Received: 25 Apr 2023 | **Accepted:** 02 Oct 2023 **Genel Tıp Derg. Volume** 33/**Issue** 6 (December), 703-710
DOI: 10.54005/geneltip.1287570

ORIGINAL ARTICLE

Correlation of Measurable Body Fat and Muscle Composition Parameters and Visceral Adipose Tissue on Computed Tomography with COVID-19 Severity

Bilgisayarlı Tomografide Ölçülebilir Vücut Yağ ve Kas Bileşimi Parametreleri ile Visseral Yağ Dokusunun COVID-19 Şiddetiyle Korelesi

[1]Duygu Imre Yetkin, [2]Yeliz Çiçek, [3]Erkan Büyükdemirci

[1]Adıyaman Training and Research Hospital, Adıyaman, Türkiye
[2]Bingöl State of Hospital, Department of Clinical Microbiology and Infectious Diseases, Bingöl, Türkiye
[3]Ankara provincial health directorate, Department of Public Health, Ankara, Türkiye

Correspondence

Yeliz Çiçek, Bingöl State of Hospital, Department of Clinical Microbiology and Infectious Diseases, Türkiye

E-Mail: dr.yelizcicek@gmail.com

How to cite ?

İmre Yetkin D, Çiçek Y, Büyükdemirci E. Correlation of Measurable Body Fat and Muscle Composition Parameters and Visceral Adipose Tissue on Computed Tomography with COVID-19 Severity. Genel Tıp Derg. 2023;33(6):703-10.

ABSTRACT

Background/Aims: Obesity increases the risk of having COVID-19. To evaluate the relationship between body fat, muscle composition and visceral adipose tissue on computed tomography (CT) with COVID-19 outcome.
Materials and Methods: One hundred forty-nine patients who had chest CT and a positive reverse transcriptase-polymerase chain reaction test were included. We measured the epicardial adipose tissue thickness (EAT) and liver density (LD), thoracic subcutaneous adipose tissue /pectoralis major (TSAT/PMJ), abdominal subcutaneous adipose tissue /psoas major muscle (ASAT/PSM), abdominal subcutaneous adipose tissue/erector spina muscle (ASAT/ESM) thickness ratios from thorax CT. Lymphocyte, platelet, neutrophil count, lymphocyte/neutrophil ratio and CRP were recorded.
Results: The mean EAT was high in patients with a poor clinical course (in severe patients: 7.06±2.39 mm, in critical patients: 7.89±2.08 mm). The mean EAT of the ICU group was 7.70±2.14 mm, and it was 8.50±2.10 mm in the deceased patients. TSAT/PMJ was lower in deceased patients (0.90±0.36, p=0.038). ASAT/PSM and ASAT/ESM were also higher in the moderate group (2,27±1,60 and 0,51±0,25) (p=0.003. and p=0.019) than mild one (1.59±1.80, and 0.40±0.26). There was no difference in terms of DM, malignancy or gender.
Conclusion: EAT was high in ICU admitted and deceased patients and should be used as a predictor of poor prognosis.

Keywords: Adipose tissue, computed tomography, COVID-19, epicardium.

ÖZ

Arka Plan/Amaçlar: Obezite, COVID-19'a yakalanma riskini artırır. Amacımız bilgisayarlı tomografide (BT) vücut yağı, kas bileşimi ve iç organ yağ dokusu ile COVID-19 hastalık şiddetiyle arasındaki ilişkiyi değerlendirmektir.
Gereç ve Yöntem: Toraks BT'si olan ve ters transkriptaz-polimeraz zincir reaksiyonu testi pozitif olan 149 hasta çalışmaya dahil edildi. Epikardiyal yağ dokusu kalınlığını (EAT) ve karaciğer dansitesi (LD), torasik deri altı yağ dokusu/pektoralis majör (TSAT/PMJ), karın deri altı yağ dokusu/psoas majör kası (ASAT/PSM), karın deri altı yağ dokusu/erector spina kas (ASAT/ESM) kalınlık oranlarını Toraks BT'den ölçtük. Lenfosit, trombosit, nötrofil sayısı, lenfosit/nötrofil oranı ve CRP kaydedildi.
Bulgular: Klinik gidişi kötü olan hastalarda ortalama EAT yüksekti (ağır hastalarda: 7,06±2,39 mm, kritik hastalarda: 7,89±2,08 mm). Yoğun bakım grubunun ortalama EAT'si 7,70±2,14 mm, ölen hastalarda ise 8,50±2,10 mm idi. Ölen hastalarda TSAT/PMJ daha düşüktü (0,90±0,36, p=0,038). ASAT/PSM ve ASAT/ESM de orta grupta (2,27±1,60 ve 0,51±0,25) (p=0,003 ve p=0,019), hafif gruptan (1,59±1,80 ve p=0,019) daha yüksekti. 0,40±0,26). DM, malignite ve cinsiyet açısından fark yoktu.
Sonuç: YBÜ'ye başvuran ve ölen hastalarda EAT yüksekti ve kötü prognozun bir göstergesi olarak kullanılabilir.

