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Visceral adipose tissue area predicts intensive care unit admission in COVID-19 patients

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ABSTRACT

We retrospectively investigated, in 62 consecutive hospitalised COVID-19 patients (aged 70 ± 14 years, 40 males), the prognostic value of CT-derived subcutaneous adipose tissue and visceral adipose tissue (VAT) metrics, testing them in four predictive models for admission to intensive care unit (ICU), with and without pre-existing comorbidities. Multivariate logistic regression identified VAT score as the best ICU admission predictor (odds ratios 4.307–12.842). A non-relevant contribution of comorbidities at receiver operating characteristic analysis (area under the curve 0.821 for the CT-based model, 0.834 for the one including comorbidities) highlights the potential one-stop-shop prognostic role of CT-derived lung and adipose tissue metrics.

Introduction

A clear definition of severity-determining risk factors for COVID-19 could improve patient management in pandemic clusters and peaks, considering that the high volume of patients attending Emergency Departments (ED) in such circumstances potentially overcomes the resources even of well-funded healthcare systems. A higher risk of hospitalisation and severe complications for patients with obesity, already observed with diseases caused by the Middle East Respiratory Syndrome Coronavirus [1] and by Orthomyxoviruses [2], has also been reported for COVID-19, with a correlation between high body mass index and the rate of intensive care unit (ICU) admission [3–7].

Chest computed tomography (CT) has been up to now widely used for suspected COVID-19 patients, albeit with oscillating specificity and a high organizational burden on ED workflow [8]. Even if chest x-ray showed interesting diagnostic performance [9,10], chest CT was extensively used for patients' staging and monitoring, since it allows to evaluate disease severity as well as pulmonary, extra-pulmonary, and vascular features [8,11,12]. CT-derived additional data to stratify patients' risk could be provided by quantification and distribution analysis of abdominal fat, both obtainable with post-processing software including automatic and semiautomatic segmentation tools [13,14].

In this study, involving COVID-19 patients from two different Italian hospitals, we aimed to assess the relationship between subcutaneous tissue (SAT) or visceral adipose tissue (VAT) and lung disease severity, then testing their potential as predictors of ICU admission compared to models integrating the anamnestic investigation of pre-existing comorbidities.

Methods

This retrospective study involved two Italian hospitals, "Azienda Ospedaliero-Universitaria Policlinico Umberto I" (Roma) and "IRCCS Policlinico San Donato" (San Donato Milanese), and was approved by the competent Ethical Committees (Comitato Etico Policlinico Umberto I; Comitato Etico Ospedale San Raffaele).

From March 9th to May 5th, 2020, consecutive COVID-19 patients with CT scans encompassing the third lumbar vertebra were included in this study. No time limitation was set for CT performance, considering both scans performed on admission and during hospitalization. In patients performing multiple CT exami-

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nations during hospitalization, we considered the one performed during the worst disease phase.

Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) infection was confirmed by positive reverse transcriptase-polymerase chain reaction (RT-PCR) assay on pharyngeal swabs. Symptoms on admission such as fever (increase in body temperature equal to or greater than 37.5 °C), dyspnoea, and cough were recorded along with other clinical characteristics, such as oxygen therapy or mechanical ventilation and ICU admission. Comorbidities (diabetes, cardiovascular disease, hypertension, chronic obstructive pulmonary disease, oncological history) were recorded on ED admission.

CT examinations were performed with the patient in supine position using two different scanners (Somatom Sensation 64 and Somatom Definition; Siemens Healthineers, Erlangen, Germany), both allowing to acquire ≥16 slices/rotation. Acquisition parameters, adjusted according to the clinical question and patient's body size, included: standard tube voltage 120 kVp; adjusted tube current; layer spacing 5 mm; and acquisition layer thickness 0.625 mm.

All CT scans were reviewed by two chest radiologists with at least 5 years of experience in body CT. Lung disease severity was assessed according to Chung et al. [15]. Lung severity score was calculated for each lobe as follows: no involvement (0%), minimum (1%–25%), mild (26%–50%), moderate (51%–75%), or severe (76%–100%). Each percentage category was then assigned a score from 0 (no involvement) to 4 (severe involvement) on an ordinal scale, the sum of each lobe score determining a lung disease severity score ranging from 0 to 20.

