

Outcome of primary percutaneous coronary intervention at public sector tertiary care hospital in Pakistan

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Abstract

Objectives: To determine the outcome of Primary Percutaneous Coronary Intervention (PCI) in our setup and compare the results with the west.

Methods: This study was conducted at a tertiary care teaching Hospital (National Institute of Cardiovascular Diseases Karachi, Pakistan) during January 1st, 2008 to December 31st, 2008. A total of 113 patients were enrolled who came with STEMI and agreed to go for Primary PCI. We excluded the patients who had history of Thrombolytic therapy within 24 hours, presented with Non ST-elevation Myocardial Infarction (NSTEMI) and coronary angiogram revealed significant left Main or equivalent disease. All Patients received Aspirin, Clopidogrel and Platelet Glycoprotein IIB IIIA Inhibitor. After Primary PCI patients were planned to follow at one month, 3 months and 6 months. Primary end point was to document death, MI, CABG and re-hospitalization.

Results: Out of 113 cases, 102 (90.3%) were male and 11 (9.7%) were female, Mean age was 51.2 ± 11.7 years, 54 (47.8%) patients had Hypertension, 28 (24.8%) were Diabetics and 44 (38.9%) were Smokers. Immediate success was achieved in 111 (98.2%) cases. In hospital mortality was 5.3% (3.5% in cardiogenic shock, 1.7% in non-shock patients). Mean Door to Balloon time remained 98.4 minutes. Twelve patients were lost to follow up. Therefore at 6 months, out of 101 patients, 8 (7.9%) died, 5 (4.9%) underwent Coronary Artery Bypass Graft (CABG) surgery and 5 (4.9%) had been re-hospitalized either for recurrent myocardial infarction or heart failure.

Conclusion: Optimal results of primary percutaneous coronary intervention can be achieved for acute STEMI in a developing country at a tertiary care public sector hospital. The results are comparable and nearly similar to the west.

Keywords: ST-segment elevation Myocardial Infarction, Primary Percutaneous Coronary Intervention, Mortality (JPMA 61:575; 2011).

Introduction

Percutaneous coronary Intervention (PCI) in patients with acute ST elevation myocardial infarction (STEMI) is an established and preferable method of revascularization. Considerable body of evidence now suggests that revascularization with primary PCI provides better outcome as compared to pharmacological treatment.¹ Primary PCI significantly reduces mortality, re-infarction and stroke rates.² This is true not only for patients admitted to PCI centers but also for patients transferred from non PCI centers.³ Despite this fact among the third world nations, this mode of treatment has not been widely adopted yet as a first line treatment particularly in public sector hospitals. This is mainly due to financial reasons as the state funding for health sector is very minimal and patients have to bear most of the expenses. Therefore, it is not surprising if the data is scarcely available from the developing nations including indo-Pak subcontinent.

Primary PCI is being done at our centre since 1999, but it was offered to those in whom Thrombolytic treatment was contraindicated. Recently we reorganized our Primary PCI programme and now it is offered to every patient who comes with acute STEMI. The key question, however, is whether we can

truly offer this health care facility in a public sector tertiary care centre. The primary object of our study was to determine the outcome and predictors of mortality in patients undergoing primary PCI for STEMI in a tertiary care public sector hospital in Pakistan. Our secondary outcome was to compare our results with the published literature from developed countries.

Patients and Methods

This study was conducted at the National Institute of Cardiovascular diseases (NICVD) Karachi during January 1st 2008 to December 31st 2008. All Patients presenting with acute STEMI were offered Primary PCI. Patients who chose primary PCI as a mode of reperfusion were included in the study. Informed consent was taken and detailed questionnaire was filled for those patients who fulfilled the following inclusion criteria: (1) chest pain lasting > 30 minutes with (2) an ST elevation of > 1 mm in > 2 contiguous leads and (3) time from symptom-onset to presentation > 24 hours. Patients who received Thrombolytic therapy within 24 hours of hospital admission, those who were diagnosed as Non ST elevation Myocardial Infarction (NSTEMI) and those presenting beyond 24 hours with resolved symptoms were excluded from the analysis.