Anahtar Kelimeler: Yağ dokusu, bilgisayarlı tomografi, COVID-19, epikardiyum.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of COVID-19 illness and it is responsible for morbidity and mortality (1). Obesity is an important risk factor for the poor prognosis (2). Obesity is considered to create an exaggerated chronic inflammation with high levels of pro-inflammatory proteins (3). In the severe COVID-19 illness, excessive inflammatory host response to SARS-COV-2 leads to high levels of circulating cytokines, and this cytokine storm may result in death (4). Body mass index (BMI) is commonly used to assess obesity, but cardiometabolic risk and mortality may show differences among the patients with the same BMI, which can be due to the variations in body composition (5). Body composition means the distribution and the amount of adipose tissue, muscle, and bone in the body (6). Visceral adipose tissue (VAT) is more strongly related to hypertension (HT), diabetes mellitus (DM), and metabolic syndrome than subcutaneous adipose tissue (SAT) (3). DM, HT, and cardiopulmonary diseases have been stated as risk factors for the severe clinical outcome (7). The spectrum of COVID-19 illness ranges from asymptomatic state to severe illness requiring hospital stay, mechanical ventilation, and death (8). There is a need to identify and validate biomarkers that can estimate the prognosis and allow taking caution reduce morbidity and mortality.

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - iThenticate
Complaints: geneltip@selcuk.edu.tr

Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

In the present study, we measured the epicardial adipose tissue thickness (EAT) and liver density (LD), as visceral obesity indicators, thoracic subcutaneous adipose tissue thickness/pectoralis muscle thickness (TSAT/PMJ), abdominal subcutaneous adipose tissue thickness/psoas major muscle thickness (ASAT/PSM), abdominal subcutaneous adipose tissue thickness/ erector spina muscle thickness (ASAT / ESM) ratios from thorax computerized tomography (CT) of the SARS-CoV-2 positive patients, which can be used as indicators of peripheral adiposity to see whether these biomarkers can affect the clinical, radiological and laboratory outcome of the disease. We aimed to assess the relationship of measurable body fat and muscle composition parameters, and visceral adipose tissue on CT with the clinical, radiological and laboratory outcome of the COVID-19.

Material and Methods

Ethical Committee

The present study was a retrospective study and informed consent was waived. Ethics approval was obtained from the local committee (Gazi Yaşargil Training and Research Hospital, number:81, date:06.05.2022) and study approval was also obtained from the Ministry of Health. This study was conducted with the principles of the Helsinki Declaration.

Patients

We included 149 patients admitted to our hospital between April 1, 2020 – August 1, 2020, with both chest CT for clinical requirements and a positive reverse transcriptase-polymerase chain reaction (RT- PCR) test result. If a patient had more than one thorax CT, measurements were made from the initial examination. Patients under the age of 15, CT of patients with motion, respiratory and pulsation artifacts that would prevent the measurement of EAT, patients with significant ventral diastasis, and the patients with cardiac pacemakers were excluded from the study because they may cause errors in the measurements. Patients with massive pericardial effusion, with polycystic liver disease were also excluded.

Age, gender, and comorbidities (DM, HT, cardiovascular and airway diseases, malignancy) of the patients were recorded from the hospital database. Lymphocyte, platelet, neutrophil count, lymphocyte/neutrophil ratio, and CRP values were recorded from the blood sample results taken together with or within 24 hours of a positive PCR test.

The worst clinical status was collected from the hospital database during the observation period of 22 days beginning with admission to the hospital; because it was reported that 22 days was the maximum survival time of deceased patients (15.0–22.0 days) (9). The symptoms of the patients were divided into 4 groups: mild, moderate, severe, and critical. Mild cases had mild symptoms with no imaging findings, moderate cases had a fever, respiratory tract infection, and pneumonia findings on imaging. In severe cases, there was a need for oxygen, or imaging findings increase by more than 50% within 1-2 days. The critical group consisted of the patients with shock, need for mechanical ventilation (MV), and/or intensive care unit (ICU) admission (10).

CT acquisition parameters

All CT examinations were performed in a Somatom Emotion 16-slice (Siemens Healthcare, Muenchen, Germany) with 1 mm slice thickness, in the supine position, without contrast agent, with breath-holding, from the thoracic inlet to mid-portion of the kidneys. We used the initial CT scan of the patients at the time of diagnosis. Technical parameters for CT scans were: tube voltage:110 kilovolt, mAs (milliampere-per second) was calculated with automatic exposure control system (CARE Dose 4D), pitch:0.8, gantry rotation time:0.6 second, collimation:1.2 mm, window width:400 HU, window level:40 HU, FOV:364 mm, Kernel: B30S medium smooth.

All images were obtained from picture archiving communication systems (PACS). All images were evaluated at the workstation (Siemens Healthcare, Germany) by a 7-year-experienced board certificated radiologist unaware of clinical status. To show intraclass reliability, a second measurement was obtained in a sample of 90 randomized patients by the same radiologist after one month.

Measurements

Pneumonia severity scores (PSS) for COVID-19 illness were calculated as stated before (12). Patients were divided into 6 groups according to the rate of pneumonic involvement in each of the five lobes of the lung on CT; no involvement was scored as 0, those with <5% involvement as 1, 5-25% involvement as 2, 26-49% as 3, 50-75% as 4, and >75% involvement as 5 (Figure 1) (11).

