Original Article

Reperfusion Delay and its Main Correlates in Patients with ST-Segment Elevation Myocardial Infarction under Primary PCI

Azadeh Sadrzadeh[1*]

[1] Cardiology Department, Shahid Modares Hospital, Tehran, Iran

Received: 25 September, 2018; Accepted: 16 December, 2018

Abstract

Background: Various strategies have been proposed to minimize reperfusion delay in patients who are candidate for primary percutaneous coronary intervention (PCI). Reperfusion time may be affected by both intra- and extra-hospital factors. The study attempted to identify factors affecting reperfusion time to reduce mortality and morbidity.

Materials and Methods: In this cross-sectional study, 95 patients with chest pain who were admitted to a hospital emergency in Tehran (capital city of Iran) were admitted and those who were diagnosed with ST-segment elevation myocardial infarction (STEMI) were candidates for primary PCI. Basic information was asked from the patients or companion of them. In addition, the PCI time recorded in the patient file was entered in the checklist.

Results: The mean interval between the onset of symptoms and primary PCI was 218.6±21.69 min. The interval between the first medical contact (FMC) and primary PCI was determined to be 87.122±183.66 minutes. The mean time of door to balloon in the hospital was 42.49±78.53 min. In addition, the mean time interval from symptom onset to FMC was 19.47±11.84 minutes. In 31 cases (32.6%), the emergency service (EMS) contacted. Three factors were identified to be associated with a delay between the onset of symptoms to primary PCI (or delay reperfusion time) including the previous history of myocardial infarction (MI) (p=0.034), the severity of coronary artery disease, based on angiography (p=0.043) and the type of vehicle used to transfer the patient to the hospital (p=0.007).

Conclusion: The reperfusion delay seems to be higher in our treatment center than in other centers. Three preceding factors of MI, the severity of coronary artery disease and the transmission of patients via EMS are considered factors associated with the reduction of reperfusion delay.

Keywords: Systolic blood pressure, Pulmonary emboli, CT index

***Corresponding Author:** Azadeh Sadrzadeh, Cardiology Department, Modares Hospital, Tehran, Iran, Fax: (+98) 21 22074087; E-mail: azadesadrzadeh@gmail.com

Please cite this article as: Sadrzadeh A. Reperfusion Delay and its Main Correlates in Patients with ST-Segment Elevation Myocardial Infarction under Primary PCI. Novel Biomed. 2020;8(1):7-12.

Introduction

The primary percutaneous coronary intervention (PCI) procedure is currently considered as a predominant strategy in the treatment of acute myocardial infarction (MI) associated with ST-segment elevation (STEMI) when it is done in due time by an experienced operator. This technique has far more satisfactory results than thrombolytic treatment, even when the time interval between the event and hospital transferring is prolonged[1-6]. Delaying reperfusion in determining the prognosis of patients with STEMI, play

an important role. In this regard, both the time interval between the patient's arrival to the percutaneous coronary intervention (PCI) lab (door to balloon time) and total ischemic time relate to the increased risk for motility in most patients[7-9]. New guidelines have suggested that the delay in door to balloon time should be reduced to less than 90 to 120 minutes[10,11]. However, latencies in performing the primary PCI are usually longer than those given in the guidelines[12,13] and this makes the primary therapeutic effects of PCI less effective than thrombolysis[14,15]. To solve this problem, various strategies have been proposed, and national steps, especially in Europe and America, have been taken to manage time in the primary PCI process. All of these strategies are aimed at bypass of the emergency services (EMS), the faster transferring the patient to the catheter lobe and also minimizing the delay time in the reperfusion.

In the treatment of patients with STEMI, the goal is to open the access in the artery to supply the ischemic tissue with either a thrombolytic drug or PCI. Factors that cause reperfusion delay include pre-hospital delay (due to advanced age, previous history of MI, referral by personal vehicle and no contact with EMS), and intra-hospital delay due to prolonged door to Balloon Time[16,17]. Information to emergency centers is one of the most important steps that should be taken by the patient. Patients with STEMI should receive emergency coronary reperfusion within 12 hours[18]. The more reperfusion is done sooner, the more health benefits are gained and the mortality rate is reduced. Current guide lines recommend that the time between the first medical contact with the patient and the balloon during angioplasty should not be over 90 minutes[19]. This time may be affected by both intra- and extra-hospital factors that should be clearly identified to minimize this time interval[20]. The study attempted to identify factors affecting reperfusion time to reduce mortality and morbidity. In total, the following questions were answered in this study: What is the frequency of reperfusion delay in STEMI patients under primary PCI? What is the TIMI flow grade based on what is observed at the primary PCI time? And what are the effective factors in reperfusion delay?

