RESEARCH ARTICLE / *Araştırma Makalesi*

The Relationship of Mitral Anular Calcification with Mortality and Myocardial Injury in COVID-19 Patients

COVID-19 Hastalarında Mitral Anüler Kalsifikasyonun Mortalite ve Miyokard Hasarı ile İlişkisi

Savaş Özer[1], Eser Bulut[2], Ercan Aydin[1], Dilek Cahide Haznedar Kırcı[1], Ali Gökhan Özyıldız[3], Mustafa Peker[2], Oğuzhan Ekrem Turan[4]

[1] Trabzon Kanuni Training and Research Hospital Cardiology Clinic, Trabzon, Turkey
[2] Trabzon Kanuni Training and Research Hospital Radiology Clinic, Trabzon, Turkey
[3] Recep Tayyip Erdogan University Training and Research Hospital Cardiology Clinic, Rize, Turkey
[4] Dokuz Eylul University Faculty of Medicine Department of Cardiology, İzmir, Turkey

Yazışma Adresi / *Correspondence:*
Ercan Aydin
Trabzon Kanuni Training and Research Hospital Cardiology Clinic, Trabzon, Turkey
T: **+90 530 527 61 28** E-mail **: ercanaydin112@yahoo.com**

Geliş Tarihi / Received : **07.06.2022** Kabul Tarihi / Accepte: **07.09.2022**

Orcid :

Savaş Özer https://orcid.org/0000-0002-7073-4021
Eser Bulut https://orcid.org/0000-0002-6765-6552
Ercan Aydin https://orcid.org/0000-0001-8743-3762
Dilek Cahide Haznedar Kırcı https://orcid.org/0000-0002-2708-1408
Ali Gökhan Özyıldız https://orcid.org/0000-0003-0679-9434
Mustafa Peker https://orcid.org/0000-0002-9445-3355
Oğuzhan Ekrem Turan https://orcid.org/0000-0003-3557-1682

(Sakarya Tıp Dergisi / *Sakarya Med J* 2022, 12(3):544-551) DOI: 10.31832/smj.1126067

Abstract

Objective Coronavirus disease-2019 (COVID-19) can particularly affect the respiratory and cardiovascular systems and cause serious mortality. Mitral annular calcification (MAC) is a mitral valve pathology associated with cardiac mortality. We aimed to evaluate the effect of MAC on myocardial injury (MI) and mortality, which can develop secondary to COVID-19 infection.

Materials and Methods After applying the exclusion criteria, thorax computed tomography (CT) images of the remaining 1151 consecutive COVID-19 patients were evaluated. Calculation of MAC scores was done by two expert radiologists blinded to the study data. MI was defined as those with hs-TnI level (≥34 ng/dl). Patients included in the study were classified as having mortality and not occurring.

Results Male gender, advanced age (>65), hypertension, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease (CKD), coronary artery disease, heart failure and atrial fibrillation rates were statistically higher in the mortality group (p<0.05). The presence of MAC was 34.1% in the mortality group, while it was 16% in the survival group (p<0.001). MI was observed 49.3% in the mortality group, while it was 16.2% in the survival group (p<0.001). Presence of MAC was associated with MI (14.8% vs 38.7%, p<0.001). Age (OR=1.976, 95% CI 1.166-3.346, p=0.011), male gender (OR=1.784, 95% CI 1.101-2.892, p=0.019), CKD (OR=2.293, 95% CI 1.085-4.485, p=0.030), MI (OR=2.893, 95% CI 1.735-4.823, p<0.001) and advanced lung involvement on CT (OR=2.231, 95% CI 1.084-4.594, p=0.029) were the independent predictors of mortality

Conclusion In terms of MI and mortality risk in COVID-19 patients, it may be recommended to evaluate MAC from the CT images.

