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Correlation of Pectoralis Muscle Volume and Density with Severity of COVID-19 Pneumonia in Adults

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Rationale and Objectives: The aim of our study was to evaluate whether there is any correlation between a histogram analysis of the pectoralis muscle derived from chest computed tomography (CT) and the mortality rate for COVID-19 pneumonia in the adult population.

Method: Chest CT derived measurements were evaluated retrospectively for 217 patients with a diagnosis of COVID-19 pneumonia. Using a CT histogram analysis, we measured pectoralis muscle volume (PV) and pectoralis muscle density (PD). Patients were divided into groups first according to gender and then subgroups, which are age and outcome.

Results: The COVID-19 diagnoses were confirmed by RT-PCR testing, chest CT and clinical findings in 217 patients (108 men, 109 women), aged 21−92 years (mean 61 years). PD measurements were lower in the exitus group ($p = 0.001$) and in patients aged ≥65 than in those aged <65 years ($p < 0.05$). There was a significant difference between PD measurements of outpatient and inpatient under 65 years age ($p < 0.05$). Additionally, there was a statistically significant difference between fatty volume measurements according to the exitus status of cases ($p < 0.05$).

Conclusion: CT-derived measurements of the pectoralis muscle can be useful in predicting disease severity and mortality rate of COVID-19 pneumonia in adult patients.

Key Words: Chest computed tomography; pectoralis muscle; COVID-19 pneumonia.

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INTRODUCTION

On December 31, 2019, a new coronavirus appeared in the Wuhan region of China, and by February 11, 2020 this human-to-human transmittable virus had been recognized as SARS-CoV-2 by The International Committee on Taxonomy of Viruses (1). COVID-19 disease eventually spread worldwide, being declared a pandemic on March 11, 2020, and officially recognised as a pandemic in the world by the WHO.

COVID-19 pneumonia is a contagious disease and spreads rapidly among the population. In the adult population, chest computed tomography (CT) examination is an important diagnostic modality in the diagnosis of COVID-19 pneumonia (2).

The clinical signs of COVID-19 infection show a very wide range, patients can be asymptomatic, may present with mild to severe upper respiratory tract illness or respiratory failure and death. Many factors and comorbidities have been described that may affect the prognosis, such as age and cerebrovascular diseases. However, COVID-19 may cause death in the young population and in patient groups with no chronic disease (3,4).

It has been shown that muscle quality correlates with the general health status of a patient and that quantitative muscle measurements can be used as a prognostic factor in a range of health conditions including lung disease, cancer, and surgery outcomes (5−14). Sonographic or cross-sectional measurements of muscles quantity found to be related with general health condition of patients and general outcomes of diseases (15). In this study, we evaluated retrospectively the volume and density of the pectoralis muscle and its correlation with the clinical outcomes of COVID-19 pneumonia in the adult population. To our knowledge, this has not been described previously.

MATERIALS AND METHODS

Data Collection

Chest CT studies of 220 adult patients aged between 18 and 95 were evaluated retrospectively. The diagnosis had been confirmed by the real-time fluorescence polymerase chain (RT-PCR) test and chest CT. Patients with chronic lung or

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other diseases, any type of cancer, malnutrition which may cause sarcopenia and affect muscle volume, were excluded from the study. The patients who do not have any type of known chronic disorders were included to the study. The patients with chronic lung diseases and cancer, both of which may cause sarcopenia and affect muscle volume, were excluded from the study. RT-PCR, demographic details and clinical features were obtained from the medical records, and the thorax CT images were evaluated using Picture Archiving and Communication Systems. Images were evaluated by a radiologist with a minimum of 15 years of experience of thoracic imaging. All cases confirmed as COVID-19 infection by RT-PCR were evaluated by clinicians, and due to the severity of the disease, the patients were followed up in hospital or through outpatient clinics. Severity was evaluated from the patient's clinical condition and the CT findings (4,16). After evaluation, patients were divided according to gender and then according to their outcomes: into the exitus group, or the survival group, with the survival group being subdivided into in-patient and out-patient groups according to hospitalization status. Finally, all groups were subdivided into age groups: ≥65 and <65 years.The institutional review board of our hospital approved the study protocol (approval number: 2020/334).

