ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 31(1): 28-34, 2026
DOI: 10.5505/ejm.2026.56750

Decrease In Epicardial Adipose Tissue Volume Predicts Mortality In Covid-19: A New Biomarker

Betül Akdal Dölek[1*], Eren Çamur[2], Erdem Özkan[3], Muhammet Batuhan Gökhan[4], Murat Vural[1]

[1]*Ankara Bilkent City Hospital*
[2]*29 Mayıs Hospital*
[3]*Kastamonu Training and Research Hospital*
[4]*Yerkoy Hospital*

ABSTRACT

COVID-19 caused by SARS-CoV-2 has been associated with cardiovascular complications, including increased epicardial adipose tissue (EAT) volume. While prior studies have explored the association between EAT volume and COVID-19 severity, none have investigated dynamic changes in EAT over time and their connection to mortality. The aim of this study was to investigate the relationship between changes in EAT volume and prognosis in COVID-19 patients and to examine EAT's role in COVID-19 pathophysiology by correlating volume changes with laboratory markers.

A retrospective analysis was performed on 134 patients with COVID-19 who underwent two thoracic CTs on different days of scans during hospitalization. EAT volume was quantified using segmentation software, and differences between survivors and non-survivors were analyzed. Logistic regression models and ROC curve analysis were used to evaluate predictive biomarkers for mortality.

Among the 134 patients, 64 (47.7%) died. Non-survivors had significantly higher D-dimer, IL-6, cTnI, and ferritin levels ($p < 0.05$). The reduction in EAT volume was significantly greater in non-survivors ($p < 0.001$). ROC analysis revealed an optimal cut-off value of -3.78% for EAT volume decrease in predicting mortality (AUC 0.867). EAT volume change (AUC 0.86) and troponin (AUC 0.92) were highly predictive of mortality.

A decrease in EAT volume of 3.78% or more is a significant predictor of mortality in COVID-19 patients. EAT appears to actively contribute to COVID-19's inflammatory and cardiovascular effects, and EAT volume change may be a novel biomarker for mortality risk in this disease.

Keywords: COVID-19, epicardial adipose tissue, mortality, severe disease, biomarkers

Introduction

COVID-19, caused by the SARS-CoV-2 virus, was first detected in December 2019. The rapid spread of this disease has resulted in over 6 million deaths and has become a global health crisis (1). Therefore, COVID-19 must be thoroughly investigated and its pathophysiology must be clearly understood. Current research has identified several risk factors for severe COVID-19, including age, smoking history, hypertension, diabetes mellitus, and obesity (2-4). Among these factors, obesity - particularly visceral obesity - is thought to exacerbate disease severity by increasing inflammation (5). Studies have shown that visceral adipose tissue (VAT) is hormonally active and influences metabolic regulation via the inflammatory cytokines it secretes (1-6). The two primary parameters used to assess VAT are abdominal visceral adipose tissue and epicardial adipose tissue (EAT), both measured by computed tomography (CT) (7). In particular, EAT has been shown to trigger proinflammatory cytokine release via angiotensin-converting enzyme 2 (ACE2) and to induce myocardial cell death via a paracrine effect (8). Routine thickness or volume measurements on chest CT images are used to assess EAT in patients. Given the success of EAT in predicting prognosis in chronic lung disease, researchers have begun to question whether EAT could serve as a novel biomarker for COVID-19. All studies to date have reported a positive correlation between EAT thickness or volume at diagnosis and COVID-19 disease severity. However, to our best knowledge, there is no study that investigates the relationship between changes in EAT volume - an active endocrine tissue - during the course of COVID-19 (9-11).

In this study, we aimed to determine the relationship between changes in EAT volume

***Corresponding Author:** Betul Akdal Dolek, Ankara Bilkent City Hospital
e-mail: b_akdal@yahoo.com
ORCID ID: Betül Akdal Dölek: 0000-0002-8556-6278, **Eren Çamur:** 0000-0002-8774-5800, **Erdem Özkan:** 0000-0001-8120-7051, **Muhammet Batuhan Gökhan:** 0000-0002-3579-7887, **Murat Vural:** 0000-0001-6815-5269
Received: 18.10.2025, **Accepted:** 01.12.2025

during the course of COVID-19 and mortality, while also highlighting the active role of EAT in the pathophysiology of the disease by examining its volume changes in relation to laboratory markers such as cardiac troponin I (cTnI), IL-6, D-dimer and ferritin.

