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The Outcome of Smoker Patients with ST-Elevation Myocardial Infarction(STEMI) Undergone Primary Percutaneous Coronary Intervention(P-PCI) Versus Thrombolytic Therapy

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ABSTRACT

Background: Coronary artery disease is the leading cause of cardiac diseases in Iran. It usually happens in people aged the 70s, but nowadays, the prevalence of cardiac events has risen upin middle-aged people.This study aims to compare the mortality rate, re-hospitalization, and ejection fraction (EF)of smoker patients who have undergone P-PCI with those who received thrombolytic therapy.

Methods: The study group consisted of 42 smoker patients referred to the hospitals with the diagnosis ofSTEMIand have undergone P-PCI or thrombolytic therapy. Complications such as death and re-hospitalization were noted, and the EFof each patient was recorded.

Results: The Independent Samples t-test showed no significantdifference between two groups of PCI and thrombolytic therapy regarding EFat the time of admission. Also,there was no considerableEF difference after three months of follow-up between 2 groups in bothsmoker and ex-smoker ones ($P>0.05$). The paired samplet-test showed no significant difference between EF at the time of admission and after three months in the ex-smoker group, but there was a considerable difference in the smoker group ($P<0.05$). The three-monthmortality rate was estimatedat 23.1% in smokers with PCI and 7.1% in patients treated with thrombolytic therapy.

Conclusion: Thrombolytic therapy can increase the EF of smoker patients with STEMI for a long time, indicating a beneficial effect of thrombolytic therapy to prevent heart failure.

Keywords: Smokers, ST-Elevation Myocardial Infarction, Percutaneous Coronary Intervention, Cardiovascular Disease, Thrombolytic Therapy

INTRODUCTION

Cardiovascular diseases are the most common cause of death in many countries, especially in Iran(1). Coronary artery disease (CAD) is the leading cause of cardiac diseases in Iran. It usually

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happens in people aged the 70s, but nowadays, the prevalence of cardiac events has risen up to 45% in middle-aged people (aged 40s and 50s) (2).

ST-Elevation Myocardial Infarction (STEMI) is a severe type of heart attack during which one of the heart'smain arteries isoccluded. The ST-segment elevation is an abnormality detected on the 12-lead ECG.This sudden disturbance in blood flow can be due to an obstructing thrombosis caused by erosion, fissuring, or dissection.Platelet gathering can form a thrombus in the vessel and thus cause stenosis(3,4).Sometimes it can block blood flow completely(5,6). The pain usually occurs when myocardial demand for oxygen increases and blood flow is insufficient for this demand(7).Diagnosis of STEMI in the very first stages is crucial because delayed diagnosis and subsequently delayed reperfusion results in higher mortality(8).

Smoking is one of the most critical factors in developing cardiovascular disease, and according to some studies, it is the leading risk factor for myocardial infarction. MI is usually caused by atherosclerotic plaques, and smoking makes these plaques more susceptible to thrombosis (9,10).It has been proven that smokers have a significantly higher risk of having another infraction that may result in heart failure or even death. Also, their STEMI onset is ten years earlier in comparison to non-smokers. In addition, in patients with STEMI, the most common adjustable risk factor is cigarette Smoking,and despite all concerns and warnings,it remains the major cause of preventable death (10,11).In both STEMI and NSTEMI groups, the risk of a recurring cardiac event during the first year after MI in smoker patients was higher than non-smoker patients, and quitting smoking after MI can have a significant role in decreasing cardiovascular mortality (12,13). In addition, history of hypertension and diabetes are the most critical risk factors for occurring STEMI in smoker patients.

