



## Epidemiological, clinical, and economic burden of myocardial infarction patients in Iran during the COVID-19 pandemic

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### ABSTRACT

**Background:** To define changes in AMI case rates, patient demographics, cardiovascular comorbidities, treatment approaches, in-hospital outcomes, and the economic burden of COVID-19 during the pandemic.

**Methods:** We conducted a multicenter, observational survey with selected hospitals from three medical universities in Tehran city. A data collection tool consisting of three parts. The first part included socio-demographic information, and the second part included clinical information, major complications, and in-hospital mortality. Finally, the third part was related to the direct medical costs generated by AMI in COVID-19 and non-COVID-19 patients. The study cohort comprised 4,560 hospitalizations for AMI (2,935 for STEMI [64%] and 1,625 for NSTEMI [36%]).

**Results:** Of those hospitalized for AMI, 1,864 (76.6 %) and 1,659 (78 %) were male before the COVID-19 outbreak and during the COVID-19 era, respectively. The length of stay (LOS), was significantly lower during the COVID-19 pandemic era ( $4.27 \pm 3.63$  vs  $5.24 \pm 5.17$ ,  $p = 0.00$ ). Results showed that there were no significant differences in terms of patient risk factors across periods. A total of 2,126 AMIs were registered during the COVID-19 era, with a 12.65 % reduction (95 % CI 1.5–25.1) compared with the equivalent time in 2019 ( $P = 0.179$ ). The risk of in-hospital mortality rate for AMI patients increased from 4.9 % in 2019 to 7.0 % in the COVID-19 era (OR = 1.42; 95 % CI 1.11–1.82;  $P = 0.004$ ). Major complications were registered in 9.7 % of cases in 2020, which is higher than the rate of 6.6 % reported in 2019 (OR = 1.46, 95 % CI 1.11–1.82;  $P = 0.000$ ). Total costs in hospitalized AMI-COVID patients averaged \$188 more than in AMI patients ( $P = 0.020$ ).

**Conclusion:** This cross-sectional study found important changes in AMI hospitalization rates, worse outcomes, and higher costs during the COVID-19 periods. Future studies are recommended to examine the long-term outcomes of hospitalized AMI patients during the COVID-19 era.

**Abbreviations:** AMI, Acute Myocardial Infarction; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; COVID-19, Coronavirus Disease 2019; LOS, length of stay; CI, confidence interval; OR, Odds ratios; RR, Risk ratios; ICCUs, Incentive cardiac care unite; VSD, ventricular septal defect; ACS, Acute coronary syndrome.

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## 1. Introduction

The still ongoing “Coronavirus Disease 2019” (COVID-19) outbreak, a novel viral respiratory illness caused by the “Severe Acute Respiratory Syndrome Coronavirus type 2” (SARS-CoV-2), started to spread in late 2019 and quickly developed into a global pandemic in early 2020 [1]. The immediate and direct global effects of the COVID-19 outbreak on public health have been dreadful [2]. During the pandemic, the surge in infections has put a strain on healthcare facilities: the global regulations implemented and the measures taken, on the one hand, have reduced viral transmission and mitigated the associated burden in terms of infections and mortality, partially relieving weak infrastructure. On the other hand, they have led to devastating effects on public health, by delaying/postponing the treatment of other diseases, including non-communicable disorders [3]. For instance, despite being primarily a respiratory illness, COVID-19 may have potential, either direct or indirect, cardiovascular sequelae, that were initially underestimated, as shown by an accumulating body of scholarly evidence, which has reported relevant cardiac complications also in patients with COVID-19, with or without prior cardiovascular disease [4,5].

Besides, the COVID-19 outbreak has also had major psychological, emotional, and behavioral impacts, and may have compromised mental health, leading to secondary issues and conditions, including those increasing the risk of affecting the cardiovascular system [6].

Nonetheless, the pandemic might have even had more severe cardiovascular effects than initially expected. Importantly, despite all the efforts made by health authorities to fight the infection, the surge of infected patients in demand for Intensive Care Unit (ICU) admission has been overwhelming. Consequently, further Intensive Cardiac Care Units (ICCU) have been dedicated to the treatment of COVID-19 patients, but, despite this, clinical critical settings such as acute myocardial infarction (AMI) might have missed proper medical care and management [7,8].

The massive pressure exerted on the healthcare system during the pandemic and the reluctance of patients experiencing chest pain to seek timely medical care apparently resulted in a significant reduction in AMI hospitalizations [9–11]. Although fewer patients were admitted during the COVID-19 pandemic in comparison with the pre-COVID-19 era, mortality rate and unfavorable patient outcomes were shown to be higher during the outbreak, since AMI patients were hospitalized with more severe symptoms [12].

However, limited data is currently available regarding the effects of the COVID-19 outbreak on AMI admission rates, pre-hospital patient characteristics, clinical outcomes, and associated costs in Iran. Therefore, the present study investigated the characteristics of hospitalized AMI patients, their admission rate, clinical outcomes, and associated medical costs for a period of 7 months during the COVID-19 era and equivalent months of 2019 in selected hospitals based in Tehran City, Iran.

## 2. Material and methods

We conducted a multicenter, observational survey with selected hospitals from three medical universities in Tehran city, including the Tehran University of Medical Sciences, the Iran University of Medical Sciences, and the Shahid Beheshti University of Medical Sciences. We aimed at evaluating consecutive AMI patients admitted to ICCUs throughout the 7 months during the COVID-19 outbreak in Iran from 19 February 2020 (when Iran reported its first confirmed COVID-19 case) to 22 September 2020. The same data was collected for the equivalent months of 2019.