Materials and Methods

Study Design: This study is a retrospective observational study conducted at our institution. This study was approved by the International Review Board of our institution (approval number: E1-21-2113) and was conducted in full accordance with the tenets of the Declaration of Helsinki. Informed consent could not be obtained from the patients because this was a retrospective study.

All subjects admitted to the hospital between March 2021 and April 2021 with a diagnosis of SARS-CoV-2 confirmed by PCR test were analyzed. Patients' medical information was anonymized for research purposes. Patients who had undergone two thoracic CT scans during hospitalization were included in the study. The first CT scans were taken during the patient's admission to the hospital. The mean interval between two CT scans was 21 days. Exclusion criteria are shown in Figure 1. Demographic information, laboratory findings, and comorbidities were obtained from the hospital information management and automation system. Additionally, medical histories and outcomes, including mortality due to COVID-19, were documented. While those who were hospitalized due to COVID-19 and survived were defined as the survivor group, those who lost their lives due to COVID-19 were defined as the non-survivor group.

Image Acquisition and Image Evaluation: All scans were acquired on a 128-slice CT (GE Revolution EVO, GE Medical Systems, Milwaukee, WI, USA) with the patient in the supine position during inspiration and without an intravenous contrast agent. Acquisition parameters included a tube voltage of 120 kV, a tube current of 180-300 mA, a spiral step factor of 0.98, a collimation thickness of 0.625 mm, a slice thickness of 1.3 mm, and sharp kernel reconstruction for image clarity.

EAT volume was assessed quantitatively using segmentation software (GE Medical Systems, 4.7 version, Milwaukee, WI, USA). The density of EAT was determined using Hounsfield units ranging from -30 to -190. The superior border of EAT measurements was determined as the pulmonary trunk bifurcation. The inferior border of EAT was determined as the posterior descending coronary artery in the inferior atrioventricular groove. The contour of the epicardium was automatically drawn by the software and corrections were made by radiologists if necessary. Nine patients whose epicardial contour could not be clearly seen due to artifacts were excluded from the study.

Statistical analysis: Statistical analyses were performed using the R programming language. Differences between the two groups were evaluated using the Wilcoxon rank-sum test. The EAT volume (cm^3) values between the two groups were compared using an independent two-sample t-test, and Mann-Whitney U tests were applied to the cTnI and EAT volume (cm^3) variables. A logistic regression model was constructed to predict survival outcomes in COVID-19 patients based on significant variables. These variables included D-Dimer, Ferritin, HDL, IL-6, LDH, LDL, N/L Ratio, Spleen Density (HU), Test Date, Total Cholesterol, cTnI, and EAT volume (cm^3). The model's diagnostic performance was assessed using ROC curve analysis, and post-hoc power analysis was conducted for the significant p-values. p-value < 0.05 was considered statistically significant.

Results

Among 134 patients (76 women and 58 men), included in the study 64 patients (47.7%) died due to COVID-19. The mean age of those who died was 70.2 years, whereas the mean age of the survivors was 61.1 years. 36 (56%) of the group of non-survivors and 40 (57%) of the group of survivors were male. There was no difference between the two groups in terms of gender. Significant differences were observed in the laboratory markers of IL-6, D-dimer, ferritin, cTnI, LDL, and total cholesterol between the two groups ($p < 0.001$; 0.002; 0.04; <0.001; 0.01 and 0.03, respectively). The non-survivor group demonstrated elevated levels of D-dimer, IL-6, cTnI, and ferritin in comparison to the survivor group (Table 1). On the CT scan taken at the time of first hospitalization, the EAT volume was 132 cm^3 ($\pm$ 37.84) in the survivor group and 148.9 cm^3 ($\pm$ 64.29) in the non-survivor group. The change in EAT volume between two CT scans were evaluated for each patient (Fig 2). Upon evaluating the changes in EAT between the two groups, a significant difference was observed ($p<0.001$) (Fig. 3). EAT volume decreased more

Table 1: Comparison of Groups In Terms of Laboratory Markers

Laboratory Findings	Non-survivor group (n: 64)	Survivor group (n: 70)	p value
CRP	0.10 ± 0.082	3.79 ± 21.79	0.98
cTnI	665.03± 2422.6	13.49 ± 33.10	<0.001*
D-dimer	5.38 ± 6.88	3.16 ± 6.34	0.002*
Ferritin	3032.27 ± 7884.40	418.70 ± 430.58	0.04*
IL6	412.95 ± 1489.67	328.43 ± 1688.81	<0.001*
LDL	71.26 ± 40.44	93.52 ± 43.74	0.01*
Total cholesterol	128.00 ± 59.02	157.03 ± 65.29	0.03*
Triglyceride	150.72 ± 99.22	68.91 ± 95.54	0.1

