MN participated in writing the manuscript. All authors read and approved the final manuscript.

Funding

No financial support was used in this study.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. The material is fully explained in the "Methods" section.

Declarations

Ethics approval and consent to participate

In this study, written consent was obtained from the patients. All information was kept confidential, and all provisions of the Declaration of Helsinki were observed at every stage of the research.

Consent for publication

Patients were given permission to publish the results of the study.

Competing interests

The authors declare that they have no competing interests.

Received: 11 November 2023 Accepted: 14 March 2024
Published online: 25 March 2024

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