

Low thoracic skeletal muscle index is associated with negative outcomes in 244 patients with respiratory COVID-19

S. Grigioni, V.-E. Lvovschi, F. Tamion, L.-M. Joly, M. Coëffier, H. van Elslande, Marie Galmiche, M. Gâté, U. Traore-Ouattara, B. Marais, et al.

▶ To cite this version:

S. Grigioni, V.-E. Lvovschi, F. Tamion, L.-M. Joly, M. Coëffier, et al.. Low thoracic skeletal muscle index is associated with negative outcomes in 244 patients with respiratory COVID-19. Clinical Nutrition, 2023, 42 (2), pp.102-107. 10.1016/j.clnu.2022.11.011. hal-03977635

HAL Id: hal-03977635 https://normandie-univ.hal.science/hal-03977635v1

Submitted on 29 May 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.





Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu



Covid-19

Low thoracic skeletal muscle index is associated with negative outcomes in 244 patients with respiratory COVID-19



S. Grigioni ^{a, b, c}, V.-E. Lvovschi ^{b, d}, F. Tamion ^{e, f}, L.-M. Joly ^d, M. Coëffier ^{a, b, c}, H. Van Elslande ^{a, b, c}, Marie Galmiche ^a, M. Gâté ^a, U. Traore-Ouattara ^e, B. Marais ^e, I. Michel ^d, P. Dechelotte ^{a, b, c}, C. Savoye-Collet ^g, N. Achamrah ^{a, b, c, *}

- ^a Nutrition Department, CHU Rouen, Rouen, France
- ^b Normandie Univ, UNIROUEN, INSERM UMR 1073, Nutrition, Inflammation et axe microbiote-intestin-cerveau, IRIB, Rouen, France
- ^c Clinical Investigation Centre CIC 1404, INSERM and CHU Rouen, France
- d Emergency Department, CHU Rouen, Rouen, France
- ^e Medical Intensive Care Unit, CHU Rouen, France
- f Normandie Univ, UNIROUEN, INSERM U1096, F-76000 Rouen, France
- g Radiology Department, QUANTIF-LITIS EA 4108, France

ARTICLE INFO

Article history: Received 13 June 2022 Accepted 9 November 2022

Keywords: Sarcopenia COVID-19 Skeletal muscle index Computed tomography Emergency care

SUMMARY

Background: Sarcopenia is associated with negative outcomes in intensive care unit (ICU) patients and during chronic diseases. We aimed to evaluate if low skeletal muscle index (SMI) measured by computed tomography (CT) at the thoracic level is associated with poor outcomes in hospitalized patients with respiratory COVID-19.

Methods: Patients admitted to the hospital between March 1st and June 9, 2020 with a confirmed diagnosis of respiratory COVID-19 in the Emergency Department were included in this retrospective cohort study. SMI was assessed from a transverse CT image at the T12 level. We analysed the association between thoracic SMI and mortality, ICU admissions, infections, length of stay and gravity scores.

Results: We included 244 patients, whose median age was 62 (20–95) years, mean body mass index was 28,6 kg/m², and 34% were obese patients. 102 patients (41,8%) had low thoracic SMI. On multivariable analysis, low thoracic SMI was associated with more infections (OR = 1,88 [1,06-2,98]) and increased length of stay (OR = 1,87 [1,14-3,49]) but not with mortality (OR = 1.37 [0.54–3.52]), whereas it was inversely associated with ICU admission (OR = 5,56 [1,96-16,67].

Conclusion: Low SMI measured by CT at the thoracic level T12 is associated with negative outcomes in patients with respiratory COVID-19.

© 2022 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Sarcopenia is a clinical condition in which skeletal muscle mass and strength gradually decline, leading to adverse outcomes including poor quality of life, disability, and death. Sarcopenia is defined in the literature as a progressive degeneration of muscle tissue, with a prevalence in older people. An agreement on defining sarcopenia, as well as diagnostic criteria, was proposed by the European Working Group on Sarcopenia for Older People Sarcopenia [1]. Younger subjects are also at risk in some conditions due to lifestyle (sedentary), nutritional status (malnutrition), or during pathologies promoting the loss of muscle mass (obesity, diabetes,

E-mail address: najate.achamrah@univ-rouen.fr (N. Achamrah).

