PHARMACOVASIVE VERSUS THROMBOLYSIS IN STEMI COHORT – OUTCOMES FROM A TERTIARY CARE CENTRE OF NORTH INDIA

Cardiology

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ABSTRACT

STEMI is an event where transmural myocardial ischemia induces myocardial necrosis. PI strategy is a promising strategy in the management of STEMI. It is prospective registry study conducted in Cardiology Department, KGMU between January-June 2016 to know 30 day outcome of thrombolysis alone or thrombolysis followed by PCI in north India. At 30 day follow up, patients undergoing PI strategy, complained less of angina and dyspnea compared to thrombolysis arm.

KEYWORDS

STEMI, PI, ECG

INTRODUCTION

ST-Elevation Myocardial Infarction (STEMI) is a serious heart attack that blocks one of the arteries supplying the heart muscle with oxygen and nutrient-rich blood, associated with persistent electrocardiogram (ECG) ST elevation and subsequent release of myocardial necrosis biomarkers.

Patients of STEMI can be managed by primary percutaneous coronary intervention (primary PCI), thrombolysis, pharmacoinvasive strategy (PI) or optimal medical therapy. However, approved therapies for the treatment of STEMI largely involves thrombolysis and primary PCI.

Primary PCI was more effective than thrombolysis in the STEMI therapy, the main constraint being limited availability and logistically challenging in countries like India. Since there are often delays in restoring successful reperfusion, thrombolysis seems to remain an option for prompt reperfusion. Fibrinolytic therapy, however, has limitations, even if the best thrombolytic agent currently available is used (recombinant tissue plasminogen activator-rTPA). Thus, to overcome this, and to avail the combined benefit of thrombolysis and mechanical revascularization, PI strategy is a promising strategy in the management of STEMI. Patients undergoing thrombolysis as initial management further go for PI therapy within 24 hours (Fernandez-Avilés *et al.*, 2004; White, 2008). The present research was therefore planned to study the outcome in patients undergoing treatment by either PI strategy or thrombolysis and predictors of mortality in both groups of patients.

MATERIAL AND METHODS

The present study was a prospective registry study conducted in Cardiology Department, King George Medical University between January-June 2016 to know 30 day outcome of thrombolysis alone or thrombolysis followed by PCI in north India. The predictors of major adverse cardiovascular outcome (MACE) in both the groups were studied. After STEMI diagnosis, all patients (>18 years) who were screened and either referred from periphery or presenting at tertiary care centre, undergoing thrombolysis within 12 hours, were included in the study while those willing to undergo primary PCI and/or having contraindication to thrombolysis were excluded from the study. After obtaining informed consent, all patients were loaded with 325mg aspirin, 300mg clopidogrel and 80mg atorvastatin. All patients were thrombolysed with streptokinase. Following thrombolysis, patients with informed consent were taken for PCI within 24 hours of symptom onset (PI approach). In multi-vessel disease (MVD), performance of infarct related artery was also at operator's discretion. Patients were transferred to coronary care unit post procedure and discharged on the third day when hemodynamically stable. The primary outcome was MACE upto 30 days while secondary outcomes consisted of occurrence of angina and dyspnea in patients till 30 days. At 30 days,

all patients were reviewed in the outpatient department or contacted telephonically. All statistical analysis comprised of calculating means and proportions. Fischer's exact test was used to test differences in categorical measures. Statistical significance was set at $p < 0.05$.

RESULTS

Out of total 856 patients screened as STEMI, 199 patients (96 patients underwent primary PCI, 34 patients sent for rescue PCI, 69 patients didn't receive any reperfusion therapy) were excluded from the study, 285 underwent PI therapy and 372 received thrombolysis alone (Table 1). Table 1 also shows other baseline characteristics of the study.

Table 1: Baseline Characteristics Of The Study Subjects

Variables	Groups	PI N= 285	Mean	Only Thrombolysis N=372	Mean
Age	<35	21(7.30%)	52.90±10.87	36(9.6%)	54.39±14.42
	>35-45	65(22.80%)		67(18.01%)	
	>45-55	78(27.36%)		104(27.95%)	
	>55-65	95(33.33%)		115(30.91%)	
	>65	26(9.12%)		50(13.44%)	
Sex	Male	257(90.17%)		329(88.44%)	
	Female	28(9.83%)		43(11.83%)	
MI type	AWMI	167(58.59%)		206(55.37%)	
	NON-AWMI	118(41.41%)		166(44.62%)	
Smoking	Present	160(56.14%)		239(64.25%)	
Hypertension	Present	55(19.29%)		67(23.50%)	
Diabetes	Present	71(24.91%)		74(19.89%)	
Heart rate		81.67±13.45bpm		80.82±9.57bpm	
LVEF	<35%	1(0.35%)		14(3.76%)	
	35-45%	122(42.80%)		162(43.54%)	
	>45%	162(56.84%)		182(48.92%)	
Kilip class	1	261(91.58%)		313(84.14%)	
	2	17(5.96%)		23(6.18%)	
	3	2(0.70%)		8(2.15%)	
	4	2(0.70%)		27(7.26%)	
Creatinine Clearance	<15	2(0.70%)		32(8.60%)	
	15-30	2(0.70%)		11(2.96%)	
	>30-60	48(16.84%)		69(18.55%)	
	>60-90	158(55.44%)		155(41.67%)	
	>90	75(26.32%)		105(28.23%)	

Mean time from Symptom to Thrombolysis		5.70 hours		5.39 hours	
Mean time from Symptoms to Balloon		22.99 hours			
Mean time from Thrombolysis to Balloon		17.8 hours			

Furthermore, angiographic findings in patients going for PI strategy revealed that final TIMI 3 flow was achieved in 89.82% of patients (Figure 1).