AMI was defined according to the Fourth Universal Definition of Acute Myocardial Infarction, that is to say, the presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of clinical evidence of acute myocardial ischemia. Major complications were defined as cardiogenic shock, life-threatening arrhythmias, cardiac rupture/ventricular septal defect (VSD), or severe

functional mitral regurgitation. Direct medical costs included the costs of a defined intervention and all the follow-up costs for other medication and health care interventions in ambulatory, inpatient, and nursing care. Data were divided and analyzed for AMI patients and two sub-groups of patients: 1) ST-segment elevation myocardial infarction (STEMI); and 2) non-ST segment elevation myocardial infarction (NSTEMI).

### 2.1. Data collection

An *ad hoc* data collection tool was utilized, that is to say, a self-made form consisting of three parts. The first part included socio-demographic information (patient’s first and last name, age, sex/gender, admission and discharge date, and length of hospitalization). The second part included clinical information (smoking, diabetes, dyslipidemia, blood pressure, family background of coronary artery diseases), major complications, and in-hospital mortality. Finally, the third part was related to the direct medical costs generated by AMI in COVID-19 and non-COVID-19 patients.

### 2.2. Statistical analysis

Categorical variables were presented as absolute (numbers), and relative (percentages) figures, as well as risk ratios (RR) with 95 % confidence interval (95 % CI), and compared by the chi-square test. Continuous variables were presented as mean and standard deviation (Mean  $\pm$  SD) and compared by the Student’s *t*-test. A dedicated commercial software (IBM SPSS Statistics 23) was used for all analyses. A logistic regression model was utilized for the multi-variable analysis to evaluate parameters affecting the medical costs of AMI in COVID-19 and non-COVID-19 patients. P-values less than 0.05 were considered statistically significant.

## 3. Results

### 3.1. Pre-hospital information and LOS

Three selected medical universities participated in the study. The study cohort comprised 4,560 hospitalizations for AMI (2,935 for STEMI [64 %] and 1,625 for NSTEMI [36 %]). Of those hospitalized for AMI, 1,864 (76.6 %) and 1,659 (78 %) were male before the COVID-19 outbreak and during the COVID-19 era, respectively (Table 1). The mean age of AMI patients was  $61.35 \pm 12.09$  and  $60.37 \pm 11.77$  years before and during the COVID-19 era, respectively. Overall, the mean age for AMI was significantly different between the pre-COVID-19 and the COVID-19 era ( $p = 0.005$ ). However, when stratifying based on the STEMI/NSTEMI status, in STEMI patients the mean age ( $61.02 \pm 12.28$  vs  $60.61 \pm 12.12$ ) was not significantly different between the pre-COVID-19 and the COVID-19 era ( $p = 0.37$ ), whilst, in NSTEMI patients, the mean age ( $61.86 \pm 11.77$  vs  $59.83 \pm 10.94$ ) was significantly different between the pre-COVID-19 and the COVID-19 era ( $p = 0.00$ ).

The length of stay (LOS), as an important hospitalization index, was significantly lower during the COVID-19 pandemic era ( $4.27 \pm 3.63$  vs  $5.24 \pm 5.17$ ,  $p = 0.00$ ). Sub-group analysis showed that for STEMI patients ( $4.38 \pm 3.61$  vs  $5.44 \pm 5.53$ ) and NSTEMI patients ( $4.14 \pm 3.64$  vs  $4.96 \pm 4.56$ ), the average of LOS during the pandemic period is 1.06 and 0.82 days less than the pre-pandemic period, and these changes are statistically significant ( $p = 0.00$ ). Results showed that there were no significant differences in terms of patients’ risk factors such as diabetes, hypertension, family history of CVD, dyslipidemia and current smoking rates in the COVID-19 era compared with the pre-COVID-19 period.

### 3.2. Reduction of hospitalizations for AMI in the COVID-19 era

A total of 2,126 AMIs were registered during the COVID-19 era, with a 12.65 % reduction (95 % CI 1.5–25.1) compared with the equivalent

time in 2019 (P = 0.179), when 2,434 patients had been hospitalized for the same diagnosis (Table 1). Results for STEMI and NSTEMI patients are reported in Table 2. The reduction for NSTEMI patients was higher than in the STEMI group. The admission rate for STEMI patients remained almost constant and has not changed significantly; reduced from 1,473 in 2019 to 1,462 in 2020 (0.7 % reduction; 95 % CI -0.9–40.6; P = 0.974). also, hospitalizations for NSTEMI went down from 961 in 2019 to 664 in 2020 (30.9 % reduction; 95 % CI 13.03–42.28; P = 0.25), this decrease is not statistically significant.

### 3.3. Mortality for AMI

Table 3 shows the result of the mortality rate in AMI patients and STEMI and NSTEMI subgroups. The risk of in-hospital mortality rate for AMI patients increased from 4.9 % in 2019 to 7.0 % in the COVID-19 era (OR = 1.42; 95 % CI 1.11–1.82; P = 0.004), this increase is statistically significant. for STEMI patients' mortality rate increased from 5.1 % in 2019 to 7.9 % in the COVID-19 era (OR = 1.53; 95 % CI 1.14–2.07; P = 0.004), this increase is statistically significant. NSTEMI subgroup patients' mortality rate increased from 4.6 % in 2019 to 5.1 % in the COVID-19 era (OR = 1.11; 95 % CI 0.7–1.75; P = 0.64), this increase is not statistically significant.

