Association of Paraspinal Muscle Measurements on Chest Computed Tomography with Clinical Outcomes in Patients with Severe Coronavirus Disease 2019

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Abstract

Background: Skeletal muscle depletion is common in the elderly and individuals with chronic comorbidities, who have an increased risk of developing severe coronavirus disease 2019 (COVID-19), which is defined by hypoxia requiring supplemental oxygen. This study aimed to determine the association between skeletal muscle depletion and clinical outcomes in patients with severe COVID-19.

Methods: One hundred and sixteen patients with severe COVID-19 who underwent chest computed tomography (CT) scan on admission were included in this multicentre, retrospective study. Paraspinal muscle index (PMI) and radiodensity (PMD) were measured using CT images. The primary composite outcome was the occurrence of critical illness (respiratory failure requiring mechanical ventilation, shock, or intensive care unit admission) or death, and the secondary outcomes were the duration of viral shedding and pulmonary fibrosis in the early rehabilitation phase. Logistic regression and Cox proportional hazards models were employed to evaluate the associations.

Results: The primary composite outcome occurred in 48 (41.4%) patients, who were older and had lower PMD (both $P < 0.05$). Higher PMD was associated with reduced risk of critical illness or death in a fully adjusted model overall (OR per SD increment: 0.87, 95% CI: 0.80-0.95; $P = 0.002$) and in female patients (OR per SD increment: 0.71, 95% CI: 0.56-0.91; $P = 0.006$), although the effect was not statistically significant in male patients ($P = 0.202$). Higher PMD (HR per SD

increment: 1.08, 95% CI: 1.02-1.14; *P* = 0.008) was associated with shorter duration of viral shedding among female survivors. However, no significant association was found between PMD and pulmonary fibrosis in the early rehabilitation phase, or between PMI and any outcome in both men and women.

Conclusion: Higher PMD, a proxy measure of lower muscle fat deposition, was associated with a reduced risk of disease deterioration and decreased likelihood of prolonged viral shedding among female patients with severe COVID-19.

Keywords: Coronavirus disease 2019; Severe pneumonia; Clinical outcome; Computed tomography; Paraspinal muscle measurement.

Introduction

The rapid escalation of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has become the newest global health threat [1]. About 10-20% of COVID-19 patients develop severe illness, characterized by hypoxia requiring supplemental oxygen, who require more medical resource utilization and have a worse prognosis with a case fatality rate about 20 times higher than patients with non-severe disease, especially for those with critical illness [2, 3]. Thus, the identification of patients who are at higher risk of unfavourable clinical outcomes has the potential to facilitate more individually aligned treatment plans and medical resource allocation.

Skeletal muscle depletion or sarcopenia is common in the elderly and in patients with chronic comorbidities, who have been confirmed to be at an increased risk of developing severe COVID-19 by several recent reports [4-6]. For elderly patients in the intensive care unit (ICU) or with critical illness, skeletal muscle loss adversely affects clinical outcomes and may result in a deadly intersection of disease processes [7, 8]. However, the impact of skeletal muscle depletion on the clinical outcomes in severe COVID-19 patients remains unclear. Computed tomography (CT) has been recognised in precisely quantifying skeletal muscle cross-sectional area and radiodensity to further identify the presence of diminished muscle mass and increased muscle fat deposition, respectively [9, 10]. In a recent study, Lenchik et al. reported that higher CT-derived paraspinal skeletal muscle area and density at the T12 level were associated with better survival in a large multicentre cohort of community-

dwelling older men [11]. Likewise, our study workflow selects a single CT image at the level of the T12 vertebra from routine chest CT examinations and segments the paraspinal muscles, recording the paraspinal muscle area (PMA) and muscle radiodensity (PMD).

Therefore, based on a multicentre cohort of patients with severe COVID-19, our study aimed to assess the association of skeletal muscle depletion determined by paraspinal muscle measurements on chest CT examinations with several unfavourable clinical outcomes. We hypothesised that reduced paraspinal muscle index (PMI, i.e. PMA adjusted by height squared) or PMD would be associated with an increased risk of disease deterioration, prolonged viral shedding, and pulmonary sequela.

