Total Ischemic Time has Prognostic Implications on Short Term Outcome of Primary Percutaneous Coronary Intervention (pPCI)

Md. Golam Morshed, Muhammad Azmol Hossain, Housneara Begum, Md Shamsuzzaman, Kazi Mohammed Zafrul Haq, Md. Mozammel Haque, Md. Khurshid Alam & Poppy Bala

ABSTRACT

Objectives: Primary percutaneous coronary intervention (pPCI) is being increasingly done as the treatment of acute ST elevation myocardial infarction (STEMI). Time until treatment is paramount in the management of STEMI. But the total ischemic time before pPCI how much influencing the outcome is a matter of interest. So we evaluated the influence of total ischemic time on myocardial reperfusion and short term clinical outcome in patients with STEMI treated with primary PCI.

Methods: This prospective observational study was conducted from August 2017 to July 2018 in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka.

Forty eight (48) acute STEMI patients were selected by purposive sampling based on inclusion and exclusion criteria dividing into two groups as short total ischemic time in whom pain to pPCI time was <6 hours and long total ischemic time in whom pain to pPCI time was 6-12 hours. Angiographic (TIMI flow grade 3 & MBG 3) & short term clinical outcome (MACE, heart failure, major bleeding, minor bleeding, cardiogenic shock, significant arrhythmia, instent thrombosis) were observed and compared between these two groups.

Keywords: total ischemic time, primary PCI (pPCI), prognostic implications.

Classification: NLM Code: WG 166.5

Language: English

Great Britain Journals Press

LJP Copyright ID: 392815

London Journal of Medical and Health Research

Volume 24 | Issue 5 | Compilation 1.0

Total Ischemic Time has Prognostic Implications on Short Term Outcome of Primary Percutaneous Coronary Intervention (pPCI)

Md. Golam Morshed[α], Muhammad Azmol Hossain[σ], Housneara Begum[ρ], Md Shamsuzzaman[Ↄ], Kazi Mohammed Zafrul Haq[¥], Md. Mozammel Haque[§], Md. Khurshid Alam[χ] & Poppy Bala[ν]

ABSTRACT

Objectives: Primary percutaneous coronary intervention (pPCI) is being increasingly done as the treatment of acute ST elevation myocardial infarction (STEMI). Time until treatment is paramount in the management of STEMI. But the total ischemic time before pPCI how much influencing the outcome is a matter of interest. So we evaluated the influence of total ischemic time on myocardial reperfusion and short term clinical outcome in patients with STEMI treated with primary PCI.

Methods: This prospective observational study was conducted from August 2017 to July 2018 in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka.

Forty eight (48) acute STEMI patients were selected by purposive sampling based on inclusion and exclusion criteria dividing into two groups as short total ischemic time in whom pain to pPCI time was <6 hours and long total ischemic time in whom pain to pPCI time was 6-12 hours. Angiographic (TIMI flow grade 3 & MBG 3) & short term clinical outcome (MACE, heart failure, major bleeding, minor bleeding, cardiogenic shock, significant arrhythmia, instent thrombosis) were observed and compared between these two groups.

Results: The 30-day mortality & morbidity were assessed and compared between short and long total ischemic time before pPCI. The overall 30-day mortality rate was 4.2%, heart failure was 6.2%, cardiogenic shock was 4.2%, major bleeding was 2.1% and minor bleeding was 14.6%. Mortality and morbidity were higher in longer ischemic time group than shorter ischemic time group. In multivariate regression analysis, the factors independently influencing the adverse short term outcome were advance age (OR 1.51, 95% CI 1.105 to 4.101, p=0.03), hypertension (OR 2.44, 95% CI 1.102 to 4.281, p=0.02), diabetes mellitus (OR 2.51, 95% CI 1.200 to 4.987, p=0.02), anterior MI (OR 1.38, 95% CI 1.001 to 2.872, p=0.03), multivessel disease (OR 2.35, 95% CI 1.010 to 5.371, p=0.02), pain to door time (OR 1.66, CI 1.099 to 2.2.722, p=0.04), and total ischemic time (OR 2.67, 95% CI 1.122 to 5.784, p=0.02). Even after correction for predictive baseline and procedural variables of the univariate analysis, longer total ischemic time was the most significant independent predictor (OR 2.67, p=0.02) of short term adverse outcome of primary PCI.

