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IN-HOSPITAL MORTALITY RATE AND TRENDS IN DOOR-TO-BALLOON TIME IN PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH ACUTE ST ELEVATION MYOCARDIAL INFARCTION IN AFIC-NIHD RAWALPINDI

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ABSTRACT

Objective: To determine in-hospital mortality rate and trends in Door-to-Balloon Time in Primary percutaneous coronary intervention (Primary-PCI) in patients with acute ST elevation Myocardial Infarction (AMI).

Study Design: Descriptive cross sectional study.

Place and Duration of Study: This study was conducted at AFIC/NIHD Rawalpindi from Oct 2011 to Jan 2015.

Material and Methods: Total of 1256 patients with acute ST elevation Myocardial Infarction (AMI) from Oct 2011 to Jan 2015 who underwent primary PCI were included in this study. We determined the in-hospital mortality and yearly trend in door to balloon time (DTBT). Procedural success was defined as restoration of TIMI-III flow in the Infarct Related Artery (IRA) or culprit artery with less than 30% residual stenosis and discharge from hospital.

Results: Overall in-hospital mortality was 3.82% (48) including 1.12% (14) procedural mortality. Most of the patients' fall into the category of < 60 minutes. Patients with longer door-to-balloon time > 90 minutes had higher mortality amongst the door-to-balloon time groups (< 60 minutes = 4.8%, 60-89 minutes = 2.85%, 90-120 minutes = 15.27% $p < 0.001$).

Conclusion: Door-to-balloon time is associated with mortality in patients undergoing primary percutaneous coronary intervention for ST elevation myocardial infarction. Time to treatment should be as short as possible, even in centers currently providing primary percutaneous coronary intervention within 90 minutes. Further studies are needed to take into account total ischemic time and pre-hospital delays.

Key words: Primary PCI, mortality, Acute STEMI & Door To Balloon Time (DTBT).

INTRODUCTION

Ischaemic heart disease is the leading cause of death in Pakistan[1]. ST Elevation Myocardial Infarction (STEMI) is usually due to rupture of an inflamed thin-capped fibro-atheroma containing a lipid-rich necrotic core. This leads to secondary thrombosis, which can cause coronary artery occlusion and acute coronary syndrome[2]. Effective reperfusion in STEMI can be achieved by either thrombolytic therapy or primary percutaneous coronary intervention (PCI) without preceding thrombolysis (known as primary angioplasty). Primary PCI is currently the preferred treatment option for acute ST-segment elevation myocardial infarction. Studies have collectively shown improved survival and reduced major adverse cardiovascular events with primary PCI compared with thrombolysis[2].

Door-to-balloon time was defined as the time in minutes between a patient's arrival at the hospital and the first balloon inflation or device deployment as documented in the patient's medical record[3]. Time duration from onset of symptoms to reperfusion for patients with ST-segment elevation myocardial infarction (STEMI) consistently predicts mortality for fibrinolytic therapy. Compared with thrombolytic therapy, the benefits of primary PCI include a reduction in the frequency of total stroke and hemorrhagic stroke, a reduction in the frequency of re-infarction, and an increase in the frequency of infarct-related artery patency, resulting in improved in-hospital mortality and long-term

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survival[3,4]. Clinical guidelines recommend that hospitals providing primary percutaneous coronary intervention to patients with ST segment elevation myocardial infarction should treat patients within 90 minutes of first medical contact or admission to hospital[4]. Most studies point to an independent association between longer time to treatment and higher mortality[5,7].

Door-to-balloon time has become the main focus of all cardiac care centers and quality-improvement initiatives and is currently documented by different clinical registries[7,8]. Many studies have shown that mortality is reduced in patients with shorter symptom onset-to-reperfusion time and increased in those with longer total ischemic time[9,10].

American College of Cardiology / American Heart Association (ACC/AHA) guidelines for management of patients with STEMI suggested door-to-balloon times of 90 min or less as the target and give this a class-1 recommendation[11]. Although widely adopted as the default strategy for patients presenting with STEMI in developed nations, there are limited data on the acceptability, success and outcomes of primary PCI in our patient population. As developing countries are preparing themselves for a cardiovascular epidemic, the question arises; is primary PCI a viable therapeutic option in our country with limited resource and trained staff?

