

# Prevalence and risk factors of myocardial injury in patients with COVID-19: A retrospective study

Siti Nurul Azimah Mat Jusoh, Msc<sup>1</sup>, Laily Noor Zuliaty Anuar, Msc<sup>1</sup>, Sharifah Shafinaz Sh Abdullah, PhD<sup>1</sup>, & Huzairi Sani, MMed<sup>2</sup>

<sup>1</sup>Centre for Nursing Studies Faculty of Health Sciences, Universiti Teknologi MARA Cawangan Selangor Kampus Puncak Alam, Bandar Puncak Alam, Selangor, Malaysia, <sup>2</sup>Faculty of Medicine, Universiti Teknologi MARA Cawangan Selangor Kampus Puncak Alam, Bandar Puncak Alam, Selangor, Malaysia

## ABSTRACT

**Introduction:** The coronavirus disease of 2019 (COVID-19) predominantly impacts the pulmonary system; however, it also has harmful consequences for the cardiovascular system through the occurrence of myocardial injury.

**Materials and Methods:** This retrospective study analysed 119 COVID-19 patients admitted to Al-Sultan Abdullah Hospital (HASA) from March until December 2020. Demographics, medical histories, admission laboratory results, electrocardiogram (ECG), echocardiogram (echo), were captured from the hospitals' health records. Myocardial injury is an injury to the myocardium that can be diagnosed by elevated cardiac troponin T or I level above the 99th percentile upper reference limit (URL), an abnormal ECG, and an abnormal echo. Data were analysed using Statistical Package for Social Sciences (SPSS) Version 27.

**Results:** From this study, it was founded that the prevalence of myocardial injury is 36.1% (43 subjects out of 119). The risk factors are older age (odds ratio, 2.347;  $p=0.028$ ), males (odds ratio, 2.019;  $p=0.125$ ), Indians (odds ratio, 3.659;  $p=0.296$ ), hypertension (odds ratio, 2.776;  $p=0.009$ ), diabetes mellitus (odds ratio, 1.732;  $p=0.155$ ) and category 4 and 5 COVID-19 patients (odds ratio, 2.325;  $p=0.038$ ).

**Conclusion:** Myocardial injury is prevalent among patients affected by COVID-19 and is associated with older age, hypertension and category 4 and 5 COVID-19. The researchers suggested conducting a more thorough investigation of the sizable population in multiple settings and conducting a prospective study where all infected COVID-19 patients have to undergo several tests, such as ECG, troponin T, and echocardiogram.

## KEYWORDS:

Prevalence, myocardial injury, COVID-19, risk factor.

## INTRODUCTION

COVID-19 is a disease that is spread by the novel acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China.<sup>1</sup> It is becoming a pandemic and causing an effect on the whole world. SARS-CoV-2 is categorised as a beta coronavirus, characterised by its huge size, spherical shape, enveloped structure, and non-segmented positive-sense

single-stranded RNA genome, which spans around 30 kilobases.<sup>1</sup> Despite being largely a respiratory illness, observational studies have demonstrated a close relationship between COVID-19 and cardiovascular disease.<sup>2</sup> This then triggers the activation of immunological mechanisms, including T-cells and B-cells, which create antibodies, mediators, and cytokines, leading to myocardial inflammation.<sup>2</sup>

Numerous published studies have indicated a correlation between higher fatality rates in COVID-19 infections and myocardial injury among patients with COVID-19. 28% of patients inflicted with COVID-19 signs of myocardial injury and elevated troponin levels in the blood.<sup>3</sup> Additionally, the mortality rates of patients with cardiac damage evidence were higher than those of those without (51.2% vs. 4.55%,  $p<.001$ ).<sup>5</sup> The study also found that acute renal failure, electrolyte abnormalities, and acute respiratory distress syndrome (ARDS) were complications that frequently occurred in heart injury patients, indicating that the involvement of the heart negatively impacts these patients' prognosis.<sup>3</sup>

