sciendo

Journal of Cardiovascular Emergencies 2020
DOI: 10.2478/jce-2020-0013

CLINICAL UPDATE

Differential Diagnosis of Myocardial Injury in the SARS-CoV-2 Era – Myocarditis Versus Acute Coronary Syndrome

Cosmin Țolescu[1], Renata Gerculy[1], Camelia Libenciuc[1], Istvan Kovacs[1,2,3]

[1] Clinic of Cardiology, Emergency Clinical County Hospital, Târgu Mureș, Romania
[2] "George Emil Palade" University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania
[3] Center of Advanced Research in Multimodality Cardiac Imaging, CardioMed Medical Center, Târgu Mureș, Romania

ABSTRACT

COVID-19 is a disease caused by the new coronavirus discovered in 2019, which may lead to a severe acute respiratory syndrome and has a major impact on public health worldwide, being declared a pandemic by World Health Organization. In Italy, and especially in the region of Lombardia, the healthcare system has faced a huge overload, which led to significant consequences on cardiology resources. The accessibility to cardiology care units has been drastically reduced, and scheduled interventions, such as elective primary percutaneous coronary interventions, have been significantly delayed. During this time, there was a global concern regarding the management of the SARS-CoV-2 pandemic, but also the management of main cardiovascular emergencies. Under usual circumstances, the differential diagnosis of myocardial injury does not confront many difficulties. Unfortunately, there are several limitations in the management of patients with SARS-CoV-2 infection in the current pandemic state. The aim of the present manuscript is to provide an overview on the main causes of myocardial injury during the COVID-19 pandemic.

Keywords: COVID-19, myocardial injury, ischemia, myocarditis, acute coronary syndrome

ARTICLE HISTORY

Received: August 18, 2020
Accepted: September 9, 2020

CORRESPONDENCE

Renata Gerculy
Str. Gheorghe Marinescu nr. 50
540136 Târgu Mureș, Romania
Tel: +40 265 212 111
E-mail: gerculy_renata@yahoo.com

INTRODUCTION

COVID-19 is a disease caused by the new coronavirus discovered in 2019, which may lead to a severe acute respiratory syndrome and has a major impact on public health worldwide, being declared a pandemic by World Health Organization. Multiple cardiovascular complications that may occur in the context of COVID-19 have been described, separately or in addition with pulmonary manifestations.[1] There appears to be a special interrelation between SARS-CoV-2 and cardiovascular disease (CVD). Despite the fact that COVID-19 has predominantly respiratory manifestations, a significant number of patients with COVID-19 present with preexisting CVD or evolve to new-onset myocardial damage amid the course of the novel type of coronavirus-induced disease.[2] Although the clinical picture of COVID-19 is usually dominated by respiratory symptoms, these patients may also develop ful-

Cosmin Țolescu: Str. Gheorghe Marinescu nr. 50, 540136 Târgu Mureș, Romania. Tel: +40 265 212 111, E-mail: tolescu.cosmin@yahoo.com
Camelia Libenciuc: Str. Gheorghe Marinescu nr. 50, 540136 Târgu Mureș, Romania. Tel: +40 265 212 111, E-mail: camelialibenciuc@gmail.com
Istvan Kovacs: Str. Gheorghe Marinescu nr. 38, 540139 Târgu Mureș, Romania. Tel: +40 265 215 551, E-mail: kov_istvan@yahoo.com

minant myocardial injury, leading to a major increase in mortality rates. Among the cardiovascular complications that have been reported, the most frequent are myocarditis, acute coronary syndromes (ACS), congestive heart failure (HF), pulmonary embolism (PE), and cardiogenic shock. Thereby, understanding the myocardial damage caused by SARS-CoV-2 and its foremost mechanisms is of great importance. During treatment for COVID-19, a vigilant attitude is required to identify potential cardiovascular damage or antiviral treatment-induced cardiac side effects.[3] The aim of the present manuscript is to provide an overview of the main causes of myocardial injury during the COVID-19 pandemic.

