

## Original Research Article

# Evaluation of clinical outcome of thrombolytic therapy in elderly patients in Western Rajasthan: a single centre experience

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### ABSTRACT

**Background:** Heart disease is the leading cause of mortality in population above the age of 65 years. Severity and prevalence of coronary artery disease (CAD) increase with increasing age. Thrombolysis remains the standard of care in the management of acute ST-elevation myocardial infarction (STEMI) in developing countries like India where primary percutaneous coronary intervention (PCI) is still not possible in the majority of patients. The risks and benefits of thrombolytic reperfusion therapy among the elderly patients with STEMI is much less known. Authors aimed to evaluate the outcome and complications of thrombolytic therapy in elderly patients admitted with acute STEMI.

**Methods:** The present observational study was done between January 2017 and January 2019 in the department of cardiology, Dr. S.N. Medical College, Jodhpur, India. It included a study group comprising 102 consecutive elderly patients who had acute STEMI and underwent thrombolytic therapy and a control group comprising 102 consecutive elderly patients who had STEMI who were not given thrombolytic therapy. Both groups were evaluated for an outcome (in-hospital mortality) and complications.

**Results:** The overall in-hospital mortality was less in thrombolytic therapy group as compared to control group although not statistically significant (8.82% versus 14.70%,  $p=0.277$ ). Similarly, in-hospital mortality was less in thrombolytic therapy subgroup A (age 66-74 years) as compared to control subgroup A (6.45% versus 10.75%,  $p=0.583$ ) and also less in thrombolytic therapy subgroup B (age 75-85 years) as compared to control subgroup B (12.50% versus 21.62%,  $p=0.445$ ). Among the traditional risk factors, co-morbid conditions and complications, there was less prevalence of diabetes mellitus (4.90% versus 15.68%,  $p=0.021$ ), hypertension (5.88% versus 6.86%,  $p=1.000$ ), cardiogenic shock (8.82% versus 9.80%,  $p=1.000$ ), left ventricular failure (LVF) (0.98% versus 3.92%,  $p=0.365$ ) and atrioventricular (AV) block (0% versus 4.90%,  $p=0.245$ ) but more acute kidney injury (AKI) (2.94% versus 0%,  $p=0.070$ ) in thrombolytic therapy group patients as compared to control group patients. Cerebrovascular accident (CVA) did not occur in both group patients.

**Conclusion:** Despite the higher prevalence of co-morbidities and high risk features in elderly patients of acute STEMI, timely thrombolysis is beneficial. A mortality benefit was seen in all groups suggesting net benefit regardless of increasing age up to the age of 85 years.

**Keywords:** Elderly, ST-elevation myocardial infarction, Thrombolytic therapy

### INTRODUCTION

Heart disease is the leading cause of mortality in population above the age of 65 years.<sup>1-3</sup> Severity and the prevalence of coronary artery disease (CAD) increase

with the increasing age. About 50% of the patients above 60 years of age have been found to be having severe CAD including triple vessel disease (TVD) and/ or left main (LM) disease, in various autopsy studies.<sup>4</sup> It is common to find peripheral artery disease (PAD) in elderly patients who present with acute myocardial infarction (AMI). Such abnormalities were detected in about 33% of men between 65 and 70 years and 45% of men above 85 years of age.<sup>5,6</sup> Incidence of ST-elevation myocardial infarction (STEMI) is high among the elderly population, however many large randomised trials have excluded this age group.<sup>7-11</sup>

Thiemann et al. evaluated the risk of intracranial bleed following thrombolysis in STEMI in elderly.<sup>12</sup> Factors associated with intracranial haemorrhage were: age >75 years, female sex, prior history of stroke, black race, hypertension (systolic blood pressure >160 mm Hg), use of tissue plasminogen activator (t-PA), international normalized ratio (INR) >4 and weight <65 kg for females and <80 kg for males.<sup>13</sup> Thrombolytic therapy was recommended in patients <75 years with STEMI or new onset left bundle branch block (LBBB), presenting within 12 hours of onset of symptoms.<sup>14</sup> Recent guidelines however, have extended the recommendation to the patients of more than 75 years also.<sup>15,16</sup> In view of the above review of literature, it is clear that the recent recommendation of use of thrombolytic therapy in the elderly patients which is a high risk group has caveats related to morbidity and mortality. The present study was planned to find out the benefits and complications related to thrombolytic therapy in elderly patients when compared to the elderly patients who were not thrombolysed.