Materials and Methods

Study population

The Institutional Review Board of the Third Xiangya Hospital approved our study and waived the informed consent of patients due to the retrospective nature of this study. We were authorised by the Hunan Provincial Health Commission for the collection of clinical and radiological data under anonymization according to the standard of care. All consecutive patients with severe COVID-19 who underwent chest CT scan on admission at the Third Xiangya Hospital, First Hospital of Changsha, First Hospital of Yueyang, Central Hospital of Shaoyang, and Second Hospital of Changde between January 17, 2020, and February 17, 2020, were included in this multicentre, retrospective study (n = 137). Patients who had a CT scan without covering the level

of the 12th thoracic (T12) vertebra (n = 12) and those without complete clinical or laboratory data (n = 9) were excluded. A total of 116 patients were ultimately included (**Figure 1**). The diagnosis of SARS-CoV-2 infection was established on the basis of the World Health Organization interim guidelines, and a confirmed case was defined as positive on the basis of the presence of SARS-CoV-2 RNA on high-throughput sequencing or real-time reverse transcription-polymerase chain reaction (RT-PCR) assay in nasal and pharyngeal swab specimens. Severe COVID-19 cases were defined as those with one of the following: 1) respiratory distress (respiratory rate ≥ 30 beats/min); 2) hypoxia (oxygen saturation ≤ 93% in the resting state); or 3) hypoxaemia (arterial blood oxygen partial pressure/oxygen concentration ≤ 300mmHg) [12].

Clinical, laboratory, and radiological assessment

Data on demographic, epidemiological history, chronic comorbidities, clinical symptoms, and laboratory findings were obtained on admission from electronic medical records. All laboratory tests were performed according to the clinical care needs of the patient during hospitalisation, including a complete blood count, liver and renal function, coagulation testing, and measures of electrolytes, creatine kinase, lactate dehydrogenase, procalcitonin, and C-reactive protein. The respiratory tract specimens of patients were collected daily during hospitalisation and tested for SARS-CoV-2 viral RNA. All patients underwent a chest high-resolution CT scan at the time of admission, and the recovered patients repeated the CT scan one month after discharge. The CT images on admission were reviewed by two experienced

radiologists with consensus for assessment of bilateral involvement and CT severity score. The extent of lesions (opacification or consolidation) within each lung lobe was evaluated by scoring from 0 to 5, and the total score was calculated by summing up the scores of all five lobes to provide a CT severity score ranging from 0 to 25 [13]. The CT images at one month after discharge (early rehabilitation phase) were reviewed by the two experienced radiologists with consensus for the evidence of pulmonary fibrosis, which was defined as a combination of findings including parenchymal band, coarse reticular pattern, irregular interface, and traction bronchiectasis [14, 15].

Paraspinal muscle measurement

The CT scans used for paraspinal muscle measurement were carried out as part of the assessment of disease severity. Unenhanced axial CT images of patients at the T12 level were selected and assessed by two trained observers who were blinded to the clinical outcomes, using the Chest Imaging Platform plug-in in 3D Slicer software (version 4.8.1, Boston, MA, USA), which enables paraspinal muscles (including the erector spinae and multifidus muscles) demarcation using specific Hounsfield unit (HU) thresholds [16, 17]. Skeletal muscle is identified and quantified by HU thresholds of -29 to +150. The cross-sectional PMA (cm^2) was automatically computed by summing tissue pixels and multiplying by pixel surface area and then normalised to the height squared to calculate the PMI (cm^2/m^2). The PMD (HU) was measured from the same region of interest of PMA, which indirectly measures fat infiltration in muscles. The average of the values calculated by the two observers was

used for the subsequent analysis. Body mass index (BMI, kg/ m^2) was calculated as weight divided by height squared.

Study outcomes

The primary composite outcome of this study was the occurrence of critical illness or death. Critical illness for COVID-19 was defined as a case with one of the following: 1) respiratory failure requiring mechanical ventilation; 2) shock; or 3) ICU admission required for combined organ failure. Secondary outcomes were the duration of viral shedding after illness onset, which was considered the interval from symptom onset to persistent negative results of respiratory tract viral RT-PCR test, without converting positive thereafter, and the development of pulmonary fibrosis in the early rehabilitation phase. All samples from the same patient were tested until two consecutive samples (at least 24 hours apart) were negative with the first negative sample defining the duration of viral shedding.