Methods

In this descriptive cross-sectional study, patients with chest pain who were admitted to an emergency ward of a hospital in Tehran (capital city of Iran) were admitted and those who were diagnosed with STEMI were candidates for primary PCI. Basic information including gender, age, previous history of heart disease, risk factors for heart disease (smoking, hypertension and diabetes) as well as the time for starting chest pain, the time interval between pain initiation and transfer to hospital, duration of treatment, and oral medications were asked from patients or companions. In addition, the PCI time was entered in the checklist. On the other hand, the severity of chest pain, type of pain, how it was disseminated and associated symptoms were also asked. During the course of angiography, TIMI flow rate was also recorded.

The results were presented as mean±standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with t test or Mann U test. For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used and p values of 0.05 or less were considered statistically significant.

Results

Baseline characteristics of the study subjects were summarized in Table 1. A total of 95 patients were evaluated. The mean age of the patients was 59.24±13.22 years old in the range of 28-86 years old and 83 (87.4%) patients were men and 12 (12.6%) were women. History of MI was found in 4.2%, 43.2% were hypertensive, 26.3% were diabetic, 27.4% had hyperlipidemia, 43.2% were smokers, and 4.2% were opium misuser. In addition, 6.3% had previous experience of PCI, 4.2% underwent coronary artery bypass grafting (CABG) previously, and 7.4% had history of brain stroke. Family history of heart disease was found in 21.1% and only 1.1% was obese. History of cardiac care unit (CCU) admission was found in

Table 1: Baseline characteristics of study population.

Mean age, year	59.42 ± 13.22
Gender	
Male	83 (87.4)
Female	12 (12.6)
Occupation state	
Employed	16 (16.8)
Worker	8 (8.4)
Self-employed	35 (36.8)
Housekeeper	10 (10.5)
Retired	24 (25.3)
Farmer	2 (2.1)
Marital status	
Married	87 (91.6)
Single	2 (2.1)
Divorced	3 (3.2)
Widow	3 (3.2)
Educational level	
Illiterate	9 (9.5)
Primary	16 (16.8)
Secondary	7 (7.4)
Diploma	36 (27.4)
Bachelor	22 (23.2)
Master	2 (2.1)
Doctorate	3 (3.2)
Living alone	4 (4.2)
Having insurance	75 (78.9)

Table 2: Cardiovascular variables of study population.

Primary complaint	
Typical chest pain	73 (76.8)
Atypical chest pain	1 (1.1)
Non-specific chest pain	21 (22.1)
Medical history	
Myocardial infarction	4 (4.2)
Hypertension	41 (43.2)
Diabetes	25 (26.3)
Hyperlipidemia	26 (27.4)
Smoking	41 (43.2)
Opium use	4 (4.2)
Previous PCI	6 (6.3)
Previous CABG	4 (4.2)
Previous brain stroke	7 (7.4)
Family history of heart disease	20 (21.1)
Obesity	1 (1.1)
CCU admission	
Once	9 (9.5)
Twice	4 (4.2)
Three times	2 (2.1)
Angiography report	
One vessel	31 (32.6)
Two vessels	35 (36.8)
Three vessels	29 (30.5)
LVEF	
< 35%	25 (26.3)
35 – 50%	49 (51.6)
> 50%	21 (22.1)
Killip class	
I	78 (82.1)
II	10 (10.5)
III	6 (6.3)
IV	1 (1.1)