inflammatory diseases). Sarcopenia is associated with negative outcomes in intensive care unit (ICU) patients by contributing to sepsis, resistant infections, neuropathy, and ventilator-associated pneumonia [2]. Physical function and muscle strength measurements are not available in ICU patients because of sedation. However, low muscle mass alone is commonly used for diagnosing sarcopenia in ICU patients. Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease associated with a wide range of clinical manifestations, ranging from alterations in smell and taste to severe respiratory distress requiring intensive care, that might be associated with weight loss and malnutrition. Prevalence of malnutrition in hospitalized COVID-19 patients is estimated at about 50% (31.7–66.5%) [3]. Muscle loss appears strongly correlated with the COVID-19 disease severity [4]. Skeletal muscle mass can be assessed with various methods including bioelectrical impedance (BIA), dual-energy x-ray absorptiometry (DXA), magnetic resonance

^{*} Corresponding author. Department of Clinical Nutrition, Rouen University Hospital, 1 Rue de Germont, 76000 Rouen, France.

imaging (MRI) and transverse computed tomography (CT) at the lumbar level L3 [5]. Previous findings reported that low muscle mass is a predictor of negative clinical outcomes in COVID-19 patients [6–9]. In a recent meta-analysis of eight retrospective studies including 1059 COVID-19 patients, the pooled prevalence of low skeletal muscle mass (SMM) was 33.6%. The pooled odds ratio for the effect of low SMM on in-hospital mortality was 5.84 (95% CI 1.07–31.83) in univariate analysis, and 2.73 (95% CI 0.54–13.70) in multivariate analysis [10]. Most COVID-19 patients only receive thoracic CT scans. Recently, the diagnosis of sarcopenia by using skeletal muscle measurement at the T12 level has been validated compared to the L3 level [11] and has been associated with clinical outcomes in patients undergoing CT limited to the chest [12,13].

In the Emergency Department (ED), malnutrition remains not carefully screened, by lack of time and suitable tools. This new CT based method could allow an easier and earlier detection of sarcopenia in critically patients, particularly in the pandemic context, as CT is one of the routine diagnostic tool for respiratory COVID-19 severe forms. Automatization of the CT scans analysis using artificial intelligence may improve the diagnosis efficiency [14].

In this study, we aimed to evaluate if low skeletal muscle index (SMI) measured by CT at the thoracic level (T12) is associated with clinical outcomes in hospitalized patients with respiratory COVID-19 hospitalized after admission in the ED.

2. Methods

2.1. Study population

Patients hospitalized after an admission in the ED of Rouen University hospital, from March 2020 to June 2020 were included if they had a thoracic CT-scan in the ED (CT Revolution Evo - General Electric — Medical Systems) and a positive nasopharyngal swab for diagnosis of COVID-19 infection. Minor patients were excluded. The calculation of the SMI was carried out retrospectively. This retrospective study was approved by the Institutional Review Board of Rouen University Hospital.

2.2. Skeletal muscle assessment

CT DICOM (Digital Imaging and Communications in Medicine) images were analysed by a senior radiologist blinded to the clinical data. On a single CT image, skeletal muscle area was segmented by a dedicated plugin running on Carestream - Picture Archiving and Communication System. Skeletal muscle was identified and quantified by use of Hounsfield Unit thresholds (–29 to + 150) according to the widely accepted muscle tissues thresholds validated by Derstine et al. A single cross-sectional CT slice at the T12 level was used for segmentation of skeletal muscle. The skeletal muscle included rectus abdominis, external oblique, internal oblique, latissimus dorsi, intercostal and erector spinae muscles. The cross-sectional surface area of muscle was obtained by summing the given tissue's pixels and multiplying the sum by the absolute unit pixel surface area. The skeletal muscle index (SMI) was calculated by dividing the surface area by the height squared.

In our study, we used Derstine et al. sex specific cut-offs for low SMI in T12: for female SMI<20.8 cm^2/m^2 ; for male SMI<28.9 cm^2/m^2 .

2.3. Outcomes definition

We have studied the association between low SMI and four main outcomes: in-hospital mortality, acquired nosocomial infection, length of stay (LOS), and ICU admission. Nosocomial infection was conventionally defined as occurring at least 48 h after

hospitalisation and not present or incubating at the time of admission. A long LOS gathered patients who stayed hospitalized more than 23 days for COVID-19, this threshold corresponding to the 4th quartile of our population.

2.4. Data and co-variables

Data were obtained from the electronical medical records of each patient: Sex, age (>65 years old), smoking status (smoker/no smoker) comorbidities (chronic lung disease, cardiovascular disease, chronic kidney disease, diabetes) and obesity (defined by BMI >30 kg/m²). The clinical severity at admission in the emergency unit was evaluated by the NEWS 2 (National Early Warning Score 2) score [15]. This score, ranging from 0 to 20 points, was determined from respiration rate, oxygen saturation, need of supplemental oxygen, systolic blood pressure, pulse rate, level of consciousness and temperature. According to the total score, we identified 4 degrees of clinical severity at admission: low (score from 0 to 4), moderate (score from 5 to 6); high (score from 7 to 8) and severe (score \geq 9). We also selected biological variables including polynuclear neutrophils cell count, C-reactive protein (CRP (mg/l)), albumin (g/l) and creatinine (umol/l). Finally, we collected chest CT findings including severity of lung lesions due to COVID-19 classified in 3 classes: moderate (<25%), high (25–50%) and severe (>50%) and the presence or not of a pulmonary embolism associated.