PMJ (pectoralis major muscle) thickness was calculated at the level of just above the aortic arch, because it was found to give better results (12), in a single axial slice, at the midline, the antero-posterior diameter (A-P) of the muscle was measured on the right and left. The TSAT measurement was obtained for each side at the same level and location as PMJ thickness was measured. A-P thickness of TSAT was obtained from the PMJ's anterior border to the dermis. The final TSAT/ PMJ ratio was found by taking the average of the two sides (Figure 2 A).

The EAT mean was measured from the myocardial wall to the pericardium (13), by taking the average of the right atrioventricular groove, left atrioventricular groove and interventricular groove values (Figure 2 B). Measurements were taken from a one-slice, four-chamber horizontal mediastinal view.

The ASAT was measured at the level of L1-L2 vertebrae (lowest level of the thorax CT sections in our institute), 5 cm lateral to the linea alba as stated previously (14), on the right and left separately in a single axial section. The PSM thickness was measured in the middle part of the muscle at the L1-2 level (Figure 2 C). L3 level

was reported as the best point for this measurement (15), this level was not present in thorax CT sections. The ASAT/PSM ratio was found for each side. The results were recorded by averaging the ratios.

ASAT/ESM ratios were calculated at the same level as ASAT/PSM. The ESM thickness was measured from the vertebral transverse process to the posterior border of ESM (Figure 2 C). ASAT was measured with the same method as above described, ASAT/ESM ratios were calculated for each side, and the mean of the ratios were recorded.

An attenuation value of ≤ 40 Hounsfield units (HU), on the unenhanced CT correlates with a pathological fat content of ≥ 30%, and it is compatible with the moderate hepatic steatosis (16). Although previous data have reported that liver fat is homogeneous and measuring from a single section is sufficient (17), our measurements were made from 3 different segments in order not to miss the effect of inhomogeneous fatty areas. The LD was measured for every 10 cm2 area from three axial views, segments 2-3, 5-8, and 6-7 with a freehand region of interest (ROI). Vascular structures, biliary tree, and cystic-solid lesions were spared from the ROI space. The average density of the three segments was recorded.

Statistical Analysis

Research data were uploaded to the computer environment and evaluated via IBM SPSS Statistics 25 Macosx Version: 25.0.0.0 (Armonk, New York). Descriptive statistics were presented as mean (±) standard deviation, median (min-max), frequency distribution, and percentage. Chi-Square Test or Fisher's Exact Test was used to compare categorical variables. The conformity of the variables to the normal distribution was examined using visual (histogram, box-line plot, Q-Q plot…etc) and analytical methods (Kolmogorov-Smirnov Test/Shapiro-Wilk Test). If two independent groups fitted to the normal distribution, the T-test was used. Mann Whitney U test was used when the two groups did not fit to the normal distribution. In the comparison of more than two groups, one-way ANOVA was applied if it was suitable for normal distribution, and Kruskal Wallis Test was applied if it did not comply with the normal distribution. The Mann-Whitney U test was used (for post-hoc test) to compare the significant results between the groups according to the Kruskal Wallis test. The results were evaluated with Bonferroni correction to control for type 1 error. Tukey or Tamhane's T2 test was applied according to the homogeneity of variances to determine between which groups the difference was in one-way ANOVA, and the results were evaluated with Bonferroni correction to control type 1 error. Eta Correlation analysis was applied to assess the correlational relationship between various continuous variables and the severity of the disease, which is a four-category. Intra-class correlation test was used to determine the intrareader agreement (If Intra-class correlation coefficient (ICC) was <0.5, it was evaluated as poor reliability, between 0.8-0.9 values were evaluated as good, and >0.9 ICC was noted as excellent reliability). Logistic regression analysis was used to evaluate the selected risk factors for ICU admission according to the results of the univariate analysis. Omnibus tests were used for the significance of the model, Hosmer-Lemeshow tests were used for the goodness of fit. In the last stage of the logistic regression model, a table of statistically significant variables was made. In the comparison of the variables, the first group was accepted as the reference group. In the present study, ICU admission was accepted as the gold standard, and the diagnostic features of the CT measurements for ICU admission were examined with ROC curve analysis. In the presence of significant breakpoints, the sensitivity and specificity values of these limits were calculated. A p-value of <0.05 was considered significant in statistical evaluations.

Results

General Findings

One hundred forty-nine patients were included in our study. The mean age of the patients was 49.98±18.69 years. The mean age of men was 53.7±18.4. The mean age of women was 45.5±18.2. While 83.2% (n=124) of the patients had no need for oxygen (O2), 6.0% (n=9) required non-invasive O2 therapy and 10.7% (n=16) needed for ICU admission, 5.4% (n=8) of the patients died and all deceased patients were admitted to the ICU.

There was no statistically significant difference between clinical severity according to gender, DM, HT, malignancy, additional disease and the number of additional diseases (p>0.05). As the age increased, the frequency of severe and critical illness increased (p<0.001). In patients with respiratory system disease, the frequency of severe and critical illness was significantly higher than in mild and moderate ones (p=0.004). The PSS increased as the course of the disease worsened (p<0.001) (Table 1).

