# CT-Defined Pectoralis Muscle Density Predicts 30-Day Mortality in Hospitalized Patients with COVID-19: A Nationwide Multicenter Study

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**Rationale and Objectives:** The prognostic role of computed tomography (CT)-defined skeletal muscle features in COVID-19 is still under investigation. The aim of the present study was to evaluate the prognostic role of CT-defined skeletal muscle area and density in patients with COVID-19 in a multicenter setting.

**Materials and Methods:** This retrospective study is a part of the German multicenter project RACOON (Radiological Cooperative Network of the COVID-19 pandemic). The acquired sample included 1379 patients, 389 (28.2%) women and 990 (71.8%) men. In each case, chest CT was analyzed and pectoralis muscle area and density were calculated. Data were analyzed by means of descriptive statistics. Group differences were calculated using the Mann–Whitney-U test and Fisher's exact test. Univariable and multivariable logistic regression analyses were performed.

**Results:** The 30-day mortality was 17.9%. Using median values as thresholds, low pectoralis muscle density (LPMD) was a strong and independent predictor of 30-day mortality, HR = 2.97, 95%-CI: 1.52–5.80, p = 0.001. Also in male patients, LPMD predicted independently 30-day mortality, HR = 2.96, 95%-CI: 1.42–6.18, p = 0.004. In female patients, the analyzed pectoralis muscle parameters did not predict 30-day mortality.

For patients under 60 years of age, LPMD was strongly associated with 30-day mortality, HR = 2.72, 95%-CI: 1.17;6.30, p = 0.019. For patients over 60 years of age, pectoralis muscle parameters could not predict 30-day mortality.

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**Conclusion:** In male patients with COVID-19, low pectoralis muscle density is strongly associated with 30-day mortality and can be used for risk stratification. In female patients with COVID-19, pectoralis muscle parameters cannot predict 30-day mortality.

**Key Words:** COVID-19; CT; Skeletal muscle; Sarcopenia; Body composition.



## INTRODUCTION

The coronavirus disease 2019 (COVID-19) posed a significant threat to global health. The clinical course of COVID-19 varies widely, with most cases presenting mild symptoms, while others progress rapidly to a fatal outcome (1,2).

Early prediction of adverse outcomes in COVID-19 is therefore of critical importance. Established predictors of severe disease in COVID-19 patients include age over 60 years, male sex, and comorbidities like dementia, heart failure, and peripheral vascular diseases (3,4). Imaging plays a crucial role in diagnosing and guiding therapy in COVID-19. Computed tomography (CT) is the preferred imaging modality for detection of pulmonary consolidations and complications such as thrombosis and pulmonary embolism in patients with COVID-19 (5,6).

Recent literature highlights the significance of extrapulmonary findings in COVID-19 patients (7). Studies have identified coronary calcifications, pleural effusion, pericardial effusion, and mediastinal lymphadenopathy as independent predictors of severe disease (7–9). For instance, the presence of pleural and/or pericardial effusion has been reported as a strong independent predictor of mortality in COVID-19 (7,10). Additionally, parameters of the skeletal musculature and visceral and/or subcutaneous adipose tissue may have prognostic relevance, though findings on the issue are preliminary and often contradictory (11). While some researchers have found associations between sarcopenia and important clinical outcomes in patients with COVID-19, others have not (11–13).

The aim of this multi-center study is to evaluate the prognostic value of the pectoralis muscle area and density, measured in a single slice on chest CT scans, for 30-day mortality in COVID-19 patients.

## MATERIAL AND METHODS

The present retrospective study is a subproject of the German research infrastructure project RACOON (Radiological Cooperative Network) (14). It has been collaboratively created by all radiological departments within the German Network of University Medicine (NUM) as partner sites (14).

