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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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The Association of Chest CT-based Measurements with Myocardial Injury in Critically Ill Patients with COVID-19

COVİD-19'lu Kritik Hastalarda Toraks BT Tabanlı Ölçümlerin Miyokard Hasarı ile İlişkisi

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ABSTRACT *Objective:* Myocardial injury incidence is high in critically ill patients with coronavirus disease-2019 (COVID-19) and mortality increases in COVID-19 patients with myocardial injury. Our objective was to determine the association between chest computed tomography (CT)-based measurements and myocardial injury in critically ill patients with COVID-19.
Materials and Methods: We conducted a single-center cohort study of patients admitted to the intensive care unit (ICU) with a diagnosis of COVID-19 who underwent chest CT. Myocardial injury was defined as high-sensitivity troponin I blood levels above the 99th percentile upper reference limit, independent of new abnormalities in electrocardiography and echocardiography. Demographic, clinical, laboratory results, and chest CT findings were collected at ICU admission.
Results: A total of 213 patients were included. Of the 213 patients, 69 (32.4%) were female, and 144 (67.6%) were male. Myocardial injury incidence was 61.0% (n=130). Acute Physiology and Chronic Health Evaluation-II score [odds ratio (OR): 1.07, 95% confidence interval (CI): 1.02-1.12, p=0.005], having a chest CT severity score ≥18 (OR: 2.85, 95% CI: 1.29-6.32, p=0.010), having any coronary artery calcification (CAC) (OR: 2.45, 95% CI: 1.09-5.52, p=0.030), and age (OR: 1.04, 95% CI: 1.01-1.08, p=0.041), as factors independently associated with an increased risk of myocardial injury.
Conclusion: The incidence of myocardial injury is high in critically ill COVID-19 patients. Chest CT severity score ≥18 and presence of CAC are practical and valuable tools readily available from existing chest CT to predict myocardial injury in critically ill patients with COVID-19.
Keywords: Chest CT severity score, coronary artery calcification, critical care, intensive care unit, myocardial injury, SARS-CoV-2

ÖZ *Amaç:* Koronavirüs hastalığı-2019 (COVİD-19) olan kritik hastalarda miyokardiyal yaralanma insidansı yüksektir ve miyokard yaralanması olan COVİD-19 hastalarında mortalite artar. Amacımız, COVİD-19'lu kritik hastalarda toraks bilgisayarlı tomografi (BT) tabanlı ölçümler ile miyokard hasarı arasındaki ilişkiyi belirlemekti.
Gereç ve Yöntem: Tek merkezli kohort çalışmamız toraks BT çekilen ve COVİD-19 tanısı ile yoğun bakım ünitesine kabul edilen hastalar üzerinde gerçekleştirildi. Miyokard hasarı, elektrokardiyografi ve ekokardiyografideki yeni anormalliklerden bağımsız olarak, high-sensitivity troponin I kan seviyesinin 99. persentil üst referans sınırının üzerinde olması olarak tanımlandı. Hastaların demografik, klinik, laboratuvar sonuçları ve toraks BT bulguları kaydedildi.
Bulgular: Toplam 213 hasta dahil edildi. İki yüz on üç hastanın 69'u (%32,4) kadın, 144'ü (%67,6) erkekti. Miyokardiyal yaralanma insidansı %61,0 (n=130) idi. Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II skoru [olasılık oranı (OO): 1,07, %95 güven aralığı (GA): 1,02-1,12, p=0,005], toraks BT şiddet skoru ≥18 (OO: 2,85, %95 GA: 1,29-6,32, p=0,010), herhangi bir koroner arter kalsifikasyonu varlığı (OO: 2,45, %95 GA: 1,09-5,52, p=0,030) ve yaş (OO: 1,04, %95 GA: 1,01-1,08, p=0,041), miyokardiyal yaralanma riskini bağımsız olarak artıran faktörlerdi.
Sonuç: Kritik hastalığı olan COVİD-19 hastalarında miyokard yaralanması insidansı yüksektir. Toraks BT şiddet puanı ≥18 ve koroner arter kalsifikasyonu varlığı, COVİD-19'lu kritik hastalarda miyokard hasarını tahmin etmek için halihazırda çekilmiş olan toraks BT üzerinden kolayca elde edilebilen pratik ve değerli parametrelerdir.
Anahtar Kelimeler: Toraks BT şiddet skoru, koroner arter kalsifikasyonu, yoğun bakım, yoğun bakım ünitesi, miyokard yaralanması, SARS-CoV-2

Introduction

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), can cause various cardiovascular disorders such as myocardial injury (1,2).

