Treatment delays and in-hospital outcomes in acute myocardial infarction during the COVID-19 pandemic: A nationwide study

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Abstract

Objective: Delayed admission of myocardial infarction (MI) patients is an important prognostic factor. In the present nationwide registry (TURK-MI-2), we evaluated the treatment delays and outcomes of patients with acute MI during the Covid-19 pandemic and compaired with a recent pre-pandemic registry (TURKMI-1).

Methods: The pandemic and pre-pandemic studies were conducted prospectively as 15-day snapshot registries in the same 48 centers. The inclusion criteria for both registries were aged ≥18 years and a final diagnosis of acute MI (AMI) with positive troponin levels. The only difference between the 2 registries was that the pre-pandemic (TURKMI-1) registry (n=1872) included only patients presenting within the first 48 hours after symptom-onset. TURKMI-2 enrolled all consecutive patients (n=1113) presenting with AMI during the pandemic period.

Results: A comparison of the patients with acute MI presenting within the 48-hour of symptom-onset in the pre-pandemic and pandemic registries revealed an overall 47.1% decrease in acute MI admissions during the pandemic. Median time from symptom-onset to hospital-arrival increased from 150 min to 185 min in patients with ST elevation MI (STEMI) and 295 min to 419 min in patients presenting with non-STEMI (NSTEMI) (p-values <0.001). Door-to-balloon time was similar in the two periods (37 vs. 40 min, p=0.448). In the pandemic period, percutaneous coronary intervention (PCI) decreased, especially in the NSTEMI group (60.3% vs. 47.4% in NSTEMI, p<0.001; 94.8% vs. 91.1% in STEMI, p=0.013) but the decrease was not significant in STEMI patients admitted within 12 hours of symptom-onset (94.9% vs. 92.1%; p=0.075). In-hospital major adverse cardiac events (MACE) were significantly increased during the pandemic period [4.8% vs. 8.9%; p<0.001; age- and sex-adjusted Odds ratio (95% CI) 1.96 (1.20–3.22) for NSTEMI, p=0.007; and 2.08 (1.38–3.13) for STEMI, p<0.001].

Conclusion: The present comparison of 2 nationwide registries showed a significant delay in treatment of patients presenting with acute MI during the COVID-19 pandemic. Although PCI was performed in a timely fashion, an increase in treatment delay might be responsible for the increased risk of MACE. Public education and establishing COVID-free hospitals are necessary to overcome patients' fear of using healthcare services and mitigate the potential complications of AMI during the pandemic. *(Anatol J Cardiol 2020; 24: 334-42)*

Keywords: acute myocardial infarction, COVID-19, pandemic, total ischemic time, treatment delay

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Introduction

The prognosis of patients suffering from acute myocardial infarction (MI) directly depends on rapid diagnosis and early treatment. Therefore, fast transport and early admission to the hospital are crucial in improving prognosis after MI (1, 2). Patient-related factors can contribute to delays in treatment after the onset of symptoms. In addition, geographical or logistical factors or the organization of the healthcare management system can contribute to treatment delays (3, 4). The sudden outbreak of the Coronavirus Disease in 2019 (COVID-19) caused intense pressure on the community and the healthcare system. Recent observations suggest that the number of patients presenting with acute MI decreased with the emergence of the outbreak (5-11). Moreover, acute MI patients may be presenting at later stages during the pandemic due to fear of acquiring coronavirus in healthcare facilities (5-11). The extent of the delays, the stage at which the delay is prominent, and the potential effects of delays on outcomes are unclear. The Turkish Acute Myocardial Infarction (TURKMI)-2 registry was planned to assess delays in MI patient care at each step from symptom-onset to treatment. The effects of delays on in-hospital outcomes during the COVID-19 outbreak were also investigated. Data from TURKMI-2 are compared to the results from a recent nationwide registry (TURKMI-1) (12) that was conducted just prior to the pandemic.

Methods

TURKMI-2 was planned as a nationwide, observational, 15-day snapshot registry of patients presenting with acute MI during the COVID-19 pandemic. The Institutional Review Board of Ankara University Medical School, Turkey (May 2020; No: i4-225-20) and the Ministry of Health COVID-19 Scientific Board (May 2020; No: 66175679.99.E.110223) approved the protocol and informed consent was obtained from all participants.