Conclusion: According to this study finding, there is prognostic implication of total ischemic time in patients with STEMI undergoing primary PCI. Therefore, all efforts should be made to shorten total ischemic time, including reduction in patient related delays, to improve clinical outcome of STEMI patients.

Keywords: total ischemic time, primary PCI (pPCI), prognostic implications.

α §: Assistant Professor, Department of cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.

σ: Assistant professor (cardiology), Department of cardiology, Faridpur Medical College, Faridpur, Bangladesh.

ρ: Associate professor & lieutenant colonel, Combined Military Hospital (CMH), Dhaka, Bangladesh.

London Journal of Medical & Health Research

ↀ: Specialty registrar (acute medicine), Ipswich Hospital, East of England, UK.
¥: Senior Consultant, Department of cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.
χ: Assistant Registrar, Department of cardiology, National Institute of Cardiovascular Diseases (NICVD), Assistant Professor, Department of cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.
v: Registrar, Clinical and interventional cardiology, Apollo Hospitals, Dhaka, Bangladesh.

I. INTRODUCTION

Coronary artery disease (CAD) is the most common form of heart disease and single most important cause of premature death in most part of the world. By the year 2020 it will become the major cause of death in all the region of the world.[1] Acute myocardial infarction (AMI) is one of the leading causes of death and disability. It generally occurs due to sudden occlusion of a coronary artery by formation of thrombus at the site of fissured or ruptured atherosclerotic plaque.[2] The resultant thrombus that is formed interrupts blood flow and leads to an imbalance between oxygen supply and demand, if this imbalance is severe and persistent, it leads to myocardial necrosis.[3] The major aspect of treatment of STEMI is reperfusion of the infarct related artery. Reperfusion therapy aims at restoration of antegrade flow in the occluded infarct related artery, which reduce infarct size and improves clinical outcome[4].

II. MATERIALS AND METHODS

This was a prospective observational study and was done in the department of cardiology in National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from August 2017 to July 2018. Patients presented with acute STEMI admitted in CCU in National Institute of Cardiovascular Diseases who full filled inclusion and exclusion criteria were my study population. Sampling was purposive.

Considering nonresponse, unavailability of some respondent, inflation in the desired sample size is planned. Targeted sample size for the study = 40 + 8= 48. Study subjects were divided into two groups on the basis of time delay to reperfusion: Group A (shorter ischemic time): Patients whose symptom onset to first balloon/ stent time was < 6 hours were included in this group and Group B (longer ischemic time): Patients whose symptom onset to first balloon/ stent time was 6-12 hours were included in this group.

Patients presented within 12 hours of onset of typical chest pain with ST segment elevation in ECG and diagnosed as a case of acute STEMI (ST segment elevation myocardial Infarction) were included in this study. Patients having LBBB (left bundle branch block). Patients with history of old myocardial infarction. Patients who received thrombolytic therapy. Patients with high bleeding risk. Patients with valvular heart disease. Patients with cardiomyopathies Patients with established renal failure (S. Creatinine > 2mg/dl.). Patients with stroke. Patients with malignancy were excluded in this study.

All variables were entered into the Statistical Package for Social Sciences, version 16 (SPSS Inc., Chicago, Illinois). Data was presented as frequency and percents for categorical variables and as mean with standard deviation for quantitative variables. Paired t-test was done for quantitative variables where applicable.

Univariate and multivariate regression analysis were done with variables may be related to adverse outcome with calculated risk ratios & odds ratios [OR] for independent variables with 95% confidence intervals [CI]. P value <0.05 were considered as significant.

III. RESULTS AND DISCUSSIONS

This prospective observational study was conducted in the National Institute of Cardiovascular Diseases (NICVD), Dhaka during the period of August 2017 to July 2018. The main objective of this study was to assess the prognostic implication of total ischemic time on short term outcome of primary Percutaneous Coronary Intervention (PCI) among a case series of population presented with acute ST elevation myocardial infarction (STEMI).