The etiology of COVID-19 associated myocardial injury, which is mostly defined by the elevation of troponin I level in the absence of acute coronary syndrome, has not yet been fully clarified. The trigger of acute coronary events, a direct viral effect, inflammatory damage of the heart, and development of exacerbation of heart failure are several putative mechanisms (3,4).

The incidence of COVID-19 associated acute myocardial injury ranges from 16.1% to 23.8% in hospitalized patients (5) and up to 53.2% in critically ill patients (6,7). Mortality increases in patients with myocardial injury with a diagnosis of COVID-19, independent of the presence of cardiovascular disease (8,9).

Non-contrast chest computed tomography (CT) provides significant benefits in diagnosing, managing, and monitoring the progression of the COVID-19 disease (10). Chest CT enables measurements of CT severity score, which is associated with inflammation, oxygen requirement, length of hospital stay, and mortality in COVID-19 patients (11-13). Chest CT can provide additional potential clinical significant parameters including ascending aortic (AA) diameter, cardiothoracic ratio (CTR), pulmonary artery (PA) diameter, and coronary artery calcification (CAC) (14-17). A recent study of hospitalized patients, including both stable and intensive care unit (ICU) patients, demonstrated that enlarged PA diameter was independently associated with myocardial injury (18). However, since many potential factors can cause myocardial injury, the association between myocardial injury and chest CT-based measurements should be analyzed in detail with other proven risk factors such as underlying cardiovascular disease (6-9), COVID-19-specific high inflammatory burden (6), and critical illness disease severity (6,7).

In this study, we aimed to determine the association between chest CT-based measurements and myocardial injury in critically ill patients with COVID-19.

Materials and Methods

Study Population

This retrospective cohort study was conducted in the adult ICU of our center after the approval of the Dokuz Eylül University Non-Invasive Research Ethics Committee (decision no: 2021/05-08, date: 15.02.2021) and the Turkish Ministry of Health. All adult patients (age ≥18 years) who were admitted to the ICU with the diagnosis of COVID-19 disease between March 2020 and January 2021 and had a chest CT image were included in the study. A reverse transcriptase-polymerase chain reaction test was used in respiratory samples to confirm SARS-CoV-2.

Factors affecting high-sensitivity (HS)-troponin levels, such as a history of the acute coronary syndrome, cardiopulmonary resuscitation, and pulmonary thromboembolism after the diagnosis of COVID-19, were determined as the exclusion criteria of the study. Patients with a history of coronary artery stenting were excluded for impaired quantitative CAC measurement.

Definitions and Measurements

Myocardial injury was defined as serum HS-troponin-I levels above the 99th percentile upper reference limit without any new and specific abnormality in echocardiography and electrocardiography (2). Patients were categorized into two groups according to the presence or absence of myocardial injury. In this study, only the patients' initial CT examinations at admission were evaluated. The highest value of serum HS-troponin-I levels was recorded in the first 24 hours of admission to the ICU.

Chest CT Technique and Image Interpretation

Non-contrast chest CT was performed in clinically suspected patients in line with the recommendations of our national COVID-19 guidelines. Images were obtained from A 64-channel multidetector CT scanner (Brilliance, Philips Medical Systems) reserved for only COVID-19 suspected patients. CT examinations were performed without an intravenous contrast medium. Chest CT imaging protocol was as follows: 120 kVp, 80 mA, slice thickness 1.5 mm, and high-spatial-frequency reconstruction algorithm (bone algorithm). 2 mm reconstruction interval and 1.5 mm slice thickness were used for coronal and sagittal image reconstruction.

Chest CT examinations were independently interpreted by radiologists with 15 and 4 years of experience and the final decision was reached by consensus. Radiologists were blinded to clinical characteristics and laboratory data of the patients.

All scans were reviewed for the assessment of pneumonia associated with COVID-19. A scoring system

that demonstrates a typical and indeterminate appearance for COVID-19 was used to estimate the pulmonary involvement of CT scans (11-13). Each of the five lung lobes was visually scored on a scale of 0 to 5. No involvement was scored as 0 points. Involvements were scored, 1 point for less than 5%; 2 points for 5-25%; 3 points for 26-49%; 4 points for 50-75%; and 5 points for more than 75%. The total CT score was obtained by summing the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement). Patients were categorized into mild (7 or less), moderate (8-17), and severe (18 or more) groups according to the total score. Atypical CT scans were not scored because the radiological findings were not compatible with COVID-19. CTR measurements (dividing the largest transverse cardiac diameter from outer-to-outer myocardium by the largest transverse thoracic diameter from inner to the inner chest wall, usually at the level of the diaphragmatic apex) were obtained from axial CT images. PA/AA ratio was calculated from the axial CT slice by dividing the diameter of PA measured at the level of the PA bifurcation by AA diameter measured at the level of the right PA. The average transverse/anteroposterior inferior vena cava (IVC) diameter ratio was measured by dividing the maximum transverse diameters of IVC by maximum anteroposterior diameters at the level of the right diaphragmatic crus (Figure 1, 2) (19). In this study, we also measured the maximum transverse diameter of the arcus aorta from axial CT images and the maximum transverse diameter of the trachea at the same slice. Abnormal twists and turns (tortuosity) of the aorta were also evaluated at coronal and sagittal CT images and were recorded. The presence of CAC was determined using a simple patient-based score (17) and defined as any area

