



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

Diabetes Care 2020;43:e129–e130 | <https://doi.org/10.2337/dc20-1333>

Sofia Battisti,^{1,2,3} Claudio Pedone,⁴
Nicola Napoli,^{5,6} Emanuele Russo,⁷
Vanni Agnoletti,⁷
Stefano Geniere Nigra,⁸
Caterina Dengo,¹ Martina Mughetti,¹
Caterina Conte,⁹ Paolo Pozzilli,^{5,10}
Emanuela Giampalma,¹ and
Rocky Strollo⁵

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 Brilliance 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

¹Radiology Department, AUSL Romagna M. Bufalini Hospital, Cesena, Italy

²Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy

³Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES), Alma Mater Studiorum-Università di Bologna, Bologna, Italy

⁴Unit of Geriatrics, Department of Medicine, Campus Bio-Medico University of Rome, Rome, Italy

⁵Unit of Endocrinology and Diabetes, Department of Medicine, Campus Bio-Medico University of Rome, Rome, Italy

⁶Division of Bone and Mineral Diseases, Washington University in St. Louis, St. Louis, MO

⁷Anesthesia and Intensive Care Unit, AUSL Romagna M. Bufalini Hospital, Cesena, Italy

⁸Emergency Department, Dipartimento Chirurgico e Grandi Traumi, AUSL Romagna M. Bufalini Hospital, Cesena, Italy

⁹Department of Human Sciences and Promotion of the Quality of Life, San Raffaele Roma Open University, Rome, Italy

¹⁰Centre for Immunobiology, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, U.K.

Corresponding author: Rocky Strollo, r.strollo@unicampus.it

Received 2 June 2020 and accepted 10 July 2020

E.G. and R.S. contributed equally to this work.

This article is part of a special article collection available at <https://care.diabetesjournals.org/collection/diabetes-and-COVID19>.

© 2020 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://www.diabetesjournals.org/content/license>.

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.

Funding. R.S. is supported by the European Foundation for the Study of Diabetes Mentorship Programme 2018, by the Italian Ministry of Health (grant number GR-2018-12365982), and by the Young Investigator fellowship from the Salerno Academy of Physicians (OMCeO Salerno).

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. S.B. conceived the study, collected the data, and contributed to

the interpretation of the data and the writing of the manuscript. C.P. analyzed the data and contributed to the interpretation of the data and the writing of the manuscript. N.N., C.C., and P.P. contributed to the interpretation of the data and the writing of the manuscript. E.R. contributed to data analysis. S.G.N. and C.D. contributed to data collection. V.A. and M.M. contributed to data interpretation. E.G. contributed to data collection and interpretation. R.S. wrote the first draft and contributed to the interpretation of the data and to data analysis. All authors critically revised the manuscript for intellectual content. All authors saw and approved the final draft. S.B. and R.S. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Tamara A, Tahapary DL. Obesity as a predictor for a poor prognosis of COVID-19: a systematic review. *Diabetes Metab Syndr* 2020;14:655–659
2. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest* 2020;130:2620–2629
3. Mathis D. Immunological goings-on in visceral adipose tissue. *Cell Metab* 2013;17:851–859
4. Fried SK, Bunkin DA, Greenberg AS. Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid. *J Clin Endocrinol Metab* 1998;83:847–850
5. Sungnak W, Huang N, Bécavin C, et al.; HCA Lung Biological Network. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. *Nat Med* 2020;26:681–687