



Troponin is a useful marker in clinical decision making in hospitalized patients with COVID-19 infections

Fahimeh Safarnezhad-Tameshkel PhD⁽¹⁾ , Nima Motamed MD⁽²⁾ ,
 Mohammad Hadi Karbalaie Niya PhD⁽³⁾ , Dhayaneethie Perumal MD⁽⁴⁾ , Nader Rezaie MD⁽⁵⁾ ,
 Shirin Izadi MD⁽⁶⁾ , Mitra Ranjbar MD⁽⁷⁾ , Mahdi Yadollahzadeh MD⁽⁸⁾ ,
 Behnam Behdad MD⁽⁹⁾ , Gholamreza Hemmasi MD⁽¹⁰⁾ , Vahid Kaveh MD⁽¹¹⁾ ,
 Ali Arash Anoushirvani MD⁽¹²⁾ , Mojtaba Malek MD⁽¹³⁾ , Behzad Farahani MD⁽¹⁴⁾ ,
 Ramin Eskandari MD⁽¹⁴⁾ , Mahshid Panahi MD⁽¹⁵⁾ , Mandana Rahimi MD⁽¹⁵⁾ ,
 Sepideh Emami MD⁽¹⁴⁾ , Farhad Zamani MD⁽¹⁶⁾ , Mohsen Farrokhpour MD⁽⁸⁾ 

Original Article

Abstract

BACKGROUND: COVID-19 was introduced by the World Health Organization (WHO) as a global pandemic. The disease manifestations ranges from a mild common cold to severe disease and death. It has a higher mortality rate in people with a history of comorbidities, including cardiovascular disease (CVD) and can also contribute to cardiac injury. This study was conducted to evaluate the relationship between troponin levels as a cardiac marker and adverse outcomes in this disease.

METHODS: The study sample included 438 patients hospitalized with COVID-19; however, the troponin data of 6 patients were not available. The need to be admitted to the intensive care unit (ICU), and death were considered the adverse outcome in patients with COVID-19. Troponin levels were checked in all patients on day 1 and day 3 of hospitalization. Multiple logistic regression analysis was performed to determine whether there was an independent association between the adverse outcomes and troponin enzyme in hospitalized patients with COVID-19.

RESULTS: The mean age of patients was 61.29 ± 15.84 years. Among the 432 patients tested on day 1 of hospitalization, 24 patients (5.6%) tested positive (Troponin 1), and among the 303 patients tested on day 3, 13 patients (4.3%) tested positive (Troponin 2). Based on our results, Troponin 1 showed an independent association with both death (3.008 [95%CI = 1.091-8.290]; $P = 0.033$) and need for ICU admission (8.499 [95%CI = 3.316-21.788]; $P < 0.001$) in multiple logistic regression analysis. Moreover, the status of Troponin 2 had an independent significant association with both death (4.159 [95%CI = 1.156-14.961]; $P = 0.029$) and ICU admission (7.796 [95%CI = 1.954-31.097]; $P = 0.004$).

CONCLUSION: Troponin showed a significant association with adverse outcomes in people who were hospitalized with COVID-19. The periodical assessment of this enzyme from the time of hospitalization may improve the clinical decision making of clinicians.

Keywords: Troponin; COVID-19; Mortality

Date of submission: 29 June 2020, *Date of acceptance:* 12 Jan. 2021

- 1- Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran
 - 2- Associate Professor, Department of Social Medicine, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran
 - 3- Assistant Professor, Gastrointestinal and Liver Diseases Research Center AND Department of Virology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
 - 4- Assistant Professor, School of Science, Engineering and Computing, Kingston University, Kingston, United Kingdom
 - 5- Associate Professor, Department of Pulmonology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
 - 6- Assistant Professor, Department of Pulmonology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
 - 7- Professor, Department of Infectious Diseases, Iran University of Medical Sciences, Tehran, Iran
 - 8- Assistant Professor, Department of Internal Medicine, School of Medicine, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
 - 9- Resident, Department of Internal Medicine, School of Medicine, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
 - 10- Associate Professor, Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran
 - 11- Assistant Professor, Department of Hematology and Medical Oncology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
 - 12- Associate Professor, Department of Hematology and Medical Oncology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
 - 13- Associate Professor, Research Center for Prevention of Cardiovascular Disease, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran
 - 14- Assistant Professor, Department of Cardiology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
 - 15- Assistant Professor, Department of Pathology, Iran University of Medical Sciences, Tehran, Iran
 - 16- Professor, Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran
- Address for correspondence: Mohsen Farrokhpour; Assistant Professor, Department of Internal Medicine, School of Medicine, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran; Email: mohsenfrkh@gmail.com