### 3.4. Major complications in AMI

Table 4 illustrates the numbers and percentages of major complications in AMI patients. Major complications were defined as cardiogenic shock, life-threatening arrhythmias, and cardiac rupture/ventricular septal defect (VSD) or severe functional mitral regurgitation. Major complications were registered in 9.7 % of cases in 2020, which is higher than the rate of 6.6 % reported in 2019, in a statistically significant fashion (OR = 1.46, 95 % CI 1.11–1.82; P = 0.000).

### 3.5. Total costs

The multi-variable logistic regression model showed that sex/gender, age, readmission, Diagnosis, COVID-19, and Results of Angiography were independent factors influencing total direct costs in AMI patients (Table 5).

Table 6 shows that on average, direct medical costs in men are \$105 less than in women, however, this relationship is not statistically significant (p = 0.156). Costs for STEMI patients are on average \$112 more than for NSTEMI patients. There is a relationship between living conditions and total expenses, so that total expenses for living people are on average \$62 more than for deceased people, although this difference is not statistically significant (P = 0.578). There is a statistically significant relationship between contracting COVID-19 and the total costs of AMI patients. Total costs in hospitalized AMI-COVID patients averaged \$188 more than in AMI patients (P = 0.020). The estimation results show that

total costs in patients with SVD angiography are \$96, in patients with 2VD \$136, and in 3VD \$127 more than in patients with mild CAD.

Table 7 represents cost itemized for AMI-COVID and AMI patients. Results show that most percent of total medical cost for AMI-COVID patients are drug and device (37.4 %), hospital bed & CCU (26.3 %), respectively. For AMI patients therapeutic and surgical interventions (29 %) and hospital bed & CCU (21.7 %), respectively.

## 4. Discussion

In this observational survey, we investigated the impact of COVID-19 on hospitalizations, health outcomes, and costs in AMI patients during the COVID-19 era and the equivalent period of 2019. The key findings of the current study are:

- 1) The mean age of AMI patients was significantly lower during the COVID-19 period, significantly among patients presenting with NSTEMI;
- 2) Admitted AMI patients had significantly lower LOS;
- 3) AMI Hospitalization during the COVID-19 pandemic was reduced;
- 4) Mortality rate during the COVID-19 era increased significantly among STEMI patients;
- 5) Major complications rate was significantly higher during the COVID-19 outbreak;
- 6) Total direct costs among hospitalized AMI-COVID-19 patients were demonstrably higher than AMI patients.

Our study revealed a lower mean age of admission among ACS patients compared to the pre-COVID-19 era. However, the mentioned reduction was more significant among NSTEMI patients. Since the COVID-19 outbreak, several studies evaluated changes in AMI patients' characteristics and in-hospital outcomes [13–18]. A recent meta-analysis showed similar results regarding the mean age of admission among ACS patients during the COVID-19 pandemic [11]. The lower mean age of admission may have several explanations. The initial pandemic response involved national lock-downs and recommendations for social distancing and remaining at home. These measures might have led to the reluctance of ACS patients to seek medical care. Furthermore, NSTEMI may cause milder symptoms and therefore, is more likely to be ignored. During latent COVID-19 phases, medical care services were more adopted and the COVID-19 infection rate was more controlled. Consequently, several studies resulted in the same or higher mean age of hospitalization among AMI patients [13,14,19].

We found shorter LOS during the COVID-19 period among both STEMI and NSTEMI subgroups in comparison with pre-COVID-19-era. Milovancev et al. obtained similar results [20]. Shorter LOS may be justified by the general policy of allocating cardiac beds for non-AMI patients in the early COVID-19 pandemic. Besides, during the initial pandemic phases, admitted ACS patients were more likely to get medical

**Table 1**  
The demographic and pre-hospital information.

Variable	AMI (4,560)			STEMI (2,935)			NSTEMI (1,625)		
	Before n = 2434	COVID-19 Era n = 2126	P value	Before n = 1473	COVID-19 Era n = 1462	P value	Before n = 961	COVID-19 Era n = 664	P value
Age, mean (SD),	61.35 12.09	60.37 11.77	0.005	61.02 12.28	60.61 12.12	0.37	61.86 11.77	59.83 10.94	0
Male (sex)	1864(76.6 %)	1659(78 %)	0.85	1159(78.6 %)	1148(78.5 %)	0.87	709(73.8 %)	513(77.3 %)	0.94
LOS	5.24(5.17)	4.27(3.63)	0	5.44(5.53)	4.38(3.61)	0	4.96(4.56)	4.14(3.64)	0
Comorbidities (%)									
CS	619(25.46)	559(26.29)	0.45	448(30.43)	489(33.44)	0.72	159(16.22)	86(12.98)	0.06
DM	309(12.69)	270(12.69)	0.47	187(12.67)	240(16.39)	0.35	123(12.76)	101(15.23)	0.88
DLP	266(10.94)	294(13.82)	0.53	168(11.42)	222(15.15)	0.25	93(9.67)	68(10.29)	0.45
HTN	489(20.08)	507(23.86)	0.65	320(21.76)	374(25.56)	0.8	150(15.64)	128(19.34)	0.65
FH	158(6.49)	198(9.31)	0.1	111(7.54)	157(10.72)	0.14	36(3.70)	37(5.56)	0.47
CAD	746(30.66)	811 (38.16)	0.99	509(34.57)	625(42.75)	0.83	196(20.45)	193(26.14)	0.94