Imaging Techniques

We used a 64 slice multidetector CT scanner (Siemens Medical Solutions, Erlangen, Germany) to obtain chest CT exams with 1-mm slice thickness in the supine position without contrast. We also used "SAFIRE reconstruction software" to adjust mAs 120kV for tube voltage. Gantry rotation was 0.5 s, collimation was 0.6 mm, pitch was 1.2. Multiplanar reconstruction was made 4 -mm image thickness. We used the first CT scan of patients, which are used for diagnosis at the beginning of the disease. CT scanning boundaries was between thoracic inlet and adrenal glands. We measured pectoralis muscle volume (PV) and pectoralis muscle density (PD) on a single axial slice of the chest CT scan above the aortic arch at baseline CT using the Synapse 3D Picture Archiving and Communication Systems system (Fujifilm Synapse 3D, Tokyo, Japan). It has been shown that this level gives the best results and is highly reproducible (5). ROI was placed on the right pectoralis muscle and the borders of the muscle were traced and shaded manually. The pectoral muscle fat infiltration was calculated as the mean volume of the voxel attenuation within ROI (Fig 1). The attenuation thresholds ranged from −1000 to 250 Hounsfield units (HU). Ten groups were created for volume evaluation from the histogram analysis map. Groups 1 to 10 were called total volume. Group 1 to 3 ranged between −1000 and 0 HU; these showed the most fatty attenuation and were called fatty volume groups. Group 4 to 10 ranged between 1 and 250,which showed muscle attenuation, and these were called muscle volume groups. The radiologist was blinded to the clinical condition of the patients during the analyses. PD was described as the mean attenuation of pectoralis muscle within the ROI.

Statistical Analysis

The NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for the statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used for evaluating the descriptive data. The suitability of quantitative data for assessing normal distribution was tested by Kolmogorov-Smirnov, Shapiro-Wilk test, and by graphical evaluation. The Mann Whitney *U* test was used for comparing two groups of non-normally distributed data. A p value <0.05 was regarded as statistically significant. The calculation for the cut-off point for PD was considered on the basis of this significance. ROC (Receiver Operating Characteristic) analysis and diagnostic screening tests were used to determine the cut-off point according to mortality. The intraobserver agreement for PD and PV was assessed with the concordance correlation coefficient (CCC).

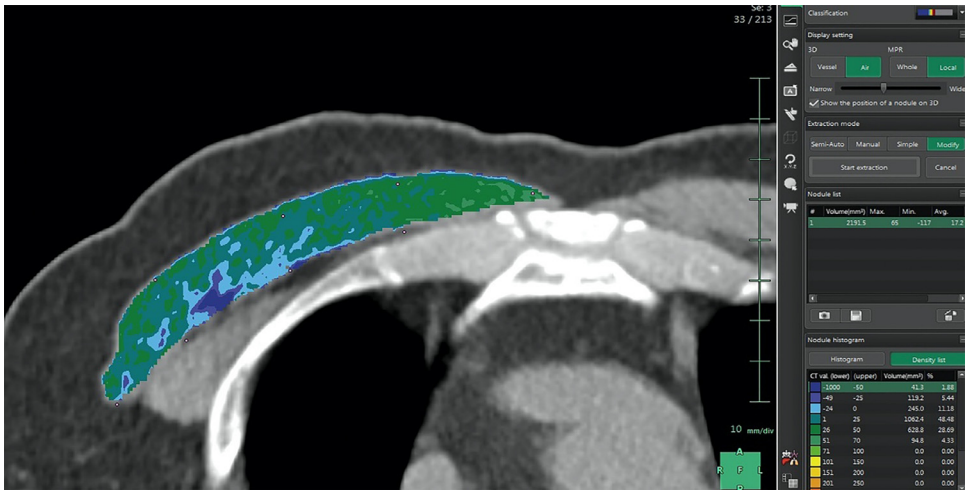

Figure 1. Histogram analysis of pectoralis major muscle. (Color version of figure is available online.)

