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Research Article

The Impact of Thoracic CT Findings, Adiposity Parameters, and Laboratory Data on COVID-19 Prognosis

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Abstract

Aim: Numerous studies have been conducted concerning the clinical, laboratory, and radiological methods and markers to predict the prognosis of Coronavirus disease 2019 (COVID-19). In this study, we aim to explore the impact of COVID-19 severity scores, adiposity parameters, and laboratory findings on the prognosis of COVID-19.
Material and Method: A retrospective study was performed with 98 patients who were both computed tomography (CT) and polymerase chain reaction positive. Clinical outcomes, laboratory findings, thorax CT findings, and adiposity parameters (such as hepatic steatosis and visceral fat amount) obtained from thorax CTs were evaluated.
Results: The frequency of hepatic steatosis, lung severity score, and C-reactive protein (CRP) levels were higher, whereas lymphocyte count was lower in hospitalized patients than in patients treated at home. Among hospitalized patients, in addition to previous laboratory and radiological findings d-dimer and ferritin levels were higher in patients requiring intensive care. Among patients admitted to intensive care unit (ICU), the visceral to subcutaneous adipose tissue ratio was higher in patients who died than in patients who survived; none of the other parameters showed a significant difference.
Conclusion: COVID-19 CT score, adiposity parameters, and laboratory results were related to the prognosis of COVID-19. These results align with those of other recent research. A formula based on patient age, CT score, and CRP levels can be employed to determine if the patient requires hospital admission.

Keywords: COVID-19, quantitative evaluation, tomography, visceral adipose tissue, subcutaneous adipose tissue

INTRODUCTION

The World Health Organization stated in March 2020 that the Coronavirus disease 2019 (COVID-19) outbreak had reached pandemic levels, leading to a rapid increase in global cases. Numerous risk factors, such as male gender, smoking, and pre-existing conditions like cardiovascular disease and diabetes, have been recognized as potential contributors to severe pneumonia, hospitalization, and death during the pandemic.

According to various studies, patients who have higher Body Mass Index (BMI) are more severely affected by COVID-19 and tend to develop more severe forms of illness, obesity has been linked to an increased risk of hospitalization and mortality in COVID-19 patients (1-3). Several studies have also explored the connection between visceral adiposity and the severity of COVID-19, it has been suggested that visceral fat tissue area is associated with COVID-19 severity and may predict the need for intensive care (4-6).

Laboratory data is crucial in diagnosing and monitoring COVID-19 (7). These data include viral load, inflammation markers, organ functions, and other critical parameters. A detailed analysis of these parameters is crucial for comprehending the gravity of the disease and anticipating potential complications.

In our study, radiological markers of obesity, such as hepatic steatosis, waist circumference, visceral and subcutaneous fatty tissue amount, radiological extent of COVID pneumonia, and laboratory findings were evaluated to investigate their relationship with COVID severity and their potential effects on hospitalization, intensive care unit (ICU) admission, or mortality.

CITATION
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MATERIAL AND METHOD

Population and Study Design

This retrospective study was conducted at our hospital's radiology department between December 30, 2022, and February 15, 2023. The study received approval from Karamanoğlu Mehmetbey University's Institutional Ethics and Research Committee (approval number: 10-2022/07, approval date: 08.11.2022).

We retrospectively examined patients who applied to the pandemic clinic with flu-like symptoms and underwent non-contrast chest computed tomography (CT) between June 1, 2020, and July 15, 2020. All CT images were assessed using the guidelines set forth by the Radiological Society of North America (RSNA) (8). One hundred twenty-four patients with typical and indeterminate results according to RSNA classification were further evaluated. A total number of 98 patients who also had a positive real-time reverse transcription polymerase chain reaction (PCR) test were included in the study. Laboratory results and clinical outcomes were collected from hospital records. Patients were categorized according to their clinical outcome (Figure 1). Two main groups were established at the beginning of the study: "home treatment" and "hospital admission." Subsequently, the Hospital Admission cohort was further categorized into “COVID ward admission” and “ICU admission". Finally, the ICU admission group was divided into "ICU-mortality" and "ICU-survival" subgroups.