**Table 2**  
Admissions for specific diagnoses.

	Before COVID-19			COVID-19 era			Change	95 % CI	P-value
	Admission	Sex <sup>M</sup>	Age	Admission	Sex <sup>M</sup>	Age			
AMI	2434	1864	61.35 ± 12.09	2126	1659	60.37 ± 11.77	12.65 %	(1.5–25.1)	0.179
STEMI	1473	1159	61.02 ± 12.28	1462	1148	60.61 ± 12.12	0.70 %	(-0.9–40.6)	0.974
NSTEMI	961	709	61.86 ± 11.77	664	513	59.83 ± 10.94	30.90 %	13.03–42.28	0.25

**Table 3**  
Mortality rate.

	Before COVID-19		Covid era		Risk Ratio (95 % CI)	Odds Ratio (95 % CI)	P-value
	Admission	Mortality (%)	Admission	Mortality (%)			
AMI	2434	120(4.9)	2126	150(7.0)	1.39 (1.10–1.76)	1.42 (1.11–1.82)	0.004
STEMI	1473	76(5.1)	1462	116(7.9)	1.49 (1.13–1.98)	1.53 (1.14–2.07)	0.004
NSTEMI	961	44(4.6)	664	34(5.1)	1.1 (0.71–1.71)	1.11 (0.70–1.75)	0.64

**Table 4**  
Major complications rates.

	Before COVID-19		Covid era		Risk Ratio (95 % CI)	Odds Ratio (95 % CI)	P-value
	Admission	Complications (%)	Admission	Complications (%)			
AMI	2434	160(6.6)	2126	206(9.7)	1.39 (1.10–1.76)	1.46 (1.11–1.82)	0

**Table 5**  
Variable coding.

Variable	Category	Parameter coding
<b>Independent variables coding</b>		
Sex	Female	0
	Male	1
Second admission	No	0
	Yes	1
Diagnosis	NSTEMI	0
	STEMI	1
State	Dead	0
	Live	1
COVID Present	MI	0
	MI-COVID	1
Angiography	Mild CAD	0
	SVD	1
	2VD	2
	3VD	3

treatment instead of traditional interventional treatment. It must be noted that, however, admission rate and LOS were much lower during the COVID-19 as to pre-COVID-19-era, in-hospital complications and mortality were shown to be higher revealing the fact that admitted patients were more critical. The decrease in the LOS makes it possible to underestimate the possibility of in-hospital mortality and complications. Probably with the LOS prolongation, an increase in in-hospital mortality and complications may be expected. This may highlight the importance of the excess mortality caused by the COVID-19 pandemic [21].

Considering hospitalization rates, a significant reduction was confirmed by several studies [1,8,9,13–15]. An observation common to studies was that during the pandemic a higher proportion of patients were hospitalized with STEMI as compared to NSTEMI [22–24].

Our results show that the reduction for NSTEMI patients was higher than in the STEMI group. These results are in line with two recent systematic reviews and meta-analyses by Sofi et al., that show the overall incidence rate ratio (IRR) of NSTEMI hospitalizations over the reference period higher decreased than STEMI (IRR 0.70 vs 0.80), the study also states that importantly, wide variations were observed among, and within, countries. [25–27]. The greater decrease in NSTEMI

**Table 6**  
Variables in the equation.

Total costs (USD)	Coef.	Std. Err.	t	P > t	[95 % Conf.	Interval]
Sex	-104.5385	73.46285	-1.42	0.156	-249.1527	40.07557
Age	-1.147934	2.866698	-0.40	0.689	-6.791127	4.495259
Length of Stay	-4.443881	6.819293	-0.65	0.515	-17.86789	8.980129
Second Admission	204.3225	132.4563	1.54	0.124	-56.42214	465.0672
STEMI vs NSTEMI	112.5022	70.08281	1.61	0.110	-25.45816	250.4626
State	62.75191	112.7195	0.56	0.578	-159.1403	284.6441
COVID	188.6139	80.39249	2.35	0.020	30.35855	346.8693
<b>Results of Angiography</b>						
1	96.93764	249.5783	0.39	0.698	-394.3657	588.241
2	136.8868	163.5644	0.84	0.403	-185.0952	458.8688
3	127.4092	151.4354	0.84	0.401	-170.6964	425.5149
Constant	575.1401	278.5848	2.06	0.040	26.73647	1123.544



**Table 7**  
Costs items for specific diagnoses.

Costs Item	MI-COVID (% Total Costs)	AMI (% Total Costs)
Physician/Nursing Services	6.7	3.8
Drug & device	37.4	18.2
CT-Scan, Angiography, Echocardiography	9.1	14.1
diagnostic tests & Laboratory	10.3	13.2
Therapeutic and surgical interventions	10.2	29
Hospital bed & CCU	26.3	21.7
<b>Total Costs</b>	<b>100 %</b> (\$1,059.09 ± 944.76)	<b>100 %</b> (\$871.09 ± 657)
Basic insurance	75.6	74.2
Supplementary insurance	8.6	10.8
Out of Pocket	12.1	11.8

hospitalizations may have several explanations. Possibly patients with NSTEMI did not seek medical help since their symptoms were less frequently characterized by precordial pain or chest discomfort. This would have, therefore, along with national lockdowns and recommendations for social distancing, increased their reluctance to expose themselves to the in-hospital risk of COVID-19 infection [11]. The lower hospitalization rate was, however, associated with higher in-hospital mortality and complications. This may point out the excess mortality during the pandemic. Moreover, AMI may lead to chronic settings such as HF if left untreated, which may impose a further burden on patients and health care systems. This mandates the importance of providing proper medical care for emergent cardiovascular patients and the prevention of patients missing during the pandemic. On the other hand, according to some studies, an actual decrease in the incident cardiovascular events during the COVID-19 pandemic cannot be ruled out mostly because staying at home may limit exposure to ACS-triggering factors [26,28].

