

Original Article



Twelve-Year History of STEMI Management in Tehran Heart Center: Concomitant Reduction of In-Hospital Mortality and Hospitalization Length

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Abstract

Background: Cardiovascular-related death remains the major cause of mortality in Iran despite significant improvements in its care. In the present study, we report the in-hospital mortality, hospitalization length, and treatment methods for patients with ST-elevation myocardial infarction (STEMI) in Tehran Heart Center (THC).

Methods: Records pertaining to patients with STEMI from March 2006 to March 2017 were extracted from the databases of THC. Besides a description of temporal trends, multivariable regression analysis was used to find factors associated with in-hospital mortality.

Results: During the study period, 8,295 patients were admitted with STEMI with a mean age of 60.4 ± 12.5 years. Men accounted for 77.5% of the study population. Hospitalization length declined from 8.4 to 5.2 days, and in-hospital mortality was reduced from 8.0% to 3.9% (both P values < 0.001). In a multivariable model adjusted for age, sex, conventional cardiac risk factors, prior cardiac history, and indices of event severity, primary percutaneous coronary intervention (PCI) (OR: 0.280, 95% CI: 0.186 to 0.512; $P < 0.001$), coronary artery bypass graft (CABG) surgery (OR: 0.482, 95% CI: 0.220 to 0.903; $P = 0.025$), and rescue or facilitated PCI (OR: 0.420, 95% CI: 0.071 to 0.812; $P = 0.001$) were all associated with reduced in-hospital mortality in comparison with medical treatment. Furthermore, primary PCI was a crucial protective factor against prolonged length of hospital stay (OR: 0.307, 95% CI: 0.266 to 0.594; $P < 0.001$).

Conclusion: In-hospital mortality and hospitalization length were almost halved during the study period, and primary PCI has now replaced thrombolysis in the management of STEMI.

Keywords: Coronary artery disease, Fibrinolytic agents, Hospital mortality, Percutaneous coronary intervention, Reperfusion; ST-elevation myocardial infarction

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Introduction

Cardiovascular death remains the major cause of death in Iran^{1,2} and one of the cardinal issues in policymaking.³ ST-elevation myocardial infarction (STEMI) management is one of the key components of acute cardiovascular care. Given its high burden, many operational and research plans are currently performed in this field.^{4,7} Developed countries have devised a comprehensive program for the management of patients with STEMI, resulting in successful replacement of thrombolytic drugs with primary percutaneous coronary intervention (P-PCI).^{8,9}

A comprehensive STEMI management program has been commenced in Iran recently. This national program aims to provide P-PCI all around the country in a well-coordinated geographic coverage in a 24/7 fashion. All aspects of STEMI management including dispatch center, on-site electrocardiogram (ECG), electronic ECG transfer

system, transportation plan, and P-PCI team activation before the ambulance arrival are incorporated in this program. However, reports are still lacking on the success of this program.

In the present study, we report the frequency and temporal trend of STEMI patients, as well as its annual distribution, in-hospital mortality, hospitalization length, and treatment methods between March 2006 and March 2017 in Tehran Heart Center (THC).

Materials and Methods

Study Design

The present study enrolled patients admitted into THC between March 2006 and March 2017 with STEMI diagnosis, whether or not they were initially admitted into THC or were transferred from another center. For each admitted patient, questionnaires comprising detailed

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information on demographic characteristics, risk factors, past medical history, paraclinical findings, ischemic heart disease presentation, and treatment were filled in by well-trained nurses. The obtained data, in combination with follow-up information and additional electronic health records, were combined to set up the ischemic heart disease databank of THC, which presently contains data on more than 120 000 patients.