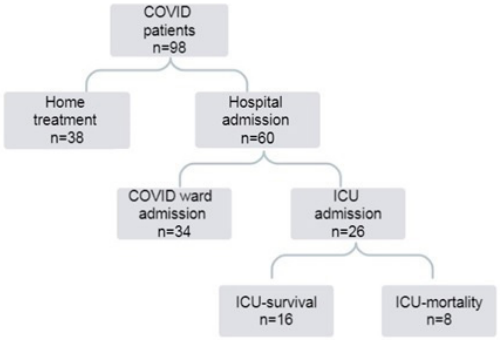

Figure 1. Flow chart of the study population

CT Acquisition and Evaluation

A non-contrast chest CT scan was performed on each patient as part of their initial clinical assessment in the emergency department. Images were obtained on a 16-detector CT scanner (Toshiba, Alexion) with the patients in supine position at full inspiration. CT scan parameters are as follows: X-ray tube parameters, 100 KVp; automatic tube current modulation (145–300 mAs); rotation time, 0.5 s; pitch, 1.43; section thickness, 5 mm.

The CT images were reviewed by a team of two radiologists (GMA and TG), each with eight and seven years of experience. The final agreement was made by consensus.

Chest CT scans were examined to detect the ground-glass opacities, consolidations, crazy paving appearance, and atoll sign.

The extent of pneumonia was visually scored following the previous method, “Total Severity Score (TSS)” (9). The technique involved evaluating each lobe and giving it a rating on a 4-point scale depending on the degree of lobar involvement: 0 for no involvement, 1 for 1-25%, 2 for 25-50%, 3 for 51-75%, and 4 for 76-100% involvement. TSS was equal to the sum of the scores of five lobes with a maximum score of 20 points.

CT Evaluation of Adiposity Parameters

CT scans were reviewed for hepatic steatosis, waist circumference, and visceral adipose tissue area.

On unenhanced CT, liver density less than 40 Hounsfield units (HU) is widely accepted as hepatic steatosis. For this study, we measured liver density from the right lobe, preferably from segment VIII, by positioning a region of interest (ROI) of approximately 10 cm^2, avoiding vessels, the biliary tree, and any focal lesions.

For visceral and subcutaneous adipose tissue (VAT and SAT) measurements, we used a semiautomatic software called BMI_CT (10). Measurements were made from a slice at the L2 corpus level. A manually drawn line separated the abdominal muscles and peritoneal cavity, and the software was employed to calculate SAT and VAT. These two areas were added together to calculate the total adipose tissue (TAT) area (Figure 2).

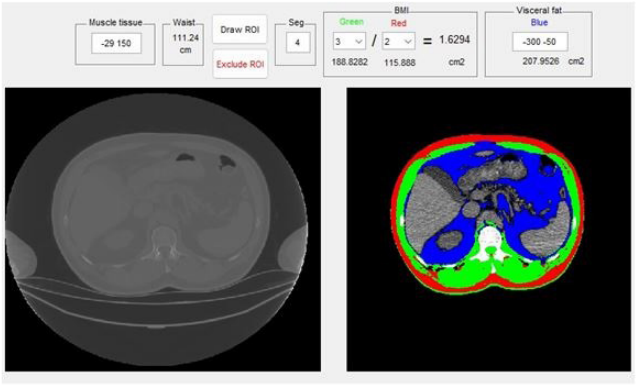

Figure 2. The process of semiautomatic quantification of body composition using the software. Subcutaneous adipose tissue is shown in red, visceral adipose tissue in blue, and muscle tissue in green

Statistical Analysis

IBM's SPSS 22.0 software (Chicago, IL) was performed for statistical analysis. Correlation heatmap plots were created using the Python 3.7.9 (Delaware, USA) software program. Shapiro Wilk, Mann-Whitney U Test, Independent Two-Sample t-test, Continuity Correction, and Fisher's Exact Tests, and Kruskal-Wallis H Test were employed in the analysis of the data set.