The previous TURKMI study (clinicaltrials.gov NCT04241770) was also a 15-day registry (November 1-15, 2018) that prospectively enrolled patients with acute MI in Turkey (12, 13). All consecutive patients admitted to the hospital within 48 hours of symptom-onset were registered in TURKMI-1. Fifty cardiology centers capable of 24/7 service for primary percutaneous coronary intervention (PCI) were selected in the 12 Eurostat NUTS statistical regions of Turkey proportional to the 2018 Turkey census. The clinical characteristics and delay at each step from symptom-onset to the appropriate treatment were assessed (12). In the present study (TURKMI-2 registry), the same information was obtained from the same centers during the COVID-19 pandemic. Of note, 2 centers of the former registry did not participate in the TURKMI-2 study. Accordingly, all consecutive patients presenting with acute MI during a 15-day period (April 17-May 2, 2020) at 48 centers that participated in the TURKMI-1 registry were enrolled. The inclusion criteria were the same as the original registry: 1) aged ≥18 years, 2) a final (discharge) diagnosis of acute MI, either ST elevation MI (STEMI) or non-STEMI (NSTEMI), with positive troponin levels, and 3) written, informed consent. Patients unwilling or unable to consent were excluded. The only difference between the 2 registries in terms of the inclusion criteria was the time frame from symptom-onset to hospital admission. The TURKMI-1 registry, conducted before the pandemic outbreak, only included patients admitted to the hospital within 48-hour of the onset of symptoms. Since some delays in admission due to the pandemic were expected, we included all of the acute MI patients in the TURKMI-2, regardless of the time of symptom-onset. However, for the comparison of pre-pandemic and pandemic data, we primarily focused on the patients who were admitted to the study centers within 48-hour of symptom-onset in both registries.

All outcomes and diagnoses were defined in accordance with the previous TURKMI-1 definitions (12-14). Patients who were admitted to emergency departments without emergency medical service (EMS) were accepted as self-transported. Major adverse cardiovascular events (MACE) were defined as the composite in-hospital endpoint of death, heart failure, or cardiogenic shock. The time variables between symptom-onset to hospital arrival obtained from each patient were the number of minutes reflecting symptom-onset to EMS contact (for those who called EMS), EMS contact to EMS arrival patient's location, EMS arrival patient's location to EMS arrival at the hospital, and time for transportation from a non-PCI-capable hospital to a PCI-capable study center (for transferred patients). The sum of these variables was defined as symptom-onset to hospital arrival. Door-to-balloon time was defined as the time between arrival at the study center and balloon inflation in the culprit artery for STEMI patients and, similarly, door-to-needle time was calculated for those who received fibrinolytic treatment. Total ischemic time was defined as the time from symptom-onset to balloon-inflation (or the initiation of fibrinolytic therapy) for STEMI patients. Since the indication for coronary angiography and PCI varies according to the risk categories in NSTEMI patients, the length of time from symptom-onset to arrival at the study centers was used to compare the delay in NSTEMI patients and all patients (STEMI+NSTEMI) between the 2 periods. During the study period, a lockdown was implemented for several days in major cities. Thus, the time variables were also compared between lockdown and non-lockdown periods in these major cities (Supplementary Online Material).

Statistical analysis

All of the analyses were performed using Predictive Analytics Software (PASW) for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). Categorical variables are presented as the number and percentage and compared using chi-square or Fisher's exact tests. Continuous variables are shown as mean and standard deviation or median and interquartile range (IQR), depending on

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the presence of normal distribution, and compared using an independent t-test or the Mann-Whitney U test. The risk of MACE for the pandemic versus non-pandemic periods was assessed using logistic regression analysis, adjusted for age and sex. Due to the observational nature of the registries and the second part of the study (TURKMI-2) occurring during the pandemic period, changes in the characteristics of patients admitted to the hospital between the 2 periods might create a selection bias in estimating the outcome risk. Therefore, we performed a sensitivity analysis to assess the potential selection bias. In this analysis, the period (pre-pandemic or pandemic) was modeled using a logit link function and covariates of age, sex, history of hypertension, diabetes mellitus, hyperlipidemia, smoking, coronary artery disease, and EMS use, and then inverse probability weighting was applied for the comparison of the risk of outcome between the 2 periods. The balance was assessed with standardized differences after weighting (all had ≤2%). A p value of <0.05 was considered significant.

