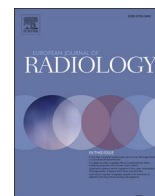




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Research article

Association of body composition parameters measured on CT with risk of hospitalization in patients with Covid-19

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ABSTRACT

Purpose: To assess prognostic value of body composition parameters measured at CT to predict risk of hospitalization in patients with COVID-19 infection.

Methods: 177 patients with SARS-CoV-2 infection and with abdominopelvic CT were included in this retrospective IRB approved two-institution study. Patients were stratified based on disease severity as outpatients (no hospital admission) and patients who were hospitalized (inpatients). Two readers blinded to the clinical outcome segmented axial CT images at the L3 vertebral body level for visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), muscle adipose tissue (MAT), muscle mass (MM). VAT to total adipose tissue ratio (VAT/TAT), MAT/MM ratio, and muscle index (MI) at L3 were computed. These measures, along with detailed clinical risk factors, were compared in patients stratified by severity. Various logistic regression clinical and clinical + imaging models were compared to discriminate inpatients from outpatients.

Results: There were 76 outpatients (43%) and 101 inpatients. Male gender ($p = 0.013$), age ($p = 0.0003$), hypertension ($p = 0.0003$), diabetes ($p = 0.0001$), history of cardiac disease ($p = 0.007$), VAT/TAT ($p < 0.0001$), and MAT/MM ($p < 0.0001$), but not BMI, were associated with hospitalization. A clinical model (age, gender, BMI) had AUC of 0.70. Addition of VAT/TAT to the clinical model improved the AUC to 0.73. Optimal model that included gender, BMI, race (Black), MI, VAT/TAT, as well as interaction between gender and VAT/TAT and gender and MAT/MM demonstrated the highest AUC of 0.83.

Conclusion: MAT/MM and VAT/TAT provides important prognostic information in predicting patients with COVID-19 who are likely to require hospitalization.

1. Introduction

COVID-19 illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to severe global morbidity and mortality. According to the Centers for Disease Control (CDC), between January 2020 and January 2021, over 25 million Americans have been diagnosed with COVID-19 and over 400,000 have died. Unfortunately, the number of new cases, hospitalizations, and deaths continues to rise in the United States and worldwide. The spectrum of COVID-19 illness ranges from asymptomatic presentation to severe illness requiring hospitalization and potentially mechanical ventilation, to even death [1,2].

Therefore, there is an urgent need to identify and validate biomarkers that are associated with severe disease and hospitalization as this may have direct impact on patient management, timely intervention, and an opportunity to reduce mortality. Reliable selection of patients that may require hospitalization can help to optimize resources and closely monitor high-risk patients. Furthermore, such evaluation and analysis may also be useful in future for other infectious and inflammatory disease processes.

Age, male sex, race, diabetes mellitus, hypertension, cardiopulmonary diseases, and obesity have been identified as risk factor for disease severity [1–8]. In a recent systematic review and meta-analysis, obesity

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assessed by the body-mass index (BMI) has been identified as a risk factor for hospitalization, need for invasive mechanical ventilation, and death in patients with COVID-19 [9–11]. In addition to BMI, higher visceral adipose tissue (VAT) measured on CT has also been shown to be associated with hospitalization and the need for mechanical ventilation [9]. A recent small study demonstrated that the addition of VAT measured on abdominopelvic CT at the L3 level to the clinical model, which included age, sex, and BMI, improved discrimination between hospitalized patients and outpatients [12]. This study found no significant correlation between VAT and BMI, which implied that VAT provides important information about obesity and patient's metabolic health that is not captured by BMI.

It is well known that sarcopenia, muscle fat or steatosis, and low muscle mass are associated with poor outcome in patients with malignancy and in critically ill patients [13–15]. A recent study has shown that lower volume and density of the pectoralis muscle on chest CT was associated with severe COVID-19 disease [16]. Similarly, decreased attenuation of skeletal muscle was associated with disease severity in the hospitalized patients [17]. Measures of cross sectional muscle area (muscle mass, MM) and muscle adipose tissue (MAT) may thus serve as biomarkers of overall health, and lower MM and higher MAT may suggest poor health.

The purpose of our two-center study, motivated by this evidence, was two-fold: (1) Evaluate if the ratio of muscle adipose tissue (MAT) to MM (MAT/MM) measured at abdominopelvic CT is higher in patients with COVID-19 who required hospitalization compared to the outpatients, and (2) test if a model that includes MAT/MM in addition to CT measures of VAT can improve identification of patients that require hospitalization.