VAT and SAT areas were manually segmented (Fig. 1) on axial images at the lower margin of the third lumbar vertebra [16], using a dedicated software (Osirix Lite, v11.0.3, Bernex, Switzerland). As described by Murray et al. [17], a VAT area 100–129 cm^2 indicates an overweight status, while a VAT area greater than 130 cm^2 indicates an obesity status. Therefore, patients with normal weight were assigned a VAT score, patients with overweight a VAT score 1, and patients with obesity a VAT score 2.

The Mann–Whitney *U* test was used for variable comparison between patients with and without ICU admission, the Kruskal–Wallis test being used to assess such differences between men and women. Correlations were assessed with Spearman's ρ. Odds ratios (ORs) for the prediction of ICU admission were calculated through multivariate binary logistic regression. Receiver operating characteristic (ROC) analysis, with area under the curve

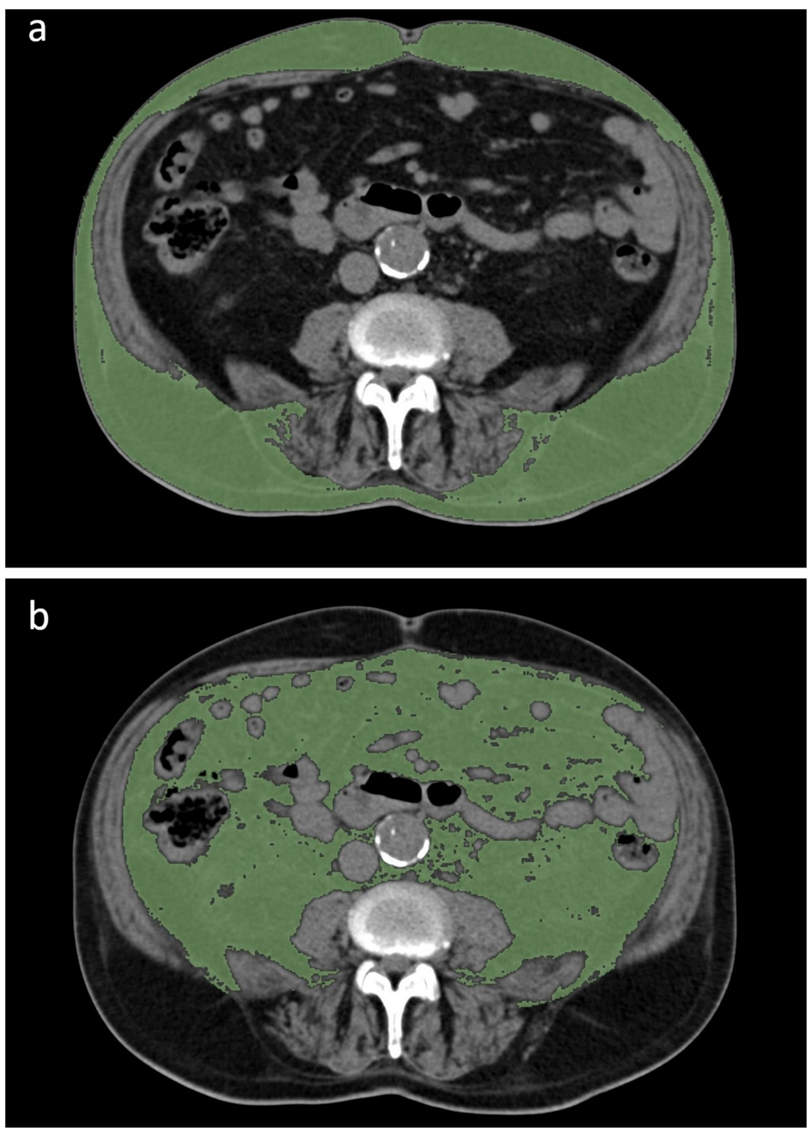

Fig. 1. Adipose tissue segmentation in an axial unenhanced CT image at the lower margin of the third lumbar vertebra. (**a**) the green area shows the segmented subcutaneous adipose tissue area. (**b**) the green area shows the segmented visceral adipose tissue area.

Table 1
Demographic, clinical, and computed tomography characteristics of the study population.