Definitions

STEMI was defined as the presence of more than a 1-mm ST-segment elevation in two contiguous ECG leads persisting for more than 20 minutes and accompanied by acute symptoms. Along with self-reports about previously diagnosed diseases necessitating medical treatment, diabetes mellitus was defined as a fasting blood glucose level of 126 mg/dL or greater and/or an HbA1C level of greater than 7% mmol/mol. Hypertension was defined as the current consumption of antihypertensive drugs or at least two blood pressure measurements of 140/90 mm Hg or greater after the acute phase. Dyslipidemia was defined as a high-density lipoprotein cholesterol level of less than 40 mg/dL in men and less than 50 mg/dL in women, a triglyceride level of greater than 150 mg/dL, and a total cholesterol level of more than 200 mg/dL. Chronic kidney disease was defined as a glomerular filtration rate of less than 60 mL/min. Peripheral artery disease was defined as an ankle-brachial index of less than 0.9 or previous revascularization of peripheral arteries. Patients who left the hospital alive were considered the discharged group and those who died during hospitalization were considered the deceased group. For the discharged group, hospitalization length was calculated by subtracting the admission date from the discharge date; and for the deceased group, the expiration date was considered the end of hospitalization. STEMI complications were considered to be ventricular septal defects, free wall rupture and tamponade, advanced atrioventricular block (second or third degree), acute mitral regurgitation, and ventricular tachycardia/fibrillation. A current smoker was defined as a patient having ever smoked more than 100 cigarettes with a concomitant history of smoking over the preceding month. A family history of early coronary artery disease (CAD) was defined as diagnosed CAD in first-degree relatives before 55 in men and 65 in women.

The patients were divided into five groups based on the reperfusion strategy adopted for them: 1) the medical treatment group: if no reperfusion strategy was used in the first 24 hours following STEMI; 2) the thrombolytic group: if a thrombolytic agent was used as the first treatment and there was no PCI during the first 24-hour post STEMI period; 3) the rescue or facilitated (R/F) PCI group: if PCI was performed in patient who had received thrombolytic within 24 hours after STEMI; 4) the P-PCI group: if P-PCI was performed as the initial strategy

for reperfusion; and 5) the coronary artery bypass graft (CABG) group: if this surgical modality constituted the initial strategy for reperfusion.

Statistical Analysis

The dichotomous variables were presented as numbers (percentages) and the continuous variables as mean \pm the standard deviation for those with normal distributions, and as median (interquartile ranges [IQRs]) for those without normal distributions. Group comparisons for the categorical and continuous variables were performed using the χ^2 test, the Mann–Whitney test, or the *t*-test, as appropriate. A *P* value of less than 0.05 was considered statistically significant. Logistic regression was applied to calculate the crude and adjusted effects of each variable on the outcome of interest. Hospitalization length was expressed as both the median (IQRs) and the 5% trimmed mean with relatively equal manners and identical results. In a further multiple regression analysis, the cutoff point of 5 days (overall median) was used to differentiate between prolonged and short hospitalization lengths. All variables were tested in univariate analysis and those with a *P* value of less than 0.2 were included in the final multivariate binary logistic regression. Enter and backward stepwise methods in the regression were utilized to find adjusted significant associations. The final step is shown to avoid data overload.

Results

From 2006 to 2017, a total of 8295 patients were hospitalized in THC with a STEMI diagnosis. The mean age of the study population was 60.4 ± 12.5 years, and men represented 77.5% of the entire study subjects. The basic demographic and clinical features of all the patients are presented in Table 1. As shown in Figure 1, the biannual number of the admitted patients during these years increased from 1,214 in the period of 2006–2008 to 1,506 in the period of 2015–2017 ($P = 0.018$). Despite some differences between various months of the year, there was no statistically significant difference in the number of hospitalization cases per month ($P = 0.342$). Almost half of the patients (48.7%) had arrived between 9 am to 4 pm (an 8-hour period), while the rest of them (51.3%) had arrived between 5 pm and 8 am (a 16-hour period).