Data are shown as mean ± SD
CRP: C-reactive protein; IL6: Interleukin 6; LDL: low-density lipoprotein, cTnI: Cardiac Troponin I
*p value < 0.05 was considered statistically significant

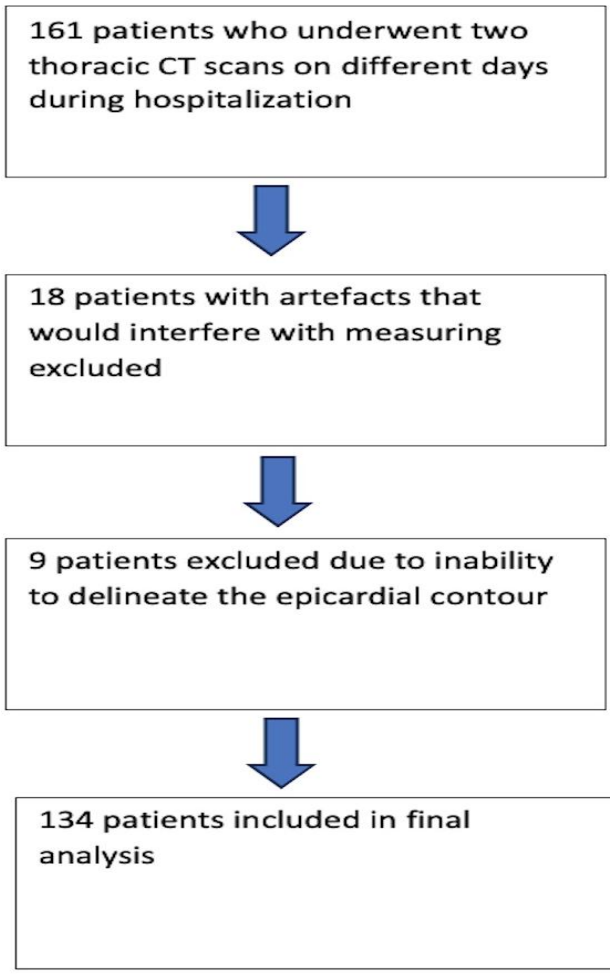

Fig. 1. Flowchart of the study

in the non-survivor group than in the survivor group.

ROC curve analysis was conducted to evaluate the power of EAT volume changes and laboratory markers to predict mortality (cTnI, IL-6, D-dimer,

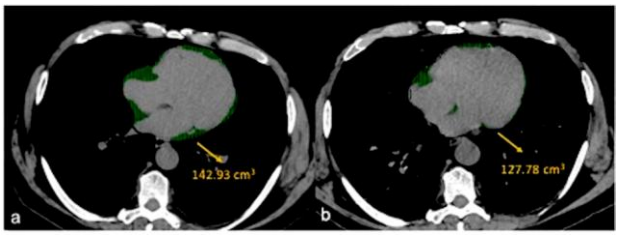

Fig. 2. EAT volume change in a patient who died due to COVID-19. a) EAT volume measurement on CT taken at the time of application. b) EAT volume measurement on CT taken 21 days after application

