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Original Article

Percutaneous Coronary Intervention

IN-HOSPITAL OUTCOME OF PERCUTANEOUS CORONARY INTERVENTION AFTER THROMBOLYSIS AS PART OF INVASIVE STRATEGY IN ANTERIOR ST-ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT

Objective: In-hospital outcome of percutaneous coronary intervention after thrombolysis as part of invasive strategy in anterior ST-elevation myocardial infarction.

Study Design: Cross-sectional study.

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, from Dec 2020 to Apr 2021.

Methodology: Permission was sought from hospital ethics committee. Written informed consent was taken from participants of study. Charges of the tests and procedures were borne by hospital administration and not by the patient. Particulars of all the patients who meet the inclusion and exclusion criteria were recorded. Patients who present in ED after thrombolysis with streptokinase after anterior wall ST elevation myocardial infarction from any other non- percutaneous coronary intervention capable/percutaneous coronary intervention capable center were acknowledged. If the patient qualifies for facilitated percutaneous coronary intervention i.e. within 3-24 hours of fibrinolytic therapy, pathway for coronary angiogram with intent to perform percutaneous coronary intervention was initiated.

Results: Total 234 patients were included according to the inclusion criteria of the study. Mean age (years) in the study was 56.71 ± 15.83 with ranges from 18-70 years. There were 164 (70.1%) male and 70 (29.9%) female patients who were included in the study according to the inclusion criteria. Out of 234 cases, 21 (8.9%) cases presented with non-fatal MI (acute stent thrombosis), 16.23% died and 4 (1.7%) stroke patients noted in patients after thrombolysis with streptokinase suffering from anterior ST-elevation myocardial infarction.

Conclusion: The study concluded that those areas where percutaneous coronary intervention centers are not readily available, a pharmaco-invasive strategy can be proposed. As, this strategy comprises the use of fibrinolysis with subsequent transfer to a PCI-capable facility for angiography within 24 hours of presentation.

Keywords: Percutaneous coronary intervention, Pharmaco-invasive facilitated percutaneous coronary intervention, ST-segment elevation myocardial infarction.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is a life threatening manifestation of coronary artery disease (CAD) requiring timely reperfusion. The incidence of STEMI is higher in this population when compared to developed countries and results in significant mortality[1].

The current recommendations maintain primary percutaneous coronary intervention (PCI) as the treatment of choice in the management of STEMI, contingent upon rapid initiation of treatment at centers with a skilled PCI laboratory within suggested timelines. However, unavailability of primary PCI capable hospitals across Pakistan and delays in transport have restricted the access to this life-saving modality to <10% of patients with STEMI[2].

Of those, patients who do reach the hospital early still have to deal with other issues, such as arranging for finances, as most Pakistani patients pay out-of pocket, even for the emergency services, such as primary PCI[3].

On the other hand, introduction of fibrin-specific lytic agents like tenecteplase (TNK) has improved the infarct-related artery (IRA) patency rates significantly. Rapid fibrinolytic treatment after STEMI improved the outcomes in patients treated within an hour of symptom onset, with tapering benefits after 3 hours[4]. The time to treatment with primary PCI is an important determinant of the clinical outcome among patients who have had an acute myocardial infarction, and current guidelines from the American College of Cardiology call for a time of <90 minutes from the first medical contact to inflation of the balloon[5]. Conceptually, the

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door-to-balloon time may be most important for patients with potentially large infarcts who present early, since they have the most myocardium to salvage[6].

However, fibrinolysis is associated with high rates of re-occlusion of IRA, hence a strategy of initial bolus lysis followed by early coronary angiogram within 3–24 hof fibrinolysis, with an appropriate PCI, now known as pharmaco-invasive strategy or facilitated PCI, has been considered as a good alternative in the treatment of STEMI, especially in a developing country such as Pakistan[7].

Welsh *et al* shows that composite event rate for MACE were 18.7% vs 11.8% with primary PCI arm. This finding shows that pharmaco-invasive strategy as compared with primary PCI in the management of STEMI was equivalent in terms of composite primary outcome. There was no significant difference between the secondary outcomes between the two groups[7].