COVID-19 AND MYOCARDIAL INJURY

Myocardial injury, demonstrated by elevated cardiac biomarkers, was documented among early cases in China. In a study that included 138 hospitalized patients with COVID-19 in Wuhan, China, cardiac damage (demonstrated by elevated high-sensitivity cardiac troponin I [hs-cTnI] and new electrocardiographic or echocardiographic abnormalities) was confirmed in 7.2% of patients overall, and in 22% of patients who required admission to the intensive care unit (ICU).[4] Remarkably, hs-cTnI was above the 99th percentile upper reference limit in 46% of non-survivors as opposed to 1% of survivors.[5] This indicates an increased risk of death in COVID-19 patients who present associated myocardial injury.

Initial reports specify that there are two patterns of myocardial injury with COVID-19. One study established that at four days after the onset of symptoms, the median hscTnI levels were 8.8 pg/mL in non-survivors as opposed to only 2.5 pg/mL in survivors. Throughout follow-up, the average hscTnI did not present a marked change in survivors (2.5 to 4.4 pg/mL), but patients that had deceased presented significant increase during hospitalization (24.7 pg/mL on day 7, to 55.7 pg/mL on day 13, 134.5 pg/mL on day 19, and 290.6 pg/mL on day 22).[6] Particularly, the median time to the end-point from the onset of symptoms was 18.5 days. The increase in hs-cTnI tracks with other inflammatory biomarkers (D-dimer, ferritin, interleukin-6, lactate dehydrogenase), indicating that this is more a reflection of the cytokine storm, than an isolated myocardial injury.[7]

The precise mechanism of myocardial involvement in COVID-19 remains unclear. One proposed mechanism is direct myocardial injury mediated by angiotensin converting enzyme 2 (ACE2). A murine prototype revealed pulmonary infection with SARS-CoV-2 also causing an ACE2-dependent myocardial damage.[8]

Other evoked mechanisms of COVID-19-linked myocardial injury include the cytokine storm, interposed by an overexpressed response among subtypes of T helper cells, and the intracellular accumulation of calcium due to a hypoxic mechanism, leading to myocyte apoptosis.[9]

WHAT DOES RAISED TROPONINS SUGGEST IN COVID-19?

A group from Wuhan Renmin University described, in a cohort of 671 COVID-19 patients, the importance of increased troponin I (cTnI) levels in patients who required respiratory support. The authors noticed that a cTnI value of >0.026 ng/mL was the finest limit for predicting in-hospital mortality, the value being in the normal population range for this test (<0.04 ng/mL).[10]

Patients with CVD and risk factors, such as high blood pressure and diabetes mellitus, are at high risk of presenting severe manifestations of COVID-19. Whether this reflects a higher susceptibility to infection, or its severe consequences, is presently unclear. There is ample speculation over the role of the ACE2 receptor for CoV-2 cellular docking, which may be influenced by CVD and/or its treatment.[11]

Elevated troponin levels are common in patients with chronic stable CVD, particularly when it is associated with heart failure, which foretells a worse scenario. Moderate troponin elevation during COVID-19 infection may just be a surrogate indicator for the underlying severity of pre-existing cardiovascular disease.[12]

Two editorials issued in JAMA Cardiology from two academic hospitals from Wuhan, China, the epicenter of the COVID-19 pandemic,[11,13] have proposed multiple mechanisms that brought us a more accurate representation of the impact of SARS-CoV-2 infection on patients with cardiovascular disease. Shi *et al.* reported a study on 416 hospitalized patients with SARS-CoV-2-related disease, confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR). From the total number of enrolled patients, 82 (19.7%) had evidence of myocardial damage, revealed by increased high-sensitivity troponin I (TnI) levels. Patients with myocardial injury had presented a drastic increase of in-hospital mortality rates (51.2%) compared to the group of patients in whom no myocardial injury was detected (4.5%). Furthermore, patients with myocardial injury who presented greater levels of troponin I, showed increasingly higher death rates.[11]

