

COMPARISON OF SURVIVAL TIMES AMONGST PATIENTS UNDERGOING PRIMARY PERCUTANEOUS CORONARY INTERVENTION, PHARMACO-INVASIVE AND THROMBOLYTIC THERAPY FOR ACUTE ST ELEVATION MYOCARDIAL INFARCTION IN A TERTIARY CARE HOSPITAL: A SURVIVAL ANALYSIS

Javeria Kamran, Tahir Iqbal, Mehwish Ujala, Abdul Hameed Siddiqui, Siddra Ihsan*, Anum Tahir**, Sohail Aziz, Tariq Hussain Khattak, Shuja Abbas

Armed Forces Institute of Cardiology (AFIC)/National Institute of Heart Diseases (NIHD)/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Armed Forces Bone Marrow Transplant Centre/National University of Medical Sciences (NUMS) Rawalpindi Pakistan
**Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Background: Acute myocardial infarction remains a time-sensitive medical emergency associated with significant morbidity and mortality. Research supports the superiority of PPCI over fibrinolytic therapy that can improve outcomes when delivered within a specified timeframe, however; effectiveness of treatment options in the terms of survival over the period of time has not been tested in our setup.

Objective: To compare the survival times in patients with acute myocardial infarction treated with PPCI, PI and streptokinase.

Material and Methods: A prospective study was conducted in Armed Forces Institute of Cardiology, Rawalpindi from Jan 2016 to July 2018 using consecutive sampling. Total 294 patients fulfilling the inclusion criteria were stratified into three groups i.e group I patients who underwent PPCI and group II who underwent pharmaco-invasive therapy and group III who were administered streptokinase. All the groups were followed for 30 months. In this study the probability of the patients to survive after PPCI at the end of 6 months duration was found to be 96% for PPCI, 93% for PI and 75% for SK. Similarly, probability of the patients to survive at the end of 30 months in case of PPCI was 91%, 89% in case of PI and 64% for SK.

Conclusions: This study will help determine the benefits of PPCI over fibrinolysis in terms of survival and will play a pivotal role in policy decisions for sustainability of a 24/7 PPCI reperfusion strategy to decrease overall mortality related to acute myocardial infarction.

Keywords: Acute myocardial infarction, Primary percutaneous coronary intervention, Survival analysis.

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INTRODUCTION

Acute myocardial infarction (AMI) is a vital health issue worldwide. 40% of patients reporting to emergency department are diagnosed as ST Elevation Myocardial Infarctions (STEMI). In USA, 258,000 STEMI patients present in emergency department per year result in 7.3 per 10000 of STEMI incidence rate¹.

Acute Myocardial Infarction (AMI) occurs due to atherosclerotic plaque rupture leading to thrombolysis or coronary artery occlusion. Occlusive thrombus is then dealt with either by thrombolytic therapy (infusion of streptokinase),

mechanical initiation of coronary artery blood flow by wiring followed by angioplasty (stenting) within 90 minutes of STEMI diagnosis (PPCI) or pharmaco-invasive therapy (PI) which involves thrombolysis (streptokinase) followed later on by percutaneous transluminal coronary angioplasty (PTCA)².

Most STEMI patients do not report directly to a Cardiac Care facility leading to failure of performing PPCI within the recommended timeframe thus posing a significant logistic challenge in many healthcare systems across the world³. Decision at such a time regarding thrombolysis, transfer of a patient to PCI center despite the delay or PPCI for complete reperfusion is critical.

Correspondence: Dr Javeria Kamran, Department of Cardiology, AFIC/NIHD Rawalpindi Pakistan
Email: jk.ny@hotmail.com

Recent evidence suggests that there has been a decline in morbidity and mortality owing to medical and technical advances, improved accessibility to PCI centers and latest clinical guidelines for STEMI patients⁴.

Primary percutaneous Coronary Intervention (PPCI) is the best treatment option in patients reporting to emergency departments with ST-Segment Elevation Myocardial Infarction

flexible options for emergent reperfusion, we think that it may be of considerable interest to conduct similar work at our institution⁶.

The clinically relevant question with regard to reperfusion strategy is which treatment modality is better in terms of long term benefits and survival score in the event of availability of all treatment modalities? Evidence based research seconds the superiority of PPCI over

Table-I: Selection of participants in the study.