This subproject received approval from the Review Board (number 20–719). All RACOON sites were contacted to provide the data on hospitalized patients with COVID-19. Overall, 19 sites provided data in this study (Fig 1). The participating university centers were:

- Institute of Diagnostic and Interventional Radiology, University Hospital Frankfurt
- Department of Radiology and Nuclear Medicine, University Hospital of Magdeburg
- Department of Radiology, University Hospital of Leipzig
- Department of Radiology, University Hospital of Halle
- Department of Radiology, University Hospital of Erlangen
- Department of Radiology, University Hospital of Rostock
- Institute of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen
- Department of Diagnostic Interventional Radiology, University Hospital RWTH Aachen
- Department of Radiology, University Hospital of Berlin
- Department of Diagnostic and Interventional Radiology, University Medical Center Mainz
- Department of Radiology, University Hospital of the Ludwig-Maximilian University Munich
- Department of Radiology, Hannover Medical School
- Clinic for Radiology, University Hospital of Münster
- Department of Radiology, University Hospital of Kiel
- Department of Radiology, University Hospital of Hamburg
- Institute of Radiology, Neuroradiology and Nuclear Medicine Minden, Ruhr-University-Bochum
- Clinic for Diagnostic and Interventional Radiology and Neuroradiology, University Hospital of Augsburg
- Department of Radiology, University Hospital Schleswig-Holstein-Campus Luebeck
- Clinic for Diagnostic and Interventional Radiology, University Hospital Heidelberg

Inclusion criteria for the present study were:

- Diagnosis of COVID-19 confirmed by Polymerase chain reaction (PCR);
- First pretreatment chest CT examination of diagnostic image quality;
- Complementary data about 30-day mortality.

Exclusion criteria were:

- Missing or incomplete documentation of clinical parameters
- Non-diagnostic image quality of CT studies
- Missing documentation of SARS-CoV-2 infection by PCR
- Primary/secondary malignant diseases

### Measurement of the Pectoralis Muscle on CT

All measurements were manually performed by experienced radiologists using dedicated reporting and viewing software