A notable analysis conducted by Guo *et al.* in 187 patients with SARS-CoV-2 positive test, revealed that 27.8% of patients had presented myocardial injury illustrated by

increased levels of troponin T (TnT). The in-hospital mortality rate was 59.6% (31 of 52) in those with higher TnT levels compared with 8.9% (12 of 135) in those with normal TnT. Additionally, a higher mortality rate was observed in patients with underlying CVD (69.4%). However, high levels of mortality were observed even in those without CVD but with high levels of troponin (37.5%). In contrast, a relatively favorable prognosis was observed in patients with diagnosed CVD but without high troponin levels, who presented a mortality of 13.3%. Guo *et al.* proposed an additional explanation according to which increased levels of TnT are directly related to higher levels of C-reactive protein (CRP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP). This hypothesis could connect the myocardial injury to the magnitude of the inflammatory response and the presence of systolic dysfunction. Their article also showed a gradual increase in troponins and NT-proBNP levels in patients with a worsening clinical status. On the other hand, in patients with a favorable evolution and response to antiviral therapy, a constantly low level of serum biomarkers was maintained.[11]

MYOCARDITIS IN THE CONTEXT OF SARS-CoV-2 INFECTION

Myocarditis is an inflammatory disease characterized by non-ischemic myocardial injury and accumulation of a cellular infiltrate in the myocardium. Esfandiarei *et al.* and Lee *et al.* proposed that the mechanism of viral myocarditis is a combination of direct damage to myocardial cells and cytotoxicity caused by T lymphocytes, a phenomenon intensified by the occurrence of the cytokine storm. Interleukin 6 (IL-6) is thought to be the central element of the cytokine storm, consequently coordinating all proinflammatory activities.[14,15]

The entry of the SARS-CoV-2 virus into the cell is achieved by attaching its spike protein to the protein membrane of ACE2, which can also be found on the ciliated columnar epithelial cells of the respiratory tract, type II pneumocytes, and cardiomyocytes.[16]

Due to the fact that the initial reports often did not have specific diagnostic methods for the evaluation of myocardial injury, Driggin *et al.* strengthened the idea that the real incidence of myocarditis is unknown. Nevertheless, it is suggested that approximately 7% of COVID-19 deaths are caused by myocarditis.[17]

Elevated levels of lactate and other inflammatory markers have been observed, including CRP, erythrocyte sedimentation rate, and procalcitonin, which are typically elevated according to clinical presentation. Increases in both troponins and NT-proBNP have been observed in patients with myocarditis associated with SARS-CoV-2 infection.[18]

In myocarditis, the electrocardiogram (ECG) revealed pericarditis-like changes, such as elevation of the ST segment and PR depression. However, the method is not sensitive for the detection of myocarditis, and the absence of these changes does not exclude the diagnosis. Other changes can be observed, such as newly appeared bundle branch blocks, infarction patterns, ventricular arrhythmias, or high-grade atrioventricular blocks.[19]

The American Heart Association (AHA) recommends that all patients with clinical signs positive for myocarditis should be investigated by one or more imaging diagnostic methods such as transthoracic echocardiography or cardiovascular magnetic resonance (CMR).[20]

Echocardiography is the first used imaging method due to its portability and the short time of issuing a presumptive diagnosis. The cardinal indicators of myocarditis on echocardiography are increased wall thickness, dilation of the heart cavities, and pericardial effusion, accompanied by systolic dysfunction. Although CMR represents the main diagnostic imaging method, it is limited by the long period of analysis and, given the high contagion of SARS-CoV-2, the need to sanitize materials and the room after examination. The results obtained must be interpreted in accordance with the revised Lake Louise criteria, which include: (1) edema; (2) irreversible cell damage; and (3) hyperemia.[21,22]

Endomyocardial biopsy (EMB) is recommended by the European Society of Cardiology (ESC) as the main diagnostic method for myocarditis. However, there are certain limitations of this technique, especially false negative results and infectious risk associated with the current pandemic state. If CMR cannot be performed, contrast-enhanced computed tomography (CT) can be used, especially if the patient undergoes a CT scan for the assessment of dyspnea or other clinical elements related to the respiratory distress. In the absence of CMR or contrast-enhanced CT results, it is very challenging to differentiate myocarditis from other similar diagnoses.[18]

ACUTE CORONARY SYNDROMES AND COVID-19

Arising from the well-known association between acute myocardial infarction and respiratory infections caused mostly by influenza viruses, recent studies regarding the potential pathophysiological correlations between SARS-CoV-2 and acute coronary syndromes (ACS) are of the

utmost importance and relevance. Preliminary data have shown an apparent decrease in the overall number of ACS presentations during the SARS-CoV-2 pandemic, but mortality and morbidity associated with this condition remain very high.[22]