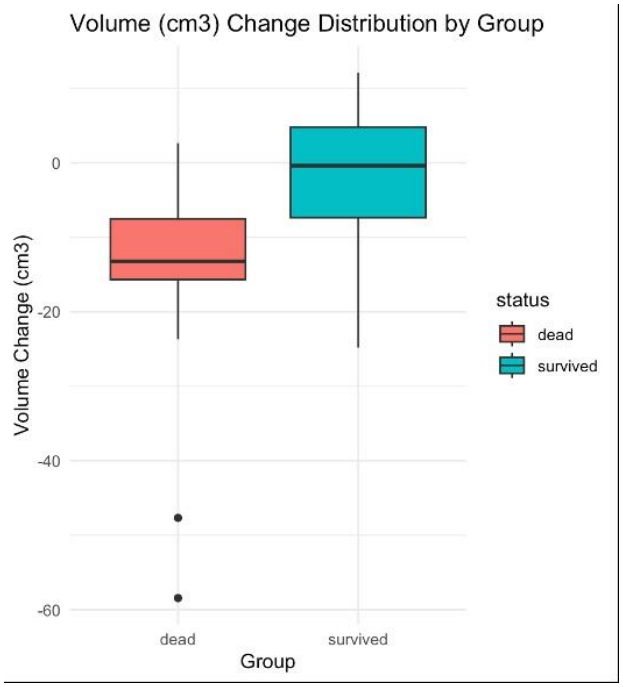

Fig. 3. EAT volume (cm^3) change distribution by group

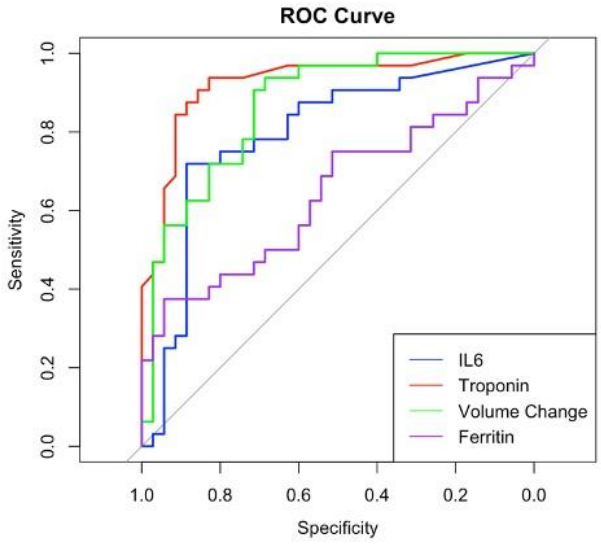

Fig. 4 ROC curve analysis of EAT volume changes and laboratory markers (cardiac troponin I, IL-6, D-dimer and ferritin)

and Ferritin). The optimal cut-off value for EAT volume change was −3.78%, corresponding to a sensitivity of 87.5% and a specificity of 74.3% (AUC 0.867) (Fig. 4). When power assessment was performed on data with significant p-values, cTnI (AUC 0.92) and EAT volume change (AUC 0.86) showed the highest power to predict mortality (Fig. 3). In contrast, ferritin (AUC 0.64) exhibited the lowest power to predict mortality.

Discussion

COVID-19 primarily targets the respiratory system, but it has been reported in the literature to lead to multiple organ failure by impacting various systems, including the heart, kidneys, and vasculature, ultimately increasing mortality and morbidity (12).

VAT, located in the mesentery and omentum, has a more complex cellular, vascular, and neural structure than subcutaneous adipose tissue. It contains more inflammatory and immune cells, less preadipocyte differentiation capacity, and a greater number of large adipocytes (13).

EAT is a component of VAT, and in particular, it and the myocardium share a microcirculation that allows rapid exchange of inflammatory and metabolic chemicals (11). This anatomical relationship implies that under acute or chronic inflammatory conditions, these interactions may adversely affect cardiovascular function. Changes in epicardial adipogenesis trigger the secretion of pro-inflammatory adipokines that contribute to atrial and ventricular damage (14,15). In the context of COVID-19, EAT is thought to play a role in creating an imbalance between the production of anti-inflammatory and pro-inflammatory adipokines, thereby contributing to the enhanced cytokine storm and multisystem involvement observed in severe COVID-19 cases (9). Increased EAT accumulation has been shown to correlate with increased cardiac injury and a hypercoagulable state through its influence on fibrinogen levels, thereby increasing the risk of COVID-19 severity and mortality. The prothrombotic and inflammatory adaptive responses to SARS-CoV-2 infection, combined with direct myocardial injury, have been associated with a higher risk of cardiovascular complications in COVID-19 (16,17). Greater EAT thickness was associated with an increased risk of in-hospital myocardial infarction and elevated cardiac troponin levels, possibly indicating direct cardiovascular injury. Our results are consistent with existing findings in the literature indicating that troponin levels are a robust biomarker of cardiac damage associated with SARS-CoV-2 infection. Furthermore, our results indicate that EAT volume change may serve as a valuable biomarker in the assessment of cardiac effects associated with the disease.

In this analysis, we investigated how EAT, known to be an important prognostic biomarker in cardiovascular disease, changes during the clinical course of COVID-19, which is known to cause direct cardiac damage, including myocarditis. Due to the high spatial resolution of CT and the distinct attenuation values of adipose tissue, EAT volume and changes in EAT can be measured accurately and precisely (13,18). Recent literature has shown a positive correlation between EAT volume and COVID-19 disease severity (19,20). Although there is some variation between studies, it has been reported that the disease is more severe in patients with an EAT volume of approximately 97 cc and above (19,20).