2.5. Statistical analysis

Data are presented as means (\pm SD) for continuous variables, and categorical data are represented as frequencies and percentages. Chi-squared tests were used for categorical variables and Student-t-test or ANOVA for continuous variables to study differences between low and normal SMI groups. In order to identify risk factors, we performed univariate logistic regression analyses using the different outcomes (death, LOS >23 days, acquired infection and ICU admission) as the dependent variables and low SMI and other co-variables as independent variables. Then, only variables with a p < 0.05 on the univariate regression were included in a multivariate model. Statistical analysis was performed with SPSS version 20.0.

3. Results

3.1. Flow chart of the study population

From 1328 patients with chest CT scan performed in the ED from march to june 2020, 854 patients had a negative COVID 19 swab diagnosis, 11 were minor, and 203 had no height measure (necessary for the calculation of BMI and SMI) (Fig. 1). In addition, SMI could not be calculated from the CT in 16 patients for technical reasons (Fig. 1). At the end, 244 patients were included in the study.

3.2. Baseline characteristic data

The median age was 62.1 years (± 14.5) and the majority were male (54.9%). Obesity (33.7%), chronic cardiac disease (24.4%) and diabetes (20.7%) were the most frequent comorbidities. Mean NEWS2 at baseline was 5.10 (± 3.05) and 40 patients (17.6%) had severe lung lesions (>50%) on chest CT (Table 2).

3.3. Prevalence and characteristics of patients with low SMI

Of all 244 patients, 102 patients (41.8%) had low SMI in T12 according to the Derstine thresholds corresponding to 68 male

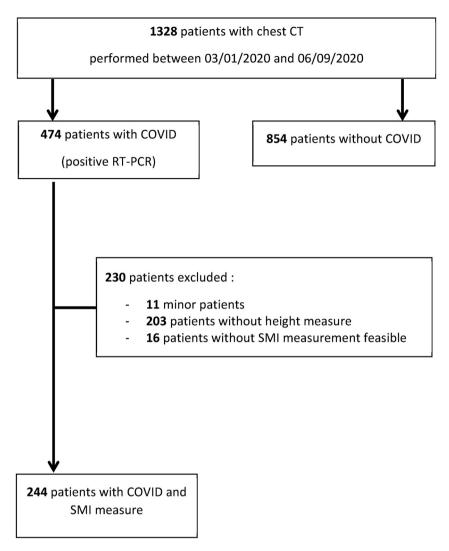


Fig. 1. Flowchart.

Table 1Prevalence of low SMI.
Patients with low SMI measured at T12 level defined by the Derstine thresholds: SMI <28.9 cm²/m² and SMI <20.8 cm²/m² for males and females respectively.

| | SMI (cm2/m2) | Low SMI % (n) |
|--------------------|---------------|------------------|
| Male (n = 134) | 30.42 (±6.84) | 50.7% (68) |
| Female $(n = 110)$ | 24.55 (±5.78) | 30.9% (34) |
| All (n = 244) | 27.89 (±7.02) | 41.8% (102) |

patients (50.7%) with SMI <28.9 cm^2/m^2 and 34 female patients (30.9%) with SMI <20.8 cm^2/m^2 (Table 1).

Compared to patients with a normal SMI, patients with a low SMI were older (69.7 (± 14.5) vs 56.7 (± 16.0), p < 0.001)), were more men (66.7% versus 45.7%,p = 0.002), had a lower BMI (26.9 (± 4.6) vs 30.0 (± 6.1), p < 0.001)) and had a higher number of comorbidities (2 (± 1.3) vs 1.4(± 1.2), p < 0.05), including lung (21.6% vs 11.4%, p = 0.03) and cardiac (35.3% vs 16.4%, p = 0.001) chronic disease. Furthermore, they had a higher NEWS score (5.8 (± 3.1) vs 4.6 (± 3.1), p = 0.002)) and concerning biological data, they had a higher creatinine (109 umol/l (± 95.5) vs 86.3 umol/l (± 83.8), p = 0.04)) and CRP (112.5 mg/l (± 96.5) vs 83.5 mg/l (± 94.7), p = 0.02)) means.

