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Association of Total Ischemic Times and In-Hospital Outcomes of Acute STEMI Patients who Underwent Primary Angioplasty at a Tertiary Cardiac Care Facility

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Authors' contributions

This work was carried out in collaboration among all authors. Authors AAS, SDAS, and MSK conceived, designed and did statistical analysis & editing of manuscript. Authors AAS, FA, IA, FF and DK did data collection and manuscript writing authors AAS, SDA and MSK did review and final approval of manuscript

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Original Research Article

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ABSTRACT

Aims: To determine the association between total ischemic time and in-hospital outcome of acute ST elevation myocardial infarction (STEMI) patients who underwent primary angioplasty.
Study Design: Prospective observational study.
Place & Duration of Study: Department of Cardiology, Dow university of health sciences Karachi between October 2017 till March 2021.
Methodology: Data for total ischemic time analysis were collected from 366 STEMI patients who consecutively underwent primary angioplasty. Total ischemic time was measured from the onset of chest pain to o the first balloon inflation during primary angioplasty and in hospital outcome was measured.
Results: Total ischemic times were available in 366 STEMI patients which was ≥ 30 minutes and < 24 hours: ≤ 2 hours in 15.5%, >2-3 hours in 11.4%, >3-5 hours in 25.4%, and >5 hours in 47.5% of

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STEMI patients. In addition, STEMI patients with total ischemic times <5 hours demonstrated complete ST-segment resolution and reduced death rate than those with total ischemic times >5 hours.

Conclusion: This study showed that shorter ischemic times are significantly related to improved myocardial reperfusion and decreased mortality.

Keywords: ST-segment elevation myocardial infarction; total Ischemic time; primary angioplasty; outcomes.

1. INTRODUCTION

Acute ST segment elevation myocardial infarction (STEMI) is increasingly becoming a dominant cardiovascular condition in bringing significant morbidity and mortality to vast majority of patients in developing countries [1]. With the inception of the therapeutic landmark for STEMI known as Percutaneous Coronary Intervention (PCI) or angioplasty, its timely intervention has been a major focus. Considering the evidence-based positives of timely angioplasty, clinical guidelines suggested the angioplasty for STEMI patients to be accomplished within 90 minutes of arrival at hospital [2]. Despite its significance, there is a lack of clinical evidence regarding its ideal implementation as demonstrated by Majid et al in their study which showed that only 32% PCI were done in agreement with recommended guidelines for door-to-balloon time [3].

According to the National Registry of Myocardial infarction (NRMI) database, it has been shown that those STEMI subjects who received early angioplasty are far more benefited in terms of in-hospital mortality, length of stay, recurrent ischemia and cardiogenic shock compared to late ones [4-5]. Moreover, it has been established that off-hours angioplasty tend to be associated with longer door-to-balloon time and resultant possible complications related to it [3]. Therefore, management of STEMI is directed towards the effort to limit the interval in institution of PCI and patients arrival at hospital. Several speculators have indicated different methods to achieve timely angioplasty [6-9]. A significant body of evidence featured, in terms of clinical outcome, the merits of immediate reperfusion and demerits of late reperfusion in patients with STEMI [10-11].

In this study, we aimed at determining the association between total ischemic times and in-hospital outcomes of acute STEMI patients who underwent primary angioplasty at Department of Cardiology of Dr. Ruth K.M. Pfau, CHK during the period from October 2017 till March 2021.

2. METHODS

From October 2017 till March 2021, Data for total ischemic time analysis were available in 366 patients who consecutively underwent primary angioplasty after being diagnosed, in emergency, with acute STEMI. Total ischemic time is defined as the time from the onset of chest pain to the first balloon inflation during primary angioplasty [12]. Inclusion criteria were patients aged above 18 years, Evidence of ST segment elevation MI (electrocardiographic findings of ST-segment elevation 0.1 mV in at least two contagious leads, new or presumed new left bundle branch block, isolated ST-segment depression greater than or equal to 0.5 mm in leads V1-V3 or ST elevation of 0.5 mm in leads V7-V9 with the use of posterior leads). Exclusion criteria were Patients aged < 18 years, STEMI patients who already received fibrinolytic therapy, who presented with cardiogenic shock and who received coronary artery bypass grafting (CABG) after primary angioplasty. When patient with typical chest pain landed up in emergency department, 12 lead ECG is performed within 10 minutes of arrival and interpreted by our emergency physician, After STEMI was confirmed, treatment protocol was started and patient transferred to catheterization laboratory keeping in view the door to balloon time within 90 minutes. The study protocol was approved by Ethics committee of Dow University of Health Sciences. Karachi, Pakistan.

