Analysis of Cardiac Injury Biomarkers in COVID-19 Patients

Salma Abdeladim1,2, Sara Oualim1, Amal Elouarradi1, Ilham Bensahi1, Rita Aniq Filali2, Mahassine EL Harras1, Soukaina Scadi1, El Arbi Bouaiti3, Naitlho Abdelhamid2 and Mohamed Sabry1

1Department of Cardiology, Cheick Khalifa International University Hospital, Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco
2Department of Internal, Cheick Khalifa International University Hospital, Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco
3Laboratory of Biostatistics, Clinical Research and Epidemiology, Faculty of Medicine and Pharmacy Mohammed V University in Rabat, Casablanca, Morocco

*Corresponding author: MD, Department of Cardiology, Cheick Khalifa International University Hospital, Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco. Email: salma.abdeladim56@gmail.com

Received 2020 May 23; Accepted 2020 September 13.

Abstract

Background: Infection with the novel coronavirus, named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), producing a clinical syndrome known as COVID-19, is a budding infectious disease that first manifested in December 2019 in China and subsequently spread worldwide.

Objectives: We performed an analysis of cardiac injury markers to determine their usefulness as predictors of severity and mortality.

Methods: In a retrospective study, we enrolled 73 patients with confirmed diagnoses of COVID-19, from March 21, 2020, to April 24, 2020. Serial tests of cardiac injury markers, including cardiac troponin I (cTnI), N-terminal pro-brain natriuretic peptide (NT-proBNP), and Lactate dehydrogenase (LDH), were considered for the analysis of potential cardiac damage.

Results: Among 149 patients with confirmed COVID-19, data from 73 patients were studied. Of them, 58 (79.46%) patients were discharged, and 15 (20.54%) patients died. The mean age was 58.50 (14.66) years. Patients were classified into mild (39 cases), severe (17 cases), and critical (17 cases) groups. The peak cardiac troponin I level (0.11 ng/mL [IQR: 0.33–0.20]), peak NT-pro BNP level (5840.35 pg/mL [IQR: 1609.39 – 10071.32]), and peak LDH level (578.65 IU/l[IQR: 313.40 – 843.90]) were significantly higher in the critical group, and the three cardiac injury parameters were significantly higher in the death group, suggesting that they are significantly associated with a higher risk of in-hospital mortality.

Conclusions: The understanding of cardiovascular system injury caused by SARS-CoV-2 and its underlying mechanisms is of great importance for the early clinical management of these patients and mortality reduction.

Keywords: COVID-19, Cardiac Troponin I, NT-proBNP, Lactate Dehydrogenase, Severity

1. Background

Novel Coronavirus Disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is an emerging infectious disease that first manifested in December 2019 in Wuhan and subsequently spread worldwide. Coronavirus disease 2019 has become a major public health problem resulting in considerable morbidity and mortality. As of April 30, 2020, there were 3,090,445 confirmed cases and 217,769 deaths in the world (1).

In addition to the severe state of pneumonia, the new coronavirus can cause multiple organ failure by attacking several important organs. The heart is one of these organs. It is very likely that viral myocarditis and myocardial damage are involved and may even be one of the main causes of death from COVID-19. Regardless of previous cardiac history, heart failure is described in severe cases of COVID-19 (2, 3). This increases the levels of myocardial markers, especially cardiac N-terminal pro-brain natriuretic peptide (NT-proBNP), and troponin I (cTnI), specifically in severe cases (4).

2. Objectives

In the present study, we tried to determine the role of laboratory indicators of heart injury including cardiac troponin I (cTnI), NT-proBNP, and Lactate Dehydrogenase (LDH) in predicting the disease severity and outcome in 73 patients with COVID-19 at Cheikh Khalifa International University Hospital, Mohammed VI University of Health Sciences (UM6SS), Morocco.
3. Methods

In a retrospective study, we enrolled 149 patients from March 21, 2020, to April 24, 2020, at Cheikh Khalifa International University Hospital, Mohammed VI University of Health Sciences (UM6SS), Morocco. The final follow-up date was April 30, 2020. The laboratory confirmation of COVID-19 was done as recommended (5). We excluded 76 patients because of incomplete data, leaving 73 patients for final analysis. The Ethics Committees of the Mohammed VI University of Health Sciences approved this study.