Of the 8,295 patients, 7,852 (94.6%) patients were discharged and 443 (5.4%) died in the hospital. As demonstrated in Table 1, the comparison between the expired patients and the discharged patients using the univariate analysis indicated that the deceased patients were older (69.5 ± 12.1 years vs 59.9 ± 12.4 years; $P < 0.001$), more frequently hypertensive (54.1% vs 42.8%; $P < 0.001$), and more frequently diabetic (42.1% vs 29.4%; $P < 0.001$). While 77.0% of the deceased group did not receive any reperfusion treatment, only 6.7% in the discharged group did not receive it ($P < 0.001$).

Table 1. Baseline Clinical Characteristics of the Study Population (N = 8295)

	Discharged (n = 7852)	Deceased (n = 443)	Total (n = 8295)	P*
Age (y)	59.9 ± 12.4	69.5 ± 12.1	60.4 ± 12.5	<0.001
Men	78.2% (6140)	65.9% (292)	77.5% (6432)	<0.001
Hypertension	42.8% (3361)	54.1% (240)	43.4% (3601)	<0.001
Diabetes	29.4% (2308)	42.1% (187)	30.1% (2495)	<0.001
Hyperlipidemia	39.4% (3094)	37.5% (166)	39.3% (3260)	0.435
Family history of CAD	11.8% (927)	3.3% (15)	11.4% (942)	<0.001
Smoking				
Current	35.5% (2787)	21.4% (95)	34.7% (2882)	<0.001
Former	8.2% (644)	4.8% (21)	8.0% (665)	0.021
Opium				
Current	12.5% (982)	8.8% (39)	12.4% (1021)	0.032
Former	2.2% (173)	0.7% (3)	2.1% (176)	0.018
Hospitalization length	6 (4–8)	3 (1–7)	5 (4–8)	<0.001
History of				
CABG	5.0% (393)	5.7% (25)	5.1% (418)	0.553
CHF	1.6% (126)	8.0% (35)	1.9% (161)	<0.001
PAD	0.6% (47)	0.9% (4)	0.6% (51)	0.374
CKD	2.7% (212)	13.9% (62)	3.3% (274)	<0.001
COPD	1.2% (94)	1.4% (6)	1.2% (100)	0.780
Ejection fraction (%)	40.5 ± 9.5	28.9 ± 10.7	39.9 ± 9.84	<0.001
Complication				
VSD	0.1% (8)	2.3% (10)	0.2% (18)	<0.001
VT/VF	2.0% (157)	30.5% (135)	3.5% (292)	<0.001
AV block	0.8% (63)	4.5% (20)	1.0% (83)	<0.001
Treatment				
Medical treatment	6.7% (526)	77.0% (341)	10.5% (867)	<0.001
Thrombolytic	38.5% (3023)	3.2% (14)	36.6% (3037)	<0.001
R/F PCI	22.2% (1743)	3.4% (15)	21.2% (1758)	<0.001
Primary PCI	28.8% (2261)	14.0% (62)	28.0% (2323)	<0.001
CABG	3.8% (298)	2.4% (10)	3.7% (308)	0.098

AV, Atrioventricular; CABG, Coronary artery bypass graft; CAD, Coronary artery disease; CHF, Congestive heart failure; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; PAD, Peripheral artery disease; PCI, Percutaneous coronary intervention; R/F, Rescue or facilitated; VSD, Ventricular septal defect; VT/VF, Ventricular tachycardia/fibrillation. * *P* value of univariate analysis by adjusted χ^2 for the categorical parameters or the Student *t*-test for the continuous variables.