RESULTS

Patients' Information

COVID-19 diagnoses were confirmed by RT-PCR testing, chest CT, and clinical findings in 217 patients (108 men, 109 women),whose ages ranged between 21 and 92 years, with an average age of 61 years. Of all patients, 63.6% (n = 138) were under the age of 65, and 36.4% (n = 79) were over 65 years of age. Of all cases included in the study, 31.8% (n = 69) lost their lives due to the COVID-19 infection. The intraobserver CCC for both PD and PV at the aortic arch level was 1.00.

Chest CT-derived Measurements

PD Analysis of the Groups

We obtained a statistically significant decrease in PD measurements of both male and female exitus groups compared to survival group($p = 0.001$). Besides, there was a statistically significant negative correlation with age status, which means PD values were lower in patients older than 65 years ($p < 0.05$). Also, PD measurements were lower in the exitus group compared to the survival group at all age groups. Additionally in exitus female group, it was found that patients aged ≥65 had lower PD measurements compared to patients under the 65 years of age (Table 1).

PD of Inpatient and Outpatient Groups Among Survival Patients

There was no statistically significant difference between the PD measurements of female patients who were treated in an outpatient clinic or an inpatient clinic (Table 2). However, a statistically significant difference was found between PD measurements according to the outpatient or inpatient treatment of surviving female cases <65 years of age ($p < 0.05$). PD measurements of inpatient cases <65 years of age were lower than those treated in the outpatient clinic. PD measurements of inpatient treated male cases were also lower than those treated in the outpatient clinic ($p < 0.05$).

ROC Analysis of PD

We obtained a statistically significant difference on the basis of presence of mortality which means PD measurements were found to be lower in patients who died ($p < 0.05$). Based on this significance, the calculation of the cut-off point for PD was considered. We designated threshold levels by ROC analysis and diagnostic screening tests in accordance with mortality.

The threshold level of PD in female group was obtained as 15.9 and below. For a cut-off value for PD measurement of 15.9, sensitivity was 61.11%, specificity was 73.97%, positive predictive value was 53.66%, negative predictive value was 79.41%, and accuracy was 69.72% (Table 3a). In the ROC

TABLE 1. PD Measurements of Groups

Gender			PD (HU)			p
			n	Min-Max (Median)	Mean ± Sd	
Female (n = 109)		Survival	73	−16.5−56.3 (23.8)	23.38 ± 13.76	0.001**
		Exitus	36	−27.3−40.1 (12.2)	11.11 ± 16.58	
	Survival	<65 yrs	49	−9.1−56.3 (25.6)	26.51 ± 13.16	0.026*
		≥65 yrs	24	−16.5−32.1 (23.8)	16.98 ± 12.94	
	Exitus	<65 yrs	17	−27.3−40.1 (19.8)	17.31 ± 17.21	0.020*
		≥65 yrs	19	−20.1−28.3 (6.6)	5.56 ± 14.23	
	<65 yrs	Survival	49	−9.1−56.3 (25.6)	26.51 ± 13.16	0.096
		Exitus	17	−27.3−40.1 (19.8)	17.31 ± 17.21	
	≥65 yrs	Survival	24	−16.5−32.1 (23.8)	16.98 ± 12.94	0.013*
		Exitus	19	−20.1−28.3 (6.6)	5.56 ± 14.23	
Male (n = 108)		Survival	75	6−58.1 (39.3)	38.05 ± 11.45	0.001**
		Exitus	33	−3.8−50.8 (29.5)	27.96 ± 12.86	
	Survival	<65 yrs	52	6−58.1 (42.1)	40.21 ± 11.28	0.010*
		≥65 yrs	23	14.4−51.5 (33.4)	33.18 ± 10.49	
	Exitus	<65 yrs	20	8.8−50.8 (32.6)	30.66 ± 12.23	0.210
		≥65 yrs	13	−3.8−39.8 (23.9)	23.82 ± 13.18	
	<65 yrs	Survival	52	6−58.1 (42.1)	40.21 ± 11.28	0.004**
		Exitus	20	8.8−50.8 (32.6)	30.66 ± 12.23	
	≥65 yrs	Survival	23	14.4−51.5 (33.4)	33.18 ± 10.49	0.054
		Exitus	13	−3.8−39.8 (23.9)	23.82 ± 13.18	