Statistical analysis

Continuous variables are presented as the median and interquartile range (IQR), and categorical variables are presented as frequency and percentage. Differences between groups were analysed using Student's t-test or the Mann-Whitney U test for continuous variables according to the normal distribution and the Chi-square test or Fisher's exact test for categorical variables. Unadjusted and adjusted logistic regression analyses were used to evaluate the associations between paraspinal muscle measurements and the primary composite outcome, and the corresponding odds ratios

(ORs) and 95% confidence intervals (CIs) were calculated. Unadjusted and adjusted Cox proportional hazard models were adopted for the identification of potential risk factors associated with the discontinuation of viral shedding, and the corresponding hazard ratios (HRs) and 95% CIs were calculated. Subgroup analysis by gender was performed. The cumulative percentage of patients with positive SARS-CoV-2 RNA was calculated using Kaplan-Meier curves, and comparisons between groups were conducted using the log-rank test. All statistical analyses were performed using the SPSS statistics software (version 22.0, IBM Inc., Chicago, IL, USA). A two-sided *P* value of < 0.05 was considered statistically significant.

Results

The clinical characteristics of patients according to the presence of primary composite outcome are displayed in **Table 1**. Of the 116 included patients, 63 (54.3%) were men, the median age was 57 (range, 29-84) years, and the median BMI was 23.5 (range, 16.4-30.0) kg/m^2. During hospitalisation, the composite outcome occurred in 48 patients (41.4%), including 45 patients who developed critical illness and 3 deceased cases. Patients who presented with the composite outcome were significantly older ($P = 0.001$) and were more likely to have a BMI of ≥ 25 kg/m^2 ($P = 0.008$), had lower albumin ($P = 0.010$) levels, higher D-dimer ($P = 0.027$), and creatine kinase ($P = 0.042$) levels compared with those who did not. There was a higher PMD ($P < 0.001$) in patients who presented with the composite outcome in contrast to those who did not, while no significant difference was found in PMA and PMI (both $P > 0.05$). **Figure 2 A-F** illustrate the pulmonary involvement and

paraspinal muscle measurements of two patients. Also, patients who presented with the composite outcome had significantly longer hospital length of stay ($P < 0.001$) and duration of viral shedding after illness onset ($P = 0.002$), and were more likely to develop pulmonary fibrosis in the early rehabilitation phase ($P = 0.003$) than those who did not.

Patients were assigned as low or normal PMI and PMD based on the corresponding sex-specific medians. The clinical and biochemical characteristics of patients according to the presence of low muscle index or radiodensity are shown in **Supplementary Table 1**. Longer hospital length of stay was found in patients with low muscle paraspinal muscle index ($P = 0.034$) or radiodensity ($P < 0.001$) than in those without. Patients with low paraspinal muscle radiodensity were more likely to develop the primary composite outcome ($P = 0.001$), present prolonged viral shedding ($P = 0.020$), and develop pulmonary fibrosis in the early rehabilitation phase ($P = 0.011$) than those without.

An overview of the association of paraspinal muscle measurements with the presence of primary composite outcome in patients with severe COVID-19 is shown in **Table 2**. Univariate analysis showed that age ($P = 0.001$) and PMD ($P < 0.001$) were significantly associated with the presence of composite outcome. In the multivariate analysis, CT severity score (OR per standard deviation [SD] increment and 95% CI, 1.09 [1.02-1.17]; $P = 0.011$) and PMD (OR per SD increment and 95% CI, 0.87 [0.80-0.95]; $P = 0.002$) were associated with the occurrence of critical illness or death after adjustment for other confounding factors. Per SD increment in PMD was

associated with a 13% decrease in risk of critical illness or death. Subgroup analysis by gender further confirmed the significant association between PMD and the presence of composite outcome only among female patients (OR per SD increment and 95% CI, 0.71 [0.56-0.91]; *P* = 0.006) adjusted for age, any comorbidities, CT severity score, BMI, and PMI. Per SD increment in PMD was associated with a 29% decrease in risk of critical illness or death in female patients.