Several medications are used for the treatment of myocardial infarction (MI). To name some, there arebeta-blockers, statins, aspirin, P2Y inhibitor,and nitroglycerin(14).Antiplatelet medication choice can be affected by the previous percutaneous coronary intervention (PCI) or fibrinolytic treatments. According to recent trials, ticagrelor and prasugrel are shown superior to clopidogrel and are preferred in patients with a history of PCI, (15,16)but clopidogrel should be prescribed in patients who are undergoing fibrinolytic therapy(17). Sometimes the plaque ruptures, and the diagnosis of STEMI ismade by ECG changing and troponin rising,and symptoms cannot be controlled with medications.The golden time to performPCI in PCI-capable hospitals is 90 minutes, or if not, the patient should be transferred to a PCI-capable hospital in 120 minutes(18).Thrombolytic therapy should be started for the patient in the first 30 minutes of patient's presentation in the hospital if PCI is unavailable within 120 minutes of first medical contact(19). Most patients who die from STEMI usually expire shortly after MI and before getting to the hospital (20). The goal of thrombolytic therapy is to remove life-threatening clots in blood vessels, facilitate blood flow, and protect the tissues and organs from being damaged. Thrombolysis can be performed by injecting clot-dissolving drugs using an intravenous (IV) line or a long catheter to deliver the thrombolytic agent to the blockage site. The clot can also be removed or broken physically using a long catheter with an attached mechanical device to the catheter’stip (19). Indication for thrombolytic therapy in emergenciesdissolves clots in the heart, brain, and lungs (21). PCI is a non-surgical procedure that involves a combination of angioplasty with stenting and is used to treat narrowing of the heart's coronary arteries. In this procedure, femoral or arterial arteries are used to access the bloodstream. Then X-ray imaging is used to determine the path of coronary arteries and the exact site of the blockage. After that, a coronary angioplasty can be done to relieve the narrowing of coronary arteries using balloon catheters or keep them open using stents. CABG (coronary artery bypass grafting) involves replacing the

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stenotic arteries with harvested vessels from elsewhere in the body. PCI can be an alternative to CABG, but in some instances, CABG may be superior (22,23).

To evaluate the cardiac performance,usually,Ejection fraction (EF) and stroke volume (SV)are measured in emergency rooms or cardiac care unit (CCU). However, SV and EF do not always change in parallel and are affected differently by changes in cardiac load(24).

EF is defined as the percentage of the ejected blood to diastolic volume during ventricular contraction. Echocardiography is used to determine EF in the CCU, which usually is about 55% for LV(24). In patients with acute STEMI who have undergone P-PCI and thrombolysis, the objective is to enhance the blood flow to ischemic sites andpreservethe quality and quantity of the patient's life (25).

Previous studies have released controversial results. Some of them demonstrated no significant difference in mortality rate and re-hospitalization of patients who underwent PCI with those who received thrombolytic therapy (26–28).However, according to long-term outcomes, some studies showthat PCI is superior to thrombolytic therapy (29).Another study reports that in patients older than 65 years, TT and P-PCI had similarresults. According to this study, one-year mortality in patients who had undergone TT was more,but it was not statistically meaningful(8). Asadpour-Piranfaret al. (2021) compared 3-month outcomes between P-PCI and TT in 43 patients and concluded that the effects of these two methods were not significantly different (30).To determine the prognosis in patients with STEMI, left ventricular ejection fraction (LVEF) is a reliable predictor of clinical outcomes; therefore, we aimedto compare the mortality rate, re-hospitalization,and ejection fraction of smoker patients who underwent PCI with those who receivedthrombolytic therapy in Ayatollah Taleghaniand Labbafinejadhospitals ofShahid Beheshti University of Medical Sciences, Tehran City, Iran, in autumn2018.

METHODS

This cross-sectional study was done inAyatollah Taleghani and Labbafinejad hospitals. The institutional Human Subjects Review Board approved the study protocol, and all patients signed informed consent. The study group consisted of 42 cigarette smoker patients referred to the hospitals with the diagnosis of STEMIfrom September 2018 to December2018.

During the present study,at first, 66 patients were admitted to hospitals with STEMI,ofwhom 54 patients were smokers and ex-smokers. Out of 54 smoker and ex-smoker patients admitted with STEMI, eight patients passed away in the next three months, and four patients refused to cooperate. Among the patients who passed away,six patients had undergone PCI, and two patients had undergone treatment with thrombolytic therapy. Eventually, 42 patients were included in the study (Figure 1).