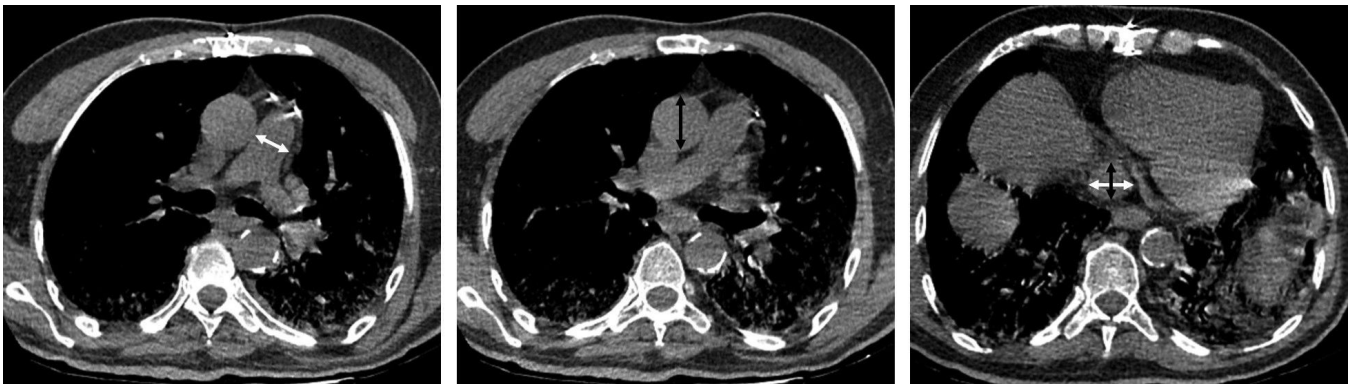

Figure 1. PA to A ratio was calculated from the axial CT slice by dividing the diameter of PA measured at the level of the PA bifurcation (white arrow) (A) by ascending aortic diameter measured at the level of right pulmonary artery (black arrow) (B). The average diameters of IVC were measured at the level of the right diaphragmatic crus by dividing the maximum transverse diameters of IVC (white arrow) by maximum anteroposterior diameters (black arrow) (C)
PA: Pulmonary artery, CT: computed tomography, IVC: inferior vena cava

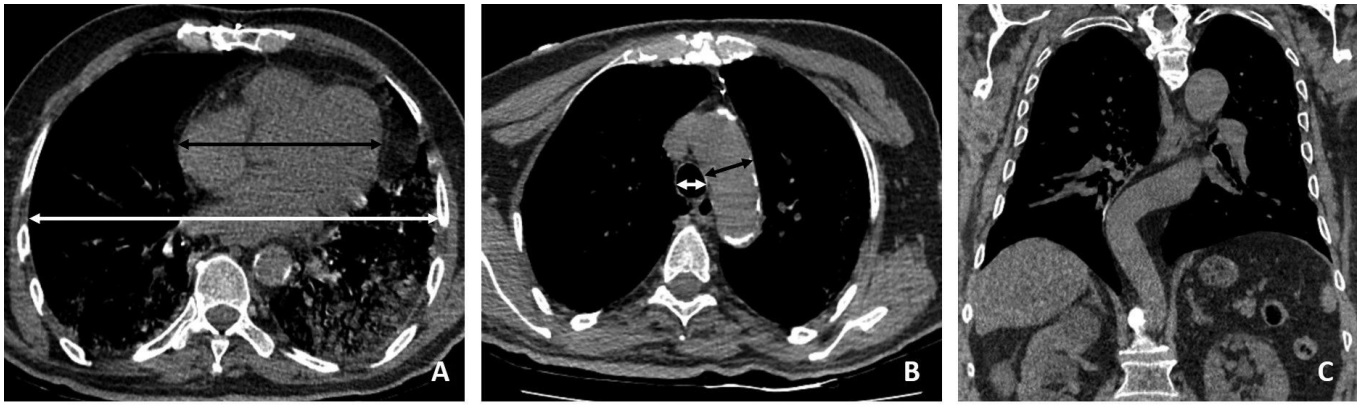

Figure 2. Cardiothoracic ratio was calculated from axial CT images by dividing the greatest transverse cardiac diameter from outer to outer myocardium (black arrow) by the greatest transverse thoracic diameter from inner to inner chest wall (white arrow), usually at the level of the diaphragmatic apex (A). Measurement of maximum transverse diameter of arcus aorta from axial CT images and the maximum transverse diameter of trachea at the same slice (B). Abnormal twists and turns (tortuosity) of the aorta wasvels evaluated at coronal and sagittal CT images (C)
CT: Computed tomography

≥1 mm^2 in the coronary artery tract with a density >130 Hounsfield units (20). All measurements were performed using mediastinal windows.