As the severity of the disease increased, the mean age, CRP, EAT increased, and LD decreased (p<0.001; p<0.001; p<0.001; p=0.016, respectively). Lymphocyte count, and lymphocyte/neutrophil ratio were lower in severe and critical patients (p<0.001; p=0.005; p=0.016, respectively). There was no significant differences between groups in terms of neutrophil, platelet count and TSAT/PMJ ratio (p>0.05). The mean values of ASAT/PSM and ASAT/ESM were statistically significantly different between the groups (p=0.003; p=0.019) (Table 2).

A strong and statistically significant correlation was found between age, lymphocyte count and epicardial adipose tissue thickness and the severity of the disease. (Table 3).

For EAT, the area under the curve in the ROC analysis was found as 0.743 (at 95% confidence interval, 0.624-0.862), which was statistically significant (p=0.002) (Table 4 and Figure 3).

Table 1. Comparison of demographic and comorbid disease parameters according to the clinical severity of the disease.

	Clinical Outcome								p*
	Mild (n=30)		Moderate (n=95)		Severe (n=9)		Critical (n=15)		
	n	%	n	%	N	%	n	%	
Age									
15-29	13	48.1	14	51.9	0	0.0	0	0.0	<0.001
30-49	9	20.0	34	75.6	2	4.4	0	0.0	
50-69	5	9.8	36	70.6	3	5.9	7	13.7	
≥70	3	11.5	11	42.3	4	15.4	8	30.8	
Gender									
Male	17	21.0	47	58.0	4	4.9	13	16.0	0.054
Female	13	19.1	48	70.6	5	7.4	2	2.9	
DM									
No	27	21.6	78	62.4	9	7.2	11	8.8	0.259
Yes	3	12.5	17	70.8	0	0.0	4	16.7	
HT									
Yes	25	23.8	66	62.9	4	3.8	10	9.5	0.141
No	5	11.4	29	65.9	5	11.4	5	11.4	
Airway Disease									
No	29	21.0	91	65.9	7	5.1	11	8.0	0.004
Yes	1	9.1	4	36.4	2	18.2	4	36.4	
Malignancy									
No	30	20.5	92	63.0	9	6.2	15	10.3	0.628
Yes	0	0.0	3	100.0	0	0.0	0	0.0	
Additional Illness									
No	16	18.4	57	65.5	5	5.7	9	10.3	0.927
Yes	14	22.6	38	61.3	4	6.5	6	9.7	
Number of Additional Illness									
0	16	18.4	57	65.5	5	5.7	9	10.3	0.092
1	9	20.0	29	64.4	2	4.4	5	11.1	
2	4	33.3	8	66.7	0	0.0	0	0.0	
≥3	1	20.0	1	20.0	2	40.0	1	20.0	
PSS									
0	20	90.9	0	0.0	0	0.0	2	9.1	<0.001
1	6	11.3	45	84.9	2	3.8	0	0.0	
2	1	2.3	34	77.3	6	13.6	3	6.8	
3	2	11.1	14	77.8	1	5.6	1	5.6	
4	1	10.0	2	20.0	0	0.0	7	70.0	
5	0	0.0	0	0.0	0	0.0	2	100.0	

*: Chi square test; n: number; PSS: Pneumonia severity score

Table 3. Correlation of the relationship between laboratory findings and measured parameters on CT and clinical severity.

	Clinical Outcome (Mild/Moderate/Severe/ Critical) (n=149)	
	r*	p
Age	0.716	0.032
CRP	0.922	0.235
Lymphocyte	0.938	0.005
Neutrophil	0.924	0.695
Lymphocyte/neutrophil	0.997	0.310
Platelet	0.892	0.187
Liver Density	0.953	0.865
Epicardial Adipose Tissue	0.961	0.004
Thoracic subcutaneous adipose tissue/Pectoralis Major Thickness	0.925	0.357
Abdominal subcutaneous adipose tissue/Psoas Major Thickness	0.872	0.921
Abdominal subcutaneous adipose tissue thickness/Erector spina thickness	0.659	0.873

*: Eta correlation coefficient; HU: Hounsfield Unit; n: number; cm2: centimeter square; mm: millimeter.

Table 4. Roc curve values of the power to diagnose ICU admission (critical disease) according to CT measurements.

	ICU Admission (For critical outcome)		
	Area Under Curve (AUC)	%95Confident interval	p
Liver Density (Hu/10 Cm^2)	0.555	0.433-0.677	0.473
Epicardial Adipose Tissue (Mm)	0.743	0.624-0.862	0.002
Thoracic subcutaneous adipose tissue/Pectoralis Major Thickness	0.603	0.459-0.747	0.178
Abdominal subcutaneous adipose tissue/Psoas Major Thickness	0.559	0.409-0.710	0.438
Abdominal subcutaneous adipose tissue thickness/Erector spina thickness	0.597	0.461-0.733	0.208

Cm2: Centimeter square; HU: Hounsfield Unit; ICU: Intensive care unit; mm: millimeter.

Table 2. Comparison of laboratory findings and parameters measured in CT according to the clinical severity of the disease.