Procedure:

Primary PCI of the infarct related artery was performed in standard fashion using a variety of guiding catheters, coronary wires, balloons and stents. The majority of interventions were performed via the femoral route. However, the choice of route was on discretion of operators and considerable number of interventions was performed via radial route. All patients received 5000-10,000 units of intravenous unfractionated heparin, Aspirin 300 mg, clopidogrel 600 mg (loading dose), and Platelet glycoprotein IIb IIIa inhibitor. Thrombus extraction catheter, nitroprusside, and adenosine use were at the discretion of operators. All patients were prescribed Aspirin 300 mg, Clopidogrel 75 mg and Atorvastatin 20-40 mg daily at the time of discharge from the hospital. Patients were followed at 4th week, 3rd month and 6th month of procedure.

Data collection:

The prospective information on variables including age, gender, history of diabetes (defined as fasting glucose > 126 mg/dl or on treatment), hypertension (systolic blood pressure > 140/90 mmHg or on treatment), hyperlipidaemia (fasting cholesterol > 190 mg/dl or on treatment), Smoking, prior to PCI or coronary artery bypass grafting (CABG), presence of cardiogenic shock (defined as systolic blood pressure [SBP] of < 90 mmHg for at least 30 minutes, or requirement of inotropes to maintain a SBP > 90 mmHg), need of intubation and/or Intra aortic balloon pump (IABP), angiographic and procedural details (culprit vessel, number of diseased vessels, use of stents, GP IIb IIIa inhibitors, Thrombolysis in Myocardial Infarction [TIMI] flow, and Tissue Myocardial perfusion [TMP] grade) and Electrocardiogram (ECG) findings were recorded. Timing variables were documented as follows: (1) Symptom onset to Emergency Room (ER) time was defined as the time interval between the onset of symptoms, as obtained from the history, and the time of presentation to the ER. (2) Door-to-Lab time was defined as the time taken for the shifting of patient into the Catheterization Laboratory from the point of arrival to the ER. (3) Door-to-balloon time was defined as the time taken for the first ballooning from the point of entry to the ER.

TIMI flow, TMP grades and ST resolution (on 12- lead ECG strips) were visually determined and documented by two independent observers before and after PCI and in case of controversy third expert opinion was taken as final. PCI success was defined as achievement of vessel patency to a residual < 30 %. Major bleeding was defined as a haematoma > 10 cm in diameter or bleeding requiring transfusion, vascular surgery or resulting in major morbidity. Patients were followed in out patients department (OPD) at 30th day, 3rd month and at 6th month. Those who did not come to the OPD, they were contacted via telephone and follow up documented. We failed to contact 12 patients. The primary

outcome was to determine major adverse cardiac events (MACE) i.e. death, MI, CABG and re-hospitalization from the time of intervention till six months.

Data management and analysis plan:

Statistical Package for Social Sciences (SPSS) version 14.0 was used for data entry and analysis. The analysis was carried out two levels univariate and multivariate analysis. Mean and standard deviation (SD) were calculated for quantitative variable (age, door to balloon time, symptom onset to ER time, etc.) and proportions for categorical variables. Univariate logistic regression analysis was performed to measure association of outcome with each independent variable. Relative risk (RR) and 95% confidence intervals (CI) was calculated for each association. Associations among independent variables were assessed using appropriate test before performing multivariate analysis. Multiple logistic regression models were used to examine the association between the independent variables and the main outcomes variable, MACE in patients undergoing primary PCI for AMI controlling for the effects of other covariates. P-value < 0.05 was considered as statistically significant.

Results

A total of 137 patients opted primary PCI out of them 113 underwent PCI and remaining 24 were excluded from the study due to significant left main or left main equivalent disease or severe diffusely diseased three vessel disease (3VD).

Table-1: Characteristics of patients undergoing primary PCI at NICVD.