PD, pectoralis muscle density.
Mann Whitney U Test.
* $p < 0.05$.
** $p < 0.01$.

TABLE 2. PD Measurement of Survival Patients due to Follow-Up Protocol (In-Patient - Out-Patient)

Gender	Survival		PD (HU)			p
			n	Min-Max (Median)	Mean ± Sd	
Female (n = 73)	Follow-up	Out-p	51	−2.4−51.5 (25.8)	25.10 ± 13.21	*0.091*
		In-p	22	−16.5−56.3 (19.6)	19.39 ± 14.47	
	<65 yrs	Out-p	37	7.6−51.5 (26.7)	28.93 ± 11.38	*0.014**
		In-p	12	−9.1−56.3 (17.9)	19.05 ± 15.86	
	≥65 yrs	Out-p	14	−2.4−32.1 (11.8)	14.98 ± 12.67	*0.482*
		In-p	10	−16.5−29.9 (24.6)	19.79 ± 13.44	
Male (n = 75)	Follow-up	Out-p	41	12.9−58.1 (41.9)	40.59 ± 10.87	*0.032***
		In-p	34	6−56.8 (35.2)	34.99 ± 11.54	
	<65 yrs	Out-p	33	12.9−58.1 (42.4)	41.28 ± 10.62	*0.419*
		In-p	19	6−56.8 (36.9)	38.35 ± 12.42	
	≥65 yrs	Out-p	8	17.2−51.5 (41.3)	37.74 ± 12.13	*0.138*
		In-p	15	14.4−46.5 (31.9)	30.75 ± 9.00	

PD, pectoralis muscle density.
Mann Whitney U Test.
* $p < 0.05$.
** $p < 0.01$.

TABLE 3A. The Relationship Between Diagnostic Screening Tests and ROC Curve Results

Female	Diagnostic Scan					ROC Curve		p
	Cut off	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Area	95% Confidence Interval	
PD	*≤15.9*	61.11	73.97	53.66	79.41	0.703	0.597-0.809	*0.001***

PD, pectoralis muscle density.
** $p < 0.01$.

curve obtained, the area lying under the 70.3% standard error was 5.4% (Table 3b).

There was a statistically significant relationship between mortality and a PD cut-off level of 15.9 for women ($p = 0.001$). The risk of mortality is 4.466 times higher in women with PD levels of 15.9 and below. The ODDS ratio for PD is thus 4.466 (95% CI: 1.909−10.448) (Table 2b).

In the male group, the cut off point for PD was 34.1 and below. For a cut-off value for PD measurement of 34.1, sensitivity was 69.70%, specificity was 65.33%, positive prediction value was 46.94%, negative prediction value was 83.05%, and accuracy was 66.67%(Table 3c). In the ROC curve obtained, the area lying under the 72.2% standard error was determined as 5.2% (Fig. 2).

There was a statistically significant relationship between mortality and PD cut-off level 34.1 for men ($p = 0.001$). The risk of mortality was 4.3 times higher in male cases with PD level of 34.1 and below. The ODDS ratio for PD is thus 4.3 (95% CI: 1.795−10.468).