Results

A total of 1113 patients with acute MI were admitted to the TURKMI-2 study centers during a 2-week period of the pandemic. We present the comparison of the previous TURKMI-1 and a subgroup of TURKMI-2 patients who were admitted to the study centers within 48-hour of symptom-onset. The details of the entire TURKMI-2 population in comparison with the TURKMI-1 registry are presented as supplementary material (Online text, eTable 1, and eFig. 1).

Characteristics of the TURKMI-1 and TURKMI-2 registries

Table 1 displays the baseline characteristics, delays, and in-hospital outcomes of the patients in the pre-pandemic and pandemic periods. There were no significant differences between the 2 registries in terms of the sex, the presence of diabetes mellitus or hypertension, history of coronary artery disease, or the MI location.

Change in the number of admissions

Among the patients registered in the TURKMI-2, 991 patients were admitted to the hospital within 48-hour of symptom-onset (51.1% NSTEMI and 48.9% STEMI). A total of 1872 patients were enrolled in the TURKMI-1 (62.0% NSTEMI and 38.0% STEMI). Acute MI admissions decreased by 47.1% during the pandemic time frame studied. This reduction in admission was more prominent in patients with NSTEMI compared with STEMI (56.4% vs. 31.8%, respectively, Fig. 1).

EMS call and delays

EMS transport significantly increased during the pandemic period (11.7% vs. 20.7%; p<0.001), though EMS transport use was very low in both registries. Changes in EMS transport were similar in NSTEMI and STEMI patients. The time elapsed between symptom-onset to EMS call was significantly prolonged in the pandemic period (median 52.5 min vs 90 min, p<0.001 for all; 67.5 min vs. 125 min for NSTEMI, p=0.080; 32.5 min vs. 80 min for STEMI, p=0.003). Though the difference between EMS arrivals was not "clinically" significant; and the median time was 15 minutes for both NSTEMI and STEMI patients in both periods. The median time for EMS arrival to the hospital was 20 min vs. 19 min for NSTEMI patients and 20 min vs. 20 min for STEMI patients in the TURKMI-1 and the TURKMI-2 studies, respectively. Moreover, there were no statistically significant differences in the time delay for patients who were transferred from a non-PCI-capable hospital when the pre-pandemic and pandemic periods were compared.

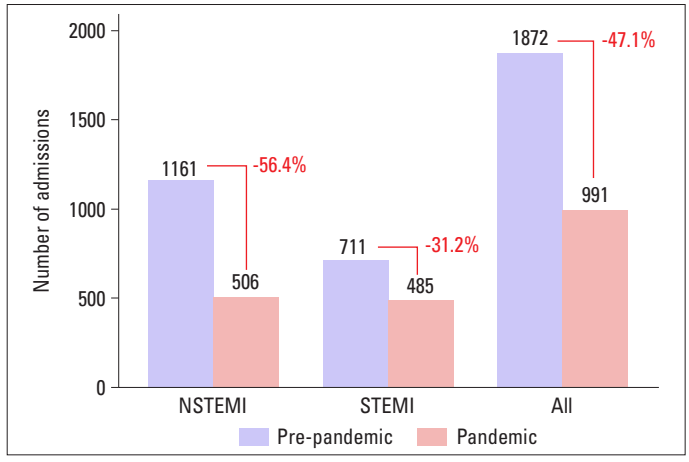

Figure 1. Decreased number of the patients with acute myocardial infarction during the pandemic (TURKMI-2) compared to the non-pandemic period (TURKMI-1) in the patient cohort admitted to the study centers within 48 hours of symptom onset
MI - myocardial infarction, NSTEMI - non-ST elevation MI, STEMI - ST elevation MI

The time elapsed between symptom-onset to study center arrival was significantly longer during the pandemic compared with the pre-pandemic period (median arrival delay: 215.5 min vs. 270 min in total, p<0.001) and was more prominent in the NSTEMI group. The total ischemic time for patients with STEMI who were treated with PCI was significantly longer during the pandemic period compared with the pre-pandemic period (Fig. 2). However, the door-to-balloon time was similar between the 2 registries. Time delays at each step for STEMI patients transferred directly to the study centers using EMS are presented in Figure 3. Of note, the time from hospital arrival to coronary angiography for NSTEMI patients was significantly less during the pandemic period (median 1050 min for TURKMI-1 vs. 502 min for TURKMI-2; p=0.001).