84.2%. Regarding severity of coronary artery disease (CAD), one, two and three-vessel disease based on angiography was revealed in 32.6%, 36.8% and 30.5% respectively. Overall, 26.3% had left ventricular ejection fraction (LVEF) lower than 35%. Regarding functional status, Killip class I, II, III, and IV was found in 82.1%, 10.5%, 6.3%, and 1.1% respectively. Regarding thrombolysis in myocardial infarction (TIMI) flow before PCI, TIMI 0 was found in 86.3%, TIMI I in 1.1%, TIMI II in 10.5%, and TIMI III in 2.1%, while these rates after PCI were 0%, 1.1%, 7.4%, 91.6%. The mean TIMI frame count was also 16.77±2.55. In total, 24.2% underwent thrombectomy. The mean interval between the onset of symptoms and primary PCI was 218.6±21.69 min. The interval between the first medical contact (FMC) and primary PCI was determined to be 87.122±183.66 minutes. The mean time of door to balloon in the hospital was 42.49±78.53 min. Also, the mean time interval from symptom onset to FMC was 19.47±11.84 minutes. In 31 cases (32.6%), the EMS service was contacted. The centers covered by FMC cases included government centers in 2 cases (1.2%), private clinics in 4 cases (4.2%), other hospitals in 22 cases (23.2%) and referred hospital in 67 cases (70.6%). The use of motor vehicles also recorded as personal cars in 59 (62.1%), taxi service in 4 cases (4.2%) and EMS in 32 cases (33.7%). Based on the multivariate linear regression model and the presence of all the underlying factors of the study, there were three factors in total associated with a delay between the onset of symptoms to primary PCI (or delay reperfusion time). They included the previous history of MI (p=0.034), the severity of coronary artery disease, based on angiography (p=0.043), and the type of vehicle used to transfer the patient to the hospital (p=0.007). In this regard, the mean time between the onset of symptoms and primary PCI in patients with and without previous history of MI was 155.1±91.88

Table 3: Multivariate linear regression model to determine the correlates of delayed reperfusion time.

Factor	Beta	T score	P value
Age	1.557	0.631	0.530
Gender	131.95	1.403	0.165
Job	-23.210	-1.028	0.307
Marital	48.144	0.697	0.488
Education level	6.397	0.349	0.728
Living alone	-14.785	-0.190	0.850
Insurance	-42.018	-0.657	0.513
Income	-42.372	-1.418	0.161
Previous MI	314.424	2.165	0.034
Hypertension	15.956	0.289	0.774
Diabetes	-77.563	-1.248	0.216
Hyperlipidemia	51.563	0.819	0.416
Smoking	2.936	0.116	0.908
Opium use	-12.197	-1.051	0.297
Previous PCI	112.766	0.757	0.451
Previous CABG	50.589	0.389	0.699
Previous stroke	-25.347	-0.242	0.810
Family history of CAD	-68.768	-1.084	0.282
CCU admission	46.076	0.754	0.436
Severity of CAD	76.576	2.064	0.043
Type of MI	-4.547	-0.381	0.704
LVEF	9.891	0.244	0.808
Killip class	61.712	1.438	0.155
FMC	-0.576	-0.112	0.911
Type of transferring	-69.417	-2.769	0.007

minutes and 2886.07±27.62 minutes, respectively, that was lower in the group with previous history of MI. Also, the mean time between the onset of symptoms and primary PCI in patients with single coronary involvement was 2645.16±19.27 minutes, in cases with two-vessel involvement was 258.4±166.53 min, and in the cases with three vessels involvement was 347.41±264.97 minutes, which increased with increasing number of involved vessels. The average time between the onset of symptoms and primary PCI in patients with transmission using personal vehicle was 327.29 236.66 minutes, in the cases of using the taxi service to be 290.22±21.66 minutes, and in the case of EMS use was 160.55±180.33 minutes, which was the shortest related to the use of EMS. The mean time between the onset of symptoms and primary PCI in men and women was 264.46±11.122 min and 396.62±38.31 min, respectively with no statistical significant difference. In addition, there was no significant correlation between the time between the onset of symptoms and primary PCI with the age of the patients (correlation coefficient equal to 0.109, p=0.295). The mean time between the onset of symptoms and primary PCI in hypertensive and normotensive groups was 259.75±26.26 and 129.29±49.26 minutes, respectively, which did not differ between the two groups (p=0.427). The mean of this time in patients with and without diabetes mellitus was 336.38±25.88 and 272.85±229.26 minutes, respectively, which did not differ between the two groups (p=0.352). Similarly, the mean pointed time in those with and without hyperlipidemia was 277.50±244.81 minutes and 282.53±28.42 minutes respectively (p=0.925). The mean time between the onset of symptoms and primary PCI in patients with and without smoking history were 288.88±250.88 and 272.26±226.22, respectively, which did not differ between the two groups (p=0.910).