The mean±standard deviation was used to express continuous data that lined up to a normal distribution; the median (Q1-Q3) was used to represent those that did not. For categorical data, percentages (%) and frequencies were employed. Box-Plot (95% CI) was used to compare the median of TSS between “home treatment” and “hospital admission” groups. Pairwise comparison was applied for multiple sub-groups. The cut-off value was determined by applying receiver operating characteristic (ROC) analysis. Binary logistic regression with the enter method was applied

to investigate the factors affecting the follow-up status. The Hosmer-Lemeshow Test was used to model goodness of fit in regression analysis. The threshold for statistical significance was set at p<0.05.

RESULTS

Ninety-eight patients participated in the study. Forty percent were male, and 60 percent were female. They ranged in age from 23 to 84, with a mean of 56.19±15.88.

Comparison of Home Treatment and Hospital Admission Groups

Table 1 compares the groups of patients treated at home and admitted to the hospital. Age was notably higher in the hospital admission group, although gender did not differ. Among biochemical markers, neutrophil, lymphocyte, and C-reactive protein (CRP) were higher in the latter group. D-dimer and ferritin levels were elevated in hospitalized patients, but these data could not be compared to the home treatment group due to their unavailability.

Among obesity parameters, patients in the hospital admission group had notably lower liver HU and significantly higher waist circumference (p<0.05). VAT, SAT, or TAT areas did not significantly differ between the two groups.

Lung severity score was significantly higher in the hospital admission group (p<0.001) (Figure 3). The ROC curves for the TSS were done, and the area under the curve (AUC) was calculated for the diagnostic effectiveness of TSS in detecting patients needed hospital admission. ROC analysis showed the AUC of TSS for deciding hospital admission was 0.800 (95%CI 0.715–0.885). The sensitivity and specificity of the TSS cutoff of 5.5 were 56.7% and 86.8%, respectively (Figure 4).

Binary logistic regression with the enter method was applied with age, lung severity score, and CRP parameters to decide if the patient requires hospitalization. It was significant and fit (p<0.001 and p=0.523, respectively).

To decide between outpatient management and hospitalization, status can be calculated according to the formula: Follow-up status=-6.168 + 0.047*age + 0.591*TSS + 0.022*CRP.

The classification table is shown in Table 2.

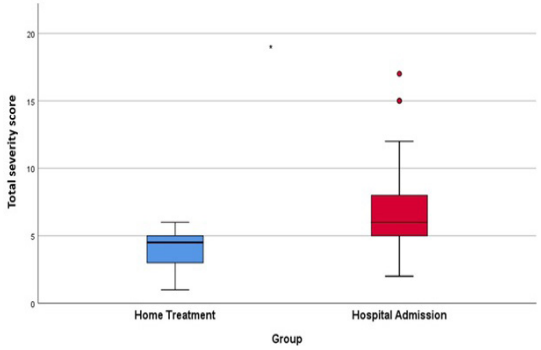

Figure 3. Box-plots for comparison of median differences of Total Severity Score (TSS) between "home treatment" and "hospital admission" groups, which represents a statistically significant difference between the two groups (p<0.001), * represents statistically significant differences between groups (p<0.001)

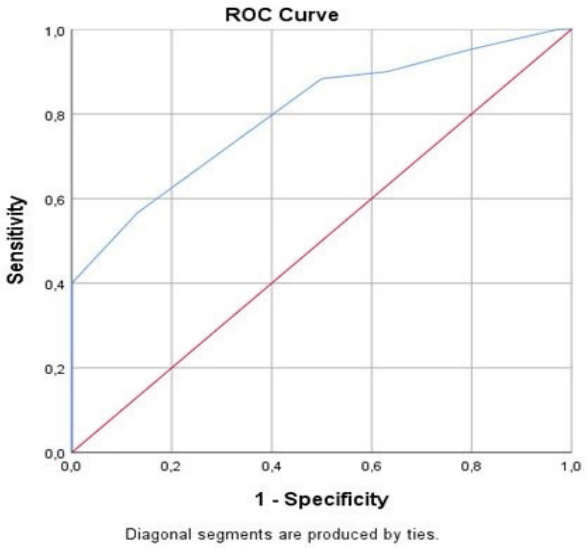

Figure 4. ROC curve for diagnostic performance of TSS in detection patients who need hospital admission. ROC analysis showed the area under the curve (AUC) of TSS for deciding "hospital admission" was 0.800 (95%CI 0.715–0.885); The TSS cutoff of 5.5 had 56.7% sensitivity and 86.8% specificity