In-hospital management and outcomes

There was a significant reduction in the overall frequency of coronary angiography during the pandemic period compared to the pre-pandemic period. However, the reduction was significant only in the NSTEMI group. The frequency of PCI decreased

Table 1. Characteristics, time delays, and in-hospital outcomes in patients with acute myocardial infarction admitted within the first 48 hours of symptom onset during the pandemic and pre-pandemic periods

Characteristics	TURKMI-1 (Pre-pandemic registry)			TURKMI-2 (Pandemic registry)			*P*-All	*P*-NSTEMI	*P*-STEMI
	All (n=1872)	NSTEMI (n=1161)	STEMI (n=711)	All (n=991)	NSTEMI (n=506)	STEMI (n=485)			
Age, years	62 (53-71)	63 (54-72)	60 (51-70)	60 (51-69)	61 (52-71)	58 (49-66)	<0.001	0.050	0.012
Age, years	62 (13)	63 (13)	60 (14)	60 (13)	62 (12)	59 (13)			
Female	492 (26.3)	333 (28.7)	159 (22.4)	236 (23.8)	138 (27.3)	98 (20.2)	0.149	0.557	0.373
Hypertension (self-reported)	922 (49.3)	649 (55.9)	273 (38.4)	499 (50.4)	278 (54.9)	221 (45.6)	0.575	0.717	0.013
Diabetes	633 (33.8)	432 (37.2)	201 (28.3)	335 (33.8)	184 (36.4)	151 (31.1)	0.996	0.742	0.286
Smoking	914 (48.8)	513 (44.2)	401 (56.4)	432 (43.6)	184 (36.4)	248 (51.1)	0.008	0.003	0.073
Hypercholesterolemia (self-reported)	215 (11.5)	148 (12.7)	67 (9.4)	256 (25.8)	148 (29.2)	108 (22.3)	<0.001	<0.001	<0.001
History of coronary artery disease	528 (28.2)	406 (35)	122 (17.2)	283 (28.7)	190 (37.8)	93 (19.3)	0.767	0.273	0.346
Infarct localization									
Anterior	-	-	340 (48.1)	-	-	238 (49.1)	-	-	0.739
Inferior (±posterior)	-	-	367 (51.9)	-	-	247 (50.9)			
Mode of Admission to hospital (study center)									
By Ambulance	213 (11.7)	88 (7.8)	125 (17.9)	205 (20.7)	77 (15.2)	128 (26.4)	<0.001	<0.001	<0.001
Transfer from a non-PCI-capable hospital	694 (38.1)	419 (37.3)	275 (39.3)	391 (39.5)	185 (36.6)	206 (42.5)	0.477	0.772	0.281
Self-transport	915 (50.2)	616 (54.9)	299 (42.8)	395 (39.9)	244 (48.2)	151 (31.1)	<0.001	.0013	<0.001
Mode of admission to study center for those transferred from a non-PCI-capable center									
By Ambulance	-	-	-	131 (34)	59 (32.6)	72 (35.3)	-	-	-
Self-transport	-	-	-	254 (66)	122 (67.4)	132 (64.7)			
Time delays									
Symptom-onset to EMS call, min	52.5 (15-170)	67.5 (15-290)	32.5 (15-120)	90 (30-240)	125 (30-315)	80 (30-195)	0.001	0.080	0.003
EMS call to EMS arrival, min	15 (10-20)	15 (10-20)	15 (10-20)	15 (10-20)	15 (10-20)	15 (15-20)	<0.001	0.103	<0.001
Time delay for those transferred from a non-PCI-capable hospital, min	169 (99-300)	235.5 (120-390)	120 (63-180)	180 (90-296)	265 (135-390)	120 (60-186.5)	0.691	0.084	0.710
Symptom-onset to hospital (study center) arrival, min	215.5 (90-473)	295 (120-582.5)	150 (70-300)	270 (120-630)	419 (180-840)	185 (100-360)	<0.001	<0.001	<0.001
Transferred from a non-PCI-capable center	332 (180-635)	424 (260-763)	240 (145-365)	390 (210-690)	512 (360-930)	240 (167-453)	0.036	<0.001	0.125
Directly admitted to the study center (by EMS or self-transport)	135 (60-370)	180 (74-450)	100 (56-240)	181 (90-550)	275 (120-785)	145 (70-303)	<0.001	<0.001	<0.001
In-hospital procedures and times									
Coronary angiography	1758 (93.9)	1054 (90.8)	704 (99)	871 (87.9)	396 (78.3)	475 (97.9)	<0.001	<0.001	0.122