During the mentioned period, along with a decline in the mean length of hospital stay (from 8.4 to 5.2 days; *P* <0.001), in-hospital mortality also decreased significantly (from 8.0% to 3.9%). The age-stratified plots of in-hospital mortality and hospital stay are illustrated in Figures 2 and 3, respectively. The temporal trend of the treatment strategies is presented in Figure 4. Twelve years prior to the writing of this article, pharmacologic thrombolysis was the main reperfusion strategy in the majority of cases insofar as 72.3% of the cases received this treatment and only 7.2% cases underwent P-PCI. The period of 2006–2017 witnessed a significant reduction in thrombolytic use (declined to 16.5%) and a rise in P-PCI (up to 58.6%, *P* for trend <0.001). It should be noted that the 24/7 P-PCI strategy in accordance with the 24/7 national program was established in THC in September 2015, since which time

all patients with STEMI having arrived at our center in a timely fashion have been treated with P-PCI. Accordingly, all the patients who received thrombolytic treatment after this time were those initially treated in another center before referral to THC.

In the multivariable binary logistic regression model, in comparison with medical treatment, P-PCI (OR: 0.280, 95% CI: 0.186 to 0.512; *P* <0.001), CABG (OR: 0.482, 95% CI: 0.220 to 0.903; *P* = 0.025), and R/F PCI (OR: 0.420, 95% CI: 0.071 to 0.812; *P* <0.001) were associated with reduced in-hospital mortality. All other statistically significant variables and a complete list of variables included in the model are presented in Table 2. Furthermore, primary PCI was a crucial protective factor against prolonged length of hospital stay (OR: 0.307, 95% CI: 0.266 to 0.594; *P* <0.001).

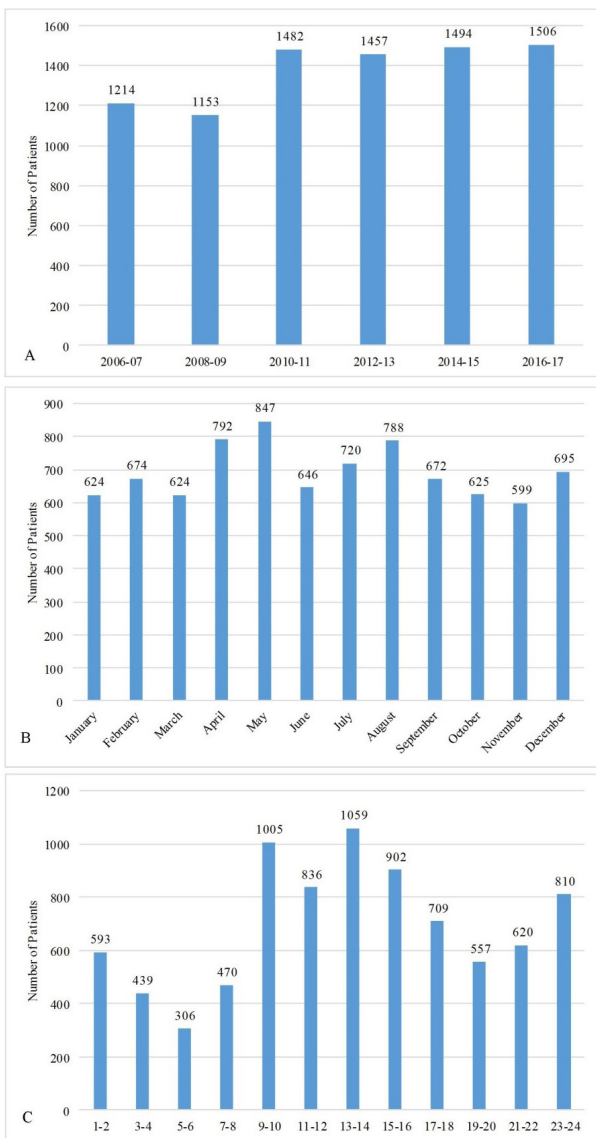


Figure 1. A) Biannual, B) Monthly, and C) Daily Distributions of Patients with STEMI from 2006 to 2017.