Our study revealed a higher mortality rate among total AMI and STEMI during the COVID-19 pandemic, yet mortality among NSTEMI patients did not rise significantly. Our findings together with the number of other studies revealed higher mortality rates among AMI patients hospitalized during the pandemic [22,29–32]. COVID-19 infection may compromise outcomes in hospitalized ACS patients as a recent study revealed poorer prognosis among hospitalized STEMI patients with concurrent COVID-19 infection in comparison with uninfected patients [19]. Additionally, infection with coronavirus may reportedly lead to AMI in several ways [18,33,34]. Moreover, the COVID-19 outbreak has as well, had a serious impact on the mental health of the general population. This may influence cardiovascular diseases because of worsened risk factor control [6]. Higher mortality rate may suggest patients hospitalized with more critical health conditions, which together with lower hospitalization rate, brings out the fact of excess mortality rate during the COVID-19 pandemic [21].

We demonstrated major complications (cardiogenic shock, life-threatening arrhythmias, cardiac rupture/ventricular septal defect (VSD), or severe functional mitral regurgitation) increased among AMI patients during the COVID-19 pandemic. An important finding based on recent studies indicates that patients with STEMI had greater infarct size, as assessed by the peak of troponin or creatine kinase levels [31,35], lower left ventricular ejection fraction [31,36], greater intracoronary thrombotic burden [37], and, therefore, more common in-hospital unfavorable outcomes during the pandemic compared with pre-COVID-19 era. Additionally, we focused on major complications, which indicated severe disease and were more probable to lead to death. This may specify the fact that patients were more critical and although the admission rate has reduced, complications and mortality rate are expected to be higher.

The results of the regression model estimation revealed that there was a statistically significant relationship between the state of being infected with COVID-19 and the total costs of AMI patients. In other words, being infected with COVID-19 in AMI patients significantly increases hospital costs. The results of the present study showed that due to the more acute health condition in COVID-MI patients, they needed more and longer health care and consequently, hospital costs increased. This results are in line with COVID-MI patients who were hospitalized for a longer time in ICCU and had a higher mortality rate and re-hospitalization. Furthermore, the current study demonstrated that the total costs in STEMI patients are on average \$112 more than NSTEMI patients, which may be justified by the more acute condition of STEMI patients and their need to receive more diagnostic and therapeutic care and therefore, higher LOS.

Moreover, a direct relationship between re-admission and an increase in costs could be observed. Total costs for patients who were re-hospitalized were on average \$204 more than those who were admitted for the first time. Seemingly, re-hospitalized patients had more acute health conditions, and, as a result, required more care and services. Our study also showed that there is a direct relationship between the number of vessels disease and the costs of patients (3VD and 2VD); Patients with vessels disease, a high-risk group according to therapeutic guidelines, and are a high-risk group according to therapeutic guidelines. During the initial phases of the pandemic and with the surge in the load of patients in healthcare centers, ACS patients may have received medical treatments rather than traditional cardiovascular interventions and therefore, total medical costs may have declined. However, soon, the situation was organized to provide appropriate medical care based on guidelines for hospitalized AMI patients.

## 5. Strengths and limitations

The current study collected data from 4,560 AMI patients in selected hospitals of Tehran city and, as such, results may not be generalized to the entire Iran. Furthermore, we evaluated the impact of COVID-19 on hospital costs of AMI patients, which was rarely reported in other related studies. Our study covered 14 months since the COVID-19 outbreak and the equivalent months of 2019 therefore, only the initial phases of the pandemic were evaluated. Thus, the rate of admission, major complications, and mortality among AMI patients might have changed during the latent phases of the COVID-19 pandemic. Recent studies on AMI outcomes during the COVID-19 pandemic report short-term results. Therefore, further evaluation is mandatory to study long-term outcomes in the future.

## 6. Conclusions

Our results indicated that the mean age for AMI hospitalization was significantly different compared to the pre-COVID-19 era. LOS was lower among both STEMI and NSTEMI subgroups. The reduction in hospitalization was observed in both groups and was more dominant among patients with STEMI. The mortality rate was significantly higher among patients admitted with STEMI in the COVID-19 era. The incidence of major complications in hospitalized AMI patients increased during the COVID-19 pandemic. More complications and higher mortality rate, together with a lower rate of admission suggests an excess mortality rate during the COVID-19 pandemic. Total medical costs were significantly higher among hospitalized MI-COVID patients. Our study evaluated COVID-19 pandemic effects on pre-hospital patient characteristics and short-term outcomes of hospitalized patients during the initial phases of the pandemic. Future studies are recommended to examine long-term outcomes of hospitalized AMI patients during the COVID-19 era.

## Registration number of clinical studies

This study is an extract from the research project with the Code of Ethics IR.TUMS.MEDICINE.REC.1399.1245 from Tehran University of Medical Sciences, Tehran, Iran.