Those who have cardiovascular comorbidity and exhibit high-risk variables, such as being male, advanced age, diabetes, hypertension, or obesity, are susceptible to experiencing cardiac injury and are considered part of the vulnerable group in relation to COVID-19.<sup>4</sup> It is clear that myocardial injury is a common complication in COVID-19 patients in the severe and critical intensive care units, and that advanced age, arterial hypertension, immunomodulator use, and a high Sequential Organ Failure Assessment score are independent predictors of COVID-19 occurrence and severity.<sup>5</sup> Cardiovascular problems are also common in these patients, and they are associated with a greater mortality rate.<sup>5</sup>

After conducting research, the researcher found limited published articles about COVID-19-related myocardial injury in Malaysia. The issue of insufficient concentration within a relevant field has been acknowledged and tackled in Malaysia. The researcher intends to conduct this study within the specific context of Malaysia in order to investigate and find risk factors that are linked to the prevalence of myocardial injury among individuals who have received a positive diagnosis for COVID-19.

This article was accepted: 30 December 2024

Corresponding Author: Sharifah Shafinaz Sh Abdullah

Email: shasya@uitm.edu.my

## MATERIALS AND METHODS

### Study Design and Population

This is a retrospective study that uses solely accessible secondary data. The participants must undergo one of the following examinations while hospitalised: electrocardiogram (ECG), echocardiography (echo), or troponin T. Except for those with suspected symptoms of myocardial injury, these procedures (ECG, echo, and troponin T) are not routinely performed on all COVID-19 patients admitted to Al-Sultan Abdullah Hospital (HASA). These three studies serve as markers for the diagnosis of myocardial injury in COVID-19 patients. The population of the study are 119 patients with positive COVID-19 all categories, Malaysian, age above 12 years old, and both genders.

### Research Instrument

The data collection form which consists of five different sections (Demographics, medical histories, admission laboratory results, ECG, and echo) was used as an instrument to collect data from the Al-Sultan Abdullah Hospital (HASA) medical records department.

### Sample collection

The UiTM Research Ethics Committee (Ref. number: REC/11/2021 (MR/881)) and the Director of HASA (Ref. number: 500-HUiTM (PT.8/3/1)) have approved this study. The data has been collected at the HASA medical record department. All the data patients with COVID-19 were screened and collected from hardcopy records or database files using the computer in the medical record department. Positive COVID-19 cases were screening from October 2021 until February 2022. All ECG, echo and troponin T results were interpreted and reviewed by a cardiologist who is one of research team members.

### Definition

Myocardial injury is defined as injury in the myocardial and can be detected by elevated cardiac troponin T or troponin I greater than the 99th percentile upper reference limit (URL).<sup>6</sup> In the context of COVID-19, myocardial injury, defined by an elevated troponin level, is caused primarily by non-ischaemic myocardial processes such as severe respiratory infection with hypoxia, sepsis, systemic inflammation, pulmonary thrombosis and embolism, cardiac adrenergic hyperstimulation during cytokine storm syndrome, and myocarditis.<sup>7</sup> Any injury to the myocardium can be diagnosed based on increased troponins T or troponin I, electrocardiographic changes in ST segments, and echocardiographic wall motion abnormalities or wall thickening.<sup>8</sup> This must be correlated with the COVID-19 symptoms, clinical features, and investigations (ECG, cardiac biomarkers (troponin) and echo). Investigation results were analysed to fit the clinical diagnosis of myocarditis and ruling out other possibilities of elevated troponin.

### Statistical Analysis

All respondents' socio-demographic information, medical and health history, were analysed using Statistical Packages for Social Sciences (SPSS) Version 27. Descriptives statistics were used to calculate the prevalence rate. A crosstab test was used to identify the odd ratio contributing to developing myocardial injury among patients with COVID-19 in HASA.

### Demographic characteristics of subjects

A total of 119 patients were included from October 2021 until February 2022 at HASA. Table I displays the demographics, clinical characteristics, and laboratory characteristics based on the presence of myocardial injury. Patients with myocardial injury were 81.4% male, with a mean age of 59 years old. COVID-19 patients with myocardial injuries were associated with older age ( $P=0.028$ ). Most of the myocardial injuries had occurred in those aged over 61 years (27.9%). Meanwhile, 20.9% of myocardial injuries had occurred in patients aged over 71 until 80 years of age. The predominant racial group in our dataset was Malay, comprising 79% and not being equally distributed among race groups because Malay is the largest race in Malaysia.