A total of 48 patients with acute ST elevation myocardial infarction who were consented to PCI were included in this study. Patients were classified as shorter total ischemic time (group-A) in whom treatment delay was<6 hours and longer total ischemic time (group-B) in whom treatment delay was 6- 12 hours. Two patients died at the same day of the procedure and all other patients were followed up in hospital and for one month.

Table I: Comparison of risk factors between early treatment group and late treatment group (n=48)

Variables	(Group A) n=23	(Group B) n=25	Total (n=48)	p value
Age in years	51.5±11.1	59.8±14.7	55.9±13.6	0.03^{s}
Hypertension	6 (26.1%)	14 (56.0%)	20 (41.7%)	0.03^{s}
Diabetes mellitus	7 (30.4%)	15 (60.0%)	22 (45.8%)	0.04^{s}
Dyslipidemia	11 (47.8%)	17 (68.0%)	28 (58.3%)	0.17^{ns}
Smoker	15 (65.2%)	20 (80.0%)	35 (72.9%)	0.25^{ns}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. Quantitative data expresses in mean ±SD and qualitative data expresses in no. &(%). s= Significant (p<0.05), ns = Not significant (p>0.05) p value reached from Chi Square test.

The above table depicts the comparison of risk factors between early treatment group and late treatment group among the study population. Age, hypertension and diabetes were higher in patients with longer symptom onset to balloon time than in those with shorter symptom onset to balloon time and there were statistical significant association(p=0.03,p=0.03, p=0.04) respectively. Among the study population overall 41.7% were hypertensive, 45.8% were diabetic, 58.3% were dyslipidaemic and 72.9% were smoker.

Table II: Comparison of LVEF (%) between two groups before pPCI *(n=48)*

Group A (n= 23) LVEF (%)	Group B (n=25)		Total		p value (n=48)		
	Number	%	Number	%	Number	%	
≤ 35 (Severe)	0	0.0	0	0.0	0	0.0	
36 – 44 (Moderate)	2	8.7	7	28.0	9	18.8	
45 -54 (Mild)	20	87.0	17	68.0	37	77.1	
≥ 55 (Normal)	1	4.3	1	4.0	2	4.2	
Mean ± SD (Range)	48.4±3.9 (40-60)		46.1±4.7 (38-55)		47.2±4.4 (38-60)		0.06^{ns}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. s = Significant (p<0.05), p value reached from unpaired t-test.

The above table displays that among early presenters (group A) 8.7% had moderate LV dysfunction and 87% had mild LV dysfunction but among late presenters (group B) 28% had moderate LV dysfunction and 68% had mild LV dysfunction before pPCI.

Table III: Comparison of LVEF (%) between two groups after PPCI (n=48) Group A (n= 23)

Group A (n= 23) Group B (n=25) **LVEF (%)**	Total				p value (n=48)	
	Number	%	Number	%	Number	%
≤ 35 (Severe)	0	0.0	0	0.0	0	0.0
36 – 44 (Moderate)	0	0.0	0	0.0	0	0.0
45 -54 (Mild)	2	8.7	3	12.0	5	10.4
≥ 55 (Normal)	21	91.3	22	88.0	43	89.6
Mean ± SD (Range)	63.5±5.5 (50-70)		61.6±6.7 (46-70)		62.5±6.2 (46-70)	0.28^{ns}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. s = Significant (p<0.05), p value reached from unpaired t-test.

