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Association of pectoralis major muscle cross-sectional area and mean density on chest CT with mortality in elderly COVID-19 patients: sex and side differences

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Abstract

Background COVID-19 is a disease that primarily affects the lungs and may follow a fatal course. The aim of this study was to investigate whether there are differences in the cross-sectional area and mean density of the pectoralis major (PM), an accessory respiratory muscle, between survivors and non-survivors with COVID-19, with analyses performed according to sex.

Materials and methods This retrospective study included a total of 201 patients aged 65 and over who were admitted to a tertiary healthcare center between March 2020 and May 2021. Patients with confirmed COVID-19 diagnosis by PCR and radiological evidence of pulmonary involvement on chest CT were included in the study, while patients with imaging artifacts that could affect measurements were excluded. The cross-sectional area and mean density of the right and left pectoralis major muscles were measured on axial CT images at the sternal angle level using 3D Slicer software.

Results Of the 201 patients, 103 (51.2%) died. In the overall cohort, PM CSA (cross-sectional area) and density did not differ significantly between survivors and non-survivors. However, sex-stratified analyses revealed that female survivors had significantly greater right and left PM CSA compared to non-survivors ($p = 0.015$ for both), whereas in male patients, left PM density was significantly higher in survivors ($p = 0.011$). Lymphopenia and elevated NLR, AST, LDH, CRP, and D-dimer were also associated with mortality ($p < 0.05$).

Conclusion PM muscle measurements on chest CT showed some sex-related differences between survivors and non-survivors in elderly COVID-19 patients. Lower PM CSA in women and lower PM density in men were observed in univariable analyses. However, these parameters were not independently associated with mortality after adjustment. Therefore, PM muscle assessment on routine chest CT may provide additional but limited prognostic information.

Keywords COVID-19, Cross-sectional area, Density, Geriatrics, Mortality, Pectoralis major

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in 2019 and primarily affects the respiratory system, leading to substantial mortality worldwide [25]. Although the gold standard for the diagnosis of COVID-19 is the detection of viral RNA by polymerase chain reaction (PCR), chest computed tomography (CT) is widely used both for diagnostic purposes and for assessing disease severity and clinical status [1, 4].

In the current literature, numerous studies have investigated the association between CT-derived muscle measurements and the clinical course and mortality across various diseases [5, 13]. Consequently, CT-based morphometric measurements have gained increasing attention as a potential tool for clinical assessment and prognostic evaluation [21].

Among thoracic muscles, the pectoralis major is well suited for CT-based morphometric evaluation due to its consistent visualization on routine chest CT and its well-defined anatomical boundaries. The muscle consists of clavicular, sternocostal, and abdominal parts, and inserts onto the humerus. Functionally, when the upper extremity is fixed, contraction of the pectoralis major can elevate the thoracic cage, thereby assisting inspiration [3, 13]. Previous radiologic studies have demonstrated that pectoralis major muscle CSA and mean density reflect overall skeletal muscle mass and are associated with disease severity and clinical outcomes in respiratory diseases such as chronic obstructive pulmonary disease [11]. There is also a study showing that the cross-sectional area of the pectoralis major muscle is an independent predictor of exacerbation frequency in COPD, whereas the serratus anterior and intercostal muscle areas were not found to be significant [22]. More recently, CT-derived thoracic muscle measurements such as CSA or mean density have also been investigated as potential prognostic markers in patients with COVID-19 [17].

Older age has consistently been identified as a major risk factor for poor outcomes in COVID-19, with individuals aged ≥ 65 years demonstrating significantly higher mortality during the pandemic [20]. Despite growing interest in opportunistic body composition analysis, data regarding pectoralis major muscle morphometry on chest CT in elderly patients with COVID-19 remain limited. In particular, potential sex-related and laterality-related differences in pectoralis major muscle parameters have not been sufficiently investigated. To our knowledge, few studies have specifically evaluated pectoralis major muscle morphometry on chest CT in elderly COVID-19 patients while simultaneously assessing sex- and side-related differences.

Therefore, the aim of this study was to investigate whether differences exist in the cross-sectional area and mean density of the pectoralis major muscle, as well as selected laboratory parameters, between elderly COVID-19 patients who survived and those who died. In addition, predefined analyses stratified by sex and by laterality (right and left sides analyzed separately) were performed to explore potential differences in pectoralis major muscle measurements.

Materials and methods

Study design

This study was carried out with the approval of the ethics committee of Karadeniz Technical University Faculty of Medicine, with the letter dated 12/10/2023 and numbered 2023/175. Since the study was conducted retrospectively, no volunteers were used. No financial support was provided for the study.