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Table 1. Cont.

Characteristics	TURKMI-1 (Pre-pandemic registry)			TURKMI-2 (Pandemic registry)					
	All (n=1872)	NSTEMI (n=1161)	STEMI (n=711)	All (n=991)	NSTEMI (n=506)	STEMI (n=485)	*P*-All	*P*-NSTEMI	*P*-STEMI
Fibrinolytic therapy	-	-	13 (1.8)	-	-	11 (2.3)	-	-	0.594
PCI	1374 (73.4)	700 (60.3)	674 (94.8)	682 (68.8)	240 (47.4)	442 (91.1)	0.010	<0.001	0.013
Door-to-needle time, min						30 (15-60)			
Door-to-balloon time, min	-	-	37 (25-65)	-	-	40 (25-68)	-	-	0.448
Total ischemic time, min	-	-	195 (115-331)	-	-	245 (149-469)	-	-	<0.001
Time from arrival to study center to Coronary angiography for NSTEMIs	-	1050 (300-2095)	-	-	501.5 (134-1225)	-	-	<0.001	-
In-hospital outcomes									
MACE (death, heart failure, or cardiogenic shock)	90 (4.8)	40 (3.4)	50 (7.0)	88 (8.9)	30 (5.9)	58 (12.0)	<0.001	0.020	0.004
Death	71 (3.8)	33 (2.8)	38 (5.3)	31 (3.1)	8 (1.6)	23 (4.7)	0.361	0.126	0.642
Heart failure or cardiogenic shock	53 (2.8)	23 (2)	30 (4.2)	82 (8.3)	28 (5.5)	54 (11.1)	<0.001	<0.001	<0.001

Data were expressed as mean (SD), median (interquartile range), or n (%). EMS - emergency medical service call; MACE - major adverse cardiac events; MI - myocardial infarction; NSTEMI - non-ST elevation MI; PCI - percutaneous coronary intervention; STEMI - ST elevation MI

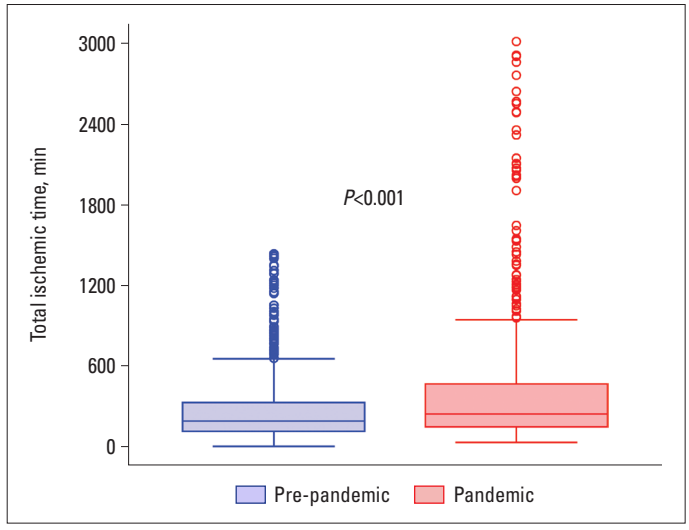

Figure 2. The total ischemic times for patients with ST elevation myocardial infarction who were treated with percutaneous coronary intervention were significantly longer during the pandemic period compared with the pre-pandemic period (median 195 min for TURKMI-1 vs. 245 min for TURKMI-2; p<0.001)