TABLE 3B. The Relationship Between PD Cut-Off Value and Mortality

		Mortality (-)		Mortality(+)		p
		n	%	N	%	
PD	>15.9	54	*74.0*	14	*38.9*	*0.001***
	≤ 15.9	19	*26.0*	22	*61.1*	

PD, pectoralis muscle density.
Pearson Ki-kare Test.
** $p < 0.01$.

PV Analysis of Groups

We obtained a significant correlation between the fatty and muscle volume measurements of the patients in accordance with gender ($p = 0.001$): fatty volume measurements of female cases were higher than those of the males; muscle volume measurements of male cases were higher than those of the women.

There was a significant positive correlation between the volume measurements according to the exitus status of the female cases ($p < 0.05$); Which means total volume measurements of exitus cases were higher than those of the survival group. It was statistically significant that fatty volume of female cases who died was higher than in the female cases who survived ($p < 0.05$).

TABLE 3C. The Relationship Between Diagnostic Screening Tests and ROC Curve Results

Male	Diagnostic Scan					ROC Curve		*p*
	Cut off	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Area	95% Confidence Interval	
PD	≤*34.1*	69.70	65.33	46.94	83.05	0.722	0.620−0.824	*0.001***

PD, pectoralis muscle density.
** $p < 0.01$.

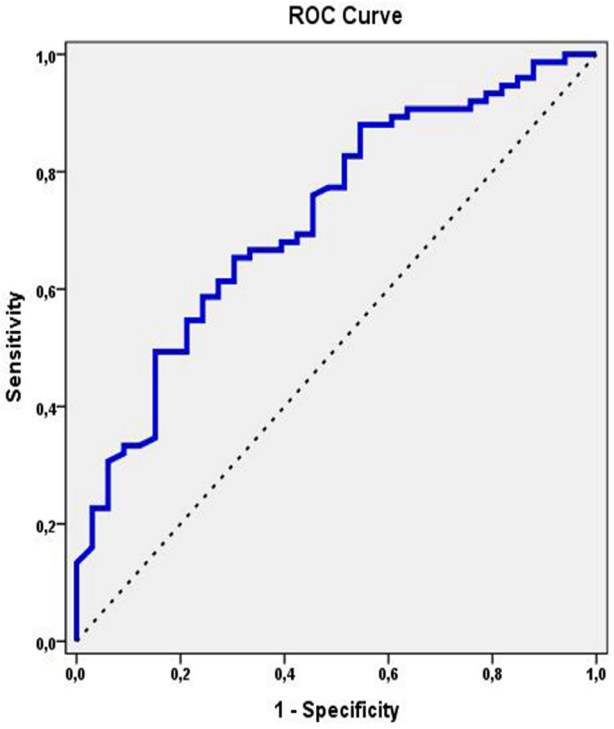

Figure 2. ROC curve of male mortality and PD measurements. PD, pectoralis muscle density. (Color version of figure is available online.)

There was no statistically significant difference between total volume measurements according to the exitus-survival status of the male cases ($p > 0.05$); however, it was statistically significant that the fatty volume of male cases who died was higher than that of males cases who survived ($p < 0.05$). We also separated the groups according to their ages and used 65 years as a threshold level. It was statistically insignificant except the survival male patients group; patients aged ≥65 had lower PD measurements compared to patients under the 65 years of age (Table 4). The distribution of patients is shown in Figure 3.

DISCUSSION

In present study we wanted to demonstrate that a new CT-derived quantitative measurement, PV, and PD, is correlated with clinical outcomes and mortality rate for COVID-19 pneumonia. The measurements were taken at the level above the aortic arch, and were therefore highly reproducible. We separated patients on the basis of gender as male and female groups for evaluation, because it is known that muscle volume and density may differ between genders and between races (7). PD measurements of patients in both male and female groups aged 65 and over were lower than those below 65 years of age, which was predictable due to muscle loss with age. In our study, we found that a lower PD was associated with higher mortality from COVID-19 disease and older age in both gender groups. However, PD measurements of patients in both exitus and survival groups in the same age group showed that the PD of patients who died and were younger than 65 was lower than that of those who survived and were younger than 65.