Data sources

The study was conducted on a total of 201 patients aged ≥ 65 years who presented to the emergency department of a tertiary care hospital (Recep Tayyip Erdoğan Training and Research Hospital) between March 2020 and May 2021. All patients had RT-PCR–confirmed COVID-19 infection and underwent chest CT during their initial clinical evaluation in the emergency department. Chest CT images were evaluated by radiologists and classified according to the CO-RADS (COVID-19 Reporting and Data System) classification [16]. Only patients with CO-RADS category ≥ 3 were considered to have CT findings compatible with COVID-19 infection and were included in the study. Depending on their clinical condition, patients were either hospitalized or managed as outpatients after emergency department evaluation. Patients with any known muscle disease or with imaging artifacts that could interfere with muscle measurement were excluded. Information regarding muscle diseases was obtained through review of the patients' medical records, and patients with a documented history of neuromuscular or muscle-related disorders were not included in the study. Laboratory blood parameters were obtained from blood samples collected during the patient's initial emergency department visit. If these data were unavailable, results obtained within the first 24 h after hospital admission were used. Cases without available blood test results were excluded. The measured laboratory parameters included leukocyte count, neutrophil count, lymphocyte count, hemoglobin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), C-reactive protein (CRP), D-dimer, fibrinogen, international normalized ratio (INR), and neutrophil-to-lymphocyte ratio (NLR). Comorbidities were identified based on documented diagnoses recorded in the hospital information system. Because of the retrospective design of the study,

comorbid conditions were grouped into broader categories including cardiovascular disease, diabetes mellitus, chronic lung disease, and chronic renal failure. The patients were divided into two groups according to clinical outcome: survivors ($n = 98$) and non-survivors ($n = 103$).

Chest CT and quantitative analysis

Chest CT examinations were performed using a 16-detector CT scanner (Alexion, Toshiba Medical Systems, Japan) with patients in the supine position during deep inspiration. The scanning parameters were as follows: tube voltage 120 kVp, tube current 50–300 mA, and slice thickness ranging from 0.625 to 5 mm according to the clinical protocol. CT images retrieved from the PACS system had a slice thickness of 1 mm in the majority of cases, while six examinations had a slice thickness of 5 mm. The CT images of the patients were taken from the radiology system as DICOM files. Later, these images were opened on the application named Slicer (ver 5.10.0). The slicer program is a free, publicly available program that can perform numerous measurements on radiological images and collect data. To ensure measurement standardization, all measurements were performed on axial CT images at the level of the sternal angle, as previously described [18]. The sternal angle was selected as the measurement level because it is a well-defined anatomical landmark corresponding approximately to the T4–T5 vertebral level and can be consistently identified on CT images. After identifying the appropriate axial plane, the segment editor module of the software was used to manually delineate the boundaries of the right and left pectoralis major muscles using the pen tool. The segmented muscle regions were then filled to obtain quantitative measurements. During segmentation, a Hounsfield unit (HU) threshold range of − 29 to + 150 HU was used to define skeletal muscle tissue, consistent with previously reported CT-based body composition analyses [14]. All measurements were initially performed by a single anatomist. To understand interobserver reproducibility, a randomly selected of 50 patients (25 survivors and 25 non-survivors) was independently remeasured by a second anatomist. Interobserver reliability was analysed using the intraclass correlation coefficient (ICC). The ICC values were 0.94 (95% CI: 0.90–0.97) for right pectoralis major muscle CSA, 0.93 (95% CI: 0.89–0.96) for left pectoralis major muscle CSA, 0.92 (95% CI: 0.87–0.95) for right pectoralis major muscle mean density, and 0.91 (95% CI: 0.86–0.95) for left pectoralis major muscle mean density. Following this, the cross-sectional area (mm^2) and mean muscle density (Hounsfield Units) of the right and left pectoralis major muscles were calculated using the quantification module of the software (Figs. 1 and 2).