The interventional procedure was performed by interventional cardiologists' once written informed consent, or if not feasible, verbal consent for treatment had been obtained. The vast majority of patients received a loading dose of two antiplatelet therapies and heparin before angioplasty. The choice of antithrombotic therapy, the use of thrombus aspiration catheter and the type of stent were left to the discretion of the attending interventionist. As primary angioplasty was done, patients were advised to take: dual antiplatelet therapies, beta blockers,

lipid lowering agents, and angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker.

After primary angioplasty, evaluation of the angiographic and clinical data record was done by two experienced observers blinded with patients' personal details. Following parameters were assessed, thrombolysis In Myocardial Infarction (TIMI) flow grade, angiographic appearance of thrombus in the infarct related artery and an electrocardiogram done 30 to 60 minutes after primary angioplasty was evaluated. ST segment elevation resolution was used as a marker for determining optimum myocardial reperfusion.

A structured pro-forma was filled out for the said subjects that encompasses continuous and categorical variables including age, gender, smoking history, diabetes, hypertension, dyslipidemia, location of myocardial infarction [anterior, inferior, lateral or posterior, and right ventricular infarction], total ischemic time (onset-to-door plus door-to-balloon time) which was systematically collected from patient itself or relatives of the patient, TIMI flow grade(pre and post procedure), number of diseased vessels, resolution of ST segment, and follow-up record at 30-day interval which was obtained through telephone or from hospital database.

Data analysis done through SPSS version 21.0. STEMI patients were categorically classified into four different quartiles based on Total ischemic times which are ≤ 2 hours, >2-3 hours, >3-5 hours, and >5 hours. The continuous variables were reported as mean and SD whereas for categorical variables Chi-square test applied in which the p-value of <0.05 considered statistically significant. Moreover, Microsoft Excel 2016 used to report the frequencies and percentages in tabulation and graphical format, as appropriate.

3. RESULTS

Total ischemic time were available in 366 patients, of which the number of patients who had ischemic time less than two hours were 57 (15.5%), those who had ischemic time more than two to three hours were 42 (11.4%), those who had ischemic time more than three to five hours were 93 (25.4%), those patient who had ischemic time more than five hours were 174 (47.5%). Ischemic time median was 3.1 hours. Total ischemic time was significantly associated with age, hypertension, and current smoking status (Table 1). Table 2 summarizes the angiographic and procedural characteristics of STEMI patients. Ischemic time was associated with presence of collateral redistribution, multi-vessel disease, stent implantation and use of Intra aortic balloon pump (IABP). Successful TIMI 3 flow was 94.7% in patients who landed up in emergency department within two hours; however, TIMI 3 flow was 70.7% in patients who presented after five hours. Thrombosis after primary PCI occurred significantly in patients who presented prolonged ischemic hours (> 5 hours). Furthermore, STEMI patients with early presentation did not need the use of IABP.

The outcome characteristics specify that STEMI patients who landed early (< 2 hours) in emergency department show greater ST segment resolution (87.7%) and lower mortality at 30-day interval (0%) compared with patients who presented late (> 5 hours) as shown in Table 3.

4. DISCUSSION

This cohort maintained that myocardial reperfusion was successfully achieved, with better cardiovascular outcomes, in those STEMI patients who suffered less ischemic hours of injury before receiving primary angioplasty.