Discussion

By studying 8,295 patients with STEMI hospitalized in THC between March 2006 and March 2017, we presented the annual number of such patients and their time distribution. This time period saw a concomitant decline in terms of in-hospital mortality (from 8.0% to 3.9%) and hospitalization length (from 8.40 days to 5.26 days). Most of the observed improvements could be attributed to the increase in the utilization of P-PCI as the main reperfusion strategy.

STEMI: A Hot Spot for Intervention

Many studies have shown that patients with STEMI benefit from cardiovascular intervention more than other patients. Given the current controversy surrounding the role of PCI in stable ischemic heart disease even for symptom relief (10), P-PCI in patients with STEMI confers survival benefits even for patients older than 80 years.^{11,12} Thus, all statistics regarding these patients are of great import and any positive intervention that results in the improvement of care for these patients would directly affect cardiovascular mortality.

Time Distribution

There is currently a dearth of accurate information on the incidence of acute MI and specifically STEMI and the temporal trend thereof in the Iranian population.^{13,14} During the study period, 8,295 patients with STEMI were hospitalized in THC. The number of patients with STEMI showed an increase over these years; nonetheless, this upturn cannot be necessarily interpreted as a rise in the incidence or prevalence of STEMI because total admission in our center also exhibited an increase over this period. Apropos of STEMI occurrence, seasonal variation with a peak in winter and a nadir in summer^{15,16} and the circadian

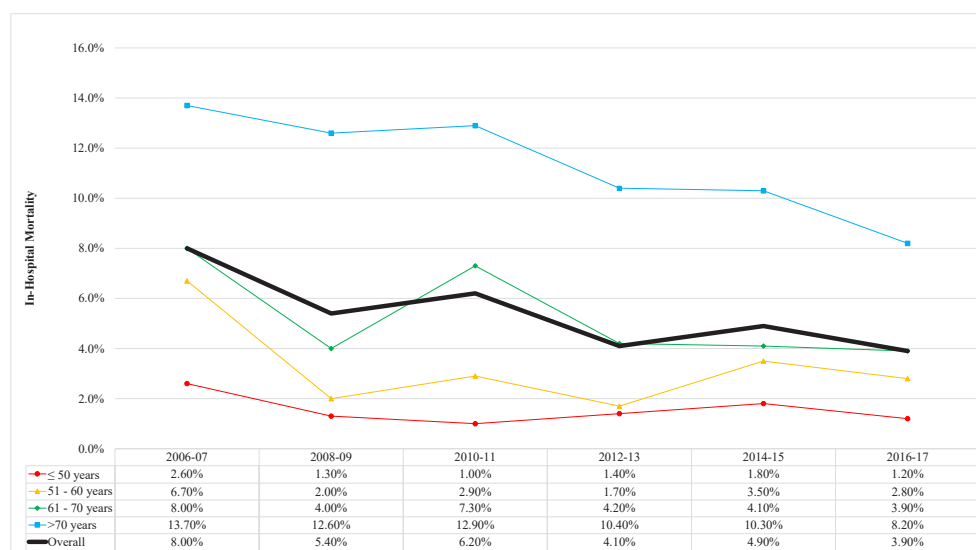


Figure 2. In-Hospital Mortality Trend of Patients with STEMI in Tehran Heart Center from 2006 to 2017 Based on Age. *P* values for trends pertaining to various age categories: age >70 : <0.001, age of 61–70: 0.042, age of 51–60: 0.037, age of <50: 0.041. *P*-value for the overall trend was also significant (*P* < 0.001).