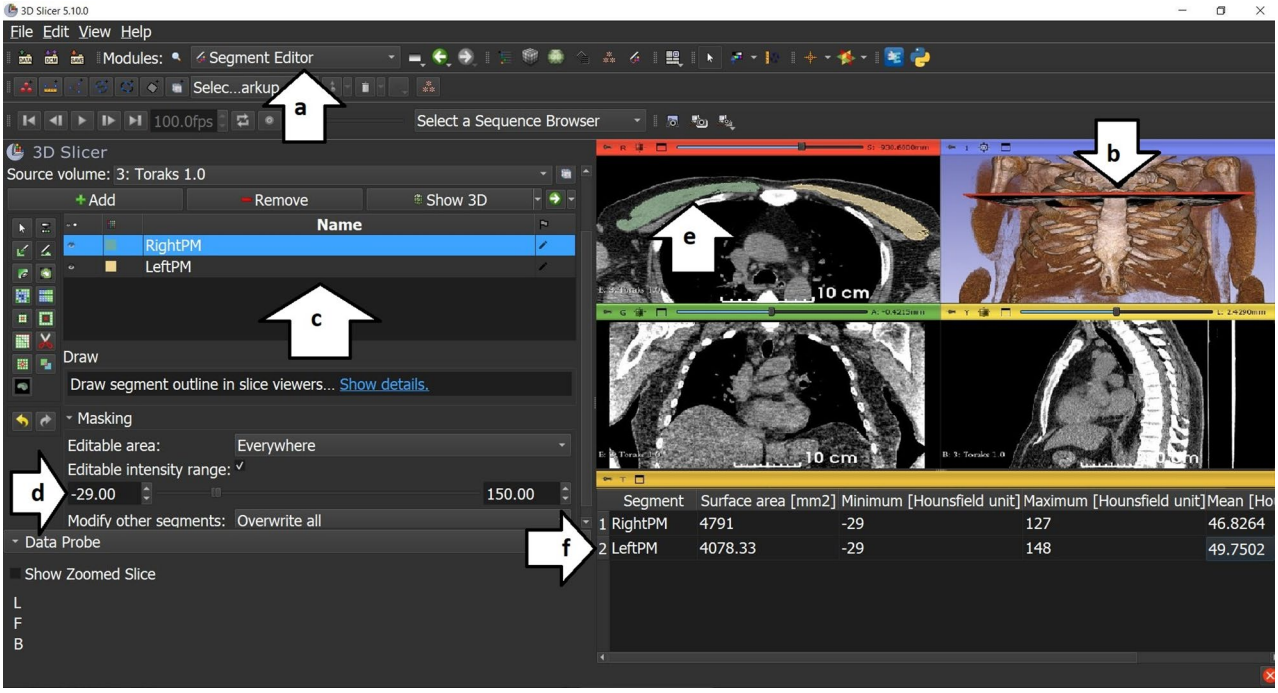

Fig. 1 Measurement of the cross-sectional area and mean density of the pectoralis major muscle. Segmentation of the pectoralis major muscles on axial CT images. **a** The Segment Editor module was selected. **b** The axial slice at the level of the sternal angle (manubriosternal junction) was identified. **c** Two separate segments were created for the right and left pectoralis major muscles. **d** A threshold of − 29 to + 150 Hounsfield units (HU) was applied to define muscle tissue. **e** Manual delineation of the pectoralis major muscle borders was performed. **f** Muscle cross-sectional area and mean density were calculated from the segmented regions. The right pectoralis major muscle is shown in green and the left in yellow

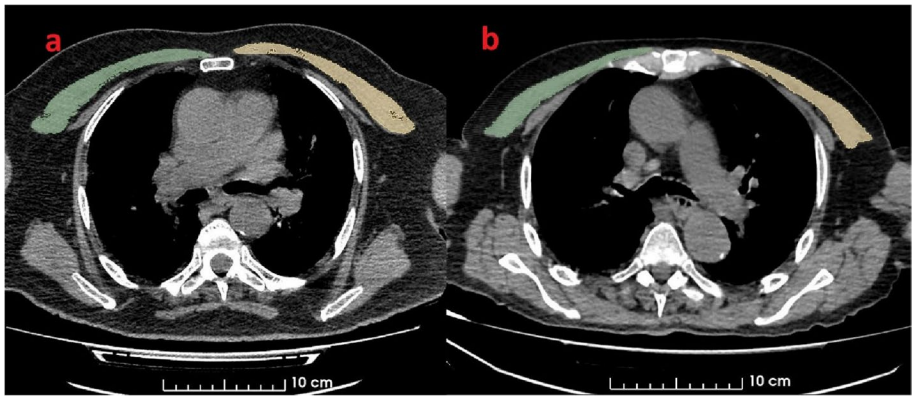

Fig. 2 Example representation of male patients of the same age, one alive and one deceased. **a** Surviving patient: right pectoralis major muscle (green) cross-sectional area 3768.4 mm2 with mean density 37.83 HU; left pectoralis major muscle (yellow) cross-sectional area 3506.49 mm2 with mean density 45.79 HU. **b** Deceased patient: right pectoralis major muscle (green) cross-sectional area 2549.32 mm2 with mean density 31.01 HU; left pectoralis major muscle (yellow) cross-sectional area 2388 mm2 with mean density 29.34 HU

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA.). The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. For variables with normal distribution, comparisons between groups were conducted using the Independent-Samples *t* test, whereas variables not conforming to normal distribution were analyzed with the Mann–Whitney U test. Categorical data were evaluated with the chi-square test, and where expected cell counts were insufficient, Fisher's exact test was applied. To evaluate whether pectoralis major muscle parameters were associated with mortality, multivariable logistic regression analyses were performed. Variables considered clinically relevant and those showing potential association with mortality were entered into the multivariable model. Age and CRP were included in the multivariable models as potential confounders because both are established predictors of COVID-19 outcomes. CRP was selected as a representative inflammatory marker since other inflammatory laboratory parameters are biologically related and may be correlated. Sex was not included as a covariate because analyses were performed separately for male and female patients. To assess the discriminatory ability of pectoralis major muscle morphometric parameters for predicting mortality, receiver operating characteristic (ROC) curve analysis was performed. The area under the curve (AUC) was calculated, and the optimal cut-off values were determined using the Youden index. Interobserver reproducibility of CT-derived pectoralis muscle measurements was evaluated using the intraclass correlation coefficient (ICC) based on a two-way random-effects model with absolute agreement, calculated from measurements repeated by a second observer in a randomly selected subset of patients. Normally distributed data are presented as mean ± standard deviation, while non-normally distributed variables are expressed as median (25th–75th percentiles). A p value < 0.05 was considered indicative of statistical significance.

