









Investigating the Impact of COVID-19 on the Incidence of Cardiovascular Diseases: A Cross-sectional Study

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Abstract:

Background: The inflammation caused by COVID-19 can cause blood clots, block the heart vessels and lead to heart attack.

Aim: This study aims to investigate the impact of COVID-19 on heart diseases in patients referred to Imam Khomeini Hospital in Jiroft City.

Methods: This is a cross-sectional (descriptive-analytical) study. The statistical population includes all cardiovascular patients who visited Imam Khomeini Hospital two years before Corona (March 2017 to March 2019) and two years after Corona (March 2019 to March 2021). Data were analyzed using SPSS software version 20. The chi-square test was used to investigate the relationship between qualitative variables in two groups. The level of significance in this study was considered less than 0.05.

Results: The average age of patients before COVID-19 was 60.02 ± 16.7 years, and during COVID-19 was 63.9 ± 16.8 years, and in group 1, 50.5% were men, and in group 2, 51% were women. COVID-19 has caused a 14.2% increase in cardiovascular diseases. Acute coronary syndrome, heart attacks, and heart failure increased by 11.3%, 32.2%, and 9.5%, respectively, during the COVID-19 pandemic compared to before the COVID-19 pandemic.

Conclusion: Based on the findings of the study, special attention should be paid to the cardiovascular support of these patients and specific diagnostic and treatment protocols should be developed to prevent cardiovascular complications and treat patients with COVID-19.

Keywords: COVID-19, Incidence, Cardiovascular diseases, Coronavirus, Hospital, Patient, Diseases.

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1. INTRODUCTION

Coronavirus disease (COVID-19) is a new infectious disease that emerged in 2019. The first infected person was observed in Wuhan, China, in late 2019 [1]. Sars-COVID-2 primarily causes a respiratory illness with symptoms ranging from asymptomatic or mild symptoms (fever, cough, shortness of breath, muscle pain, fatigue, diarrhea) to the development of acute respiratory distress syndrome [2, 3]. Countries acted in different ways to fight COVID-19, so the burden of disease varied in various countries [4, 5]. The health impact of COVID-19 was different according to age and sex [5, 6]. COVID-19 can cause cardiac damage, myocarditis, acute coronary syndrome, pulmonary embolism, stroke, arrhythmia, heart failure, and cardiovascular disease. It is recognized that it can cause severe cardiovascular disease, including autogenic shock. Cardiac manifestations of COVID-19 are due to adrenergic stimulation, peripheral and systemic inflammation, SARS-COVID-2 cytokine release syndrome, direct viral infection of cardiomyocytes and endothelial cells, and respiratory failure, Hypoxia, electrolyte imbalance, fluid overload, *etc* [7, 8]. In a study conducted on 416 COVID-19 patients, 19.7% of patients experienced an increase in troponin during hospitalization, which was recognized as an independent risk factor for in-hospital mortality [9]. Increased rates of heart damage in people with severe systemic inflammatory response syndrome and the development of shock in the face of COVID-19 also point to an important link between the immune response to the virus and the cardiovascular system. Masu. Additionally, the presence of cardiometabolic heart disease is very common in patients with COVID-19 infection, and patients with a history of cardiovascular disease are more likely to die [10, 11]. Cardiac complications are not only common but also portend a poor prognosis and may lead to more severe cases later in the course of the disease [12-14].

Coronaviruses cause a flu-like syndrome that primarily affects the respiratory tract. Like other respiratory viral infections, coronavirus disease 2019 (COVID-19) can have more severe consequences in people with cardiovascular risk factors and patients with cardiovascular disease. This is due to weak cardiopulmonary function in these patients, worsening of the underlying cardiovascular disease due to the systemic effects of the disease, or stimulation of new cardiac complications [15-17]. Limited data is available for management treatment for myocarditis due to COVID-19, but several antiviral drugs are available, for example, remdesivir, ribavirin, lopinavir, hydroxychloroquine, and antibiotics. Inflammation, *e.g.*, interferon, corticosteroids, tocilizumab, sarilumab, Siltuximab Anakinra, and Statin, are available for treatment [18].