The question of the optimal pharmacologic therapy for reperfusion before and in conjunction with primary PCI, especially when there is a delay in the initiation of therapy, remains unanswered.

Fibrinolytic therapy alone was found to be harmful among patients in the Assessment of the Safety and Efficacy of a new treatment strategy with percutaneous coronary intervention (ASSENT-4 PCI) trial, possibly owing to the deleterious effects of early activation of platelets by the fibrinolytic agents without effective antiplatelet treatment or plaque hemorrhage at the time of PCI[8].

In areas where PCI centers are not readily available, a pharmaco-invasive strategy has been proposed. This strategy comprises the use of fibrinolysis with subsequent transfer to a PCI-capable facility for angiography within 24 h of presentation.

The objective of this study was to assess the safety, efficacy and outcomes of a pharmaco-invasive strategy in the context of a realworld regional system in Pakistan.

METHODOLOGY

This Cross-sectional study was conducted in the Armed Forces Institute of Cardiology and National Institute of Heart Diseases Rawalpindi from December 2020 to April 2021. A total of 234 patients aged between 18–70 years who had anterior wall STEMI and who underwent coronary angiogram with an intent to perform PCI within 3-24 hours of thrombolysis therapy were included in the study through non- probability consecutive sampling. Patients who were candidates of Primary PCI/CABG or who had old MI, previous PCI or CABG, dilated cardiomyopathy or were unwilling for PCI were excluded from the study.

The following operational definitions were taken:

1. Pharmaco-Invasive Facilitated PCI

Coronary angiogram with an intent to perform PCI within 3-24 hours of fibrinolytic therapy.

2. Anterior STEMI

ST-Elevation of 1 mm in leads V1 – V4 with chest pain of <12 hours duration.

3. Thrombolysis

Streptokinase at a dose of 1.5 million units administered I/V over 60 min. Outcomes was measured by any of the following

4. In Hospital Death

After primary PCI patient stays at hospital for at least 48 hours in a monitored post cath ward. In hospital death will be defined in this period.

5. Acute Stent Thrombosis (non-fatal MI)

The acute stent thrombosis occurs between zero to 24 hrs after coronary stent implantation confirmed when there is angiographic confirmation of stent thrombosis

6. Stroke

Acute hemorrhagic stroke will be taken sudden acute intracranial bleed with in 48 hours after confirmation on CT

scan brain .

7. Family History of CAD

Coronary heart diseases in first degree relatives having age <55 in male and <60 for female.

8. Hyperlipidemia

LDL >70mg/dl CAD and >100mg/dl in non CAD.

Permission was sought from hospital ethics committee. Written informed consent was taken from participants of study. Charges of the tests and procedures were borne by hospital administration and not by the patient. Particulars of all the patients who meet the inclusion and exclusion criteria were recorded in the Performa.

Patients who present in ED of AFIC/NIHD after thrombolysis with strep to kinase from any other non-PCI capable/ PCI capable center were acknowledged. If the patient qualifies for facilitated PCI i.e. within 3-24 hours of fibrinolytic therapy, pathway for coronary angiogram with intent to perform PCI was initiated and if the IRA qualifies for stenting, a second genera-

tion DES was placed in a TIMI II/III IRA artery by a consultant cardiologist on-call.

After that patients were shifted to post-catheterization wards where researcher cardiologist had follow-up the patients for MACE i.e. death, stroke or non-fatal MI in terms of acute stent thrombosis keeping in view the TIMI risk score, co-morbid and number of stents placed in IRA. All in-hospital outcome data was recorded in SPSS for statistical analysis by the cardiologist under supervision of his supervisor.

Statistical analysis was performed using statistical software SPSS-23. Mean and standard deviation was calculated for quantitative variable i.e. age, time to treatment. Frequency and percentage was calculated for qualitative variable i.e. MACE in terms of death, stroke, non-fatal MI (acute stent thrombosis), IRA lesion, stent(s) placed. Effect modifier like age, gender, diabetes, hypertension, and time to treat, TIMI score, number of stent(s) placed, MACE was controlled by stratification. Post stratification chi-square test was applied. *p*-value <0.05 was significant.