The COVID-19 patients included in this study were diagnosed following the World Health Organization’s interim guidelines (1). They were classified into three groups: Mild (39 cases), severe (17 cases), and critical (17 cases). The diagnostic criteria for mild cases were a positive result in the real-time fluorescence polymerase chain reaction of COVID-19 virus RNA nucleic acid test, fever, or other respiratory symptoms, besides imaging characteristics typical of lung involvement as an additional criterion (6). For severe cases, at least one of the following criteria must be met: (a) Respiratory depression (breathing rate > 30 breaths/min), (b) need for oxygen treatment or mechanical ventilation, and (c) SpO$_2$ < 90% of ambient air (1). Critical cases must meet at least one of the following additional criteria: (a) Respiratory failure requiring mechanical ventilation, (b) shock, and (c) multiple organ failure (7).

Confirmed COVID-19 cases were hospitalized and placed in isolation for treatment. We collected data on the first detection of laboratory parameters of cardiac lesions in these 73 patients with COVID-19 on admission. The cases without cardiac biomarkers, including cardiac troponin I (cTnI), NT-proBNP, and LDH, were excluded.

We used SPSS for statistical analysis. Differences between the groups were analyzed. The Pearson correlation coefficient was used for linear correlation analyses. The categorical variables were compared using the $\chi^2$ test. $P$ value < 0.05 was considered statistically significant.

4. Results

4.1. Demographic and Clinical Characteristic

Data were collected from consecutive hospitalized COVID-19 patients. We excluded 76 patients because of incomplete data, leaving 58 discharged individuals and 15 dead ones for final analysis.

The mean age was 54.58 (17.62) years. The difference in sex and age between the three groups was significant (Table 1). Of the 73 patients, 58 (51.8%) had one or more cardiovascular risk factors. Hypertension (23 [33.8%]), diabetes (12 [17.6%]), and smoking (4 [5.9%]) were the most common cardiovascular risk factors and six patients had underlying Coronary Heart Disease (CHD) (Table 2). The most common heart-related symptoms were cough (42 [57.5%]), fever (39 [53.4%]), chest pain/tightness (34 [46.6%]), and shortness of breath (21 [28.8%]).

4.2. Laboratory Results

The values of cardiac troponin I (cTnI), NT-proBNP, and LDH were studied in all patients of mild, severe, and critical groups. The values of these indicators and their relationships with the clinical classification of the disease were analyzed and compared.

In severe and critical cases, the positive levels of LDH, cTnI, and NT-proBNP were higher than those in mild cases, and the differences between the groups were statistically significant ($P$ value < 0.05). Cardiac troponin I was elevated (over 0.03 ng/mL) in 11 (15.1%) patients during hospitalization. The peak cardiac troponin I level (0.11 ng/mL [IQR: 0.33–0.20]), peak NT-pro BNP level (5840.35 pg/mL [IQR: 1609.39–10071.32]), and peak LDH level (578.65 UI/L [IQR: 313.40–843.90]) were significantly higher in the critical group (Table 3).

4.3. Clinical Outcomes

Until April 24, 2020, the overall Case Fatality Rate (CFR) was 20.54% (15 deaths among 73 cases). The CFR was 47.05% (8 deaths among 17 cases) in the critical group, which was not much higher than the CFR of 41.17% (seven deaths among 17 cases) in the severe group. Then, the levels of cTnI, LDH, and NT-proBNP were compared between dead ($N$ = 15) and surviving ($N$ = 58) patients with COVID-19. The cardiac injury biomarkers were significantly higher in the deceased group than in the survivor group ($P$ value < 0.005) (Table 4).

5. Discussion

Influenza infection is a common risk factor for chronic cardiovascular disease. Previous epidemics have been associated with heart injury. Acute myocardial infarction, acute myocarditis, and sudden heart failure have been described in SARS and MERS (8, 9). The novel Coronavirus Disease 2019 (COVID-19) has attracted great attention around the world. Previous studies suggest that severe COVID-19 may lead to acute heart damage (7, 10, 11). Huang et al. reported that 12% of patients with mild and severe COVID-19 had increased hypersensitivity to troponin I, suggesting acute myocardial injury (10).
Table 1. Coronavirus Disease 2019 Patients Based on Age and Gender

| Age (years) | Total Cases | Mild Group, (N = 39) | Severe Group, (N = 17) | Critical Group, (N = 17) | P Value |
|-------------|-------------|----------------------|-----------------------|--------------------------|---------|
| 54.58 ± 17.62 | 49.59 ± 18.81 | 56.65 ± 16.85 | 63.94 ± 10.73 | 0.015 |