		Clinical Outcome				
	Total n=149	Mild (n=30)	Moderate (n=95)	Severe (n=9)	Critical (n=15)	p*
Age[1] (years)	49.98±18.69	39.70±19.47	48.92±17.03	65.22±17.35	68.13±7.16	<0.001**
CRP[2] (milligram/liter)	35.87±58.35	18.43±25.08	24.88±34.20	33.47±35.06	140.59±112.87	<0.001
Lymphocyte[3] (10^3/µL)	1451±712	1651±817	1466±608	1113±612	1159±1018	0.004
Neutrophil (10^3/µL)	3788±2258	3290±1196	3502±1457	4361±2035	6254±5148	0.073
Lymphocyte/neutrophil[4] (It is a ratio no unit is for that reason)	0.47±0.30	0.56±0.35	0.48±0.27	0.36±0.35	0.30±0.26	0.005
Platelet (10^3/µL)	201213±59638	199466±48734	206355±62267	167555±56914	192333±61622	0.271**
Liver Density (Hu/10 Cm^2)[5]	50.03±11.56	55.46±8.11	48.50±12.78	48.69±9.38	49.67±7.04	0.016
Epicardial Adipose Tissue (Mm)[6]	5.98±2.28	5.05±2.00	5.86±2.20	7.06±2.39	7.89±2.08	<0.001
Thoracic subcutaneous adipose tissue/Pectoralis Major Thickness	1.92±1.59	1.52±1.26	2.08±1.69	2.40±1.76	1.39±1.28	0.081
Abdominal subcutaneous adipose tissue/Psoas Major Thickness[7]	2.11±1.63	1.59±1.80	2.27±1.60	2.55±1.41	1.87±1.44	0.003
Abdominal subcutaneous adipose tissue thickness/Erector spina thickness[8]	0.48±0.25	0.40±0.26	0.51±0.25	0.58±0.29	0.39±0.18	0.019

*: Kruskal Wallis Test; **: One-way ANOVA test; n: number; HU: Hounsfield unit; mm: millimeter; cm2(centimeter square). According to the Bonferroni correction 1: difference mild-severe and mild-critical 2: difference mild-critical, moderate-critical, severe-critical 3: mild-critical and moderate-critical 4: mild-critical, moderate-critical 5: difference mild-moderate 6: mild-critical, moderate-critical, 7: mild-moderate, 8: difference arises between mild-moderate groups.

Figure 1. Unenhanced thorax CT in the parenchymal window of a 75-year-old male PCR (+), ICU admitted, survival patient, reveals peripheral patchy ground glass opacities and PSS score was calculated:2.

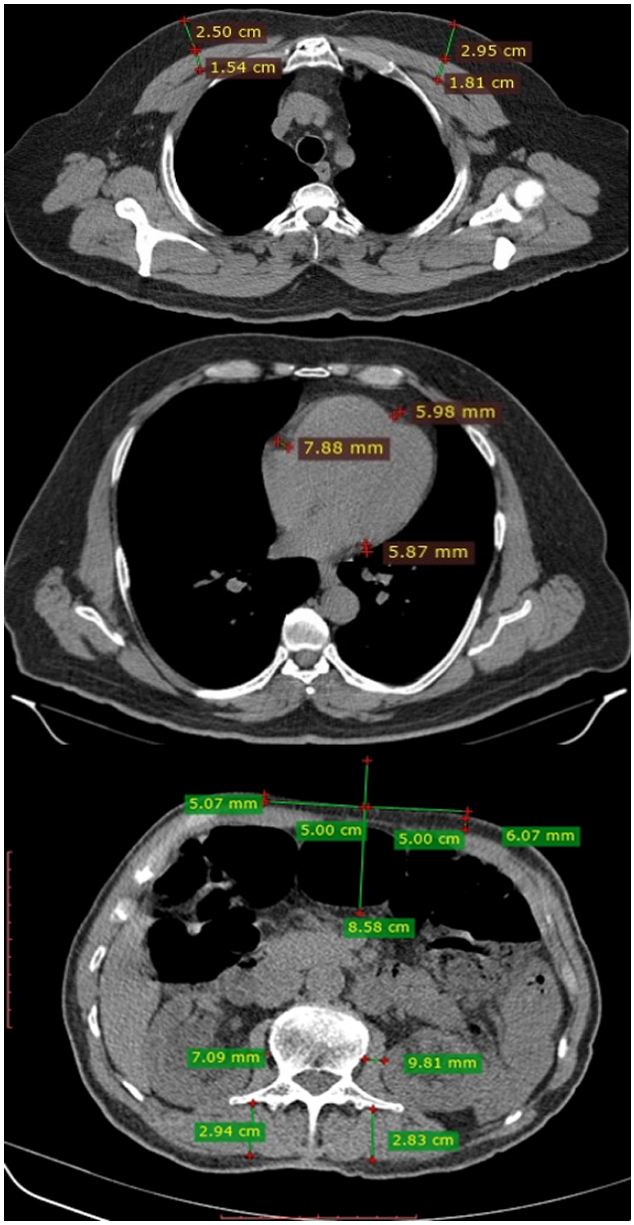

Figure 2. Unenhanced thorax CT in the mediastinal window of the same patient's ; **A.** Level of just above the aortic arc, TSAT/PMJ ratio, **B.** Four chamber horizontal view, right, left and interventricular groove EAT, **C.** At L1-L2 level, ASAT/PSM, and ASAT/ESM measurements are shown.