Table 1 Patient demographics

	All	Deceased	Survivor	*P* value
	n **= 201**	***n*** **= 103**	***n*** **= 98**	
Age	76.38 ± 7.73	77.61 ± 7.94	75.08 ± 7.41	0.020*
Gender				
Men	115 (57%)	62 (60%)	53 (54%)	0.463
Women	86 (43%)	41 (40%)	45 (46%)	

*$p < 0.05$ indicates a significant difference

Results

Patient characteristics

The study population consisted of 201 patients, with a mean age of 76.4 ± 7.7 years. When stratified by outcome, patients who died had a significantly higher mean age compared to survivors (77.6 ± 7.9 vs. 75.1 ± 7.4 years, $p = 0.020$). Regarding sex distribution, 115 patients (57%) were male and 86 (43%) were female. There was no statistically significant difference in survival between males and females (60% vs. 54% deceased, $p = 0.464$) (Table 1).

Among the study population, cardiovascular disease was the most common comorbidity, present in 154 patients (76.6%). Other frequent conditions included diabetes mellitus in 73 patients (36.3%), chronic lung disease in 27 patients (13.4%), renal failure in 28 patients (13.9%), and malignancy in 25 patients (12.4%). When comparing deceased and surviving patients, none of the comorbidities showed a statistically significant difference. Cardiovascular disease was observed in 79 deceased patients (76.7%) and 75 survivors (76.5%) ($p > 0.05$). Diabetes was present in 39 deceased (37.9%) and 34 survivors (34.7%) ($p = 0.749$). Chronic lung disease was seen in 17 deceased (16.5%) and 10 survivors (10.2%) ($p = 0.270$). Renal failure was detected in 19 deceased (18.4%) versus 9 survivors

(9.2%) ($p = 0.091$). Malignancy was present in 15 deceased (14.6%) and 10 survivors (10.2%) ($p = 0.470$). Overall, no statistically significant association between comorbid conditions and mortality was identified in this study (Table 2).

Laboratory findings

A total of 201 patients aged ≥ 65 years were included in the study, comprising 103 patients in the mortality group and 98 patients in the survival group. Comparisons of laboratory blood parameters between the two groups are summarized in Table 3.

White blood cell (WBC), neutrophil, platelet, hemoglobin, alanine aminotransferase (ALT), fibrinogen, and international normalized ratio (INR) levels did not differ significantly between the groups ($p > 0.05$). In contrast, some parameters showed significant differences. Lymphocyte counts were significantly lower in the mortality group compared to the survival group [0.95 (0.63–1.54) vs. 1.22 (0.81–1.61) $\times 10^3$/μL, $p = 0.019$]. Similarly, the neutrophil-to-lymphocyte ratio (NLR) was significantly higher among non-survivors [5.42 (3.03–7.86) vs. 3.67 (2.39–6.10), $p = 0.002$].

Comparing biochemical markers; aspartate aminotransferase (AST) [36.5 (27.25–58.75) vs. 30 (24–38) IU/L, $p < 0.001$], lactate dehydrogenase (LDH) [332.5 (249–486) vs. 274 (218–351) IU/L, $p < 0.001$], and C-reactive protein (CRP) [114.8 (54–158.9) vs. 53.4 (22.2–135.3) mg/L, $p < 0.001$] were significantly elevated in the mortality group. D-dimer levels were higher in non-survivors [0.87 (0.43–2.13) vs. 0.73 (0.40–1.07) μgFEU/mL, $p = 0.003$].

In general, lymphopenia, elevated NLR, and increases in AST, LDH, CRP, and D-dimer levels were strongly associated with higher mortality in this study.

Pectoralis major muscle measurements

The analysis of pectoralis major (PM) muscle cross-sectional area and mean density values between survivors and non-survivors is presented in Table 4.

When evaluated for the entire cohort ($n = 201$), the mean right PM cross-sectional area was 2904 ± 1066 mm^2, while the mean left PM cross-sectional area was 2730 (2192–3257) mm^2. No statistically significant differences were observed between survivors and non-survivors in terms of overall right or left PM cross-sectional area ($p = 0.082$ and $p = 0.064$, respectively).

Sex-stratified analysis revealed that female patients in the survival group had significantly larger right PM cross-sectional areas compared with those in the mortality group [2686 ± 885 mm^2 vs. 2245 ± 758 mm^2, $p = 0.015$]. Similarly, the left PM cross-sectional area was significantly higher among surviving females [2652 (2192–3011) mm^2 vs. 2073 (1718–2800) mm^2, $p = 0.015$].