Comparison of COVID Ward Admission and ICU Admission Groups

The findings are shown in Table 3. Demographic features were not different among groups. TSS was significantly higher in the ICU admission group (p=0.005) (Figure 5). Regarding biochemical markers, there were notable differences between the two groups in lymphocyte, CRP, d-dimer, and ferritin. Adiposity parameters did not differ among the two groups.

Comparison of ICU-Mortality and ICU-Survival Groups

The VAT/SAT ratio, higher in the ICU-mortality group, was the only metric that revealed a significant difference between these two groups (Table 4).

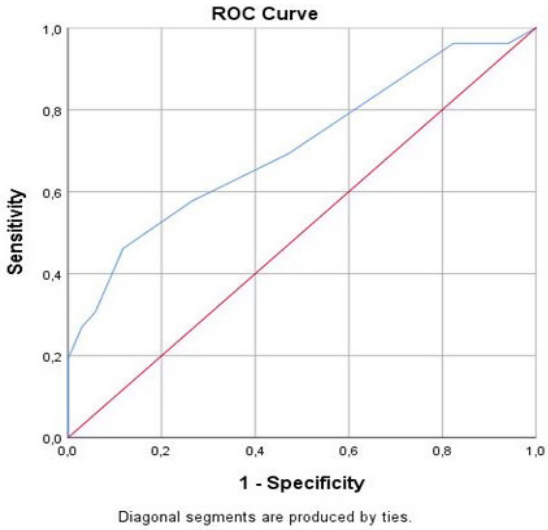

Figure 5. ROC curve for diagnostic performance of TSS in detection patients who need ICU admission. ROC analysis showed the area under the curve (AUC) of TSS for deciding "ICU admission" was 0.708 (95%CI 0.572–0.843); The LSS cutoff of 7.5 had 46.2% sensitivity and 88.2% specificity

Table 1. Comparison of home treatment and hospital admission groups

Parameters	Participant group		p value
	Home treatment (n=38)	Hospital admission (n=60)	
Age (year)	51.0 (38.5-59.8)	63.0 (48.0-72.5)	**0.002**[b]
VAT	101.8 (53.8-174.2)	142.3 (97.0-184.8)	0.072[b]
SAT	159.9±78.8	182.2±90.2	0.215[a]
TAT	283.0±128.9	327.4±114.9	0.079[a]
VAT/SAT	0.60 (0.33-1.28)	0.82 (0.51-1.31)	0.180[b]
Gender. (M/F) (M%)	14/24 (36.8)	25/35 (41.7)	0.634[c]
Waist circumference	100.3±12.3	106.6±10.0	**0.007**[a]
Liver HU	61.83 (56.95-65.46)	56.96 (49.63-62.65)	**0.013**[b]
Total severity score	4.5 (3.0-5.0)	6.0 (5.0-8.0)	**<0.001**[b]
Crazy paving (absent/present) (absent%)	30/8 (78.9)	37/23 (61.7)	0.117[c]
Atoll sign (absent/present) (absent%)	37/1 (97.4)	55/5 (91.7)	0.400[d]
Consolidation (absent/present) (absent%)	26/12 (68.4)	34/26 (56.7)	0.342[d]
White blood count	6280.0 (4900.0-6280.0)	6430.0 (4845.0-8927.5)	0.856[b]
Neutrophil	3900.0 (2430.0-4960.0)	4335.0 (3185.0-7467.5)	**0.034**[b]
Lymphocyte	1740.0 (1250.0-2680.0)	1210.0 (960.0-1590.0)	**<0.001**[b]
CRP	13.4 (5.2-24.0)*	86.2 (40.7-124.7)	**<0.001**[b]

Continuous variables are presented as mean±standard deviation or median (Q1-Q3); categorical variables are presented as numbers (%); a: Independent Samples T Test was applied, b: Mann-Whitney U Test was applied, c: Continuity Correction Test was applied, d: Fisher's Exact Test was applied, *: Some participant data was missing