During hospitalisation, 113 patients had twice negative results of the viral RT-PCR test before discharge and 3 patients died. The median duration of viral shedding after illness onset among survivors was 22 (range, 8-46) days. **Table 3** provides an overview of the association of paraspinal muscle measurements with the duration of viral shedding among survivors. Univariate Cox regression analysis showed that age (*P* = 0.005) and PMI (*P* = 0.004) were significantly associated with the duration of viral shedding. In the multivariate analysis, age (HR per SD increment and 95% CI, 0.97 [0.95-1.00]; *P* = 0.023) and CT severity score (HR per SD increment and 95% CI, 0.95 [0.92-0.98]; *P* = 0.002) were associated with the duration of viral shedding after adjustment for other confounding factors. However, subgroup analysis by gender unexpectedly identified a significant association between PMD and the duration of viral shedding among female patients (HR per SD increment and 95% CI, 1.08 [1.02-1.14]; *P* = 0.008) adjusted for age, any comorbidities, CT severity score, BMI, and PMI. Per SD increment in PMD was associated with an 8% increase in risk of shorter duration of viral shedding in female patients. The Kaplan–Meier curves between patients with low PMD versus those with normal PMD by time after illness onset in

male patients (log-rank $P = 0.275$) and female patients (log-rank $P < 0.001$) are shown in **Supplementary Figure 1 A-B**. Comparing female patients with normal PMD, those with low PMD (or myosteotosis) had longer duration of viral shedding after illness onset.

Among the 113 discharged patients, 56 developed pulmonary fibrosis in the early rehabilitation phase. **Supplementary Figure 2 A-H** display the CT scans on admission and at one month after discharge in two patients. In the multivariate analysis, CT severity score (OR per SD increment and 95% CI, 1.22 [1.11-1.33]; $P < 0.001$) and presence of critical illness (OR per SD increment and 95% CI, 6.70 [2.07-21.70]; $P = 0.002$) were associated with the development of pulmonary fibrosis in the early rehabilitation phase after adjustment for other confounding factors, but not the paraspinal muscle measurements, as presented in **Supplementary Table 2**. Subgroup analysis by gender further confirmed that no significant association was found between paraspinal muscle measurements and pulmonary fibrosis in the early rehabilitation phase.

Discussion

In the present study, we investigated the associations of CT-derived paraspinal muscle measurements with several unfavourable clinical outcomes in a multicentre cohort of 116 patients with severe COVID-19. The results showed that higher PMD was associated with a reduced risk of developing critical illness or death and decreased likelihood of prolonged viral shedding in women, but no statistically significant

association was found in men. The association persisted after adjusting for age, comorbidities, CT severity score, and BMI. Importantly, after adjusting for PMI (a measure of myopenia), PMD (a measure of myosteatosis) remained predictive of the unfavourable clinical outcomes. This indicates that myosteatosis or muscle fat deposition contributes independently to clinical outcomes in female patients with severe COVID-19.

Our results revealed that patients who developed critical illness were associated with longer hospital length of stay and duration of viral shedding, higher mortality, and increased risk of developing pulmonary fibrosis in the early rehabilitation phase, which was partly shown in previous reports [18, 19]. Severe COVID-19 patients with low PMI or PMD were significantly older than those with normal values in our cohort, which may be attributed to skeletal muscle wasting and fatty muscle infiltration with age. In turn, patients with severe lung damage and hypoxaemia could further exacerbate the loss of fat-free mass and physical disability [20]. Lower PMD was further identified to be significantly predictive of disease progression and prolonged viral shedding in female patients. Yang et al reported that COVID-19 patients with high intramuscular fat deposition had a higher risk for critical illness, which was partly consistent with our results [21]. However, the prognostic value of PMI in adult COVID-19 patients reported by Ufuk et al was not confirmed by this study [22]. We found that age was no longer a risk factor for disease progression once BMI and paraspinal muscle measurements were accounting for in a fully adjusted model, which should be interpreted with caution and needs to be further investigated.