Table 2 Comorbidity status of patients

	All	Deceased	Survivor	*P* value
	n = 201	*n* = 103	*n* = 98	
Comorbidity status				
Cardiovascular system disease	154 (76.6%)	79 (76.7%)	75 (76.5%)	> 0.05
Diabetes	73 (36.3%)	39 (37.9%)	34 (34.7%)	0.749
Chronic lung disease	27 (13.4%)	17 (16.5%)	10 (10.2%)	0.270
Renal failure	28 (13.9%)	19 (18.4%)	9 (9.2%)	0.091
Malignity	25 (12.4%)	15 (14.6%)	10 (10.2%)	0.470

$p < 0.05$ indicates a significant difference

Table 3 Laboratory blood tests of patients

Parameters	Deceased (*n* = 103)	Survivors (*n* = 98)	All (*n* = 201)	*P* values
WBC ($\times 10^3$/μL)	6.08 (5.0–8.62)	6.43 (4.77–8.03)	6.18 (4.85–8.17)	0.516
Neutrophil ($\times 10^3$/μL)	4.36 (3.4–6.8)	4.29 (3.29–6.09)	4.33 (3.32–6.46)	0.147
Lymphocyte ($\times 10^3$/μL)	0.95 (0.63–1.54)	1.22 (0.81–1.61)	1.08 (0.73–1.59)	0.019*
NLR (%)	5.42 (3.03–7.86)	3.67 (2.39–6.1)	4.58 (2.58–6.86)	0.002*
Trombocyte ($\times 10^3$/μL)	159.5 (130–217)	175 (140–229)	169 (137–218)	0.280
Haemoglobin (g/dL)	12.88 ± 1.75	13.23 ± 1.55	13.05 ± 1.66	0.138
AST (IU/L)	36.5 (27.25–58.75)	30 (24–38)	33 (26–47)	< 0.001*
ALT (IU/L)	20 (16–32.75)	20 (14–30)	20 (15–31)	0.069
LDH (IU/L)	332.5 (249–486)	274 (218–351)	294 (233–411)	< 0.001*
CRP (mg/L)	114.8 (54–158.9)	53.4(22.2–135.3)	82.4 (31.4–146.5)	< 0.001*
D-Dimer (μgFEU/mL)	0.87 (0.43–2.13)	0.73 (0.4–1.07)	0.75 (0.40–1.28)	0.003*
Fibrinogen (mg/dL)	515.78 ± 117.02	492.78 ± 111.88	503.45 ± 114.54	0.181
INR	1.04 (0.97–1.14)	1.02 (0.95–1.13)	1.03 (0.97–1.14)	0.294

Normally distributed data are presented as mean ± standard deviation, while non-normally distributed variables are expressed as median (25^{th}-75^{th} percentiles)

WBC White blood cell, *NLR* Neutrophil-to-lymphocyte ratio, *AST* Aspartate aminotransferase, *ALT* Alanine aminotransferase, *LDH* Lactate dehydrogenase, *CRP* C-reactive protein, *INR* International normalized ratio

*$p < 0.05$ indicates a significant difference

However, no significant differences were observed in male patients' muscle cross-sectional areas.

When the cohort was analyzed without sex stratification, mean right and left pectoralis major (PM) muscle density values did not differ significantly between survivors and non-survivors ($p > 0.05$). After stratification

Table 4 Pectoralis major muscle measurements

	All $n=201$	Deceased $n=103$	Survivor $n=98$	*P* values
	Men = 115 (57.2%)	Men = 62 (60.2%)	Men = 53 (54.1%)	
Right PM (mm^2)	2904 ± 1066	2776 ± 949	3039 ± 1166	0.082
Men	3225 (2515–4089)	3128 (2586–3641)	3339 (2366–3599)	0.803
Women	2476 ± 851	2245 ± 758	2686 ± 885	0.015*
Left PM (mm^2)	2730 (2192–3257)	2662 (1947–3219)	2801 (2343–3469)	0.064
Men	3183 (2418–4304)	2844 (2349–3438)	2894 (2534–3871)	0.226
Women	2440 (1914–2953)	2073 (1718–2800)	2652 (2192–3011)	0.015*
Right PM Density (HU)	32.48 ± 12.79	32.44 ± 13.40	32.52 ± 12.20	0.963
Men	37.90 ± 11.32	37.48 ± 12.76	38.39 ± 9.47	0.662
Women	25.23 ± 10.97	24.81 ± 10.51	25.61 ± 11.48	0.738
Left PM Density (HU)	31.87 ± 15.61	30.23 ± 15.91	33.59 ± 15.19	0.127
Men	38.36 (27.59–47.13)	34.73 (24.29–43.29)	42.4 (31.3–46.95)	0.011*
Women	23.61 ± 11.58	22.74 ± 11.81	24.41 ± 11.42	0.506

Normally distributed data are presented as mean ± standard deviation, while non-normally distributed variables are expressed as median (25^{th}-75^{th} percentiles)

HU Hounsfield Unit, *PM* Pectoralis major

*$p < 0.05$ indicates a significant difference

by sex, left PM density was significantly higher in male survivors compared with male non-survivors [42.4 (31.3–46.9) HU vs. 34.7 (24.3–43.3) HU, $p = 0.011$].