Table 2. Classification table for binary logistic regression

			Predicted		
			Group		Percentage correct
			1 (home treatment)	2 (hospital admission)	
Observed	Group	1 (home treatment)	26	9	74.3
		2 (hospital admission)	9	51	85.0
Overall percentage			74.3	85.0	81.1

Table 3. Comparison of COVID ward admission and ICU admission groups

Parameters	Participant group		p value
	COVID ward admission (n=34)	ICU admission (n=26)	
Age (year)	52.0 (45.5-67.0)	70.0 (56.5-78.5)	0.328[b]
VAT	153.2±39.3	160.4±80.4	0.376[a]
SAT	162.8±87.1	163.7±85.7	0.643[a]
TAT	316.0±100.6	324.0±117.2	0.882[a]
VAT/SAT	1.0 (0.6-1.8)	1.0 (0.5-2.4)	0.429[b]
Gender (M/F) (M%)	13/21 (38.2)	12/14 (46.2)	0.725[c]
Waist circumference	108.9 (104.5-114.9)	103.4 (96.5-109.8)	0.582[a]
Liver HU	53.2±10.6	55.6±14.0	0.717[a]
Total severity score	6.0 (4.0-7.0)	7.0 (5.0-10.0)	**0.005**[b]
White blood count	6000.0 (5365.0-8065.0)	8500.0 (5677.5-13090.0)	0.110[b]
Neutrophil	4350.0 (3600.0-5675.0)	6590.0 (3387.5-12095.0)	0.075[b]
Lymphocyte	1590.0 (915.0-1770.0)	1080.0 (835.0-1257.5)	**0.024**[b]
LDH	381.7±147.2	396.6±142.5	0.157[a]
CRP	68.2±31.6	123.8±83.7	**<0.001**[a]
D-dimer	700.0 (427.5-1202.0)	885.5 (587.8-2167.8)	**0.001**[b]
Ferritin	332.9 (49.1-648.7)	360.6 (117.8-541.8)	**0.034**[b]
Total cholesterol	167.7±72.3	144.3±39.4	0.508[a]
LDL cholesterol	93.8±44.3	79.3±35.7	0.471[a]
Triglyceride	173.1±80.4	170.5±69.0	0.823[a]

Continuous variables are presented as mean±standard deviation or median (Q1-Q3); a: Independent Samples T Test was applied, b: Mann-Whitney U Test was applied, c: Continuity Correction Test was applied

Table 4. Comparison of ICU-mortality and ICU-survival groups

Parameters	Participant group		p value
	ICU-mortality (n=10)	ICU-survival (n=16)	
Age (year)	70.5 (64.8-78.5)	66.5 (51.5-78.3)	0.262
VAT	166.0 (130.5-215.6)	144.1 (74.7-216.6)	0.220
SAT	60.3 (46.7-181.8)	189.8 (133.4-233.1)	0.182
TAT	283.0 ± 128.9	327.4 ± 114.9	0.698
VAT/SAT	2.6 (1.0-3.6)	0.6 (0.4-1.3)	**0.036**
BMICT	1.8 (0.7-2.5)	0.6 (0.5-0.9)	0.060
Gender (M/F) (M%)	7/3 (70.0)	5/11 (31.3)	0.105[c]
Waist circumference	100.2 (92.6-107.1)	103.8 (99.2-112.0)	0.938
Liver HU	53.1 (40.6-56.9)	61.3 (53.9-68.1)	0.109
LDH	455.0 (302.8-528.0)	353.5 (270.0-481.5)	0.251
Total severity score	7.5 (5.0-8.5)	6.5 (5.3-13.8)	0.623
White blood count	8500.0 (4492.5-10510.0)	8965.0 (6140.0-14687.5)	0.551
Neutrophil	6590.0 (3177.5-8610.0)	7595.0 (3302.5-13557.5)	0.551
Lymphocyte	1115.0 (930.0-1822.5)	1030.0 (825.0-1217.5)	0.849
CRP	107.2 (97.6-239.0)	119.0 (41.6-140.4)	0.517
D-dimer	1410.5 (458.0-3505.3)	885.5 (615.5-1970.0)	0.776
Ferritin	291.0 (107.7-797.3)	389.2 (99.8-551.9)	0.698
Total cholesterol	125.0 (86.8-199.5)	148.0 (126.3-173.5)	0.972
LDL cholesterol	455.0 (302.8-528.0)	353.5 (270.0-481.5)	0.757
Triglyceride	127.0 (68.3-193.8)	199.5 (148.0-212.0)	0.330