COVID-19 infection has a wide variety of symptoms and clinical outcomes. Older age is a very well-known prognostic factor in COVID-19 pneumonia. Du et al. have described four important prognostic factors that may affect mortality in COVID-19 pneumonia, which include age ⩾65 years; pre-existing concurrent cardiovascular or cerebrovascular diseases; CD3+, CD8+ T-cells ⩽75 cells·μL-1; and cardiac troponin I ⩾0.05 ng·mL−1. They also found that in the same age and sex group with similar comorbidities, T-cell condition and cardiac troponin can be used as predictors of mortality (17).

Other studies have investigated the risk factors causing death in adult patients with COVID-19. Zhou et al. described sequential organ failure assessment, elevated d-dimer score and older age and on appeal as risk factors for COVID-19 mortality (3). Li et al. found that hyperglycemia and high-dose corticosteroid use may indicate a high risk for death in addition to the factors mentioned above (4).

In the literature, several studies (6−15,18−22) have examined the relationship between low muscle size and mortality in different populations with different lung diseases that include COPD, cancer, idiopathic pulmonary fibrosis, and surgery outcomes. CT-derived measurements mostly show correlation with severity of health condition. It is important to mention that the term sarcopenia defined as both quantitative and qualitative loss of skeletal muscle in these studies, however, muscle quality shows more relevant information about patients' health and the prediction of outcomes than quantity of muscle (7−9). Lipid accumulation in the muscles appears as a low muscle density in CT and it is known that fat accumulation within the muscles decreases the strength, independently of muscle mass. It is also known that anemia and hypoalbuminemia are associated with low muscle density (8).

TABLE 4. PV Measurements of Fatty Volume Group (Group 1–3)

Gender			Fatty Group Volume (1.+2.+3.)			*p*
			n	Min-Max (Median)	Mean ± Sd	
Female (n = 109)		Survival	73	0.9–1891.1 (142.4)	226.86 ± 309.59	*0.001***
		Exitus	36	21–2116.5 (363)	551.71 ± 545.55	
	Survival	<65 yrs	49	0.9–1891.1 (136)	209.01 ± 311.05	*0.203*
		≥65 yrs	24	35.4–1467.2 (151.7)	263.3 ± 309.93	
	Exitus	<65 yrs	17	21–1487.2 (185.8)	402.68 ± 429.19	*0.079*
		≥65 yrs	19	57.4–2116.5 (554.7)	685.06 ± 612.57	
Male (n = 108)		Survival	75	9.3–1983.1 (81.7)	175.47 ± 322.63	*0.005***
		Exitus	33	11.2–891.1 (146.3)	261.87 ± 257.23	
	Survival	<65 yrs	52	9.3–641.9 (52.9)	102.58 ± 121.53	*0.044**
		≥65 yrs	23	11.2–1983.1 (130.1)	340.29 ± 524.33	
	Exitus	<65 yrs	20	11.2–891.1 (137.5)	231.61 ± 235.4	*0.439*
		≥65 yrs	13	27.6–884.6 (222.4)	308.43 ± 291.25	

PV, pectoralis muscle volume.
Mann Whitney U Test.
* $p < 0.05$.
** $p < 0.01$.

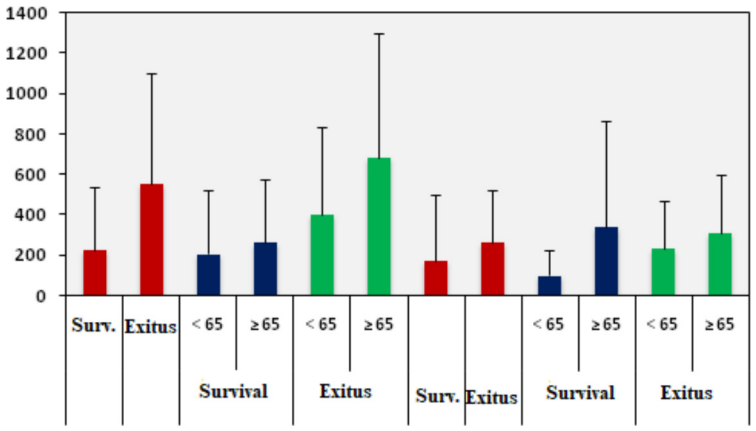

Figure 3. The distribution of PV measurements of patients. PV, pectoralis muscle volume. (Color version of figure is available online.)