3.4. Association between low SMI and outcomes

3.4.1. Low SMI and mortality

In our study, the in-hospital mortality rate was 11.9% (n = 29). Patients with low SMI had a significant higher mortality rate than patients without low SMI (17.6% versus 7.7%) (OR = 2.55 [1.15–5.67]). The other variables associated with mortality on univariate analysis were age >65 years old (OR = 10.35 [3.04–35.22]]), cardiac chronic disease (OR = 2.95 [1.32–6.57]), diabetes (OR = 3.25 [1.44–7.37]), severe lung lesions on chest CT (OR = 2.96 [1.82–4.81]) and severe level of NEWS2 score (OR = 1.58 [1.09–2.28]). After adjustment on the multivariate model, low SMI variable was no longer significantly associated with mortality (ORa = 1.37 [0.54–3.52]). Variables independently associated with mortality on the final multivariable model were age> 65 years old (ORa = 4.67 [1.24–17.61]) and severe lung lesions on chest CT (ORa = 2.70 [1.53–4.76]) (Table 3).

3.4.2. Low SMI and length of hospital stay

Patients with low SMI had significantly longer hospital stay than patients without low SMI (13.04 days vs 25.49 days; p < 0.001). Moreover, the proportion of patients with a long LOS (>23 days) was more than 2 times higher among low SMI patients than those without low SMI (36.3% vs 15.5%, p < 0.001). Long LOS was

Table 2• Characteristics of patients at admission according to SMI

Data are presented as means $(\pm SD)$ for continuous variables, and categorical data are represented as frequencies and percentages; Chi-squared tests were used for categorical variables and Student-t-test or ANOVA for continuous variables to study differences between low and normal SMI groups.

| | Low SMI n = 102 | Normal SMI n = 142 | All n = 244 | p | | | |
|------------------------------------|--------------------|-----------------------|-------------------|---------|--|--|--|
| Age, years (±SD) | 69.73 (±14.48) | 56.72 (±15.99) | 62.16 (±16.61) | <0.001 | | | |
| Male %(n) | 66.7% (68) | 46.5% (66) | 54.9% (134) | 0.002 | | | |
| Comorbidities | | | ` , | | | | |
| Chronic lung disease %(n) | 21.6% (22) | 11.4% (16) | 15.7% (38) | 0.03 | | | |
| Chronic cardiac disease %(n) | 35.3% (36) | 16.4% (23) | 24.4% (59) | 0.001 | | | |
| Kidney disease %(n) | 12.7% (13) | 7.9% (11) | 9.9% (24) | 0.21 | | | |
| Smoking %(n) | 8.8% (9) | 10.7% (15) | 9.9% (24) | 0.63 | | | |
| Diabetes %(n) | 23.5% (24) | 18.6% (26) | 20.7% (50) | 0.35 | | | |
| Obesity %(n) | 18.8% (16) | 45.4% (49) | 33.7% (65) | < 0.001 | | | |
| BMI kg/m2, mean (±SD) | 26.93 | 29.99 (±6.08) | 28.64 | < 0.001 | | | |
| | (± 4.60) | | (± 5.67) | | | | |
| Chest CT findings | | | | | | | |
| Severity of lung lesions | | | | | | | |
| Moderate (<25%) %(n) | 54.7% (52) | 64.4% (85) | 60.4% (137) | 0.16 | | | |
| Extensive (25-50%) %(n) | 22.1% (21) | 22.0% (29) | 22.0% (50) | | | | |
| Severe (>50%) %(n) | 23.2 (22) | 13.6% (18) | 17.6% (40) | | | | |
| Pulmonary embolism %(n) | 8.8% (8) | 8.5% (11) | 8.6% (19) | 0.93 | | | |
| Clinical severity at ED adm | ission | | | | | | |
| NEWS2 score, mean (±SD) | 5.79 (±3.05) | 4.59 (±3.09) | 5.10 (±3.05) | 0.002 | | | |
| Biological data at admission | | | | | | | |
| Polynuclear neutrophils mean (±SD) | 6.70 (±4.09) | 5.64 (±6.66) | 6.09 (±5.73) | 0.16 | | | |
| Créatinine, umol/l mean (±SD) | 109.86 (±95.45) | 86.31 (±83.75) | 96.33 (±89.49) | 0.04 | | | |
| CRP, mg/l mean (±SD) | 112.45 (±96.54) | 83.45 (±94.68) | 95.88 (±96.35) | 0.02 | | | |
| Albumin, g/l mean (±SD) | 28.05 (±6.34) | 29.79 (±5.65) | 28.93 (±6.05) | 0.08 | | | |

Table 3Association between low SMI and outcomes.
Odds ratio (OR) for the effects of low SMI on in-hospital mortality, length of stay, acquired infection and ICU admission, in univariate (OR) and multivariate analysis

(ORa).