Variables

The demographic data, medical history, anthropometric measurements, Acute Physiology and Chronic Health Evaluation (APACHE)-II, Sequential Organ Failure Assessment (SOFA) scores, and Charlson Comorbidity index (CCI) were recorded. Blood pressure records were obtained from the first measurement of ICU admission. Major events during ICU stay [secondary bacterial infections, septic shock, acute kidney injury (AKI), renal replacement therapy, need for invasive mechanical ventilation (IMV)] were recorded. Mortality, length of stay in the ICU and hospital stay were recorded.

Outcomes

Our primary outcome was to assess the association of chest CT-based measurements with myocardial injury in ICU patients with COVID-19. The secondary outcome was to identify other clinical and biochemical risk factors for myocardial injury.

Statistical Analysis

All continuous variables were expressed as a median and interquartile range, and categorical variables were expressed as numbers and percentages. Continuous variables between groups were compared with the Mann-Whitney U test. Categorical variables were compared with chi-square or Fisher's Exact test. A multivariate logistic regression analysis model was performed to evaluate the independent risk factors for myocardial injury. To construct the model, a purposeful selection method was used to select a subset of the covariates considered clinically important, adjusting for confounding factors and statistical significance. For each independent risk factor, an adjusted odds ratio (OR) and a 95% confidence interval (CI) were reported. A two-tailed p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences Version 24, IBM Corp., Armonk, N.Y., USA).

Results

General Characteristics

A total of 213 eligible ICU patients, 69 (32.4%) female and 144 (67.6%) male, with a diagnosis of COVID-19 infection were included in the study. Of them, 130 had (61.0%) myocardial injury.

Patients with myocardial injury were significantly older [75.5 (67.8-83.0) vs. 66.0 (56.0-76.0) years; p<0.001; Table 1] and had a higher prevalence of comorbidities including hypertension (84.6% vs. 69.9%; p=0.015) and congestive heart failure (18.5% vs. 7.2%; p=0.026) than patients without myocardial injury. The median CCI score was higher in patients with myocardial injury than the patients without myocardial injury as well [6.0 (4.0-8.0) vs. 4.0 (2.0-5.0); p<0.001]. In patients with myocardial injury median APACHE-II score [24.0 (16.0-30.0) vs. 16.0 (11.0-23.0); p<0.001], and median SOFA score at admission to ICU [6.0 (5.0-8.0) vs. 4.0 (3.0-6.0); p<0.001] were higher than in patients without myocardial injury.

Laboratory Findings

In patients with myocardial injury, median D-dimer levels [1.80 (1.20-4.70) vs. 1.10 (0.60-2.30) µg/mL; p<0.001], and median B-type natriuretic peptide levels [165.0 (46.0-519.8) vs. 53.6 (27.0-118.0) pg/mL; p<0.001] were higher than in patients without myocardial injury. The median levels of blood urea nitrogen, creatinine, aspartate transaminase, C-reactive protein, and procalcitonin were higher in patients with myocardial injury than in patients without myocardial injury.

Major Events During ICU Stay

The need for the IMV was higher in patients with myocardial injury than patients without myocardial injury (90.0% vs. 61.4%; p<0.001). In patients with myocardial injury, vasopressor use (76.2% vs. 57.8%; p=0.006), AKI (73.8% vs. 50.6%; p=0.001), and secondary bacterial infections (63.1% vs. 48.2%; p=0.034) were more frequent than patients without myocardial injury. Both ICU mortality (80.8%, vs. 54.2%; p<0.001) and hospital mortality (83.8%, vs. 54.2%; p<0.001) were higher in patients with myocardial injury than in patients without myocardial injury.

CT Findings

In patients with myocardial injury median chest CT severity score was higher when compared with patients without myocardial injury [16.0 (12.0-20.0) vs. 13.5 (10.0-18.3); p=0.021; Table 2]. Patients with a chest CT severity score ≥18 were more common in the myocardial injury group than the no myocardial injury group (43.9% vs. 26.9%; p=0.021). CAC was detected in 153 (71.8%) patients. Patients with CAC were more common in the myocardial

injury group than the no myocardial injury group (81.5% vs. 56.6%; p<0.001). In patients with myocardial injury median CTR was higher when compared with patients without myocardial injury [0.54 (0.50-0.59) vs. 0.51 (0.47-0.54); p<0.001].