The physiopathology of ACS is related to the sudden decrease of coronary blood flow, leading to the appearance of acute myocardial ischemia. This is clinically illustrated by the occurrence of ST- and non-ST-segment elevation, and unstable angina.[23,24] The most important mediators involved in the regulation of the contractile apparatus of myocardial cells are cTnI and cTnT, these biomarkers being used also in the evaluation of myocardial lesions. However, it is important to emphasize that any type of myocardial injury can lead to a substantial release of cTnI into the bloodstream, but this increase in cTn cannot differentiate the underlying pathophysiological mechanisms.[25]

STEMI: WHERE DID THEY ALL DISAPPEAR?

One of the most important consequences of the COVID-19 pandemic was reflected in the approach to the diagnosis and management of patients with ACS, delaying their hospitalization due to suspicion or confirmation of SARS-CoV-2 infection. In patients with STEMI, the ischemic period is critical in terms of myocardial necrosis, therefore prompt activation of emergency medical services (EMS) is very important. Also, in terms of mortality and morbidity associated with ACS, of particular importance are the prompt detection and early application of specific treatment. During the pandemic, the radical decrease in the total number of ACS admissions was considered to be in the middle of the healthcare crisis, especially given the circumstances in which patients refused to be admitted to EMS, as these were considered unsafe places. Therefore, hospital admissions for ACS were reduced by up to 75%.[26,27]

Furthermore, in Italy, especially in the region of Lombardia, the healthcare system has faced a huge overload, which has led to significant consequences for the cardiology resources. Accessibility to cardiology care units (CCU) has been drastically reduced, and the scheduled interventions, such as primary percutaneous coronary interventions (PCI) have been delayed. Due to the redistribution of most financial resources and medical staff to COVID-19 management, there are fewer resources for the management of ACS or other cardiovascular emergencies.[27]

During this time, there has been a global concern for the management of the pandemic generated by SARS-COV-2 but also for the correct management of the main cardiovascular emergencies. Regularly, according to the guidelines, PCIs bypassing the ED are the standard management for STEMI patients.[28] Percutaneous interventions

TABLE 1. The main studies focused on myocardial injury in patients with SARS-CoV-2-related disease

Study, year	Population	Evaluation and timeline	Cases with myocardial injury	Suspected ACS	In-hospital mortality
Huang *et al.*, 2020	*n* = 41 ICU = 13 Non-ICU = 28	Myocardial injury – elevated cardiac biomarkers or new ECG/ echo abnormalities during hospitalization	*n* = 5 (12%) ICU = 4 (31%) Non-ICU = 1 (4%)	NA	*n* = 6 (15%)
Wang *et al.*, 2020	*n* = 138 ICU = 36 Non-ICU = 102	Myocardial injury – elevated cardiac biomarkers or new ECG / echo abnormalities during hospitalization	*n* = 10 (7.2%) ICU = 8 (22.8%) Non-ICU = 2 (2%)	NA	*n* = 6 (43%)
Zhou *et al.*, 2020	*n* = 191 Non-Survivor = 54 Survivor = 137	Myocardial injury – elevated cardiac biomarkers or new ECG / echo abnormalities during hospitalization	*n* = 33 (17%) Non-Survivor = 32 (59%) Survivor = 1 (1%)	First autopsy performed – strongly evidence of AMI	*n* = 54 (28.3%)
Shi *et al.*, 2020, Journal of American Medical Association	*n* = 416	Myocardial injury – elevated cardiac biomarkers or new ECG / echo abnormalities during hospitalization	*n* = 82 (19.7%)	ECG features consistent with myocardial ischemia	*n* = 57 (13.7%) With cardiac injury – 42 (51.2%) Without cardiac injury – 15 (4.5%)

ACS – acute coronary syndromes; AMI – acute myocardial infarction; ECG – electrocardiogram; ICU – intensive care unit; NA – not available

should remain the main reperfusion strategy in patients with myocardial infarction and SARS-CoV-2 infection, with careful protection of medical staff, according to myocardial infarction guidelines in the COVID-19 era.