### Prevalence of myocardial injury in patients with COVID-19

The majority of the myocardial injury had occurred in those in COVID-19 categories 4 (44.2%) and 5 (27.9%). A total of 43 patients (36.1%) had abnormal ECG, abnormal echo and laboratory-confirmed troponin T positivity for myocardial injury during the hospitalisation. The result showed that 3 in 10 patients with COVID-19 might develop myocardial injury (Table I).

Risk factors of myocardial injury in patients with COVID-19 To determine the risk factors for myocardial injury in patients with COVID-19, a crosstab analysis of myocardial injury among COVID-19 patients with clinical data was performed (Table I). The result showed that older age (odds ratio, 2.347;  $p=0.028$ ), male (odds ratio, 2.019;  $P=0.125$ ), Indian (odds ratio, 3.659;  $P=0.296$ ), hypertension (odds ratio, 2.776;  $p=0.009$ ), diabetes mellitus (odds ratio, 1.732;  $P=0.155$ ) and category 4 and 5 COVID-19 patients (odds ratio, 2.325;  $p=0.038$ ) are risk factors associated with the incidence of myocardial injury. Older age, hypertension and category 4 and 5 COVID-19 patients are significant with occurrence of myocardial injury among patients with COVID-19. Due to the small sample size, there is no significant correlation between Indians and the occurrence of cardiac injury.

### Electrocardiogram (ECG), Echocardiogram (echo) and Troponin T Characteristics of Patients COVID-19

The ECG was tested in 57 patients (47.8%), and 24 (42.2%) were abnormal. 14 (58.3%) sinus tachycardia, 1 (0.04%) sinus bradycardia, 1 (0.04%) atrial flutter, 2 (0.08%) atrial fibrillation, 2 (0.08%) ST elevation, and 4 (0.16%) ST depression (Table II). 22 (18.48%) did echo, and 19 (86.36%) was abnormal, while 24 (20.16%) underwent testing for high-sensitivity troponin T level, and 12 (50%) were raised ( $>14$  ng/L). 13 did ECG and echo, 6 (46.1%) had abnormal ECG and echo, 1 (7.7%) had sinus tachycardia with abnormal echo, 2 (15.4%) had sinus bradycardia with abnormal echo, and 3 (23%) had ST depression with abnormal echo. 21 did the ECG and troponin T test; abnormal ECG and troponin T were 7 (33.33%) ST depression and 2 (28.5%) raised in troponin T, sinus tachycardia and 3 (42.8%) raised in troponin T and atrial fibrillation and 2 (28.5%) raised in troponin T. 5 did echo and troponin T; 3 (60%) had abnormal echo and were raised in troponin T. 3 did ECG, echo, and troponin T; 3 (100%) had abnormal ECG, echo, and were raised in troponin T.

Table I: Demographic data of patients with COVID-19 (n=119)