Risk Factors for Myocardial Injury

Multivariable analysis (Table 3) showed APACHE-II score (OR: 1.07, 95% CI: 1.02-1.12, p=0.005), having a chest CT severity score ≥18 (OR: 2.85, 95% CI: 1.29-6.32, p=0.010), having any CAC (OR: 2.45, 95% CI: 1.09-5.52, p=0.030), and age (OR: 1.04, 95% CI: 1.01-1.08, p=0.041), as factors independently associated with an increased risk of myocardial injury.

Discussion

This retrospective cohort study has some important results. First, myocardial injury incidence in critically ill COVID-19 patients is 61.0%. Second, APACHE-II score, chest CT severity score ≥18, presence of any CAC, and age are independently associated with myocardial injury in critically ill COVID-19 patients. Third, hospital mortality is higher in patients with myocardial injury than in patients without myocardial injury.

The incidence of acute myocardial injury is between 16.1-23.8% in hospitalized patients with COVID-19 (5), and up to 53.2% in critically ill patients with COVID-19 (7). In this study, the incidence of myocardial injury was relatively high, with a rate of 61.0%. As emphasized in previous studies, advanced age and underlying cardiovascular comorbidities are important risk factors for myocardial injury (6-9). Similarly, in our study, hypertension and congestive heart failure comorbidities were more common in patients with myocardial injury than the patients without myocardial injury. Additionally, advanced age was an independent risk factor for the risk of myocardial injury in our analysis. The high incidence of myocardial injury in our study may be due to the relatively advanced age of our population and the presence of multiple complicated comorbid diseases.

Previous studies evaluated the correlation between myocardial injury and disease severity scores, and they demonstrated that patients with myocardial injury had higher APACHE-II scores than patients without myocardial injury (6,7). Similarly, in our study, high APACHE-II scores were independently associated with myocardial injury. APACHE-II score is a predictive scoring system that measures disease severity to predict mortality in the ICU (21). However, since the APACHE-II score is not a disease-specific score, it may not predict the severity of the COVID-19 disease. Some studies used a chest CT score to estimate COVID-19 disease severity and outcomes (11-13). CT severity score was positively correlated with inflammatory biomarkers (11-13), oxygen requirement (11), disease severity (12,13), disease progression (13), and length of hospital stays (11) in patients with COVID-19. Likewise, short-term mortality was highly predicted with a CT score ≥18 (12). In this study, we evaluated the association between chest CT score and myocardial injury. We demonstrated that a CT score ≥18 is also independently associated with myocardial injury.

CAC is an important biomarker that represents atherosclerosis burden and the absence of calcification most likely indicates a low atherosclerotic plaque load (22). CAC is a strong predictor of cardiovascular events (especially coronary heart disease) and all-cause mortality in the general population (23,24). CAC has been studied in patients with COVID-19 as well. In a study of 209 hospitalized COVID-19 patients without pre-existing cardiovascular disease, the presence of any CAC on chest CT was significantly associated with the mechanical ventilation requirement (non-invasive or invasive) or death within 30 days of hospitalization (20). In another study of 180 COVID-19 patients who underwent non-contrast chest CT, patients with any CAC were more likely to need intubation and die than those who did not have CAC (25). In the present study, we demonstrated that the presence of any CAC is independently associated with myocardial injury.

Mortality in patients with myocardial injury is high, ranging between 37.4-59.6% in hospitalized patients (2,9,26), and 85.3% in ICU patients (6,7). Mortality increases in COVID-19 patients with myocardial injury regardless of the presence of cardiovascular disease (8,9). The myocardial injury was an independent risk factor for high mortality in a small study including 64 critically ill patients with COVID-19 (6). In our study, the hospital mortality rate was higher in patients with myocardial injury than the patients without myocardial injury.

This study has several limitations. First, cardiac complications related to myocardial injury were not evaluated. Second, the effect of cardiac movements and respiratory changes on the chest CT measurements was not evaluated.