The above table displays that after pPCI 91.3% patients had good LV function among those who are early presenter having total ischemic time <6 hours and those who are late presenter having longer total ischemic time (6-12 hours) among them 88% had good LV function

Table IV: Adverse outcomes between group A (early treatment group) and group B (late treatment group) (n=48) at one month

Adverse outcome	Group (n=23)		A Group (n=25)		B Total (n=48)		p value
	No.	(%)	No.	%	No.	%	
Death	0	0.0	2	8.0	2	4.2	0.49^{ns}
Heart failure	0	0.0	3	12.0	3	6.2	0.24^{ns}
Cardiogenic shock	0	0.0	2	8.0	2	4.2	0.49^{ns}
Major bleeding	0	0.0	1	4.0	1	2.1	0.69^{ns}
Minor bleeding	1	4.3	6	24.0	7	14.6	0.04^{s}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. S= Significant (p<0.05), ns = Not significant (p>0.05) p value reached from Fisher's Exact test

The above table depicts that mortality in 1 month was 4.2%, heart failure was 6.2%, cardiogenic shock was 4.2%, major bleeding was 2.1% and minor bleeding was 14.6%. Most of the adverse outcomes occurred in late treatment group (6-12 hours from symptom onset to primary PCI) within one month. So it can be concluded that delay in symptom onset to balloon time (6-12 hrs) adversely affects the prognosis in patients with STEMI.

Table V: Univariate logistic regression of adverse short term outcome of pPCI

Variables of interest	B	S. E.	p value	OR	95% CI
Advance age (>60 years)	0.368	0.431	0.02[s]	1.82	1.143-4.219
Male gender	0.152	0.101	0.30[ns]	1.24	0.057-1.541
Hypertension	0.589	0.379	0.01[s]	2.66	1.110-5.581
Diabetes mellitus	0.470	0.465	0.01[s]	2.78	1.110-3.811
Smoker	0.678	0.473	0.33[ns]	0.78	0.120-2.111
Anterior MI	0.439	0.351	0.02[s]	1.54	1.110-3.245
Multi vessel disease	0.578	0.354	0.01[s]	2.55	1.220-6.37
Lower LVEF (<45 %)	0.248	0.176	0.12 ns	1.99	0.494-2.872
Pain to door time	0.420	0.378	0.03[s]	1.92	1.071-2.824
Door to balloon time	0.119	0.101	0.31[ns]	0.99	0.110-1.780
Longer total ischemic time (6-12 hrs)	0.591	0.312	0.01[s]	2.97	1.154 – 7.889

Dependent variable: Adverse in-hospital outcome; Independent variables: Advance age, male gender, hypertension, diabetes mellitus, smoking, anterior MI, multi vessel disease, lower LVEF (<45%), pain to door time, door to balloon time and longer total ischemic time (6-12 hrs). s= Significant (p<0.05), ns= Not significant (p>0.05)

Above table demonstrates the binary logistic regression analysis of odds ratio (OR) for characteristics of the subjects likely to develop adverse short time outcome of primary PCI. The variables revealed to be significantly associated with univariate analysis were entered into the model directly. In regression analysis advance age, hypertension, diabetes mellitus, anterior MI, multi vessel disease, pain to door time and longer total ischemic time (6-12hrs) were found to be the significant predictors for developing adverse short term outcome of primary PCI.

Table VI: Multivariate logistic regression of adverse short term outcome of pPCI

Variables of interest	B	S. E.	p value	OR	95% CI
Advance age (>60yrs)	0.302	0.290	0.03[s]	1.51	1.105-4.101
Male gender	0.141	0.101	0.45[ns]	1.11	0.017-1.541
Hypertension	0.479	0.361	0.02[s]	2.44	1.102-4.281
Diabetes mellitus	0.435	0.304	0.02[s]	2.51	1.200 – 4.987
Smoker	0.220	0.119	040[ns]	0.88	0.111-2.509
Anterior MI	0.339	0.279	0.03[s]	1.38	1.001-2.872
Multi vessel disease	0.478	0.342	0.02[s]	2.35	1.010-5.371
Lower LVEF(<45 %)	0.232	0.107	0.27 ns	1.44	0.549-1.770
Pain to door time	0.410	0.301	0.04[s]	1.66	1.099-2.722
Door to balloon time	0.110	0.101	0.4 ns	0.88	0.120-1.699
Longer total ischemic time (6-12 hrs)	0.569	0.300	0.02[s]	2.67	1.122 – 5.784