Characteristics	Myocardial injury			p-value ( <sup>2</sup> )	Odds ratio
	All (n=119)	With (n=43)	Without (n=76)		
<b>Demographic</b>					
<b>Age (years old)</b>					
<b>Younger</b>				0.028	0.426
12 - 20	1 (0.8%)	0 (0%)	1 (1.3%)		
21 - 30	21 (17.6%)	3 (7%)	18 (23.7%)		
31 - 40	10 (8.4%)	3 (7%)	7 (9.2%)		
41 - 50	16 (13.4%)	7 (16.3%)	9 (11.8%)		
51 - 60	23 (19.3%)	7 (16.3%)	16 (21.2%)		
<b>Older</b>					2.347
61 - 70	28 (23.5%)	12 (27.9%)	16 (21.1%)		
71 - 80	14 (11.8%)	9 (20.9%)	5 (6.6%)		
81 - 90	6 (5%)	2 (4.7%)	4 (5.3%)		
<b>Gender</b>				0.125	2.019
Male	87 (73.1%)	35 (81.4%)	52 (68.4%)		
Female	32 (26.9%)	8 (18.6%)	24 (31.6%)		0.495
<b>Race</b>					
Malay	95 (79.8%)	34 (79%)	61 (80.3%)	0.876	-
Chinese	21 (17.6%)	7 (16.3%)	14 (19.2%)	0.768	-
Indian	3 (2.5%)	2 (4.7%)	1 (0.5%)	0.296*	-
<b>Comorbid</b>					
Hypertension	53 (44.5%)	26 (60.5%)	1 (2.3%)	0.009	2.776
Diabetes Mellitus	48 (40.3%)	21 (48.8%)	27 (22.7%)	0.155	1.732
Hyperlipidemia	36 (30.3%)	13 (30.2%)	27 (35.5%)	0.997	-
Asthma	8 (6.8%)	2 (4.7%)	23 (30.3%)	0.709*	-
Cancer	6 (5%)	1 (2.3%)	6 (8%)	-	-
Chronic obstructive pulmonary disease (COPD)	1 (0.8%)	1 (2.3%)	5 (6.6%)	-	-
Ischemic heart disease (IHD)	9 (7.6%)	5 (11.6%)	0 (0%)	-	-
Chronic kidney disease (CKD)	3 (2.5%)	1 (2.3%)	4 (5.3%)	-	-
Chronic kidney disease (CKD)	1 (0.8%)	1 (2.3%)	2 (2.6%)	-	-
Transient ischemic attack (TIA)	1 (0.8%)	1 (2.3%)	0 (0%)	-	-
Acute kidney injury (AKI)	1 (0.8%)	1 (2.3%)	0 (0%)	-	-
<b>COVID-19 categories</b>					
<b>Mild - Moderate</b>				0.038	0.430
Category 1	8 (6.7%)	2 (4.7%)	6 (7.9%)		
Category 2	31 (26.1%)	6 (14%)	25 (32.9%)		
Category 3	9 (7.6%)	4 (9.3%)	5 (6.6%)		
<b>Severe and critically ill</b>					2.325
Category 4	49 (41.2%)	19 (44.2%)	30 (39.5%)		
Category 5	22 (18.5%)	12 (27.9%)	10 (13.2%)		
<b>Point prevalence of myocardial injury</b>	43/119 x 100 = 36.1 % 3:10 patients with COVID-19 develop MI				

\*Fishers exact test

## DISCUSSION

In this study, the prevalence of myocardial injury was 36.1% (43 out of 119), indicating that 3 out of every 10 COVID-19 patients developed myocardial injury. A study conducted in China, Germany, and the United States similarly found that myocardial damage is common in COVID-19 patients.<sup>9-12</sup> These studies covered 42 to 985 participants and reported a prevalence of myocardial damage ranging from 28.9% to 46%.<sup>9-12</sup>

Older patients, males, Indians, hypertension, diabetes mellitus, and COVID-19 categories 4 and 5 are all risk factors for myocardial injury. Consistent with prior studies,<sup>13,14</sup> the myocardial injury patients in our study were older. Similar to these observations, the researchers also found that patients with cardiac injury tended to be older.<sup>15,16</sup> Elderly patients were considered "frail" due to increased comorbidities, low cognitive condition, diminished resistance to shocks, and impaired compensatory abilities.<sup>17</sup> Elderly people are more prone to cardiac injury due to vascular ageing, myocardial remodelling, and immunological senescence.<sup>18,19</sup>

The study also discovered that COVID-19 patients with myocardial injury were more likely to be men. This finding was reinforced by a prior study, which indicated that male COVID-19 patients are at a higher risk of developing myocardial injury.<sup>13,20-23</sup> Previous research discovered that the clearance function of inhaled particles in small airway sections decreased with age.<sup>24</sup> Upper airway size decreases with age, which is especially noticeable in males.<sup>25</sup> Furthermore, aged males have fewer immune cells and an inverted CD4/ CD8 T-cell ratio than females, resulting in reduced immune surveillance and clearance.<sup>26</sup> However, the study from Italy found different results.<sup>27</sup> Their study showed that myocardial injury could be associated with female patients.<sup>27</sup>

This study was conducted in Malaysia, which has a multiracial population, including Malay, Chinese, and Indian. According to the study, Indian patients with COVID-19 are at a higher risk of developing myocardial injury. A study conducted in the United States discovered that the majority racial group in their sample was white, accounting

