Computed Tomography Highlights Increased Visceral Adiposity Associated With Critical Illness in COVID-19

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Obese subjects with coronavirus disease 2019 (COVID-19) are at increased risk of requiring critical care (1), suggesting that excess body fat associates with greater disease severity. BMI does not discriminate between fat and lean body mass and poorly reflects fat distribution. Cardiometabolic diseases and increased systemic inflammation, two conditions associated with visceral adiposity, are also linked to COVID-19 severity and fatality (1,2). The aim of this study was to assess the relationship between abdominal fat distribution and COVID-19 severity. We hypothesized that excess visceral adipose tissue (VAT), as identified by an increased VAT to subcutaneous adipose tissue (SAT) ratio (VAT/SAT), is associated with COVID-19 severity, as defined by intensive care unit (ICU) admission.

This was a single-center cohort study of 441 patients consecutively admitted to the Emergency Department (ED) of the Trauma Center Public Hospital Bufalini, Cesena, Italy, between 26 February and 6 April 2020 for a clinical suspicion of COVID-19. Of these patients, 144 had confirmed COVID-19 based on positive RT-PCR from a nasal and/or throat swab together with high-resolution computed tomography (HR-CT) findings suggestive of COVID-19 pneumonia. Of those, 61 (42%) were admitted to ICU (ICU-COVID-19 group). One-hundred thirty-six patients evaluated in the ED for clinical suspicion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection who tested negative by nasopharyngeal swab and had no HR-CT signs of pneumonia served as the control group. We excluded 161 subjects due to unavailability of RT-PCR data or absence of HR-CT signs of pneumonia despite a positive RT-PCR. Upper abdominal fat was assessed on sagittal image from chest HR-CT (Philips Diamond Select Brillance CT 64-slice) performed upon ED admission and acquired up to a plane transverse to L2. SAT was defined as the greatest thickness between the skin–fat interface and the muscle wall; VAT was defined as the greatest distance between the inner muscular wall and the anterior liver surface (intrareader agreement by Cohen $\kappa \geq 0.98$ for both). The primary exposure and outcome measures were VAT amount and ICU admission, respectively. Logistic regression models were used to estimate the odds ratios (OR) of ICU admission by VAT.

There were no differences between patients with COVID-19 and control subjects in terms of age and BMI (Table 1). Male sex was more prevalent among COVID-19 patients than control subjects. BMI was higher in ICU-COVID-19 versus COVID-19 subjects not requiring intensive care (nICU-COVID-19). In the overall COVID-19 population, BMI positively correlated with VAT and SAT ($r = 0.407$ and $r = 0.289$, respectively; $P < 0.003$) but was unrelated to VAT/SAT ratio ($r = 0.085$; $P = 0.378$). Subjects with COVID-19 had thicker VAT than control subjects (Table 1). This difference was driven by the ICU-COVID-19 group and might suggest that visceral adiposity influences

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Table 1—Clinical features and fat distribution of the studied population. The table reports comparisons between the non-COVID-19 and the overall COVID-19 population, as well as comparison between subjects with COVID-19 not requiring intensive care (nICU-COVID-19) and those admitted to ICU (ICU-COVID-19).

	Non-COVID-19 (n = 136)	Overall COVID-19 population (n = 144)	P value	nICU-COVID-19 (n = 83)	ICU-COVID-19 (n = 61)	P value
Age, years	61.9 (20.4)	60.3 (17.0)	0.476	59.3 (19.0)	61.7 (13.8)	0.393
Males, n (%)	63 (46.3)	87 (60.4)	0.005	46 (55.4)	41 (67.3)	0.153
BMI, kg/m^2	26.2 (4.0)	27.0 (5.1)	0.306	25.8 (4.3)	29.6 (5.8)	<0.001
VAT, mm	12.3 (6.7)	15.1 (6.6)	<0.001	13.1 (6.0)	17.9 (6.5)	<0.001
SAT, mm	16.3 (8.4)	17.7 (8.9)	0.205	19.2 (9.7)	15.6 (7.4)	0.011
VAT/SAT	0.94 (0.70)	1.16 (0.93)	0.987	0.90 (0.73)	1.53 (1.04)	<0.001

Continuous data are expressed as mean (SD). Differences in continuous data were tested by ANOVA (two-tailed). Categorical data were analyzed by χ^2 (two-tailed).

COVID-19 severity. In COVID-19 patients, fat thickness and distribution were unrelated to age and sex, except for SAT, which was thicker in females than males (mean [SD] 19.7 [9.6] vs. 16.3 [8.3] mm; $P = 0.030$). Admission to ICU was associated with a 30% higher VAT ($P < 0.001$) and a 30% lower SAT ($P = 0.011$), independent of age and sex (Table 1). VAT thickness was associated with increased risk of ICU admission (age-, sex-, and BMI-adjusted OR [aOR] for unit [mm] increase 1.16, 95% CI 1.07–1.26; $P < 0.0001$), as was VAT/SAT (aOR for 20% VAT/SAT increase 1.25, 95% CI 1.10–1.42; $P < 0.0001$), with a predictive area under the receiver operating characteristic curve of 0.728 (95% CI 0.647–0.810).

Our data indicate that abdominal fat distribution characterized by increased VAT and lower SAT increased the risk of ICU admission for COVID-19, independent of BMI. Visceral adiposity is associated with local and systemic inflammation, characterized by increased production of proinflammatory cytokines such as interleukin-6 and tumor necrosis factor-α, which are also markedly increased in severe COVID-19 (2). Omental fat can release two- to threefold higher levels of interleukin-6 and chemokines compared with SAT (3,4). We hypothesize that excess visceral adiposity sustains a proinflammatory milieu that promotes hyperinflammation, exacerbating disease severity. SARS-CoV-2 infection might also enhance VAT inflammation. Enterocytes coexpress high levels of the SARS-CoV-2 entry ligands ACE2 and TMPRSS2 (5), serving as potential entry sites. Virus recognition by the gut immune system may trigger an immunoinflammatory response spreading to mesenteric VAT and exacerbating local inflammation.

Our study is limited by the lack of inflammatory biomarkers, diabetes status, and a total abdomen scan. A strength of our approach is the use of routine chest CT for measuring upper abdominal fat distribution, without the need for additional or repeated ad hoc imaging.

In conclusion, our findings indicate that COVID-19 severity is associated with abdominal adipose tissue distribution, highlighting the potential pathogenic role of visceral adiposity in acute illness.

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