2. Methods

2.1. Patients

This HIPAA-compliant, retrospective, two-institution study (institutions A and B, located in different cities) was approved by each institution's review board and received a waiver of informed consent. At each institution, a retrospective search of the patient database was performed to identify all adults (≥ 18 years of age) who had a diagnosis of SARS-CoV-2 infection during the period of March to June 2020. Inclusion criteria for the study was patients with diagnosis of SARS-CoV-2 infection who either underwent abdominopelvic CT during their acute presentation of SARS-CoV-2 infection or had prior abdominopelvic CT performed within 6 months of the diagnosis of SARS-CoV-2 infection. Exclusion criteria were patients whose CT exams showed poor image quality and extensive ascites. In patients with multiple exams, the CT exam closest to the acute presentation was selected.

At institution A, 2850 patients were diagnosed with SARS-CoV-2 infection from March to June 2020. Among these, 176 abdominopelvic CT exams were performed either during acute presentation or within 6 months prior to the acute presentation. After excluding repeat exams, exams with incomplete abdominopelvic imaging, or with sub-optimal image quality, the study cohort at institution A consisted of 99 patients. The electronic medical record (EMR) was reviewed to obtain the clinical outcome of COVID-19 disease and categorize patients based on disease severity into two groups: (1) patients who did not require hospital admission (outpatients), and (2) patients who were hospitalized (inpatients) due to severe COVID-19 illness. There were 62 inpatients and 37 outpatients. A subset of patients ($n = 50$) from institution A were included in a previously published study [12]. Similarly, at institution B, 1700 patients were diagnosed with SARS-CoV-2 infection during the same time period, and 252 abdominopelvic CT examination were performed in these patients. After excluding repeat exams and exams with poor image quality, a subset of patients from institution B consisted of 39 inpatients and 39 outpatients were randomly selected. Thus, 99 patients from institution A and 78 patients from an institution B were included

for a total combined cohort of 177 patients.

Data on age, sex, race/ethnicity, BMI, hypertension (HTN), diabetes mellitus (DM), history of pulmonary disease, and cardiac disease were collected in all patients from EMR.

2.2. CT acquisition

Abdominopelvic CT examinations were acquired in supine position on a variety of state-of-the-art 64-slice or 128-slice multi-detector scanners. Axial images through the abdomen were constructed on the scanner console. Section thickness averaged 3.7 mm (range, 2.5–5 mm). 69% of CT exams (122 out of 177) were performed with intravenous contrast.

2.3. CT segmentation

The goal of quantitative CT image analysis workflow is to reliably and quickly estimate the composition of abdominal fat and muscle. At each institution, segmentation and quantitative adipose tissue analyses were performed by a reader who was blinded to the clinical outcome. Processing was done using FireVoxel (build 314), a freely available software (www.firevoxel.org).

In the first step, the observer located the CT slice corresponding to the superior endplate of the L3 vertebral body. This was facilitated by sagittal and coronal projections of the axial image stack. In the next step, the observer then drew the interior boundary (C) of the abdominal wall (red contour in Fig. 1). Subsequent steps are applied automatically. In these steps, median filtering, background detection and connectivity are