## METHODS

The present observational study was done between January 2017 and January 2019 in the department of cardiology, Dr. S.N. Medical College, Jodhpur, India, which included study group comprising 102 consecutive elderly patients who had acute STEMI and underwent thrombolytic therapy with streptokinase (STK) (n=100) and reteplase (n=2) and control group comprising 102 consecutive patients who had STEMI but were not given thrombolytic therapy. All patients received loading doses of aspirin 325 mg, clopidogrel 300 mg if age was <75 years and 75 mg if age >75 years and age adjusted doses of low molecular weight heparin (LMWH). All patients received other guideline directed medical therapy. Both groups were evaluated for outcome (in-hospital mortality) and complications. The patients were followed up till the index hospitalization.

### Inclusion criteria

Between January 2017 and January 2019, a total of 204 consecutive patients of age 66-85 years, who presented with acute STEMI and underwent thrombolysis (n=102) and control group which included elderly STEMI patients who were not thrombolysed because they came out of

window period or had contraindications for thrombolysis (n=102) were included in the study.

### Exclusion criteria

1. Age <66 years and >85 years.
2. Patients were excluded from the thrombolytic therapy group if they had absolute contraindications to thrombolytic therapy.

- Any previous intracranial hemorrhage.
- Known structural cerebral vascular lesion (e.g. arteriovenous malformation).
- Known malignant intracranial neoplasm (primary or metastatic).
- Ischemic stroke within 3 months except acute ischemic stroke within 4.5 hours.
- Suspected aortic dissection.
- Active bleeding or bleeding diathesis (excluding menses).
- Significant closed-head or facial trauma within 3 months.
- Intracranial or intraspinal surgery within 2 months.
- Severe uncontrolled hypertension (unresponsive to emergency therapy).
- For streptokinase, previous treatment within the previous 6 months.

### Statistical analysis

Categorical data were expressed as frequency and percentage and were analyzed using Chi square test/ Fischer exact test as applicable. Statistical significance was considered at the p value <0.05. The statistical analysis was performed using epi info version 7.2.1.0

## RESULTS

A total of 204 patients of acute STEMI of which, 102 patients in each group (thrombolytic therapy group and control group) were observed during the study period from January 2017 to January 2019 at our institution. Table 1 presents the in-hospital mortality of both groups. Out of the 102 patients in the study group, 65(63.72%) were male and 37(36.27%) were female; and of 102 patients of acute STEMI in control group, 64(62.74%) were male and 38 (37.25%) were female.

Among the traditional risk factors, comorbid conditions and complications, there was less prevalence of diabetes mellitus (4.90% versus 15.68%, p=0.021), hypertension (5.88% versus 6.86%, p=1.000), cardiogenic shock (8.82% versus 9.80%, p=1.000), left ventricular failure (LVF) (0.98% versus 3.92%, p=0.365) and atrioventricular (AV) block (0% versus 4.90%, p=0.245) but more acute kidney injury (AKI) (2.94% versus 0%, p=0.070) in thrombolytic therapy group patients as compared to control group patients. The complication

cerebrovascular accident (CVA) was not found in either group as shown in Table 2.