RESULTS

Data was entered and analyzed in SPSS version 23. A total of 234 patients were included according to the inclusion criteria of the study. Mean age (years) in the study was 56.71 ± 15.83 with ranges from 18-70 years. Mean time to treat in the study was 6.56 ± 1.86. There were 164 (70.1) male and 70 (29.9) female patients included in the study.

Out of 234 cases, there were 21 (8.9%) cases presented with non-fatal MI (acute stent thrombosis), 38 (16.23%) died and 4 (1.7%) cases presented with stroke. There were 174 (74.4%) patients of diabetes presented in the study with hyperlipidemia in 151 (64.5%) and hypertension in 200 (85.5%) patients.

Time to treat (PCI after thrombolysis) of <6 hours there were 8 (3.41%) cases presented with non-fatal MI (acute stent thrombosis), 16 (6.83%) died and 2 (0.85%) cases presented with stroke. Time to treat less (PCI after thrombolysis) of >6 hours there were 13 (5.5%) cases presented with non-fatal MI (acute stent thrombosis), 22 (9.40%) died and 2 (0.85%) cases presented with stroke.

TIMI score <2 there were 10 (4.2%) cases presented with non-fatal MI (acute stent thrombosis), 22 (9.4%) died and 1 (0.42%) cases presented with stroke. TIMI score >2 there were 11 (4.7%) cases presented with non-fatal MI (acute stent thrombosis), 16 (6.83%) died and 3 (1.28%) cases presented with stroke.

Regarding number of stents placed ≤2 have MACE (in hospital outcome), there were 8 (3.41%) cases presented with non-fatal MI (acute stent thrombosis), 18 (7.69%) died and 1 (0.42%) cases presented with stroke. In patents with stents placed more than 2 there were 13 (5.5%) cases presented with non-fatal MI (acute stent thrombosis), 20 (8.54%) died and 3 (1.28%) cases presented with stroke. Rests of the results are shown in the table-I, II & III

Table-I: Demographics and Co-morbids of study population (n= 234).

Variable	Mean ± SD / n(%)
Age (Mean ± SD)	56.71 ± 15.83
Gender	
Male	164 (70.1%)
Female	70 (29.9%)
Diabetes	174 (74.4)
Hypertension	200 (85.5)
Smoking	157 (67.1)
Hyperlipidemia	151 (64.5)
Family History	115 (49.1)
Diabetes	174 (74.4)
Hypertension	200 (85.5)

Table-II: Association between Co-morbids and MACE

	MACE (In-Hospital Outcomes)			*p*-value
	Non fatal MI (Acute stent thrombosis	Death	Stroke	
Age (Years)				
18-50	6 (2.56%)	9 (3.84%)	1 (0.42%)	0.476
51-70	15 (6.41%)	29 (12.39%)	3 (1.28%)	
Gender				
Male	12 (5.12%)	24 (10.25%)	2 (0.85%)	0.071
Female	9 (3.8%)	14 (5.88%)	2 (0.85%)	2
Diabetes Mellitus				
Yes	17 (7.26%)	32 (13.64%)	4 (1.7%)	0.040
No	4 (1.7%)	6 (2.56%)	-	2
Hypertension				
Yes	16 (6.83%)	30 (12.82%)	3 (1.28%)	0.049
No	5 (2.1%)	8 (3.41%)	1 (0.42%)	

Table-III: Association between effect modifiers and MACE.

	MACE (In-Hospital Outcomes)			*p*-value
	Non fatal MI (Acute stent thrombosis)	Death	Stroke	
Time to treat (for facilitated PCI from 3-24 hrs)				
≤6 hrs	8 (3.41%)	16 (6.83%)	2 (0.85%)	0.038
>6 hrs	13 (5.5%)	22 (9.4%)	2 (0.85%)	
TIMI Score				
≤2	10 (4.2%)	22 (9.4%)	1 (0.42%)	0.329
>2	11 (4.7%)	16 (6.83%)	3 (1.28%)	
No. of Stents placed				
≤ 2	8 (3.41%)	18 (7.69%)	1 (0.42%)	0.465
>2	13 (5.5%)	20 (8.54%)	3 (1.28%)	

DISCUSSION

PPCI is considered to be the best reperfusion option in STEMI when it can be performed in a timely fashion and by an expert team[9,10]. However, PPCI is not universally available, and delays in performing PPCI are common in real-world practice[11]. Even in some large cities, patients have a high chance of presenting to hospitals not providing around-the-clock PPCI service[12].