The includedpatients had a history of cigarette smoking or were smokers at the time. If they had a particularpast medical history, they should not have contraindications for thrombolytic therapy. They should also have had acute myocardial infarction symptoms, accompanied by an ECG with ST-segment elevation of more than 1 mm (0.1 mV) in two or more contiguous leads (STEMI). The other inclusion criteria were completing the follow-up sessions and undergoing echocardiography in the 3-month follow-up.The patients who received other treatments than P-PCI, thrombolytic therapy, or both, were excluded from the present study.

The stages of this study were explained to the patients.After signing an informed consent form, a doctor filled out a questionnaire, including the baseline information, demographic characteristics (age, sex), past medical history, family history, smoking history, and pack-year.

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After evaluating patients' ECG and other medical records, the type of MI and its features were recorded, and the first day EF at the time of admissionwas measured by echocardiography.
Given that the medical facilities in the two hospitals were different, the patients who were presented to the Labbafinejad hospital received thrombolytic therapy, and those who were presented to the Taleghani hospital underwent P-PCI. After discharging the patients, they were asked to return for a 3-month follow-up to perform echocardiography. They were also asked to return to the hospital if any side effects occurred, specially bleeding. At their 3-month follow-up, the echocardiography and the examination were performed again by the same doctor using the same equipment, and complications such as death and re-hospitalization were also noted.
The statistical analyses were performed using SPSS version 25. Comparisons were made using the Independent Samplest-test and paired sample t-test. The Chi-square test was used to compare the categorical parameters. Statistical significance was considered at $P<0.05$.

RESULTS

In this study, 42 smoker patients completed all stages of this study, of which 41 were male (97.62%), and 1 was female (2.38%). The most common risk factors were hypertension (45.24%), diabetes (42.86%), and family history of ischemic heart disease (21.42%), which are shown separately or in combination with other factors in Table 1.
According to the angiographic records of patients, simultaneous involvement of left anterior descending (LAD) and right coronary artery (RCA) vessels with a frequency of 17 cases (40.47%) were the most commonly involved vessels. After that, LAD artery involvement and simultaneous involvement of LAD, RCA, and left circumflex artery (LCX) were the most frequently involved vessels with a frequency of 9 cases (21.43%). The number of patients with RCA involvement was 7 (16.67%).
Since admission time after the onset of MI symptoms is crucial for making treatment decisions, the duration is taken to get the patient into the hospital after the symptoms are summarized in Table 1. As this Table shows,most patients were admitted after one hour, and only 7.14% of them were admitted in the golden time of 30 minutes.
24 patients were admitted to a hospital not capable of performing PCI from the whole study sample. Of them, 8cases (33.33%) received thrombolytic therapy in less than 30 minutes, and 16 patients (66.67%) got the treatment after 30 minutes of arrival. Also, 18 patients were admitted to a hospital capable of PCI, the time of door-to-balloon for 5 of them (27.78%) was less than 90 minutes, and for 13 of them (72.22%) was more than 90 minutes (Table 1).

Table 1. Demographic and clinical characteristics and recorded time frames for the onset of MI symptoms to patient response and door-to-balloon and door-to-needle of the patients**.**

			Absolute frequency	**Percentage**
Demographic and clinical characteristics	Sex	Male	41	97.62
		Female	1	2.38
	Age	≤50	12	28.57
		>50	30	71.43
		Mean: 54.90 ±8.93		
	Risk factors	Hypertension	9	21.43
		Diabetes	8	19.05
		Dyslipidemia	6	14.29

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				Absolute frequency	**Percentage**
		Family history of ischemic heart disease		5	11.90
		Past MI history		2	4.76
		Hypertension +Diabetes		6	14.29
		Hypertension +Diabetes+Family history of Ischemic heart disease		3	7.14
		Hypertension +Diabetes+Family history of Ischemic heart disease+ Past MI history		1	2.38
		None		2	4.76
		Total		42	100.00
	Location of Culprit lesion	LAD		9	21.43
		RCA		7	16.67
		LAD+RCA		17	40.47
		LAD+RCA+LCX		9	21.43
		Total		42	100
	Vascular involvement	One Vessel		16	38.10
		Two Vessels		17	40.47
		Three Vessels		9	21.43
		Total		42	100
Recorded time frames for the onset of MI symptoms to patient response	Onset of MI to patient response	<30 minutes		3	7.14
		30 to 60 minutes		12	28.57
		>60 minutes		27	64.29
		Total		42	100
	Door to Balloon	PCI	≤90 minutes	5	27.78
			> 90 minutes	13	72.22
			Total	18	100
	Door to Needle	Thrombolytic Therapy	≤30 minutes	8	33.33
			> 30 minutes	16	66.67
			Total	24	100