| In-Hospital mortality | | | | | | | | |
|-----------------------|--------------------------|----------------|----------------------|----------------------|--|--|--|--|
| | Yes (n = 29) | No (n = 215) | OR [IC 95%] | ORa [IC 95%] | | | | |
| Normal SMI % (n) | 7.7% (11) | 92.3% (131) | 1.00 | 1.00 | | | | |
| Low SMI % (n) | 17.6% (18) | 82.4% (84) | 2.55 [1.15 -5.67] | 1.37 [0.54 -3.52] | | | | |
| Length of stay > | Length of stay > 23 days | | | | | | | |
| | Yes (n = 59) | No $(n = 185)$ | OR [IC 95%] | ORa [IC 95%] | | | | |
| Normal SMI % (n) | 15.5% (22) | 84.5% (120) | 1.00 | 1.00 | | | | |
| Low SMI % (n) | 36.3% (37) | 63.7% (65) | 3.11 [1.69 -5.70] | 1.87 [1.14 -3.49] | | | | |
| Acquired Infecti | Acquired Infection | | | | | | | |
| • | Yes (n = 85) | No $(n = 159)$ | OR [IC 95%] | ORa [IC 95%] | | | | |
| Normal SMI % (n) | 27.5% (39) | 72.5% (103) | 1.00 | 1.00 | | | | |
| Low SMI % (n) | 45.1% (46) | 54.9% (56) | 2.17 [1.27 -3.71] | 1.88 [1.06 -2.98] | | | | |
| ICU admission | | | • | • | | | | |
| | Yes (n = 86) | No $(n = 158)$ | OR [IC 95%] | ORa [IC 95%] | | | | |
| Normal SMI % (n) | 35.9% (51) | 64.1% (91) | 1.00 | 1.00 | | | | |
| Low SMI % (n) | 34.3% (35) | 65.7% (67) | 0.93 [0.55 -1.59] | 0.18 [0.06 -0.51] | | | | |

significantly associated with longer ventilation periods (27 days vs 12 days, p < 0.05). On univariate model, low SMI was associated with a long LOS (OR = 3.11 [1.69–5.70]). Several variables were associated with a longer LOS: age >65 years old (OR = 3.10 [1.65–5.85]), diabetes (OR = 2.07 [1.06–4.06]), severe lung lesions on chest CT (OR = 1.92 [1.31–2.80]), severe level of NEWS2 score (OR = 1.65 [1.23–2.21]), high level of CRP (OR = 1.73 [1.19–2.50]) and low level of serum albumin (OR = 2.94 [1.79–4.55]). After adjusting for all the significant variables in the univariate model, low SMI appeared to be an independent risk factor for long LOS (ORa = 1.87 [1.14–3.49]) as well as age >65 years old (ORa = 3.01 [1.10–8.20]), diabetes (ORa = 2.80 [1.00–7.88]) and low level of serum albumin (ORa = 3.44 [1.75–6.67]).

3.4.3. Low SMI and acquired infection

We recorded a total of 116 confirmed infectious complications (66 patients had one infection, 10 patients had 2 different sites of infection, 6 patients had 3, and 3 patients had 4). Data regarding the type of infection are shown in Fig. 2. The most frequent site of infections were lower respiratory tract (59 cases, 50.9%), followed by urinary tract (31 cases, 26.7%), blood stream (20 cases, 17.2%), and gastrointestinal tract infection (6 cases, 5.2%). During their stay, 85 patients (34.8%) developed at least one confirmed infectious complication. Infectious complications occurred significantly more frequently in patients with low SMI (45.1% vs 27.5%, p < 0.001). On univariable model, low SMI is associated with infection (OR = 2.17[1.27–3.71]). This association remained significant after adjustment in the multivariate model (ORa = 1.88 [1.06-2.98]). Three other variables were also associated with infection in the multivariable model: severe lung lesions on chest CT (ORa = 1.59 [1.26-2.53]), severe level of NEWS2 score (ORa = 1.54 [1.01-2.34]) and polynuclear neutrophilis count at admission (ORa = 1,22 [1,06-1,39]).

3.4.4. Low SMI and ICU admission

Overall, more than one third of our patients (35.2%) were admitted in ICU. There was no significant difference between patients with and without low SMI (34.3% vs 35.9%, p = 0.79. The univariate model showed a significant risk of ICU admission in male patients (OR = 2.84 [1.62-4.98]), non-smoker patients (OR = 4.35[1.25-14.29]), patients with severe lung lesions on chest CT (OR = 3.85 [2.56-5.79]), patients with pulmonary embolism (OR = 3.78 [1.42-10.06]), patients with severe level of NEWS2 score (OR = 2.33 [1.73-3.14]), high level of CRP (OR = 2.85 [1.97-4.12])and low level of albumin (OR = 2.86 [1.85-4.35]). No significant association was found for patients with low SMI (OR = 0.93 [0.55–1.59]) concerning ICU admission on univariate model. Nevertheless, after adjustment, the multivariate model revealed a significant increasing risk of ICU admission for patients with normal SMI (ORa = 5.56 [1.96-16.67]) and patients with low level of albumin (ORa = 1.85 [1.00 - 3.45]).