Several studies have been conducted on potent antiviral drugs with cardiovascular-favoring effects and their effectiveness against different variants of SARS-CoV-2, including the Omicron variant. A study discussed the efficacy of nirmatrelvir and ritonavir in treating COVID-19. It was found that nirmatrelvir was effective against all currently known Variants of Concern (VOCs),

including the Omicron variant [19]. The results of another study showed that Molnupiravir, an oral antiviral agent, has emerged as a promising new drug against COVID-19. [20]. Various classes of drugs, including antivirals, anti-SARS-CoV-2 antibody agents, anti-inflammatory drugs, immunomodulators, and anticoagulants, have been proposed for the treatment of COVID-19. These drugs work by interfering with the SARS-CoV-2 replication cycle and reducing viral entry. The review also highlighted the latest important guidelines and FDA approvals regarding the use of these drugs [21]. These studies provide valuable insights into the effectiveness of different antiviral drugs against SARS-CoV-2, including the Omicron variant, and their potential cardiovascular benefits.

Early in the outbreak, risk factors such as heart disease, high blood pressure, and diabetes were associated with an increased risk of severe illness and death from COVID-19. Viruses can affect the heart and cause various heart complications. They can also directly attack the body and cause inflammation, affecting the heart and causing myocarditis or pericarditis (the outer wall of the heart muscle or pericardium). This is because it can cause inflammation in the heart. Additionally, the inflammation caused by COVID-19 can cause blood clots to block blood vessels in the heart and brain, potentially leading to heart attacks and strokes [22, 23]. This study was conducted with the aim of studying the impact of COVID-19 on cardiovascular diseases in patients referred to Imam Khomeini Hospital in Jiroft City, as such studies have not yet been conducted in Jiroft City.

2. METHODS

This is a cross-sectional (descriptive-analytical) study. The statistical population included all cardiovascular patients who visited Imam Khomeini Hospital two years before COVID-19 (March 2017 to March 2018) and two years after COVID-19 (March 2019 to March 2021). The inclusion criteria included the records of all cardiovascular patients two years before and two years after COVID-19 in Imam Khomeini Hospital, and the exclusion criteria were excluded from the study if the records were incomplete. After the proposal was approved by this committee and the code of ethics and necessary permits were obtained with the help of the relevant faculty, necessary coordination was made with Imam Khomeini Hospital (RA), patients' files were reviewed, and the necessary information was recorded. Sampling was performed using the census method, and the sample size consisted of 5635 cardiovascular patients two years before COVID-19 (March 2017 to March 2019) and two years during COVID-19 (March 2019 to March 2021) who were admitted to Imam Khomeini Hospital. Data collection in this study was conducted in the form of a checklist, including demographic characteristics of the patients (age, sex, department, reason for hospitalization), determined and recorded by the researcher.

After collecting the data, they were analyzed using SPSS software version 20. Qualitative data were reported

as numbers (percentages). The chi-square test was used to investigate the relationship between qualitative variables in two groups. The level of significance in this study was considered less than 0.05. Obtaining permission from the Vice-Chancellor of Research and obtaining the Code of Ethics Committee of Jiroft University of Medical Sciences (IR.JMU.REC.1402.012), observing ethical principles in the use of texts and sources, patient information remained confidential.

3. RESULTS

This study is a cross-sectional (descriptive-analytical) study that examined 5635 cardiovascular patients two years before COVID-19 (group 1) and two years during COVID-19 (group 2) who were referred to Imam Khomeini Hospital. The average age of patients before the COVID-19 was 60.02 ± 16.7 years, and during the COVID-19 was 63.9 ± 16.8 years; in group 1, 50.5% were men, and in group 2, 51% were women. (Table 1).

Table 2 demonstrates the trend of cardiovascular diseases before contracting COVID-19 disease and during the COVID-19 disease in the form of numbers and percentages in both groups.

Table 3 shows the information related to the age and sex variables of patients with heart attacks. The average age of patients in group 1 was 62.2 ± 16.8 years, and in group 2, was 62.4 ± 15.1 years, including 61.9% and 62.2% male patients in group 1 and group 2, respectively.

Table 4 shows the reason for hospitalization of patients with heart attacks in groups 1 and 2 in the form of numbers and percentages.