The findings of ICU-admitted patients

16 patients were admitted to ICU. Age, male gender and airway disease were significantly higher in ICU admitted patients (p=0.001, p=0.022, p=0.019 respectively). Higher CRP, neutrophil counts, lower lymphocyte values and lymphocyte/neutrophil ratio were frequently detected in ICU patients (p=0.001, p=0.012, p=0.001, p=0.001 respectively). The EAT means were higher (7.70±2.14 mm, p=0.002) in this group. When the EAT was 6.34 mm and above, it estimated the possibility of ICU admission (clinically severe disease) with 75% sensitivity, 72.2% specificity, 24.5 % positive predictive value, and 96.0% negative predictive value.

In univariate analysis, being >50 years old, male gender, and having another respiratory system disease increased the risk of ICU admission (p<0.05). An age of > 50 years- old increased the risk of ICU admission 38.902 times (p=0.011); male gender increased it 4.142 times (p=0.032) and having respiratory system disease increased 6.000 times (p=0.010).

The findings of deceased patients

8 patients died. Older age and male gender predominated in deceased patients (p<0.001 and p=0.008). In univariate analysis, >50- year-old-age increased the risk of death 17.730 times (p=0.049). These patients had a higher CRP value and a lower lymphocyte count (p=0.001, and p=0.031). The EAT means were higher (8.50±2.10 mm, p=0.002), and TSAT/PMJ ratio was lower (0.90±0.36, p=0.038) in this group.

According to multivariate logistic regression analysis, a rise in EAT thickness increased the risk of death 2.466 times and ASAT / PSM increased it 7.837 times (p=0.042; p=0.038 respectively) (Table 5).

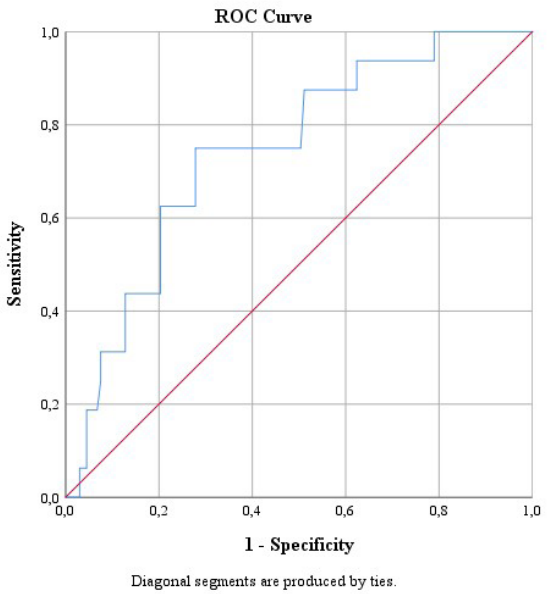

Figure 3. ROC curve of epicardial adipose tissue for differantiation of patients with intensive care unit administration.

Table 5. Logistic regression analysis of age, gender, laboratory findings and CT measurements for death status.

	Death			
	p	Odd's Ratio	95% Confident İnterval	
			Lower	Upper
Age	0.086	1.287	0.965	1.718
Gender	0.987	0.000	0.000	.
Airway Disease	0.113	0.017	0.000	2.654
CRP	0.176	1.013	0.994	1.032
Lymphocyte Count	0.771	1.000	0.999	1.002
Lymphocyte Neutrophil	0.729	0.140	0.000	9296.473
Liver Density (Hu/1 Cm2)	0.865	0.981	0.792	1.217
Epicardial Adipose Tissue (Mm)	0.042	2.466	1.032	5.890
Thoracic subcutaneous adipose tissue/Pectoralis Major Thickness	0.091	0.039	0.001	1.687
Abdominal subcutaneous adipose tissue/Psoas Major Thickness	0.038	7.837	1.120	54.830
Abdominal subcutaneous adipose tissue thickness/ Erector spina thickness	0.075	250963.690	0.287	219287601267.559

Cm2: Centimeter square; HU: Hounsfield Unit; mm: millimeter

Intrareader agreement

The intrareader agreement was excellent for EAT and LD (ICC was between 0.95 and 1.00), TSAT/PMJ, ASAT/PSM, and ASAT/ESM (ICC was 0.90, 0.93, and 0.91 respectively).

Discussion

The most important findings of the present study were that the mean EAT was high in the patients with poor prognosis. The LD was different between the mild and moderate groups, however, values were similar in the other groups. The TSAT/PMJ ratio was lower in deceased patients. ASAT/PSM and ASAT/ESM rates were also higher in the moderate group than in the mild one. The fact that these values were determined although there was no difference in terms of DM, malignancy, or gender, which may affect the patient's body composition, makes the findings more valuable.