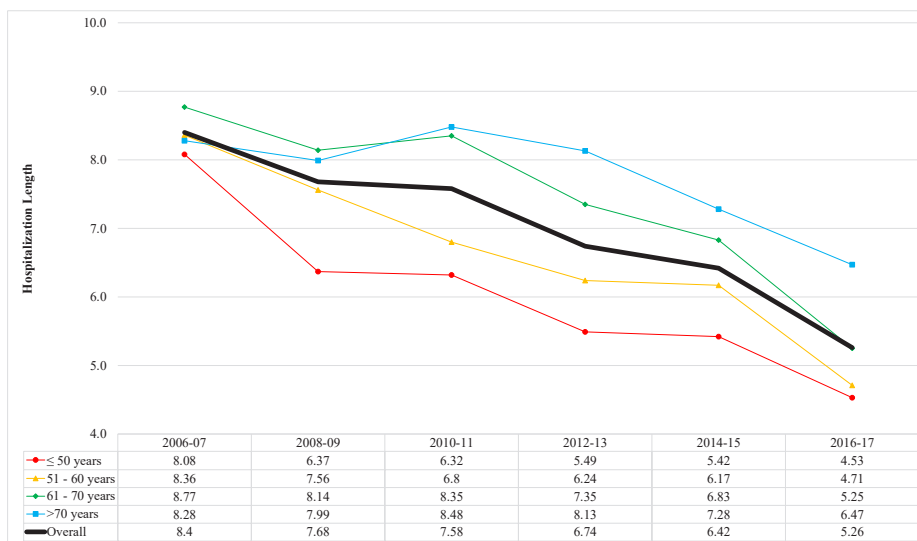


Figure 3. Mean Length of Hospitalization (in Days) Pertaining to Patients with STEMI in Tehran Heart Center from 2006 to 2017 Based on Age. A 5% trimmed mean was shown in this graph, which was substantially close to median values. All P-values for trends were < 0.001.

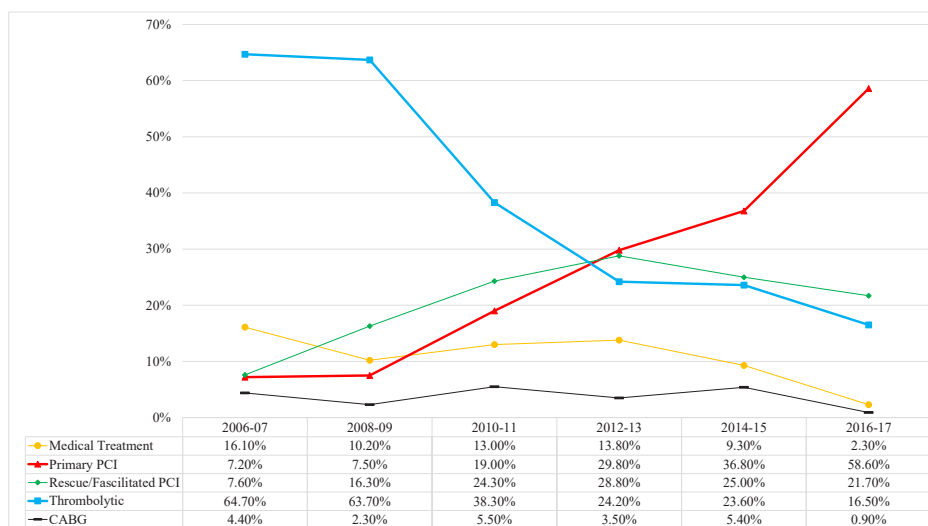


Figure 4. Different Treatment Strategies for Patients with STEMI in Tehran Heart Center from 2006 to 2017. Except for CABG ($P > 0.05$), all other P values for trends were significant ($P < 0.001$). Abbreviation: CABG, Coronary artery bypass graft; PCI, Percutaneous coronary intervention.

rhythm with a morning peak have been propounded. Mogabgab et al reported a higher incidence of STEMI between 10 am and 2 pm¹⁷ and Kanth et al reported 11 am as the peak time for STEMI incidence.¹⁸ At first glance, our results appear to be completely similar to these studies inasmuch as most of our admissions occurred between 9 am and 4 pm. It is worthy of note, nevertheless, that whereas the aforementioned studies reported the time of chest pain onset, we reported the time of arrival at the hospital. Considering a mean time period of 4 hours as a prehospital delay in Iranian patients with STEMI in the P-PCI era⁶ could be helpful to interpret this finding.