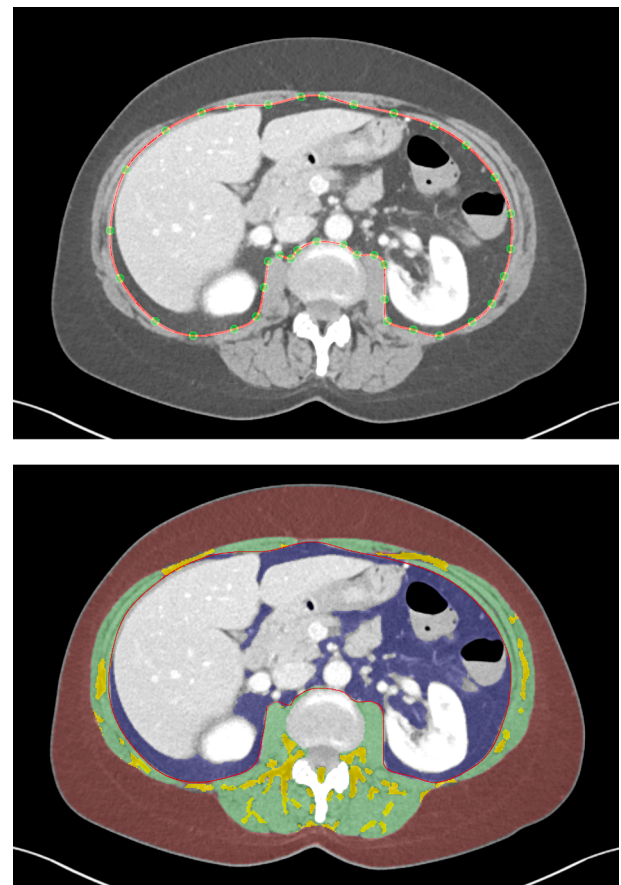


Fig. 1. CT image post processing with FireVoxel. Top panel: slice is selected at the L3 level and the contour (shown in red) is drawn along the abdominal wall. Bottom: segmented tissues: dark red = subcutaneous fat (SAT); green = muscle (MM); blue = visceral fat (VAT); yellow = muscle fat (MAT).

used to mask out features that are external to the abdomen, including the patient's arms, clothing, tubes, and supporting table. Morphological erosion was used to further exclude the 2.2-mm layer of abdominal skin. The resulting tissue was thresholded to $[-150, +73]$ Hounsfield units (HU) attenuation range. A further threshold of -10 HU and morphological noise removal was used to define the muscle (>-10 HU) and total abdominal fat compartments. Finally, the location with respect to the contour *C* and the topological relationship to the muscle were applied to partition the total fat into (a) subcutaneous, (b) visceral, and (c) muscle fat compartments (Fig. 1). In the final manual step, the operator checks and corrects muscle ROI by erasing a small area in spinal medullary canal that can be erroneously classified as muscle.

2.4. Measures of muscle and visceral adiposity

Measures of adipose tissue area VAT, subcutaneous adipose tissue (SAT), MAT were obtained from the segmented areas at the L3 vertebral body level. Cross-sectional area of muscle tissue at the L3 level was defined as Muscle Mass (MM). Mean muscle index (MI) which is the MM normalized to height² was computed. Ratios of MAT/MM and VAT to total value TAT = SAT + VAT + MAT were also computed.

Clinically acceptable speed (1–2 min per exam) and inter-observer reliability of CT segmentation workflow has been reported previously [12].

2.5. Statistical analysis

In the initial analysis, age, sex, race, BMI, and raw measures of abdominal tissue volume VAT, SAT, MAT, MI, and MM (computed at the L3 vertebral body level) were compared between outpatients and inpatients. For each continuous measure, the normality assumption was checked by means of a Shapiro-Wilk test with the significance level of 0.05. For normally distributed variables ($p > 0.05$), we then used the two-tailed *t*-test. For non-normally distributed variables, we used a Mann-Whitney nonparametric test for independent samples. Box and whisker plots were used to visualize the effect of continuous predictors on hospitalization. To assess the association of clinical risk factors, such as HTN, DM, and history of heart disease or pulmonary disease, with hospitalization, inpatients and outpatients with each of the risk factors were compared using one-sided proportion test. The correlations of BMI with VAT/TAT and MAT/MM were assessed with Pearson correlation coefficient *r*.

In the next step, we built multivariate models to predict which patients would require hospitalization. Based on the initial analyses, we selected as potential predictors age, sex, race (Black or not Black), BMI, MI, and VAT/TAT. Abdominal tissue distribution is known to depend on sex and race, and thus we also considered two types of interactions: VAT/TAT versus sex/race and MAT/MM versus sex/race. Using the best subset selection approach, we have constructed the logistic regression model defined as the model with the smallest value of Akaike information criterion (AIC) [18] among all subsets. This optimal model was compared to (1) a clinical model that included age, sex, and BMI, and to (2) a previously proposed clinical + CT model that included age, sex, BMI, and VAT/TAT [12]. Receiver operating characteristic (ROC) analysis was performed and the area under the curve (AUC) was computed for each of these models. The comparison between the AUCs was performed using the DeLong method [19]. For each model and each predictor, we computed the odds ratio. In addition, leave-one-out cross-validation was also performed in conjunction with each model fit for a more realistic estimate on how the model is likely to perform in a new setting. MedCalc (version 19.2.6) and R (version 3.6.3) were used to perform statistical analyses.