The EAT located between the myocardium and the visceral pericardium (18) has an important role in cardioprotective effects under physiological states (19). The EAT can be dangerous by secreting pro-inflammatory cytokines like interleukin 1β (IL1β), IL 6, and tumor necrosis factor alfa (TNF-a) (20). High levels of these cytokines can lead to severe outcomes and death. Several studies have reported a possible association between increased adipose tissue and poor prognosis of COVID-19 as in our study (21-23). Although EAT volume was used in most of the studies, thickness measurement was performed in our study and it may be possible to predict the outcome of the disease without the need for advanced applications and software. Iacobellis et al. indicated that, EAT thickness was not significantly different among different degrees of COVID-19 patients contrary to our study (24). The small number of patients may be the reason for the difference.

Duyuler et al. reported that a cut-off- point of 6.64mm EAT had a sensitivity of 82.7% and a specificity of 66.7% (25). Similarly, in our study, when the EAT was 6.34 mm and above, it predicted the possibility of admission to the ICU (clinically severe disease) with 75% sensitivity, 72.2% specificity (present study's result). In the present study, similar sensitivity and specificity values were obtained at lower EAT cut-off values to predict ICU admission.

Parlak et al. contrary to our study, found lower LD in ICU patients (26). We just found a difference between mild and moderate group individuals. Increased secretion of infection and stress-related hormones and agents in ICU-admitted patients has been shown to increase lipolysis, glycogenolysis, and neo-gluconeogenesis. (27-28), which may explain the lack of difference in liver density measurements. Although the measurements were made from the first CT examinations of the patients, no difference in liver density between the subgroups may indicate that the patients are faced with intense inflammation mediators in the early period. The virus has the ability to provoke immune system aggression against its tissues in the form of an autoinflammatory process (29).

In a study by Hocaloğlu et al. showed that the pectoralis muscle volume was higher in the deceased group than in the survival individuals (30). Although the measurements were made at a similar level in our study, TSAT/PMJ ratios were made as a measurement of thickness, and the adipose tissue in the muscle was not evaluated separately. This high rate in deceased patients may be explained by the excessive use of an auxiliary respiratory muscle of the pectoralis major due to the respiratory distress and increasing the thickness.

Low skeletal muscle mass (LSMM) was identified as a predictor of critically ill patients (31). Meyer et al. found an association between the poor prognosis of COVID- 19 and LSMM (32). In our study, we did not find ASAT/PSM and ASAT/ESM rates different in critically ill patients, but we found these rates lower in mild patients than in moderate patients. This finding was important to show that people with more muscle mass and less subcutaneous adipose tissue might have the disease without symptoms, however, these ratios were not successful in predicting disease prognosis. There was no difference between the groups in terms of gender, which made the findings strong, but the fact that the elderly patients were in the group with poor prognosis could be the reason of low muscle mass without any additional factor in the present study. In this study, there was no difference between the groups in terms of gender, but the fact that the elderly patients were in the poor prognosis group might be the reason for their low muscle mass without any additional factor. In addition, since the patients who died and were hospitalized in the ICU constituted a small part of the patients in our study. Evaluating these ratios with a higher number of critically ill patients will make the results more reliable.

The limitations of our study can be listed as being retrospective, lack of BMI data, fewer patients admitted to ICU (16) and fewer deseased patients

(8), measuring EAT thickness instead of volume or area, not adding the density values of epicardial and subcutaneous adipose tissue, measuring abdominal muscle thickness at the L1-2 level, not L3, which is the most appropriate level, because it was not included in the thorax CT examinations. The strengths of the study are that the CT-mediated measurements of the patients were evaluated together with clinical and laboratory data, and the study was not conducted with only image evaluation. However, as it is the first study to examine the relationship between CT measurements and clinical outcomes in COVID-19, it can provide an idea about prognosis and help in the follow-up of patients with early detection of possible complications.

In conclusion, EAT was high in ICU admitted and deceased patients and is a simple measurement method that can be used as a predictor of poor prognosis without additional imaging. Older age, male gender, higher CRP, and lower lymphocyte and lymphocyte/neutrophil values are also predictors of critical disease. The ASAT/PSM and ASAT/ESM ratios and LD should be used to discriminate mild from moderate patients.

Author Contributions

Concept: D.İ.Y., Y.Ç, E.B., Design:D.İ.Y., Y.Ç, Data Collection or Processing: D.İ.Y., Y.Ç, Analysis or Interpretation: D.İ.Y., Y.Ç,E.B., Literature Search:D.İ.Y., Y.Ç,E.B., Writing: D.İ.Y., Y.Ç, E.B.

References

1.Chandarana H, Pisuchpen N, Krieger R, Dane B, Mikheev A, Feng Y, et al. Association of body composition parameters measured on CT with risk of hospitalization in patients with Covid-19. Eur J Radiol 2021;145:110031.

2.Cai Q, Chen F, Wang T, Luo F, Liu X, Wu Q, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. Diabetes Care 2020;43:1392–8.

3.Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation 2007;116:39–48.

4.Merad M, Martin JC. Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. Nat Rev Immunol 2020; 20:355–62.

5.Haines MS, Dichtel LE, Santoso K, Torriani M, Miller KK, Bredella MA. Association between muscle mass and insulin sensitivity independent of detrimental adipose depots in young adults with overweight/ obesity. Int J Obes 2020;44:1851–8.

