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Original Research

Is There a Relationship Between Epicardial Adipose Tissue, Inflammatory Markers, and the Severity of COVID-19 Pneumonia?

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ABSTRACT

Objectives: Epicardial adipose tissue (EAT) is a type of visceral adipose tissue with pro-inflammatory properties. We sought to examine the relationship between the EAT volume and attenuation measured on non-contrast chest computed tomography (CT), inflammation markers, and the severity of COVID-19 pneumonia.

Methods: One hundred and twenty-five patients who are over 18 years old who applied to our hospital and were found to have COVID-19 polymerase chain reaction (+) on nasopharyngeal swab sample and COVID-19 pneumonia on chest CT were included in the study. At admission, C-reactive protein (CRP), procalcitonin, fibrinogen, leukocytes, neutrophil–lymphocyte ratio, platelet-lymphocyte ratio, lactate dehydrogenase (LDH), ferritin, and d-dimer were evaluated. EAT volume and attenuation were measured on chest CT. Patients who were hospitalized and discharged from the ward were categorized as Group 1, whereas patients who required intensive care admission and/or died were classified as Group 2. The primary endpoint of our study was defined as death, hospitalization in the intensive care unit, and discharge. The relationship between disease severity and EAT and other inflammatory markers was investigated.

Results: One hundred and six individuals were in Group 1 and 19 patients were in Group 2. Of the 125 individuals, 46 were women and 79 were men. The mean age was 58.5±15.9 years. Group 2 patients were older. Regarding measurements of the EAT volume and attenuation; there was no statistically significant difference between the groups determined. The patients in Group 2 had statistically substantially higher values for urea, creatinine, LDH, d-dimer, troponin T, procalcitonin, CRP, and neutrophil/lymphocyte ratio in their laboratory tests. When compared to patients in Group 1, patients in Group 2 had statistically significantly lower albumin values ($p<0.001$). In obese patients, EAT volume was statistically significantly higher and EAT attenuation was found to be lower.

Conclusion: In our study, no relationship was found between critical COVID-19 disease and EAT volume and attenuation, which is an indicator of EAT inflammation. Inflammatory markers from routine laboratory tests can be used to predict critical COVID-19 disease. No relationship was found between obesity and critical COVID-19 disease.

Keywords: Computed tomography, COVID-19, Epicardial adipose tissue

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Severe acute respiratory syndrome Coronavirus-2, the virus responsible for the COVID-19 disease, emerged in Wuhan, China, and rapidly spread worldwide. On March 11, 2020, the World Health Organization declared COVID-19 a pandemic. COVID-19 is a highly contagious RNA-type virus that can cause severe respiratory tract infections, ranging from asymptomatic cases to respiratory failure, sepsis, multi-organ failure, and mortality.[1] Several studies have investigated risk factors for severe disease and have identified markers such as C-reactive protein (CRP), ferritin, and inflammation parameters in the blood.[2-5]

Obesity is a significant public health concern and a modifiable risk factor for COVID-19. Clinical studies have demonstrated a link between obesity and the severity of the disease, with overweight and obese individuals being at higher risk for death and intensive care hospitalization.[6-8]

Epicardial adipose tissue (EAT), a metabolically active visceral adipose tissue, is located between the visceral pericardium and the myocardium. It acts as a hormonal and inflammatory organ, secreting pro-atherogenic and pro-inflammatory cytokines.[9] EAT is primarily distributed in the atrioventricular and interventricular grooves, as shown by studies using multi-detector computed tomography (CT).[10]

In our country, individuals with a high clinical suspicion of COVID-19 infection usually undergo a chest CT. EAT volume and attenuation can be measured easily and precisely on CT. A correlation was found between the epicardial fat volume assessed on chest CT and the lung capacity of patients with chronic obstructive pulmonary disease.[11] In the study by Grodecki et al.,[12] increases in EAT volume or attenuation were found to independently indicate clinical deterioration or mortality in COVID-19 patients.

EAT is visceral adipose tissue that secretes inflammatory cytokines such as monocyte chemoattractant protein-1, IL-6, and tumor necrosis factor-alpha.[13] The relationship of EAT with severe COVID-19 infection has not been clarified. Ryan et al. [14] claimed that EAT functions as a COVID-19 reservoir in obese patients and facilitates viral spread. Moreover, various cells in adipose tissue have been accepted as proven targets for various viruses such as influenza A, SARS-CoV, adenovirus, human immunodeficiency virus, cytomegalovirus, and H1N1.[15-19]

In this study, we aimed to investigate the relationship between the severity of COVID-19 pneumonia, EAT, and inflammation markers.

Methods

The study comprised 125 patients older than 18 who registered at our hospital between October 2020 and June 2021, tested positive for COVID-19 polymerase chain reaction using nasopharyngeal swab samples, and had chest CT results suggesting they might have COVID-19 pneumonia. The study protocol was approved by the Sisli Hamidiye Etfal SUAM Local Ethics Committee (February 22, 2022, protocol number 3406). The study adhered to the World Medical Association's Declaration of Helsinki's ethical criteria. The exclusion criteria included individuals under 18 years old and pregnant. At the time of admission, demographic characteristics of the patients, laboratory findings such as urea, creatinine, creatine phosphokinase, CRP, lactate dehydrogenase (LDH), d-dimer, ferritin, fibrinogen, troponin T, lactate, leucocyte, platelet, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, MPV/lymphocyte ratio, clinical features, temperature, arterial blood pressure (BP), and oxygen saturation (SpO_2) level measured by a pulse oximeter on room air were recorded. The patients' complaints at admission included cough, sore throat, fever, diarrhea, fatigue, abdominal pain, and dyspnea. The primary endpoint of our study was defined as death, admission to the intensive care unit (ICU), and discharge. Each hospitalized patient was given favipiravir as antiviral therapy and enoxaparin as an anticoagulant. Steroids, pulse steroids, tocilizumab, antibiotics, and plasma therapy administered during hospitalization were recorded. Patients were followed up by phone for up to 3 months after discharge, observed in terms of mortality, and their data were recorded.