3. Results:

3.1. Demographics and disease severity

The mean \pm stdev age of the patients was 59 ± 16 years; 80 patients (45%) were female and 97 patients were male (55%). Out of the 177 patients, 76 were outpatients (43%) and 101 were inpatients (57%). Inpatients were older compared to the outpatients (62.4 ± 15.2 years vs. 53.8 ± 15.8 years; $p < 0.001$). Among female patients, 46.3% (37/80) were inpatients, whereas among male patients, 66.0% (64/97) were inpatients, and therefore male sex was significantly associated with hospitalization (46.3% vs. 66.0%; $p = 0.013$). In our study cohort, 49% of the patients were White, 19% Black, 16% Hispanic, 6% Asian, and 11% other/nonspecific. We did not find statistically significant differences in the proportion of inpatients by ethnicity.

Table 1 summarizes the data on clinical risk factors and their association with hospitalization. Among all patients, 52.0% (92/177) had HTN; 68.5% of patients with HTN were inpatients and 31.5% were outpatients. This difference was statistically significant ($p < 0.001$). Approximately 27.7% (49/177) of all patients had DM. Of all the diabetic patients, 77.6% were inpatients, whereas 22.4% were outpatients ($p < 0.001$). Furthermore, 21.5% (38/177) of all patients had history of heart disease and 20.3% (36/177) of all patients had history of pulmonary disease. Higher percentages of patients with heart and pulmonary disease were inpatients compared to the outpatients (Table 1). This difference was statistically significant for patients with history of heart disease ($p = 0.007$), but did not reach significance for patients with pulmonary disease ($p = 0.067$).

3.2. CT measures and disease severity

3.2.1. Muscle adiposity

There was a larger amount (area in cm²) of muscle adipose tissue (MAT) in inpatients compared to the outpatients (17.8 ± 9.4 cm² vs. 12.1 ± 7.0 cm²; $p < 0.001$). There was no significant difference in the muscle area (measured in cm²) at the L3 level between inpatients and outpatients (122.7 ± 34.5 cm² vs. 131.0 ± 32.8 cm²; $p = 0.112$). However, mean muscle index (MM normalized to height²) was significantly smaller for inpatients (0.00437 ± 0.00118) than for outpatients (0.00482 ± 0.00119 , $p = 0.012$). MAT/MM ratio was significantly higher in the inpatients compared to the outpatients (0.131 ± 0.070 vs. 0.088 ± 0.054 ; $p < 0.001$). When stratified by sex, MAT/MM was significantly higher in hospitalized males ($p < 0.001$) and hospitalized females ($p = 0.002$) compared to the outpatient males and females, respectively (Fig. 2A).

There was no significant correlation between BMI and MAT/MM ($r = 0.13$; $p = 0.113$).

3.2.2. Adipose tissue

VAT (234.8 ± 112.1 cm² vs. 157.9 ± 92.4 cm²; $p < 0.001$) and VAT/

Table 1

Clinical risk factors and their association with hospitalization. The p-value is the result of the one-sided proportion test comparing inpatients and outpatients with a given risk factor.

Clinical risk factor	% patients with risk factor	% with risk factor who are outpatients	% with risk factor who are inpatients	p value
HTN	52.0% (92/177)	31.5% (29/92)	68.5% (63/92)	0.0003
DM	27.7% (49/177)	22.4% (11/49)	77.6% (38/49)	0.0001
History of heart disease	21.5% (38/177)	28.9% (11/38)	71.1% (27/38)	0.007
History of pulmonary disease	20.3% (36/177)	36.1% (13/36)	63.9% (23/36)	0.067