Pharmaco-invasive (PHI) strategy, an early reperfusion strategy encompassing initial prompt fibrinolysis with subsequent early catheterization, has been proposed as a therapeutic option for STEMI patients when timely PPCI is not feasible[13–15]. Clinical trials and registry data have shown that clinical outcomes with pharmaco-invasive strategy are comparable to the outcomes with PPCI[16-18]. However, current evidence on the efficacy and safety of a PhI strategy in patients with STEMI remains limited, and its role is a matter of debate. The recent STREAM trial showed that a PhI strategy could be a reasonable alternative to PPCI in STEMI patients presenting ≤3 hours of symptom onset and with an expected time delay from first-medical-contact (FMC) to PPCI >1 hour. The only downside of the PhI arm was that its rate of intracranial hemorrhage with full-dose tenecteplase was 5 times higher than that of the PPCI group. However, the difference was not significant after a trial protocol amendment reducing tenecteplase dose by 50% in the elderly[2]. The latter observation suggested that a half-dose fibrinolytic regimen might be a safe and effective option for PhI treatment in eligible patients with STEMI. Interestingly, in an observational registry study in the United States in patients with STEMI with long PCI-related delays, a PhI strategy utilizing half-dose fibrinolysis (97% tenecteplase, 3% reteplase) combined with transfer for PCI achieved similar efficacy outcomes as PPCI without increased bleeding risk. Consistent with these findings, in our pilot study in the Chinese population, early routine PCI after half-dose alteplase fibrinolysis appeared promising in the treatment of patients with STEMI who could not undergo timely PPCI[2].

In our study, mean age (years) in the study was 56.71 ± 15.83 with ranges from 18-70 years. Similarly, in a study conducted by Alex *et al*[6] found that mean age in years was 57.6 ± 12.2.

In our study, there were 164 (70.1%) male and 70 (29.9%) female patients. Likewise, in a study conducted in 2018[6] observed that frequency and percentage of male and female patients were 89 (93.7%) and 6 (6.3%) respectively.

In a study by Welsh *et al*[7] the composite event rate for MACE were 18.7% versus 11.8% with primary PCI arm. Likewise, the frequency and percentage of in-hospital outcomes of pharmaco-invasive procedure was 26.5% in the study.

CONCLUSION

The study concluded that those areas where PCI centers are not readily available, a pharmaco-invasive strategy can be proposed.