How to cite this article: Safarnezhad-Tameshkel F, Motamed N, Karbalaie Niya MH, Perumal D, Rezaie N, Izadi S, et al. **Troponin is a useful marker in clinical decision making in hospitalized patients with COVID-19 infections.** ARYA Atheroscler 2021; 17: 2191.

Introduction

Coronaviruses are a group of RNA viruses with a very large genome size of about 27 to 34 kb. In previous decades, infections with human strains have usually caused mild and limiting respiratory infections such as the common cold.¹⁻³ However, in the 2 past decades, the 3 betacoronaviruses of SARS CoV, MERS-CoV, and SARS-CoV-2 have caused severe human illnesses with high morbidity and mortality rates.^{4,5} Epidemiologically, 2019-nCoV, now designated as SARS-CoV-2, is highly contagious with a latency period of 4-8 days.^{6,7}

All age groups are susceptible to the virus. Elderly patients with the disease are more likely to develop severe illness.^{6,7} Most importantly, asymptomatic patients may be the primary sources of infection their diagnosis is for the prevention and control of the epidemic.⁸ Severe cases of the disease comprise 20% of all cases according to estimates by the World Health Organization (WHO). Based on some estimates, the mortality rate varies from 3.6% in people of 60 years of age to 8.14% in people of over the age of 80.^{9,10}

The prognosis of patients with COVID-19 in the general population can range from simple cold symptoms to viral pneumonia, septic shock, or even death. Death has been observed in all ages, but mainly in the elderly, those with immunodeficiency or with a history of underlying disease.^{6,7} Previous studies have shown that infection with SARS-CoV-2 may lead to higher adverse outcomes in people with underlying cardiovascular diseases (CVD), and infection with the virus itself can be linked to adverse cardiovascular outcomes.^{11,12}

Due to the relatively high morbidity and mortality rate of COVID-19, early identification of high-risk individuals is of critical importance. High-sensitivity cardiac troponin (hs-cTn) assessment is an integral part of the diagnostic management of acute coronary syndromes. Although a rising titer of troponin does not necessarily indicate the occurrence of acute myocardial infarction (AMI), it may indicate myocardial injury, regardless of the underlying cause.¹³ Troponin levels may also be elevated in

many other critical conditions, such as sepsis or renal failure.¹⁴⁻¹⁶

These complications can occur in severe conditions and contribute to an increase in the mortality rate of involved patients. As a result, this study was conducted to determine the association between serum troponin and adverse outcomes in patients with COVID-19, including the need for intensive care unit (ICU) admission, prolonged ICU stay (LOS), and death.

Materials and Methods

This study was conducted in Firoozgar Hospital in Tehran, the capital city of Iran. This study was performed on 438 hospitalized patients with COVID-19 from 15 March 2020 to 15 July 2020. All patients enrolled were diagnosed on the basis of real time reverse transcription polymerase chain reaction (RT-PCR). Written informed consent was obtained from each of the participants. The study was approved by the Ethics Committee of Iran University of Medical Sciences, Tehran, Iran.

Death, admission into the ICU, and LOS were considered the adverse outcomes in patients with COVID-19. We categorized age into the 4 categories of 18-39, 40-64, 65-79, and 80 years and older. The LOS was categorized into the 3 categories of ≤ 3 days, 4-7 days, and more than 7 days.