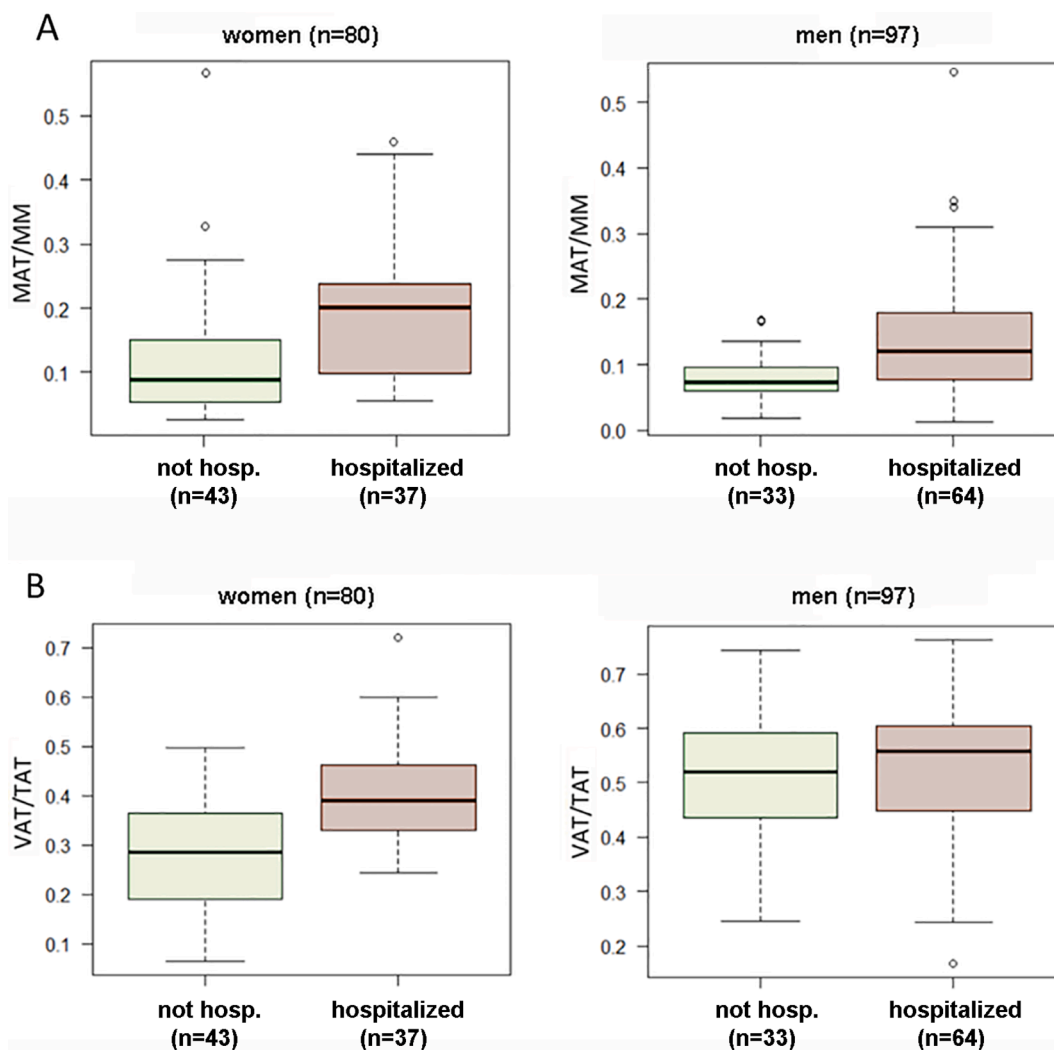


Fig. 2. The distribution of adipose tissue ratios in hospitalized vs non-hospitalized individuals, stratified by gender. Top row: Muscle fat (MAT/MM). Bottom row: Visceral fat (VAT/TAT).

TAT (0.48 ± 0.14 vs. 0.38 ± 0.16 ; $p < 0.001$) were significantly higher in inpatients compared to the outpatients. Furthermore, these measures when stratified by sex were significantly different in hospitalized women compared to the outpatient women ($p < 0.001$), but were not significantly different in hospitalized and outpatient men ($p = 0.39$). These differences are illustrated by a box plot in Fig. 2B.

3.2.3. Correlation between MAT/MM and VAT/TAT

There was no significant correlation between MAT/MM and VAT/TAT ($r = 0.04$; $p = 0.692$).

3.3. Models for predicting hospitalization:

A clinical model (age, sex, BMI) had AUC of 0.70 with leave-one-out cross validation error of 0.29 and AIC of 226.44. A model that added VAT/TAT to the clinical model improved the AUC to 0.73 with AIC of 221.66.

The optimal model contained seven predictors: sex, BMI, race (Black or not Black), MI, VAT/TAT, as well as the interactions between VAT/TAT and sex and between MAT/MM and sex. The odds ratios for the optimal model variables are shown in Table 2. The optimal model demonstrated the highest AUC of 0.83 (95% CI: 0.76–0.88). This model had the lowest AIC of 190.74 and leave-one-out-cross validation error of 0.24 (Fig. 3). This model is available online (https://www.firevoxel.org/im/hospitalization_calculator.xlsx).

Table 2

The optimal model to predict hospitalization contains seven variables. The odds ratios* are for hospitalization, as predicted by each of the model variables.

