Comparison of Thrombolysis Outcome in Early and Late Thrombolysis in Acute STEMI Patients

Dr. Uddhav Khaire[1], Dr. Shweta Shinde[2]

[1]MD Medicine, Associate Professor, Department of General Medicine, Govt. medical college Aurangabad, India

[2]MD Medicine, Junior Resident, Department of General Medicine, Govt. medical college Aurangabad, India

Abstract: _Introduction:_ _"A short distance from its origin, the left coronary artery was completely obstructed by a red thrombus that had formed at a point of great narrowing…The hope for the damaged myocardium lies in the direction of securing a supply of blood"(James B Herrick. 1912.) Acute myocardial infarction is usually due to disruption of an atherosclerotic plaque in a coronary artery followed by thrombus formation. The complete occlusion of the lumen of a major epicardial coronary artery leads to acute ST – Elevation Myocardial Infarction (STEMI). Prompt, complete and sustained restoration of antegrade flow in the infarct related artery is essential to salvage the myocardium at risk, improve ventricular function and reduce short term morbidity and mortality.[1] Thrombolytic therapy for acute myocardial infarction reduces case fatality and improves clinical outcomes.[6,7] The thrombolytic agent available for clinical outcome in our study is streptokinase._ _Material and methods:_ _We conducted cross sectional observational study in 200 patients of acute ST segment elevation myocardial infarction. Outcome of early (within 6 hours) and late (after 6 hours) thrombolysis in patients of STEMI studied and compared._ _Results:_ _In our study 148 males were admitted while 52 were females showing male predominance in acute STEMI. Maximum number of patients (26.5%) were from age group 61-70 yrs. The outcome of therapy showed that 18 % patients of STEMI were died and 82 % were discharged from hospital About the complication after receiving thrombolytic therapy 37 % were in cardiogenic shock, 27.5 % land up in CCF, 15% showed arrhythmias, 12.5 % were having Post infarction angina and very few patients 4.5 % having reinfarction & bleeding 2.5%. most of cases 85 (42.5 %)ST segment resolution > 50% were seen where there is initiation of therapy before 6 hours, whereas only 41 (20.5%) of cases shows improve ST segment > 50% after 6 hours of initiation of therapy._ _Conclusion:_ _Complications like cardiogenic shock, CCF were significantly less in patients thrombolysed within 6 hours of onset of chest pain compared to those who thrombolysed after 6 hours, however no difference in death rate was observed in both groups. Patients who were thrombolysed earlier had better ST segment resolution and better outcome than who were thrombolysed later._

1. Introduction

"A short distance from its origin, the left coronary artery was completely obstructed by a red thrombus that had formed at a point of great narrowing…

The hope for the damaged myocardium lies in the direction of securing a supply of blood"

- James B Herrick. 1912

Acute myocardial infarction is usually due to disruption of an atherosclerotic plaque in a coronary artery followed by thrombus formation. The complete occlusion of the lumen of a major epicardial coronary artery leads to acute ST – Elevation Myocardial Infarction (STEMI). Prompt, complete and sustained restoration of antegrade flow in the infarct related artery is essential to salvage the myocardium at risk, improve ventricular function and reduce short term morbidity and mortality[1]. Cardiovascular diseases, especially coronary heart disease (CHD), are epidemic in India. The Registrar General of India reported that CHD led to 17% of total deaths and 26% of adult deaths in 2001-2003, which increased to 23% of total and 32% of adult deaths in 2010-2013. The World Health Organization (WHO) and Global Burden of Disease Study also have highlighted increasing trends in years of life lost (YLLs) and disability-adjusted life years (DALYs) from CHD in India. In India, studies have reported increasing CHD prevalence over the last 60 years, from 1% to 9%-10% in urban populations and <1% to 4%-6% in rural populations[2].The most common form of CHD is the myocardial infarction. It is responsible for over 15% of mortality each year, among the vast majority of people suffering from non-ST-segment elevation myocardial infarction (NSTEMI) than ST-segment elevation myocardial infarction (STEMI). The prevalence of myocardial infarction (MI) is higher in men in all age-specific groups than women. Although the incidence of MI is decreased in the industrialized nations partly because of improved health systems and implementation of effective public health strategies, nevertheless the rates are surging in the developing countries such as South Asia, parts of Latin America, and Eastern Europe [3].

Since 1987 Anthon K et al. work on critical role of coronary thrombosis in acute myocardial infarction has been confirmed. This provides the scientific basis for thrombolytic therapy, the advent of which has been the cause of much global excitement and revolutionized the treatment of AMI[4].