Troponin I levels were determined in the blood serum of each patient on day 1 and 3 of hospitalization via the VIDAS troponin I Ultra assay (BioMerieux, Marcy L'Etoile, France) according to the manufacturer's protocol. For measurement, 200 µl of each patient's sample was used. This assay limit of detection (LOD) is < 0.01 µg/l. Of the 438 patients who had consented to participate in the study, the troponin data of 6 patients were not available on day 1. As a result, the related analyses were performed on the data of 432 patients. Furthermore, some patients (129 patients) were discharged on or before the third day, hence day 3 troponin levels were performed on the 303 remaining patients.

Statistical analysis: In descriptive statistics, mean and standard deviation (SD) were reported for continuous data, while the percentage (and frequency) was obtained for nominal data. To determine the differences between nominal data, chi-square test was performed. Simple and multiple logistic regression analysis was performed in which either death or need for ICU admission were individually considered as an outcome and troponin level as a predictor. We conducted 3 models

including the crude model (model 1), adjusted based on age and sex (model 2), and further adjusted based on LOS and ICU admission in addition to age and sex (model 3) with death considered as the related outcome. Moreover, for ICU admission, we adjusted model 3 only based on age, sex, and LOS. All analyses were performed in SPSS software (version 21; IBM Corp., Armonk, NY, USA). The significance level was considered as less than 0.05.

Results

The mean age of the study participants was 61.29 ± 15.84 years. Mean LOS was 4.35 ± 3.59 days. Of the 432 patients tested on day 1, a positive test of troponin (Troponin 1) was detected in 24 patients (5.6%). The day 3 troponin test (troponin 2) was conducted among 303 patients and was positive in 13 patients (4.3%).

Table 1 shows the basic characteristics of patients with COVID-19 in the present study. Based on our results, 62.3% of patients were men, and 10.9% of all participants were in the age group of 18-40 years, 43.8% in the age group of 40-64 years, 32.9% in the age group of 65-79 years, and 12.2% in the age group of 80 years and higher. The frequency of death in this cohort study was 12.3%.

Table 1. Basic characteristics of patients (n = 432) with COVID-19 in the present study

Variable	Categories	Based on percent (n)
Sex	Male	62.3 (269)
	Female	37.7 (163)
age group (years)	18-39	10.9 (47)
	40-64	43.8 (189)
	65-79	33.1 (143)
	≥ 80	12.2 (53)
ICU admission	Yes	19.4 (84)
	No	80.6 (348)
Hospital length of stay (days)	≤ 3	45.0 (195)
	4-7	36.4 (157)
	> 7	18.6 (80)
Death	Yes	12.0 (52)
	No	88.0 (380)

ICU: intensive care unit

Table 2 shows the data on the outcomes (death, ICU admission, and LOS) of COVID-19 patients based on the serum troponin status on day 1 (Troponin 1; n = 432) and day 3 (Troponin 2; n = 303) of hospitalization. Both troponin status 1 and 2 of patients had a significant association with death and ICU admission; people with a positive troponin 1 and 2 status were at a higher risk of death and ICU admission.

Table 2. Evaluated association between outcomes and serum troponin status of patients on day 1 and day 3 of hospitalization

Outcome	Categories	Outcome % (n)		P*
		Troponin on day 1 (positive)** [n = 24]	Troponin on day 1 (negative)** [n = 408]	
Death	Yes	45.8 (11)	10.0 (41)	< 0.001
	No	54.2 (13)	90.0 (367)	
ICU admission	Yes	66.7 (16)	16.7 (68)	< 0.001
	No	33.3 (8)	83.3 (340)	
Hospital length of stay	≤ 3	62.5 (15)	43.8 (162)	0.131
	4-7	25.0 (6)	37.0 (137)	
	> 7	8.3 (2)	19.2 (71)	
Outcome	Categories	Troponin on day 3 (positive) [n = 13]	Troponin on day 3 (negative) [n = 290]	P
Death	Yes	61.5 (8)	9.7 (28)	< 0.001
	No	31.5 (5)	90.3 (262)	
ICU admission	Yes	23.1 (3)	21.7 (63)	< 0.001
	No	76.9 (10)	78.3 (227)	
Hospital length of stay	≤ 3	61.5 (8)	31.8 (85)	0.051
	4-7	15.4 (2)	43.8 (117)	
	> 7	23.1 (3)	24.3 (65)	

ICU: intensive care unit

*Statistical significance level was considered to be less than 0.05.