Table 1. Demographic and clinical characteristics in patients with and without myocardial injury (univariate analysis)				
Characteristics	**All cases**	**Myocardial injury**	**No myocardial injury**	**p-value**
	(n=213)	**(n=130)**	**(n=83)**	
Age, years	71.0 (62.0-80.0)	75.5 (67.8-83.0)	66.0 (56.0-76.0)	<0.001
Gender				
Female	69 (32.4)	48 (36.9)	21 (25.3)	0.09
Male	144 (67.6)	82 (63.1)	62 (74.7)	
Smoking history	46 (21.6)	27 (20.8)	19 (22.9)	0.74
Body mass index, kg/m^2	26.7 (24.2-29.5)	26.4 (24.2-29.4)	27.3 (24.0-30.1)	0.19
Comorbidities				
Hypertension	168 (78.9)	110 (84.6)	58 (69.9)	0.015
Congestive heart failure	30 (14.1)	24 (18.5)	6 (7.2)	0.026
Chronic atrial fibrillation	10 (4.7)	10 (7.7)	1 (1.2)	0.054
Coronary artery disease	55 (25.8)	38 (29.2)	17 (20.5)	0.20
Neurological disease [1]	38 (17.8)	29 (22.3)	9 (10.8)	0.043
Chronic kidney disease	51 (23.9)	41 (31.5)	10 (12.0)	0.001
Dialysis dependent	6 (2.8)	5 (3.8)	1 (1.2)	0.41
Diabetes mellitus	91 (42.7)	53 (40.8)	38 (45.8)	0.48
Hyperlipidemia	45 (21.1)	27 (20.8)	18 (21.7)	0.87
COPD	25 (11.7)	13 (10.0)	12 (14.5)	0.38
Malignancy [2]	23 (10.8)	18 (13.8)	5 (6.0)	0.11
Chronic liver disease	1 (0.5)	1 (0.8)	0 (0.0)	N/A
Blood pressure measurement				
Systolic blood pressure	135 (110-151)	128 (110-150)	140 (110-159)	0.10
Mean arterial blood pressure	84 (71-100)	82 (70-99)	73 (87-100)	0.94
Prior medication history				
ACE-inhibitors or ARBs	97 (45.5)	60 (46.2)	37 (44.6)	0.89
Diuretics	82 (38.5)	52 (40.0)	30 (36.1)	0.67
Beta-blockers	75 (35.2)	44 (33.8)	31 (37.3)	0.66
Calcium channel blockers	50 (23.5)	29 (22.3)	21 (25.3)	0.62
Alfa-blockers	11 (5.2)	7 (5.4)	4 (4.8)	1.00
Anti-arrhythmic agents	6 (2.8)	5 (3.8)	1 (1.2)	0.41
Anti-hyperlipidemic agents	45 (21.1)	28 (21.5)	17 (20.5)	1.00
Insulin	45 (21.1)	27 (20.8)	18 (21.7)	0.87
1 oral antidiabetic agent	34 (16.0)	19 (14.6)	15 (18.1)	0.57
>1 oral antidiabetic agents	31 (14.6)	14 (10.8)	17 (20.5)	0.07
APACHE-II	22.0 (13.0-28.0)	24.0 (16.0-30.0)	16.0 (11.0-23.0)	<0.001
SOFA [3]	5.0 (4.0-7.0)	6.0 (5.0-8.0)	4.0 (3.0-6.0)	<0.001
CCI	5.0 (3.0-7.0)	6.0 (4.0-8.0)	4.0 (2.0-5.0)	<0.001
Laboratory data [4]				
HS-troponin I, ng/L	27.0 (9.6-142.5)	84.0 (30.7-465.2)	8.60 (6.0-11.4)	<0.001
D-dimer, µg/mL	1.50 (0.90-3.50)	1.80 (1.20-4.70)	1.10 (0.60-2.30)	<0.001
BNP (plasma), pg/mL	87.0 (38.2-290.5)	165.0 (46.0-519.8)	53.6 (27.0-118.0)	<0.001
BNP >100 pg/mL [5]	101 (47.4)	78 (60.0)	23 (27.7)	<0.001
BUN, mg/dL	31.6 (24.0-52.5)	40.5 (25.0-59.4)	29.0 (20.0-39.0)	<0.001
Creatinine, mg/dL	1.10 (0.81-1.78)	1.31 (0.89-1.98)	0.96 (0.74-1.20)	<0.001
AST, U/L	54.0 (37.0-90.0)	63.0 (40.0-102.8)	48.0 (34.0-75.0)	0.005
ALT, U/L	37.0 (24.0-62.5)	37.0 (23.0-61.5)	39.0 (27.0-63.0)	0.50