Based on the multivariate linear regression model, none of the underlying factors was able to predict other times, including the interval between the first medical contact (FMC) and primary PCI, the door to balloon time in the hospital, or the time interval between the occurrence of the symptoms and the FMC.

Discussion

In various studies, the time interval between the clinical manifestations of STEMI occurrence prior to the primary PCI procedure is considered as an important prognostic factor, especially hospital mortality in these patients. In this regard, studies have evaluated various factors predicting this delay to minimize the time gap to improve PCI-related implications. In this regard, the present study aimed to investigate the delayed reperfusion of primary PCI in patients with STEMI and in this regard, factors that are positively associated with increasing delay in reperfusion were assessed. At the beginning of the study, we found that the mean time interval between the onset of symptoms and primary PCI was 238.16±31.69 minutes. The interval between

the FMC and primary PCI was determined to be 87.122±183.66 minutes. The mean time of door to balloon in the hospital was also 42.49±78.53 min. In addition, the mean time interval from symptom to FMC was 19.47±11.84 minutes. According to a review of related studies, the door to balloon interval was equivalent to other studies. For example, according to the instructions given, the optimal time for door to balloon is considered less than 90 to 120 minutes. In our study, 96.8% of patients had a door to balloon time of less than 105 minutes. However, the time of reperfusion delay or the interval between the onset of symptoms and primary PCI was higher in our study than in other studies and it was varying between 35 and 990 minutes. The major reason for this delay was that, firstly, many of the patients referred to the center were due to their referral from surrounding cities and even distant areas and therefore, long distance between clinical symptoms and PCI increases significantly. Second, due to the non-specificity of symptoms and clinical manifestations in most of patients, patients who referred to the hospital or contact with the EMS delayed and sometimes even until 24 hours after the onset of symptoms referral to health centers.

In the second step, and in evaluating the factors associated with delayed reperfusion and the PCI process, we found that patients with a history of MI had a much lower latency for reperfusion. It is due to the greater awareness of patients with a history of MI of prominent manifestations, as well as to the need for quick referral for treatment as soon as possible for these patients. In addition, with increasing severity of coronary artery disease, the latency of PCI also increases that may be due to the more delayed these patients in emergency centers for initial evaluations. As it has been mentioned in some studies, the initial referral of patients to emergency centers is a factor in increasing the delay in referring patients to cat lab.

As a third factor in predicting reperfusion delay, the patient's transfer to hospital is an effective factor to increase the delay. Because it is evident that the EMS referral is accompanied with the lowest delay and personalized referrals has the greatest delays, since EMS is trying to minimize this time in coordination with the patient accepting centers for the PCI. While transferring through personal methods in coordination with the receiving centers would make it impossible to move between different centers to the final receiving center.

In total, the reperfusion delay predictive factors were different in different studies. In the study of Blankenship et al., the most important factors related to the interval between the onset of symptoms and the arrival of the PCI hospital, as well as the door to balloon time, were the initial transfer of patients to non-PCI centers, which is equivalent to the analysis we have just mentioned. In addition, the referral of the patient with the symptoms of respiratory distress, the referral of patients to non-adherent clocks and the presence of comorbidities such as diabetes and heart failure were predictors that were not considered as prognostic factors in our study[21]. In the study of Rodríguez-Leor et al., the shortest total delaying time was related to the use of EMS, which was completely consistent with our study[22]. In the study of Shavelle *et al*., the factors associated with delay in the onset of treatment include referral in days and unannounced dates and shutting down, failure to perform ECG within 10 minutes of hospitalization, previous CABG history, black race, older age, and female gender. The only previous history of MI in our study was consistent with this study[23].

Conclusion

Overall, the reperfusion delay seems to be higher in our treatment center than in other centers. Based on the analysis, the three preceding factors of MI, the severity of coronary artery disease and the transmission of patients via EMS are considered factors associated with the reduction of reperfusion delay. Therefore, by evaluating the clinical history of patients as well as initial evaluation of patients through electrocardiographic evaluation during transmission with EMS, the time for transferring to clinical settings for performing primary PCI can be minimized.