Sex-stratified multivariable logistic regression analyses are presented in Table 5. In female patients, two separate models were developed to avoid multicollinearity between right and left PMCSA measurements. In Model 1, which included age, CRP, and right PMCSA, age was identified as a statistically significant predictor of survival (OR = 0.941, 95% CI: 0.886–0.999, $p = 0.048$). CRP was not significantly associated with survival (OR = 0.994, 95% CI: 0.988–1.000, $p = 0.060$), whereas right PMCSA was not independently associated with survival (OR = 1.000, 95% CI: 1.000–1.001, $p = 0.210$). In Model 2, which included age, CRP, and left PMCSA, neither variable reached statistical significance. However, age (OR = 0.943, 95% CI: 0.888–1.000, $p = 0.052$) and CRP (OR = 0.994, 95% CI: 0.988–1.001, $p = 0.074$) were not statistically significant. Left PMCSA was not associated with survival (OR = 1.000, 95% CI: 0.999–1.001, $p = 0.882$). In male patients, the multivariable model including age, CRP, and left mean density revealed that CRP was the only independent predictor of survival. Higher CRP levels were associated with lower odds of survival (OR = 0.993, 95% CI: 0.987–0.998, $p = 0.008$). Left mean density was not significantly associated with survival (OR = 1.028, 95% CI: 0.999–1.057, $p = 0.055$), whereas age was also not significantly associated (OR = 1.003, 95% CI: 0.946–1.062, $p = 0.929$). The explanatory power of the models was modest, with Nagelkerke R^2 values of 0.109 for Female Model 1, 0.104 for Female Model 2, and 0.096 for the Male Model.

ROC analysis was performed to evaluate the discriminative performance of pectoralis major muscle morphometric parameters for predicting mortality (Fig. 3). In male patients, the highest discriminative ability was observed for left PM density (AUC = 0.639). The optimal cut-off value determined by the Youden index was 37.12 HU, corresponding to a sensitivity of 0.63 and a specificity of 0.64. In female patients, the best discriminative performance was observed for PM cross-sectional area, particularly left PM CSA (AUC = 0.653). The optimal cut-off value was 2073 mm^2, with a sensitivity of 0.51 and a specificity of 0.84. Overall, ROC analyses indicated limited discriminatory performance of pectoralis major muscle morphometric parameters for predicting mortality, with sex-specific differences in the most informative parameter (muscle density in males and cross-sectional area in females).

Table 5 Sex-stratified multivariable logistic regression analyses of pectoralis major muscle parameters and survival

Variable	Female Model 1 (Right PMCSA) OR (95% CI)	*P* value	Female Model 2 (Left PMCSA) OR (95% CI)	*P* value	Male Model OR (95% CI)	*P* value
Age	0.941 (0.886–0.999)	0.048*	0.943 (0.888–1.000)	0.052	1.003 (0.946–1.062)	0.929
CRP	0.994 (0.988–1.000)	0.060	0.994 (0.988–1.001)	0.074	0.993 (0.987–0.998)	0.008*
PMCSA (Right)	1.000 (1.000–1.001)	0.210	-	-	-	-
PMCSA (Left)	-	-	1.000 (0.999–1.001)	0.882	-	-
Left PM mean density	-	-	-	-	1.028 (0.999–1.057)	0.055

Separate models were constructed for female and male patients. In female patients, two different models were generated to avoid multicollinearity between right and left PMCSA measurements. Model 1 included age, CRP and right PMCSA, whereas Model 2 included age, CRP and left PMCSA. In male patients, the model included age, CRP and left PM mean density. Odds ratios (ORs) with 95% confidence intervals (CIs) are presented. Survival was coded as 1 and mortality as 0. Nagelkerke R^2 values were 0.109 for Female Model 1, 0.104 for Female Model 2, and 0.096 for the Male Model

OR odds ratio, *CI* confidence interval, *PM* pectoralis major, *CSA* cross-sectional area, *CRP* C-reactive protein