Table 5 shows the information related to age and sex variables of patients with acute coronary syndrome. The average age of patients in group 1 was 58.9 ± 16.1 years, and in group 2 was 61.4 ± 16.04 years. In group 1, 51.5%, and group 2, 55.9% of patients were women.

Table 6 mentions the reason for the hospitalization of patients with acute coronary syndrome in groups 1 and 2 in the form of numbers and percentages.

Table 7 demonstrates the information related to the variables of age and gender of patients with heart failure. The average age of patients in group 1 was 68.4 ± 17.1 years, and in group 2 it was 69.3 ± 18.3 years, in group 1, 50.9% were women, and in group 2, 51.3% of patients were men.

Table 1. Demographic variables of cardiovascular patients referred to Imam Khomeini Hospital Jiroft city.

Variable		Frequency Group 1 (%)	Frequency Group 2 (%)	p-value
Sex	Male	1217 (50.5)	1580 (49)	P<0.04
	Female	1194 (49.5)	1644 (51)	
Age	< 20	24 (0.9)	26 (0.8)	P<0.01
	20-35	103 (4.2)	109 (3.4)	
	35-50	428 (17.7)	469 (14.5)	
	50-80	1519 (63.3)	2021 (62.7)	
	> 80	337 (13.9)	599 (18.6)	
Number	Total	2411 (100)	3224 (100)	-

Table 2. Variables of cardiovascular diseases before and during COVID-19 of cardiovascular patients referred to Imam Khomeini Hospital Jiroft city.

Variable	Frequency Group 1 (%)	Frequency Group 2 (%)
Myocarditis	5 (0.2)	3 (0.1)
Pericarditis	9 (0.4)	4 (0.2)
Heart Attack	314 (13.1)	615 (19)
Acute Coronary Syndrome	1623 (67.1)	2042 (63.4)
Heart failure	461 (19.2)	560 (17.3)
Total	2411	3224

Table 3. Demographic variables of patients suffering from heart attacks.

Variable		Frequency Group 1 (%)	Frequency Group 2 (%)	p-value
Sex	Male	195 (61.9)	382 (62.2)	P<0.02
	Female	120 (38.1)	232 (37.8)	

(Table 3) contd....

Variable		Frequency Group 1 (%)	Frequency Group 2 (%)	p-value
Age	<20	5 (1.6)	3 (0.3)	P<0.01
	20-35	18 (5.7)	8 (1.5)	
	35-50	37 (11.7)	86 (14)	
	50-80	201 (63.8)	382 (62.3)	
	> 80	54 (17.2)	135 (21.9)	
Total		315	614	

Table 4. The reason for hospitalization of patients with a heart attack.

Variable	Frequency Group 1 (%)	Frequency Group 2 (%)
Heart disease	28 (8.9)	180 (29.3)
Loss of consciousness	5 (1.6)	18 (2.9)
Chest pain	135 (42.9)	278 (45.3)
Shortness of breath	17 (5.4)	27 (4.4)
Stomach ache	8 (2.5)	8 (1.3)
Heartbeat	0 (0)	5 (0.8)
Changes in blood pressure	3 (1)	5 (0.8)
Other cases	119 (37.7)	93 (15.2)
p-value	P<0.05	

Table 5. Demographic variables of patients suffering from acute coronary syndrome.

Variables		Frequency Group 1 (%)	Frequency Group 2 (%)
Sex	Male	788 (48.5)	899 (44.1)
	Female	836 (51.5)	1139 (55.9)
Age	< 20	6 (0.7)	8 (0.4)
	20-35	71 (4.4)	83 (4.1)
	35-50	353 (21.6)	344 (16.9)
	50-80	1047 (64.1)	1332 (65.3)
	> 80	147 (9.2)	271 (13.3)
P-value		P<0.05	

Table 6. The reason for the hospitalization of patients with acute coronary syndrome in groups 1 and 2 in the form of numbers and percentages.