**Positive troponin test is defined as troponin ≥ 0.1 ng/ml.

Table 3. The results of multiple logistic regression for troponin assessed on day 1

Model	OR (95% CI)	P*
Outcome: Death		
Model 1 (crude model)	5.312 (1.934-14.594)	0.001
Model 2 (adjusted based on age and sex)	3.180 (1.058-9.552)	0.039
Model 3 (Further adjusted based on LOS and ICU admission)	3.008 (1.091-8.290)	0.033
Outcome: ICU admission		
Model 1 (crude model)	8.226 (2.999-22.562)	< 0.001
Model 2 (adjusted based on age and sex)	6.381 (2.258-18.038)	< 0.001
Model 3 (Further adjusted based on LOS)	8.499 (3.316-21.788)	< 0.001

ICU: Intensive care unit; LOS: Length of stay

*Statistical significance level was considered as less than 0.05.

Table 3 shows the results of multiple logistic regression analysis in which death and ICU admission were considered as an outcome, and troponin 1 (assessed on day 1), sex, age, and LOS were considered as potential predictors (for death, ICU admission was also included in the model). Based on our results the status of troponin 1 had significant association with both death (3.008 [95%CI = 1.091-8.290]; P = 0.033) and ICU admission (8.499 [95%CI = 3.316-21.788]; P < 0.001). The results of the 2 other models (crude model and model adjusted based on age and sex) are displayed in table 3.

Table 4 shows the results of multiple logistic regression analysis in which death and ICU admission were separately considered as outcomes, and troponin 2 (assessed on day 3), sex, age, and LOS were considered as potential predictors (for death, ICU admission was also included). Based on our results the status of troponin 2 had significant association with both death (4.159 [95%CI = 1.156-14.961]; P = 0.029) and ICU admission (7.796 [95%CI = 1.954-31.097]; P = 0.004). The results of the 2 other models (crude model and model adjusted based on age and sex) are displayed in table 3.

Discussion

We evaluated the association between serum

troponin level and outcomes of patients with COVID-19 including mortality rate and need for ICU admission in 432 patients with COVID-19. Our results showed that the troponin status of patients had a significant independent association with death and the need for ICU admission. In a systematic review, Li et al. found that 8.0% of COVID-19 patients suffered from an acute cardiac injury.¹⁷ Huang et al. reported cardiac injury in 5 of the 41 studied COVID-19 patients based on a high troponin level (more than 28 pg/ml).⁶ Zhou et al. demonstrated that troponin levels increased early in critically ill patients who subsequently died relative to surviving patients.¹⁸

Chen et al. reported that elevated concentrations of troponin and previous heart disease may be considered as independent risk factors for an adverse outcome in COVID-19 patients.¹⁹ They also concluded that both factors can be considered as mediators for the clinical status of patients with COVID-19 disease.²⁰ Li et al. also concluded that patients with severe forms of COVID-19 have a significantly higher level of troponin than those with milder forms.⁵ Yang et al. also concluded that it is reasonable to hypothesize that routine assessment of troponin level and other related evaluations during the hospitalization period may be useful in the prediction of adverse outcomes.²¹

Table 4. The results of the three models of logistic regression for troponin assessed on day 3

Model	OR (95% CI)	P*
Death		
Model 1 (crude model)	14.971 (4.585-48.886)	< 0.001
Model 2 (adjusted based on age and sex)	8.466 (2.344-30.579)	0.001
Model 3 (Further adjusted based on LOS and ICU admission)	4.159 (1.156-14.961)	0.029
ICU admission		
Model 1 (crude model)	12.011 (3.208-44.963)	< 0.001
Model 2 (adjusted based on age and sex)	8.213 (2.124-31.753)	0.002
Model 3 (Further adjusted based on LOS)	7.796 (1.954-31.097)	0.004

ICU: Intensive care unit; LOS: Length of stay

*Statistical significance level was considered as less than 0.05.