Table 1. continued

Characteristics	All cases	Myocardial injury	No myocardial injury	p-value
	(n=213)	(n=130)	(n=83)	
CRP, mg/L	156 (85-235)	172 (104-254)	137 (68-215)	0.014
Procalcitonin, ng/mL	0.34 (0.14-1.49)	0.54 (0.20-1.81)	0.17 (0.08-0.41)	<0.001
Glucose, mg/dL	139 (110-185)	143 (108-190)	135 (112-162)	0.22
Total bilirubin, mg/dL	0.83 (0.63-1.12)	0.88 (0.63-1.12)	0.78 (0.61-1.16)	0.35
LDH, U/L	546 (428-699)	554 (451-728)	521 (388-659)	0.10
Ferritin ng/mL	617 (363-1129)	615 (345-1156)	632 (374-1115)	0.99
WBC, $x10^3$/µL	11.3 (80.5-150.5)	12.6 (9.2-15.6)	10.1 (7.0-13.1)	0.002
Neutrophil, $x10^3$/µL	9.8 (6.8-13.8)	10.4 (7.5-14.4)	8.6 (5.6-11.6)	0.004
Lymphocyte, $x10^3$/µL	0.50 (0.30-0.90)	0.50 (0.40-10.25)	0.50 (0.30-0.80)	0.28
Lymphocyte percentages, %	5.5 (3.1-8.5)	5.1 (2.8-8.6)	5.7 (3.9-8.2)	0.55
Hemoglobin, g/dL	12.4 (10.8-13.8)	11.8 (10.2-13.5)	13.2 (12.0-14.3)	<0.001
Platelet, $x10^3$/µL	255 (171-335)	243 (170-332)	275 (177-354)	0.31
Arterial blood gas analysis[4]				
pH	7.41 (7.34-7.47)	7.39 (7.31-7.46)	7.44 (7.37-7.47)	0.006
HCO_3, mmol/L	22.0 (19.9-25.0)	22.0 (18.7-24.0)	24.0 (21.0-26.0)	0.001
PaO_2, mmHg	61.0 (52.0-70.7)	61.0 (51.8-70.1)	62.0 (52.0-74.0)	0.30
PaO_2/FiO_2	110 (93-132)	106 (88-127)	115 (98-148)	0.010
PaO_2/FiO_2 <150, n (%)	191 (89.7)	121 (93.1)	70 (84.3)	0.06
$PaCO_2$, mmHg	34.0 (29.0-43.0)	35.0 (29.0-44.0)	33.0 (30.0-38.0)	0.27
Lactate, mmol/L	2.00 (1.40-3.00)	2.05 (1.40-3.00)	2.00 (1.40-3.10)	0.98
Events/therapies during ICU stay				
IMV	168 (78.9)	117 (90.0)	51 (61.4)	<0.001
Vasopressor requirement[6]	147 (69.0)	99 (76.2)	48 (57.8)	0.006
Acute kidney injury	138 (64.8)	96 (73.8)	42 (50.6)	0.001
Renal replacement therapy	51 (23.9)	37 (28.5)	14 (16.9)	0.07
Secondary bacterial infections	122 (57.3)	82 (63.1)	40 (48.2)	0.034
New-onset atrial fibrillation	28 (13.1)	16 (12.3)	12 (14.5)	0.68
Treatment for COVID-19				
Favipiravir	203 (95.3)	121 (93.1)	82 (98.8)	0.09
LMWH	203 (95.3)	123 (94.6)	80 (96.4)	0.74
ASA	164 (77.0)	96 (73.8)	68 (81.9)	0.19
Dipyridamole	130 (61.0)	76 (58.5)	54 (65.1)	0.39
Corticosteroids	167 (78.4)	99 (76.2)	68 (81.9)	0.39
Pulse corticosteroid	87 (40.8)	53 (40.8)	34 (41.0)	1.00
Hydroxychloroquine	47 (22.1)	31 (23.8)	16 (19.3)	0.50
Tocilizumab	24 (11.3)	12 (9.2)	12 (14.5)	0.27
Azithromycin	7 (3.3)	5 (3.8)	2 (2.4)	0.71
Length of ICU stay, days	8.0 (4.0-14.0)	9.0 (4.0-15.0)	8.0 (5.0-14.0)	0.99
Length of hospital stay, days	14.0 (9.0-21.0)	13.0 (8.0-20.0)	16.0 (12.0-21.0)	0.012
ICU mortality	150 (70.4)	105 (80.8)	45 (54.2)	<0.001
Hospital mortality	154 (72.3)	109 (83.8)	45 (54.2)	<0.001

All values are expressed as numbers (percentages) or median (interquartile range), [1]history of cerebrovascular disease or dementia, [2]includes hematological and solid organ malignancies, [3]calculated on the day of ICU admission, [4]tested on the day of ICU admission, [5]laboratory upper limit of BNP (100 pg/mL), [6]use of any dose of vasopressor. APACHE-II: Acute Physiology and Chronic Health Evaluation-II, ALT: alanine transaminase, AST: aspartate transaminase, ASA: acetylsalicylic acid, BUN: blood urea nitrogen, BNP: brain natriuretic peptide, CCI: Charlson Comorbidity index, COPD: chronic obstructive pulmonary disease, CPR: cardiopulmonary resuscitation, CRP: C-reactive protein, FiO_2: fraction of inspired oxygen, HS troponin I: high-sensitivity troponin I, ICU: intensive care unit, IMV: invasive mechanical ventilation, LDH: lactate dehydrogenase, LMWH: low molecular weight heparin, N/A: not applicable, PaO_2: partial pressure of arterial oxygen, $PaCO_2$: partial pressure of arterial carbon dioxide, RT-PCR: reverse transcription-polymerase chain reaction, SOFA score: The Sequential Organ Failure Assessment score, WBC: white blood cell count