Gender, %

| Gender | Total Cases | Mild Group, (N = 39) | Severe Group, (N = 17) | Critical Group, (N = 17) | P Value |
|--------|-------------|----------------------|-----------------------|--------------------------|---------|
| Men | 38.40 | 48.90 | 15.60 | 35.60 | 0.004 |
| Women | 61.60 | 60.70 | 35.70 | 3.60 |  |

Table 2. Cardiovascular Risk Factors and Cardiovascular Disease of Coronavirus Disease 2019 Patients

| Risk Factor | Mild Group, (N = 39) | Severe Group, (N = 17) | Critical Group, (N = 17) | P Value |
|-------------|----------------------|-----------------------|--------------------------|---------|
| Hypertension | 10 (41.5) | 5 (21.7) | 8 (34.8) | 0.186 |
| Diabetes | 5 (41.7) | 3 (25.0) | 4 (33.3) | 0.525 |
| Smoking | 1 (25.0) | 2 (50.0) | 1 (25.0) | 0.376 |
| Coronaropathy | 1 (16.7) | 1 (16.7) | 4 (66.7) | 0.02 |

Table 3. Coronavirus Disease 2019 Patients’ Levels of Cardiac Troponin, LDH, and NT-proBNP

| Biomarker | Total, (N = 73) | Mild Group, (N = 39) | Severe Group, (N = 17) | Critical Group, (N = 17) | P Value |
|-----------|----------------|----------------------|-----------------------|--------------------------|---------|
| Troponin (ng/ml) | 0.0320 (0.0105 - 0.0534) | 0.005 (0.002 - 0.006) | 0.005 (0.005 - 0.203) | 0.188 (0.013 - 0.203) | < .001 |
| < 0.03 | 62 (84.9 %) | 37 (50.7 %) | 17 (23.3 %) | 8 (11.9 %) | < 0.001 |
| ≥ 0.03 | 11 (15.1 %) | 2 (2.7 %) | 0 (0.0 %) | 9 (12.3 %) |  |
| NT-pro BNP (pg/mL) | 1432.14 (361.99 - 2502.29) | 80.74 (46.66 - 104.83) | 124.18 (72.27 - 176.08) | 5840.35 (1609.39 - 10071.32) | < .001 |
| < 125 | 44 (60.3 %) | 32 (41.8 %) | 9 (12.3 %) | 3 (4.1 %) | < 0.001 |
| ≥ 125 | 29 (39.7 %) | 7 (9.6 %) | 8 (11.0 %) | 14 (19.2 %) |  |
| LDH (UI/L) | 326.89 (259.27 - 394.51) | 239.21 (215.52 - 262.89) | 276.29 (224.03 - 328.56) | 578.65 (313.40 - 843.90) | < .001 |
| < 250 | 38 (52.1 %) | 28 (38.4 %) | 9 (12.3 %) | 1 (1.4 %) | < 0.001 |
| ≥ 250 | 35 (47.9 %) | 11 (15.1 %) | 8 (11.0 %) | 16 (21.9 %) |  |

Table 4. Correlation Between the Levels of cTnI, LDH and NT-proBNP and Mortality

| Biomarker | Death (Mean ± SD) | Survival (Mean ± SD) | P Value |
|-----------|------------------|----------------------|---------|
| Troponin (ng/ml) | 0.0049 ± .004 | 0.1322 ± 0.172 | 0.001 |
| NT-pro BNP (pg/mL) | 127.74 ± 129.088 | 6540.72 ± 8537.188 | 0.001 |
| LDH UI/L | 245.22 ± 540.021 | 654.93 ± 540.021 | 0.002 |

In this study, the association of COVID-19 with heart injury was confirmed, and the correlation of the severity of SARS-CoV-2 infection and cardiac involvement was analyzed. We focused on the biomarkers of heart injury in mild, severe, and critical COVID-19 patients. We proved the elevation of cTnI, Pro BNP, and LDH in the critical group. In the critical group, 12.3% of the patients had a cTnI level above the reference level while it was 2.7% in the mild group. Moreover, the difference in the level and positivity rate of LDH and NT-proBNP was statistically significant among the three groups. This suggests that a rise in heart injury markers could be a potential indicator of critical disease and predict the severity of COVID-19. Also, the high values of cTnI, Pro BNP, and LDH in the group of dead patients compared to survivor patients indicated a higher fatality risk associated with the increased level of heart injury markers.