	Patients without ICU admission (36 patients)	Patients with ICU admission (26 patients)	
Demographics	Sex	16 F / 20 M	6 F / 20 M
	Median age (interquartile interval)	76.5 years (68–82.5 years)	66.5 years (61–73 years)
Symptoms and treatment needs	Fever[a] (%)	18/36 (50%)	20/26 (77%)
	Dyspnoea (%)	23/36 (63%)	13/26 (50%)
	Cough (%)	10/36 (28%)	11/26 (42%)
	Need of oxygen therapy (%)	22/36 (61%)	26/26 (100%)
	Need of mechanical ventilation (%)	0/36 (0%)	20/26 (77%)
Comorbidities	Diabetes (%)	7/36 (19%)	6/26 (23%)
	Cardiovascular disease (%)	9/36 (25%)	8/26 (31%)
	Hypertension (%)	14/36 (39%)	10/26 (38%)
	Chronic obstructive pulmonary disease (%)	4/36 (11%)	4/26 (15%)
	Oncological history (%)	7/36 (19%)	4/26 (15%)
CT findings	Median VAT area (interquartile interval)	154.8 cm^2 (92.3–256.3 cm^2)	258.3 cm^2 (199.5–292.6 cm^2)
	Median SAT area (interquartile interval)	170.5 cm^2 (113.8–234.9 cm^2)	199.2 cm^2 (146.9–301.3 cm^2)
	Median lung disease severity score (interquartile interval)	13 (9–16)	16 (14–19)

ICU intensive care unit, F females, M males, CT computed tomography, VAT visceral adipose tissue, SAT subcutaneous adipose tissue.
[a] Body temperature >37.5 °C.

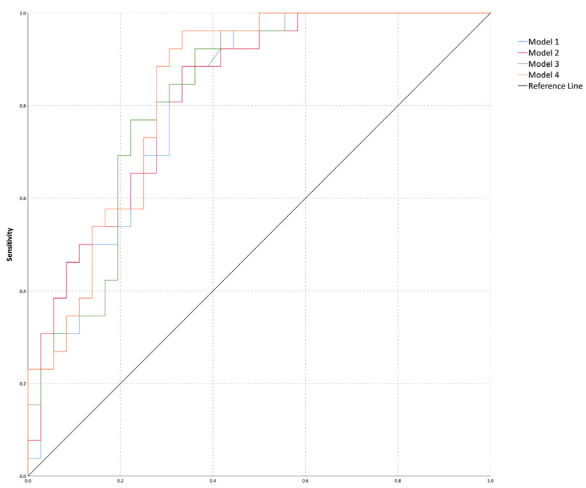

Fig. 2. Receiver operating curve analysis for the prediction of intensive care unit admission. Area under the curves (with 95% confidence interval): Model 1 = 0.807 (0.701–0.913); Model 2 = 0.823 (0.721–0.924); Model 3 = 0.821 (0.717–0.924); Model 4 = 0.834 (0.736–0.933).

(AUC) as output, was then used to compare the predictive performance of four different models, all including patients' age and sex: Model 1 (considering lung disease severity and comorbidities), Model 2 (VAT, SAT, and comorbidities), Model 3 (VAT, SAT, and lung disease severity), Model 4 (VAT, SAT, lung disease severity, and comorbidities). IBM SPSS Statistics v.26 (IBM SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis, *p* values < 0.05 being considered significant.

Results

Among consecutive suspected COVID-19 patients referring to the two centres during the study period, 479 had a positive RT-PCR for SARS-CoV-2 and a chest CT, 62 (40 males, mean age 70 ± 14 years) of them also having performed abdominal CT. Twenty-six patients (41.9%) were then admitted to ICU (Table 1). Abdominal CT metrics found 40/62 (64.5%) patients with obesity, 10/62 (16.1%) with overweight, and 12/62 (19.4%) with normal weight. Pulmonary involvement greater than 50% was found in 48/62 (77.4%) patients. Notably, 26/62 patients (41.9%) had a pulmonary involvement higher than 75%.

Patients admitted to ICU compared to the non-admitted ones showed significantly higher lung disease severity (p < 0.001), SAT areas (p = 0.047), VAT areas (p = 0.011), and VAT scores (p = 0.003). Considering men and women who did and did not require ICU admission, the Kruskal–Wallis test showed significant differences in lung disease severity (p = 0.006), VAT areas (p < 0.001), and VAT scores (p < 0.001), while no significant difference was found for SAT areas (p = 0.065).