In acute myocardial infarction, early identification of patients at a high mortality risk is important for planning further therapeutic strategies. Previous studies have demonstrated that the extent of early resolution of ST-segment elevation may represent a simple, quick and noninvasive assessment to identify high risk groups of patients[5].

Thrombolytic therapy for acute myocardial infarction reduces case fatality and improves clinical outcomes[6,7].

However, in up to 60% of patients the treatment does not restore perfusion in the myocardium at risk[8] and such failure indicates a worse prognosis[9].

By contrast, ST segment resolution 90–180 minutes after thrombolysis is an excellent marker of successful myocardial reperfusion [10] and a strong predictor of survival and preservation of left ventricular function[11-13].

In most regions in the world in general, and in Europe in particular, thrombolytic therapy is still the fastest and best accessible reperfusion treatment for most patients presenting with acute STEMI, as indicated in the international guidelines [14-15].

Therapy of acute ST-elevation myocardial infarction (STEMI) has undergone dramatic improvements during the past three decades, and in-hospital and 30-day mortality rates have tremendously decreased from .15–20% in the pre-thrombolytic area to 8–10% using fibrin-non-specific agents, to 6–8% using fibrin-specific thrombolytic agents. Registry data show mortality rates of .20% in patients who do not undergo reperfusion therapy within 12 h, of 10% in thrombolysed patients, and of up to 6–8% in patients treated by PPCI. The overall success rate depends not only on the individual patient's risk (high-risk patients, e.g. patients in cardiogenic shock, or the elderly, usually have not been included into controlled trials) [16,17] but also on the optimal organization and the use of the available reperfusion strategies.

The thrombolytic agent available for clinical outcome in our study is streptokinase.

2. Material and methods

A cross sectional observational study at a tertiary healthcare hospital. The study was conducted after formal approval from institutional ethics committee. The study was conducted with 200 patients of acute STEMI includingdiagnosed cases of Acute ST elevated myocardial infarction as per WHO criteria requiring at least 2 of following 3 elements to be present1.History of ischemic type of chest pain (resting chest pain lasting for more than 30 minutes).2.Evolutionary change on serially obtained ECG tracings (atleast 2 mm in adjacent chest leads and/or ST segment elevation atleast 1 mm in 2 or more standard leads)3.A rise of serum cardiac markers. Patients who are eligible for the study and who received streptokinase and patients above 18 years of age excluding patients Below 18 years of age,Those patients who are not willing,Patients with recent history of stroke, active bleeding, recent major operation, recent non compressible vascular puncture, previous treatment with streptokinase and patient those who have contraindication for thrombolytic therapy.

The demographic features of patients were recorded which included age ,sex,dateadmission,date of discharge,date of death. Baseline screening process and recording done includingDetail clinical history**,**Thorough clinical examination**,**Routine blood investigation-blood group, complete blood count, kidney function test, liver function test, blood sugar level, lipid profileElectrocardiogram (ECG).

2.1 Procedure of data collection

After applying inclusion and exclusion criteria total cases were studied.Data was collected from cases with proforma on admission till discharge from ICCU or death. Detailed case proforma used which is already validated by department faculties for entering all details of patient. After written valid informed consent of patient and her relatives, case proforma filled with all details like basic demographic data name, age, sex, clinical features on arrival, previous significant histories contributing to the present condition (DM / HTN / H/o old MI), habits like smoking / alcoholism are recorded. After initial diagnosis, details regarding the status of the patient on admission with respect to vitals, killip's classification and ECG.

The samples were categories by using blood pressure by using American college of cardiology / American heart association hypertension guidelines.

Analysis of data is done using SPSS Inc., (Statistical Program for Social Science Inc.,) Chicago, IL, USA, version 20. Qualitative variables were expressed as frequency and percentage. Chi-square test, Logistic Regression, ANNOVA was used to compare qualitative variables. Level of significance "P" value was evaluated, where P value < 0.05 was considered statistically significant. Multivariable logistic regression analysis was done to identify independent risk factors for mortality.

3. Results

A study of early & late thrombolytic therapy in patients with acute STEMI studied in 200 cases. Data were analysed using computer based SPSS software by frequency, percentage etc. The p-value < 0.05 was considered as statistically significant.