We used a semi-automated technique to calculate epicardial fat volume. We have an appropriate tool in our workstation for measuring the volume of epicardial fat (Volume Viewer, Siemens, Germany). The visceral fat between the cardiac surface and the visceral layer of the pericardium was defined as epicardial fat.

By manually tracing the pericardium on axial images from the division of the pulmonary artery to the apex of the heart, the volume of epicardial fat was segmented. The pericardium must be manually outlined by the operator at each cross-section. A threshold of −190 to −30 Hounsfield unit (HU), which is characteristic of EAT attenuation, was applied. The data obtained from all sections were then summed, resulting in the total epicardial fat volume.

Statistical Analysis

The statistical investigation was carried out using the SPSS version 25.0 application (SPSS Inc., Chicago, Illinois, USA). The conformity of the variables to the normal distribution was examined using histogram graphics and the Kolmogorov–Smirnov test. The mean, standard deviation, median, min–max values were used during the performance of descriptive analyses. The Chi-square test was used to evaluate categorical variables. The Mann–Whitney U test and the Kruskal–Wallis test were used to compare non-normally distrib-

uted (non-parametric) variables between two groups and more than two groups, respectively. The Spearman correlation test was utilized to analyze the measured data together. It was determined that a p<0.005 was statistically significant.

Results

One hundred and twenty-five individuals aged >18 years with COVID-19 pneumonia were included in our study. There were 46 women and 79 men. Patients who were hospitalized and discharged from the ward were categorized as Group 1, whereas individuals who required intensive care admission and/or died were categorized as Group 2. There were 106 individuals in Group 1 and 19 individuals in Group 2. Age, gender, and body mass index did not show statistically significant differences between the two groups. There were no statistically significant differences between the two groups when comparing comorbidities and admission symptoms. In Group 2, patients who received pulse steroid (p=0.037) and tocilizumab (p=0.001) treatments were observed to have statistically significantly higher

Table 1. Demographic and clinical characteristics of patients on admission

	Group 1		Group 2		Total		p
	n	%	N	%	n	%	
Gender							
Female	39	(36.79)	7	(36.84)	46	(36.80)	0.997
Male	67	(63.21)	12	(63.16)	79	(63.20)	
BMI (body mass ındex)							
Normal	23	(23.47)	5	(35.71)	28	(25.00)	0.595
Overweight	45	(45.92)	5	(35.71)	50	(44.64)	
Obese	30	(30.61)	4	(28.57)	34	(30.36)	
Diabetes mellitus	39	(36.79)	6	(31.58)	45	(36.00)	0.663
Hypertension	39	(36.79)	11	(57.89)	50	(40.00)	0.084
Hyperlipidemia	11	(10.38)	3	(15.79)	14	(11.20)	0.491
Chronic kidney disease	4	(3.77)	2	(10.53)	6	(4.80)	0.205
Kidney transplant	1	(0.94)	0	(0.00)	1	(0.80)	0.671
Liver transplant	1	(0.94)	0	(0.00)	1	(0.80)	0.671
COPD*	11	(10.38)	3	(15.79)	14	(11.20)	0.491
Ischemic heart disease	17	(16.04)	5	(26.32)	22	(17.60)	0.279
Previous cerebrovascular event	5	(4.72)	3	(15.79)	8	(6.40)	0.069
Use of ACE inhibitor/ARB**	22	(20.75)	5	(26.32)	27	(21.60)	0.588
Cough	63	(59.43)	8	(42.11)	71	(56.80)	0.160
Dyspnea	90	(84.91)	18	(94.74)	108	(86.40)	0.250
Headache	10	(9.43)	1	(5.26)	11	(8.80)	0.555
Diarrhea	5	(4.72)	1	(5.26)	6	(4.80)	0.918
Fatigue	72	(67.92)	13	(68.42)	85	(68.00)	0.966
Abdominal pain	4	(3.77)	1	(5.26)	5	(4.00)	0.760
Fever	49	(46.23)	7	(36.84)	56	(44.80)	0.449
Back pain	9	(8.49)	3	(15.79)	12	(9.60)	0.320
Steroid	77	(72.64)	17	(89.47)	94	(75.20)	0.118
Pulse steroid	10	(9.43)	5	(26.32)	15	(12.00)	**0.037**
Tocilizumab	3	(2.83)	4	(21.05)	7	(5.60)	**0.001**
Antibiotic	53	(50.00)	12	(63.16)	65	(52.00)	0.290
Immune plasma	1	(0.94)	0	(0.00)	1	(0.80)	0.671
Mortality	0	(0.00)	9	(47.37)	9	(7.20)	**<0.001**
ICU (ıntensive care unit)	0	(0.00)	16	(84.21)	16	(12.80)	**<0.001**
Discharged	106	(100.00)	10	(52.63)	116	(92.80)	**<0.001**
Lower extremity DVT***	3	(2.83)	2	(10.53)	5	(4.00)	0.115
Upper extremity DVT	1	(0.94)	2	(10.53)	3	(2.40)	**0.012**
Death within 3 months after discharge	2	(1.89)	0	(0.00)	2	(1.60)	0.546

*: Chronic obstructive pulmonary disease; **: Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ***: Deep vein thrombosis.

numbers. Both groups showed no statistically significant difference in terms of the incidence of lower extremity venous thrombosis. However, it was shown that the incidence of upper extremity vein thrombosis was statistically significantly higher in Group 2 participants (p=0.012). Out of the 19 patients in Group 2, 9 patients died. When the patients were followed up for 3 months after discharge, it was observed that 2 individuals in Group 1 died (Table 1).