Keywords Coronavirus; COVID-19 infection; mitral annular calcification; myocardial injury, computed tomography

Öz

Amaç *Koronavirüs hastalığı-2019 (COVID-19) özellikle solunum ve kardiyovasküler sistemleri etkileyerek mortaliteye ve ciddi morbiditelere neden olabilir. Mitral halka şeklindeki kalsifikasyon (MAC), kardiyak mortalite ile ilişkili bir mitral kapak patolojisidir. Bu çalışmada, MAC'ın COVID-19 enfeksiyonuna sekonder gelişebilen miyokard hasarı (MI) ve mortalite üzerine etkisini değerlendirmeyi amaçladık.*

Gereç ve Yöntemle *Dışlama kriterleri uygulandıktan sonra geriye kalan 1151 ardışık COVID-19 hastasının toraks bilgisayarlı tomografi (BT) görüntüleri değerlendirildi. MAC puanlarının hesaplanması, çalışma verilerine kör olan iki uzman radyolog tarafından yapıldı. MI, hs-TnI düzeyi (≥34 ng/dl) olanlar olarak tanımlandı. Çalışmaya dahil edilen hastalar mortalitesi olan ve olmayan olarak sınıflandırıldı.*

Bulgular *Mortalite grubunda erkek cinsiyet, ileri yaş (>65), hipertansiyon, diabetes mellitus, kronik obstrüktif akciğer hastalığı, kronik böbrek hastalığı (KKD), koroner arter hastalığı, kalp yetmezliği ve atriyal fibrilasyon oranları istatistiksel olarak daha yüksekti (p<0.05). Mortalite grubunda MAC varlığı %34.1, sağkalım grubunda ise %16 idi (p<0.001). Miyokardiyal hasar mortalite grubunda %49.3, sağkalım grubunda ise %16.2 olarak saptandı (p<0.001). MAC varlığı MI ile ilişkiliydi (%14.8'e karşılık %38.7, p<0.001).Yaş (OR=1.976, 95% CI 1.166-3.346, p=0.011), erkek cinsiyet (OR=1.784, 95% CI 1.101-2.892, p=0.019), kronik böbrek yetersizliği (OR=2.293, 95% CI 1.085-4.485, p=0.030), MI (OR=2.893, 95% CI 1.735-4.823, p<0.001) ve küçük hücreli akciğer tutulumu (OR=2.231, 95% CI 1.084-4.594, p=0.029) mortalitenin bağımsız belirleyicileri idi.*

Sonuç *COVID-19 hastalarında MI ve mortalite riski açısından BT görüntülerinden MAC değerlendirilmesi önerilebilir.*

Anahtar Kelimeler *Koronavirüs; COVID-19 enfeksiyonu; mitral anüler kalsifikasyon; miyokard hasarı; bilgisayarlı tomografi*

INTRODUCTION

Coronavirus-2 (SARS-CoV-2) is a viral disease that causes severe acute respiratory syndrome. Coronavirus disease-2019 (COVID-19) affects the respiratory system and cardiovascular system and can cause mortality.[1] As the COVID-19 pandemic threatens global health, learning about the pathogenesis and clinical course of the disease can help identify therapeutic targets and guide the clinical approach.

Mitral annular calcification (MAC) is a chronic degenerative process in which micro-injuries and endothelial dysfunction result in calcium deposition on the fibrous support structure of the mitral valve.[2,3] Mitral annular calcification primarly develops in the posterior part of the mitral annulus and is often associated with athero-thrombosis risk factors.[4] The prevalence of MAC is between 8% and 15%, and it tends to increase in the elderly patient group, hypertension (HT), dyslipidemia, hypertrophic cardiomyopathy, aortic stenosis, and chronic kidney disease (CKD).[5] Mitral annular calcification is associated with cardiovascular mortality and various comorbidities including cardiovascular events.[6,7] Although MAC is usually asymptomatic, its clinical significance is its association with cardiovascular diseases and mortality.

Various pathologies have been identified associated with an increased risk of mortality in COVID-19 patients, such as embolic events, cardiovascular involvement secondary to the infection, presence of CAD, HT, chronic obstructive pulmonary disease (COPD), and CKD priot to the infection.[8,9] It has been reported that myocardium can be affected directly or through the cytokine storm in COVID-19 infection.[10] It has also been shown that increased cardiac troponin levels may be associated with poor prognosis in COVID-19 patients.[11] There is no literature data on myocardial injury and mortality rates in COVID-19 patients with MAC. In our study, we assessed the effect of MAC, which was evaluated by computed tomography (CT), on the development of myocardial injury and mortality rates in COVID-19 patients.