CONFLICT OF INTEREST

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

REFERENCES

1. Victor SM, Vijayakumar S, Alexander T, Bahuleyan CG, Srinivas A, Selvamani S, et al. Two-year follow-up data from the STEPP-AMI study: A prospective, observational, multicenter study comparing tenecteplase-facilitated PCI versus primary PCI in Indian patients with STEMI. Indian Heart J 2016; 68(2): 169-73.
2. Pu J, Ding S, Ge H, Han Y, Guo J, Lin R, et al. Efficacy and safety of a pharmaco-invasive strategy with half-dose alteplase versus primary angioplasty in ST-segment-elevation myocardial infarction: EARLY-MYO trial (early routine catheterization after alteplase fibrinolysis versus primary PCI in acute ST-segment-elevation myocardial infarction).Circulation 2017; 136(16): 1462-73.
3. Rashid MK, Guron N, Bernick J, Wells GA, Blondeau M, Chong AY, et al. Safety and efficacy of a pharmacoinvasive strategy in ST-segment elevation myocardial infarction: a patient population study comparing a pharmacoinvasive strategy with a primary percutaneous coronary intervention strategy within a regional system. JACC Cardiovasc Interv 2016; 9(19): 2014-20.
4. Dalal JJ, Alexander T, Banerjee PS, Dayasagar V, lyengar SS, Kerkar PG, et al. Consensus statement for early reperfusion and phar-maco-invasive approach in patients presenting with chest pain diagnosed as STEMI (ST elevation myocardial infarction) in an Indian setting. J Assoc Physicians India. 2014; 62(6): 473-83.
5. Sim DS, Jeong MH, Ahn Y, Kim YJ, Chae SC, Hong TJ, et al. Pharmacoinvasive strategy versus primary percutaneous coronary intervention in patients with ST-segment-elevation myocardial infarction: a propensity score-matched analysis. Circ Cardiovasc Interv 2016;9(9): e003508.
6. Alex AG, Lahiri A, Devika, Geevar T, George OK. Observational study comparing pharmacoinvasive strategy with primary percutaneous coronary intervention in patients presenting with ST elevation myocardial infarction to a tertiary care center in India. J Postgrad Med 2018; 64(2): 80-85.
7. Welsh RC, Van de Werf F, Westerhout CM, Goldstein P, Gershlick AH, Wilcox RG, et al. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the STrategic reperfusion early after myocardial infarction [STREAM] study). Am J Cardiol. 2014; 114(6): 811-19.
8. Frans Van De Werf. Assessment of the safety and efficacy of a new treatment strategy with percutaneous coronary intervention (Assent-4 PCI) investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-

segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. Lancet 2006; 367(9510): 569-78.
9. Jahic E. Experience and outcomes of primary percutaneous coronary intervention for patients with ST-segment elevation myocardial infarction of tertiary care center in Bosnia and Herzegovina. Med Arch. 2017; 71(3): 183–87.
10. Choudhury T, Magdi O. ST elevation myocardial infarction. Clin Med (Lond) 2016; 16(3): 277–82.
11. Lee SH, Kim HK, Jeong MH, Lee JM, Gwon HC, Chae SC et al. Pre-hospital delay and emergency medical services in acute myocardial infarction. Korean J Intern Med 2020; 35(1): 119–32.
12. Khraishah H, Alahmad B, Secemsky E, Young MN, ElGuindy A Siedner MJ. Comparative effectiveness of reperfusion strategies in patients with st-segment elevation myocardial infarction: a secondary analysis of the acute coronary syndrome quality improvement in Kerala (ACS QUIK) trial. Glob Heart 2020; 15(1): 68.
13. Zubaid M. Efficacy and safety of pharmacoinvasive strategy compared to primary percutaneous coronary intervention in the management of ST-segment elevation myocardial infarction: a prospective country-wide registry. Ann Glob Health 2020; 86(1): 13.
14. Capodanno D, Dangas G. Facilitated / pharmaco-invasive approaches in STEMI. Curr Cardiol Rev 2012; 8(3): 177–80.
15. Welsh RC, Werf FV, Westerhout CM, Goldstein P. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the STrategic reperfusion early after myocar-dial infarction [STREAM] study). Am J Cardiol 2014; 114(6): 811-19.
16. Larson DM, McKavanagh P, Henry TD, Cantor WJ. Reperfusion options for ST elevation myocardial infarction patients with expected delays to percutaneous coronary intervention. Interv Cardiol Clin 2016; 5(4): 439-50
17. Siontis KC, Barsness GW, Lennon RJ, Holmen JL, Wright RS, Bell MR. Gersh BJ. Pharmacoinvasive and primary percutaneous coronary intervention strategies in ST-elevation myocardial infarction (from the Mayo Clinic STEMI Network). Am J Cardiol. 2016; 117(12): 1904-10
18. Danchin N, Coste P, Ferrières J, Steg PG, Cottin Y, Blanchard D. FAST-MI Investigators. Comparison of thrombolysis followed by broad use of percutaneous coronary intervention with primary percutaneous coronary intervention for ST-segment-elevation acute myocardial infarction: data from thefrench registry on acute ST-elevation myocardial infarction (FAST-MI) Circulation 2008; 118(3): 268-76.

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