Variables	Frequency Group 1 (%)	Frequency Group 2 (%)
Heart disease	133 (8.2)	616 (30.2)
Loss of consciousness	1 (0.1)	6 (0.3)
Chest pain	703 (43.3)	838 (41.1)
Shortness of breath	73 (4.5)	73 (3.6)
Stomach ache	7 (0.4)	16 (0.8)
Heartbeat	1 (0.1)	14 (0.7)
Changes in blood pressure	18 (1.1)	14 (0.7)
Other cases	688 (42.3)	461 (22.6)
P-value		P<0.05

Table 7. Demographic variables of patients with heart failure.

Variable		Frequency Group 1 (%)	Frequency Group 2 (%)	p-value
Sex	Male	227 (49.1)	287 (51.3)	P<0.05
	Female	235 (50.9)	272 (48.7)	

(Table 7) contd....

Variable	Frequency Group 1 (%)	Frequency Group 2 (%)	p-value	
Age	< 20	10 (2.1)	15 (2.6)	P<0.05
	20-35	11 (2.4)	18 (3.3)	
	35-50	26 (5.7)	31 (5.6)	
	50-80	289 (62.6)	305 (54.6)	
	> 80	126 (27.2)	190 (33.9)	

Table 8 shows the information related to the inpatient department of patients with heart failure, the results indicate that of the 462 people examined in group 1, 191 people (8.2%) were in CCU, 138 people (29.9%) in the

internal department, 31 people (6.7%) ICU, 38 people (4.1%) emergency, 34 people (7.4%) surgery, 23 people (5%) in the neurology department and 7 people (5.5%) 1%) in other departments and of 559 people in group 2, 160

Table 8. Inpatient department for heart failure patients.

Variables	Frequency Group 1 (%)	Frequency Group 2 (%)
CCU	191 (41.3)	160 (28.6)
Internal	138 (29.9)	324 (58)
ICU	31 (6.7)	24 (4.3)
Emergency	38 (8.2)	46 (8.2)
Surgery	34 (7.4)	3 (0.5)
Neurology	23 (5)	1 (0.2)
Other departments	7 (1.5)	1 (0.2)
p-value	P<0.05	

Table 9. Reason for hospitalization of patients with heart failure.

Variables	Frequency Group 1	Frequency Group 2
Heart disease	28 (6.1)	139 (24.9)
Loss of consciousness	12 (2.6)	13 (2.3)
Chest pain	243 (52.6)	258 (46.2)
Shortness of breath	85 (18.4)	75 (13.4)
Stomach ache	8 (1.7)	8 (1.4)
Heart beat	0 (0)	4 (0.7)
Changes in blood pressure	5 (1.1)	1 (0.2)
Other cases	81 (17.5)	61 (10.9)
p-value	P<0.05	

people (28.6%) in CCU, 324 people (58%) internal, 42 people (4.3%) ICU, 46 people (8.2%) emergency and 3 (0.5%) surgery, 1 (0.2%) neurology and 1 (0.2%) in other departments.

Table 9 reveals the reason for hospitalization of patients with heart failure in groups 1 and 2 in the form of numbers and percentages.

4. DISCUSSION

This study aims to determine the frequency of cardiovascular disease patients referred to Imam Khomeini Hospital in Jiroft City and its association with the COVID-19 pandemic. Viral pneumonia is known to be a typical clinical manifestation of COVID-19 [24]. Studies have found that some patients who present without the usual symptoms of fever or cough develop cardiac symptoms as the first clinical manifestation of COVID-19 [25]. Studies conducted have reported the comorbidity rate of cardiovascular disease in SARS and MERS patients to be 10% and 30%, respectively [26-28].

According to the study results, acute coronary syndromes increased by 11.3% during the coronavirus pandemic compared to pre-coronavirus times. In a study by Ahmadi *et al.*, this cardiovascular disease increased by 120% in women and 137% in men between 2017 and 2021. Although acute coronary syndromes are decreasing in European and American countries, they remain the leading cause of death in cardiovascular disease subgroups [29]. Kwong *et al.*'s study concluded that, like other infectious diseases such as SARS and influenza, COVID-19 can cause acute coronary syndrome. An early study conducted in China found that a small number of COVID-19 patients experienced chest pain upon admission, but the characteristics of the chest pain were not described [30]. In 2020, 18 COVID-19 patients underwent ST-segment elevation in New York. This result suggests the possibility of acute myocardial infarction, and five out of six patients with myocardial infarction require percutaneous coronary intervention [24].