Table 2. Chest CT-based measurements in patients with and without myocardial injury (univariate analysis)				
Characteristics	**All cases**	**Myocardial injury**	**No myocardial injury**	**p-value**
	(n=213)	**(n=130)**	**(n=83)**	
Chest CT severity score[1]	15.0 (10.0-20.0)	16.0 (12.0-20.0)	13.5 (10.0-18.3)	0.021
Chest CT severity score of 18 or more (severe group), n (%)[1]	68 (36.8)	47 (43.9)	21 (26.9)	0.021
Patients with any coronary artery calcification, n (%)	153 (71.8)	106 (81.5)	47 (56.6)	<0.001
Cardiothoracic ratio	0.52 (0.48-0.57)	0.54 (0.50-0.59)	0.51 (0.47-0.54)	<0.001
Aortic tortuosity, n (%)	32 (15.0)	27 (20.8)	5 (6.0)	0.003
AA diameter, mm	36.5 (34.1-39.1)	36.6 (34.1-39.6)	36.3 (34.1-38.7)	0.64
Arcus aorta diameter, mm	29.8 (27.7-31.9)	30.0 (27.5-32.5)	29.7 (27.7-31.4)	0.34
PA diameter, mm	28.5 (25.5-31.7)	28.8 (25.4-32.6)	28.5 (25.5-31.2)	0.49
PA/AA diameter ratio	0.77 (0.69-0.86)	0.77 (0.69-0.87)	0.77 (0.70-0.84)	0.71
T/AP IVC diameter ratio	1.26 (1.11-1.44)	1.26 (1.09-1.46)	1.27 (1.13-1.43)	0.84
T/AP trachea diameter ratio	0.96 (0.85-1.07)	0.96 (0.85-1.06)	0.97 (0.86-1.09)	0.43

All values are expressed as numbers (percentages) or median (interquartile range). [1]Chest CT severity score was calculated on 185 patients.
AA: Ascending aorta, CT: computed tomography, IVC: inferior vena cava, PA: pulmonary artery, T/AP: transverse/anteroposterior

Table 3. Logistic regression analysis for risk factors of myocardial injury		
	OR (95% CI)	**p-value**
APACHE-II score	1.07 (1.02-1.12)	0.005
Chest CT severity score of 18 or more	2.85 (1.29-6.32)	0.010
Patients with any coronary artery calcification	2.45 (1.09-5.52)	0.030
Age	1.04 (1.01-1.08)	0.041
Gender	1.06 (0.48-2.36)	0.886
Hypertension	1.16 (0.46-2.98)	0.751
Congestive heart failure	1.21 (0.36-4.04)	0.757
Coronary artery disease	0.73 (0.29-1.81)	0.503
Cardiothoracic ratio	1.05 (0.98-1.11)	0.192

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CI: confidence interval, CT: computed tomography, OR: odds ratio

Conclusion

Myocardial injury incidence in critically ill COVID-19 patients is 61.0%. The APACHE-II score, chest CT severity score ≥18, presence of any CAC, and age were independently associated with myocardial injury in critically ill patients with COVID-19. The chest CT severity score and the presence of CAC can be easily obtained from existing chest CT and are valuable in predicting the development of myocardial injury in critically ill patients with COVID-19.

Ethics

Ethics Committee Approval: This retrospective cohort study was conducted in the adult intensive care unit of our center after the approval of the Dokuz Eylül University Non-Invasive Research Ethics Committee (decision no: 2021/05-08, date: 15.02.2021) and the Turkish Ministry of Health.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.E., M.K., M.N.Y., M.C.Ö., B.C., N.G., Be.E., Design: B.E., N.S.G., M.K., M.N.Y., E.Y., N.G., Be.E., Data Collection and Process: B.E., M.K., M.N.Y., M.C.Ö., M.D., Analysis or Interpretation: B.E., N.S.G., M.K., M.N.Y., M.C.Ö., B.C., N.G., Be.E., Literature Search: B.E., M.K., M.N.Y., M.C.Ö., E.Y., B.C., N.G., Be.E., Writing: B.E., M.K., M.N.Y., M.C.Ö., E.Y., N.G., Be.E.

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