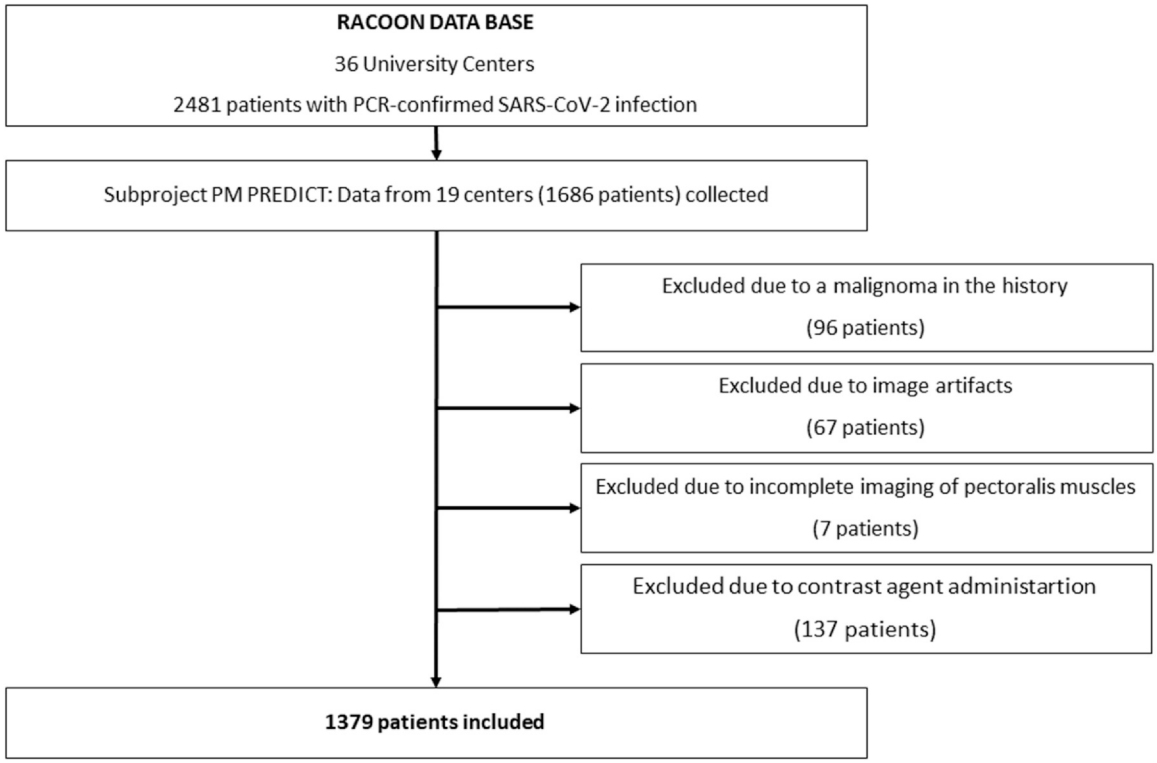


**Figure 1.** Flow chart of the data acquisition.

(Mint Lesion, Mint Medical GmbH, Heidelberg, Germany). The radiologists underwent training in two virtual meetings before data aggregation. Also, all readers were blinded to clinical outcomes.

The measurements were performed on axial images reconstructed with a soft tissue kernel at the T4 vertebral level. A polygonal region of interest (ROI) was drawn along the contours of the pectoralis major and minor muscles on both sides (Fig 2). The pectoralis muscle area (PMA) was defined as a sum of the bilateral areas of the pectoralis major and minor muscles. Furthermore, pectoralis muscle density (PMD) was measured within the ROIs (15). Additionally, skeletal muscle gauge (SMG) was calculated by multiplying PMA with mean muscle density (15). Gender-specific median values were used as thresholds for estimating low or normal pectoralis muscle area and density. There were as follows: male patients, pectoralis muscle area: 1868 $mm^2$, pectoralis muscle density: 40.30 HU; female patients: pectoralis muscle area: 1495 $mm^2$, pectoralis muscle density: 33.68 HU.

Furthermore, pathological lung involvement due to COVID-19 was visually assessed for each patient, according to a lung damage CT scoring system. Each of the five lung lobes was visually assessed to determine the presence of ground glass opacities (GGO) or consolidation and degree of extension of either GGO areas alone or combined with condensation opacity areas (16). Each lung lobe was classified with a score of 0, 1, 2, 3, or 4, corresponding to none, minimal (1–25%), mild (26–50%), moderate (51–75%), or severe (> 75%) visual estimations, respectively (16).

### Statistical Analysis

Statistical analysis was performed using SPSS (IBM SPSS Statistics for Windows, version 25.0, IBM corporation). Descriptive statistics, including absolute and relative frequencies, were used to summarize the data. The investigated group differences (survivors vs non-survivors; patients requiring mechanical ventilation or ICU admission vs patients without) were assessed using the Mann–Whitney-U test. Univariable binary logistic regression analysis was performed to investigate the associations between skeletal muscle parameters and 30-day mortality. Statistically significant variables were further analyzed in multivariable logistic regression analysis to adjust for potential confounding factors. In all instances, a $p$-value of $< 0.05$ was considered indicative of statistical significance.

## RESULTS

The final cohort consisted of 1379 patients, with 389 (28.2%) women and 990 (71.8%) men. The baseline characteristics of the patients and the measurements of the pectoralis muscle are summarized in Table 1.

Of the included patients, 248 (17.9%) died within the 30-day observation period. Non-survivors had lower pectoralis muscle density (LPMD) (Table 2). However, the pectoralis muscle area did not differ significantly between survivors and non-survivors ($p = 0.16$).