Continuous variables are presented as mean ± standard deviation or median (Q1-Q3); a: Independent Samples T Test was applied, b: Mann-Whitney U Test was applied, c: Fisher's Exact Test was applied, *: Some participant data was missing

DISCUSSION

Numerous studies have been conducted concerning the clinical, laboratory, and radiological methods and markers used to foresee the outcome of COVID-19 (11,12). The purpose of this study was to explore the impact of obesity markers and COVID-19 severity markers obtained from thorax CT and laboratory findings on the prognosis of COVID-19.

Many studies showed that older age significantly predicts severe COVID-19 and hospitalization (13,14). It is thought to result from weaker immune function combined with the underlying chronic diseases in older age. Similarly, our study found that patients in the hospital admission subgroup were notably older than those in the home treatment group. Although several studies suggest that advanced age is a significant predictor of COVID-19 mortality (15-17), our study found no significant age difference between the COVID ward and ICU admission subgroups, nor between ICU-survival and ICU-mortality subgroups.

Laboratory parameters have been reported as essential markers for monitoring COVID-19 pneumonia. Among the laboratory parameters frequently investigated were neutrophil and lymphocyte count, d-dimer as a coagulation biomarker, and inflammatory biomarkers such as CRP and ferritin.

Research indicates that individuals who develop severe COVID-19 have markedly decreased lymphocyte counts. Our findings also showed that patients who required hospitalization had lower lymphocyte counts.

Higher levels of CRP and ferritin were observed in severe COVID-19 patients and were indicative of poor prognosis (18-21). Our research showed an increase in CRP levels among hospitalized patients and an even greater increase among those admitted to the ICU. It is an acute inflammatory protein and is closely tied to severe illness. We observed elevated ferritin levels in patients who needed ICU admission. Severe COVID-19 patients have been found to have higher levels of ferritin due to a cytokine storm (22). This storm triggers the release of inflammatory cytokines, stimulating ferritin secretion by hepatocytes and macrophages (23).

In COVID-19 patients, endothelial dysfunction caused by the virus and activation of the coagulation cascade may lead to COVID-19-associated coagulopathy (7). Therefore, coagulation biomarkers were widely investigated as markers for COVID-19 severity.

As one of the initial coagulation biomarkers affected in COVID-19 patients, D-dimer has also revealed its potential as a prognostic factor for mortality upon admission (24). Our findings showed a significant correlation between elevated D-dimer levels and the need for ICU admission in hospitalized patients. D-dimer and ferritin levels could not be compared in the home treatment subgroup as they were not routinely evaluated in the emergency room.

Thorax CT scans are a reliable method for diagnosing and predicting the course of COVID-19 (25). The severity of COVID-19 infections has been evaluated using a variety of scoring systems (11,26).

Li et al. found that TSS could predict severe disease in COVID-19 patients (9). Our research revealed that TSS levels were notably elevated in hospitalized patients compared to those treated at home. We found that the TSS cutoff of 5.5 had 56.7% sensitivity and 86.8% specificity. Binary logistic regression was applied with age, TSS, and CRP parameters; the resulting formula had 74.3% sensitivity and 56.7% sensitivity in predicting hospitalization. We believe this formula could be easy to apply in emergency departments and help clinicians decide if the patients require hospitalization.

The TSS score was also higher in patients requiring ICU admission than those treated in COVID wards. The TSS cutoff of 7.5 had 56.7% sensitivity and 86.8% specificity for deciding ICU admission.