At univariate analysis, a significant correlation was found between VAT and SAT area (ρ = 0.49; p < 0.001) as well as between each of them and lung disease severity (ρ = 0.55, p < 0.001, and ρ = 0.56, p < 0.001, respectively). At multivariate binary logistic regression (detailed in Appendix A), the VAT score was the best predictor of ICU admission in all models incorporating this parameter, with an OR = 12.842 (95% CI 2.045–80.652) in Model 2, an OR = 4.307 (95% confidence interval [CI] 0.709–26.153) in Model 3, and an OR = 5.518 (95% CI 0.745–40.876) in Model 4. Among predictive models for ICU admission (Fig. 2), Model 3 obtained an AUC of 0.821 (95% CI 0.717–0.924), very close to the one of Model 4 (AUC 0.834, 95% CI 0.736–0.933).

Discussion

The stratification of COVID-19 patients according to their risk of developing severe complications and of being subsequent admitted to ICU remains a priority, several clinical and radiological cofactors having been investigated to this purpose [11,12]. In this study, we assessed the role of visceral and subcutaneous adipose tissue in predicting disease severity of hospitalised COVID-19 patients, highlighting how patients needing ICU admission showed significantly higher CT-derived metrics of increased adipose tissue. Area-based measurements of VAT obtained at the level of the third and fourth lumbar vertebrae are known to be strongly associated with total VAT volumes and cardiometabolic risk factors in men and women [18]. While also VAT area measured at the lower limits of the standard chest CT field of view (i.e. at the first or second lumbar vertebra) were recently shown to be correlated with ICU admission in a pilot study [19], VAT area measured at the lower margin of the third lumbar vertebra is known to provide the best proxy of VAT burden for both sexes and different ages [18]. We therefore chose to include in our analysis only patients with available abdominal CT scans. At multivariate logistic regression, the VAT score constantly yielded the highest odds ratio for ICU admission, while multiparametric models (Model 2, 3, and 4) including adipose tissue metrics had a higher AUC than Model 1, which considered only lung disease severity and comorbidities. Of note, the non-relevant contribution of comorbidities to diagnostic performance, highlighted by the 0.012 increase in AUC between Model 3 and Model

4, underlines the one-stop-shop prognostic capabilities of CT, as well as the capability of VAT to act as a proxy of obesity-related comorbidities. The limited sample size of this study hindered a more complete understanding of the role of those comorbidities that were underrepresented in our population (oncological history, chronic obstructive pulmonary disease). Other limitations, apart from the retrospective design, include the overrepresentation of patients with obesity. Only a minority of our population (19.4%) had a VAT area <100 cm^2, while the majority presented a VAT area >130 cm^2 (64.5%), being therefore overrepresented than in the general population of our country, as observed also at a regional level in another Italian study involving 92 hospitalized COVID-19 patients [20]. Those patients showed, moreover, a more frequent need for assisted ventilation and ICU admission during hospitalization.

In conclusion, we showed that in COVID-19 patients the VAT area is significantly correlated to the extent of lung parenchymal involvement, a combined model integrating lung disease severity and VAT being able to reliably predict ICU admission, without sizable contribution from the inclusion of comorbidities. Further studies in larger populations will need to ascertain prognostic and treatment implications of these findings.

Ethical statement

The authors of this Ethics Committee-approved retrospective study declare they have read and have abided by the statement of ethical standards for manuscripts submitted to Obesity Research & Clinical Practice.

Conflict of interest statement

S. Schiaffino declares to be member of speakers' bureau for General Electric Healthcare and to have received travel support from Bracco Imaging. F. Sardanelli declares to have received grants from or to be member of speakers' bureau/advisory board for Bayer Healthcare, Bracco Group and General Electric Healthcare. All other authors declare that they have no conflicts of interest and nothing to disclose.

CRediT authorship contribution statement

Federica Pediconi: Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Veronica Rizzo:** Conceptualization, Investigation, Data curation, Writing - original draft, Writing - review & editing. **Simone Schiaffino:** Conceptualization, Methodology, Investigation, Data curation, Validation, Writing - original draft, Writing - review & editing. **Andrea Cozzi:** Methodology, Formal analysis, Data curation, Visualization, Writing - original draft, Writing - review & editing. **Gianmarco Della Pepa:** Investigation, Data curation, Writing - review & editing. **Francesca Galati:** Investigation, Data curation, Writing - review & editing. **Carlo Catalano:** Conceptualization, Validation, Resources, Funding acquisition, Supervision, Writing - review & editing. **Francesco Sardanelli:** Conceptualization, Methodology, Validation, Resources, Funding acquisition, Supervision, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.orcp.2020.12.002.

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