*$p < 0.05$ indicates a significant difference

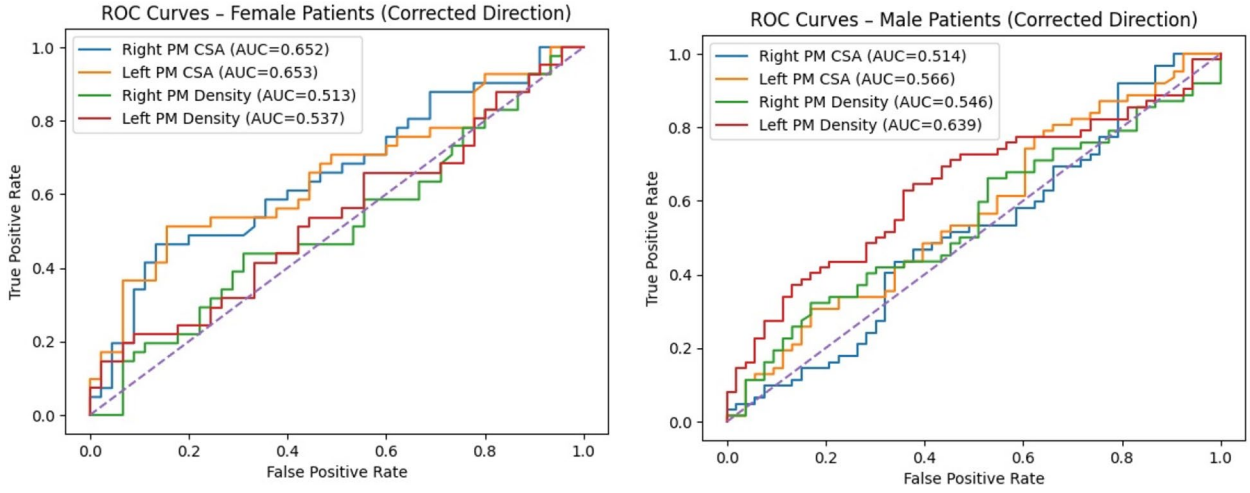

Fig. 3 Receiver Operating Characteristic (ROC) curve analysis of pectoralis major muscle metrics in female and male patients. Receiver operating characteristic (ROC) curves demonstrating the predictive performance of pectoralis major (PM) muscle cross-sectional area (CSA) and density for female and male patients. The left panel represents female patients, where right PM CSA (AUC = 0.652) and left PM CSA (AUC = 0.653) showed moderate discrimination, while right (AUC = 0.513) and left (AUC = 0.537) PM density demonstrated lower predictive ability. The right panel represents male patients, where left PM density (AUC = 0.639) showed the highest discriminatory performance, followed by left PM CSA (AUC = 0.566), right PM density (AUC = 0.546), and right PM CSA (AUC = 0.514). The diagonal dashed line indicates the reference line for no discrimination

Discussion

In this study conducted among patients aged 65 and older—a population at high risk for COVID-19—some limited findings related to mortality were identified between survivors and those who died. In the analyses, a decrease in the cross-sectional area of both the right and left pectoralis major muscles was found to be statistically significantly associated with higher mortality in female patients, whereas in male patients, a decrease in the mean density of the left pectoralis major muscle was associated with higher mortality. However, these parameters did not yield significant results when analyzed using multivariate models. Based on our results, measurements related to the morphology of the pectoralis major muscle may provide some insights into the general condition of COVID-19 cases but may not serve as independent predictors. Future multicenter studies with larger case numbers may yield more meaningful parameters.

Morphometric measurements of skeletal muscle are being studied for their association with mortality in critically ill patients, not only because they reflect physical strength but also due to their contribution to respiratory mechanics [3]. The PM muscle, as one of the accessory respiratory muscles, is particularly relevant in diseases affecting pulmonary function, including COVID-19 [9]. Previous studies have shown that a lower muscle cross-sectional area or density measured on chest CT scans is associated with worse clinical outcomes—including longer hospital stays, the need for mechanical ventilation, and death—in various conditions such as COPD, cancer, and sepsis [11, 23]. Studies in the literature have reported that muscle density decreases with age, obesity, and chronic diseases, and it is thought that density may better reflect functional impairment compared to CSA [6]. Our finding that female mortality was linked to reduced CSA, while male mortality was linked to reduced density may be related to sex-related differences in muscle morphology or physiological reserve. However, these interpretations remain speculative because mechanistic data were not available in the present study and should be investigated in future research. Women typically have lower absolute muscle mass than men; thus, a further reduction in CSA may disproportionately impair their reserve [10]. Conversely, men patients may have relatively preserved bulk, but poorer muscle quality may be more critical for outcomes. These sex differences warrant further mechanistic investigation.

Several prior studies have demonstrated some prognostic role of thoracic muscle measurements in COVID-19. Ufuk et al. reported that low PM muscle density on chest CT was associated with increased mortality and need for intensive care [19]. Grigioni et al. similarly found that a reduced thoracic skeletal muscle index predicts adverse outcomes [7]. In another study by Hocaoğlu et al. involving COVID-19 patients aged 65 and older, it was noted that a decrease in average pectoralis major muscle density was associated with high mortality in women, whereas no such association was found in men; however, it should be noted that this study evaluated only the right-sided muscle morphology [8]. Our results are in line with these findings and extend previous observations by highlighting sex-specific associations and focusing on patients aged 65 years and older, a population at higher risk for severe disease. Unlike some previous studies

that included mixed age groups, our cohort allows for insights specifically into geriatric patients, who may experience accelerated sarcopenia and altered inflammatory responses. In the literature, there are studies examining muscle cross-sectional area or mean density, many of which do not stratify by sex. In some, right and left sides were not measured separately and were analyzed together, or—as in the previous example—only one side was assessed. Since morphological characteristics may vary by sex and by laterality (right vs. left), considering these factors in studies may yield more meaningful results [15].

Nevertheless, the clinical relevance of side-specific differences in pectoralis major muscle measurements remains uncertain. Although some anatomical asymmetry may exist, the finding observed only on the left side in male patients should be interpreted cautiously. It may be incidental or due to statistical variation. Factors such as limb dominance or individual anatomical differences may also play a role. Therefore, these findings should be confirmed in larger studies. In addition, ROC analyses performed separately for male and female patients suggested modest discriminatory performance of pectoralis major muscle measurements for predicting mortality. These findings further suggest that such imaging markers should be interpreted as complementary indicators rather than standalone prognostic tools.