The mean age was 58.5±15.9 years. The mean age of the individuals in Group 2 was observed to be statistically significantly higher when compared to that of the individuals in Group 1 (p=0.022). The mean EAT volume was 113.5±40.3 cm^3, and the EAT attenuation was −77.4±13.5 HU. There were no statistically significant differences between the two groups in terms of EAT volume and attenuation. The laboratory values of urea, creatinine, LDH, d-dimer, troponin T, procalcitonin, CRP, and neutrophil/lymphocyte ratio were observed to be statistically significantly higher in the individuals in Group 2. The albumin level was observed to be statistically significantly lower in individuals in Group 2 when compared to that in individuals in Group 1 (p<0.001). The individuals in Group 2 had a statistically significantly higher systolic BP value (p=0.022). The individuals in Group 2 had significantly lower percentages of SpO_2 as determined by a pulse oximeter when on room air (p<0.001). There was no statistically significant difference in the length of hospitalization between the two groups (Table 2).

A positive correlation was found between body weight, body mass index, and EAT volume, and a negative correla-

Table 2. Comparison of demographic, clinical, and laboratory characteristics among the groups

	Group 1		Group 2		Total		p
	Mean±SD	Median (Min-Max)	Mean±SD	Median (Min-Max)	Mean±SD	Median (Min-Max)	
Age, years	57.1±15.8	55 (21–91)	66.3±14.8	65 (36–97)	58.5±15.9	58 (21–97)	**0.022**
Body Mass Index	28.8±5.7	27.8 (17.8–44.6)	28.1±5	26.6 (23.2–39.1)	28.7±5.6	27.7 (17.8–44.6)	0.465
EAT volume, mm^3	115.4±42.5	107 (31–325)	102.8±22.5	106 (31–126)	113.5±40.3	107 (31–325)	0.531
EAT attenuation, HU	−77.4±14	−78.5 (−98–8)	-77.5±11	−76 (−96–−46)	−77.4±13.5	−78 (−98–8)	0.845
Urea, mg/dL	38.57±24.06	31.5 (11–137)	75.63±65.86	49 (19–280)	44.2±36.03	33 (11–280)	**0.001**
Creatinine, mg/dL	1.14±.92	0.89 (0.39–6.6)	2.94±4.23	1.12 (0.77–15.39)	1.41±1.93	0.94 (0.39–15.39)	**0.001**
Uric acid, mg/dL	6.4±2.6	5.9 (3.2–11.1)	3.7±1.1	3.7 (2.9–4.4)	6.1±2.6	5.9 (2.9–11.1)	0.117
LDH, u/L	371.7±128.3	352.5 (139–831)	501.8±171.1	472 (204–929)	392.1±143.2	375 (139–929)	**0.001**
Albumin, g/L	3.61±.42	3.59 (2.62–4.77)	3.08±.40	3.09 (2.24–3.78)	3.51±.46	3.5 (2.24–4.77)	**<0.001**
Sodium, mg/dL	134.1±4.6	135 (121–145)	134.7±3.7	135 (128–143)	134.2±4.5	135 (121–145)	0.874
Potassium, mg/dL	4.15±0.57	4.07 (2.53–5.84)	4.23±0.62	4.07 (3.37–5.35)	4.16±0.57	4.07 (2.53–5.84)	0.744
D–Dimer, ug/L	739.9±804.1	500 (110–6233.1)	2415.8±3590.1	1410 (200–16300)	996.7±1673.4	534.9 (110–16300)	**<0.001**
Ferritin, ug/L	555.3±472.1	440.2 (9.7–2832)	833.6±839.6	515.1 (78.9–3170)	597.9±549.3	454.5 (9.7–3170)	0.314
Troponin T, ng/L	0.45±2.83	0.01 (0–27.7)	9.71±28.28	0.03 (0.01–104.1)	1.88±11.66	0.01 (0–104.1)	**0.002**
Lactate, mmol/L	1.87±.67	1.73 (0.76–4.25)	2.21±1.21	2.02 (0.76–5.81)	1.93±0.79	1.74 (0.76–5.81)	0.312
Procalcitonin, ug/L	0.25±.55	0.11 (0.03–3.85)	1.55±4.07	0.26 (0.03–18)	0.45±1.71	0.12 (0.03–18)	**0.001**
CRP, mg/dL	93.04±61.85	87.07 (1.12–328.86)	159.46±98.39	144.61 (2.2–390)	103.14±72.24	95.32 (1.12–390)	**0.003**
Fibrinogen, g/L	6.14±1.31	6.18 (3.21–10.04)	6.15±1.63	6.32 (3.34–9.14)	6.14±1.36	6.18 (3.21–10.04)	0.873
Leukocyte 10^3mm^3	6.9±3.25	5.76 (1.73–16.41)	8.88±4.62	7.71 (2.58–17.49)	7.2±3.55	6.06 (1.73–17.49)	0.071
Neutrophil 10^3mm^3	5.39±2.97	4.55 (1.25–14.41)	7.31±4.27	6.15 (1.4–15.15)	5.68±3.26	4.75 (1.25–15.15)	0.056
Lymphocyte10^3mm^3	1.09±.49	0.99 (0.39–3.01)	1.02±.58	0.86 (0.19–2.19)	1.08±0.50	0.97 (0.19–3.01)	0.386
Platelet 10^3mm^3	207.51±79.20	190 (89–547)	186.53±64.59	194 (83–342)	204.32±77.30	191 (83–547)	0.409
MPV*	10.33±1.19	10.3 (8.5–14.7)	10.64±1.43	10.6 (8.3–13)	10.37±1.23	10.3 (8.3–14.7)	0.355
N/L**	5.72±3.81	4.67 (1.06–18.83)	9.76±8.50	6.78 (1.51–36.84)	6.34±4.99	4.86 (1.06–36.84)	**0.031**
P/L***	217.72±104.07	207.26 (60.92–612.24)	239.82±150.11	210.26 (66.21–715.79)	221.08±111.83	208.33 (60.92–715.79)	0.757
MPV/L****	11.42±5.26	10.22 (2.99–29.74)	15.12±12.26	12.33 (4.29–58.95)	11.98±6.86	10.31 (2.99–58.95)	0.306
Temperature, °C	36.71±.63	36.6 (36–39)	36.61±.50	36.5 (36–38)	36.69±.61	36.6 (36–39)	0.626
Sistolic BP, mmHg	115±15.97	116.5 (70–150)	127.68±23.07	120 (100–190)	116.93±17.73	120 (70–190)	**0.022**
Diastolic BP, mmHg	70±10.82	70 (40–94)	73.84±12.90	71 (57–110)	70.58±11.19	70 (40–110)	0.329
SAO2, %	89.84±4.02	90 (80–99)	84.84±6.11	85 (70–98)	89.08±4.73	89 (70–99)	**<0.001**
LOS, days*****	9.97±6.19	8.5 (1–36)	9.26±8.21	9 (1–37)	9.86±6.50	9 (1–37)	0.329
ICUS, days******			9.25±7.53	7.5 (1–26)	9.25±7.53	7.5 (1–26)	