Retrospective cohorts have shown that the increased levels of cardiac injury markers at the onset of disease are associated with a more severe prognosis (12, 13). Guo et al. (3) could prove a direct relationship between troponin and the levels of highly sensitive C-reactive protein (CRP), an important inflammatory marker that strengthens the link between inflammation and myocardial damage. This fact should be raised as a warning because the risk of death from myocardial injury exceeds that of factors such as age,
the presence of diabetes, and previous chronic lung and heart disease.

Despite the strong evidence, there is still no proof for the presence of the virus in the myocardium; however, we suggest the occurrence of direct and indirect heart injury attributed to the virus. Indirect damage can be caused by a cardiac overload due to systemic inflammation and hypoxemic respiratory failure whereas direct lesions would be caused by tissue infection leading to the death of cardiomyocytes (14). The finding of inflammatory infiltrates of mononuclear cells in autopsies in cardiac tissue is another argument suggesting direct cardiac injury by COVID-19 (15). In the study by Yi Han et al., the LDH elevation was positively associated with cTnI and BNP and showed that LDH could be identified as a strong predictor for the early identification of severe cases of COVID-19 (16). In another study by Zhou et al., the elevation of cTnI and LDH in critical cases was proven (17).

In a single-center study by Han et al. in Wuhan, China, the roles of cardiac troponin I and NT-pro BNP were studied. The authors assessed the results of 273 patients with COVID-19 and indicated that higher concentrations of these enzymes were associated with the severity of the disease and poor outcomes (18). Cardiac troponin I is a sensitive marker for myocardial injury (19), and NT-pro BNP is an optimal biomarker for heart failure (20). The mechanism of cardiac injury markers’ elevation in COVID-19 infection is not fully understood. The underlying pathophysiology suggests a heart-inflammatory response because a large series of severe cases of COVID-19 show a parallel elevation of inflammatory markers in the acute phase, such as C-reactive protein (CRP), procalcitonin, and ferritin (21). This can present clinically as fulminant myocarditis. Another mechanism involves the angiotensin-converting enzyme 2 (ACE2), which is a human cell receptor that binds strongly to the SARS-CoV-2 protein Spike. ACE2 is highly expressed in the heart (22, 23). SARS-CoV-2 can mediate myocardial inflammation and damage associated with the down-regulation of the myocardial ACE2 system, which may be responsible for the myocardial dysfunction and adverse cardiac outcomes in patients with SARS (24). However, a recent pathologic study reported rare mononuclear interstitial inflammatory infiltrations into heart tissue without substantial myocardial damage in a patient with COVID-19 (15), which may suggest that COVID-19 may not directly affect the heart.

Myocardial damage and heart failures presented in critical cases before death may be due to other reasons, such as severe hypoxia, which may be responsible for myocardial ischemia, management of mechanical ventilation, multiple organ failure, severe unbalance in water and electrolytes, or irreversible metabolic acidosis, which would cause serious systemic disorders in COVID-19 patients. All of these factors can influence the heart and cause secondary myocardial damage and heart failure (25).

Some limitations existed in this study. Some data, such as magnetic resonance imaging or echocardiography data and cytokine level measurements, were lacking to determine the characteristics of myocardial injury. Our study was also limited to patients whose data were complete, which decreased our sample size.

In conclusion, although it has not been confirmed that the presence of the novel coronavirus is linked to direct cardiac damage, the elevation of cardiac markers should be considered as a warning sign. We have shown that increased biomarkers of heart damage are associated with worsening outcomes in patients with COVID-19, and could be a powerful predictor for the early detection of severe COVID-19 cases. Serious monitoring of myocardial enzymes is of great importance to prevent complications and mortality in COVID-19 patients.

Footnotes

Authors’ Contribution: Study concept and design, data analysis and interpretation, and manuscript drafting: S.A and S.O; Critical revision of the manuscript for important intellectual content: S.A, S.O, A.E, I.B, R.F., M.E, S.S, A.N, and S. M; Statistical analysis: E. B.

Clinical Trial Registration Code: 47513

Conflict of Interests: The authors report that they have no relationships relevant to the contents of this paper to disclose.

Funding/Support: This manuscript was not funded.