MATERIALS and METHODS

Patients, who were hospitalized between November 2020 and January 2021 with the diagnosis of COVID-19 and underwent thoracic CT were included in the study. COVID-19 was detected as a result of a sample taken from the nasopharynx using the polymerase chain reaction (PCR) test. Patients under 18, pregnant women, and those with suboptimal image quality were determined as exclusion criteria. A total of 55 patients were excluded from the study for various reasons; 14 patients under the age of 18, 23 were pregnant, and 54 had suboptimal image quality (Figure 1).

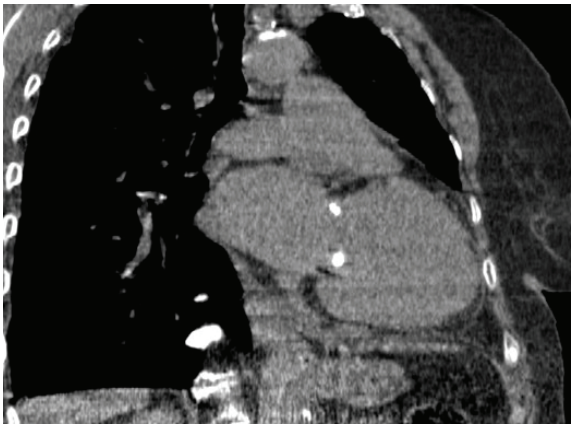

Figure 1.Evaluation of mitral anular calcification
A
• Sagittal plane: It is evaluated whether the calcification extended to the mitral valve in this plane.
• Mitral annular calcification was observed.
• Extension of calcification to mitral valves was not detected

The study continued with the remaining 1151 patients. Thoracic CT images of patients were performed within the first two days of hospitalization. The higher limit value of the troponin test kit in our laboratory in hospital was 34 ng/L. Myocardial injury was defined as being high-sensitive troponin I (hs-TnI) level ≥34 ng/dl at the time of hospitalization. Patients were divided into groups as those who died during hospitalization and those who were disc-

harged. The study was conducted within the framework of the principles stated in the Declaration of Helsinki and was approved by the ethics committee of the hospital where the study was conducted (No: 2021/61). Before the patients were included in the study, the patients were informed about the study and the patients signed an informed consent document that they agreed to participate in the study.

During follow-up, the survival status of the patients was obtained using the hospital data system and confirmed through the national death notification system. D-dimer, C-reactive protein (CRP), hs-TnI, glucose, whole blood analysis, and kidney function test, obtained at the day of hospitalization, were searched and recorded through the hospital's laboratory data.

Low-dose unenhanced thoracic CT scans were performed on the patients at admission. Patients were CT scanned in the supine position during end-inspiration using a 128-slice scanner (General Electric, Revolution EVO, USA). A low-dose CT protocol was performed with the following scanning parameters: 0.5 s gantry rotation time, 0.625 mm×64 detector array, 1.375mm/s step, table speed/rotation, 80 mA, 100 kV, and 512x512 matrix. ASIR was on and Auto mA scan parameter was off; 0.625 mm slice thickness and 0.625 mm reconstruction interval were used for sagittal and coronal image reconstruction.

The thoracic CT images were interpreted by two experienced radiologists who were blind to the patients' data. The measurements were recorded based on the consensus of two radiologists. The repeated measurement of each image was performed by one radiologist and confirmed by another. If a consensus could not be reached, a third radiologist's opinion was sought. All CT images were taken in axial, sagittal and coronal planes.

Mitral annular calcification was evaluated in the cardiac software (CardIQ Xpress) on the workstation of the CT device. 'CT-based mitral annular calcification scoring', previously published in the literature, was used to evaluate mitral annular calcification. Mean annulus calcium thickness (<5 mm 1 point, 5-9.9 mm 2 points, 10 mm≤ 3 points); calcium distribution in the annulus (<180' 1 point, 180'-270' 2 points, 270'≤ 3 points); trigone calcification (absent 0 point, anterolateral 1 point, posteromedial 1 point); and mitral leaflet calcification (absent 0 point, anterior 1 point, posterior 1 point) were analysed in the scoring. Mild MAC was defined as 3 points or less, moderate MAC 4 to 6 points, and severe MAC 7 points or above (Figure 2).[12]