Baseline Demographic and clinical characteristics	N=113 (%)
Age (mean years)	51.2±11.7
Male gender	102 (90.3)
Past Medical history	
Hypertension	54 (47.8)
Diabetes	28 (24.8)
Current Smoker	44 (38.9)
Prior MI	28 (24.7)
Prior PCI	03 (2.6)
Prior CVA	04 (3.5)
Admission Characteristics	
Anterior wall MI	75 (66.4)
Cardiogenic Shock	08 (7.0)
Inotrops required	11 (9.7)
Intubation required	03 (2.6)
IABP required	08 (7.0)
Timing Variables (minutes {SD})	
Chest pain to ER	125.4 {149.6}
Door to Laboratory	66.2 {52.4}
Door to Balloon	98.4 {53.5}
Major Events (In-hospital)	
Death (all patients)	06 (5.3)
Death (cardiogenic shock)	04 (50)
Death (no cardiogenic shock)	02 (1.7)
Urgent CABG	01 (0.8)
Stroke (haemorrhagic)	01 (0.8)

PCI = percutaneous coronary intervention; SD = standard deviation; MI = Myocardial infarction; CVA = cerebrovascular accident; IABP = intra-aortic balloon counterpulsation; ER = emergency room; CABG = coronary artery bypass grafting.

Table-1 shows the baseline demographic and clinical characteristics as well as hospital outcome of the studied cohort. The mean age was just under 52 years. Nearly half of our patients were hypertensive and approximately one-third were diabetic. Twelve (10.6%) patients presented with Killip III-IV out of them 7% were in cardiogenic shock and we put them on Intra aortic balloon counter pulsation (IABP).

The mean door to balloon time was 98.4±53.5 minutes. Six patients died in the hospital (5.3 %), and another two died during follow up. Major bleed occurred in one patient and one patient went for urgent Coronary artery bypass graft (CABG) surgery.

Table-2: Angiographic and procedural characteristics of patients undergoing Primary PCI for STEMI at NICVD, Karachi.

Angiographic and procedural characteristics	N=113 (%)
Culprit vessel	
LAD/ Diagonal	71 (62.8)
LCx / OM	18 (15.9)
RCA	24 (21.2)
Single Vessel CAD	73 (64.6)
Two Vessel CAD	11 (9.7)
Multivessel CAD	29 (25.7)
TIMI flow (pre procedure)	
0	69 (61.1)
I	13 (11.5)
II & III	31 (27.4)
TIMI flow (post procedure)	
I	1 (0.8)
II	3 (2.6)
III	109 (96.5)
Glycoprotein IIb/IIIa inhibitor use	113 (100)
Use of stents	106 (93.8)
BMS	103 (91.2)
DES	3 (2.7)
POBA	7 (6.1)
Use of Export Cathter	88 (77.9)
Clot retrieval	45 (39.8)
Use of Adenosine	24 (21.2)
Tissue Myocardial Perfusion	
0	22 (19.5)
I	49 (43.4)
II	36 (31.9)
III	6 (5.3)
Procedural success	111 (98.2)
Urgent CABG	01 (0.8)
Table Death	01 (0.8)

STEMI = ST-elevation myocardial infarction; LAD = left anterior descending; LCx = left circumflex; OM = obtuse marginal; RCA = right coronary artery; CAD = coronary artery disease; TIMI = thrombolysis in myocardial infarction; BMS = bare metal stent; DES = drug eluting stent; CABG = coronary artery bypass grafting.

Table-2 shows the angiographic and procedural details of the patients undergoing primary PCI. Significant multivessel disease (defined as > 70 % lesion in > 2 epicardial coronary arteries) was present in 35.3% patients. GP IIb/IIIa inhibitor was used in all patients and stenting was done in ~ 94% patients. Aspiration catheter for clot retrieval was also used in majority of patients (~ 78%). Procedural success was achieved in 98% patients.

Table-3: Outcome of patients undergoing Primary PCI at 6 months of follow up.

Major Adverse Cardiac Event (MACE)	N = 101 * (%)
Death : in-hospital	06 (5.9)
Death : follow up	02 (1.9)
Death (cardiogenic shock)	04 (50)
Death (no cardiogenic shock)	04 (3.9)
Death : all patients	08 (7.9)
CABG : in-hospital	01 (0.9)
CABG : follow up	04 (3.9)
CABG : all patients	05 (4.9)
Heart Failure	02 (1.9)
Recurrent MI	03 (2.9)
Stroke	01 (0.9)
Total event rate	19 (18.8)

PCI = Percutaneous Coronary Intervention; CABG = Coro-nary artery bypass grafting; MI = Myocardial Infarction.