Reperfusion Strategies

Over these years, P-PCI has shown its efficacy, in comparison with pharmacologic thrombolysis, as the

treatment of choice for patients with STEMI by reducing mortality, complications,¹⁹⁻²¹ and hospitalization length.²² P-PCI was a treatment strategy in THC even before the initiation of the 24/7 national program. In September 2015, under the aegis of the Iranian Ministry of Health and Medical Education, the 24/7 national program was launched to provide P-PCI 24/7 in designated hospitals. Currently, any patient with STEMI referring to THC at any hour and on any day is treated by P-PCI. A recent study reported a median of the-door-to-device time of 55 minutes (IQR: 40–82) in 2016, which was reduced to 46 minutes (IQR: 34–70) in 2017.⁴ Once again, it is deserving of note that the rate of 16.5% for thrombolytic administration in our study represents patients initially treated in another center before referral to THC.

Table 2. Multivariate Logistic Regression Analysis for the Prediction of In-Hospital Mortality and Prolonged Hospitalization

	In-Hospital Mortality	<i>p</i> *	Prolonged Hospitalization (> 5 d)	<i>p</i> *
	OR (95% CI)		OR (95% CI)	
Treatment strategy				
Medical treatment	Ref.	NA	Ref.	NA
Primary PCI	0.280 (0.186–0.512)	<0.001	0.307 (0.266–0.594)	<0.001
CABG	0.482 (0.220–0.903)	0.025	-	-
R/F PCI	0.420 (0.071–0.812)	0.001	-	-
Thrombolytic	0.871 (0.171–1.213)	0.120	-	-
Age (per 1 year's increase)	1.062 (1.021–1.086)	<0.001	1.029 (1.022–1.035)	<0.001
Gender (men vs. women)	0.538 (0.287–0.948)	0.022	1.432 (1.203–1.703)	<0.001
Opium use	1.863 (1.126–4.462)	0.018	1.146 (0.970–1.354)	0.101
Diabetes mellitus	2.611 (1.508–4.910)	<0.001	1.365 (1.174–1.588)	<0.001
Creatinine (per 0.1 mg/dL increase)	1.363 (1.125–1.812)	0.002	1.239 (1.021–1.502)	0.030
Pulmonary edema	6.085 (1.043–8.071)	0.002	2.013 (0.793–13.823)	0.173
VT/VF	8.403 (2.062–17.466)	<0.001	2.256 (1.304–3.902)	0.004
VSD	3.316 (1.280–6.711)	<0.001	1.156 (0.686–7.179)	0.181

AV, Atrioventricular; CABG, Coronary artery bypass graft; CAD, Coronary artery disease; CHF, Congestive heart failure; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; OR, Odds ratio; PAD, Peripheral artery disease; PCI, Percutaneous coronary intervention; R/F, Rescue or facilitated; VSD, Ventricular septal defect; VT/VF, Ventricular tachycardia/fibrillation.

In addition to variables brought in the table, the multivariable model is also adjusted for hypertension, smoking, hyperlipidemia, prior angina, prior myocardial infarction, prior peripheral artery disease, prior stroke, left ventricular ejection fraction, underlying valvular disease, post infarction mitral regurgitation, post infarction atrial fibrillation, post infarction conductive block, and troponin level at the presentation. Only variables that showed a statistical significance with at least one of the outcomes of interest were brought in the table.

In-Hospital Mortality and Hospitalization Length

There are only a few reports regarding the in-hospital mortality of patients with STEMI in Iran. In a study conducted by Ghadimi et al in 2006, the in-hospital mortality rate was reported as high as 15.1% at Shariati Hospital, Tehran, Iran.²³ A more recent study by Ahmadi et al., conducted in 2012 on the pooled data of 20,750 patients with STEMI from 31 provinces of Iran, showed a 12.1% rate of in-hospital mortality.²⁴ With respect to in-hospital mortality among patients with STEMI in developed countries, rates of 5.1% in 2014 in Belgium and 5.5% in 2016 in Switzerland were reported.^{25,26} With less than 5% in-hospital mortality in the past 6 years, the status of THC is more favorable than the rate in other hospitals of Iran and comparable with or even better than that in developed countries.