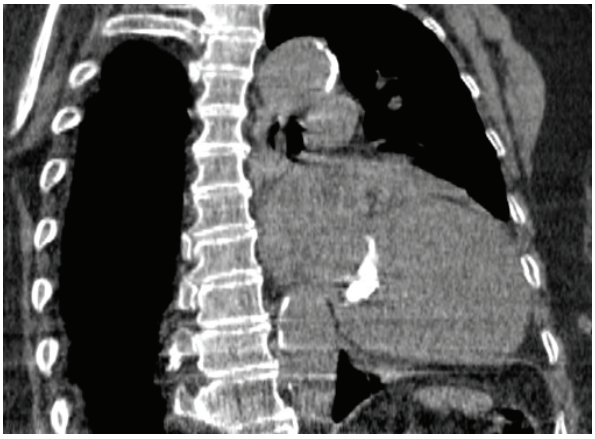

Figure 2.Evaluation of mitral anular calcification
B
• Plane showing the level of the mitral annulus in the cardiac software program.
• Degree that calcification surrounds the mitral annulus, the thickness of the calcification, and trigon involvement are evaluated.

According to the rate of involvement in itself, the severity of parenchymal involvement of COVID-19 infection is based on scoring the lobar involvement, which is a semi-quantitative CT score. Lobar involvement and scoring in each lobe: 0: % 0; 1: <% 5; 2: % 5–25; 3: 26–50%; 4: % 51–75; 5: >% 75. The total score ranges from 0 to 25.13 In the present study, we considered 0-8 points as mild, 9-16 points as moderate and 17-25 points as severe parenchymal involvement.

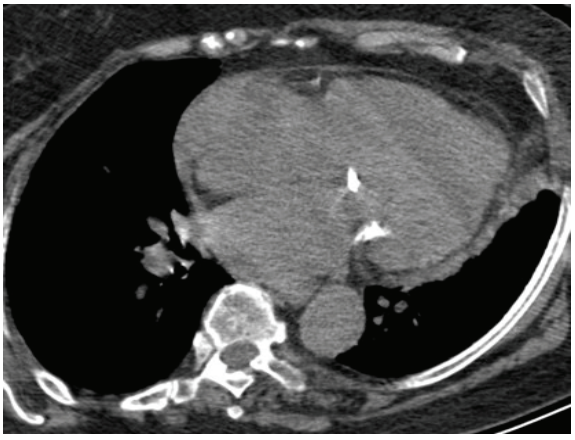

Figure 3 .Evaluation of mitral anular calcification
C
- *Axial plane*
- *Mitral annular calcification was observed.*
- *Extension of calcification to mitral valves was not detected.*

The study protocol was designed in accordance with the principles of the Helsinki Declaration and approved by the Ethics Committee of Trabzon Kanuni Education and Research Hospital (Approval number:2021/61, date: 4.4.2021).

Statistical analysis

The Social Sciences Statistical Program (for windows 22; SPSS Inc, Chicago) was used for all statistical calculations. Normal distribution of continuous variables was evaluated using the Kolmogorov-Smirnov test. The Student's t-test was used for continuous univariate analysis. The Chi-Square test was used for categorical variables. The kappa statistic was used to measure intraobserver agreement (one week apart) and interobserver agreement. In multivariate analyses, possible factors identified by univariate analyses were used to determine the independent determinants of mortality. P value below 0.05 was considered significant.

RESULTS

The study continued with the remaining 1151 patients after the exclusion criteria were met from 1242 consecutive hospitalized COVID-19 patients. Of the patients, 658 (57.2%) were male, 493 (42.8%) were female, and the mortality rate was higher in males (p=0.004). The mean age was 74 ±10.8 in the mortality group, while 62.7±14.9 in the survival group (p<0.001). HT (p<0.001), diabetes mellitus (DM) (p=0.042), COPD (p<0.001), CKD (p<0.001), CAD (p<0.001), heart failure (HF) (p<0.001) and AF (p<0.001) were statistically higher in the group that developed mortality during the hospitalization period (Table 1).

Glucose (p<0.001), CRP (115.8±73.6 vs. 67.2±60.7, p<0.001), and troponin levels (157.8±697.3 vs. 34.7±201, p<0.001) were statistically higher in the death group. While the number of patients with myocardial injury in the mortality group was 146 (49.3%), it was 138 (16.2%) in the survival group (p<0.001). D-dimer, white blood cell (WBC), neutrophil levels and neutrophil/lymphocyte ratio were higher in the mortality group (p<0.001 for all). Hemoglobin, platelet, and lymphocyte levels were higher in the survival group (p=0.025, p<0.001, and p=0.005, respectively) (Table 1).