* 12 patients lost follow up and therefore outcome was analyzed in remaining 101 patients.

Table-3 shows the outcome of patients at six months follow up. Twelve patients were lost to follow up. Therefore outcome was analyzed in remaining 101 patients. Eight patients died and 5 went for CABG, another 5 were re-hospitalized either with recurrent MI or heart failure. Total MACE calculated at 6 months follow up was 19 (18.8 %) in 101 patients.

Table-4: Univariate analysis of factors associated with major adverse cardiac events (MACE) in patients undergoing primary PCI for STEMI at tertiary care centre.

	Patients with MACE (%) N = 19	Patients with No MACE (%) N = 82	R - R (95 % CI)	P - value
Baseline characteristics				
Age (years) - < 50	06 (31.6)	44 (41.5)	1.42 (0.58-3.43)	0.427
≥ 50	13 (68.4)	48 (58.5)		
Gender: - Male	16 (84.2)	77 (93.9)	0.46 (0.16-1.24)	0.159
Female	03 (15.8)	05 (6.1)		
Diabetes	05 (26.3)	21 (25.6)	1.03 (0.41-2.58)	0.949
Hypertension	11 (57.9)	38 (46.3)	1.45 (0.64-3.32)	0.364
Current Smoker	07 (36.8)	33 (40.2)	0.89 (0.38-2.06)	0.785
Prior MI: - Yes	07 (36.8)	20 (24.4)	1.59 (0.70-3.63)	0.269
No	12 (63.1)	62 (75.6)		
Infarcted territory				
Anterior wall	15 (78.9)	51 (62.2)	1.98 (0.71-5.53)	0.167
Inferior wall	04 (21.1)	31 (37.8)		
Resolution of ST (> 50%) - Yes				
	13 (68.4)	81 (98.8)	6.19 (3.44-11.16)	0.001
No	06 (31.6)	01 (1.2)		
Infarct related artery				
LAD/Diagonal	13 (68.4)	49 (59.8)	1.36 (0.56-3.28)	0.485
RCA/LCX/OM	06 (31.6)	37 (40.2)		
Lesion Risk				
Type C	15 (78.9)	41 (50.0)	3.01 (1.07-8.44)	0.022
Type A & B	04 (21.1)	41 (50.0)		
Vessels Involved				
Multi vessel	12 (63.2)	26 (31.7)	2.84 (1.22-6.58)	0.011
Single vessel	07 (36.8)	56 (68.3)		
Chest pain to ER time				
≤ 120 (minutes)	13 (68.4)	64 (78.0)	1.48 (0.63-3.47)	0.347
> 120 (minutes)	06 (31.6)	18 (22.0)		
Door to Balloon time				
≤ 90 (minutes)	12 (63.2)	38 (46.3)	1.74 (0.75-4.07)	0.186
> 90 (minutes)	07 (36.8)	44 (53.7)		
TIMI Flow				
Zero I & II	03 (15.8)	01 (1.2)	4.55 (2.21-9.36)	0.003
III	16 (89.2)	81 (98.8)		
TMP Grade				
Zero & I	16 (84.2)	48 (58.5)	3.08 (0.96-9.88)	0.036
II & III	03 (15.8)	34 (41.5)		

RR = relative risk; CI = confidence interval; MI = myocardial infarction; LAD = left anterior descending; RCA = right coronary artery; LCx = left circumflex; OM = obtuse marginal; ER = emergency room; TIMI = thrombolysis in myocardial infarction; TMP = tissue myocardial perfusion.

Table-4 shows the univariate predictors of adverse events in patients undergoing primary PCI at our institution with the associated hazards ratios and 95% confidence intervals. Five variables were associated significantly with MACE (p-values <0.05). On multivariate analysis out of these five variables only ST-resolution after primary PCI was found significant in association with MACE.