*: Mean platelet volume; **Neutrophil/lymphocyte; ***: Platelet/lymhocyte; ****: Mean platelet volume/lymphocyte; *****: Length of hospital stay; ******: Length of intensive care unit stay.

tion was found between EAT attenuation. A negative correlation was found between troponin T and EAT attenuation (Table 3).

When the patients were divided into normal, overweight, and obese according to body mass index, EAT volume was determined to be statistically significantly higher in overweight and obese patients, whereas EAT attenuation was determined to be statistically significantly lower (p<0.001). No statistically significant difference was discovered with respect to the need for hospitalization in the ICU, lower extremity deep vein thrombosis, and mortality in normal, overweight, and obese patients (Table 4).

When patients who required ICU admission and/or who died were classified into normal, overweight, and obese groups based on body mass index, it was discovered that the mean age was statistically significantly greater in patients who were of normal weight (p=0.015). No statistically significant difference was discovered in individuals classified as normal, overweight, and obese with regard to the volume and attenuation of EAT, comorbid disease, and the

Table 3. Correlation between EAT volume, EAT attenuation, and investigated variables

	Epicardial adipose tissue volume						Epicardial adipose tissue attenuation					
	Total		Group 1		Group 2		Total		Group 1		Group 2	
	r	p	r	p	r	p	r	p	r	p	r	p
Age, years	−0.057	0.524	−0.036	0.711	−0.207	0.396	−0.025	0.781	−0.094	0.338	0.434	0.064
Height	−0.236	**0.012**	−0.185	0.068	−0.589	**0.027**	0.052	0.586	0.066	0.516	−0.311	0.279
Weight	0.581	**<0.001**	0.628	**<0.001**	0.148	0.615	−0.389	**<0.001**	−0.373	**<0.001**	−0.637	**0.014**
Body Mass Index	0.740	**<0.001**	0.764	**<0.001**	0.526	0.053	−0.451	**<0.001**	−0.426	**<0.001**	−0.569	**0.034**
Urea, mg/dl	−0.102	0.260	−0.096	0.325	−0.192	0.430	0.009	0.921	−0.008	0.933	0.316	0.187
Creatinine, mg/dl	−0.089	0.321	−0.086	0.380	0.036	0.884	−0.044	0.624	−0.090	0.357	0.341	0.153
Uric acid, mg/dl	−0.081	0.757	−0.143	0.610	1.000		0.148	0.570	0.082	0.772	1.000	
LDH, u/l	0.099	0.282	0.157	0.116	0.001	0.997	0.033	0.722	0.021	0.834	0.207	0.394
Albumin, g/l	0.069	0.497	0.043	0.703	0.210	0.402	−0.063	0.535	−0.031	0.788	−0.295	0.235
Sodium, mg/dl	0.100	0.265	0.079	0.423	0.229	0.345	0.016	0.863	0.031	0.750	−0.066	0.788
Potassium, mg/dl	−0.136	0.130	−0.136	0.165	−0.130	0.596	0.153	0.088	0.110	0.261	0.399	0.091
D−Dimer, ug/l	0.025	0.783	0.063	0.524	−0.011	0.963	−0.055	0.546	−0.130	0.185	0.425	0.069
Ferritin, ug/l	0.025	0.780	0.043	0.661	0.037	0.881	0.056	0.538	0.089	0.367	−0.165	0.499
Troponin T, ng/l	−0.012	0.892	0.023	0.819	−0.097	0.691	−0.217	**0.016**	−0.302	**0.002**	0.249	0.304
Lactate, mmol/l	−0.077	0.411	−0.001	0.990	−0.371	0.118	0.081	0.385	0.034	0.744	0.220	0.366
Procalcitonin, ug/l	−0.058	0.525	−0.023	0.820	−0.144	0.557	−0.014	0.881	−0.018	0.860	−0.016	0.949
CRP, mg/dl	−0.034	0.708	−0.040	0.685	0.017	0.946	0.027	0.767	0.054	0.581	−0.098	0.689
Fibrinogen, g/l	−0.080	0.468	−0.065	0.592	−0.075	0.799	0.195	0.074	0.176	0.141	0.219	0.453
Leukocyte, 10^3mm^3	−0,017	0.849	0.023	0.813	−0.187	0.444	0.147	0.103	0.113	0.250	0.402	0.088
Neutrophil, 10^3mm^3	−0,042	0.645	−0.023	0.812	−0.104	0.670	0.143	0.112	0.129	0.186	0.274	0.256
Lymphocyte, 10^3mm^3	0,077	0.396	0.113	0.250	−0.101	0.681	0.046	0.609	−0.026	0.794	0.450	0.053
Platelet, 10^3mm^3	−0,122	0.176	−0.115	0.239	−0.121	0.621	0.047	0.602	0,001	0.989	0.313	0.192
MPV*	0,146	0.105	0.211	**0.030**	−0.201	0.410	0.059	0.511	−0.004	0.971	0.436	0.062
N/L**	−0,096	0.289	−0.102	0.299	−0.066	0.789	0.090	0.320	0.136	0.165	−0.116	0.636
P/L***	−0,153	0.089	−0.175	0.073	−0.057	0.817	−0.013	0.882	0.046	0.639	−0.341	0.153
MPV/L****	−0,020	0.829	−0.033	0.736	0.041	0.867	−0.043	0.636	0.006	0.948	−0.362	0.128
Sistolic BP, mmHg	0,040	0.659	0.039	0.694	0.112	0.648	0.026	0.775	0.008	0.936	0.103	0.673
Diastolic BP, mmHg	0,206	**0.021**	0.221	**0.023**	0.105	0.670	0.072	0.427	0.036	0.717	0.301	0.210
SAO2,%	−0,048	0.593	−0.091	0.351	0.022	0.928	0.108	0.232	0.080	0.417	0.419	0.074
LOS, days*****	<0,001	0.999	0.033	0.737	−0.099	0.686	0.079	0.382	−0.013	0.898	0.505	**0.028**
ICUS, days******	0,186	0.491			0.186	0.491	−0.443	0.085			−0.443	0.085