The findings of the study conducted by Stefanini *et al.*

involving 28 patients with COVID-19 and ST-segment elevation myocardial infarction in Italy revealed that 17 of these patients exhibited evidence of a culprit lesion necessitating the reopening of the vessels [31]. Despite the potential of COVID-19 to induce acute coronary syndromes, the incidence of reported cases during the COVID-19 outbreak in Italy, Spain, and the United States was notably lower compared to pre-COVID-19 periods. This resulted in a significant reduction of 42-48% in the number of hospitalizations for acute coronary syndromes and a 38-40% decrease in percutaneous coronary interventions for ST-segment elevation myocardial infarction [32]. Conversely, there was an increase in out-of-hospital cardiac arrests during the COVID-19 outbreak in Italy, which exhibited a strong correlation with the cumulative incidence of COVID-19 [33]. It is worth noting that among the 28 patients who underwent coronary angiography, 24 of them presented with ST-segment elevation myocardial infarction as the initial clinical manifestation of COVID-19 despite not having received a positive COVID-19 test result at the time. These observations suggest that COVID-19 can induce this syndrome even in the absence of significant systemic inflammation. However, the exact incidence of acute coronary syndromes in COVID-19-infected patients remains unknown. Considering the limitations of healthcare resources and treatment facilities in many cities during the COVID-19 outbreak, it is possible that the number of cases of acute myocardial infarction among COVID-19 patients may have been underestimated in initial studies. Plaque rupture, coronary artery spasm, or microthrombi resulting from systemic inflammation or cytokine storm are potential underlying mechanisms for COVID-19-induced acute coronary syndromes [34].

Several studies have reported on the effectiveness of various antiviral drugs against different variants of SARS-CoV-2, including the Omicron variant, and their potential impact on COVID-19 disease treatment. Some of the antiviral drugs, as well as the drugs that have antiviral properties and their effectiveness against different types of SARS-CoV-2, have been proven in numerous studies, are Ensitrelvir, simotrelvir, cordycepin, riboprime, molnupiravir, didanosine, remdesivir, teriflunomide, strychnine bush ingredients, pineapple ingredients, ginger ingredients, Oxadiazoles, gallates, and other similar nucleoside/nucleotide analogs [35-38]. A study by José Luis Piñana *et al.* in 2023 reported an overall COVID-19-related mortality of 5% in hematological patients and cell therapy recipients treated with remdesivir or nirmatrelvir/ritonavir. The study found a higher antiviral effect in the nirmatrelvir/ritonavir cohort. *In vitro*, models have shown that both nirmatrelvir and ritonavir have equipotent antiviral activity against the Beta, Gamma, Delta, and Omicron variants [35].

In another study in 2023, Sawsan Aboul-Fotouh *et al.* discussed using different drug classes for COVID-19 treatment and prevention, such as antivirals and anti-SARS-CoV-2 antibody agents. The Omicron variant was found to have a high ability to spread and escape double-

dose vaccination, leading to an increase in the number of patients requiring hospital care [21]. Also, a study conducted in Poland during the dominance of the Omicron variant found that molnupiravir use did not decrease hospitalization time nor the frequency of mechanical patients receiving such pharmacotherapy, but it did require oxygen supplementation less often. In this study, A phase 3 double-blind, placebo-controlled trial of nirmatrelvir/ritonavir in non-hospitalized high-risk adults with COVID-19 found that the risk of progression to severe disease was reduced by 89% in participants using nirmatrelvir/ritonavir [39].

In conclusion, these studies have shown the potential of various antiviral drugs in treating COVID-19 and combating the effects of the Omicron variant on the cardiovascular system. However, more research is needed to determine the most effective and safe treatments for COVID-19 patients.