Low muscle radiodensity is believed to reflect skeletal muscle depletion and intramuscular fat deposition. The reduction in the size and number of type II myofibres is the major cellular change in sarcopenic muscle, which is partly due to the transition of type II muscle fibres into type I with age, together with intramuscular and intermuscular fat infiltration [23]. A recent study suggested that mouse skeletal muscle maintained interleukin (IL)-15 production and inhibited the $CD8^+$ T cell exhaustion phenotype during viral infection, and further concluded that skeletal muscle antagonises T cell exhaustion and enhances antiviral CD8+ T cell responses [24]. Intramuscular fat deposition can delay and blunt immune responses, especially natural killer lymphocytes involved in innate immunity [25]. Thus, lower PMD may be associated with a decreased antiviral immune response against SARS-CoV-2 attack. Besides, the hallmark of the critically ill COVID-19 patients is excessive systemic inflammation or cytokine storm, which is characterised by increased levels of serum proinflammatory cytokines [26]. Intramuscular fat is a metabolically active component of muscle, which can secrete inflammatory cytokines leading to systemic inflammation and then increase the risk of critical illness [27]. Previous studies have suggested that low muscle radiodensity, a robust indicator of overall health and physical activity level, is an important predictor of poor clinical outcomes in various chronic diseases and malignancies [28, 29]. Likewise, our results demonstrated that PMD may serve as a novel biomarker for disease deterioration in female patients with severe COVID-19.

We noticed that there was a sex disparity in the association between lower PMD and disease deterioration or prolonged viral shedding in severe COVID-19 patients. An alternative explanation may be that our sample was too small to detect effects in men and that no true sex difference exists. Further studies with larger sample size are needed to explore whether there are associations between PMD and clinical outcomes in men. It has been reported that among patients with COVID-19, men had significantly higher mortality than women [30]. There are differences in immune functions between women and men, which are manifested by stronger immune responses in women against SARS-CoV-2 [31, 32].

Currently, few studies have focussed on the clinical follow-up findings of patients who recovered from severe COVID-19 [14]. In our study, follow-up CT scans at one month after discharge showed evidence of fibrosis in almost half of the patients. Post-inflammatory pulmonary fibrosis is an important prognostic manifestation of severe pneumonia. Our results showed that patients with higher CT severity scores and who developed critical illness during hospitalisation had an increased risk of developing pulmonary fibrosis in the early rehabilitation phase, but no significant association was found between paraspinal muscle measurements and the pulmonary sequela. It also has been reported that pulmonary fibrosis may develop early in patients with SARS who have been discharged after treatment, especially in patients with the more severe disease during treatment [33]. Whether pulmonary fibrosis in the rehabilitation phase of COVID-19 can clear without treatment or would continue to progress with declining lung function needs to be further clarified by long-term follow-up.

Clinical Relevance

If future studies confirm our results and show that CT-derived muscle measurements are independently associated with clinical outcomes in severe COVID-19 patients, institutions could take advantage of routine CT examinations to identify at-risk patients. These patients could be prioritised for care management referrals. Future research should explore how the incorporation of these muscle measurements into prediction models improves the stratification of risk. Research should also examine the generalisability of these findings at other institutions. Measurement of muscularity (particularly PMD) on chest CT scans on admission may provide additive risk stratification and guide nutritional interventions for patients with severe COVID-19.

Strengths and Limitations

Our study has several important strengths. This is one of the first studies using chest CT-derived muscle measurements describing skeletal muscle depletion in severe COVID-19 patients. T12 landmark was selected for skeletal muscle quantification since the T12 level is included in the field of view of routine chest CT scans for the individuals with COVID-19. The CT examinations in our study were acquired at five hospitals, using different CT vendors and scanning protocols, likely generalizable to other health care systems.

Our study also has some limitations. First, our study was retrospectively conducted. There may be a selection bias when determining the association of skeletal muscle depletion with clinical outcomes in patients with severe COVID-19. Second, the

estimated duration of viral shedding may be limited by the frequency of specimen collection and the relatively low positive rate of viral RNA detection in throat swabs. Finally, the interpretation of our findings might be limited by the relatively small sample size. Further research into the prevalence of sarcopenia in COVID-19 pandemic and rehabilitation is also needed.