Table 1: Age & sex distribution of study populationn = 200

AGE (in years)	No. of cases		
	Male	Female	Total
21-30	06 (3 %)	01 (0.5 %)	07 (3.5 %)
31-40	14 (7 %)	03 (1.5 %)	17 (8.5 %)
41-50	42 (21 %)	07 (3.5 %)	49 (24.5 %)
51-60	36 (18 %)	14 (7 %)	50 (25 %)
61-70	33 (16.5 %)	20 (10 %)	53 (26.5 %)
≥ 71	17 (8.5 %)	07 (3.5 %)	24 (12 %)
Total	148 (74%)	52 (26 %)	200

In present study of 200 samples most of cases were above 40 years of age. Maximum number of cases 53 (26.5%) belongs to 61-70 years followed by 50 (25%) were belongs to 51-60 years, 49 (24.5%) in 41-50 years, 24 (12%) belongs to > 71 years and 17 (8.5%) in 31-40 years of age group.

Also in present study out of 200 samples males were having 148 (74 %) samples and females were having 52(26 %) samples of total study population.

The mean age was 56.58 and standard deviation was 12.88.

Table 2: Distribution of cases according time of initiation of therapy (n = 200)

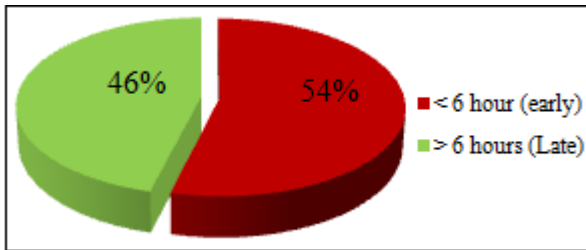| Sr.No.	Time	No. of cases	Percentage
1	< 6 hours (Early)	108	54.00
2	> 6 hours (Late)	92	46.00

Figure 1: Cases acc. to time of thrombolytic therapy

In present study of 200 samples maximum number of cases 108 (54 %) were received thrombolytic therapy before 6 hours from attack of AMI, whereas 92 (46 %) cases were received therapy after 6 hours from initial attack of AMI.

Table 3: Distribution of cases according complication, n = 200

S.N.	Time	No. of cases	Percentage
1	Reinfarction	09	04.50
2	Post infarction angina	25	12.50
3	Arrhythmias	30	15.00
4	Bleeding	05	02.50
5	Cardiogenic Shock	74	37.00
6	CCF	55	27.50

In present study of 200 samples maximum number of cases 74 (37%) went in cardiogenic shockinspite of thrombolytic therapy whereas 55 (27.50 %)were developed CCF. The other complication seen in cases were arrhythmias 30(15 %) cases, post infarction angina in 25 (12.5 %) cases, reinfarction in 9 (4.5 %) and bleeding in 5(2.5 % of cases).

Table 4: Correlation of ST segment resolution and time of initiation of therapy (n = 200)

Time	ST segment resolution		Odds ratio	95 % of CI	P – value
	< 50%	> 50%			
< 6 hours (Early)	23 (11.5%)	85 (42.5%)	4.60	2.48 – 8.52	0.000
> 6 hours (Late)	51 (25.5%)	41 (20.5%)	0.22	0.12 – 0.40	0.000

23 (11.5%) cases show < 50% ST segment before 6 hours of therapy and 51 (25.5%) cases have < 50% ST segment after 6 hours of therapy.

It was found that there was significant Correlationbetween time of initiation of therapy and ST segment improvement (p < 0.05).

Table 5: Correlation of individual complication with time of initiation of therapy (n = 200)

Complication	Time of initiation of therapy		Odds ratio	95% confidence interval	p-value
	< 6 hrs	> 6 hrs			
Reinfarction	5 (2.5 %)	4(2 %)	0.936	0.244 – 3.595	0.249
Post infarction angina	14 (7 %)	11(5.5 %)	0.912	0.392 – 2.120	0.830
Arrhythmias	17(8.5 %)	13(6.5 %)	0.881	0.403-1.926	0.751
Bleeding	01(0.5 %)	04(2 %)	4.864	0.534- 44.308	0.161
Cardiogenic Shock	23(11.5 %)	32(16 %)	1.995	1.115-3.571	0.020
CCF	26(13 %)	29 (14.5 %)	2.004	1.067-3.765	0.031

In present study of 200 samples, correlation between complication and time of initiation of thrombolytic therapy shows that in< 6 hrs. of initiation of therapy cardiogenic shock 23(11.5%) was seen followed by CCF 26(13%). Similarly in initiation of thrombolytic therapy shows that in> 6 hrs. of initiation of therapy cardiogenic shock 32(16%) was seen as most of cases followed by CCF 29(14.5%).

It was found that there was significant correlationbetween of initiation of therapy and complication such as cardiogenic shock and CCF (p < 0.05).