Furthermore, LPMD (HR = 2.97, 95%-CI:1.52–5.80, p = 0.001) was a strong and independent predictor of

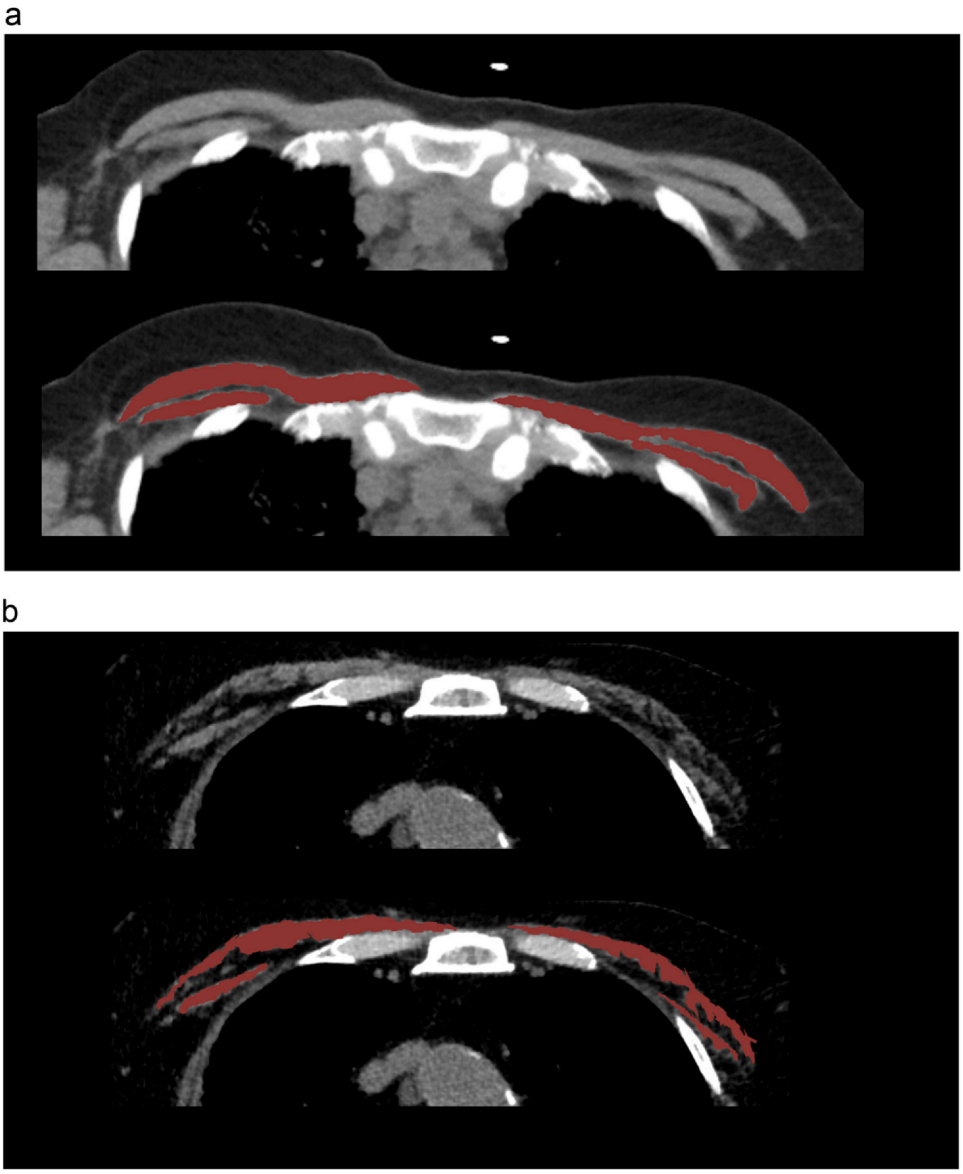


**Figure 2.** Estimation of the pectoralis muscle parameters in two patients of the sample. Regions of interest around the pectoralis major and minor muscles. **(a)** Parameters of the pectoralis musculature in a 56-year-old man Pectoralis muscle area = 1780 $mm^2$, pectoralis muscle density = 30 HU. The patient was discharged in good condition. **(b)** Parameters of the pectoralis musculature in a 61-year-old man. Pectoralis muscle area = 1142 $mm^2$, pectoralis muscle density = 18 HU. The patient died on day 22 after admission.