Conclusion

This is the first multicentre study of patients with severe COVID-19 where CT-derived PMD showed a robust association with disease deterioration and prolonged viral shedding, which was only significant in women but not men. Therefore, reduced paraspinal muscle radiodensity or muscle fat deposition may be an important prognostic biomarker for female patients with severe COVID-19, and a better understanding of the association should help target interventions to improve clinical outcomes.

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Conflict of Interest

None of the authors has declared a conflict of interest.

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Table 1. Characteristics of Patients with Severe COVID-19 According to the Presence of Composite Outcome

Characteristic	No (n = 68)	Yes (n= 48)	*P* value
Age (years)	53 (43-66)	64 (55-67)	0.001
≥ 65 years	17 (25.0%)	21 (43.8%)	0.034
Male gender	40 (58.8%)	23 (47.9%)	0.245
BMI (kg/m^2)	23.3 (22.2-24.5)	24.0 (21.0-25.3)	0.973
≥ 25 kg/m^2	13 (19.1%)	20 (41.7%)	0.008
Chronic comorbidities			
Any	45 (66.2%)	32 (66.7%)	0.956
Hypertension	16 (23.5%)	15 (31.3%)	0.355
Diabetes	7 (10.3%)	9 (18.8%)	0.193
Cardiovascular disease	4 (5.9%)	5 (10.4%)	0.369
COPD	6 (8.8%)	8 (16.7%)	0.202
Laboratory findings			
Platelet count (×10□/L)	183.0 (126.0-256.0)	157.5 (141.8-201.3)	0.253
White blood cell count (×10□/L)	5.6 (4.0-7.4)	5.5 (3.9-9.4)	0.534
Neutrophil count (×10□/L)	3.9 (2.5-6.2)	4.5 (2.8-8.4)	0.244
Lymphocyte count (×10□/L)	0.8 (0.6-1.2)	0.7 (0.5-1.1)	0.176
Alanine aminotransferase (U/L)	23.9 (16.9-38.2)	22.8 (16.4-36.6)	0.701
Aspartate aminotransferase (U/L)	32.8 (25.4-44.5)	37.4 (27.2-54.2)	0.064

Total bilirubin (μmol/L)	11.6 (7.5-15.9)	11.0 (8.3-17.7)	0.754
Albumin (g/L)	36.4 (33.1-39.5)	34.3 (30.9-37.6)	0.010
Creatinine (μmol/L)	64.1 (55.4-80.0)	65.1 (48.4-92.5)	0.823
D-dimer (μg/mL)	0.47 (0.21-0.70)	0.61 (0.42-1.16)	0.027
Creatine kinase (U/L)	76.5 (39.0-155.5)	98.0 (61.3-280.0)	0.042
Lactic dehydrogenase (U/L)	299.0 (203.2-373.2)	286.3 (240.7-370.7)	0.715
Procalcitonin (ng/mL)	0.06 (0.05-0.10)	0.06 (0.05-0.12)	0.522
C-reactive protein (mg/L)	44.0 (27.7-72.8)	40.3 (19.3-74.7)	0.825
Chest CT findings			
Bilateral involvement	59 (86.8%)	48 (100%)	0.009
CT severity score	14 (8-19)	16 (11-21)	0.062
Paraspinal muscle measurements			
PMA (cm^2)	32.5 (25.4-37.5)	28.1 (25.9-34.0)	0.140
PMD (HU)	41.9 (36.1-47.4)	35.0 (28.1-42.8)	< 0.001
PMI (cm^2/m^2)	11.8 (10.5-13.1)	10.7 (9.8-13.2)	0.136
Clinical outcomes			
Respiratory failure	29 (41.2%)	38 (79.2%)	< 0.001
Septic shock	0 (0)	7 (14.6%)	0.001
Acute cardiac injury	0 (0)	8 (16.7%)	< 0.001
Acute kidney injury	0 (0)	14 (29.2%)	< 0.001
Requiring mechanical ventilation	0 (0)	31 (64.6%)	< 0.001
ICU admission	0 (0)	48 (100%)	< 0.001
Death	0 (0)	3 (6.3%)	0.037
Hospital length of stay (days)	16 (11-19)	21 (17-26)	< 0.001
Duration of viral shedding after illness	20 (17-26)	24 (20-30)	0.002

onset (days)			
Pulmonary fibrosis in early rehabilitation phase	26/68 (38.2%)	30/45 (66.7%)	0.003