Table 1. Baseline characteristics

Variables	Myocardial Ischemic Time (hours)				P-value
	≤2 (n = 57)	>2-3 (n = 42)	>3-5 (n = 93)	>5 (n = 174)	
Ischemic time (hours)	1.67 ± 1.09	2.57 ± 0.51	3.94 ± 0.45	13.69 ± 10.83	<0.001
Age (years)	58.51 ± 14.86	55.98 ± 12.18	58.00 ± 10.43	54.64 ± 10.31	0.049
Men	45 (78.9%)	30 (71.4%)	68 (73.1%)	127 (73.0%)	0.805
Hypertension	35 (61.4%)	20 (47.6%)	68 (73.1%)	107 (61.5%)	0.036
Dyslipidemia	27 (47.4%)	16 (38.1%)	42 (45.2%)	63 (36.2%)	0.336
Diabetes Mellitus	29 (50.9%)	14 (33.3%)	43 (46.2%)	82 (47.1%)	0.341
Current smoker	18 (31.6%)	14 (33.3%)	52 (55.9%)	83 (47.7%)	0.010

Data are expressed as number (percentage) or as mean ± S.D

Table 2. Angiographic and procedural characteristics

Variables	Myocardial Ischemic Time (hours)				P-value
	≤2 (n = 57)	>2-3 (n = 42)	>3-5 (n = 93)	>5 (n = 174)	
Pre-PCI angiography					
Anterior infarction	24 (42.1%)	22 (52.4%)	43 (46.2%)	58 (33.3%)	0.057
Multi-vessel disease	20 (35.1%)	12 (28.6%)	23 (24.7%)	26 (14.9%)	0.007
Collateral arteries	14 (24.6%)	8 (19.0%)	14 (15.1%)	17 (9.8%)	0.036
TIMI grade 0 or 1 before PCI	36 (63.2%)	32 (76.2%)	82 (88.2%)	168 (96.6%)	<0.01
Procedural					
Balloon dilatation	42 (73.7%)	32 (76.2%)	86 (92.5%)	134 (77%)	0.008
Stent Implantation	51 (89.5%)	40 (95.2%)	88 (94.6%)	163 (93.7%)	0.59
Intra-aortic balloon pump	0 (0%)	4 (9.5%)	3 (3.2%)	5 (2.9%)	0.066
Post-PCI angiography					
TIMI grade 3 after PCI	54 (94.7%)	36 (85.7%)	74 (79.6%)	123 (70.7%)	0.01
Thrombus after PCI	45 (78.9%)	25 (59.5%)	23 (24.7%)	54 (31.0%)	<0.01

Table 3. Outcome characteristics

Variables	Myocardial Ischemic Time (hours)				P-value
	≤2 (n = 57)	>2-3 (n = 42)	>3-5 (n = 93)	>5 (n = 174)	
ST-segment resolution >70%	50 (87.7%)	35 (83.33%)	74(79.56%)	132 (75.86%)	0.02
Mortality at 30 days	0 (0%)	3 (7.1%)	4 (4.3%)	9 (5.1%)	0.05

Data are expressed as number (percentage)

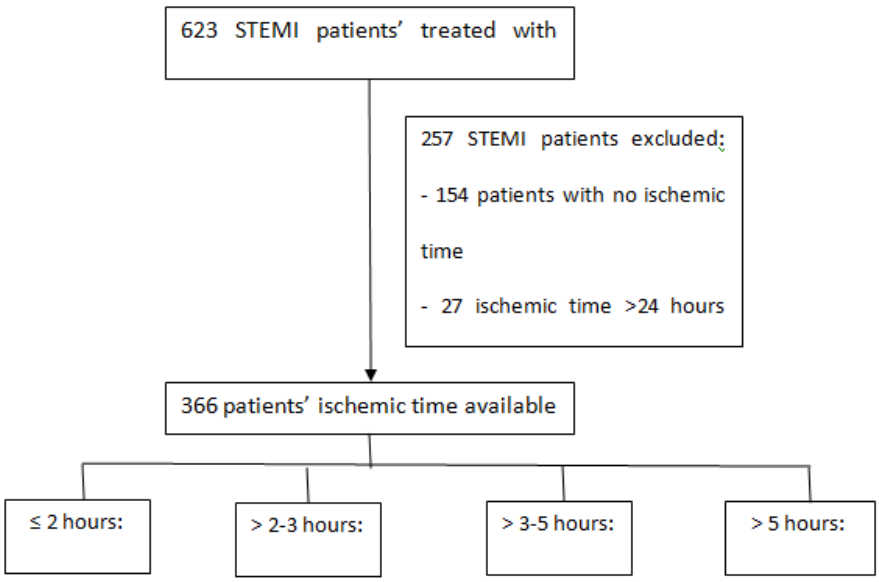

Chart 1. 623 STEMI patients' treated

Our study findings are in line with the previous speculations that prolonged ischemia (>5 hours) is linked to poor myocardial salvage. Cardio-protection and prevention of transmural necrosis can only be achieved by minimizing the time to reperfusion as evident by latest Cardiac magnetic resonance (CMR) techniques [13]. CMR pointed out the significance of total ischemic time as a prime predictor of transmural necrosis and severe microvascular obstruction (risk of transmural necrosis increased by 37% for every half an hour delay) [14].