The incidence of mitral annular calcification was 101 (34.1%) in the mortality group and 137 (16%) in the survival group (p<0.001). While the mean MAC score was 0.96±1.6 in the mortality group, it was 0.47±1.3 in the survival group (p<0.001). Higher rates of death were observed in patients with advanced lung parenchyma involvement on thorax CT (p<0.001) (Table 1).

Table 1. Demographic, laboratory and tomography data of patient groups.

Variables	Mortality (n=296)	Survival (n=855)	p value
Age	74±10.8	62.7±14.9	<0.001
>65 y/o, n(%),	246 (83.1)	412 (48.2)	<0.001
Male gender, (n %)	179 (60.5)	434 (50.8)	0.004
Hypertension,(n %)	248 (83.8)	590 (69)	<0.001
Diabetes mellitus, (n %)	137 (46.3)	338 (39.5)	0.042
COPD, (n %)	85 (28.7)	131 (15.3)	<0.001
CKD, (n %)	65 (22)	70 (8.2)	<0.001
CAD, (n %)	107 (36.1)	189 (22.1)	<0.001
HF, (n %)	48 (16.2)	35 (4.1)	<0.001
AF, (n %)	49 (16.6)	69 (8.1)	<0.001
Glucose, mg/dl	167.7±91.1	143.9±68.5	<0.001
GFR	53.3±29.9	72.2±23.4	<0.001
CRP, mg/l	115.5±73.6	67.2±60.7	<0.001
Troponin, ng/dl	157.8±697.3	34.7±201	<0.001
D-dimer, mg/dl	2473.7±4908.3	1319.7±3788.5	<0.001
WBC, x103/μL	8.7±5.1	6.9±3.1	<0.001
Hb, g/dl	13.1±2.1	13.7±4.7	0.025
Plt, x103/μL	184.2±70.6	204.9±85.7	<0.001
Plt<100, x103/μL	25 (8.4)	34 (4)	0.003
Neutrophyl, x103/μL	6.9±4.5	4.9±2.8	<0.001
Lymphocyte, x103/μL	1.2±2.3	1.4±0.9	0.005
NLR	10.1±11.3	4.5±4.4	<0.001
MAC score	0.96±1.6	0.47±1.3	<0.001
MAC, (n %)	101 (34.1)	137 (16)	<0.001
MI, (n %)	146 (49.3)	138 (16.2)	<0.001

COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, CAD: Coronary artery disease, HF: Heart failure, AF: Atrial fibrillation, GFR: Glomerular filtration rate, CRP: C reactive protein, WBC: White blood cell, Hb: Hemoglobulin, Plt: Platelet, NLR: Neutrophyllymphocyte ratio, MAC: Mitral annular calcification,MI: Myocardial injury

As a result of multivariate regression analysis, age (OR=1.976, 95% CI 1.166-3.346, p=0.011), male gender (OR=1.784, 95% CI 1.101-2.892, p=0.019), CKD (OR=2.293) in COVID-19 patients, 95% CI 1.085-4.485, p=0.030), myocardial injury development (OR=2.893, 95% CI 1.735-4.823, p<0.001) and advanced lung parenchymal involvement on computed tomography (OR=2.231, 95% CI 1.084-4.594, p=0.029) were independently associated with mortality (Table 2). It was observed that the presence of MAC was associated with the development of myocardial damage (14.8% - 38.7%, p<0.001) and CKD (18.8% - 34.8%, p<0.001).

Table 2.Mortality predictors.