## Data availability

The data and materials presented in this study are available in the article. The dataset is available to request.

## CRediT authorship contribution statement

**Hamid Poursaghari:** Conceptualization, Supervision, Writing – review & editing. **Pirhossein Kolivand:** Investigation. **Samad Azari:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Peyman Saberian:** Investigation, Validation, Writing – original draft. **Masoud Behzadifar:** Data curation, Visualization, Writing – original draft, Writing – review & editing. **Negar Omidi:** Investigation, Supervision, Writing – original draft, Writing – review & editing. **Shahzad Salehbeigie:** Data curation, Writing – review & editing. **Behzad Raei:** Formal analysis, Methodology, Software. **Soheila Rajaie:** Data curation. **Nicola Luigi Bragazzi:** Methodology, Visualization, Writing – review & editing. **Reza Golpir:** Supervision. **Mohammad Rafie Khorgami:** Writing – review & editing. **Mohammad Khani:** Supervision. **Sara Montazerinamin:** Writing – original draft, Writing – review & editing. **Farhad Lotfi:** Data curation. **Masih Tajdini:** Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## References

- [1] O. Toscano, N. Cosentino, J. Campodonico, A.L. Bartorelli, G. Marenzi, Acute myocardial infarction during the COVID-19 pandemic: an update on clinical characteristics and outcomes, *Front. Cardiovasc. Med.* 8 (2021), 648290.
- [2] A.S. Fauci, H.C. Lane, R.R. Redfield, Covid-19—navigating the uncharted, *Mass Medical Soc.* 382 (13) (2020) 1268–1269.
- [3] G. Lavie, E. Battat, W. Saliba, M.Y. Flugelman, Change in hospitalizations and 30-day mortality of patients with acute myocardial infarction during the first COVID-19 lockdown—A pure social isolation effect? *Cardiovasc. Revasc. Med.* 38 (2022) 38–42.
- [4] D. Bandyopadhyay, T. Akhtar, A. Hajra, M. Gupta, A. Das, S. Chakraborty, I. Pal, N. Patel, B. Amgai, R.K. Ghosh, G.C. Fonarow, C.J. Lavie, S.S. Naidu, COVID-19 pandemic: cardiovascular complications and future implications, *Am. J. Cardiovasc. Drugs* 20 (4) (2020) 311–324.
- [5] M. Boukhris, A. Hillani, F. Moroni, M.S. Annabi, F. Addad, M.H. Ribeiro, et al., Cardiovascular implications of the COVID-19 pandemic: a global perspective, *Can. J. Cardiol.* 36 (7) (2020) 1068–1080.
- [6] M. Komiyama, K. Hasegawa, Coronavirus disease, psychological stress and cardiovascular diseases, *Eur. Cardiol. Rev.* 2021 (2019) 16.
- [7] G. Grasselli, A. Pesenti, M. Cecconi, Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response, *J. Am. Med. Assoc.* 323 (16) (2020) 1545–1546.
- [8] G. Grasselli, A. Zangrillo, A. Zanella, M. Antonelli, L. Cabrini, A. Castelli, D. Cereda, A. Coluccello, G. Foti, R. Fumagalli, G. Iotti, N. Latronico, L. Lorini, S. Merler, G. Natalini, A. Piatti, M.V. Ranieri, A.M. Scandroglio, E. Storti, M. Cecconi, A. Pesenti, E. Agosteo, V. Alaimo, G. Albano, A. Albertin, A. Alborghetti, G. Aldegheri, B. Antonini, E. Barbara, N. Belgioirno, M. Belliati, A. Benini, E. Beretta, L. Bianciardi, S. Bonazzi, M. Borelli, E. Boselli, N. Bronzini, C. Capra, L. Carnevale, G. Casella, G. Castelli, E. Catena, S. Cattaneo, D. Chiumello, S. Cirri, G. Citerio, S. Colombo, D. Coppini, A. Corona, P. Cortellazzi, E. Costantini, R. D. Covello, G. De Filippi, M. Dei Poli, F. Della Mura, G. Evasi, R. Fernandez-Olmos, A. Forastieri Molinari, M. Galletti, G. Gallioli, M. Gemma, P. Gnesin, L. Grazioli, S. Greco, P. Gritti, P. Grosso, L. Guatterri, D. Guzzon, F. Harizay, R. Keim, G. Landoni, T. Langer, A. Lombardo, A. Malara, E. Malpetti, F. Marino, G. Marino, M. Mazzoni, G. Merli, A. Micucci, F. Mojoli, S. Muttini, A. Nailescu, M. Panigada, P. Perazzo, G.B. Perego, N. Petrucci, A. Pezzi, A. Protti, D. Radrizzani, M. Raimondi, M. Ranucci, F. Rasulo, M. Riccio, R. Rona, C. Roscitano, P. Ruggeri, A. Sala, G. Sala, L. Salvi, P. Sebastiano, P. Severgnini, I. Sforzini, F.D. Sigurta, M. Subert, P. Tagliabue, C. Troiano, R. Valsecchi, U. Viola, G. Vitale, M. Zambon, E. Zoia, Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy, *Jama* 323 (16) (2020) 1574.
- [9] A. Aldujeli, A. Hamadeh, K. Briedis, K.M. Tecson, J. Rutland, Z. Krivickas, S. Stikloraitis, K. Briede, M. Aldujeli, R. Unikas, D. Zaliaduonyte, R. Zaliunas, R. C. Vallabhan, P.A. McCullough, Delays in presentation in patients with acute myocardial infarction during the COVID-19 pandemic, *Cardiology Research.* 11 (6) (2020) 386–391.
- [10] S. Fagioli, F.L. Lorini, G. Remuzzi, Adaptations and lessons in the province of Bergamo, *N. Engl. J. Med.* 382 (21) (2020) e71.
- [11] G. Lavie, Y. Wolff Sagy, M. Hoshen, W. Saliba, M.Y. Flugelman, Continuous decline in myocardial infarction and heart failure hospitalizations during the first 12 months of the COVID-19 pandemic in Israel, *J. Clin. Med.* 11 (6) (2022) 1577.