*: Mean platelet volume; **: Neutrophil/lymphocyte; ***: Platelet/lymhocyte; ****: Mean platelet volume/lymphocyte; *****: Length of hospital stay; ******: Length of intensive care unit stay.

Table 4. Comparison of EAT measurement and severity of COVID-19 disease for normal/overweight/obese patients

	BMI (Body Mass Index)						p
	Normal		Overweight		Obese		
	Mean±SD	Med (Min-Max)	Mean±SD	Med (Min–Max)	Mean±SD	Med (Min–Max)	
EAT volume	94.9±15.9	97 (31–112)	105.7±11.1	106 (84–134)	148.1±61	125 (100–325)	**<0.001**
EAT attenuation	−71.8±12.6	−72.5 (−98–25)	−77.8±15.4	−78.5 (−98–8)	−82.9±9.4	−83.5 (−97–48)	**<0.001**
	n	%	n	%	n	%	
Mortality							
No	25	(89.29)	48	(96.00)	33	(97.06)	0.340
Yes	3	(10.71)	2	(4.00)	1	(2.94)	
ICU*							
No	25	(89.29)	45	(90.00)	31	(91.18)	0.968
Yes	3	(10.71)	5	(10.00)	3	(8.82)	
DVT**							
No	26	(92.86)	50	(100.00)	32	(94.12)	0.181
Yes	2	(7.14)	0	(.00)	2	(5.88)	

*: Intensive care unit; **: Deep vein thrombosis.

Table 5. Demographic, clinical characteristics of normal/overweight/obese patients in Group 2

Group 2	BMI (Body mass ındex)						p
	Normal		Overweight		Obese		
	n	%	n	%	n	%	
Gender							
Female	1	20	2	40	2	50	0.627
Male	4	80	3	60	2	50	
Diabetes mellitus	1	20	2	40	1	25	0.769
Hypertension	4	80	2	40	1	25	0.223
Hyperlipidemia	0	0	2	40	1	25	0.298
Chronic kidney disease	1	20	0	0	1	25	0.511
Kidney transplant	0	0	0	0	0	0	***
Liver transplant	0	0	0	0	0	0	***
COPD	1	20	0	0	1	25	0.511
Ischemic heart disease	2	40	0	0	1	25	0.298
Previous cerebrovascular event	0	0	0	0	0	0	***
Use of ACE inhibitor/ARB	2	40	1	20	1	25	0.769
Cough	3	60	4	80	1	25	0.250
Dyspnea	4	80	5	100	4	100	0.379
Headache	0	0	1	20	0	0	0.379
Diarrhea	0	0	1	20	0	0	0.379
Fatigue	4	80	5	100	2	50	0.191
Abdominal pain	0	0	1	20	0	0	0.379
Fever	2	40	3	60	2	50	0.819
Back pain	0	0	1	20	1	25	0.511
Steroid	3	60	5	100	4	100	0.122
Pulse steroid	1	20	3	60	0	0	0.122
Tocilizumab	1	20	2	40	1	25	0.769
Antibiotic	2	40	4	80	2	50	0.417
Immune Plasma	0	0	0	0	0	0	***
Mortality	3	60	2	40	1	25	0.566
ICU (ıntensive care unit) stay	3	60	5	100	3	75	0.298
Discharged	2	40	3	60	3	75	0.566
Lower extremity DVT	1	20	0	0	0	0	0.379
Upper extremity DVT	0	0	1	20	1	25	0.511
Death within 3 months after discharge	0	0	0	0	0	0	***

requirement for critical care unit and/or mortality. In laboratory testing, normal-weight patients' urea values were found to be statistically significantly greater than those of overweight and obese patients (p=0.011). No statistically significant difference was found in other laboratory values. It was found that patients who were overweight or obese had statistically significantly lower percentages of room air SpO_2 than patients who were of normal weight (p=0.013). Regarding admission complaints, no statistically significant difference was discovered in terms of cough, dyspnea, headache, diarrhea, weakness, abdominal pain, fever, and back pain. Regarding the treatments used, there was no statistically significant difference in terms of steroid, pulse steroid, tocilizumab, and antibiotic. Overweight patients were shown to have a statistically significantly longer hospital stay (p=0.010) (Tables 5 and 6).

Discussion

The severity and mortality of COVID-19 pneumonia depend on hyperinflammation and cytokine storm. Cy-

Table 6. Comparison of EAT(Epicardial adipose tissue) measurement and laboratory characteristics for normal/overweight/obese patients in Group 2