	Group 1(PPCI)	Group 2(PI)	Group 3(SK)
At the start of study	388 / 4 months out of 1000/year	135 pt reported in 2016	111 pt reported in 2016
Lost to follow up	188	87	65
Included in the study	200	48	46

(STEMI). As per European Society of Cardiology Guidelines, PPCI is indicated as class I treatment modality of STEMI patients⁵.

Evidence supports that PPCI reduces mortality and improves outcome in comparison to fibrinolytic and PI therapy⁵. Contemporary clinical trials demonstrated equivalency of early

fibrinolytic therapy, however, the effectiveness of treatment options in terms of long term survival has not been tested in our setup and data regarding long term prognostic outcomes is also unavailable.

The basic aim of this study is to compare the long-term survival benefits in patients with Segment Elevation Myocardial Infarction treated with PPCI vs Streptokinase and PTCA (PI) or Streptokinase (SK) only.

Table-II: Baseline clinical characteristics of participants according to the different treatment strategies.

		PPCI		PI		SK	
		n=200	%	n=48	%	n=46	%
Gender	Male	169	83.5	43	89.7	42	91.3
	Female	33	16.5	5	10.3	4	8.7
HTN		21.5	21.5	22	45.8	25	54.3
DM		33	16.5	21	43.8	20	43.5
Smoking		48	24	10	20.8	10	21.7
Family history of IHD		18	9	15	31.3	11	23.9
Previous H/O of IHD		2	.9	11	22.9	13	28.3

(3-12 hrs) routine post-thrombolysis PCI to standard PPCI in patients with STEMI eligible for reperfusion. In the light of encouraging results of trials comparing these two management strategies for STEMI which could give those patients more

MATERIAL AND METHODS

This was a prospective cross-sectional single centered study conducted in Armed Forces Institute of Cardiology using consecutive sampling for the duration of 2.5 years (Jan 2016 to July 2018).

The aim was primarily to compare in hospital short and long term outcome of primary PCI versus Pharmacoinvasive strategy (immediate fibrinolysis then coronary angiography with possible PCI within 3-24 hr or later) and thrombolytic therapy for reperfusion in eligible patients with STEMI. Ethical approval was sought from institutional review board coupled with patients signing written informed consent.

Patients were stratified into three groups.

In group I (PPCI), 388 patients were selected by consecutive sampling who presented in emergency within 12 hours of onset the symptoms of chest pain, ST segment elevation greater than 1mm or more in contiguous limb leads or greater than 2mm in contiguous chest leads and new LBBB on ECG were included in group I for PPCI as per hospital protocol.

Initial standard 12 lead ECG, taken/recorded immediately after the patient's admission to the emergency department was considered as baseline. Patients who had previous history of MI, signs of heart failure or CCF and critical patients who required ventilator support were excluded from the study. 188 patients were lost to

Group III (SK) constituted of patients who received thrombolytic therapy (streptokinase) were 111. Out of which 65 were lost to follow up and 46 were followed for 2.5 years prospectively as shown in table-I.

All the groups were followed for 2.5 years and data regarding complications and status of survival was updated at 6,12,18,24 and 30 months interval through contacts. Follow-up data were collected through contacts, the attending physicians, the patients, or their family.

Data Analysis

Statistical analysis was carried out using statistical software SPSS 23.

Mean and standard deviation was calculated for quantitative variables i.e. age and door to

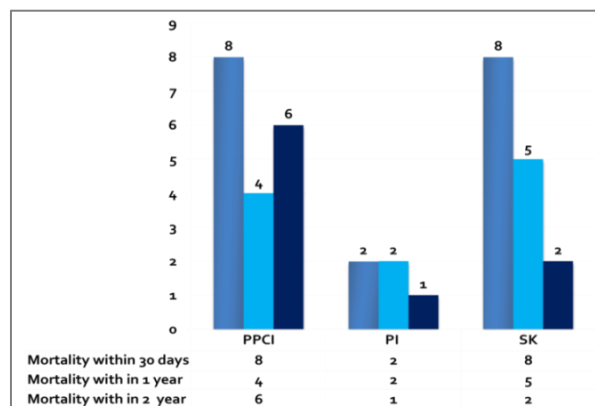
Table-III: Association between co-morbids and different treatment strategies.