Variables	%95 CI	Odds Ratio	p value
Age>65 y/o	1,166-3,346	1,976	**0,011**
Male gender, (n %)	1,101-2,892	1,784	**0,019**
Hypertension,(n %)	0,491-1,631	0,895	0,717
Diabetes mellitus, (n %)	0,677-1,832	1,114	0,670
COPD, (n %)	0,802-2,566	1,435	0,223
CKD, (n %)	1,085-4,845	2,293	**0,030**
CAD, (n %)	0,537-1,572	0,919	0,758
HF, (n %)	0,577-3,111	1,339	0,497
AF, (n %)	0,461-2,170	1,000	0,999
Glucose, mg/dl	1,000-1,006	1,003	0,089
GFR	0,979-1,004	0,992	0,198
CRP, mg/l	1,000-1,007	1,003	0,061
D-dimer, mg/dl	1,000-1,000	1,000	0,215
WBC, x103/μL	0,214-1,367	0,541	0,194
Hb, g/dl	0,949-1,045	0,996	0,871
Plt<100, x103/μL	0,301-2,248	0,823	0,704
Neutrophyl, x103/μL	0,790-5,224	2,031	0,142
Lymphocyte, x103/μL	0,702-5,054	1,884	0,208
MAC	0,838-2,681	1,499	0,172
MI, (n %)	1,735-4,823	2,893	**<0.001**

COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, CAD: Coronary artery disease, HF: Heart failure, AF: Atrial fibrillation, GFR: Glomerular filtration rate, CRP: C reactive protein,Hb: Hemoglobulin, Plt: Platelet, MAC: Mitral annular calcification,MI: Myocardial injury

DISCUSSION

The present research provides info about the relationship between MAC data obtained from thorax CT images performed in hospitalized COVID-19 patients with mortality and myocardial injury. We observed that the presence of MAC was associated with an increased risk of death in COVID-19 patients. Advanced age, male gender, chronic kidney failure, myocardial injury development, and advanced lung parenchyma involvement were found to be pathologies independent of mortality in COVID-19

patients. In addition, MAC was associated with the development of CKD and myocardial injury, which were independent predictors of mortality in COVID-19 patients. The current study showed that it might be useful to assess the presence of MAC, which can be evaluated on routine thorax CT images performed in patients with COVID-19 infection in terms of mortality and risk of myocardial injury development due to COVID-19 infection.

COVID-19 causes a hypercoagulable state associated with mortality.[14] Microvascular and macrovascular thromboembolic complications have been demonstrated in the brain, lung, intestine, spleen, and peripheral vascular system in COVID-19.[8,15] Pulmonary embolism (PTE) and deep vein thrombosis are thromboembolic events frequently encountered in COVID-19.16In a study conducted in patients who were diagnosed with COVID-19 and received their follow-up and treatment in the intensive care unit, it was reported that the possibility of thromboembolic events was 49% and the possibility to development mortality from all causes in patients with thromboembolic complications was reported to be five times higher.[8] Acute ischemic stroke has been reported in COVID-19 patients.[17] The incidence of acute ischemic stroke in COVID-19 patients receiving treatment in the intensive care unit has been reported as 2.5%.[8] The critical increase in mortality due to the mentioned thromboembolic complications dictates the need to take precautions against thromboembolic events in COVID-19 patients. Mitral annular calcification is a disorder with crucial clinical, and prognostic consequences and its pathophysiology is nebulous.[18] It is suggested that MAC predisposes to thrombus formation and is associated with thromboembolic complications.[19] However, there is no clear information about the pathophysiology of thromboembolic complications of MAC. In our study, we observed the association of MAC with higher rates of mortality in COVID-19 patients. The increased mortality rates in COVID-19 patients with MAC might be due to the increased thromboembolic complication rates of MAC in these patients. The most vital thromboembolic complications may be the myocardial injury. However, it is thought that myocardial injury in COVID-19 patients may develop with direct myocardial damage mediated by angiotensin-converting enzyme 2 (ACE2) or secondary to hypoxia, microvascular dysfunction, or systematic inflammatory response syndrome.[20] We found the presence of MAC to be associated with a higher rate of myocardial injury in COVID-19 patients. In order to elucidate this relationship, it is necessary to investigate whether thromboembolic complications that may develop in COVID-19 patients are directly related to the presence of MAC.

Mortality rates increase with advanced age in COVID-19 patients.[21] According to data from the United States and Italy, mortality is higher in men.[18,22] Increased mortality rates were detected in COVID-19 patients with arterial hypertension, diabetes mellitus, atrial fibrillation, chronic obstructive pulmonary disease, and ischemic heart disease.23 It has been shown that COVID-19 patients with a history of CKD are at higher risk of being in the ICU, exposed to mechanical ventilation, and dying.[22,23] The presence of CKD is an independent risk factor for the development of mortality in COVID-19 patients.[24] In the current study, advanced age, male gender, arterial HT, diabetes mellitus, atrial fibrillation, chronic obstructive pulmonary disease, chronic renal failure, and presence of coronary artery disease were associated with increased risk of mortality in COVID-19 patients. In the regression analysis, advanced age, male gender, and CKD were independently associated with mortality. Study results were correlated with literature data. The fact that MAC in COVID-19 patients is associated with CKD, an independent predictor of mortality, suggests that attention should be paid to the presence of MAC in these patients.