Figure 1: Angiographic Findings

Table 4: Factors Affecting Mortality In Each Group

Variables	Groups	PI survivors N=268	PI non survivors (n=17)	% of non survivors	p-value	OR	Thrombolysis survivors (n=308)	Thrombolysis non survivors (N=64)	% of non survivors	p-value	OR
Age	<35	20	1	4.76%	0.029	Ref.	34	2	5.55%	<0.001	Ref.
	>35-45	63	2	3.07%			60	7	10.44%		
	>45-55	77	1	1.28%			93	11	10.57%		
	>55	108	13	10.74%			121	44	26.66%		
Sex	Male	244	13	5.05%	0.0025 ⁵	0.32	272	56	17.07%	0.8548	0.93
	Female	24	4	14.28%			36	8	18.18%		
MI	Non AAMI	116	2	1.69%	0.011	0.17	146	20	12.04%	0.018	0.50
	AAMI	152	15	8.9%			162	44	21.35%		
Smoking	NO	118	7	5.60%	0.8182	0.89	111	23	17.16%	0.9877	1.004
	Yes	150	10	6.25%			197	41	17.22%		
HTN	NO	215	15	6.52%	0.549	1.85	252	53	17.37%	0.9923	1.07
	Yes	53	2	3.63%			56	11	16.66%		
LVEF	<35	01	0	0	0.003	-	14	14	100%	<0.0001	1.76 (<45vs >45)
	>35-45	108	14	11.47%			136	26	16.04%		
	>45	159	3	1.85%			158	24	13.18%		
Timi Flow	0	0	2	100%	<0.001	57.21 (0+1 vs 2+3)					
	1	1	1	50%							
	2	13	12	48%							
	3	254	2	1.55%							
MVD		129	10	7.19%	0.393	0.65					
SVD		139	7	4.79%	0.393	1.54					
Diabetes	No	202	12	5.60%	0.658	1.28	254	44	14.76%	<0.001	0.47
	Yes	66	5	7.04%			54	20	27.07%		
Kilip Class	1	249	15	5.68%	0.0694	0.18 (1+2 vs 3+4)	276	41	12.93%	<0.0001	0.11 (1+2 vs 3+4)
	2	16	1	5.88%			18	4	18.18%		
	3	1	1	50%			4	3	45%		
	4	2	0	0			10	16	61.53%		
CrCl	<15	2	0	0	0.959	0.58 (<60 vs >60)	12	19	61.29%	<0.0001	5.95 (<60 vs >60)
	>15=30	2	0	0			4	8	66.66%		
	>30-60	46	2	4.16%			55	14	20.28%		

Table 2 shows the primary endpoint which was a composite of MACE at 30 days. For all adverse events the odds were higher in thrombolysis compared to PI group.

Table 2: Comparison Of Primary Outcomes In Thrombolysis Vs Pharmacoinvasive Group

		Thrombolysis (n=372)		PI(n=285)		Statistical significance	
		No.	%	No.	%	p-value	OR
Death	Dead	64	17.20	17	5.96	<0.0001	3.276
Stroke	Present	3	0.81	1	0.35	0.637 ⁵	2.309
Major Bleeding	Total	8	2.15	4	1.40	0.479	1.54
Rehospitalization	HF Present	14	3.76	3	1.05	0.030	3.676
	MI Present	18	4.84	3	1.05	0.006	4.78
	Total	32	8.60	6	2.11	<0.001	4.38
Primary Outcome	Total	107	28.76	28	9.82	<0.001	3.71

⁵Fisher exact test

The secondary outcomes of angina and dyspnea at 30 day follow up was significant in patients undergoing only thrombolysis(p<0.0001 and p=0.017)(Table 3).

Table 3 Secondary Outcomes In Thrombolysis And PI Group At 30 Days Follow Up

Variable	Outcomes	Only Needle (n=298)		PCI+Needle (n=268)		Statistical significance	
		No.	%	No.	%	p-value	OR
Angina	Present	63	21.14	26	9.70	<0.0001	2.495
Dyspnoea	Present	35	11.74	16	5.97	0.017	2.096

Factors affecting mortality were represented in table 4. In both groups, odds of mortality showed significant incremental trend with increasing age.

>60-90	148	10	6.32%		144	11	7.09%		
>90	70	5	6.66%		93	12	11.42%		

Table 5 showed that there occurred maximum deaths when patient was thrombolized, maximum between 9-12 hours ($p < 0.001$).