The main studies conducted in China during the COVID-19 pandemic that analyzed the degree of myocardial injury in a variable group of patients (based on elevated cardiac biomarkers or new ECG/echocardiographic abnormalities), as well as in-hospital mortality are listed in Table 1.

DIFFERENTIAL DIAGNOSIS BETWEEN MYOCARDITIS AND ACUTE CORONARY SYNDROMES

Myocarditis may mimic myocardial infarction, and established tests lack enough specificity for proper differential diagnosis. CMR can noninvasively depict distinct abnormal tissue patterns: edema, hyperemia, and myocyte necrosis/fibrous scar tissue. Nuclear imaging is a complementary procedure, even though is hampered by radiation and reduced specificity.[29] In the context of elevated cTnI levels, the diagnosis of ACS is very likely, but the involvement of the epicardial arteries can be ruled out by coronary angiography. However, numerous COVID-19 patients were identified to have a detectable cTnI level, even when they had no substantial cardiac symptoms.[30] It is possible that the raised troponin level is the outcome of a sepsis-linked exacerbation of the patient's subclinical CAD, leading to an increased myocardial oxygen demand that triggers the ischemic cascade.[31] However, at this point, it is unknown whether the myocardial injury documented in COVID-19 patients develops in a direct manner from myocardial infection, such as SARS-CoV-2 viral myocarditis, or indirectly, from the complications of COVID-19.[32]

Under usual circumstances, the differential diagnosis of myocardial injury does not confront many difficulties. However, during the current pandemic state, there are several limitations regarding the management of patients with SARS-CoV-2 infection.

Even though studies have shown myocardial injury to be a poor prognostic factor in SARS-CoV-2 infection, it is unknown whether attenuating the myocardial damage would adjust the final endpoint. Furthermore, it is still unclear whether myocardial injury serves as the transitional state between COVID-19, systemic inflammation, and mortality, or whether the injury of the myocardium is a signal of systemic organ failure and, implicitly, a marker for the extent of the viral disease.[31]

CONCLUSIONS

Currently, there are insufficient data regarding an accurate diagnosis of myocardial injury caused by SARS-CoV-2 infection, and there is limited evidence of direct damage of the myocardium in COVID-19. Complementary research and particularly autopsy studies are required to expose the virus's potential to cause myocardial injuries or vascular damages. Additional studies should be performed to firmly conclude whether the virus has cardiotrophic properties and, furthermore, to obtain a clear image of myocardial involvement in patients with SARS-CoV-2 infection, and of its effects on duration of hospitalization, need for endotracheal intubation, mortality, and long-term outcomes.

CONFLICT OF INTEREST

Nothing to declare.

REFERENCES

1. Long B, Brady W, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med. 2020;38:1504-1507. doi: 10.1016/j.ajem.2020.04.048.
2. Paramasivam A, Priyadharsini JV, Raghunandhakumar S, et al. A novel COVID-19 and its effects on cardiovascular disease. Hypertens. 2020;43:729-730. doi: 10.1038/s41440-020-0461-x.
3. Fried JA, Ramasubbu K, Bhatt R, et al. The variety of cardiovascular presentations of COVID-19. Circulation. 2020;141:1930-1936. doi: 10.1161/CIRCULATIONAHA.120.047164.
4. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323:1061-1069. doi: 10.1001/jama.2020.1585.
5. Zhou F, Ting Y, Ronghui D, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-1062. doi: 10.1016/S0140-6736(20)30566-3.
6. Huang C, Wang Y, Ren L, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506. doi: 10.1016/S0140-6736(20)30183-5.
7. Hu H, Ma F, Wei X, Fang Y, Hongde H. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin. Eur Heart J. 2020;ehaa190. doi: 10.1093/eurheartj/ehaa190.
8. Oudit GY, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest. 2009;39:618-625. doi: 10.1111/j.1365-2362.2009.02153.x.
9. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17:259-260. doi: 10.1038/s41569-020-0360-5.
10. Shaobo S, Qin M, Cai Y, et al. Characteristics and clinical significance of myocardial injury in patients with severe