Although several studies have investigated the relationship between EAT volume and COVID-19 disease severity, our study is unique in highlighting the dynamic changes in EAT over time in COVID-19 patients that lead to mortality and in demonstrating the relationship between volume change and mortality. Furthermore, we highlighted that a decrease in epicardial adipose tissue volume of 3.78% or more during the clinical course of COVID-19 is highly valuable for predicting mortality. The decrease in EAT volume over time in COVID-19 patients who succumb to the disease may be attributed to the fact that EAT and

myocardium share the same microvascular circulation. Thus, the microvascular perfusion of the myocardium is compromised, affecting its metabolic functions and biochemistry. However, further multi-center, multi-participant clinical, and radiological correlated studies are required to confirm this hypothesis.

The levels of CRP, d-dimer, ferritin, cardiac troponin, and IL-6 have shown to be elevated in patients with COVID-19 and can also be considered significant predictors of adverse clinical outcomes (21). The meta-analysis by Lippi et al. showed that elevated cTnI, a cardiac biomarker, can detect cardiac damage and predict disease progression (22). In our study, of all the laboratory markers, cTnI had the highest predictive value for mortality. The high diagnostic power of these biomarkers indicates a significant potential for use in clinical applications.

The present study highlights the significant role of EAT volume changes in predicting mortality in patients with COVID-19. The findings demonstrate that a decrease in EAT volume exceeding 3.78% during hospitalization is a robust predictor of mortality, emphasizing its potential as a novel biomarker for risk stratification. Furthermore, the microvascular and endocrine interactions between EAT and the myocardium highlight its active contribution to the pathophysiology of the disease, including inflammatory and thrombotic processes.

This study further validates the predictive utility of cardiac cTnI alongside EAT volume changes, both of which demonstrated high diagnostic power in mortality prediction. These findings provide a deeper understanding of the interplay between inflammation, cardiac injury and adipose tissue dynamics induced by SARS-CoV-2.

The need for further studies with larger, multicenter cohorts and prospective designs is indicated to confirm these results and explore the long-term implications of EAT volume changes. The integration of EAT volume assessment with other laboratory markers in clinical practice holds the potential to enhance prognostic accuracy and guide individualized treatment strategies for patients with severe acute respiratory syndrome caused by the novel coronavirus.

Limitations: This study has several limitations. First, its retrospective design inherently limits the ability to establish causality and introduces potential selection bias. Second, we did not include long-term follow-up data, which could provide valuable insights into the persistence of EAT volume changes and their long-term impact on cardiovascular health and overall prognosis in COVID-19 patients. Further prospective studies with larger cohorts and extended follow-up periods are warranted to confirm and expand upon our findings. Third, BMI, a major determinant of visceral adiposity and EAT volume, was not available for all patients and therefore could not be incorporated into the analysis. This omission may confound the relationship between EAT dynamics and mortality, as baseline adiposity could influence both EAT volume and clinical outcomes. Fourth, the cohort reflects patients from early 2021, a period before widespread vaccination and before standardized treatment protocols, including routine use of corticosteroids and antiviral agents. Consequently, the applicability of our findings to contemporary patient populations may be limited. Finally, the pathophysiological mechanisms we propose to explain the association between decreases in EAT volume and mortality—such as microvascular injury, metabolic stress, and altered adipokine profiles—are hypothetical and were not directly investigated in this study. Future mechanistic and prospective studies integrating imaging, biochemical, and clinical data are needed to validate these hypotheses.

Authors' Contributions

BAD: Conceptualization, Formal Analysis, Methodology, Writing – review & editing.

EC: Conceptualization, Formal Analysis, Writing – original draft.

EO: Conceptualization, Data curation, Formal Analysis.

MBG: Formal Analysis, Data curation, Writing – original draft.

MV: Conceptualization, Methodology, Formal Analysis, Writing – review & editing.

List of Abbreviations:

EAT: Epicardial adipose tissue

cTnI: Troponin I

CT: computed tomography

CRP: C-reactive protein

VAT: Visceral adipose tissue

ACE2: Angiotensin-converting enzyme 2

IL-6: Interleukin 6

HDL: high density lipoprotein

LDH: Lactate dehydrogenase

LDL: Low-density lipoprotein

N/L Ratio: Neutrophil-to-lymphocyte ratio

Declaration

Funding: The authors have no financial or proprietary interests in any material discussed in this article.