Median (IQR) for continuous variables and n (percentage) for categorical variables. BMI = body mass index; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; CT = computed tomography; HU = Hounsfield unit; ICU = intensive care unit; IQR = interquartile range; PMA = paraspinal muscle area; PMD = paraspinal muscle radiodensity; PMI = paraspinal muscle index.

Table 2. Association of Paraspinal Muscle Measurements with Presence of Composite Outcome

Characteristic	Univariate OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Age (years)	1.06 (1.02-1.09)	0.001	1.02 (0.96-1.07)	0.585
Male gender	0.64 (0.31-1.36)	0.247	1.26 (0.38-4.15)	0.701
Any comorbidities	1.02 (0.47-2.24)	0.956	0.79 (0.30-2.10)	0.635
CT severity score	1.06 (1.00-1.12)	0.065	1.09 (1.02-1.17)	0.011
BMI (kg/m^2)	0.98 (0.84-1.14)	0.801	0.96 (0.78-1.18)	0.696
PMI (cm^2/m^2)	0.89 (0.76-1.04)	0.138	0.95 (0.52-1.74)	0.858
PMD (HU)	0.90 (0.85-0.95)	< 0.001	0.87 (0.80-0.95)	0.002
Male				
PMI (cm^2/m^2)	0.90 (0.70-1.16)	0.418	1.37 (0.91-2.07)*	0.135
PMD (HU)	0.92 (0.85-0.99)	0.029	0.93 (0.82-1.04)*	0.202
Female				
PMI (cm^2/m^2)	0.92 (0.71-1.18)	0.495	0.98 (0.62-1.57)*	0.945
PMD (HU)	0.84 (0.76-0.93)	0.001	0.71 (0.56-0.91)*	0.006

P values are calculated using the logistic regression model. BMI = body mass index; CI = confidence interval; CT = computed tomography; HU = Hounsfield unit; OR = odds ratio; PMD = paraspinal muscle radiodensity; PMI = paraspinal muscle index.

*Adjusted for age, any comorbidities, CT severity score, BMI, and PMD (or PMI).

Table 3. Association of Paraspinal Muscle Measurements with Duration of Viral Shedding among Survivors

Characteristic	Univariate HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Age (years)	0.97 (0.95-0.99)	0.005	0.97 (0.95-1.00)	0.023
Male gender	0.98 (0.57-1.69)	0.944	1.07 (0.62-1.86)	0.798
Any comorbidities	1.02 (0.91-1.14)	0.729	1.44 (0.91-2.27)	0.119
CT severity score	1.09 (0.97-1.22)	0.158	0.95 (0.92-0.98)	0.002
BMI (kg/m^2)	1.02 (0.98-1.06)	0.464	1.02 (0.92-1.13)	0.721
PMI (cm^2/m^2)	0.96 (0.93-0.99)	0.004	0.99 (0.89-1.10)	0.796
PMD (HU)	0.96 (0.53-1.74)	0.890	1.03 (0.99-1.07)	0.100
Male				
PMI (cm^2/m^2)	1.09 (0.97-1.22)	0.158	0.91 (0.79-1.05)	0.201
PMD (HU)	1.02 (0.98-1.06)	0.464	0.96 (0.90-1.03)	0.244
Female				
PMI (cm^2/m^2)	1.15 (1.00-1.32)	0.045	1.08 (0.91-1.29)	0.394
PMD (HU)	1.08 (1.03-1.12)	0.001	1.08 (1.02-1.14)	0.008

P values are calculated using the Cox proportional hazards model. BMI = body mass index; CI = confidence interval; CT = computed tomography; HR = hazard ratio; HU = Hounsfield unit; PMD = paraspinal muscle radiodensity; PMI = paraspinal muscle index. *Adjusted for age, any comorbidities, CT severity score, BMI, and PMD (or PMI).