**Table II: Electrocardiogram, Echocardiogram and Troponin T characteristics of patients with COVID-19**

Test	Finding Myocardial Injury (n=43)
<b>ECG</b>	n = 57
Normal	33 (57.8%)
Abnormal;	24 (42.2%)
Sinus Tachycardia	14 (58.3%)
Sinus Bradycardia	1 (0.04%)
Atrial Flutter	1 (0.04%)
Atrial Fibrillation	2 (0.08%)
ST Elevation	2 (0.08%)
ST Depression	4 (0.16%)
<b>Echo</b>	n = 22
Normal	3 (13.6%)
Abnormal	19 (86.4%)
<b>Troponin T</b>	n = 24
Normal	12 (50%)
Raised	12 (50%)
<b>ECG and ECHO</b>	n = 13
Normal	
Abnormal;	
Sinus Tachycardia	1 (7.7%)
Sinus Bradycardia	2 (15.4%)
ST Depression	3 (23%)
<b>ECG and Troponin T</b>	n = 21
Normal	14 (66.7%)
Abnormal;	7 (33.3%)
Sinus Tachycardia and raised troponin T	3 (42.8%)
Atrial Fibrillation and raised troponin T	2 (28.5%)
ST Depression and raised troponin T	2 (28.5%)
<b>Echo and Troponin T</b>	n = 5
Normal Echo and no raised in troponin T	2 (40%)
Abnormal Echo and raised in troponin T	3 (60%)
<b>ECG, Echo and Troponin T</b>	n = 3
Abnormal ECG, Echo and raised in troponin T	3 (100%)
ST Depression	2
Sinus Tachycardia	1
Abnormal Echo	3
Raised in Troponin T	3

for 79.5% and equally dispersed throughout both categories.<sup>28</sup> The findings suggest that non-Hispanics were more likely than Hispanics to have myocardial damage (20.1% vs. 12.4%).<sup>28</sup> Another study conducted in the United States discovered that an African American patient with COVID-19 had a 43% prevalence of cardiac injury, which was higher than previously published findings.<sup>29</sup> Patients with elevated troponin levels showed a sixfold greater risk of death compared to those without.<sup>29</sup>

Furthermore, this study discovered a history of comorbidities (hypertension and diabetes mellitus) are high risk to get myocardial injury among patients infected with COVID-19. The previous research also found that hypertension and diabetes mellitus are high-risk factors for myocardial injury.<sup>22,27,30-32</sup> In this study, patients have comorbidities but no previous history of myocardial injury. Patients infected with COVID-19 may have myocardial injury due to the wide-ranging effects of cardiac inflammation, which appears to be the primary feature of the infection.<sup>33</sup>

The researchers found that COVID-19 categories 4 (severe) and 5 (critically ill) are high risk to get myocardial injury. Pneumonia that requires extra oxygen and a catastrophic illness involving several organ failures are the main causes of

cardiac injury in COVID-19 categories 4 and 5.<sup>34</sup> Various studies have revealed that categories 4 and 5 patients infected with COVID-19 are more likely to get myocardial injury. A mendelian randomisation research on COVID-19 discovered that severe respiratory symptoms and hospitalisation may increase the risk of myocardial injury.<sup>35</sup> Furthermore, myocardial injury and cardiovascular issues were common in patients hospitalised to the intensive care unit with severe and critical COVID-19, and both were related to higher mortality.<sup>5</sup> A systematic study discovered that myocardial injury appears to be associated with severe COVID-19 illnesses, particularly in hospitalised patients, who should be constantly watched and treated.<sup>36</sup>

#### *Limitations and recommendations for future studies*

This study has some limitations, which the authors have noted. As with much other research in this field, this one was retrospective, and the selection of participants for cardiac troponin testing will have introduced a significant bias. This study is a retrospective study, where the researchers only used the available secondary data from October 2021 until February 2022. Recommendation for future researchers could be included more sample size and conduct a prospective study where all infected COVID-19 patients have to do several testings' such as ECG, troponin T and echocardiogram



test. This prospective study could provide conclusive finding regarding the incidence of myocardial injury among infected COVID-19 patients. Apart from study design, the sample size and study duration also have to improve in future study. Due to the small size, the researchers recommended doing an in-depth study of the population and setting for a conclusive finding.