References

1. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-covpdf?sfvrsn=bc7da517_2.
2. Tan ZC, Fu LH, Wang DD, Hong K. Cardiac manifestations of patients with COVID-19 pneumonia and related treatment recommendations. Zhonghua xin xue guan bing za zhi. 2020;48(5):E005.
3. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). Jama Cardiol. 2020;5(7):811–8. doi: 10.1001/jamacardio.2020.1017. [PubMed: 32293558]. [PubMed Central: PMC7015508].
4. Chen C, Yan JT, Zhou N, Zhao JP, Wang DW. Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19. Zhonghua xin xue guan bing za zhi. 2020;48(5):E008.
5. National Health Commission of China. New coronavirus pneumonia prevention and control program. 4th edn. 2020. Available from: http://www.gov.cn/zhengce/zhengceku/2020-01/28/5472673/files/0f96c10cc09d4d36af69a9f0b42d972b.pdf.
6. Liu R, Han H, Liu F, Lv Z, Wu K, Liu Y, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. Clin Chim Acta. 2020;505:172-5. doi: 10.1016/j.cca.2020.01.009. [PubMed: 32566071]. [PubMed Central: PMC7094385].
7. Wang D, Hu B, Hu C, Zhu F, Liu X, Zeng J, et al. Clinical characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(4):1066-9. doi: 10.1001/jama.2020.1585. [PubMed: 32035700]. [PubMed Central: PMC7042881].
8. Peiris JSM, Chiu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLM, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. The Lancet. 2003;361(9370):1767-72. doi: 10.1016/S0140-6736(03)13414-2.
9. Alhobiani T. Acute myocarditis associated with novel Middle east respiratory syndrome coronavirus. Ann Saudi Med. 2016;36(1):78-80. doi: 10.5444/0255-4947.2016.78. [PubMed: 26922892]. [PubMed Central: PMC6074274].
10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.
11. 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. The Lancet. 2020;395(10223):507-13. doi: 10.1016/S0140-6736(20)30217-4.
12. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8. doi: 10.1007/s00134-020-05999-x. [PubMed: 32125452]. [PubMed Central: PMC7080106].
13. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020;395(10229):1054-62. doi: 10.1016/S0140-6736(20)30566-3.
14. Akhmerov A, Marban E. COVID-19 and the Heart. Circ Res. 2020;126(10):1443-55. doi: 10.1161/CIRCRESAHA.120.370555. [PubMed: 32252951].
15. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet Respiratory Medicine. 2020;8(4):420-2. doi: 10.1016/s2213-2600(20)30076-x.
16. Han Y, Zhang H, Mu S, Wei W, Jin C, Xue Y, et al. Lactate dehydrogenase, a risk factor of severe COVID-19 patients. medRxiv. 2020. doi: 10.1101/2020.03.24.20040462.
17. Zhou B, She J, Wang Y, Ma X. The clinical characteristics of myocardial injury in severe and very severe patients with 2019 novel coronavirus disease. Infect. 2020;81(1):347-78. doi: 10.3143/jinf.2020.03.021. [PubMed: 32209382]. [PubMed Central: PMC716305].
18. Han H, Xie L, Liu R, Yang J, Liu F, Wu K, et al. Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. J Med Virol. 2020;92(7):819-23. doi: 10.1002/jmv.25809. [PubMed: 32232979]. [PubMed Central: PMC7228305].
19. Kimenai DM, Martens RJH, Kooman JP, Stehouwer CDA, Tan FES, Schaper NC, et al. Troponin I and T in relation to cardiac injury detected with electrocardiography in a population-based cohort - The Maastricht Study. Sci Rep. 2017;7(7):6600. doi: 10.1038/s41598-017-06978-3. [PubMed: 28747765]. [PubMed Central: PMC5529455].
20. Rorth R, Jhund PS, Yilmaz MB, Kristensen SL, Welsh P, Desai AS, et al. Comparison of BNP and NT-proBNP in Patients With Heart Failure and Reduced Ejection Fraction. Circ Heart Fail. 2020;13(2). e005644. doi: 10.1161/CIRCHEARTFAILURE.119.006541. [PubMed: 32065760].
21. 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. doi: 10.1001/jamacardio.2020.0950. [PubMed: 3221886]. [PubMed Central: PMC7097841].
22. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020;367(6483):1260-3. doi: 10.1126/science.abb2507. [PubMed: 32075877]. [PubMed Central: PMC7646637].
23. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med. 2020;14(2):185-92. doi: 10.1007/s11684-020-0754-0. [PubMed: 32170560]. [PubMed Central: PMC7088738].
24. Oudit GY, Kassiri Z, Jiang C, Liu PP, Poutanen SM, Penninger JM, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest. 2009;39(7):818-25. doi: 10.1111/j.1365-2362.2009.02153.x. [PubMed: 19453650]. [PubMed Central: PMC7857878].
25. 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;311:16-21. doi: 10.1016/j.ijcard.2020.01.087. [PubMed: 32291207]. [PubMed Central: PMC7441778].