Figure Legends

Figure 1. Flowchart displaying the study population enrolment.

Figure 2. CT images showing the pulmonary involvement and paraspinal muscle measurements in two patients with severe COVID-19 pneumonia. (A) A 56-year-old male patient with multiple, patchy ground-glass opacity or consolidation in bilateral lungs; (B) CT image at the T12 level used for the paraspinal muscle measurement; (C) Purple zone indicating the paraspinal muscle area identified using a threshold of -29 to +150 HU (PMI 13.0 cm^2/m^2, PMD 48.6 HU). (D) A 70-year-old male patient with large patchy ground-glass opacity with crazy-paving sign in right lung; (E) CT image at the T12 level used for the paraspinal muscle measurement; (F) Purple zone indicating the paraspinal muscle area identified using a threshold of -29 to +150 HU (PMI 10.3 cm^2/m^2, PMD 25.6 HU).

Figure 1

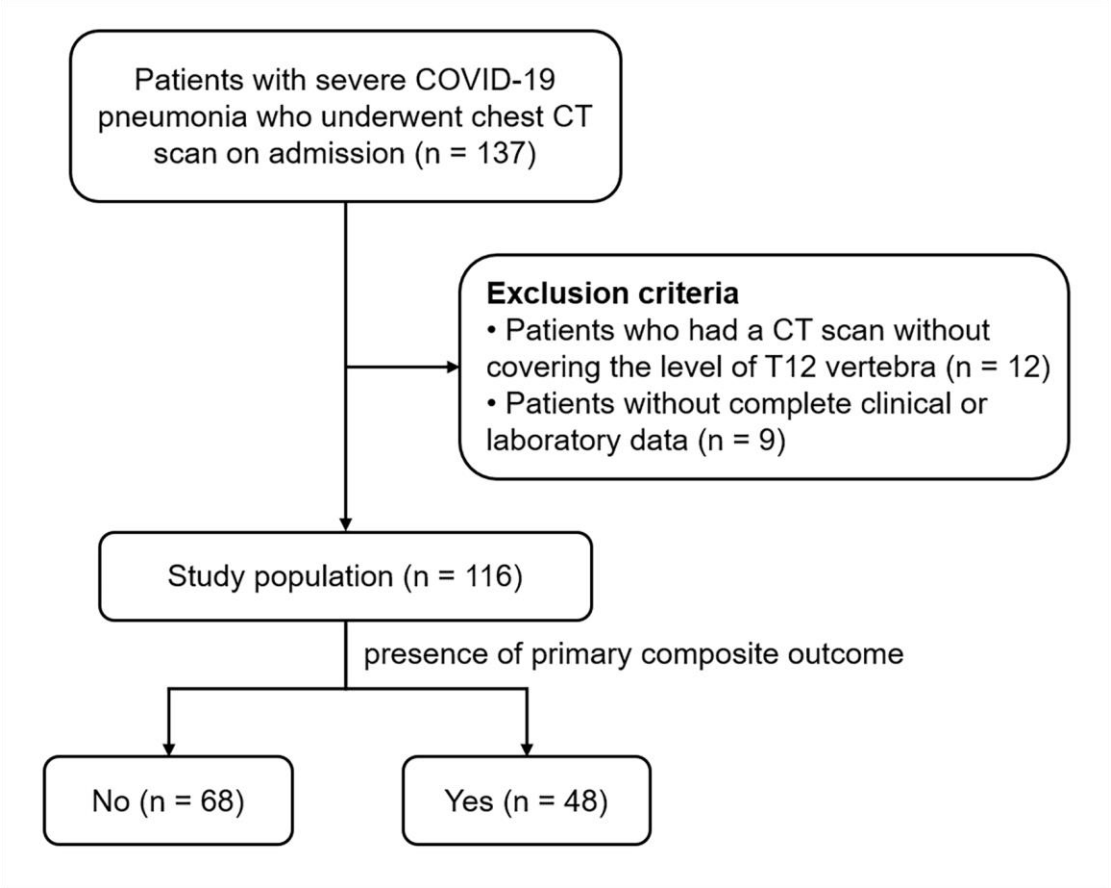

Figure 2