Table 5: Relationship between Symptoms to Time to thrombolysis and Primary Clinical Outcomes of Patients Undergoing Thrombolysis

	Outcomes	<3hr (n=110)	>3-6hr (119)	>6-9hr (86)	>9-12hr (n=54)	>12hr (n=3)	p value
Death	Dead	8 (7.27%)	17 (14.28%)	16 (18.60%)	22 (40.74%)	1 (33.33%)	<0.001
Stroke	Present	0	1(0.84%)	0	2(3.70%)	0	0.122
Bleeding	Total	0	1 (0.84%)	2 (2.32%)	2 (3.70%)	2 (66.66%)	<0.001
Rehospitalization	HF Present	1 (0.90%)	4 (3.36%)	7 (8.13%)	2 (3.70%)	0	0.126
	MI Present	1 (0.90%)	3 (2.52%)	6 (6.97%)	8 (14.81%)	0	0.001

DISCUSSION

The core aim of therapy for STEMI is the prompt restoration of antegrade flow. Delay in reperfusion is associated with higher mortality and morbidity rates. Timely reperfusion results in better myocardial salvage and preservation of left ventricular function.

The mean age of presentation in our study was comparable to NE ACS registry (Iqbal & Barkataki, 2016) while it was much higher in other studies (Fox *et al.*, 2002; Armstrong *et al.*, 2013). This showed that Indians present 10 years prior to the western population with CAD. Our study also showed much lesser females (9.9%), probably because of various factors like atypical ACS presentation in women, ignorance among majority of females, more of rural areas near tertiary centre etc.

Approximately 57% of our patients were admitted with the diagnosis of AWMi and 43.02% were non-AWMi which seemed to be in concordance with the STREAM (Armstrong *et al.*, 2013). The presence of various modifiable risk factors in our study was comparable to other studies (Investigators, 1993; Le May *et al.*, 2005; Xavier *et al.*, 2008). Similar to our study, much lesser population in higher Killip class was reported in STREAM (Armstrong *et al.*, 2013). Delayed presentation was one of the most important factors in our study determining the poor primary outcomes as compared to western data. All patients were thrombolized with streptokinase as reported for patients in CREATE registry (Xavier *et al.*, 2008). Final TIMI 3 flow was comparable to other studies such as CAPITAL AMI (Le May *et al.*, 2005) thus filling the distal coronary bed almost completely. Meta-analysis of trials of early PI strategy vs thrombolysis followed by ischemia based management shows early PI benefits over thrombolysis (Borgia *et al.*, 2010).

At 30 day follow up, patients undergoing PI strategy, complained less of angina and dyspnea compared to thrombolysis arm. This also somehow proves that, if artery is open and flow is established, the penumbra region around the infarction can be saved and hence LV remodeling will be better. It has been suggested that combining early pre-hospital thrombolysis with PCI may result in the greatest reduction in mortality (Smalling & Giesler, 2003).

REFERENCES

- Armstrong, P. W., Gershlick, A. H., Goldstein, P., Wilcox, R., Danays, T., Lambert, Y., ... Welsh, R. C. (2013). Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*, 368, 1379-1387.
- Borgia, F., Goodman, S. G., Halvorsen, S., Cantor, W. J., Piscione, F., Le May, M. R., ... Scheller, B. (2010). Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a meta-analysis. *European heart journal*, 31(17), 2156-2169.
- Fernandez-Avilés, F., Alonso, J. J., Castro-Beiras, A., Vázquez, N., Blanco, J., Alonso-Brales, J., ... Martínez-Elbal, L. (2004). Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *The Lancet*, 364(9439), 1045-1053.
- Fox, K. A., Goodman, S. G., Klein, W., Brieger, D., Steg, P. G., Dabbous, O., & Avezum, A. (2002). Management of acute coronary syndromes. Variations in practice and outcome. Findings from the Global Registry of Acute Coronary Events (GRACE). *European heart journal*, 23(15), 1177-1189.

- Investigators, G. (1993). An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *New England Journal of Medicine*, 329(10), 673-682.
- Iqbal, F., & Barkataki, J. (2016). Spectrum of acute coronary syndrome in North Eastern India—a study from a major center. *Indian heart journal*, 68(2), 128-131.
- Le May, M. R., Wells, G. A., Labinaz, M., Davies, R. F., Turek, M., Leddy, D., ... Beanlands, R. S. (2005). Combined angioplasty and pharmacological intervention versus thrombolysis alone in acute myocardial infarction (CAPITAL AMI study). *Journal of the American College of Cardiology*, 46(3), 417-424.
- Smalling, R. W., & Giesler, G. (2003). The level I cardiovascular center: is it time? *American Heart Hospital Journal*, 1(2), 170-174.
- White, H. D. (2008). Systems of care: need for hub-and-spoke systems for both primary and systematic percutaneous coronary intervention after fibrinolysis: Am Heart Assoc.
- Xavier, D., Pais, P., Devereaux, P., Xie, C., Prabhakaran, D., Reddy, K. S., ... Thanikachalam, S. (2008). Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *The Lancet*, 371(9622), 1435-1442.