4. Discussion

Our study shows that low SMI measured by CT at the thoracic level T12 was associated with more nosocomial infections and increased hospital LOS, but neither with in-hospital mortality nor ICU admission. This is the first French cohort evaluating the association between thoracic SMI and clinical outcomes in COVID-19 patients. The study was monocentric, with the same CT acquisition parameters and the same ICU admission criteria for patients with COVID-19. Similarly, image analysis was performed by the same reader using standardized criteria.

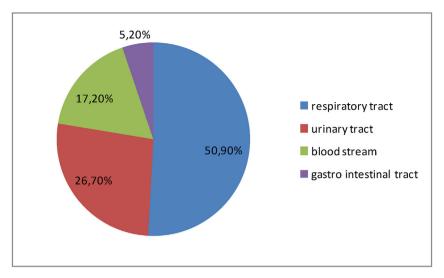


Fig. 2. Sites of acquired infections.

Few studies assessed the pronostic value of SMI measured using thoracic CT images, which have been extensively used for COVID-19 patients diagnostic, stratification and monitoring during the COVID-19 pandemic. Schiaffino et al. reported the association between a lower-than-median paravertebral muscle mass measured on chest CT images at admission and adverse outcomes of COVID-19 patients during the first pandemic peak in Italy [12]. In 552 patients admitted to the Emergency Department, a lower-thanmedian paravertebral muscle area at the T5 and T12 levels was associated with ICU admission and death. Kim et al. also reported in 121 COVID-19 patients an association between low SMI and prolonged LOS [13]. Low SMI was defined as the lowest quartile of SMI (24 cm²/m² or less for men and 20 cm²/m² or less for women), and reported in 24% of COVID-19 patients. Inversely, Moctezuma-Velázquez et al. reported that low thoracic SMI was not associated with negative outcomes in 519 patients with COVID-19 [16]. But, these authors used different cut-off values than ours for SMI identification (below 42.6 cm²/m² for men and 30.6 cm²/m² for women), which are actually the references values for L3 level reported by Derstine et al. [17]. We can also note that their patients were younger than ours (mean age = 52 years), and thus probably less sarcopenic before the onset of COVID-19 infection.

In our study, low SMI was associated with more nosocomial infections. Dysfunction of skeletal muscle may be involved in these acquired infections [18,19]. We also observed increased hospital LOS, as previously described [7]. Prolonged LOS was significantly associated with longer ventilation periods, which could be concordant with the poor function of respiratory muscles.

In accordance with other previous studies [10,11,13], low SMI was not associated with an increased mortality in our study, although patients with low SMI had significantly higher chronic lung and cardiac diseases, higher systemic inflammation (CRP), higher clinical severity at ED admission (NEWS 2) and were significantly older. Interestingly, clinical frailty has been associated with mortality in 471 UK patients with COVID-19 [20]. The relationship between frailty and other prognostic factors including age, nutritional status, obesity, sarcopenia and systemic inflammation is poorly understood. Recently, frailty was independently associated with age, comorbidities, and systemic inflammation in 106 patients with COVID-19, but not with sarcopenia (measured at L3 level), obesity and nutritional status [21]. However, relationship between frailty, sarcopenia and clinical outcomes in COVID-19 requires further study.

Moreover, we reported a significant increasing risk of ICU admission for patients with normal SMI in the multivariate analysis. Age was not significantly associated with ICU admission (median age: 63 years (± 11.7) in ICU patients vs 61 years (± 18.7), p = 0.44). Schiaffino et al. reported inversely that low thoracic SMI predicted ICU admission [12]. However, in this study, data have been collected from multiple centers with potentially different ICU admission criteria for patients with COVID-19. Giraudo et al. also found that reduced thoracic muscle mass was a predictor of ICU hospitalization in COVID-19 patients [22]. Authors did not measure thoracic SMI but the mean Hounsfield Unit (Hu) value of the right paravertebral muscle at the T12 level.