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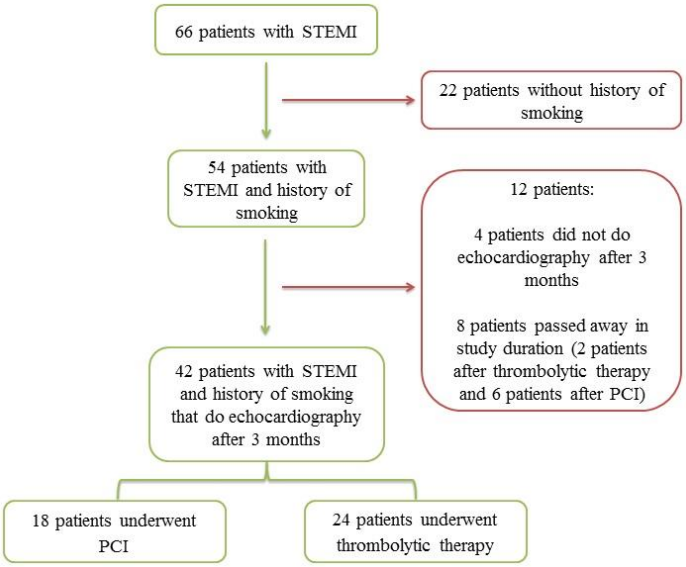

Figure 1. Participant recruitment flow diagram (STEMI, ST-Elevation Myocardial Infarction; PCI, Percutaneous Coronary Intervention)

To match the baseline characteristics, we used the Independent Samples t-testthat showed no significant difference of EF at the time of admission between two PCI and thrombolytic therapy groups.Also, there was no considerableEF differencebetween the two groups after three months of follow-upin both smoker and ex-smoker ones(Table 2).

Mean (SD) values of EF in smoker patients who underwent PCI were 41.56±9.95 at the time of admission and 45.00±10.52 after three months of follow-up. The paired sample t-test showed no significant difference between both groups regarding EF at the time of admission and after three months.Mean (SD) values of EF in smoker patients who underwent thrombolytic therapy were 40.26±8.73 at the time of admission and 48.53±5.80 after three months of follow-up (Figure 2). The paired sample t-test showed no significant difference between EF at the time of admission and after three months in the ex-smoker group, but there was a considerable difference in the smoker group (Table 2).

Table 2. The t-test to compare EF in two treatment groups and EF at the time of admission and after three months in two treatment groups

			Treatment	**Mean**	**SD**	**t**	**P-Value**
Independent Samples t-test	**Smokers**	EF1	PCI	41.56	9.95	0.411	0.683
			Thrombolytic Therapy	40.26	8.73		
		EF2	PCI	45.00	10.52	-1.154	0.262
			Thrombolytic Therapy	48.53	5.80		
		EF2-EF1	PCI	3.00	5.91	-1.804	0.081
			Thrombolytic Therapy	7.94	9.02		
	Ex-smoker	EF1	PCI	45.00	7.07	0.598	0.576
			Thrombolytic Therapy	41.00	8.21		

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		EF2	PCI	52.50	3.53	0.692	0.520
			Thrombolytic Therapy	49.00	6.51		
		EF2-EF1	PCI	7.50	5.91	-0.139	0.891
			Thrombolytic Therapy	8.00	9.02		
		Treatment	**EF**	**Mean**	**SD**	**t**	**P-Value**
Paired sample t-test	**Smokers**	PCI	EF1	41.56	9.95	-1.964	0.070
			EF2	45.00	10.52		
		Thrombolytic Therapy	EF1	40.26	8.73	-3.628	0.002
			EF2	48.53	5.80		
	Ex-smokers	PCI	EF1	45.00	7.07	-3.00	0.205
			EF2	52.50	3.53		
		Thrombolytic Therapy	EF1	41.00	8.21	-4.00	0.016
			EF2	49.00	6.52		