Among the other findings of the research was a 32.2% increase in heart attacks during the coronavirus pandemic compared to before the COVID-19, which in Shi *et al.*'s study showed that MI during the COVID-19 period is independently related to increased mortality [9]. According to preliminary studies in China, MI, which is characterized by an increase in the level of cardiac biomarkers or electrocardiogram abnormalities, was observed in 22% of patients with COVID-19 [40]. The National Health Commission of China reported that almost 12% of patients without known heart disease had an increase in troponin level or cardiac arrest during hospitalization [41]. Based on the results of studies, the presence of myocardial damage in patients with COVID-19 has been associated with a worse prognosis [9]. In a study conducted on 41 patients with COVID-19 in Wuhan, 5 patients had myocardial damage with increased cardiac troponin I levels, and 90% of these patients were admitted to the ICU [42]. In Zhou *et al.*'s study, which was conducted on 191 patients with COVID-19, 3 patients (17%) had acute heart damage, and 32 of them died [7]. In the study of Shi S *et al.*, which was conducted on 416 hospitalized patients with COVID-19, 82 patients (20%) had evidence of heart damage, which was associated with a 5-fold increase in the need for invasive mechanical ventilation and an 11-fold increase in mortality, as a result, the cardiac injury was identified as an independent risk factor for in-hospital mortality [9]. Another study confirmed this finding and reported that the mortality rate in patients with high levels of cardiac troponin T was 37.5%, while this rate in patients with cardiovascular diseases with increased cardiac troponin T levels was approximately twice as much (69.4%) [43].

Heart failure increased by 9.5% between 2017 and 2021. The most important factors influencing the development of heart failure are type 2 diabetes, hypertension, stroke, and age. A study by Chen *et al.* conducted on 799 patients in Wuhan found that heart failure was one of the most common complications of COVID-19, with 24% of all patients and 49% of deaths due to heart failure. According to The Mirror, there was a study

of pro-type natriuretic peptides, of which 85% died due to amino-terminal B, and this was observed in 49% of all patients [44].

Additionally, in a study by Zhou *et al.* conducted on patients in Wuhan, 52% of patients died, and 23% of all patients were diagnosed with heart failure [45]. In a study by Mehra *et al.*, nearly a quarter of hospitalized patients with COVID-19 had heart failure. The possibility of pulmonary congestion due to heart failure must be considered [46].

Given that COVID-19 patients are more likely to be older and have comorbidities such as coronary artery disease, hypertension, and diabetes, these underlying conditions (diagnosed or not) of Heart failure may occur as a result of worsening or the detection of subclinical heart disease. Dysfunctional. Elderly patients, especially those with reduced diastolic function, may suffer from heart failure with preserved ejection fraction during the COVID-19 pandemic, manifesting as high fever, tachycardia, excessive fluid intake, and impaired renal function. Possible [47]. In patients with heart failure and preserved ejection fraction, cardiac MRI can help detect changes caused by COVID-19 [48]. Executive limitations and the method of reducing them are the incompleteness of the files, which were excluded from the study if the files were incomplete. The emerging nature of the COVID-19 virus and the lack of complete knowledge of the disease-causing pattern of this virus were among the limitations of the project. We do not have any description of the medical history of COVID 19 disease in each patient and this study did only one center.

CONCLUSION AND RECOMMENDATIONS

The results of the study showed that the number of cardiovascular disease cases referred to Imam Khomeini Hospital in Jiroft increased by 14.2% due to COVID-19. Based on the results of the study, special attention should be paid to cardiovascular support in these patients, as well as specific diagnostic and therapeutic protocols to prevent cardiovascular complications and further treat patients with COVID-19 infection. Future studies in this case will specifically investigate the prevalence and mechanisms, the various cardiovascular effects during the course of the disease, and the diagnostic and therapeutic challenges posed by the coexistence of these two diseases.

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

ABBREVIATION

COVID-19 = Coronavirus Disease 2019

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The present study was conducted ethically in two ways. Firstly, all participants willingly volunteered to take

part in the study. Secondly, the principles of confidentiality and secrecy were upheld, ensuring that all information would be kept confidential and the results would be reported in a general manner. This project was approved by the ethics committee of Jiroft University of Medical Sciences under the ethics code IR.JMU.REC.14 02.012.

HUMAN AND ANIMAL RIGHTS

All human procedures followed were as per the guidelines of the Helsinki Declaration of 1975.

CONSENT FOR PUBLICATION

Informed consent was obtained from the participants.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author [S.D] upon reasonable request.

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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