Variables	Estimate	Std. Error	Odds Ratio
(Intercept)	-5.947	1.868	0
Gender [#]	4.610	1.772	3.01
BMI	0.113	0.035	1.12
Race (Black)	1.204	0.538	3.33
MI	-705.373	209.628	0.49
VAT/TAT	13.865	3.484	1.42
VAT/TAT × gender	-12.580	3.902	2.00 f/1.07 m
MAT/MM × gender	14.611	6.235	1.00 f/1.16 m

[#] For the model, gender was coded as 0/1, with 0 for women, and 1 for men.

* The odds ratios for the interactions between VAT/TAT and MAT/MM and gender are listed separately for female and male gender. The VAT/TAT × gender odds ratio corresponds to each 5% increase in VAT/TAT. Thus, the model indicated that among women, each 5% increase in VAT/TAT doubles the odds of hospitalization (O.R. = 2.0). For MAT/MM × gender, the odds ratio corresponds to a 1% increase in MAT/MM.

[org/im/hospitalization_calculator.xlsx](https://www.firevoxel.org/im/hospitalization_calculator.xlsx).

Fig. 4 demonstrates application of the model in two subjects for predicting risk of hospitalization.

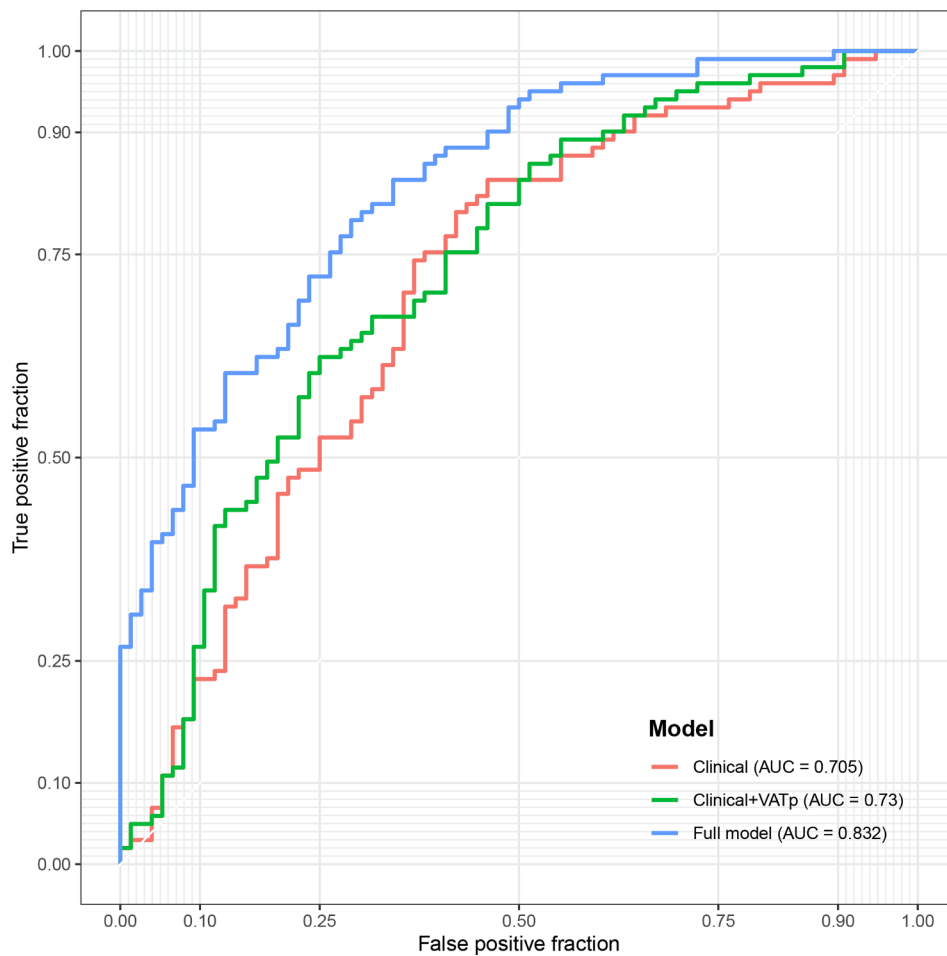


Fig. 3. Receiver operating characteristic curves for three models: Clinical, clinical + VAT/TAT (VATp) at L3, and optimal or full model.