A meta-analysis showed that increased troponin levels are associated with an increased risk of disease progression and mortality in COVID-19 patients.[25] Increased troponin levels are frequently encountered in COVID-19 patients during hospitalization, and high troponin levels

are associated with myocardial injury and fatal outcomes.[25] The mechanisms that cause myocardial injury secondary to COVID-19 infection remain unclear. Direct myocardial injury mediated by angiotensin-converting enzyme 2 (ACE2), damage secondary to hypoxia, microvascular damage, or systematic inflammatory response syndrome is considered as possible mechanisms causing myocardial injury.[20]

The presence and scoring of MAC can be calculated readily and precisely with the high 3D resolution of computed tomography.12The excessive use of CT due to the COVID-19 pandemic has allowed easier evaluation of parameters related to mortality, such as the presence and scoring of MAC. The presence of MAC is associated with cardiovascular diseases and mortality.[6,7] Myocardial injury secondary to COVID-19 is a common complication associated with an increased risk of acute coronary syndrome, cardiogenic shock, and heart failure.[26] Cardiac complications secondary to COVID-19 are associated with an increased risk of developing mortality.[27]Therefore, timely diagnosis and treatment of patients at high risk of myocardial injury secondary to COVID-19 and providing special care to prevent possible adverse events are of great importance. We analyzed the relationship between mortality and myocardial injury secondary to COVID-19 infection and MAC, and we found that MAC in COVID-19 patients was associated with a higher rate of mortality. Since the presence of MAC, which can be easily evaluated with thorax CT, is a potentially crucial parameter for increased mortality and myocardial injury development in COVID-19 patients, it may be recommended to evaluate the presence and severity of MAC in terms of possible risks at the hospital admission stage. Larger and randomized studies are required so that the presence of MAC can be used in the early risk assessment in terms of mortality and myocardial injury development in COVID-19 patients.

Limitations

The research is a single-centered study. The relationship between mortality and myocardial injury with MAC in COVID-19 patients is reported. The cross-sectional design of the study cannot explain the pathological mechanism of this relationship. Another limitation is that MAC was evaluated by non-contrast thoracic CT.

CONCLUSION

In conclusion, the presence of MAC is associated with an increased probability of developing mortality in COVID-19 patients. The presence of MAK was more frequent in COVID-19 patients with a mortal course. MAC is associated with mortality and myocardial damage in COVID-19 patients but is not an independent risk factor for mortality.

Ethics Committee Approval

Ethics Committee Approval of the study was obtained from the Ethics Committee of Trabzon Kanuni Education and Research Hospital, (Approval number: 2021/61, date: 04.4.2021).