MATERIAL AND METHODS

This was a retrospective observational study, conducted at the cardiology department of Armed Forces Institute of Cardiology & National Institute of Heart Diseases Rawalpindi. A total 1256 patients with acute ST – elevation myocardial infarction who underwent primary percutaneous coronary intervention in AFIC-NIHD from Oct 2011 to Jan 2015 were included in this study. The objectives of this study were:

- To determine in-hospital mortality of primary PCI.
- To determine trends in door-to-balloon time for patients undergoing primary PCI

Inclusion criteria:

The database was queried for patients meeting the following inclusion criteria for our study:

- Chest pain lasting > 30 minutes associated with an ST-elevation of ≥ 1 mm in ≥ 2 contiguous leads or regional wall motion abnormality.
- Time from symptom-onset to presentation ≤ 12 hours; and
- New onset LBBB with chest pain and raised cardiac-biomarkers.
- Primary PCI as the reperfusion strategy Contraindication to thrombolysis.

Exclusion criteria:

- Patients who received thrombolytic therapy.
- Non-ST-elevation myocardial infarction (NSTEMI).
- Pregnancy.
- Patients presenting beyond 12 hours with resolved symptoms.
- Those unwilling for primary PCI were excluded from this analysis.

Our primary outcome was in-hospital mortality, and the principal independent variable was door-to-balloon time. Patients were stratified based on their time from symptom onset-to-door time in different groups. For the purpose of evaluating differences in patients' characteristics associated with time to treatment, we divided patients into four groups: <60, 60-89, 90-119, and ≥120 minutes. For all other analyses, we modelled door-to-balloon time as a continuous variable.

Primary PCI protocol:

All patients on arrival were given with 300 mg aspirin, clopidogrel 600mg and received a weight adjusted unfractionated heparin dose of (10000 IU). Thrombectomy-thrombus aspiration, peri-procedural GPIIb/IIIa blockers (predominantly tirofiban).Bare metal stents (BMS) or drug eluting stents (DES) were used at the discretion of the operator, hospital policy and patient financial status. Primary PCI of the infarct-related artery-culprit artery was performed in a standard fashion using radial

access in 95.3% of patients. A variety of guiding catheters, guide wires and balloons were used. Stent size and quality (BMS or DES) was primarily based on visual assessment of vessel size and lesion length and on patient characteristics. Other medications, temporary pace-maker (TPM), Inta-Aortic-Balloon-Pump (IABP), use of DC-cardio-version and ventilatory support were determined by the patient's condition and operator assessment. Coronary blood flow and no reflow in the culprit or infarct related artery (IRA) was documented according to TIMI grading score (0-III). PCI success was defined as achieving vessel patency with TIMI-III flow and residual stenosis of less than 30%. All patients were admitted in CCU or post cath–ward for 2-5 days depending on patient's conditions and complications. Post procedure all the patients received aspirin 300 mg and clopidogrel 75 mg twice daily for 4 weeks and subsequently aspirin and clopidogrel 75 mg/day for 6 months for bare-metal and 12 months for drug-eluting stents.

Statistical analysis:

The data was entered in SPSS Statistics software (version 21). Continuous data was expressed as median and mean along with standard deviation values. Proportions were expressed as percentages with confidence intervals of 95%. Different groups were compared with chi-square test. Similarly groups of continuous variables were compared by using student's t-test and a *p*-value of 0.05 was considered significant.

RESULTS

Demographic and clinical details of patients are given in Table-1. The cohort was predominantly male (91%) and (9%) were female, with a mean age 58.4 ± 0.41 years. The mean time from onset of symptoms to arrival to hospital was 180 minutes ± 20.2 and mean door to balloon time was 52 minutes ± 15.1. Procedural success was achieved in 96.2% (1176 patients) with in-hospital mortality of 3.82% (48 /1256) including 1.12% procedural mortality (14 /1256).

The coronary angiographic and PCI details are given in Table-2. The overwhelming majority of primary PCI procedures were performed through radial access 95.3% (1197). Left anterior descending (LAD) and Right coronary artery (RCA) were the commonest infarct related arteries 673 (53.6%) and 433 (34.5%) respectively. Critical Left Main Stem disease was found in 12 patients who had in-hospital CABG surgery. Eleven patients (.9%) had normal coronaries.

Table-1: Demographic Characteristics of patients STEMI underwent Primary PCI.

Demographic and Clinical Features	Per-centage	Frequency n = 1256
Age (yrs)	58.4	60.1
Male gender (%)	91%	1144
Female	9%	112
Diabetes mellitus (%)	19%	237
Current smoker (%)	36.6%	384
Hypercholesterolemia (%)	3.34%	42.0
Hypertension (%)	29%	42.1
History of peripheral vascular disease (%)	2.7%	34
Heart Failure:		
Killip class I	60.8%	760
Killip class II	30%	375
Killip class III	3%	5
Killip class IV	1.5%	3
AMI Location		
Anterior wall MI	46.17%	580
Inferior wall MI	47.13%	590
Lateral wall MI	0.9%	11
Anterolateral wall MI	5.5%	69
Normal coronaries	0.2%	3
Time from chest pain to hospital arrival	180 minutes ± 20.2	
Door to Balloon Time (DTBT) in minutes	52 minutes ± 15.1	