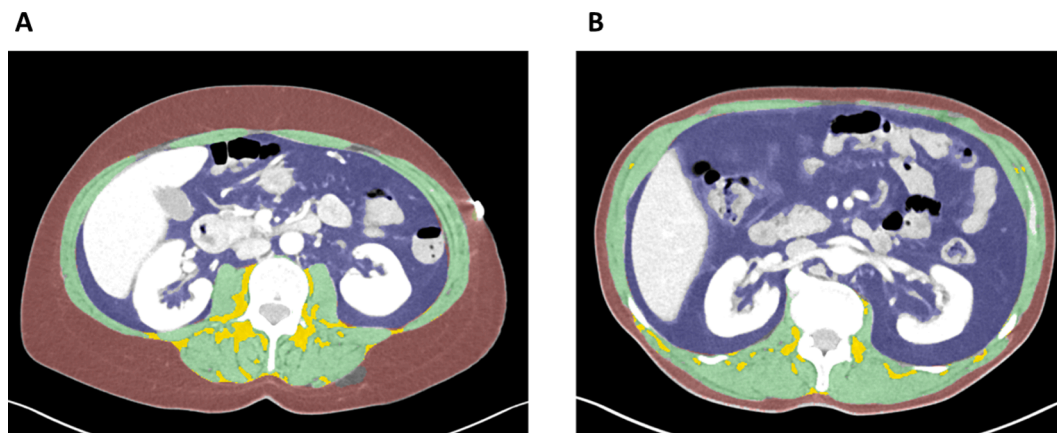


Fig. 4. Prediction of hospitalization using proposed model in two subjects. (A). White female with BMI of 27.3 kg/m². Axial image at L3 was processed with computed SAT (red) = 245.8 cm², VAT (blue) = 112.9 cm², VAT/TAT = 0.31; MAT (yellow) = 18.7 cm², Muscle (green) = 105.6 cm², and MAT/MM = 0.18. The mode computed probability of hospitalization to be 17%. This patient was not-hospitalized. (B). White male with BMI of 26.6 kg/m². Axial image at L3 was processed with computed SAT (red) = 81.1 cm², VAT (blue) = 273.9 cm², VAT/TAT = 0.77; MAT (yellow) = 12.9 cm², Muscle (green) = 121.5 cm², and MAT/MM = 0.1. The mode computed probability of hospitalization to be 75%. This patient required hospitalization.

4. Discussion

We investigated the role of muscle adiposity in addition to visceral adiposity in predicting the need for hospitalization due to severity of COVID-19 infection. In this study of 177 patients, measures of muscle adiposity (MAT and MAT/MM) were noted to be significantly higher in

patients that required hospitalization compared to the outpatients. Furthermore, there was an interaction between MAT/MM and gender such that the detrimental effect of MAT/MM was higher in males compared to females. We also noted the risk for hospitalization associated with VAT/TAT to be nearly 2 times higher in women than for men. A model that included MAT/MM and VAT/TAT, gender, race (Black or

not Black), and interactions of MAT/MM and VAT/TAT with gender had the highest AUC in identifying hospitalization. This model outperformed a clinical model (which included age, gender, BMI) as well as a model that only added VAT/TAT to the clinical model of age, gender, and BMI. These results suggest that CT-derived parameters add value to clinical parameters in predicting patients who were hospitalized due to COVID-19. It is important to note that this model did not take into account other variable such as presence of lung disease or heart disease or pulmonary involvement with COVID on chest x-ray or CT at the time of diagnosis.

Some studies have suggested that Black and Latino patients have higher incidence and greater severity of the disease [20,21]. Our multivariate model also confirmed an independent risk associated with race (Black or not Black), but this risk was much lower (nearly 4 times) than the risk of male gender. Furthermore, in a large study of six million US veterans, 30-day mortality did not differ by race or ethnicity [22]. Similarly, in a recent study, among those who tested positive for COVID-19, the odds of hospitalization were similar among White, Hispanic, and Black patients. In addition, hospitalized Black patients were less likely than White patients to have severe disease or die from the disease [23]. These studies suggest that mortality in some patients may be related to not having access to timely healthcare and hospital admission rather than underlying differences by ethnicity or race. Hence, being able to predict which patients would require hospitalization may potentially improve the outcome by triaging sicker patients to the hospital care while observing others as outpatients. Furthermore, with introduction of vaccines against SARS-CoV-2, identifying at-risk patients for hospitalization can help guide the order of vaccine deployment.