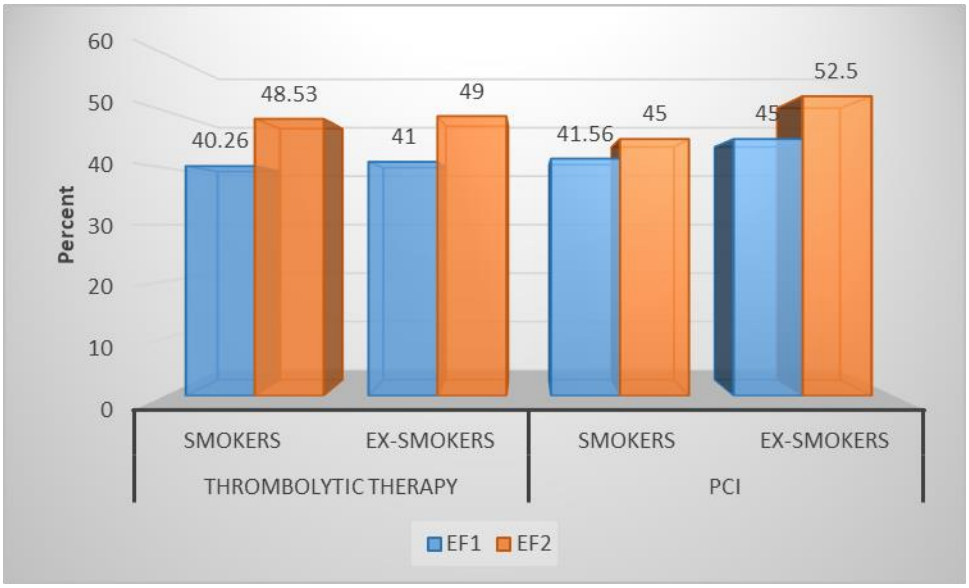

Figure 2. Ejection fraction at the time of admission and three months later in smoker patients and Ex-smoker patients

To measure MACE (Major Adverse Cardiac Events), we evaluated patients' mortality and re-hospitalization during three months of follow-up. The three-month mortality of patients who underwent PCI was 23.10% and 7.10% in those who received thrombolytic therapy. The Chi-square test showed no significant difference between the two groups. About 11.50% of smoker patients who underwent PCI were admitted to the hospital during three months of follow-up. None of those who received thrombolytic therapy had an experience of re-hospitalization in this period. Anyway, the Chi-square test showed no significant differencebetween the two groups (Table 3).

Table 3. Mortality rate and re-hospitalization of patients during three months

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		Frequency	Percentage	Chi-square	P-Value
Mortality during 3 months of follow up	PCI	6	23.10	2.712	0.100
	Thrombolytic Therapy	2	7.10		
Re-hospitalization during 3 months of follow up	PCI	3	11.50	3.421	0.064
	Thrombolytic Therapy	0	0.00		

DISCUSSION

According to the World Health Organization (WHO) report, ischemic heart disease (IHD) is responsible for 7.3 million people'sdeaths in the world with approximately 58 DALY (Disability Adjusted Life Years) global disease burden(31). In 2010, The American Heart Association announced that 15.4 million people in America were afflicted with IHD(32). Angina pectoris occurs when myocardial blood perfusion is inadequate and has two types: stable and unstable(33,34).Stable angina is caused by strenuous exercise or emotional stress and has no rest symptom; it usually responds to drugs. But in some instanceswith excessive stenosis or patients not responding to medication, revascularization is the best treatment (33). Revascularization aims to relievepatients' symptoms and quality of life, and long-term survival. Percutaneous Coronary Intervention (PCI) is a type of revascularization that has been used for more than 20 years (35). Based on studies, stent use in patients with acute coronary syndrome reduces morbidity and mortality of myocardial infarction, almost 5% more than medication only(36,37). In general, stent application removes balloon angioplasty limitations,reduces complications, and improves cardiovascular outcomes. Despite the clinical benefit of the stent, there are some unwanted outcomes like plaque rupture and emboli formation (38,39).