- [12] N.W.S. Chew, Z.G.W. Ow, V.X.Y. Teo, R.R.Y. Heng, C.H. Ng, C.-H. Lee, A.F. Low, M.-Y. Chan, T.-C. Yeo, H.-C. Tan, P.-H. Loh, The global effect of the COVID-19 pandemic on STEMI care: a systematic review and meta-analysis, *Can. J. Cardiol.* 37 (9) (2021) 1450–1459.
- [13] A. Takasaki, T. Kurita, M. Yanagisawa, A. Ino, D. Hiramatsu, A. Ikami, et al., Demographic trends and changes in the pre-and in-hospital medical management of acute myocardial infarction during the first 12 months of the COVID-19 pandemic in Mie prefecture-report from the Mie ACS Registry-, *Circulation Rep.* 4 (9) (2022) 412–421.
- [14] L. He, F. Lu, X. Du, D. Long, C. Sang, R. Tang, J. Dong, M. Guo, C. Ma, Impact of COVID-19 pandemic on hospital admissions of acute coronary syndrome: a Beijing Inpatient database study, *Lancet Regional Health-Western Pacific.* 19 (2022) 100335.
- [15] E. Altobelli, P.M. Angeletti, F. Marzi, F. D'Ascenzo, R. Petrocchi, G. Patti, Impact of SARS-CoV-2 outbreak on emergency department presentation and prognosis of patients with acute myocardial infarction: a systematic review and updated meta-analysis, *J. Clin. Med.* 11 (9) (2022) 2323.
- [16] R. Arai, D. Fukamachi, Y. Ebuchi, S. Migita, T. Morikawa, M. Monden, N. Takei, T. Tamaki, K. Kojima, N. Akutsu, N. Murata, D. Kitano, Y. Okumura, Impact of the COVID-19 outbreak on hospitalizations and outcomes in patients with acute myocardial infarction in a Japanese Single Center, *Heart Vessels* 36 (10) (2021) 1474–1483.
- [17] P. Budrys, M. Lizaitis, K. Cerlinskaite-Bajore, V. Bajoras, G. Rodevic, A. Martinonyte, L. Dieckus, I. Badaras, P. Serpytis, R. Gurevicius, R. Visinskiene, R. Buivydas, A. Volodko, E. Urbonaite, J. Celutkiene, G. Davidavicius, Increase of myocardial ischemia time and short-term prognosis of patients with acute myocardial infarction during the first COVID-19 pandemic wave, *Medicina* 57 (12) (2021) 1296.
- [18] V.L. Crudo, A.I. Ahmed, E.L. Cowan, D.J. Shah, M.H. Al-Mallah, M. Malahfji, Acute and subclinical myocardial injury in COVID-19, *Methodist Debakey Cardiovasc. J.* 17 (5) (2021) 22–30.
- [19] C. Grave, A. Gabet, J.-P. Empana, E. Puymirat, P. Tuppin, N. Danchin, V. Olié, Care management and 90-day post discharge mortality in patients hospitalized for myocardial infarction and COVID-19: A French nationwide observational study, *Arch. Cardiovasc. Dis.* 115 (1) (2022) 37–47.
- [20] A. Milovančev, M. Petrović, V. Popadić, T. Miljković, S. Klačnja, P. Djuran, A. Ilić, M. Kovačević, A. Stojić Milosavljević, M. Brajković, B. Crnokrak, L. Memon, A. Milojević, Z. Todorović, M. Čanković, M. Lukić Šarkanović, S. Bjelić, S. Tadić, A. Redžek, M. Zdravković, Characteristics and outcomes of patients with acute coronary syndrome and COVID-19, *J. Clin. Med.* 11 (7) (2022) 1791.
- [21] H. Poursaghari, H. Tavolinejad, S. Soleimanpour, Z. Abdi, J. Arabloo, N. L. Bragazzi, M. Behzadifar, S. Rashedi, N. Omidi, A. Ayoubian, M. Tajdini, S. M. Ghorashi, S. Azari, Hospitalization, major complications and mortality in acute myocardial infarction patients during the COVID-19 era: a systematic review and meta-analysis, *IJC Heart Vasc.* 41 (2022) 101058.
- [22] S. De Rosa, C. Spaccarotella, C. Basso, M.P. Calabrò, A. Curcio, P.P. Filardi, et al., Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era, *Eur. Heart J.* 41 (22) (2020) 2083–2088.
- [23] M.M. Mafham, E. Spata, R. Goldacre, D. Gair, P. Curnow, M. Bray, S. Hollings, C. Roebuck, C.P. Gale, M.A. Mamas, J.E. Deanfield, M.A. de Belder, T.F. Luescher, T. Denwood, M.J. Landray, J.R. Emberson, R. Collins, E.J.A. Morris, B. Casadei, C. Baigent, COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England, *Lancet* 396 (10248) (2020) 381–389.
- [24] S. Carugo, M. Ferlini, D. Castani, A. Andreassi, G. Guagliumi, M. Metra, C. Lombardi, C. Cuccia, S. Savonitto, L. Piatti, M. D'Urbano, C. Lettieri, P. Vandoni, M. Lettino, G. Marenzi, M. Montorfano, A. Zangrillo, B. Castiglioni, R. De Ponti, L. Oltrona Visconti, Management of acute coronary syndromes during the COVID-19 outbreak in Lombardy: the "macro-hub" experience, *IJC Heart Vasc.* 31 (2020) 100662.
- [25] F. Sofi, M. Dinu, G. Reboldi, S. Lotti, L. Genovese, I. Tritto, et al., Worldwide impact of COVID-19 on hospital admissions for non-ST-elevation acute coronary syndromes (NSTACS): a systematic review with meta-analysis of 553,038 cases, *Eur. Heart J.-Quality Care Clin. Outcomes* (2023), qcad048.
- [26] F. Sofi, M. Dinu, G. Reboldi, F. Stracci, R.F.E. Pedretti, S. Valente, G. Gensini, C. M. Gibson, G. Ambrosio, Worldwide differences of hospitalization for ST-segment