Patients who died in hospital had 45 minute longer mean door-to-balloon time than patients who survived (97 vs 52 minutes, $p < 0.001$). A greater proportion of patients who had longer door-to-balloon times were older patients belonging to low socio-economic

groups. They had more co-morbidities than patients with shorter door-to-balloon times, including a higher prevalence of previous myocardial infarction, heart failure and diabetes. Patients with longer door-to-balloon time > 90 minutes had higher mortality amongst the door-to-balloon time groups (<60 minutes = 4.8%, 60-89 minutes = 2.85%, 90-120 minutes = 15.27% $p < 0.001$). Longer door-to-balloon time was associated with increased in-hospital mortality, adjusted for patient characteristics, patients with door-to-balloon time >90 min had increased mortality (odds ratio 1.42; 95% confidence interval 1.24 to 1.62) compared with those who had door-to-balloon time ≤ 90 min.

DISCUSSION

This is the first sizable report on in-hospital mortality and DTBT in primary PCI in acute STEMI from AFIC-NIHD Rawalpindi- Pakistan. The in-hospital mortality was 3.82% showed in and our patient population, a high success rate (> 95%) of the index procedure and an excellent overall in-hospital survival rate (96.2%), particularly in the absence of cardiogenic shock. These findings support the current guideline-based recommendations for rapid PCI and provide evidence that this recommendation is valid for all patients with STEMI and presentation within 12 h of the onset of symptoms[9,10]. Primary PCI is currently the preferred treatment for acute ST-segment elevation myocardial infarction. Compared with thrombolytic therapy, the benefits of primary PCI include a reduction in the frequency of total stroke and hemorrhagic stroke, a reduction in the frequency of re-infarction, and an increase in the frequency of infarct-related artery patency, resulting in improved in-hospital and long-term survival[11]. In addition, the availability of primary PCI provides a valid alternative for patients who have contraindications to thrombolytic therapy. Our results are matching with the results of the study of primary PCI of culprit-artery only in which in-hospital MACE, 30-day mortality, and 1-year mortality rates were 4.6%, 4.7%, and 7.4%, respectively[10]. McNamara et al., in a study of data from the National Registry of Myocardial Infarction, reported an odds ratio for increased mortality

Table-2: Procedural characteristics of patients underwent primary percutaneous coronary intervention. n=1256

Angiographic Details	Percentage (n)
Access:	
Radial access	95.3% (1197)
Femoral Access	4.7%(59)
Culprit Vessel-Infarct	
Related Artery IRA	53.6% (673)
Left Anterior Descending	7.5% (94)
artery(LAD)	34.5% (433)
Left Circumflex artery(LCx)	1% (12)
Right Coronary Artery(RCA)	0.2% (3)
Left Main Stem Lesion	
(critical LMS disease)	
Normal coronaries	
Gp Iib-IIIa inhibitor use	
Pre-procedure	0%
During Procedure	85.7% (1102)
Post-procedure	90.5% (1136)
TIMI Flow Pre-procedure	
0	85.5%(1074)
I	9.5% (119)
II	2% (25)
III	3% (38)
TIMI Flow Post-procedure	
0	2.8%(35)
I	2% (25)
II	7.7%(97)
III	87.5%(1099)
Visible Thrombus	
Use of Thrombuster-	30 %(377)
Thrombus aspiration	6 %(75)
POBA	3.6 %(45)
Stents Used:	
BMS	56.6%(712)
DES	33.2%(418)
Take shots only	.9 %(11)
No-reflow	4.7%(59)
IABP used	3.5%(47)
TPM	5.3%(67)
Ventricular Tachycardia VT	7.3%(92)
Ventricular Fibrillation VF	2%(25)
Cardio-version – DCCV	5.8%(73)
Table deaths-in cath Lab	1.1(14)
In-hospital mortality	3.82(48)

of 1.42 among patients for whom the door-to-balloon time was longer than 90 minutes, as compared with those for whom the door-to-balloon time was shorter[13]. A study by Antoniucci, R. Valenti, A. Migliorini, et al quoted 5.7% mortality[14]. Our data regarding the relationship between door-to-balloon time and mortality are consistent with Berger et al. who observed lower 30-day mortality among patients with a door-to-balloon time of less than 60 minutes and an increase in mortality with increasing door-to-balloon times in data from the Global Use of Strategies to open occluded Arteries in Acute Coronary Syndromes trial[15].