**TABLE 1. Included Patients, Imaging Findings and Follow-up**

| Age mean (years) | 62.2 ± 15.1 |
|---|---|
| Female, *n* (%) | 389 (28.2) |
| Male, *n* (%) | 990 (71.2) |
| Visual lung damage CT score, M ± SD | 11.3 ± 6.1 |
| 30-day mortality, *n* (%) | 248 (17.9) |
| Pectoralis muscle area, mean ± SD, $mm^2$ | 2579 ± 3372 |
| Pectoralis muscle density, mean ± SD, HU | 36.5 ± 15.9 |

30-day mortality (Table 3). Low pectoralis muscle area, however, did not predict 30-day mortality.

Subsequently, the prognostic value of the pectoralis muscle parameters was analyzed separately for male and female patients. The frequency of LPMD and low pectoralis muscle area did not differ by gender (Table 4).

In male patients, LPMD (HR = 2.96, 95%-CI:1.42–6.18, p = 0.004) was also a strong and independent predictor of 30-day mortality (Table 5a).

In female patients, however, the pectoralis muscle parameters did not predict 30-day mortality to a statistically significant degree (Table 5b).

Finally, the role of the pectoralis musculature was analyzed in patients under and over 60 years of age. LPMD was strongly associated with 30-day mortality (HR = 2.72, 95%-CI: 1.17;6.30, p = 0.019) in patients under 60 years of age (Table 6a). For patients over 60 years of age, the pectoralis muscle parameters did not predict 30-day mortality (Table 6b).

**TABLE 2. Pectoralis Muscle Parameters According to Survivors and Non-survivors**

| Pectoralis muscle parameters | Survivors (*n* = 1135) | Non-survivors (*n* = 248) | p-values |
|---|---|---|---|
| Muscle area (mm²) | 2708 ± 3643 | 1969 ± 1500 | 0.16 |
| Muscle density (HU) | 37.4 ± 15.7 | 32.5 ± 16.3 | < 0.001 |
| Muscle gauge | 106,008 ± 165,021 | 66,382 ± 61,600 | 0.001 |
| Patients with low muscle area | 565 (49.7%) | 134 (54.0%) | 0.50 |
| Patients with low muscle density | 529 (46.7%) | 165 (66.5%) | 0.002 |
| Patients with low muscle gauge | 553 (48.7%) | 146 (58.9%) | 0.10 |

**TABLE 3. Uni- and Multivariable Regression Analysis for Prediction 30-day Mortality in the Overall Sample**

| | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95%CI | p-value | HR | 95%CI | p-value |
| Low pectoralis muscle area | 1.17 | 0.89–.55 | 0.24 | | | |
| Low pectoralis muscle density | 2.29 | 1.71–3.05 | < 0.001 | 2.97 | 1.52–5.80 | 0.001 |
| Low pectoralis muscle gauge | 1.47 | 1.11–1.94 | 0.006 | 1.53 | 1.12–2.09 | 0.007 |
| CT lung score | 1.03 | 0.99–1.07 | 0.055 | | | |
| Age | 1.01 | 1.008–1.02 | 0.01 | 1.02 | 1.001–1.03 | 0.03 |

**TABLE 4. Frequency of Low Pectoralis Muscle Area and Density in Male and Female Patients with COVID-19**

| Pectoralis muscle values | male | female | p-value |
|---|---|---|---|
| Low pectoralis muscle area, *n* (%) | 459/864 (53.1%) | 215/370 (58.1%) | 0.40 |
| Low pectoralis muscle density, *n* (%) | 441/864 (51.0%) | 182/370 (49.1%) | 0.74 |