It is certain that comorbidities in COVID-19 can lead to more adverse outcomes in patients. Yang et al. reported that severe clinical cases of COVID-19 had higher prevalence of hypertension, respiratory system disease, and CVD as compared to milder disease cases.²¹ However, based on the National Health Commission of China, an elevated level of cardiac troponin I or cardiac arrest occurred in 11.8% of patients without a history of underlying CVD during hospitalization.¹² In a study on 138 hospitalized patients with COVID-19, Wang et al. reported cardiac injury based on elevated level of hs-cTnI, new electrocardiogram (ECG) or echocardiographic abnormalities in 7.2% of all patients, and in 22% of patients admitted to the ICU.⁷ Ruan et al. reported myocarditis as the cause of death in 7% of the 68 deaths in patients with COVID-19.²²

The association between cardiac injury and COVID-19 can be affected by other mediators. For instance, age has an association with both immune functions of patients and CVD risk. Thus, a higher prevalence of CVD in people with COVID-19, particularly severe cases of the latter, can be a reflection of immunologic aging or dysregulation in patients experiencing CVD and severe COVID-19 simultaneously.¹¹ A similar argument can be made for other comorbidities such as diabetes and hyperlipidemia.^{9,11,23,24}

The mechanisms underlying myocardial injury in patients with COVID-19 infections are not fully understood, but direct myocardial damage seen in other severe respiratory illnesses is likely to play a role. Angiotensin-converting enzyme 2 (ACE2) is crucial in the functions related to the cardiovascular system. This enzyme is also a functional receptor for coronaviruses such as SARS-CoV. It is now known that SARS-CoV-2 enters target cells using ACE2 binding site and the abundance of ACE2 in cardiomyocytes may be a possible explanation for the rise in troponin levels in critically ill patients. This enzyme is also expressed in lung alveolar cells frequently, hence providing a suitable binding site for the virus to enter the host cells.^{25,26} Since ACE2 plays a role in lung protection, this ligand binding can lead to the deregulation of this protective pathway.^{11,27}

Ischemic or non-ischemic mechanisms, such as myocarditis, also play a role in the pathogenesis of myocardial injury in patients with COVID-19.¹¹ Furthermore, in severe cases of COVID-19, severe types of respiratory infection and hypoxia leading to acute respiratory distress syndrome (ARDS) may

occur. These complications can contribute to the pathogenesis of myocardial injury,¹¹ which either appears as an acute manifestation of the disease itself or as the progression of a pre-existing injury with the onset and exacerbation of the disease.²⁸

Our data show that serum troponin had a significant independent association with death and the need for ICU admission in hospitalized patients with COVID-19. Regarding death as a variable, in addition to age, sex, and LOS, we included ICU admission status of patients as potential mediator in one of our models (model 3). Consequently, we also adjusted our models for the prediction of death based on other conditions that can lead to ICU admission. As such, the serum troponin status of patients with COVID-19 infection can be considered an early reliable marker for the prediction of adverse outcomes, including death and the need for ICU admission. Due to the high mortality rate among COVID-19 patients, both in those with previous heart disease and in those with acute lesions during the course of the present disease (COVID-19), and due to the cardiovascular complications of the drugs used in COVID-19 treatment, the early identification of at-risk patients can aid in critical and timely clinical decision making.¹¹ In this respect, troponin can be a valuable marker for distinguishing these at-risk patients.

Our study had some limitations. We were not able to fully distinguish patients with acute and past lesions, although a high level of troponin mainly indicates new myocardial lesions. Moreover, previous studies have shown that critical conditions of patients, such as sepsis or severe renal failure, may artificially raise troponin levels in affected patients without any pre-existing or current myocardial injury.^{6,7,9,14-18,19-29}

However, it is worth noting that our aim was not to determine a cause and effect relationship between troponin and cardiovascular-related death in patients with COVID-19. We aimed to demonstrate that troponin is a valuable marker in predicting adverse outcomes in hospitalized patients, which our study confirms. As a result, until further evidence becomes available, the authors propose periodical troponin testing in all patients hospitalized for this disease.