### CONCLUSION

Research findings revealed that myocardial injury is prevalent in patients affected by COVID-19 and is associated with older age, hypertension and category 4 and 5 COVID-19. This study is concurrent with a previous study where the incidence of myocardial injury occurred among elderly, comorbid and category 4 and 5 COVID-19. A prospective study with a large sample size is needed for future studies.

### ACKNOWLEDGEMENTS

We would like to express our gratitude to the director of the Hospital Al Sultan Abdullah (HASA) UiTM and all the staff from the Medical Records Department, HASA.

### ETHICS APPROVAL AND INFORMED CONSENT

The UiTM Research Ethics Committee (Ref. number: REC/11/2021 (MR/881)) and the Director of UiTM Hospital (Ref. number: 500-HUiTM (PT.8/3/1)) approved this study.

### CONFLICT OF INTEREST

Authors declared no conflict of interest.

### FUNDING

600-RMC/FRGS 5/3 (177/2023).

### REFERENCES

1. Elengoe A. COVID-19 outbreak in Malaysia. *Osong public health and research perspectives.* 2020; 11(3): 93.
2. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol* 2020; 75(18): 2352-71.
3. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; 5(7): 802-10.
4. Mahajan K, Chandra KS. Cardiovascular comorbidities and complications associated with coronavirus disease 2019. *Med J Armed Forces India* 2020; 76(3): 253-60.
5. Neves AP, Machado MN, Gandolfi JV, Machado LF, Syrio JD, Luckmeyer G, et al. Myocardial injury and cardiovascular complications in COVID-19: a cohort study in severe and critical patients. *Rev Bras Ter Intensiva* 2023; 34: 443-51.
6. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth universal definition of myocardial infarction (2018). *Circulation* 2018; 138(20): e618-51.
7. Imazio M, Klingel K, Kindermann I, Brucato A, De Rosa FG, Adler Y, et al. COVID-19 pandemic and troponin: indirect myocardial injury, myocardial inflammation or myocarditis?. *Heart* 2020; 106(15): 1127-31.
8. Ammirati E, Moslehi JJ. Diagnosis and treatment of acute myocarditis: a review. *Jama* 2023; 329(13): 1098-113.
9. Dan S, Pant M, Upadhyay SK. The case fatality rate in COVID-19 patients with cardiovascular disease: global health challenge and paradigm in the current pandemic. *Current pharmacology reports* 2020; 6: 315-24.
10. Ganta N, Bonilla HM, Alebna P, Vanaparthys S, Ngwa J, Opoku-Asare I. Myocardial injury in African American patients with COVID-19. *J Am Coll Cardiol* 2021; 77(18\_Supplement\_1): 3166.
11. Lala A, Johnson KW, Januzzi JL, Russak AJ, Paranjpe I, Richter F, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol* 2020; 76(5): 533-46.
12. Mahabadi AA, Mincu R, Dykun I, Michel L, Küng A, Witzke O, et al. Frequency and prognosis of CVD and myocardial injury in patients presenting with suspected COVID-19—The CoV-COR registry. *Int J Cardiol Heart Vasc* 2023; 45: 101184.
13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395(10223): 507-13.
14. Maino A, Di Stasio E, Grimaldi MC, Luigi C, Erica R, Federico B, et al. PREVALENCE AND CHARACTERISTICS OF MYOCARDIAL INJURY DURING COVID-19 PANDEMIC. *J Am Coll Cardiol.* 2021; 77(18\_Supplement\_1): 3191.
15. Zou F, Qian Z, Wang Y, Zhao Y, Bai J. Cardiac injury and COVID-19: a systematic review and meta-analysis. *CJC open* 2020; 2(5): 386-94.
16. Barman HA, Atici A, Sahin I, Alici G, Tekin EA, Baycan ÖF, et al. Prognostic significance of cardiac injury in COVID-19 patients with and without coronary artery disease. *Coron Artery Dis* 2021; 32(5): 359-66.
17. Nishihira K, Yoshioka G, Kuriyama N, Ogata K, Kimura T, Matsuura H, et al. Impact of frailty on outcomes in elderly patients with acute myocardial infarction who undergo percutaneous coronary intervention. *Eur Heart J Qual Care Clin Outcomes* 2021; 7(2): 189-97.
18. Moccia F, Gerbino A, Lionetti V, Miragoli M, Munaron LM, Pagliaro P, et al. COVID-19-associated cardiovascular morbidity in older adults: a position paper from the Italian Society of Cardiovascular Researches. *Geroscience* 2020; 42(4): 1021-49.
19. Imazio M, Klingel K, Kindermann I, Brucato A, De Rosa FG, Adler Y, et al. COVID-19 pandemic and troponin: indirect myocardial injury, myocardial inflammation or myocarditis?. *Heart* 2020; 106(15): 1127-31.
20. Rukwal S, Kaur H, Kaur P, Shrivastava M. Study of troponin-i levels in COVID-19 patients. *Int J Med Lab Res* 2022; 7(1): 11-9.
21. Cheng R, Liu C, Yang J, Yang Y, Chen R, Ding X, et al. Sex differences in the incidence and risk factors of myocardial injury in COVID-19 patients: a retrospective cohort study. *Front Physiol* 2021; 12: 632123.
22. Li L, Zhang S, He B, Chen X, Zhao Q. Retrospective study of risk factors for myocardial damage in patients with critical coronavirus disease 2019 in Wuhan. *J Am Heart Assoc* 2020; 9(15): e016706.
23. Deng Q, Hu B, Zhang Y, Wang H, Zhou X, Hu W, et al. Suspected myocardial injury in patients with COVID-19: evidence from front-line clinical observation in Wuhan, China. *Int J Cardiol* 2020; 311: 116-21.
24. Svartengren M, Falk R, Philipson K. Long-term clearance from small airways decreases with age. *Eur Respir J* 2005; 26(4): 609-15.
25. Martin SE, Mathur R, Marshall I, Douglas NJ. The effect of age, sex, obesity and posture on upper airway size. *Eur Respir J* 1997; 10(9): 2087-90.