On the other hand, visceral obesity, defined as high visceral fat area, has been associated with in-hospital mortality in COVID-19 patients [10]. In our study, we observed that COVID-19 patients with low SMI were significantly less obese. It would be interesting to assess their fat distribution. Interestingly, epicardial adipose tissue has been recently associated with extent of pneumonia and adverse outcomes in patients with COVID-19 [23], and could be a relevant prognostic factor. All these data highlight the importance of body composition assessment in patients with COVID-19 infection. Other methods have been proposed to evaluate muscle mass in these patients. Low pectoralis muscle index (obtained by measuring the area of the pectoralis muscle on thoracic CT images) was associated with prolonged hospital stay and mortality in COVID-19 patients [24]. Gil et al. also reported that muscle mass assessed by vastus lateralis cross-sectional area using ultrasonography, and muscle strength are predictive of LOS in hospitalized patients with moderate to severe COVID-19 [7].

Muscle mass also plays a key role in the recovery from critical illness. Whether preexisting sarcopenia before the onset of COVID-19 infection and acquired sarcopenia during the ICU hospitalisation, may impact patient's recovery remains to be assessed. Many post-COVID-19 patients suffers from « post-acute sequelae of COVID-19 » (PASC), characterized by persistent symptoms such as fatigue and muscle weakness [25]. Decreased neural activation, fibre atrophy, necrosis, fibrosis, and alterations in blood flow and metabolic function may be involved in these symptoms [18]. To date, there is no consensus on optimal management strategies to treat patients with PACS. A better understanding of skeletal muscle alterations during and after COVID-19 is needed to propose adapted therapies and improve the quality of life of these patients.

Some limitations should be considered. First, because of the retrospective design, we did not assess patient's muscle function while sarcopenia is defined as loss of muscle mass and function. We did not collect informations regarding nutritional status (malnutrition score tool) or frailty. We were not able to report if comorbidities (diabetes ...) were controlled or not. Second, we did not compare SMI measured at T12 level and L3 level, because the patients had only thoracic CT scan. Third, we used cut-off values for SMI measured from thoracic CT scans that are not validated in the French population, and not adjusted to the BMI. However, to our knowledge, there are no available cut-off values based on BMI at the CT thoracic level. Finally, we only included patients of the first wave of the pandemic, which can have an impact on the results, because of less experience with COVID-19 patients, and different recommendations for their care, including ICU admission criteria [26].

In conclusion, our study showed that patients with sarcopenia were at higher risk of developing poor clinical outcomes from COVID-19, with more infections and increased hospital LOS, but not mortality. We propose that patients with sarcopenia should be considered as a population at risk which needs special identification using CT scan, and should be included as relevant prognostic biomarkers into clinical Emergency Department. Further studies are needed to also identify patients at risk of developing PACS after hospital discharge, to guide early intervention and clinical monitoring.

Funding statement

None to declare

Author contribution

Concept and design: P. D, V-E.L, N.A, F.T, C.S-C, S.G; Acquisition of data: M.G, S.G, J.M, H.VH, U.T-O, B.M, V-E.L; Analysis of CT images: C.S-C; Statistical analysis: S.G; Writing of the manuscript: N.A, S.G; Critical revision of the manuscript: V-E.L, F.T, L-M.J, P. D, C.S-C, M.C.

Conflict of interest

None to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2022.11.011.

References

- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019:48(4):601.
- [2] Meyer F, Valentini L. Disease-related malnutrition and sarcopenia as determinants of clinical outcome. Vis Med 2019;35(5):282–91.
- [3] Abate SM, Chekole YA, Estifanos MB, Abate KH, Kabthymer RH. Prevalence and outcomes of malnutrition among hospitalized COVID-19 patients: a systematic review and meta-analysis. Clin Nutr ESPEN 2021;43:174–83.
- [4] Liu H, Chen S, Liu M, Nie H, Lu H. Comorbid chronic diseases are strongly correlated with disease severity among COVID-19 patients: a systematic review and meta-analysis. Aging Dis 2020;11(3):668-78.