In respiratory medicine, Bak et al.(5) assessed the impact of the pectoralis muscle area and pectoralis muscle density to correlate the severity of COPD and changes in longitudinal pulmonary function in patients with COPD. They found that CT derived parameters were associated with baseline lung function and with the severity of emphysema($p < 0.05$). Park et al. used CT histogram analysis to obtain quantitative measurements from the intercostal muscles and the latissimus dorsi muscle to show intramuscular fat infiltration. They correlated these analyses with COPD severity. They found that intercostal mass decreased and intercostal fat increased which is related to the worsening of COPD severity (6). McDonald et al. evaluated the correlation between CT-derived pectoralis muscle area and COPD morbidity. They found a significant relationship between the pectoralis muscle area and COPD-related features, including spirometric measures, dyspnea, and walking distance (21).

Moon et al. evaluated the thoracic muscle volume and measured pectoralis, paraspinal, serratus, latissimus, and erector spinal muscles and found that low skeletal mass may be a robust risk factor for mortality in patients with idiopathic pulmonary fibrosis (23). Tzeng et al. showed on patients with long-term hospital stay and underwent for transcatheter aortic valve implantation can be predicted by the pectoralis muscle size and attenuation (7). Teigen et al. showed that pectoralis muscle size and attenuation were powerful predictors of outcomes after implantation of a left ventricular assist device (24).

In a recent study conducted by ufuk et al., researchers used pectoralis muscle volume similar to us and they differently obtained pectoralis muscle index, which is obtained by dividing muscle volume to patients height, and demonstrated that both these parameters and the affected area of lung were significantly associated with ominous results of COVID-19 diseases such as long hospital stay, intubation and exitus (25). In our study, we additionally measured PD, which is significantly decreased both male and female exitus groups compared to survival group.

In addition, many published studies demonstrated the association between PD and poor outcomes in different situations like liver cirrhosis, trauma, cancer, and major surgery by using CT measurement methods, similar to ours (6–15,18–22). These studies revealed that muscle quality determined on CT gives

prominent information about the prognosis of many diseases, similar to present study. PV may give useful information about muscle fatty enlargement if CT-histogram analysis is used to show percentage of HU window of muscle. However, if we consider it as total muscle volume, it may be affected by many health conditions and also gender and age. In this study, we found that if we combined the CT-histogram analysis (fatty and muscle groups), it gave statistically useful information; however, PD can be used as an independent risk factor for all groups.

In this study, low PD was independently correlated with mortality of patients in both male and female groups, and PD was low in patients who were older than 65. Additionally, when the outcomes of in- and outpatient groups were compared, PD was lower in the hospitalized patient group. This shows that it is correlated with COVID-19 infection severity and not only with mortality.

It is clear that our study has several limitations. It was a retrospective study using existing data and the sample size was small, coming from a single center. Second, there were not enough references in the literature regarding the correlation between PD and COVID-19 disease. We were, therefore, unable to compare our results against other studies. However, the results reported in this study will provide a useful reference for future studies. These findings may prove useful in estimating risk factors and predicting outcomes for COVID-19 infection or other infections that may cause pandemics.

CONCLUSION

CT-derived features of the pectoralis muscle were associated with COVID-19 pneumonia severity and mortality, which can be beneficial in determining treatment plans and estimating prognosis together with other estimated risk factors.

FINANCIAL DISCLOSURES

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DECLARATION OF COMPETING INTEREST

The authors declare that they have no conflict of interest.

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