Table-5: Comparison of Mortality in other trials and Registries of Primary PCI for acute STEMI.

Study	Year	Study Type	Mortality without Cardiogenic shock (%)	Mortality with Cardiogenic shock (%)
NRMI-220	1998	Registry	5.2	32
PAMI Stent ²¹	1999	Trial	3.5 [30 days]	Excluded
SHOCK Trial ²²	1999	Trial	-	46.0 [30 days]
SHOCK Registry ²³	2001	Registry	-	46.4
CAPTIM ²⁴	2002	Trial	4.8 [30 days]	Excluded
GRACIA II ²⁵	2003	Trial	3.0 [6 weeks]	Excluded
ACC-NCDR ²⁶	2005	Registry	-	59.1
ASSENT-4 ²⁷	2006	Trial	3	Virtually excluded
AKUH ⁴	2007	Registry	2.1[2.2 at 30 days]	43.9
THI ⁵	2008	Registry	1 [at 30 days]	45.4
NICVD	2009	Registry	2.9 [at 30 days] 3.9 [at 06 months]	50

PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction; ACC-NCDR = American College of Cardiology National Cardiovascular Data Registry; AKUH = Agha Khan University Hospital; THI = Tabba Heart Institute; NICVD = National Institute of Cardiovascular Diseases. Trial acronyms - see references.

Table-5 summarizes the reported mortality rates for acute STEMI treated by primary PCI in other trials and registries.

Discussion

This is the first report on outcomes of primary PCI in acute STEMI from a public sector tertiary care hospital with six months follow up data. Although few other reports have been published from Pakistan in recent years but they were all from private sector hospitals.^{4,5} The issue of resources and availability of funding complicates the decision making and hence resulting in failure of such programmes in public sector hospitals. Can we successfully run primary PCI programme in our set up? As shown in Table 1 and 2, our outcomes compare extremely favourably with those reported in national and international studies from the developed world. We found a high procedural success rate (> 98%) and an excellent overall in-hospital survival rate (94.7 %), particularly in the absence of cardiogenic shock (> 98%). The high rates of initial success and TIMI 3 flow were also comparable to western data.^{6,7} Therefore we suggest that favourable outcomes (as in developed countries) can be achieved in tertiary care public sector hospitals in Pakistan. These favourable results can be achieved in low risk (non-cardiogenic shock) as well as high-risk (with cardiogenic shock) patients and can be maintained over long term (6 months) follow up.

There are number of findings in our study that need further discussion. Ninety percent patients of our study group were male. This was not due to selection bias but it could be due to gender bias that is present in our male dominant society where female gender, in general, is a less privileged part of the society. This is consistent with other studies on acute MI, in general, and reflects the gender discrimination commonly seen in the Indo-Pakistan subcontinent.^{8,9} The mean age in our study group was less than 52 years that is lower than the reported studies from the developed world. One may argue that we selected a lower risk cohort because age itself is a strong prognostic factor. However, this lower age at presentation is again consistent with other studies in Pakistan on acute MI and probably reflects premature atherosclerosis that is commonly seen in south East Asia.¹⁰

The mean door-to-balloon (DBT) time was 98 minutes in our study group. This was slightly higher than the standard of 90 minutes.¹¹ Whereas door-to-Laboratory time was more than 66 minutes. This means that the actual delay happened in ER. This is not surprising if we consider the cost difference between the Thrombolytic and percutaneous treatment for STEMI. As we are lacking state funding for such procedures patient has to bear most (if not all) of the cost. Needless to say, this complicates the

decision making and contributes to delays in definitive therapy. If we deduct the 66 minutes of ER from our DBT then it means that we were doing Primary PCI in just 32 minutes. Although our shifting (door-to-Lab) time was higher for inevitable reasons but it was lower than the reported from the same region.⁴ Moreover, we found no significant association between door to balloon time and outcomes. Although, it has been suggested that once door-to-balloon time exceeds 90 minutes, the benefits begin to decline.¹² However, it is debatable whether the recommended DBT should be greater than 90 minutes, with the recognition that in certain patients, the mortality advantage of primary PCI compared with fibrinolytic therapy is maintained with more prolonged DBT.^{11,13} In our study group we achieved standard DBT (< 90 minutes) in 53% patients, in 23% patients it was < 110 minutes and in remaining 24% patients it remained > 110 minutes. Therefore we can say that in majority of patients we achieved the standard goal or near to standard. This may be the reason of negative association between DBT and outcomes in our study.