Group 2	BMI						p
	Normal		Overweight		Obese		
	Mean±S.D.	Median(Min-Max)	Mean±S.D.	Median(Min-Max)	Mean±S.D.	Median(Min-Max)	
Age, years	77.8±11.7	81 (64–90)	58.4±12.7	62 (36–67)	53.8±5.8	54.5 (47–59)	**0.015**
EAT volume, cm^3	100.4±17.1	107 (70–110)	102.8±14	100 (90–126)	122.8±1.5	123 (121–124)	0.075
EAT attenuation, HU	–74.4±2.1	–74 (–77–-72)	–77.6±7.2	–75 (–86–-69)	–87.8±6.6	–86.5 (–96–82)	0.058
Urea, mg/dl	111±56.62	115 (49–180)	44.2±9.78	46 (33–57)	33.75±10.24	34.5 (23–43)	**0.011**
Creatinine, mg/dL	5.1±6.00	2.62 (1.02–15.39)	0.97±0.18	0.96 (0.77–1.26)	1.98±1.94	1.07 (0.88–4.88)	0.062
Uric acid, mg/dL			3.65±1.06	3.65 (2.9–4.4)			***
LDH, u/l*	454.6±112.7	435 (321–581)	518.4±118.9	472 (403–668)	546.2±265.1	447.5 (361–929)	0.680
Albumin, g/L	3.04±0.27	3.11 (2.68–3.27)	3.24±0.55	3.49 (2.36–3.78)	3.24±.30	3.32 (2.83–3.5)	0.505
Sodium, mg/dL	136.2±4.4	134 (132–143)	134±2.8	136 (130–136)	135.8±3.8	136 (131–140)	0.722
Potassium, mg/dL	4.54±.81	4.47 (3.41–5.35)	4.51±0.50	4.5 (3.98–5.2)	3.76±.29	3.8 (3.37–4.07)	0.077
D–dimer, ug/L	1564.5±1549.1	1190 (372.5–4200)	3791.6±6992.8	700 (530–16300)	1636±1216.3	1607(200–3130)	0.914
Ferritin, ug/l	962.4±982.2	570.2 (215.4–2592)	830.6±641.8	483.6 (298–1590)	1108.1±1387.3	512.9(236.7–3170)	0.946
Troponin T, ng/l	14.66±32.61	0.08 (0.02–73)	0.01±0.01	0.01 (0.01–0.02)	27.1±51.37	2.15 (0.01–104.1)	0.167
Lactate, mmol/l	3.1±1.67	2.18 (1.74–5.81)	1.92±0.63	1.88 (1.19–2.77)	1.68±.87	1.57 (0.79–2.81)	0.277
Procalcitonin, ug/l	3.79±7.94	0.21 (0.09–18)	0.4±.44	0.17 (0.08–1.13)	0.71±1.13	0.18 (0.08–2.4)	0.835
CRP, mg/dL**	123.45±77.02	105.42 (64.59–254.82)	201.73±121.73	149.83 (77.38–390)	171.98±58.02	162.41 (114.1–249)	0.309
Fibrinogen, g/L	4.91±2.21	4.91 (3.34–6.47)	7.24±1.74	7.77 (4.43–9.14)	5.12±1.26	4.61 (4.2–6.56)	0.131
Leukocyte 10^3mm^3	11.36±5.12	8.77 (6.55–17.49)	7.34±3.68	8.55 (2.93–11.9)	5.81±1.49	5.75 (4.06–7.67)	0.125
Neutrophil 10^3mm^3	8.85±5.57	5.29 (3.92–15.15)	6.26±3.54	6.57 (2.4–10.88)	4.79±1.15	4.79 (3.41–6.15)	0.460
Lymphocyte 10^3mm^3	1.41±0.71	1.17 (0.77–2.19)	0.81±0.50	0.6 (0.43–1.64)	0.77±.35	0.71 (0.45–1.23)	0.248
Platelet 10^3mm^3	196.4±54.68	194 (140–257)	182.8±61.08	194 (83–239)	151.5±45.91	145 (112–204)	0.475
MPV, fl***	10.74±.92	10.6 (9.4–11.7)	11.32±1.72	11.9 (9.3–13)	9.13±1.01	8.8 (8.3–10.6)	0.077
N/L****	8.6±7.36	6.78 (1.79–19.06)	9.62±7.28	5.58 (3.46–18.13)	6.93±2.96	5.71 (5–11.31)	0.979
P/L*****	175.91±106.72	179.49 (66.21–333.77)	261.39±119.92	213.19 (145.73–406.98)	225.4±96.47	245.27 (91.06–320)	0.440
MPV/L******	9.35±4.41	9.83 (4.29–13.64)	17.52±8.24	21.67 (7.26–25.92)	13.57±5.31	13.71 (7.07–19.78)	0.191
Temperature, °C	36.36±0.27	36.3 (36.1–36.8)	36.52±.46	36.6 (36–37.2)	36.73±.87	36.4 (36.1–38)	0.866
Sistolic BP, mmHg	114.4±11.26	112 (100–130)	141±29.10	132 (113–190)	124.75±16.84	120 (110–149)	0.112
Diastolic BP, mmHg	71±8.31	71 (60–80)	81.6±18.85	80 (57–110)	70±8.16	70 (60–80)	0.367
SAO_2, %	91.6±4.16	91 (88–98)	80±5.87	82 (70–85)	83.5±4.20	83.5 (79–88)	**0.013**
LOS, days*******	7.4±4.04	8 (3–13)	17.6±11.24	14 (10–37)	3.25±1.26	3 (2–5)	**0.010**
ICUS, days********	7±5.29	5 (3–13)	11.8±8.44	10 (5v26)	10.33±1.53	10 (9–12)	0.650

*: Lactate dehydrogenase; **: C-reactive protein; ***: Mean Platelet Volume; ****: Neutrophil/Lymphocyte; *****: Platelet/Lymhocyte; ******: Mean Platelet Volume/Lymphocyte; *******: Length of hospital stay; ********: Length of intensive care Unit stay.

tokines and inflammatory mediators are secreted from the EAT.

In the study by Aitken-Buck et al.,[20] a statistically significant positive correlation was found between the thickness of the EAT measured by echocardiography and the body mass index.

There are limited data indicating that the size of epicardial fat is proportional to that of whole body fat. In the study by Marchington et al.,[21] no relationship was found between the amount of epicardial fat and the total amount of adipose tissue in other fat reserves of the body in various animals. In our research, EAT volume was observed to be statistically significantly higher, whereas EAT attenuation was found to be low. There was a positive correlation between body mass index and EAT volume, whereas a negative correlation was found between EAT attenuation in overweight and obese patients.

Conte et al.[22] showed that increased EAT attenuation, a marker of EAT inflammation, predicted critical COVID-19 infection. However, no relationship was found between obesity, EAT volume, and illness severity. In the research by Mehta et al.,[23] EAT thickness was determined to be significantly connected with COVID-19 severity and mortality regardless of body mass index, age, and concomitant disease.