Dependent variable: Adverse in-hospital outcome; Independent variables: Advance age, male gender, hypertension, diabetes mellitus, smoking, anterior MI, multi vessel disease, lower LVEF (<45%), pain to door time, door to balloon time and longer total ischemic time (6-12 hrs). s= Significant (p<0.05), ns= Not significant (p>0.05)

Above table demonstrates the binary logistic regression analysis of odds ratio (OR) for characteristics of the subjects likely to develop adverse short time outcome of primary PCI. The variables revealed to be significantly associated with multivariate analysis were entered into the model directly. In regression analysis advance age, hypertension, diabetes mellitus, anterior MI, multi vessel disease, pain to door time and longer total ischemic time (6-12hrs) were found to be the independent predictors for developing adverse short term outcome of primary PCI with

ORs being 1.51, 2.44, 2.51, 1.38, 2.35, 1.66 and 2.67 respectively.

In multivariate analysis, we adjusted for potential confounders associated with the endpoints in univariate analysis. After correction for predictive baseline and procedural variables of the univariate analysis, longer total ischemic time was found as the most significant independent predictor (OR 2.67, p=0.02) of short term adverse outcome of primary PCI.

Reperfusion therapy (either mechanical or pharmacologic) is indicated for patients with chest pain with a duration of 12 hours or less in association with ST-segment elevation greater than 0.1 mV in two or more contiguous electrocardiographic leads or a new (or presumed new) left bundle-branch block. Early, effective and sustained reperfusion of the culprit artery is needed to salvage myocardium, maintain left ventricular function, and reduce mortality[5]. Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for ST-segment elevated MI (STEMI) when it can be performed in a timely manner by experienced personnel[6]. PCI for the treatment of STEMI was first reported by Hartzler[7]. Primary PCI in the late eighties only comprised balloon angioplasty, resulted better survival of patients when compared with thrombolytic therapy; however the introduction of intracoronary stents showed much better clinical outcome as compared to balloon angioplasty only[8]. If high-quality PCI is available, multiple randomized trials have shown enhanced survival compared to fibrinolysis with a lower rate of intracranial haemorrhage and recurrent myocardial infarction (MI)[9].

According to ACC/AHA guidelines for the treatment of STEMI patients, the time from medical contact to PCI (door-to-balloon time) should be 90 minutes and recommends a total ischemic time within 120 minutes[10]. Compared to fibrinolysis, primary PCI restores more often angiographically normal flow, including optimal TIMI 3 flow and blush, and has additional importance in patients with a contraindication for fibrinolysis[11-15]. Moreover, about a quarter of patients receiving fibrinolytic therapy has reocclusion of the infarct-related artery within 3 months after the myocardial infarction, with a recurrent infarction, which is very rare after primary PCI[16]. Therefore, Primary percutaneous coronary intervention (PCI) is generally preferable to fibrinolytic therapy when time until treatment is short. Each 30-minute delay from symptom onset to Primary percutaneous coronary intervention (PCI) increases the relative risk for 1 year mortality by 8%[17].

However, effects of early reperfusion have been difficult to determine in STEMI patients undergoing primary PCI, with several published studies showing widely different treatment effects of early as compared to late reperfusion. While some studies have reported no effect on infarct size with shorter symptom-to-PCI timings[18,19]

In our study, after correction for predictive baseline and procedural variables of the univariate analysis, longer total ischemic time was found as the most significant independent predictor (OR 2.67, p=0.02) of short term adverse outcome of primary PCI.

IV. LIMITATION OF THE STUDY

Although the result of this study supports the research question, there were some limitations of this study. These are, as the, sample size was small, it was difficult to generalize the findings to the reference population. Non randomized sampling done. Single centered study which didn't represent the status of the whole population. Short term observation. Angiography was evaluated by visual estimation, so there was chance of inter observer and intra observer variation of interpretation of the TIMI flow and MBG.

V. CONCLUSION

The results of this study strongly support the prognostic implication of total ischemic time in patients with STEMI undergoing primary PCI. Therefore, all efforts should be made to shorten total ischemic time, including reduction in patient related delays, to improve clinical outcome of STEMI patients.