Table 6: Comparison of outcome with time of initiation of therapy (n = 200)

Outcome	Time of initiation of therapy		Odds ratio	95% confidence interval	p-value
	< 6 hrs	> 6 hrs			
Death	18 (9 %)	18 (9 %)	1.22	0.59 – 2.50	0.595
Discharged	90 (45 %)	74 (37 %)	0.82	0.40 – 1.69	0.712

In present study of 200 samples, there is no difference between the mortality in both groups of time of initiation of therapy as 18(9 %) cases died < 6 hrs. &> 6 hrs., of thrombolytic therapy. Data was not found statistically significant as p > 0.05.

4. Discussion

This study is to describe the time intervals leading to delay in thrombolytic therapy and to describe the influence of patient's clinical characteristics to delay in thrombolytic therapy in the sample of patients

Age distribution:In present study of 200 samples most of cases were above 40 years of age. Maximum number of cases 53 (26.5%) belongs to 61-70 years followed by 50 (25%) were belongs to 51-60 years, 49 (24.5%) in 41-50 years, 24 (12%) belongs to > 71 years and 17 (8.5%) in 31-40 years of age group. This is consistent with similar studies seen in below table A.

Table A: Age Distribution

Study	Present study	French et.al.[19]	Anderson et al.[13]	Karthik S.[20]	Sameer S. et al.[18]
Year	2019	2001	2002	2014	2015
Place	--	New Zealand	USA	Tamilnadu	Peshawar
Sample size	200	869	2352	60	83
Study type	Observational	Prospective	GUSTO-III TRIAL	Cross sectional	Descriptive
Result					
Mean age	56.58	56.9	62	53	52.93

Sex distribution:

In present study out of 200 samples males were having 148 (74 %) samples and females were having 52(26 %) samples of total study population. Male to female ratio was approximately 2.85:1. The findings are comparable with other studies as shown in table B;

Table B: Sex Distribution

Study	Present study	French et.al.[19]	Anderson et al.[13]	Karthik S.[20]	Sameer S. et al.[18]
Year	2019	2001	2002	2014	2015
Place	--	New Zealand	USA	Tamilnadu	Peshawar
Sample size	200	869	2352	60	83
Study type	Observational	Prospective	GUSTO-III	Cross sectional	Descriptive

			TRIAL		
Result					
Male	74 %	77 %	78 %	77%	50.6%
Female	26 %	23 %	22%	23%	49.4 %

ST SegmentResolution and Initiation Of Thrombolytic Therapy:

In present study of 200 samples maximum number of cases 126 (63 %) showed ST segment resolution > 50%, whereas in 74 (37%) cases showed ST segment resolution< 50%.most of cases 85 (42.5 %)ST segment resolution > 50% were seen where there is initiation of therapy before 6 hours, whereas only 41 (20.5%) of cases shows improve ST segment > 50% after 6 hours of initiation of therapy. Following are studies in table C comparable with findings

Table C: ST segment resolution

Study	Present study	French et.al.[19]	Anderson et al.[13]	Karthik S.[20]	Sameer S. et al.[18]
Year	2019	2001	2002	2014	2015
Place	--	New Zealand	USA	Tamilnadu	Peshawar
Sample size	200	869	2352	60	83
Study type	Observational	Prospective	GUSTO-III TRIAL	Cross sectional	Descriptive
Result					
ST SEG. Resolution > 50 %	63 %	56.5%	29%	43..3 %	62.7 %

Complication:

About the complication after receiving thrombolytic therapy 37 % were in cardiogenic shock, 27.5 % land up in CCF, 15% showed arrhythmias, 12.5 % were having Post infarction angina and very few patients 4.5 % having reinfarction & bleeding 2.5%. Findings are compared with other studies in table D.

Table D: Complication

Study	Present study	Schroder et al.[11]	Anderson et al.13	Karthik S.[20]
Year	2019	1995	2002	2014
Place	--	Germany	USA	Tamilnadu
Sample size	200	6010	2352	60
Study type	observational	Prospective	GUSTO-III TRIAL	Cross sectional
Result				
Reinfarction	4.50 %	-	-	0 %
Post infarction angina	12.50 %	13 %	3.4 %	30%
Arrhythmias	15 %	13 %	-	16 %
Bleeding	2.50 %	-	-	-
Cardiogenic Shock	37 %	2.6 %	2.2 %	0 %
CCF	27.50 %	13 %	13.9 %	12 %

Outcome:

The outcome of therapy showed that 18 % patients of STEMI were died and 82 % were discharged from hospital. Percentage of adverse events and In-hospital mortality in the present study group was higher in compare to studies in table E.