We also found no relationship on univariate analysis between symptom onset to ER (presentation) time and outcomes. The association of symptom onset to ER time with mortality was not well established previously.¹⁴ Gibson et al demonstrated the association of prolonged symptom duration prior to fibrinolytic administration with impaired epicardial flow and myocardial perfusion and poorer clinical outcomes.¹⁵ Then the strength of the evidence increased with De Luca et al report of 1072 patients.¹⁶ He demonstrated that prolonged times between symptom onset to first ballooning are associated with impaired ST-segment resolution, impaired myocardial blush grades, large infarct sizes and higher mortality.¹⁶ But why we and Cannon¹⁴ could not demonstrate this association? It may be due to smaller number of patients with prolonged symptom onset times in our study and it may be due to survival bias because those patients with prolonged symptom-to-ER times may not survive to be included in analyses.

We found significant association between ST-segment resolutions after the procedure with MACE on univariate as well as multivariate analysis. It was found to be a strong predictor of better outcome and it is consistent with other studies.^{16,17} Not surprisingly, we found significant association of Type C lesion and multivessel CAD with MACE. More than 35% of our patients had significant multivessel disease and keeping this fact in mind it is noteworthy that only 5 (4.9%) patients went for CABG surgery and 3 (2.9%) patients had re-current MI at 6 months follow up (Table-3). Similarly, better TIMI-flow and TMP grades were associated with better outcomes in our study group that is again consistent with other studies.^{16,18}

What would be the implications of our study? We have shown that Primary PCI is a viable therapeutic option and can be performed in public sector tertiary care hospitals with excellent immediate, short and long term outcomes despite relatively long symptom onset to ER and door-to-balloon times. As South East Asia faces a cardiovascular epidemic, it is obvious that acute STEMI will continue to suffer the productive lives. Even in our study mean age was just under 52 years and 80% of our patient population was having age of < 60 years. Left anterior descending artery was the culprit in majority (~63%) of them. This predicts the danger to our workforce. Although Thrombolytic therapy (Streptokinase) is widely available in urban Pakistan, the efficacy of this treatment in achieving TIMI 3 flow is around 50% at best.¹⁹ Therefore our population equally deserves widespread availability of this expensive Primary PCI treatment to save our young productive workforce. Whether the state will be ready to fund such an expensive Primary PCI programmes in public sector hospital is not evident. Keeping aside the logical analysis, the answer is that there is no choice! Cost can be reduced by using cheap stents, equipments and resterilized materials. Hands on training of the operators to perform primary PCI in other community hospitals should be the integral part of such programmes. Above all strong commitment is needed to promote and establish this mode of therapy as a first choice for most of the patients if not all.

Study Limitations:

The sample size of our study was relatively small and we need to enroll more patients to validate these results in a larger cohort. Although these were consecutive patients undergoing primary PCI but they were a very small part of patients presented with acute STEMI. Majority of our patient population opt for Thrombolytic treatment primarily due to financial reasons. Therefore, there may be a potential bias towards either low risk or high risk patients. Initially at our center, primary PCI services were given only during the day time and later on this service was extended round the clock. However, even then small number of patients (11%) were enrolled during night time. If we were freely enrolling patients round the clock, would the results be the same? The present data cannot give the answer of this question with certainty. Finally, our data represent a single centre experience and we need more data from other centers to generalize our results.

Conclusion

This is the first report from the public sector tertiary care hospital of Pakistan that provides us the outcomes of primary PCI for acute STEMI. We demonstrate a high initial success rate and excellent short and long term survival, especially in patients presenting without cardiogenic shock. Our results compare favourably to western data and suggest the need of promoting the primary PCI as a first treatment choice for acute STEMI.

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