coronavirus disease 2019. Eur Heart J. 2020;41:2070-2079. doi: 10.1093/eurheartj/ehaa408.
11. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5:1-8. doi: 10.1001/jamacardio.2020.1017.
12. Nicin L, Abplanalp W, Mellentin H, et al. CoV-2 receptor ACE2 in human hearts. Eur Heart J. 2020;41:1807-1809. doi: 10.1093/eurheartj/ehaa410.
13. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol. 2020;5:802-810. doi: 10.1001/jamacardio.2020.0950.
14. Esfandrei M, McManus B. Molecular biology and pathogenesis of viral myocarditis. Annu Rev Pathol. 2008;3:127-155. doi: 10.1146/annurev.pathmechdis.3.121806.151534.
15. Lee DW, Gardner R, Porter D, et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014;124:188-195. doi: 10.1182/blood-2014-05-552729.
16. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020;181:271-280.e8. doi: 10.1016/j.cell.2020.02.052.
17. Driggin E, Madhavan M, Bikdeli B, et al. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. J Am Coll Cardiol. 2020;75:2352-2371. doi: 10.1016/j.jacc.2020.03.031.
18. Caforio A, Pankuweit S, Arbustini E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013;34:2636-2648. doi: 10.1093/eurheartj/eht210.
19. Kociol R, Cooper L, Fang J, et al. Recognition and initial management of fulminant myocarditis: a scientific statement from the American Heart Association. Circulation. 2020;141:e69-e92. doi: 10.1161/CIR.0000000000000745.
20. Friedrich M, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: a JACC White Paper. J Am Coll Cardiol. 2009;53:1475-1487. doi: 10.1016/j.jacc.2009.02.007.
21. Sala S, Peretto G, Gramegna M, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. Eur Heart J. 2020;41:1861-1862. doi: 10.1093/eurheartj/ehaa286.
22. Schiavone M, Gobbi G, Biondi-Zoccai G, et al. Acute Coronary Syndromes and Covid-19: Exploring the Uncertainties. J Clin Med. 2020;9:1683. doi: 10.3390/jcm9061683.
23. Roffi M, Patrono C, Mueller C, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267-315. doi: 10.1093/eurheartj/ehv320.
24. Thygesen K, Alpert J, Jaffe A, et al. Fourth universal definition of myocardial infarction (2018). Eur Heart J. 2019;40:226. doi: 10.1093/eurheartj/ehy856.
25. Thygesen K, Mair J, Katus H, et al. Recommendations for the use of cardiac troponin measurement in acute cardiac care. Eur Heart J. 2010;31:2197-2204. doi: 10.1093/eurheartj/ehq251.
26. Scholz K, Maier S, Maier L, et al. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: Results from the German prospective, multicentre FITT-STEMI trial. Eur Heart J. 2018;39:1065-1074. doi: 10.1093/eurheartj/ehy004.
27. Stefanini G, Azzolini E, Condorelli G. Critical organizational issues for cardiologists in the COVID-19 outbreak: A frontline experience from Milan, Italy. Circulation. 2020;141:1597-1599. doi: 10.1161/CIRCULATIONAHA.120.047070.
28. Mahmud E, Dauerman H, Welt F, et al. Management of acute myocardial infarction during the COVID-19 pandemic. J Am Coll Cardiol. 2020;S0735-1097(20)35026-9. doi: 10.1016/j.jacc.2020.04.039.
29. Leurent G, Langella B, Fougerou C, et al. Diagnostic contributions of cardiac magnetic resonance imaging in patients presenting with elevated troponin, acute chest pain syndrome and unobstructed coronary arteries. Arch Cardiovasc Dis. 2011;104:161-170. doi: 10.1016/j.acvd.2011.01.005.
30. Clerkin K, Fried J, Raikhelkar J, et al. COVID-19 and cardiovascular disease. Circulation. 2020;141:1648-1655. doi: 10.1161/CIRCULATIONAHA.120.046941.
31. Cheng R, Leedy D. COVID-19 and acute myocardial injury: the heart of the matter or an innocent bystander? Heart. 2020;106:1122-1124. doi: 10.1136/heartjnl-2020-317025.
32. Zeng JH, Liu YX, Yuan J, et al. First case of COVID-19 infection with fulminant myocarditis complication: case report and insights. Infection. 2020;1-5. doi: 10.1007/s15010-020-01424-5.