- [5] Lenchik L, Boutin RD. Sarcopenia: beyond muscle atrophy and into the new frontiers of opportunistic imaging, precision medicine, and machine learning. Semin Muscoskel Radiol 2018;22(3):307–22.
- [6] Siahaan Ymt HV, Hariyanto TI, Kurniawan A. Coronavirus disease 2019 (Covid-19) outcomes in patients with sarcopenia: a meta-analysis and meta-regression. Clin Nutr ESPEN 2022;48:158–66.
- [7] Gil S, Jacob Filho W, Shinjo SK, Ferriolli E, Busse AL, Avelino-Silva TJ, et al. Muscle strength and muscle mass as predictors of hospital length of stay in patients with moderate to severe COVID-19: a prospective observational study. J Cachexia Sarcopenia Muscle 2021;12(6):1871—8.
- [8] Damanti S, Cristel G, Ramirez GA, Bozzolo EP, Da Prat V, Gobbi A, et al. Influence of reduced muscle mass and quality on ventilator weaning and complications during intensive care unit stay in COVID-19 patients. Clin Nutr 2022;41(12):2965–72
- [9] Osuna-Padilla IA, Rodríguez-Moguel NC, Rodríguez-Llamazares S, Orsso CE, Prado CM, Ríos-Ayala MA, et al. Low muscle mass in COVID-19 critically-ill patients: prognostic significance and surrogate markers for assessment. Clin Nutr 2022:41(12):2910-7.
- [10] Meyer HJ, Wienke A, Surov A. Computed tomography-defined body composition as prognostic markers for unfavourable outcomes and in-hospital mortality in coronavirus disease 2019. J Cachexia Sarcopenia Muscle 2022:13(1):159–68.
- [11] Molwitz I, Ozga AK, Gerdes L, Ungerer A, Köhler D, Ristow I, et al. Prediction of abdominal CT body composition parameters by thoracic measurements as a new approach to detect sarcopenia in a COVID-19 cohort. Sci Rep 2022;12(1): 6443.
- [12] Schiaffino S, Albano D, Cozzi A, Messina C, Arioli R, Bnà C, et al. CT-Derived chest muscle metrics for outcome prediction in patients with COVID-19. Radiology 2021;300(2):E328-36.
- [13] Kim JW, Yoon JS, Kim EJ, Hong HL, Kwon HH, Jung CY, et al. Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with coronavirus disease 2019. J Gerontol A Biol Sci Med Sci 2021;76(8):e110–6.
- [14] Gunraj H, Sabri A, Koff D, Wong A. COVID-net CT-2: enhanced deep neural networks for detection of COVID-19 from chest CT images through bigger, more diverse learning. Front Med 2021;8:729287.
- [15] Physicians, T.R.C.o., National early warning score (NEWS) 2: standardising the assessment of acute-illness severity in the NHS.
- [16] Moctezuma-Velazquez P, Miranda-Zazueta G, Ortiz-Brizuela E, González-Lara MF, Tamez-Torres KM, Román-Montes CM, et al. Low thoracic skeletal muscle area is not associated with negative outcomes in patients with COVID-19. Am J Phys Med Rehabil 2021;100(5):413–8.
- [17] Derstine BA, Holcombe SA, Ross BE, Wang NC, Su GL, Wang SC, et al. Skeletal muscle cutoff values for sarcopenia diagnosis using T10 to L5 measurements in a healthy US population. Sci Rep 2018;8(1):11369.
- [18] Soares MN, Eggelbusch M, Naddaf E, Gerrits KHL, van der Schaaf M, van den Borst B, et al. Skeletal muscle alterations in patients with acute Covid-19 and post-acute sequelae of Covid-19. J Cachexia Sarcopenia Muscle 2022;13(1): 11–22.
- [19] Silva CC, Bichara CNC, Carneiro FRO, Palacios VRDCM, Berg AVSVD, Quaresma JAS, et al. Muscle dysfunction in the long coronavirus disease 2019 syndrome: pathogenesis and clinical approach. Rev Med Virol 2022:e2355.
- [20] Vlachogiannis NI, Baker KF, Georgiopoulos G, Lazaridis C, van der Loeff IS, Hanrath AT, et al. Clinical frailty, and not features of acute infection, is associated with late mortality in COVID-19: a retrospective cohort study. J Cachexia Sarcopenia Muscle; 2022.
- [21] McGovern J, Al-Azzawi Y, Kemp O, Moffitt P, Richards C, Dolan RD, et al. The relationship between frailty, nutritional status, co-morbidity, CT-body composition and systemic inflammation in patients with COVID-19. J Transl Med 2022:20(1):98.
- [22] Giraudo C, Librizzi G, Fichera G, Motta R, Balestro E, Calabrese F, et al. Reduced muscle mass as predictor of intensive care unit hospitalization in COVID-19 patients. PLoS One 2021;16(6):e0253433.
- [23] Grodecki K, Lin A, Razipour A, Cadet S, McElhinney PA, Chan C, et al. Epicardial adipose tissue is associated with extent of pneumonia and adverse outcomes in patients with COVID-19. Metabolism 2021;115:154436.
- [24] Ufuk F, Demirci M, Sagtas E, Akbudak IH, Ugurlu E, Sari T, et al. The prognostic value of pneumonia severity score and pectoralis muscle Area on chest CT in adult COVID-19 patients. Eur J Radiol 2020;131:109271.
- [25] Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021;397(10270):220–32.
- [26] Domingo P, Pomar V, Mur I, Castellví I, Corominas H, de Benito N, et al. Not all COVID-19 pandemic waves are alike. Clin Microbiol Infect 2021;27(7):1040 e7—e1040 e10.