Acknowledgment

None.

References

1. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised

trials. Lancet. 2003;361:13-20.
2. Widimský P, Groch L, Zelízko M, Aschermann M, Bednár F, Suryapranata H. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J. 2000;21:823-31.
3. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003;349:733-42.
4. Widimský P, Budesínský T, Vorác D, Groch L, Zelízko M, Aschermann M, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial--PRAGUE-2. Eur Heart J. 2003;24:94-104.
5. Grines CL, Westerhausen DR, Grines LL, Hanlon JT, Logemann TL, Niemela M, et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. J Am Coll Cardiol. 2002;39:1713-9.
6. Dalby M, Bouzamondo A, Lechat P, Montalescot G. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. Circulation. 2003;108:1809-14.
7. Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. JAMA. 2000;283:2941-7.
8. McNamara RL, Wang Y, Herrin J, Curtis JP, Bradley EH, Magid DJ, et al. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol. 2006;47:2180-6.
9. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation. 2004;109:1223-5.
10. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J. 2008;29:2909-45.
11. Kushner FG, Hand M, Smith SC, King SB, Anderson JL, Antman EM, et al. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update) a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2009;54:2205-41.
12. Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation. 2005;111:761-7.
13. Chakrabarti A, Krumholz HM, Wang Y, Rumsfeld JS, Nallamothu BK. Time-to-reperfusion in patients undergoing interhospital transfer for primary percutaneous coronary intervention in the U.S: an analysis of 2005 and 2006 data from the National Cardiovascular Data Registry. J Am Coll Cardiol. 2008;51:2442-3.
14. Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything? Am J Cardiol. 2003;92:824-6.
15. Betriu A, Masotti M. Comparison of mortality rates in acute myocardial infarction treated by percutaneous coronary intervention versus fibrinolysis. Am J Cardiol. 2005;95:100-1.
16. Bradley EH, Roumanis SA, Radford MJ, Webster TR, McNamara RL, Mattera JA, Barton BA, Berg DN, Portnay EL, Moscovitz H, et al. Achieving door-to-balloon times that meet quality guidelines: how do successful hospitals do it? J Am Coll Cardiol. 2005;46:1236-41.
17. Bradley EH, Curry LA, Webster TR, Mattera JA, Roumanis SA, Radford MJ, McNamara RL, Barton BA, Berg DN, Krumholz HM. Achieving rapid door-to-balloon times: how top hospitals improve complex clinical systems. Circulation. 2006;113:1079-85.
18. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. N Engl J Med. 2006;355:2308-20.
19. Krumholz HM, Bradley EH, Nallamothu BK, Ting HH, Batchelor WB, Kline-Rogers E, et al. A campaign to improve the timeliness of primary percutaneous coronary intervention: Door-to-Balloon: An Alliance for Quality. JACC Cardiovasc Interv. 2008;1:97-104.
20. Knot J, Widimsky P, Wijns W, Stenestrand U, Kristensen SD, Van' T Hof A, et al. How to set up an effective national primary angioplasty network: lessons learned from five European countries. EuroIntervention. 2009;5:299, 301-9.
21. Blankenship JC, Skelding KA, Scott TD, Berger PB, Parise H, Brodie BR, et al. Predictors of reperfusion delay in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention from the HORIZONS-AMI trial. Am J Cardiol. 2010;106(11):1527-33.
22. Rodríguez-Leor O, Fernández-Nofrerías E, Mauri F, Salvatella N, Carrillo X, Curós A, et al. Analysis of reperfusion delay in patients with acute myocard ialinfarction treated with primary angioplasty based on first medical contactand time of presentation. Rev Esp Cardiol. 2011;64(6):476-83.
23. Shavelle DM, Chen AY, Matthews RV, Roe MT, de Lemos JA, Jollis J, et al. Predictors of reperfusion delay in patients with ST elevation myocardialinfarction self-transported to the hospital (from the American Heart)Association's Mission: Lifeline Program . Am J Cardiol. 2014;113(5):798-802.