In our study, the waist circumference value was higher, and the liver HU value was lower in the hospitalized group compared to the home-treatment group. Further studies have revealed that hepatic steatosis can independently increase the likelihood of a worse prognosis in COVID-19 infection (27,28). It has been shown that circulating IL-6 levels are higher in patients with hepatic steatosis. This situation may impact the severe course of COVID-19 (29).

It is widely recognized that obesity is connected to cardiovascular diseases, stroke, certain types of cancer, and overall mortality. The distribution of fat tissue is just as important as the amount of fat in the body. Kuk et al. showed that visceral fat is an independent predictor of mortality (30). Another study by Zhang et al. revealed that abdominal adiposity independently predicts mortality risk, especially in non-obese women (31).

Several studies have linked obesity to a more severe course of COVID-19, particularly in young patients (1-3,32,33). The connection between visceral adiposity and the severity of COVID-19 has been widely investigated. The results of multiple studies indicate that increased VAT and VAT/SAT rates are linked to a more severe course of COVID-19 and subsequent ICU admissions (4-6).

For VAT and SAT measurements in our investigation, we preferred the L2 corpus level, as a slice 3 cm above L3 level had been suggested to more accurately reflect the quantity of visceral adipose tissue than other levels (34). Similarly, L1–L2 and L2–L3 levels were suggested to correlate more strongly with VAT volume compared to the L4–L5 level (35). However, there is no widely agreed-upon level in the literature for using CT to estimate the quantity of visceral adipose tissue and studies used several different levels for adipose tissue measurements. The initial segment where the lung parenchyma is completed (6), sections that pass from the L3 level (4), and the L3-L4 intervertebral disc level (5) are all used in studies looking at the link between COVID-19 and visceral obesity. The lack of impact of adiposity factors on prognosis in our study may be attributed to the varying levels at which the assessments were conducted. Likewise, our findings may differ from other studies based on the sample size of our subgroups.

Although there were no significant differences in TSS and laboratory parameters among the two subgroups of intensive care unit patients in our study, the mortality group had a noticeably higher VAT/SAT ratio (p=0.036). Our research suggests that the VAT/SAT ratio could be a potential indicator of mortality among severe COVID-19 patients who needs intensive care.

It has long been known that adipose tissue is an active endocrine organ and a source of inflammatory interleukin and cytokines and that increased adipose tissue has pro-inflammatory effects (16). Increasing amounts of adipose tissue lead to an increase in blood vessels and connective tissue cells, particularly macrophages, that secrete proinflammatory cytokines such as interleukin-6, which was found to be higher in patients with a fatal course of COVID-19 (36). In obese people, proinflammatory cytokine levels are higher in both fatty tissue and blood circulation, which may contribute to a chronic proinflammatory state, leading to a more severe course of the disease (35).

There are various limitations to our study. Our rather small sample size led to limited subgroup sizes. Hospital records were insufficient, and anthropometric measurements (weight, height or BMI) were inaccessible and couldn't be included in the study. Likewise, important medical history, including coexisting medical conditions such as hypertension and diabetes mellitus, which might have influenced the prognosis, could not be accessible. Since our study was retrospective, some laboratory findings were not available.

CONCLUSION

In this study, CT scans were effective in detecting COVID-19 infection, assessing the extent of lung involvement, and the severity of the disease. Additionally, they are highly beneficial in evaluating adiposity parameters such as waist circumference, hepatic steatosis and visceral and adipose tissue areas, which are identified as significant risk factors for severe illness in previous studies. Our findings indicate that hepatic steatosis and elevated waist circumference could act as predictors for hospitalization, whereas the elevated VAT/SAT ratio may be associated with increased mortality risk in patients admitted to the ICU. Combining laboratory results with findings obtained from CT scans regarding the severity of COVID-19 pneumonia and radiological adiposity parameters offers valuable insights that can assist in predicting the clinical progression of COVID-19 and guide clinical decision-making.

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Conflict of interest: *The authors have no conflicts of interest to declare.*

Ethical approval: *The study received approval from Karamanoğlu Mehmetbey University's Institutional Ethics and Research Committee (approval number: 10-2022/07,* approval date: 08.11.2022*).*

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