Conclusion

In summary, troponin showed a significant association with adverse outcomes, including death and the need for ICU admission in hospitalized people with COVID-19. Regarding the high

prevalence of pre-existing underlying CVDs and new cardiac injury in patients with severe COVID-19, the periodical assessment of this protein from initial hospitalization may be considered an effective strategy to aid clinical decisions.

Acknowledgments

This study was supported by Iran University of Medical Sciences, Tehran, Iran.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contribution

Study conception and design: FST, MHKN, FZ, and NM; data collection: DP, SI, GH, MM, BF, RE, MP, BB, and MY; analysis and interpretation of results: VK, AAA, and NM; draft manuscript preparation: MHKN, MR., and SE; critical revision and final concept: NR, MR, MY, and MF

All authors reviewed the results and approved the final version of the manuscript.

References

- Malik YS, Sircar S, Bhat S, Sharun K, Dhama K, Dadar M, et al. Emerging novel coronavirus (2019-nCoV)-current scenario, evolutionary perspective based on genome analysis and recent developments. *Vet Q* 2020; 40(1): 68-76.
- Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. *Methods Mol Biol* 2015; 1282: 1-23.
- Corman VM, Muth D, Niemeyer D, Drosten C. Hosts and sources of endemic human coronaviruses. *Adv Virus Res* 2018; 100: 163-88.
- Channappanavar R, Perlman S. Pathogenic human coronavirus infections: Causes and consequences of cytokine storm and immunopathology. *Semin Immunopathol* 2017; 39(5): 529-39.
- Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. *J Med Virol* 2020; 92(4): 424-32.
- 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. *Lancet* 2020; 395(10223): 497-506.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323(11): 1061-9.
- 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.
- Saltiel AR, Olefsky JM. Inflammatory mechanisms linking obesity and metabolic disease. *J Clin Invest* 2017; 127(1): 1-4.
- Hartmann-Boyce J, Davies N, Frost R, Bussey J, Park S. Maximising mobility in older people when isolated with COVID-19. *Centre for Evidence-Based Medicine* [Online]. [cited 2020 Mar 20]; Available from: URL: <https://www.cebm.net/covid-19/maximising-mobility-in-the-older-people-when-isolated-with-covid-19/>
- 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.
- Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol* 2020; 17(5): 259-60.
- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol* 2018; 72(18): 2231-64.
- Lim W, Qushmaq I, Devereaux PJ, Heels-Ansdell D, Lauzier F, Ismaila AS, et al. Elevated cardiac troponin measurements in critically ill patients. *Arch Intern Med* 2006; 166(22): 2446-54.
- Needham DM, Shufelt KA, Tomlinson G, Scholey JW, Newton GE. Troponin I and T levels in renal failure patients without acute coronary syndrome: A systematic review of the literature. *Can J Cardiol* 2004; 20(12): 1212-8.
- Khan NA, Hemmelgarn BR, Tonelli M, Thompson CR, Levin A. Prognostic value of troponin T and I among asymptomatic patients with end-stage renal disease: A meta-analysis. *Circulation* 2005; 112(20): 3088-96.
- Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol* 2020; 109(5): 531-8.
- 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. *Lancet* 2020; 395(10229): 1054-62.
- Chen C, 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(7): 567-71. [In Chinese].
- Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin Chem Lab Med* 2020; 58(7): 1131-4.
- Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in

- patients infected with SARS-CoV-2: A systematic review and meta-analysis. *Int J Infect Dis* 2020; 94: 91-5.
22. 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.
 23. Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. *J Am Coll Cardiol* 2009; 54(23): 2129-38.
 24. Tall AR, Yvan-Charvet L. Cholesterol, inflammation and innate immunity. *Nat Rev Immunol* 2015; 15(2): 104-16.
 25. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; 579(7798): 270-3.
 26. Ge XY, Li JL, Yang XL, Chmura AA, Zhu G, Epstein JH, et al. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature* 2013; 503(7477): 535-8.
 27. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. *Intensive Care Med* 2020; 46(4): 586-90.
 28. Wadhera RK, Joynt KE. Insurance and cardiovascular health: Time for evidence to trump politics. *Circulation* 2017; 135(21): 1988-90.
 29. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. *Clin Chim Acta* 2020; 505: 190-1.