Hospitalization length has experienced a similar trend, as well. The length of hospital stay has garnered a great deal of attention in recent years, so that now, in tandem with the door-to-device time, the device-to-door time (which denotes hospitalization length) is deemed a measure of the quality control of hospitals.²⁷ Research on the safety of early discharge of patients with STEMI has resulted in the inclusion of early discharge in guidelines.²⁸⁻³⁰ Regrettably, there is no report about STEMI and hospitalization length in Iran. In developed countries, the length of hospital stay was 6.5 days in Belgium in 2010³¹ and 7.2 days in the United States in 1995, which was lessened to 5.0 days in 2005.³² However, recent evidence showed a higher rate of

adverse events in patients with STEMI discharged before 3 days, so the length of admission in the following years did not decrease further.³³ Our result is comparable with these reports from developed countries.

Re-proof of the benefits of reperfusion strategies or adverse effects of previously well-studied variables associated with in-hospital mortality like age or mechanical complications of STEMI were not our main interest in this manuscript. However, the statistically significant association of opium abuse with in-hospital mortality in the multivariable-adjusted model, while smoking lost its significance, is quite interesting. A growing body of evidence recently shows both long-term and short-term increases in cardiovascular mortality related to opium consumption³⁴⁻³⁷ that merits further consideration.

Limitations

Since the design of this research was retrospective and non-randomized, there were multiple limitations pertaining to potential missing data, the heterogeneity of baseline properties, and follow-up records. Furthermore, we encountered a considerable lack of accurate data regarding the records of the patients that were referred to THC from other medical centers. The short-term mortality and morbidity risk of CABG are substantially different from those of medical treatment or PCI. Another crucial problem is the impact of changing facilities, techniques, medications, protocols, patients' awareness and compliance, and treatment guidelines as well as the

growing expertise of P-PCI operators over a long period.

Conclusion

In conclusion, from 2006 to 2017, a total of 8295 patients with STEMI were admitted into THC. Half of the admissions were recorded between 9 AM and 4 PM. In-hospital mortality and hospitalization length were almost halved in these years, and now P-PCI has completely replaced thrombolysis in the management of STEMI. A drastic rise in the use of P-PCI (from 7.2% to 58.6%) and a concomitant decline in fibrinolytic-based reperfusion (from 64.7% to 16.5%) were eminent over this period. P-PCI, CABG, and even delayed PCI reduced mortality rates substantially when compared with medical treatment only. Still, the thrombolytic strategy was not associated with decreased in-hospital mortality after multiple adjustments. Further, P-PCI conferred remarkable protection against prolonged hospital stay. Indeed, the superiority of P-PCI over the other modalities lay in its ability to not only decrease short-term mortality but also to lower the likelihood of prolonged hospital stay.

Authors' Contribution

Study concept and design: SSe, GB, ON, SSa, GS, MSH, SM, PH. Acquisition, analysis, or interpretation of data: SSe, GS, GB, ON, MSH. Statistical analysis: SSe, GS, MSH. Drafting of the manuscript: SSe, GS, HK, GB, MSH. Critical revision of the manuscript for important intellectual content: SSe, GB, GS, SSa, ON, PH, SM, AM, KSE, AH.

Conflict of Interest Disclosures

The authors declare no conflict of interest.

Ethical Statement

This study was approved by the Tehran Heart Center Institutional Review Boards and all methods were performed in accordance to the guidelines. All patients were adult with active authorization and informed consent for use of their medical records for research.

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