**TABLE 5A. Uni- and Multivariable Regression Analysis for 30-day Mortality in Male Patients**

| | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95%CI | p-value | HR | 95%CI | p-value |
| Low pectoralis muscle area | 1.53 | 1.08–2.16 | 0.015 | 1.54 | 0.88–2.71 | 0.12 |
| Low pectoralis muscle density | 2.42 | 1.69–3.47 | < 0.0001 | 2.96 | 1.42–6.18 | 0.004 |
| CT lung score | 1.03 | 0.98–1.07 | 0.14 | | | |
| Age | 1.01 | 1.006–1.03 | 0.004 | 1.02 | 0.99–1.04 | 0.06 |

**TABLE 5B. Univariable Regression Analysis for 30-day Mortality in Female Patients**

| | HR | 95%CI | p-value |
|---|---|---|---|
| Low pectoralis muscle area | 0.67 | 0.38–1.19 | 0.18 |
| Low pectoralis muscle density | 1.61 | 0.90–2.85 | 0.10 |
| CT score | 0.98 | 0.91–1.06 | 0.77 |
| Age | 1.01 | 0.99–1.02 | 0.28 |

## DISCUSSION

This study highlights the important prognostic value of the pectoralis muscle quality in COVID-19 patients, demonstrated by a large, multicenter cohort. Because of the extensive sample size and multicenter approach, the findings can be considered representative.

There is strong evidence supporting the prognostic role of the skeletal musculature in various acute disorders. For instance, parameters such as muscle area and density, as assessed on CT, are established predictors of clinical outcomes in critically ill patients (17–19). Previous research has shown that low skeletal muscle mass is strongly associated with both mortality and recovery in critically ill patients undergoing dialysis (18), as well as with in-hospital mortality and prolonged hospitalization in sepsis patients (19).

The role of the skeletal musculature in COVID-19 has been widely studied. Yi et al. demonstrated a correlation between pectoralis muscle status and COVID-19-induced lung injury in elderly patients (20). Schiaffino et al. found that reduced skeletal muscle mass was significantly associated with both ICU admission (OR = 4.8, CI-95%:2.7–8.5, $p < 0.001$) and mortality (OR = 2.3, CI-95%: 1.0–2.9, $p < 0.027$) (11). Similarly, Kim et al. reported that reduced

**TABLE 6A. Associations Between the Pectoralis Muscle Values and 30-day Mortality in COVID-19 Patients Under 60 Years of Age**

| | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95%CI | p-value | HR | 95%CI | p-value |
| Low pectoralis muscle area | 1.11 | 0.64;1.93 | 0.68 | | | |
| Low pectoralis muscle density | 1.94 | 1.13;3.34 | 0.012 | 2.72 | 1.17;6.30 | 0.019 |
| CT lung score | 1.15 | 1.07;1.24 | 0.001 | 1.13 | 1.05;1.22 | 0.001 |

**TABLE 6B. Associations Between the Pectoralis Muscle Values and 30-day Mortality in COVID-19 Patients Over 60 Years of Age**

| | Univariable analysis | | | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95%CI | p-value | HR | 95%CI | p-value |
| Low pectoralis muscle area | 1.29 | 0.89;1.87 | 0.17 | | | |
| Low pectoralis muscle density | 1.98 | 1.33;2.94 | 0.001 | 1.65 | 0.82;3.33 | 0.15 |
| CT lung score | 1.21 | 1.15;1.28 | 0.001 | 1.22 | 1.15;1.29 | 0.001 |

skeletal muscle mass is associated with prolonged hospital stay in patients with COVID-19 (12). However, most studies have focused on skeletal muscle mass and/or area as a surrogate parameter for sarcopenia, with only a few recent studies investigating the prognostic value of skeletal muscle density (20–24). This is particularly important, as muscle density better reflects muscle quality, whereas muscle area is a surrogate for muscle quantity (20–24). The literature reports varying results for these CT-defined muscle features, especially regarding muscle density in COVID-19 patients. For instance, Palmisano et al. found that myosteatosis, reflected by low muscle density, did not predict unfavorable course of COVID-19 infection, (OR = 1.244, 95%-CI:0.937–1.653, p = 0.132) (23). On the other hand, Sabatino et al. reported an association between myosteatosis and higher mortality, (HR = 2.01, 95%-CI:1.27–3.17, p = 0.003) (22). Additionally, most studies on skeletal muscle density in COVID-19 are based on relatively small sample sizes of about 100 patients per study.