References

1. *Akbarshakh A, Marban E. COVID-19 and the heart. Circ. Res. (2010); 126(10): 1443–55.*
2. *Carpentier AF, Pellerin M, Fuzellier JF, Relland JY. Extensive calcificationof the mitral valve anulus: pathology and surgical management.JThoracCardiovasc Surg. (1996);111(4), 718–30.*
3. *RobertsWC, Perloff JK. Mitral valvular disease: a clinicopathologicsurvey of the conditions causing the mitral valve to functionabnormally. Ann Intern Med. (1972);7: 939–75.*
4. *Savage DD, Garrison RJ, Castelli WP, McNamara PM, Anderson SJ, Kannel WB, Feinleib M.Prevalence ofsubmitral (annular) calcium and its correlates in a generalpopulation-based sample (the Framingham Study). Am JCardiol. (1983);51:1375–8.*
5. *Radulescu V, Goyfman M, Mohler III ER, Gao YL, Budoff MJ, CRIC Study Investigators. (2015). Prevalence and correlates of mitral annular calcification in adults with chronic kidney disease: Results from CRIC study. Atherosclerosis. (2015);242(1): 117-22.*
6. *Fox CS, Vasan RS, Parise H, Levy D, O'Donnell CJ, D'Agostino RB, Benjamin EJ, et al. Mitral annular calcification predicts cardiovascular morbidity and mortality: the Framingham Heart Study. Circulation. (2003);107(11): 1492-6.*
7. *O'Neal WT, Efird JT, Nazarian S, Alonso A, Heckbert SR, Soliman EZ. Mitral annular calcification and incident atrial fibrillation in the Multi-Ethnic Study of Atherosclerosis. EpEuropace. (2014);17(3): 358-63.*
8. *Klok FA, Kruip MJHA, Van Der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, Kaptein FHJ, et al. Confirmation of thehigh cumulative incidence of thrombotic complications in critically illICU patients with COVID-19: an updated analysis. Thromb Res. (2020);191:148-50.*
9. *Lodigiani C, Iapichino G, Carenzo L,Cecconi M, Ferrazzi P, Sebastian T, Kucher N, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thrombosis research. (2020);191: 9-14.*
10. *Stobe S, Richter S, Seige M, Stehr S, Laufs U, Hagendorff A. Echocardiographic characteristics of patients with SARS-CoV-2 infection. Clin Res Cardiol. (2020);109(12): 1549-66.*
11. *Guo T, Fan Y, Chen M. Wu X, Zhang L, He T, Wang H, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19).JAMA Cardiol. 2020;1;5(7):811-18.*
12. *Guerrero M, Wang DD, Pursnani A, Eleid M, Haliç Ö, Urena M, Kodali S, et al. A cardiac computed tomography–based score to categorize mitral annular calcification severity and predict valve embolization. Cardiovascular Imaging, (2020);13(9): 1945-57.*
13. *Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, Panebianco V, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. European radiology. (2020);30(12), 6808-17.*
14. *Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters areassociated with poor prognosis in patients with novel coronaviruspneumonia. J ThrombHaemost. (2020);18:844-7.*
15. *Wichmann D, Sperhake JP, Lütgehetmann M, SteurerS, Edler C, Heinemann A, Heinrich F, et al. AutopsyFindings and Venous Thromboembolism in Patients With COVID-19: a Prospective Cohort Study. Ann Intern Med. (2020);173:268-77.*
16. *Middeldorp S, Coppens M, Van Haaps TF, Foppen M, Vlaar AP, Müller MC, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. Journal of Thrombosis and Haemostasis. (2020);18(8):1995-2002.*
17. *Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP,Leacy RAD, et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. New England Journal of Medicine. (2020);382(20), e60.*
18. *Massera D, Kizer JR, Dweck MR. Mechanisms of mitral annular calcification. Trends in cardiovascular medicine, (2020) ;30(5), 289-95.*
19. *Butany J, Vaideeswar P, Dixit V. Massive annular calcification: astone in the heart. Can J Cardiol. (2019) ;25(1):e18.*
20. *Malavazos AE, Goldberger JJ, Iacobellis G. Does epicardial fat contribute to COVID-19 myocardial inflammation? European heart journal. (2020);41(24), 2333.*
21. *Novel CPERE. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases(COVID-19) in China.Zhonghua Liu Xing Bing XueZaZhi (2020);41, 145–51.*
22. *Richardson S, Hirsch JS, Narasimhan M, JM Crawford, T McGinn, Davidson KW, Barnaby DP, et al. Presenting Characteristics, Comorbidities, and Outcomes among 5700 Patients Hospitalized with COVID-19 in the New York City Area. JAMA (2020);26;323(20): 2052-9.*
23. *Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. International urology and nephrology. (2020);52(6), 1193-4.*
24. *Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, L Ji, et al. Kidney disease is associatedwithin-hospital death of patients with COVID-19. Kidney Int. (2020); 1–10.*
25. *Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, Li Q, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. Journal of infection. (2020);81(2), e16-e25.*
26. *Lippi G, Salvagno GL, Pegoraro M, Militello V, Caloi, C, Peretti A, Gaino S, et al. Assessment of immune response to SARS-CoV-2 with fully automated MAGLUMI 2019-nCoV IgG and IgMchemiluminescence immunoassays. Clinical Chemistry and Laboratory Medicine (CCLM). (2020);58(7):1156-9.*
27. *Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, Madhur MS, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovascular research. (2020);116(10); 1666-87.*