Normal and pathological values for EAT volume measured on CT have not been defined. In the study by Marcucci et al.,[24] it was found that it has good sensitivity and specificity to predict a worse medical outcome in individuals with COVID-19 pneumonia with an EAT volume of 97 cm^3. In our research, no statistically significant difference was observed in terms of EAT volume and EAT attenuation when patients with COVID-19 who needed intensive care and/or died were compared with patients who were hospitalized and discharged. In the research by Rossi et al.,[25] it was emphasized that patients in intensive care who have severe COVID-19 disease and increased EAT volume and low EAT density must be followed closely.

In our study, no relationship was found between obesity and illness severity. In the research by Anderson et al.,[26] it was shown that in patients under 65 years, obesity is linked to a higher risk of intubation or mortality from COVID-19 disease.

In the study by Yang et al.,[27] individuals with COVID-19 had poor clinical outcomes when they were older and male. In our research, the age was statistically higher in the group requiring hospitalization in the ICU or the group with mortality compared to the group that was hospitalized and discharged, and no significant relationship was found regarding gender. In the group with ICU hospitalization and/or mortality, urea, creatinine, LDH, d-dimer, troponin T, procalcitonin, CRP, and neutrophil/lymphocyte ratio were determined to be statistically significantly higher, and the albumin level was statistically significantly lower. The fingertip SpO_2 measured on room air was observed to be statistically considerably lower in the group requiring ICU hospitalization or mortality, and the systolic BP was observed to be statistically significantly higher in that group.

In the meta-analysis by Ji et al.,[28] it was determined that white blood cell count, CRP, and procalcitonin levels were high in patients with severe COVID-19 disease. In another meta-analysis, higher white blood cell counts were associated with neutrophils, d-dimer, and prolonged prothrombin time in COVID-19 patients requiring intensive care.[29]

In our study, the rate of radiological lower extremity venous thrombosis detection was 4%, and the rate of upper extremity venous thrombosis was 2.4%. In the research by Al-Samkari et al.,[30] d-dimer levels were increased in COVID-19 patients, the rate of radiographically confirmed venous thromboembolism was 4.8%, and the total rate of thrombotic events was 9.5%.

The myocardial injury indicator troponin T levels and EAT volume and attenuation were not found to be correlated in our research. In the research by Grodecki et al.,[12] there was no association found between EAT attenuation and troponin T. In addition, in the study by Grodecki et al.,[12] a relationship was found between EAT volume and hospitalization in the critical care unit and mortality.

Individuals hospitalized with COVID-19 pneumonia in our hospital in Turkey consist of critically ill patients. The rate of steroid, pulse steroid, and anti-inflammatory treatment given to the patients was high. The rate of administration of pulse steroid and tocilizumab as anti-inflammatory treatments was observed to be statistically significantly higher in patients who were hospitalized in the ICU and/or died.

In the study by Iacobellis et al.,[31] dexamethasone treatment applied to COVID-19 patients was related to a significant reduction in EAT inflammation, suggesting that anti-inflammatory treatments that target visceral adipose tissue may be beneficial in COVID-19 infection. Thus, it has been shown that EAT can be used both to indicate inflammation and to function as a therapeutic target in anti-inflammatory therapy.

In our study, antibacterial agents were administered to 65 patients (52%) out of 125, since the frequency of bacterial superinfection was unclear at the beginning of the epidemic. All hospitalized patients were treated with favipiravir as an antiviral agent in accordance with the recommendations in the COVID-19 guidelines and treatment algorithm prepared by the Scientific Committee of the Republic of Turkey's Ministry of Health. Ninety-four patients

(75.2%) were treated with steroids, 15 patients (12%) with pulse steroids, 7 patients (5.6%) received tocilizumab, and 1 patient (0.8%) received immune plasma therapy. If there was a strong suspicion of a serious hyperinflammatory status based on an evaluation of inflammatory mediators and a low risk of a concurrent uncontrolled secondary infection, physicians prescribed these medications.

Our study has some limitations. We used the initial values of the inflammatory markers checked at the patients' first admission, and the markers we used can show dynamic changes in the course of the disease and affect the prognosis. Therefore, there is a need for studies with a larger number of patients in which these parameters, which change dynamically during the follow-up of the disease, are evaluated. EAT volume and attenuation measured on a non-contrast chest CT were performed by a single radiologist. Due to the low number of individuals who died in our study, the interpretation of the findings may be limited. To confirm our findings and clarify the fundamental mechanisms underlying them, additional research is required.

Conclusion

We did not find any relationship between EAT volume and attenuation measured on a non-contrast chest CT and the severity of COVID-19 pneumonia in our research. We believe that the measurement of EAT volume and attenuation should be evaluated with prospective, multicenter studies to enable its use in evaluating the risk of disease exacerbation in clinical risk classification. In addition, EAT-related measurements can be used to uncover the potential effects of drugs targeted toward adipose tissue.

Disclosures

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital (No: 3406, dated 22.02.2022).