Moreover, our findings complement studies examining other muscle groups. For example, the psoas and erector spinae muscles have also been evaluated as prognostic markers in COVID-19, with consistent evidence that lower muscle mass or density correlates with poor outcomes [2].

Our laboratory findings are generally consistent with previous reports. Blood laboratory parameters in our study also indicated that lymphopenia, elevated NLR, and increased levels of AST, LDH, CRP, and D-dimer were associated with higher mortality, consistent with previous reports linking systemic inflammation, tissue damage, and coagulopathy to adverse COVID-19 outcomes [24]. Elevated CRP and LDH levels are markers of systemic inflammation and tissue damage, and this may reflect both the severity of viral pneumonia and the underlying vulnerability of patients with reduced muscle mass [12]. Generally, our data indicate that, muscle imaging parameters should not be interpreted in isolation but in the context of systemic host responses.

In contrast to several previous studies, comorbidities were not significantly associated with mortality in our cohort. This finding may be explained by several factors. Comorbidities were categorized into broad diagnostic groups based on available hospital records, which may have limited the detection of associations with specific disease subtypes. In addition, since all patients in our cohort were elderly and comorbid conditions were highly prevalent in both groups, variability between survivors and non-survivors may have been reduced. Furthermore, the moderate sample size may have limited the statistical power to detect significant associations.

The practical importance of our findings lies in the potential integration of muscle measurements into risk stratification models for COVID-19. While clinical and laboratory parameters take important role in prognosis, CT-derived parameters may provide additional, objective insights into patients' physiological reserve. Identification of elderly patients with reduced PM CSA or density may provide additional information regarding patient frailty and physiological reserve. However, further studies are required before CT-derived muscle parameters can be incorporated into clinical decision-making or treatment planning. For example, patients with weaker muscle metrics may benefit from closer observation, early initiation of supportive therapies, or more aggressive rehabilitation and nutritional interventions once stabilized.

Our study has several strengths that merit emphasis. Our study included a relatively large sample of elderly patients ($n = 201$), all of whom had RT-PCR–confirmed COVID-19 and CT evidence of pulmonary involvement. We analyzed both CSA and density separately and stratified results by sex, revealing differential associations that might have been obscured in pooled analyses.

Conclusion

Pectoralis major muscle measurements derived from chest CT showed sex-specific associations with mortality in geriatric COVID-19 patients. Female non-survivors had lower pectoralis major cross-sectional areas, whereas male non-survivors demonstrated decreased left-sided muscle density. However, these parameters were not independently associated with mortality after multivariable adjustment for age and CRP. Pectoralis major muscle measurements on routine chest CT may therefore provide complementary information regarding patient vulnerability in elderly populations, but may not be predictors of mortality. About this topic, further prospective studies with larger cohorts and comprehensive predictive modeling are needed to clarify the clinical utility and prognostic value of these imaging-derived muscle parameters.

Study limitations

Some limitations should be acknowledged. Height and weight, which are important for calculating muscle indices normalized to body size, were not available. As a result, we could not adjust for body mass index (BMI) or directly calculate skeletal muscle index, which may have improved comparability with previous studies. Because chest CT examinations were performed according to

clinical indications during the emergency department evaluation in the COVID-19 pandemic period, the possibility of selection bias related to disease severity cannot be completely excluded. Another limitation of the present study is the number of subgroup analyses performed, including stratification by sex and by laterality. These multiple comparisons may increase the risk of type I error, and therefore the findings should be interpreted cautiously and confirmed in larger prospective studies. Our study was conducted at a single center, which may limit generalizability to other populations or healthcare systems. We did not include a control group of non-COVID-19 patients, which could have clarified whether the observed associations are specific to SARS-CoV-2 infection or reflect general vulnerability in elderly patients.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
CSA	Cross-sectional area
LDH	Lactate dehydrogenase
COVID	Coronavirus disease
CRP	C-reactive protein
COPD	Chronic Obstructive Pulmonary Disease
CoVs	Coronaviruses
MERS	Middle East respiratory syndrome
PCR	Polymerase chain reaction
PM	Pectoralis major
SARS	Severe acute respiratory syndrome
WBC	White blood cell

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None.

Authors' contributions
All authors contributed to the study conception and design. AYU, YÜ, SA, EK and AFÖ performed material preparation and data collection. AYU, YÜ, ÖFK and RA performed analysis and writing document. The first draft of the manuscript was written by AYU, EK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability
Available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was carried out in accordance with the ethical standards as laid down in the Declaration of Helsinki with the approval of the ethics committee of Karadeniz Technical University Faculty of Medicine, with the letter dated 12/10/2023 and numbered 2023/175. Due to the retrospective design of the study, no patient consent was obtained.

Consent for publication
The CT data were obtained from a retrospective review of existing imaging records.

Competing interests
The authors declare no competing interests.

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