6.Viddeleer AR, Raaphorst J, Min M, Beenen LFM, Scheerder MJ, Vlaar APJ. Intramuscular adipose tissue at level Th12 is associated with survival in COVID-19. J Cachexia Sarcopenia Muscle 2021;12:823–7.

7.Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA 2020;323:2052–9.

8.Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study BMJ 2020; 369:m1966.

9.Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.

10.Liang T, Cai H, Chen Y, et al. Handbook of COVID-19 prevention and treatment.1 st edition.China: The First Affiliated Hospital, Zhejiang University School of Medicine.2020. P.1-84.

11.Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PLoS One 2020;15:e0230548.

12.Diaz AA, Martinez CH, Harmouche R, Young TP, McDonald ML, Ross JC, et al. Pectoralis muscle area and mortality in smokers without airflow obstruction, Respir. Res 2018;19: 62.

13.Wang TD, Lee WJ, Shih FY, Huang CH, Chang YC, Chen WJ,et al. Relations of epicardial adipose tissue measured by multidetector computed tomography to components of the metabolic syndrome are region-specific and independent of anthropometric indexes and intraabdominal visceral fat. J Clin Endocrinol Metab 2009; 94: 662–9.

14.Kim J, Lim H, Lee SI, Kim YJ. The thickness of Rectus Abdominis Muscle and Abdominal Subcutaneous Fat Tissue in Adult Women: Correlation with Age, Pregnancy, Laparotomy, and Body Mass Index. Arch Plast Surg 2012; 39:528-33.

15.Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumors of the respiratory and gastrointestinal tracts: a population-based study. The Lancet Oncology 2008; 9:629–35.

16.Monjardim RDF, Costa DMC, Romano RFT, Salvadori, PS, Santos, JDVCD, Atzingen, ACV, et al. Diagnosis of hepatic steatosis by contrast-enhanced abdominal computed tomography. Radiol Bras 2013; 46:134–8.

17.Speliotes EK, Massaro JM, Hoffmann U, Foster MC, Sahani DV, Hirschhorn JN, et al. Liver fat is reproducibly measured using computed tomography in the Framingham Heart Study. J Gastroenterol Hepatol 2008;23:894-9.

18.Iacobellis G, Corradi D & Sharma, AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. Nat. Clin. Pract. Cardiovasc. Med 2005; 2:536–43.

19.Iacobellis G. Local and systemic effects of the multifaceted epicardial adipose tissue depot. Nat Rev Endocrinol 2015; 11:363-71.

20. Mazurek T, Zhang L, Zalewski A, Mannion JD, Diehl JT, Arafat H, et al. Human epicardial adipose tissue is a source of inflammatory mediators. Circulation 2003; 108:2460–6.

21.Briand-M´esange F, Trudel S, Salles J, Ausseil J, Salles JP, Chap H. Possible role of adipose tissue and the endocannabinoid system in coronavirus disease 2019 pathogenesis: can rimonabant return? Obesity 2020; 28:1580–1.

22.Kruglikov IL, Scherer PE. The role of adipocytes and adipocyte-like cells in the severity of COVID-19 infections, Obesity 2020; 28:1187–90.

23.Zbinden-Foncea H, Francaux M, Deldicque L, Hawley JA. Does high cardiorespiratory fitness confer some protection against pro-inflammatory responses after infection by SARS-CoV-2?. Obesity 2020; 28:1378–81.

24.Iacobellis G, Secchi F, Capitanio G, Basilico S, Schiaffino S, Boveri S, et al. Epicardial Fat Inflammation in Severe COVID-19. Obesity 2020;28:2260-2.

25.Turker Duyuler P, Duyuler S, Demirtaş B, Çayhan V. Epicardial and pericoronary adipose tissue in severe COVID-19 infection. Acta Cardiol 2021;6:1-8.

26.Parlak S, Çıvgın E, Beşler MS, Kayıpmaz AE. The effect of hepatic steatosis on COVID-19 severity: Chest computed tomography findings. Saudi J Gastroenterol. 2021;27:105-10.

27.Hsu CW. Glycemic control in critically ill patients, World J. Crit. Care Med 2012; 4: 31–9.

28.Marik PE, Raghavan M. Stress-hyperglycemia, insulin, and immunomodulation in sepsis, Intensive Care Med 2004;30:748–56.

29.Gusev E, Sarapultsev A, Solomatina L, Chereshnev V. SARS-CoV-2-Specific Immune Response and the Pathogenesis of COVID-19. Int J Mol Sci. 2022;23(3):1716.

30.Hocaoglu E, Ors S, Yildiz O, Inci E. Correlation of Pectoralis Muscle

Volume and Density with Severity of COVID-19 Pneumonia in Adults. Acad Radiol 2021 ;28:166-72.

31.Meyer HJ, Wienke A, Surov A. Computed tomography-defined low skeletal muscle mass as a prognostic marker for short-term mortality in critically ill patients: a systematic review and meta-analysis. Nutrition 2021;91–92:111417.

32.Meyer HJ, Wienke A, Surov A. Computed tomography-defined body composition as prognostic markers for unfavorable outcomes and in-hospital mortality in coronavirus disease 2019. J Cachexia Sarcopenia Muscle 2022 ;13:159-68.