Obesity is associated with worse outcome in patients with COVID-19, including hospitalization and need for mechanical ventilation [9,11]. In our cohort, higher VAT/TAT was associated with hospitalization, both in male and female patients, but with higher odds ratio in female subjects. In a recent study, lower volume and density of pectoralis muscle were associated with poor outcome in patients with COVID-19 [16]. Similarly, pectoralis muscle area and muscle index were associated with disease severity including death [24]. Deposition of fat in the muscle is an indicator of muscle wasting. In our study, higher MAT and MAT/MM ratio at the L3 level were associated with increased risk of hospitalization, and had higher odds ratio in male subjects. It is important to note that MAT/MM at L3 level was not significantly correlated with BMI or VAT/TAT. Hence MAT/MM provides different and synergistic information relative to BMI and visceral adiposity.

In our cohort, HTN, DM, and history of cardiac disease was significantly associated with hospitalization. Furthermore, although higher percentage of patients with history of pulmonary disease were also hospitalized, this difference was not statistically significant, possibly due to a small sample size. Moreover, when compared against the model that included body composition parameters in addition to gender and race, these clinical risk factors did not appear to provide an independent risk of hospitalization in a multi-factorial model. It is also surprising that after accounting for gender and abdominal tissue biomarkers, subject age did not constitute an independent risk for hospitalization.

A recent study evaluated the combined role of VAT and muscle adiposity in predicting critical illness in hospitalized patients with COVID-19 [17]. In this interesting study, VAT and skeletal muscle attenuation were associated with disease severity in the hospitalized patients, and with the need for mechanical ventilation and death. However, to our knowledge, no study has evaluated the role of combination of MAT/MM and VAT/TAT measured at the L3 vertebral body level on abdominopelvic CT in predicting the need for hospitalization in COVID-19 patients. Our study focuses on identifying subjects that may need hospitalization rather than severity of disease in hospitalized patients, and we believe that this information is complementary when considering resource allocation and utilization. Additional strength of our study is having data available from two institutions in different cities in the United States. We believe that this heterogeneity of data from two institutions will make our model more generalizable and robust.

Furthermore, in our study we directly measured muscle mass and MAT instead of muscle attenuation which hopefully is less influenced by anasarca and edema.

Our study had a number of limitations. It is retrospective in nature, and this model has not been evaluated prospectively to predict the need for hospitalization. Not all patients with COVID-19 will have abdominopelvic CT available or will undergo abdominopelvic CT, and hence it might be difficult to apply this model to a wider cohort of patients with COVID-19. However, patients with CT performed previously for any indication can be utilized to extract MAT/MM and VAT/TAT. Presence of edema and anasarca can impact identifying fat voxels both in the subcutaneous tissues as well as in the muscle, thus limiting the accuracy of segmented adipose tissues. We used a single slice evaluation for computing body composition parameters. Some of our studies were performed without contrast and slice thickness for CT exam ranged between 2.5 and 5 mm. However, presence or lack of intravenous contrast and CT slice thickness in the range of 2.5 mm and 5 mm does not seem to impact the accuracy of adipose tissue and muscle mass segmentation (see Supplemental Section). There has been recent work in developing deep learning based segmentation methods that also can be incorporated in such analysis [25,26]. In a recently published study, measure of muscle and visceral adiposity on chest CT at T7-T8 level was also associated with risk of hospitalization, mechanical ventilation and death [27]. In the future, we plan to develop a model that includes various measures of muscle adiposity and visceral adiposity on chest CT in addition to abdominopelvic CT to predict the need for hospitalization in patients that have chest CT but not abdominopelvic CT.

5. Conclusion

We have shown that muscle adipose tissue and the ratio of muscle adipose tissue to muscle mass measured at the L3 vertebral body level is significantly different in hospitalized patients compared to the outpatients. Furthermore, a model that includes MAT/MM in addition to visceral adiposity measures at the L3 vertebral body could help to identify patients who may require hospitalization.

CRediT authorship contribution statement

Hersh Chandarana: Conceptualization, Methodology, Project administration, Resources, Writing – original draft. **Nisanard Pisuchpen:** Data curation, Investigation. **Rachel Krieger:** Data curation, Investigation. **Bari Dane:** Data curation, Investigation, Supervision. **Artem Mikheev:** Software, Investigation. **Yang Feng:** Formal analysis. **Avinash Kambadakone:** Data curation, Methodology, Supervision. **Henry Rusinek:** Conceptualization, Data curation, Software, Methodology, Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejrad.2021.110031>.

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