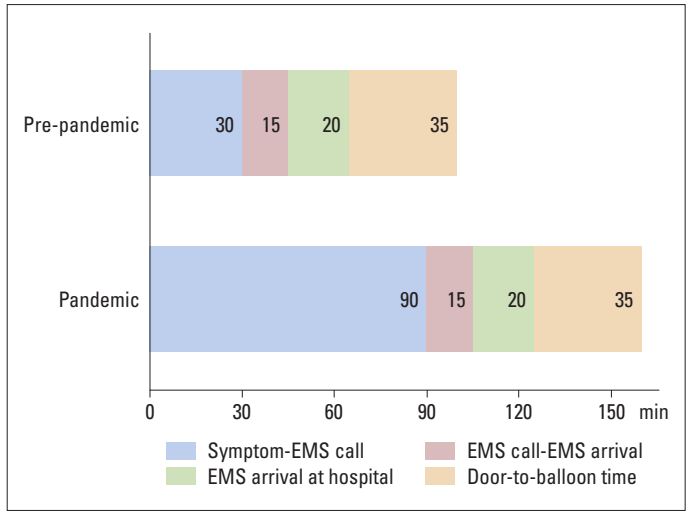

Figure 3. Comparison of treatment delays in patients admitted with acute myocardial infarction during the pandemic (TURKMI-2) and pre-pandemic (TURKMI-1) periods. Time to treatment was significantly lengthened due to patient-related delays in the pandemic period. Meanwhile, symptom-to-EMS call, EMS call-to-EMS arrival, EMS arrival at the hospital, and door-to-balloon times were similar in the pre-pandemic and pandemic periods
EMS - emergency medical service

significantly in both NSTEMI and STEMI patients during the pandemic. However, when STEMI patients who were admitted to the hospital within the guideline-recommended time frame of 12 hours were evaluated, there was no significant drop in the frequency of PCI treatment between the pre-pandemic and pandemic periods (574, 94.9% vs. 387, 92.1%, respectively; p=0.075). Meanwhile, the rate of fibrinolytic treatment was very low and statistically similar in the two registries. Of note, the number of patients who received fibrinolytic therapy was very low (13 and

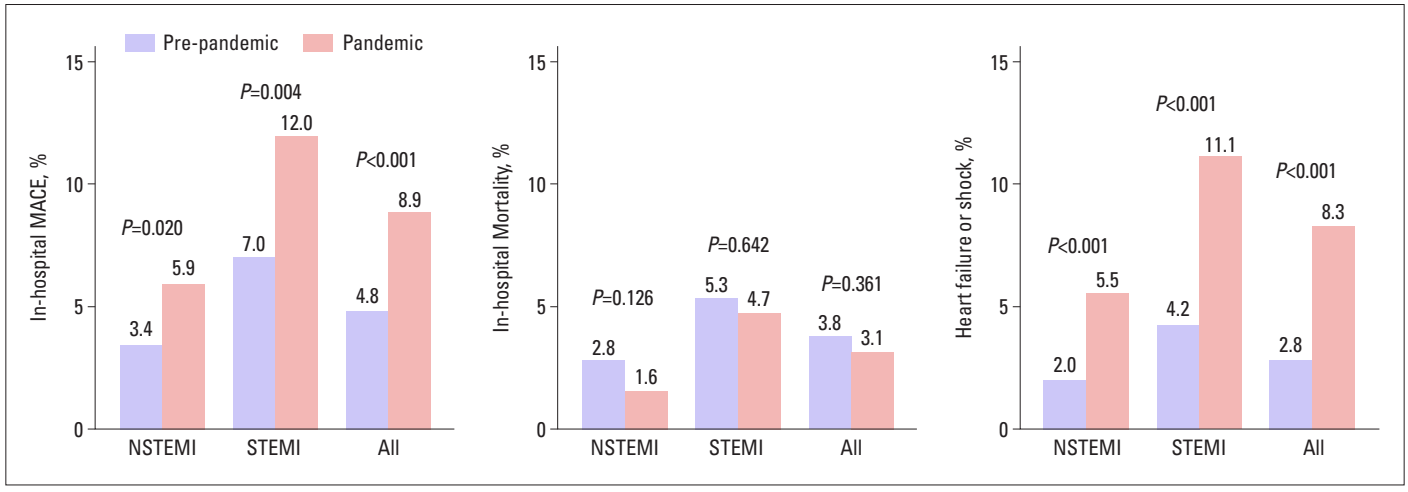

Figure 4. Comparison of the in-hospital major adverse events (defined as death, cardiogenic shock, or heart failure) between the pre-pandemic (TURKMI-1) and pandemic (TURKMI-2) periods