- elevation myocardial infarction during COVID-19: a systematic review and meta-analysis, *Int. J. Cardiol.* 347 (2022) 89–96.
- [27] Y.N. Aye, A.S. Mai, A. Zhang, O.Z.H. Lim, N. Lin, C.H. Ng, et al., Acute myocardial infarction and myocarditis following COVID-19 vaccination, *QJM: Int. J. Med.* 116 (4) (2023) 279–283.
- [28] M.A. Mohammad, S. Koul, C.P. Gale, J. Alfredsson, S. James, O. Fröbert, E. Omerovic, D. Erlinge, The association of mode of location activity and mobility with acute coronary syndrome: a nationwide ecological study, *J. Intern. Med.* 289 (2) (2021) 247–254.
- [29] N. Cosentino, A.L. Bartorelli, G. Marenzi, Time to treatment still matters in ST-elevation myocardial infarction: a call to maintain treatment effectiveness during the COVID-19 pandemic, *Eur. Heart J.-Cardiovasc. Pharmacother.* 6 (6) (2020) 408–409.
- [30] T.J. Gluckman, M.A. Wilson, S.-T. Chiu, B.W. Penny, V.B. Chepuri, J.W. Waggoner, K.J. Spinelli, Case rates, treatment approaches, and outcomes in acute myocardial infarction during the coronavirus disease 2019 pandemic, *JAMA Cardiol.* 5 (12) (2020) 1419.
- [31] U. Primessnig, B.M. Pieske, M. Sherif, Increased mortality and worse cardiac outcome of acute myocardial infarction during the early COVID-19 pandemic, *ESC Heart Failure.* 8 (1) (2021) 333–343.
- [32] B. Popovic, J. Varlot, P.A. Metzendorf, H. Jeulin, F. Goehringer, E. Camenzind, Changes in characteristics and management among patients with ST-elevation myocardial infarction due to COVID-19 infection, *Catheter. Cardiovasc. Interv.* 97 (3) (2021) E319–E326.
- [33] A. Del Prete, F. Conway, D.G. Della Rocca, G. Biondi-Zoccai, F. De Felice, C. Musto, M. Picichè, E. Martuscelli, A. Natale, F. Versaci, COVID-19, acute myocardial injury, and infarction, *Cardiac Electrophysiol. Clin.* 14 (1) (2022) 29–39.
- [34] J.P. Cooke, J.H. Connor, A. Jain, Acute and chronic cardiovascular manifestations of COVID-19: role for endotheliopathy, *Methodist Debakey Cardiovasc. J.* 17 (5) (2021) 53–62.
- [35] M. Gramegna, L. Baldetti, A. Beneduce, L. Pannone, G. Falasconi, F. Calvo, V. Pazzanese, S. Sacchi, M. Pagnesi, F. Moroni, S. Ajello, G. Melisurgo, E. Agricola, P.G. Camici, A.M. Scandroglio, G. Landoni, F. Ciceri, A. Zangrillo, A.M. Cappelletti, ST-Segment–Elevation myocardial infarction during COVID-19 pandemic: insights from a regional public service healthcare hub, *Circ. Cardiovasc. Interv.* 13 (8) (2020), e009413.
- [36] S.J. Wilson, M.J. Connolly, Z. Elghamry, C. Cosgrove, S. Firoozi, P. Lim, R. Sharma, J.C. Spratt, Effect of the COVID-19 pandemic on ST-segment–elevation myocardial infarction presentations and in-hospital outcomes, *Circ. Cardiovasc. Interv.* 13 (7) (2020), e009438.
- [37] S.J. Reinstadler, M. Reindl, I. Lechner, M. Holzknrecht, C. Tiller, F.X. Roithinger, M. Frick, U.C. Hoppe, P. Jirak, R. Berger, G. Delle-Karth, E. Laßnig, G. Klug, A. Bauer, R. Binder, B. Metzler, Effect of the COVID-19 pandemic on treatment delays in patients with ST-segment elevation myocardial infarction, *J. Clin. Med.* 9 (7) (2020) 2183.