Multiple studies have evaluated the relationship between door-to-balloon time and clinical end points and data evaluating the effect of a reduction in door-to-balloon time on patient outcomes. American College of Cardiology / American Heart Association (ACC / AHA) guidelines for management of patients with STEMI suggested door-to-balloon times of 90 min or less as the target and give this a class-I recommendation[11,16]. In our study we had high in-hospital mortality of 21 patients (2.83% in 736 patients) in 2014 because of increased volume of primary PCI and relatively high DTBT in few cases. In fact our two cardiac cath labs were out of order for few months which resulted unwanted delay, long waiting time for primary PCI cases during busy hours of the day. In 2008, Gibson et al, in an analysis of data from the National Registry of

Table-3: Mortality trends in relation to door-to-balloon time yearly trend of DTBT & mortality in primary PCI.

Year	Door-to-balloon time (minutes)				Deaths	
	Mean	SD	Median	Min	Max	Min
2011	53.22	16.36	50	25	110	2
2012	46	15.8	39	31	75	11
2013	59.5	25.8	55	20	265	14
2014	49.39	19.4	45	15	220	21
2015	45.69	15.37	45	20	120	0

Table-4: In-Hospital Mortality Trends.

Door-to-Balloon time	Number of Patients		Mortality	
	Frequency	Percentage	Frequency	Percentage
< 60 mins	290	25%	14	29.1%
61 – 90 mins	736	63%	21	44%
91 – 150 mins	72	6.1 %	11	23%
> 150 mins	76	6.4%	2	4.1%

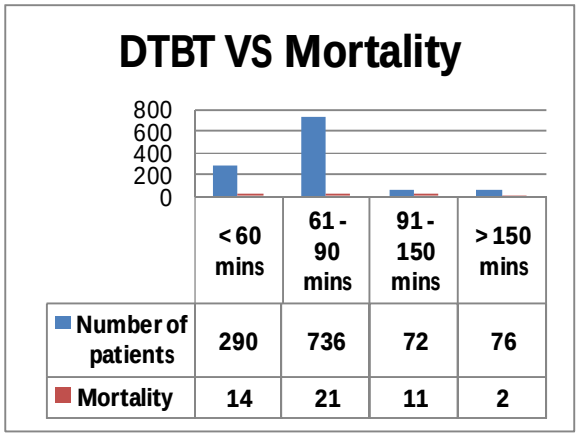

Figure-1: Comparison of Door-to-balloon time and mortality.

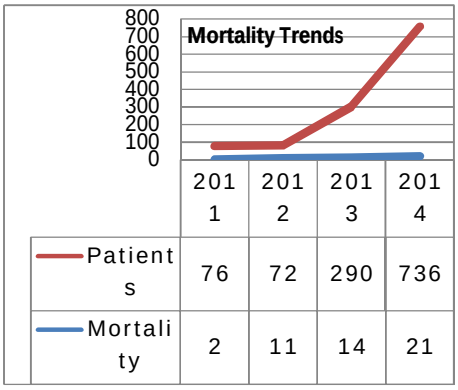

Figure-2: In hospital mortality as function of door-to-balloon time.

Myocardial Infarction, reported a significant reduction in mortality, from 8.6% to 3.1%, associated with a decline in door-to-balloon times from 111 minutes in 1994 to 79 minutes in 2006[17]. Jafery et al quoted in-hospital mortality of 8.3% in patients with KILLIP III/IV and 2.1 in non-cardiogenic shock[18]. Hussain et al from the same center determined in-hospital mortality of 2.9%[19]. In 2010, Flynn et al, in a study involving patients included in a quality-improvement database in Michigan, found no change in short-term mortality between 2003 and 2008 despite a decrease in door-to-balloon time from 113 minutes to 76 minutes[20]. Door-to-balloon time is one component of total ischemic time; as door-to-balloon time is reduced, it becomes a smaller fraction of total ischemic time, making the time before arrival at a hospital a more important factor. Therefore, efforts with potential to improve outcomes may include increasing patients' awareness of symptoms, reducing the interval from the time of symptom onset to treatment, and shortening the transfer time between medical facilities.

CONCLUSION

In conclusion, we reported a high initial success rate with acceptable in–hospital mortality of 3.82% and shorter door to balloon time. Our results compare favorably to Western data despite of few limitation in our registry system. Shorter patient-specific DTBT times were consistently associated with lower mortality over time, primarily due to our robust Primary PCI protocol, wall to wall location of catheterization lab to ER and 24 hours availability of dedicated consultant's cardiologists and trained primary PCI team in the cath lab. Nevertheless, we feel that our data do enable us to make the point that outcomes similar to the West may be possible in developing countries. Further studies are needed taking into account total ischemic time and to salvage myocardium which is greatly diminished after prolonged periods of ischemia, by reducing patients delay, transport delay, and treatment delay in primary PCI cases.

Conflict of Interest

This study has no conflict of interest to declare by any author.

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