Our findings demonstrate that low pectoralis muscle density and gauge are strong and independent predictors of 30-day mortality in patients with COVID-19. The underlying mechanisms are likely multifactorial. Primary literature suggests significant interactions between the skeletal musculature and the immune system. Skeletal muscles release numerous myokines with immunomodulatory effects (25). For example, myokines reduce the angiotensin-converting enzyme 2 levels in bronchial epithelial cells, potentially preventing the entry of COVID-19 viruses into target cells (26). The myokine irisin inhibits systemic inflammation and protects against endothelial injury and mitigates endothelial barrier dysfunction (27,28). Additionally, myokine interleukin (IL)−15 stimulates proliferation and activation of natural killer cells and CD8+ T-lymphocytes, key components of the antiviral immune defense (29). IL-15 also enhances phagocytic activity of neutrophils (30). Hypothetically, low-quality (steatotic) skeletal muscle has a diminished capacity to secrete these beneficial myokines, compared to muscles of high density.

This study demonstrates that the prognostic role of the pectoralis muscle quality, as indicated by muscle density, is superior to that of the pectoralis muscle quantity, represented by muscle area, in COVID-19 patients. Moreover, the influence of pectoralis muscle density on the 30-day mortality is greater than that of pulmonary involvement and patient age. These findings suggest that quantitative pectoralis muscle parameters should be included into radiological reports.

Interestingly, our study reveals that low pectoralis muscle density predicts 30-day mortality in male, but not in female COVID-19 patients. This finding is challenging to interpret. Previously, only few reports identified that disease outcomes and predictors of death differed by gender in patients with COVID-19 (10,31–33). For instance, Percivale et al. also observed a phenomenon that women had lower hospital admission and mortality, which was independent of CT findings between both sexes (32). Also, it has been reported that the presence of pericardial effusion was associated with 30-day mortality only in male patients (10). This may be due to the different immune responses in the two sexes. It is known that women may be less susceptible to viral infections because of different natural immunity and different activity of steroid hormones (33,34). In an experimental investigation, males were more susceptible to Sars-CoV infection and showed elevated virus load, associated with increased vascular leakage, and alveolar edema (35).

Regardless of the cause, these findings could potentially improve clinical practice by enabling personalized risk stratification in COVID-19 patients.

While the global threat of COVID-19 has diminished, the pandemic provided a unique environment in which large portions of the population were infected with the same viral agent. This allowed for the inclusion of a large number of comparable patients in this retrospective multicenter study, enhancing the reliability of our findings. From a research perspective, our results may be transferable to other diseases, as the influence of pectoralis muscle parameters on 30-day

mortality has been thoroughly analyzed and may serve as a surrogate parameter for patient frailty. These findings could also benefit future patients with other viral infections and secondary systemic inflammation.

The present study has several limitations. First, as a retrospective study, it is subject to inherent bias. Second, only hospitalized patients with COVID-19 were included and it is subject to inherent bias. However, all previously published studies show this bias. Third, our cohort includes only patients, who underwent non-contrast CT scans. This was done to ensure homogeneity of the muscle density parameters, as differences between native and contrast-enhanced scans could introduce bias. However, given the large multicenter cohort, the results of this study can be considered representative.

According to the literature, measure of the skeletal muscle mass on CT at the third lumbar vertebra level represents a standardized method to quantify the skeletal musculature (36). However, in patients with COVID-19, predominantly only chest CT investigations were performed and most studies analyzed the pectoralis musculature for this purpose (37–39).

In conclusion, low pectoralis muscle density and gauge are strongly associated with 30-day mortality in male COVID-19 patients and can be used for risk stratification. However, these parameters do not predict 30-day mortality in female patients to a statistically significant degree.

## DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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