		PPCI	PI	SK	P-value
Gender	Male	168	44	40	0.286
	Female	33	4	5	
HTN		43	26	21	0.000
DM		33	20	21	0.000
Smoking		48	10	10	0.170
Family history of IHD		18	11	15	0.000

follow up and finally 100 patients who met the study criteria for group I using consecutive sampling were selected as the study participants.

In group II (PI), 135 patients were selected who presented in emergency with MI but refused to undergo PPCI or came from periphery after administration of streptokinase or received streptokinase in AFIC emergency followed by PTCA (PI) with in hospital stay or at a later date were included in the second group. 87 were lost to follow up and finally 48 patients were followed for 2.5 years prospectively.

Table-IV: Comparison of mortality rates at 30 days, 1 year and 2 years amongst treatment groups.



balloon time. Frequency and percentage was calculated for qualitative variables i.e. gender, diabetes mellitus, hypertension and acute heart failure.

Chi-squared test was used for the comparison between qualitative variables. Statistically significant variables were identified with $p < 0.05$.

The cumulative probability of survival was determined by the Kaplan-Meier method, and statistically significant differences between curves were evaluated with the log-rank test.

RESULTS

From Jan 2016 to July 2018, 294 patients with STEMI without hemodynamic compromise underwent PPCI / PI or SK and were found suitable for the analysis. Out 294 patients, 200 underwent PPCI, 48 received PI treatment and 46 SK.

Clinical characteristics of participants in different treatment modalities are shown in table-II.

Patients in all treatment groups are mostly males (85%), SK group had more co-morbidities as

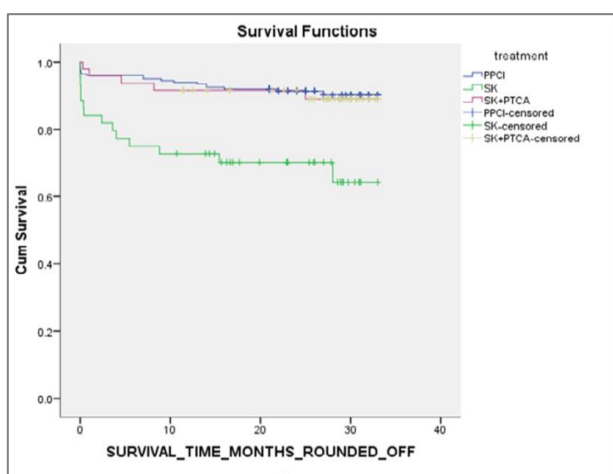


Figure-1: Comparison of overall survival experience between three treatment groups.

compared to other groups. Age of participants ranged from 28 to 76 years. In PPCI group 43 (21.5%) patients had HTN, 33 (16.5%) DM, 48 (24%) smoked and 18 (9%), 2 (2%) had F/H and previous history of IHD respectively. In PI group 22 (45.8%) patients had HTN, 21 (43.8%) DM, 10 (20.8%) smoked and 15 (31.3%), 11 (22.9%) had F/H and previous history of IHD respectively. Whereas, in SK group 25 (54.3%) had HTN, 20 (43.5%) DM, 10 (21.7%) smoked and 11 (23.9%), 13 (28.3%) had F/H and previous history of IHD respectively as shown in table-III.

Statistically significant association was seen between HTN, DM, F/H of IHD and different treatment modalities with the p -values $<.001$ whereas no statistically significant association was found between gender and F/H with p -

values of .286 and .170 and treatment groups respectively as shown in table-III.

Door to needle time for SK group was 19.29 ± 3.151 whereas door to wire time for PPCI group was 58.77 ± 70.77 .

Table-IV shows the comparison of mortality rates amongst different treatment groups over the period of 2.5 years.

Higher mortality rate of patients treated with SK 15 (32.63%) followed by 5 (10.42%) in PI and PPCI 18 (9%) in PPCI were observed at the end of period of 2.5 years.