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References

1. 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. [CrossRef]
2. Xue G, Gan X, Wu Z, Xie D, Xiong Y, Hua L, et al. Novel serological biomarkers for inflammation in predicting disease severity in patients with COVID-19. Int Immunpharmacol 2020;89:107065. [CrossRef]
3. Gong J, Dong H, Xia QS, Huang ZY, Wang DK, Zhao Y, et al. Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study. BMC Infect Dis 2020;20:963. [CrossRef]
4. Kaeuffer C, Le Hyaric C, Fabacher T, Mootien J, Dervieux B, Ruch Y, et al; Covid Alsace Study Group. Clinical characteristics and risk factors associated with severe COVID-19: prospective analysis of 1,045 hospitalised cases in North-Eastern France, March 2020. Euro Surveill 2020;25:2000895. [CrossRef]
5. Li Y, Lin S, Zhou Y, Pan J, Chen Y. Correlation between early inflammation indicators and the severity of coronavirus disease 2019. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue [Article in Chinese] 2021;33:145-9.
6. Cai Z, Yang Y, Zhang J. Obesity is associated with severe disease and mortality in patients with coronavirus disease 2019 (COVID-19): a meta-analysis. BMC Public Health 2021;21:1505. [CrossRef]
7. 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. [CrossRef]
8. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, et al; LICORN and the Lille COVID-19 and Obesity study group. High prevalence of obesity in severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity (Silver Spring) 2020;28:1195-9. Erratum in: Obesity (Silver Spring) 2020;28:1994. [CrossRef]
9. Trayhurn P. Endocrine and signalling role of adipose tissue: new perspectives on fat. Acta Physiol Scand 2005;184:285-93. [CrossRef]
10. Gorter PM, Van Lindert AS, de Vos AM, Meijs MF, van der Graaf Y, Doevendans PA, et al. Quantification of epicardial and peri- coronary fat using cardiac computed tomography; reproducibility and relation with obesity and metabolic syndrome in patients suspected of coronary artery disease. Atherosclerosis 2008;197:896-903. [CrossRef]
11. Zagaceta J, Zulueta JJ, Bastarrika G, Colina I, Alcaide AB, Campo A, et al. Epicardial adipose tissue in patients with chronic obstructive pulmonary disease. PloS One 2013;8:e65593. [CrossRef]
12. Grodecki K, Lin A, Razipour A, Cadet S, McElhinney PA, Chan C, et al. Epicardial adipose tissue is associated with extent of pneumonia and adverse outcomes in patients with COVID-19. Metabolism 2021;115:154436. [CrossRef]
13. 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. [CrossRef]
14. Ryan, PM, Caplice NM. Is adipose tissue a reservoir for viral spread, immune activation, and cytokine amplification in coronavirus disease 2019? Obesity 2020;28:1191-4. [CrossRef]

15. Maier HE, Lopez R, Sanchez N, Ng S, Gresh L, Ojeda S, et al. Obesity increases the duration of influenza A virus shedding in adults. J Infect Dis 2018;218:1378-82. [CrossRef]
16. Ponterio E, Cangemi R, Mariani S, Casella G, De Cesare A, Trovato FM, et al. Adenovirus 36 DNA in human adipose tissue. Int J Obes (Lond) 2015;39:1761-4. [CrossRef]
17. Zwezdaryk KJ, Ferris MB, Strong AL, Morris CA, Bunnel BA, Dhurandhar NV, et al. Human cytomegalovirus infection of human adipose-derived stromal/stem cells restricts differentiation along the adipogenic lineage. Adipocyte 2016;5:53-64. [CrossRef]
18. Tsatsanis C, Margioris AN, Kontoyiannis DP. Association between H1N1 infection severity and obesity-adiponectin as a potential etiologic factor. J Infect Dis 2010;202:459-60. [CrossRef]
19. Gu J, Korteweg C. Pathology and pathogenesis of severe acute respiratory syndrome. Am J Pathol 2007;170:1136-47. [CrossRef]
20. Aitken-Buck HM, Moharram M, Babakr AA, Reijers R, Van Hout I, Fomison-Nurse IC, et al. Relationship between epicardial adipose tissue thickness and epicardial adipocyte size with increasing body mass index. Adipocyte 2019;8:412-20. [CrossRef]
21. Marchington JM, Pond CM. Site- specific properties of pericardial and epicardial adipose tissue: the effects of insülin and high-fat feeding on lipogenesis and the incorporation of fatty acids on vitro. Int J Obes 1990;14:1013-22.
22. Conte C, Esposito A, De Lorenzo R, Di Filippo L, Palmisano A, Vignale D, et al. Epicardial adipose tissue characteristics, obesity and clinical outcomes in COVID-19: a post-hoc analysis of a prospective cohort study. Nutr Metab Cardiovasc Dis 2021;31:2156-64. [CrossRef]
23. Mehta R, Bello-Chavolla OY, Mancillas-Adame L, Rodriguez-Flores M, Pedraza NR, Encinas BR, et al. Epicardial adipose tissue thickness is associated with increased COVID-19 severity and mortality. Int J Obes 2022;46:866-73. [CrossRef]
24. Marcucci M, Fogante M, Tagliati C, Papiri G. Cut-off point of CT-assessed epicardial adipose tissue volume for predicting worse clinical burden of SARS-CoV-2 pneumonia. Emergy Radiol 2022;29:645-53. [CrossRef]
25. Rossi AP, Donadello K, Schweiger V, Zamboni GA, Dalla Valle Z, Zamboni M, et al. Epicardial adipose tissue volume and CT-attenuation as prognostic factors for pulmonary embolism and mortality in critically ill patients affected by COVID-19. Eur J Clin Nutr 2023;77:105-11. [CrossRef]
26. Anderson MR, Geleris J, Anderson DR, Zucker J, Nobel YR, Freedberg D, et al. Body mass index and risk for intubation or death in SARS-CoV-2 infection: a retrospective cohort study. Ann Intern Med 2020;173:782-90. [CrossRef]
27. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475-81. Erratum in: Lancet Respir Med 2020;8:e26. [CrossRef]
28. Ji P, Zhu J, Zhong Z, Li H, Pang J, Li B, et al. Association of elevated inflammatory markers and severe COVID-19: a meta-analysis. Medicine (Baltimore) 2020;99:e23315. [CrossRef]
29. Elshazli RM, Toraih EA, Elgaml A, El-Mowafy M, El-Mesery M, Amin MN, et al. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: a meta-analysis of 6320 patients. PloS One 2020;15:e0238160. [CrossRef]
30. Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JCT, Fogerty AE, Waheed A, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. Blood 2020;136:489-500. [CrossRef]
31. Iacobellis G, Malavazos AE, Basilico S, Tresoldi S, Rinaldo RF, Dubini C, et al. Epicardial fat inflammation response to COVID-19 therapies. Obesity (Silver Spring) 2021;29:1427-33. [CrossRef]