26. Perrotta F, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. *Aging Clin Exp Res* 2020; 32(8): 1599-608.
27. Ferrante G, Fazzari F, Cozzi O, Maurina M, Bragato R, D'Orazio F, et al. Risk factors for myocardial injury and death in patients with COVID-19: insights from a cohort study with chest computed tomography. *Cardiovasc Res* 2020; 116(14): 2239-46.
28. Ganta N, Bonilla HM, Alebna P, Vanaparthi S, Ngwa J, Opoku-Asare I. Myocardial injury in African American patients with COVID-19. *J Am Coll Cardiol*. 2021; 77(18\_Supplement\_1):3166.
29. Patel G, Vasavada A, Reddy S, Adak S, Jain S, Regassa H, et al. Prevalence and Outcomes of Cardiovascular Diseases in Patients with COVID-19: A Research Letter. *Int J Innov Res Med Sci* 2022; 7(10): 540-2.
30. Thapa SB, Kakar TS, Mayer C, Khanal D. Clinical outcomes of in-hospital cardiac arrest in COVID-19. *JAMA Intern Med* 2021; 181(2): 279-81.
31. Crudo VL, Ahmed AI, Cowan EL, Shah DJ, Al-Mallah MH, Malahfji M. Acute and subclinical myocardial injury in COVID-19. *Methodist DeBakey Cardiovasc J* 2021; 17(5): 22.
32. Huang S, Vignon P, Mekontso-Dessap A, Tran S, Prat G, Chew M, et al. Echocardiography findings in COVID-19 patients admitted to intensive care units: a multi-national observational study (the ECHO-COVID study). *Intensive Care Med* 2022; 48(6): 667-78.
33. Abbasi J. Researchers investigate what COVID-19 does to the heart. *JAMA* 2021; 325(9): 808-11.
34. CDC. Clinical Presentation [Internet]. COVID-19. 2024. Available from: <https://www.cdc.gov/covid/hcp/clinical-care/covid19-presentation.html>
35. Liu MJ, Sun XQ, Li LB, Wang G, Shi YF. Serious COVID-19 may have a causal relationship with myocardial injury: A Mendelian randomization study. *Front Genet* 2023; 14: 1135887.
36. Alali AH, Smaiem MS, Alsheikh AM, Alshareef AA, Smaiem FS, Alnahar BW, et al. Myocardial injuries among patients with COVID-19: a systematic review. *Infez Med* 2021; 29(3): 345.