REFERENCES

1. Walker B R, Colledge N R, Ralston S H, Penman I. Davidson's Principle and Practice of Medicine. In: Newby D E, Grubb N R, eds. Cardiovascular disease. London: Churchil living stone Elsevier; 2014:579-581.
2. Granger CB, Kenneth WM, Douglas WW. Pexelizumab, an anti C5 complement antibody, as adjunctive therapy to primary percutaneous coronary intervention in acute myocardial infarction: the complement inhibition in myocardial infarction treated with angioplasty (COMMA) trail. Circulation 2006; 108: 1184- 1190.
3. Elliott MA. Braunwald heart disease. In: ST elevation myocardial infarction: pathology, pathophysiology and clinical features. Missouri, USA: Elsevier Saunders, 2012; 1087-1109.
4. Moscucci M, Eagle KA. Door-to-balloon time in primary percutaneous coronary interven-tion: is the 90-minute gold standard an unreachable chimera? Circulation 2006; 113(8):1048-50.
5. Beohar N, Davidson CJ, Weigold G. Predictors of long-term outcomes following direct percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2001; 88:1103–7.
6. Geisler T, Muller K, Karathanos A. Impact of antithrombotic treatment on short term outcomes after PCI of left main disease: a pooled analysis from REPLACE 2, ACUITY, and HORIZONS-AMI trails. Euro interven-tion 2014; 10(1):97-104.
7. Wilhelmsson C, Vedin JA, Elmfeldt D. Smoking and Myocardial Infarction. Lancet 1975; 1:415-420.
8. Jensen LO, Maeng M, Thayssen P. Influence of diabetes mellitus on clinical outcomes following primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Am J Cardiol 2012; 109(5):629-35.
9. S. N. Willich, J. M ¨ uller-Nordhorn, M. Kulig. Cardiac risk factors, medication, and recurrent clinical events after acute coronary disease: a prospective cohort study. European Heart Journal 2001; 22(4): 307–313.
10. P. S. Yusuf, S. Hawken, S. ˆOunpuu.Eûect of potentially modiûable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364 (9438); 937–952.
11. De Luca G, Dirksen MT, Spaulding C. Impact of hypertension on clinical outcome in STEMI patients undergoing primary angioplasty with BMS or DES: insights from the DESERT cooperation. Int J Cardiol; 175:50-4.
12. Fang J, Alderman MH. Dissociation of hospitalization and mortality trends for myocardial infarction in the United States from 1988 to 1997. Am J Med 2002; 113:208.
13. Krikorian RK, Vacke JL, Beauchamp GD. Timing, mode, and predictors of death after direct angioplasty for acute myocardial infarction. Cath Cardiovasc Diag 1995; 35: 192–196.
14. Hermanides RS, Ottervanger JP, Dambrink JH. Incidence, predictors and prognostic importance of bleeding after primary PCI for STelevation myocardial infarction 2010; 6:106-11.
15. Mehta RH, Harjai KJ, Grines L. Sustained ventricular tachycardia or fibrillation in the cardiac catheterization laboratory among patients receiving primary percutaneous coronary intervention: incidence, predictors, and outcomes. J Am CollCardiol 2014; 43:1765–1772.
16. Grines CL, Browne KF, Marco J. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The primary angioplasty in myocardial infarction study group. N Eng J Med 1993; 328:673-9.
17. Fokkema, M. L., Wieringa W. G., Horst I.C.V.D., Boersma E., Zijlstra F., Smet B J. Outcome after percutaneous coronary intervention Groningen. Am J Cardiol. 2011;108:1536-1541.
18. Falk E, Thuesen L. Pathology of coronary microembolisation and no reflow. Heart 2003;89:983-985.
19. Francone M, Bucciarelli-Ducci C, Carbone I, Canali E, Scardala R, Calabrese FA, et al. Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and

microvascular damage in patients with ST-segment elevation myocardial infarction: insight from cardiovascular magnetic resonance. J Am CollCardiol 2009;54: 2145-2153.