MACE - major adverse cardiac events, NSTEMI - non-ST elevation myocardial infarction STEMI - ST elevation myocardial infarction

11 patients in the pre-pandemic and pandemic period, respectively); therefore, we excluded these patients from the analysis of in-hospital timings.

MACE was more common in the pandemic period compared to the pre-pandemic period (Fig. 4). The age- and sex-adjusted risk of MACE was 2 times higher in the pandemic period compared to the pre-pandemic period due to the increased risk of heart failure or cardiogenic shock [Odds ratio (95% confidence interval) was 1.96 (1.20–3.22) for NSTEMI, p=0.007 and 2.08 (1.38–3.13) for STEMI, p<0.001]. Sensitivity analysis for potential selection bias did not change the main outcome findings [Odds ratios and confidence intervals were 1.97 (1.18–3.30), p<0.010 for NSTEMI; and 1.79 (1.18–2.70), p=0.006 for STEMI].

Effect of lockdown period

The enrolment period of the TURKMI-2 registry covered a total of 8 days of lockdown circumstances. A comparison of patients admitting during the lockdown versus non-lockdown days is presented in the supplementary online text and eTable 2.

Discussion

Data from two nationwide TURKMI registries collected before and during the pandemic provide important insights into the impact of the COVID-19 pandemic on patients presenting with acute MI. Our results are based on the largest acute MI population studied during the COVID-19 outbreak. The results show that acute MI admissions decreased by 47.1%, with a significant treatment delay due to increased time from symptom-onset to EMS call or symptom-onset to first medical contact. These findings reflect patient-related delays during the pandemic (Fig. 3). The significant decrease (47.1%) in the number of acute MI admissions was consistent with previous reports of a 30–48.4% average reduction in acute MI presentations since the emergence of the COVID-19 outbreak (6, 8, 9, 15-20). The reduction was more pronounced in patients with NSTEMI (56.4%) compared with STEMI (31.8%), probably due to the symptom severity leading to patients seeking medical care.

The use of EMS transport was significantly greater during the pandemic compared with the pre-pandemic period. The increased use of EMS may have been due to several factors. Fear of acquiring COVID-19 may have led patients with more severe symptoms to seek medical attention via EMS. Also, the low EMS usage during the TURKMI-1 period was made public and the increased EMS use may be the effects of the successful awareness campaigns. Furthermore, restrictions on self-transport during lockdown may have contributed to the increased use of EMS.

Our results demonstrated a significant delay from symptom-onset to EMS calls for patients transported by ambulance and symptom-onset to hospital admission time for those who used self-transport. However, there were no "clinically" significant delays between the pre-pandemic and pandemic periods in terms of the EMS call to EMS arrival or the EMS arrival to hospital admission. The door-to-balloon time did not significantly change during the pandemic period. Overall, these results indicate that EMS and in-hospital care of patients with STEMI did not change during the pandemic period. Accordingly, our main findings indicate that the major time delay leading to a significantly prolonged treatment delay was patient-related (Fig. 3). Several studies have evaluated the delay in first medical contact or door-to-balloon time; (6, 10, 16-18, 21) however, only 1 study, which included 9 patients during the pandemic, assessed all of the stages from symptom-onset to balloon dilatation (17). Our study provides detailed information about delays at each step in a large nationwide population. The patient-related delay probably arose from the fear of contracting COVID-19 in the EMS ambulance or the hospital. Therefore, only patients with more severe symptoms eventually sought

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medical care and admittance to healthcare services. This fact is probably the explanation for the more pronounced drop observed in the number of NSTEMI cases compared with STEMI during the pandemic period. However, such a fear causing a refrain from seeking medical attention could be a primary denominator of increased mortality and heart failure in future as the delay in the treatment is the major determinant of infarct size and survival.