According to literature, myocardial infarction and subsequent morbidity and mortality are more common in elderly patients, and in these patients, P-PCI is preferred to TT and is more successful(8). PCI is the most efficient intervention for decreasing MI extension, so it is the best choice for patients if they arrive in less than 120 minutes at the hospitals that are capable of doing P-PCI, but since PCI is an expensive treatment, it needs lots of caution and expertise andnot all hospitals can do it; in this study, we aimed to describe the mortality rate, re-hospitalization, and ejection fraction of smoker patients with STEMI who underwent PCI versus thrombolytic therapy(20).

Results of this study showed that the three-month mortality rate of patients who underwent PCI was23.1%, and those who received thrombolytic therapy was 7.1%, but the difference was not statistically significant. So many previous studies presented the same result; some are mentioned here.Arsoet al. studied 136 patients in 2016 and evaluated MACE in patients who underwent PCI and received thrombolytic therapy. That study showed no significant difference between the two groups in MACE (26). In another study done by Danchinet al. in 2019, no significant difference was demonstrated about five years mortality after PCI versus thrombolytic therapy (27). Armstrong et al. studied 1892 patients in 2013 and evaluated mortality and re-hospitalization in patients who underwent PCI and received thrombolytic therapy. The study showed no significant difference between the two groups regarding mortality rate and re-hospitalization (28).

On the other hand, few studies show different resultsfrom those achieved in this study. For example, in 2004, Mehta et al. showed that In patients with STEMI, the mortality rate is lower in

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patients who underwent PCI than those who underwent thrombolytic therapy(29). Maybe this controversy comes out of different sample populations, as in the Mehta study, the study group was more than 70 years old, but in the current study, the mean (SD) age was 54.90±8.93 years.Thus, age can be an effective parameter in choosing the best treatment in STEMI.

The most common risk factors were hypertension (45.24%),diabetes (42.86%), and familyhistory of ischemic heart disease(21.42%). As shown in the previous studies, diabetes, hypertension, dyslipidemia,and familyhistory of ischemic heart diseaseare the most critical risk factors for occurring STEMI (40,41).

Results of the present study in smoker patients described that mean (SD) EF values of patients who underwent PCI were41.56±9.95 at the time of admission and 45.00±10.52 after three months, and statistical analyses showed no significant difference between the two numbers. Mean (SD) EF values of patients who received thrombolytic therapy were 40.26±8.73 at the time of admission and 48.53±5.80 after three months. Statistical analyses showed a significant difference between the two numbers. Also, in ex-smoker patients, mean (SD) EF values of patients who underwent PCI were 45.00±7.07 at the time of admission and 52.50±3.53 after three months, and statistical analyses showed no significant difference between the two numbers. By the way, mean (SD) EF values of patients who received thrombolytic therapy were 41.00±8.21 at the time of admission and 49.00±6.52 after three months, and statistical analyses showed a significant difference between the two numbers.Theseresults correspond with the 2021 study done by Asadpour-Piranfar et al. Itohet al. conducted a survey in 2010 to compare EF changes in both treatments. In that study, meanEF values of patients who received thrombolytic therapy were 55.4% at the time of admission and 61.6% after six months; mean EF of patients who underwent PCI was 54.3% at the time of admission and 55% after six months of follow up. The Itho study results arein line with this study, and both of them demonstrate that EF raised significantly during a long time after thrombolytic therapy (42). Controversial results of different studies may be due to many dissimilarities such as differences in medication and fibrinolytic therapy and other hospital-related factors, different habits and lifestyles, and personality differences between individuals. Considering that a short follow-up period is an essential limitation of the present study, we suggest conducting a similar study with more extended follow-up periods after treatment. It can also be noted that a larger sample size in a similar analysis can show more valuable results.

CONCLUSION

This study showed that Thrombolytic therapy could improve patients' EF after STEMI for a long time and prevent further ischemic heart disease complications. Mortality rate and re-hospitalization between two groups of PCI and thrombolytic therapy had no significant difference.In addition, only 7.1% of patients with MI are admitted to the hospital within the golden time of 30 minutes. It can be concluded that there should be more educational programs about MI symptoms and what to the when it happens in Iran.

Conflict of Interest

There are no conflicts of interest.

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