It is apparent from previous studies that time to reperfusion play a significant role in determining clinical outcomes of STEMI patients. STEMI

patients who received primary angioplasty in < 5 hours of ischemic insult tend to show better reperfusion probabilities than those who faced > 5 hours of ischemic injury [15]. In addition, maximum therapeutic benefit have been observed in patient who received primary angioplasty in <120 minutes [16].

ST-segment resolution has been recognized as a major determinant of cardiac reperfusion from epicardium up to the microvasculature level [17-18]. Complete ST-segment resolution post-angioplasty is a valid surrogate marker of optimum cardiac reperfusion which has an independent association with patients' delayed presentation to reperfusion facility [19]. In our cohort, STEMI patients with less duration of ischemia exhibited complete ST-segment resolution than those with more duration of ischemia.

The relation between total ischemic time and clinical outcomes in STEMI patients, undergoing primary angioplasty, is of paramount significance. De Luca et al highlighted the importance of time delays in cardiac reperfusion by putting forth their finding that every 30 minutes delay paralleled with 7.5% mortality at one year follow-up [20]. In addition, Kawecki D and co-workers, while studying annual trends in total ischemic times and mortalities concluded that lesser time delays translates into fewer risks of cardiovascular deaths [21]. Our study supports the above study findings as mortality (evaluated at 30 days in our study) was three fold in STEMI patients suffering from >5 hours of ischemic injury.

Our study has some limitations. Firstly, it is a single-centre study which limits its general application to other angioplasty facilities. Secondly, the retrospective nature itself inherent survivor bias along with possible influence of unidentifiable confounders. Finally, patients with cardiogenic shock were excluded from the data population which might restrict the accuracy of our study results**.**

5. CONCLUSION

In conclusion, total ischemic time is a major determinant of successful myocardial reperfusion. In addition, it has a significant link with in-hospital outcomes of STEMI patients in terms of salvaging infarcted myocardium and curbing the associated mortality.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethical approval to conduct this study was given by Institutional review board committee of Dow university of health sciences Karachi. Reference number: IRB-1767/DUHS/Approval 2020.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Writing Group Members, Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, Zheng ZJ, Flegal K, O'Donnell C, Kittner S. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2006;113(6): e85-151.
2. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, Hochman JS, Krumholz HM, Lamas GA, Mullany CJ, Pearle DL. Canadian Cardiovascular Society; American Academy of Family Physicians; American College of Cardiology; American Heart Association. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2008;51(2): 210-47.
3. Magid DJ, Wang Y, Herrin J, McNamara RL, Bradley EH, Curtis JP, Pollack CV, French WJ, Blaney ME, Krumholz HM. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. Jama. 2005;294(7):803-12.
4. Shavelle DM, Rasouli ML, Frederick P, Gibson CM, French WJ, National Registry of Myocardial Infarction Investigators. Outcome in patients transferred for

percutaneous coronary intervention (a national registry of myocardial infarction 2/3/4 analysis). The American Journal of Cardiology. 2005;96(9):1227-32.