The percentage of patients who underwent coronary angiography significantly declined during the pandemic only in NSTEMI patients. The proportion of patients who underwent PCI decreased in both the NSTEMI and STEMI groups; however, the reduction was substantial only in NSTEMI patients. The low referral to coronary procedures for NSTEMI patients might be due to the preferential selection of patients with high-risk characteristics for invasive procedures during the pandemic period. PCI rates were not decreased in STEMI patients who were admitted to the study centers within 12 hours of symptom-onset, reflecting the maintenance of guideline-recommended practice during the pandemic. Therefore, we suggest that the overall decrease in PCI rates was probably due to the late admission of patients during the COVID-19 breakout.

In NSTEMI patients, the duration between hospital arrival and coronary angiography was significantly shorter in the pandemic cohort compared with the pre-pandemic cohort. This may be due to the efforts to decrease the length of hospital stay. Additionally, the deferral of elective invasive procedures may have shortened the wait-time for elective coronary procedures in NSTEMI patients. Furthermore, patients with subtle or mild symptoms hesitated to seek care during pandemic conditions. Therefore, these patients were admitted later than the appropriate time frame with more serious symptoms, i.e. most NSTEMI patients probably presented after their condition has deteriorated. Patients would then have presented with relatively high risk, which required rapid intervention, shortening the time between hospital arrival and coronary angiography.

Another major finding of this study was that MACE were increased significantly during the pandemic period. The proportion of patients with MACE was significantly higher in the pandemic period mainly due to increased heart failure or cardiogenic shock. The increased risk of MACE may have been caused by the prolonged treatment delay in the pandemic period. There were no differences in mortality between the 2 registries. The marked increase in mortality, since the emergence of the outbreak, cannot be fully explained by COVID-19 alone, which raises the possibility of patients dying of acute coronary events due to medical care avoidance (22). As the present study included only patients who arrived alive at the study centers, some patients with high-risk characteristics for mortality were eliminated, which may have resulted in a survival bias.

To the best of knowledge, our study is the first to report a comparison of the lockdown and non-lockdown days during the pandemic period. There were no substantial differences with regard to EMS use, delays, or development of MACE between the lockdown and non-lockdown days in the major cities (n=15) of the TURKMI-2 study. Further details on the impact of lockdown are presented in the Supplementary Online Material.

Study limitation

The lack of seasonal synchronization between the registries is a limitation of the study. However, previous studies have shown that the effects of seasonal variations on prevalence, outcomes, or characteristics of acute MI presentations are <10% (23). A second limitation of the study is the source of time data. The time measurements were obtained from the patients, their relatives, and during the hospitalization period, from the attending physicians. There might be an accurate recall problem. However, as the same method was used in both registries, the effect on the comparison of the delays should be negligible. A third limitation is that the pandemic may have affected patient behavior when seeking medical care and, as in all observational studies, changes in patient characteristics may lead to a biased estimation of the outcome risk. Although the sensitivity analysis did not change the main results, we cannot completely exclude potential bias. A fourth limitation is the preference of PCI-capable centers for conducting the registries, which may have led to the low number of patients receiving fibrinolytic therapy. However, we deliberately selected the PCI-capable centers because these centers constitute the widespread practice in Turkey. We assumed that patients with MI were eventually admitted to these centers within 48 hours of symptom-onset. Finally, this study was conducted within a 2-week period 1 month after the detection of the first COVID-19 cases in Turkey. Therefore, the results may not be generalizable to other countries. However, the human response to disasters, such as fear of contracting with COVID-19 in the pandemic, is unique.

Conclusion

The TURKMI-2 study, as the largest, relevant nationwide registry, revealed that admissions of acute MI were almost halved during the pandemic compared with the pre-pandemic period. Time to treatment was significantly prolonged, largely due to patient-related delays during the pandemic period. Door-to-balloon time was not affected. Accordingly, the in-hospital MACE rate was increased significantly. Therefore, specific measures, such as increasing public awareness and establishing COVID-free hospitals, may reduce the fear of acquiring infection and mitigate the potential complications of acute MI during the pandemic.

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