Kaplan-Meier Curve provides the estimate of true survival function obtained by taking the product of a sequence of conditional probabilities. Survival curves were generated by the Kaplan-Meier method and compared with log-rank tests. Fig-1 Compares and illustrates the superiority of PPCI survival function throughout the course of 2.5 years whereas SK group has shown worst survival function. There is a dip in survival function seen in PI group at the start of study period and again at the end of 2 years time in comparison to the PPCI group.

Kaplan-Meier Estimate provides the cumulative proportion of the probability of survivors at the end of a particular time period. In this study the probability of the patients to survive after PPCI at the end of 6 months duration was found to be 96% for PPCI, 93% for PI and 75% for SK. Similarly probability of the patients to survive at the end of 30 months in case of PPCI was 91%, 89% in case of PI and 64% for SK.

Logrank test accounts for the difference in the prognostic factors between different treatment groups. Log Rank test compares the survival function curve at the later time period, Tarone Ware in the middle course and Breslow at the start of the course of time period. All three tests in the current study showed statistically significant p -values ($<.001$) throughout the course of time period between different treatment groups.

DISCUSSION

In last 25 years, high income countries encountered the burden of over half of IHD mortality but in latest years trend has been shifted to low-and-middle income countries. Rising trend in mortality i.e 80% in low and middle income countries is attributed to coronary heart diseases⁷.

Coronary artery disease is reported to be one of the leading causes of death all over the world. Therefore, PCI becomes the treatment of choice in dealing with the STEMI patients. To date, short and long term survival data are lacking in our setup⁸.

Three WHO defined goals for other countries on the basis of multiple experiences: 70% of all STEMI patients should be treated with primary PCI, Per year primary PCI rates should be more than 600/million inhabitants and PPCI should be first line treatment of choice in STEMI patients offering 24/7 services⁹.

Studies conducted before the introduction of PPCI proved the effectiveness of PTCA over thrombolysis; the fact supported by the current study too in terms of survival rates². A study conducted in Cairo by Abdalla M. Kamal reported mean door to balloon time 99.8 ± 32.8 min whereas in our study it was 58.77 ± 70.77 . In hospital mortality was reported to be 4.0% and mortality at the 6-month followup was reported in 12% of the participants whereas in our study the in hospital mortality was found to be 9% in case of PPCI, 10.41% in case of PI and 32.63% in case of SK% whereas 6 month mortality was .962 in case of PPCI, .93 in PI and .75 in SK¹⁰.

Our study has demonstrated the significance of time in relation to event (death) with regard to mortality risk after primary PCI for treatment of STEMI. In the first 7 days, there was a relatively high risk of death (3.04%) and within 1 year mortality rate was stable at 10.81%. A study conducted by Doost Hosseiny A reported similar result as 3.4% mortality within 7 days and 3.9% of within 1 year mortality 1 whereas <1 year mortality rate was stable in this study and was

reported as 10.81%. Seven day mortality in case of PPCI is 4 (2.52%) owing to the delay in transportation and severity of condition of patients, 4 (8.69%) in case of SK and 1 (2.41%) in PI group. Thirty day mortality in case of PPCI is 4 (2.52%), 6 (13.04%) in case of SK and 1 (2.41%) in PI group whereas 1 year mortality in case of PPCI is 13 (6.52%), 12 (26.08%) in case of SK and 7 (14.58%) in PI group. Mortality rate after STEMI has decreased over the past two years in parallel with more widespread use of evidence-based treatments including primary PCI and pharmacoinvasive therapy. SWEDHEART study conducted for over 10 years reported the decrease in mortality from 21% to 13.3% and management of STEMI increased from 12% to 61% and reperfusion therapy from 66% to 79%¹¹.

PPCI trend over the period of years have increased to over 55% in past years whereas in another study the rate of hospital PCI, increased from 19.5% to 86.7%¹².

The long-term follow-up data retrieved from multiple studies permitted us to show uniformity of these findings in favor of primary PCI as supported by our study¹³.

Limitation of this study was small sample size, type of thrombolytic agents, difference in time of administration of thrombolytic agent, speed of administration and transfer times were likely to be different.

CONCLUSION

This study will help determine the benefits of PPCI over fibrinolysis in terms of survival and will play a pivotal role in policy decisions for sustainability of a 24/7 PPCI reperfusion strategy to decrease overall mortality related to acute myocardial infarction.

CONFLICT OF INTEREST

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

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