5. 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(6):761-7.
6. Jacoby J, Axelband J, Patterson J, Belletti D, Heller M. Cardiac cath lab activation by the emergency physician without prior consultation decreases door-to-balloon time. The Journal of invasive cardiology. 2005;17(3):154-5.
7. Khot UN, Johnson ML, Ramsey C, Khot MB, Todd R, Shaikh SR, Berg WJ. Emergency sdepartment physician activation of the catheterization laboratory and immediate transfer to an immediately available catheterization laboratory reduce door-to-balloon time in ST-elevation myocardial infarction. Circulation. 2007; 116(1):67-76.
8. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, Roumanis SA, Curtis JP, Nallamothu BK, Magid DJ, McNamara RL. Strategies for reducing the door-to-balloon time in acute myocardial infarction. New England Journal of Medicine. 2006;355(22):2308-20.
9. Holmes DR, Bell MR, Gersh BJ, Rihal CS, Haro LH, Bjerke CM, Lennon RJ, Lim CC, Ting HH. Systems of care to improve timeliness of reperfusion therapy for ST-segment elevation myocardial infarction during off hours: the Mayo Clinic STEMI protocol. JACC: Cardiovascular Interventions. 2008;1(1):88-96.
10. Brodie BR, Hansen C, Stuckey TD, Richter S, VerSteeg DS, Gupta N, Downey WE, Pulsipher M. Door-to-balloon time with primary percutaneous coronary intervention for acute myocardial infarction impacts late cardiac mortality in high-risk patients and patients presenting early after the onset of symptoms. Journal of the American College of Cardiology. 2006; 47(2):289-95.
11. Prasad A, Gersh BJ, Mehran R, Brodie BR, Brener SJ, Dizon JM, Lansky AJ, Witzenbichler B, Kornowski R, Guagliumi G, Dudek D. Effect of ischemia duration and door-to-balloon time on myocardial perfusion in ST-segment elevation myocardial infarction: an analysis from HORIZONS-AMI trial (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction). JACC: Cardiovascular Interventions. 2015; 8(15):1966-74.
12. Song JX, Zhu L, Lee CY, Ren H, Cao CF, Chen H. Total ischemic time and outcomes for patients with ST-elevation myocardial infarction: does time of admission make a difference?. Journal of geriatric cardiology: JGC. 2016;13(8):658.
13. Kendziora B, Stier H, Schlattmann P, Dewey M. MRI for measuring therapy efficiency after revascularisation in ST-segment elevation myocardial infarction: a systematic review and meta-regression analysis. BMJ open. 2020;10(9):e034359.
14. Tarantini G, Cacciavillani L, Corbetti F, Ramondo A, Marra MP, Bacchiega E, Napodano M, Bilato C, Razzolini R, Iliceto S. Duration of ischemia is a major determinant of transmurality and severe microvascular obstruction after primary angioplasty: a study performed with contrast-enhanced magnetic resonance. Journal of the American College of Cardiology. 2005;46(7):1229-35.
15. Greulich S, Mayr A, Gloekler S, Seitz A, Birkmeier S, Schäufele T, Bekeredjian R, Zuern CS, Seizer P, Geisler T, Müller KA. Time-dependent myocardial necrosis in patients with ST-segment–elevation myocardial infarction without angiographic collateral flow visualized by cardiac magnetic resonance imaging: results from the multicenter STEMI-SCAR project. Journal of the American Heart Association. 2019;8(12):e012429.
16. Shahin M, Obeid S, Hamed L, Templin C, Gamperli O, Nietlispach F, Maier W, Yousif N, Mach F, Roffi M, Windecker S. Occurrence and impact of time delay to primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Cardiology research. 2017;8(5):190.
17. De Lemos JA. ST-Segment resolution as a marker of epicardial and myocardial reperfusion after thrombolysis: insights from the TIMI 14 and in TIME-II trials. Journal of electrocardiology. 2000;33:67-72.
18. Schröder R, Dissmann R, Brüggemann T, Wegscheider K, Linderer T, Tebbe U,

Neuhaus KL. Extent of early ST segment elevation resolution: a simple but strong predictor of outcome in patients with acute myocardial infarction. Journal of the American College of Cardiology. 1994; 24(2):384-91.

19. Fabris E, van't Hof A, Hamm CW, Lapostolle F, Lassen JF, Goodman SG, Ten Berg JM, Bolognese L, Cequier A, Chettibi M, Hammett CJ. Clinical impact and predictors of complete ST segment resolution after primary percutaneous coronary intervention: A subanalysis of the ATLANTIC Trial. European Heart Journal: Acute Cardiovascular Care. 2019;8(3):208-17.
20. 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(10):1223-5.
21. Kawecki D, Morawiec B, Gąsior M, Wilczek K, Nowalany-Kozielska E, Gierlotka M. Annual trends in total ischemic time and one-year fatalities: the paradox of STEMI network performance assessment. Journal of clinical medicine. 2019;8(1):78.

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