Table E: Complication

Study	Present study	Schroder et al.11	Anderson et al.	Karthik S.[20]
Year	2019	1995	2002	2014
Place	--	Germany	USA	Tamilnadu
Sample size	200	6010	2352	60
Study type	observational	Prospective	GUSTO-III TRIAL	Cross sectional
Result				
Mortality	18 %	4 %	3.2 %	4 % %

Conclusion

Complications like cardiogenic shock, CCF were significantly less in patients thrombolysed within 6 hours of onset of chest pain compared to those who thrombolysed after 6 hours, however no difference in death rate was observed in both groups. Patients who were thrombolysed earlier had better ST segment resolution and better outcome than who were thrombolysed later.

References

[1] SS Iyengar and Girish S Godbole, Thrombolysis in the Era of Intervention, Supplement To Japi, Deecember2011, VOL. 59, p.p.26-30.
[2] Rajeev Gupta, Indu Mohan, and JagatNarula, Trends in Coronary Heart Disease Epidemiology in India, Annals of Global Health, Volume 82, Issue 2, March–April 2016, Pages 307-315.
[3] Joshua Chadwick Jayaraj, KarapetDavatyan, S.S. Subramanian and JemmiPriya (November 5th 2018). Epidemiology of Myocardial Infarction, Myocardial Infarction, BurakPamukçu, IntechOpen, DOI: 10.5772/intechopen.74768. Available from:

https://www.intechopen.com/books/myocardial-infarction/epidemiology-of-myocardial-infarction

[4] Anthon K. Prognostic clinical significance of ST segment potential determined by body surface mapping in patients with acute myocardial infarction. Circulation 1987;76(2):287.

[5] JoergCarlsson et.al., Resolution of ST-Segment Elevation in Acute Myocardial Infarction- Early Prognostic Significance after Thrombolytic Therapy, results from the COBALT Trial

[6] GruppoItaliano per lo Studio dellaStreptochinasinell'InfartoMiocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986;i:397–402

[7] ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. Lancet 1988;ii:349–60

[8] De Belder MA., Coronary disease: acute myocardial infarction: failed thrombolysis, Heart 2001;85:104–12

[9] Group FTTFC, Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet 1994;343:311–22

[10] Santoro GM, Valenti R, Buonamici P, et al. Relation between STsegment changes and myocardial perfusion evaluated by myocardial contrast echocardiography in patients with acute myocardial infarction treated with direct angioplasty. Am J Cardiol1998;82:932–7.

[11] Schroder R, Dissmann R, Bruggemann T, et al., Extent of early ST segment elevation resolution: a simple but strong predictor of outcome in patients with acute myocardial infarction. J Am CollCardiol 1994; 24:384–91.

[12] Barbash GI, Roth A, Hod H, et al., Rapid resolution of ST elevation and prediction of clinical outcome in patients undergoing thrombolysis with alteplase (recombinant tissue-type plasminogen activator): results of the Israeli Study of Early Intervention in Myocardial Infarction. Br Heart J 1990; 64:241–7.

[13] Anderson RD, White HD, Ohman EM, et al. Predicting outcome after thrombolysis in acute myocardial infarction according to ST-segment resolution at 90 minutes: a substudy of the GUSTO-III trial. Global Use of Strategies to Open occluded coronary arteries. Am Heart J 2002; 144:81–8.

[14] Antman EM, Anbe DT, Armstrong P et al., ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarcion— executive summary. Circulation 2004;110:588–636.

[15] Van de Werf F, Ardissino D, Betriu A et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2003;24:28–66.

[16] Granger CB, Goldberg RJ, Dabbous O et al. for the Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the Global Registry of Acute Coronary Events. Arch Int Med2003;163:2345–2353.

[17] Morrow DA, Antman EM, Charlesworth A et al. TIMI risk score for ST- elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation 2000;102:2031–2037.

[18] Saleem S, Khan A, Shafiq I. Post thrombolytic resolution of ST elevation in STEMI patients. Pak J Med Sci. 2016;32(1):201–205. doi:10.12669/pjms.321.8974

[19] French JK, Andrews JMB, Manda SOM, Steward RAH, McTigue JJC, et al. Early ST segment recovery infarct artery blood flow and long term outcome after acute myocardial infarction. American Heart Journal 2002Feb;143(2):265-71.

[20] S., Karthik; Surendran, Satchi A.; A., Mohamed Kasim. Efficacy of thrombolytic therapy with IV streptokinase in acute ST elevation myocardial infarction patients. International Journal of Advances in Medicine, [S.l.], v. 6, n. 4, p. 1121-1124, july 2019. ISSN 2349-3933.

-