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

Ethics approval: This study protocol was reviewed and approved by [Ankara Bilkent City Hospital Scientific research evaluation board], approval number [E1-21-2113].

Data Availability: The data that support the findings of this study are available on request from the corresponding author.

Acknowledgements: None declared.

References

1. Fukushima T, Maetani T, Chubachi S, et al. Epicardial adipose tissue measured from analysis of adipose tissue area using chest CT imaging is the best potential predictor of COVID-19 severity. Metabolism 2024; 150.
2. Petrilli CM, Jones SA, Yang J, 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.
3. Ji D, Zhang M, Qin E, et al. Obesity, diabetes, non-alcoholic fatty liver disease and metabolic dysfunction associated fatty liver disease are proinflammatory hypercoagulable states associated with severe disease and thrombosis in Covid-19. Metabolism 2021; 115.
4. Lee H, Chubachi S, Namkoong H, et al. Effects of mild obesity on outcomes in Japanese patients with COVID-19: a nationwide consortium to investigate COVID-19 host genetics. Nutrition & Diabetes 2022; 12: 1-8.
5. Caër C, Rouault C, Le Roy T, et al. Immune cell-derived cytokines contribute to obesity-related inflammation, fibrogenesis and metabolic deregulation in human adipose tissue. Sci Rep 2017; 7(1).
6. Abraham TM, Pedley A, Massaro JM, et al. Association between visceral and subcutaneous adipose depots and incident cardiovascular disease risk factors. Circulation 2015; 132: 1639-1647.
7. Fosbøl MO, Zerahn B. Contemporary methods of body composition measurement. Clin Physiol Funct Imaging 2015; 35: 81-97.
8. Maranduca MA, Tanase DM, Cozma CT, et al. The Impact of Angiotensin-Converting Enzyme-2/Angiotensin 1-7 Axis in Establishing Severe COVID-19 Consequences. Pharmaceutics 2022; 14(9).
9. Meyer HJ, Aghayev A, Hinnrichs M, et al. Epicardial Adipose Tissue as a Prognostic Marker in COVID-19. In Vivo (Brooklyn) 2024; 38: 281-285.
10. Bihan H, Heidar R, Beloeuvre A, et al. Epicardial adipose tissue and severe Coronavirus Disease 19. Cardiovasc Diabetol 2021; 20(1).
11. Mehta R, Bello-Chavolla OY, Mancillas-Adame L, et al. Epicardial adipose tissue thickness is associated with increased COVID-19 severity and mortality. Int J Obes 2022; 46: 866-873.
12. Bouadma L, Lescure FX, Lucet JC, et al. Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. Intensive Care Med 2020; 46: 579-582.
13. Grodecki K, Lin A, Razipour A, et al. Epicardial adipose tissue is associated with extent of pneumonia and adverse outcomes in patients with COVID-19. Metabolism 2021; 115: 154436.
14. Malavazos AE, Goldberger JJ, Iacobellis G. Does epicardial fat contribute to COVID-19 myocardial inflammation? Eur Heart J 2020; 41: 2333.
15. Knight SR, Ho A, Pius R, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ 2020; 370: 22.
16. Long B, Brady WJ, Koyfman A, et al. Cardiovascular complications in COVID-19. Am J Emerg Med 2020; 38: 1504.
17. Levi M, Thachil J, Iba T, et al. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol 2020; 7: e438-e440.
18. Sonmez F, Yurtlu TS. Epicardial adipose and pre-sternal subcutaneous tissues associated with extent of pneumonia and hospitalization in COVID-19. The European Research Journal 2023; 9: 840-847.
19. Marcucci M, Fogante M, Corrado Tagliati, et al. Cut-off point of CT-assessed epicardial adipose tissue volume for predicting worse clinical burden of SARS-CoV-2 pneumonia. Emerg Radiol 2022; 1: 3.
20. Slipczuk L, Castagna F, Schonberger A, et al. Incidence of new-onset atrial fibrillation in COVID-19 is associated with increased epicardial adipose tissue. Journal of Interventional Cardiac Electrophysiology 2022; 64: 383-391.

21. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clinical chemistry and laboratory medicine. 2020; 58: 1131-1134.

22. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): evidence from a meta-analysis. Progress in cardiovascular diseases 2020; 63: 390.