**Table 1: In-hospital mortality.**

Age(Years)	Thrombolytic group (n=102)		Control group (n=102)		p Value
	No. of death	Percentage	No. of death	Percentage	
66-74 (Subgroup A)	4(62)	6.45%	7 (65)	10.75%	0.583
75-85 (Subgroup B)	5(40)	12.50%	8 (37)	21.62%	0.445
Total	9(102)	8.82%	15(102)	14.70%	0.277

**Table 2: Risk factors, comorbid conditions and complications.**

Variable	Thrombolytic group(n=102)	Control group(n=102)	p Value
Diabetes mellitus	5 (4.9%)	16 (15.6%)	0.021
Hypertension	6 (5.8%)	7 (6.8%)	1.000
Cardiogenic shock	9 (8.8%)	10 (9.8%)	1.000
LVF	1 (0.9%)	4 (3.9%)	0.365
AKI	3 (2.9%)	0 (0.0%)	0.245
AV Block	0 (0.0%)	5 (4.9%)	0.070
CVA	0 (0.0%)	0 (0.0%)	-

Thrombolytic therapy group was divided into two subgroups. There were 62 patients in subgroup A of age 66-74 years and 40 patients in subgroup B of age 75-85 years. Overall in-hospital mortality was 8.82% (9 out of 102 patients). In subgroups, in hospital mortality was 6.45% (4 out of 62 patients) in subgroup A and 12.5% (5 out of 40 patients) in subgroup B.

Control group was also divided into two subgroups. There were 65 patients in subgroup A of age 66-74 years and 37 patients in subgroup B of age 75-85 years. Overall in-hospital mortality was 14.70% (15 out of 102 patients). In subgroups, in-hospital mortality was 10.76% (7 out of 65 patients) in subgroup A and 21.62% (8 out of 40 patients) in subgroup B.

The overall in-hospital mortality was less in thrombolytic therapy group as compared to the control group although not statistically significant (8.82% versus 14.70%,  $p=0.277$ ). Similarly, in-hospital mortality was less in thrombolytic therapy subgroup A as compared to control subgroup A (6.45% versus 10.75%,  $p=0.583$ ) and also less in thrombolytic therapy subgroup B as compared to control subgroup B (12.50% versus 21.62%,  $p=0.445$ ) as shown in Table 1.

## DISCUSSION

Thiemann et al. observed a 30-day mortality of 6.8% in the patients between 65 and 75 years of age who were

treated with thrombolysis versus 9.8% in the control group. However, a higher mortality was observed among patients above 75 years of age (18.0% versus 15.4%) in the thrombolytic group.<sup>12</sup> But in the present study in-hospital mortality was less in thrombolytic therapy group as compared to control group in both subgroup A (66-74 years) (6.45% versus 10.76%) and in subgroup B (75-85 years) (12.50% versus 21.62%).

GISSI-1 trial included 1215 patients aged above 75 years and showed that the 30-day mortality was less in patients who underwent thrombolysis with STK when compared to the control group.<sup>17</sup> ISIS-2 also showed similar findings of improved mortality with thrombolysis with STK in patients >75 years of age in contrast to the control (8.1% versus 10.7%).<sup>18</sup> Together these two trials demonstrated an absolute benefit of 39/1000 patients when treated with STK versus placebo ( $p=0.02$ ). In the present study in-hospital mortality was less in thrombolytic therapy group as compared to the control group.

In the revised Fibrinolytic Therapy Trialists (FTT) data 10053 patients between 65 and 74 years of age demonstrated lower 30-day mortality with fibrinolysis than placebo (15% versus 19%).<sup>9</sup> Similar findings were observed in patients above 75 years of age. In present study in-hospital mortality was also less in thrombolytic therapy group as compared to control group in both age groups. GUSTO-1 trial included 41,021 patients of which 4625 patients were between 75 and 85 years of age and 412 patients were above 85 years of age. There was a relative reduction in mortality among patients <85 years of age. There were 17 fewer deaths or disabling strokes per 1000 patients treated between 75 and 85 years of age.<sup>19</sup> Similar advantage of thrombolytic therapy was also found in present study. Stenestrand et al. also demonstrated the beneficial effects of thrombolytic therapy among Swedish patients presenting with STEMI above  $\geq 75$  years of age, with a significant reduction in one-year mortality (relative risk [RR] 0.88; 95% CI 0.79 to 0.97).<sup>20</sup>

Thiemann et al. concluded that the outcome of fibrinolysis was dependent on many clinical factors among which time from the onset of pain, was an important one.<sup>12</sup> When performed within the first hour, as much as 50% mortality reduction has been reported and the mortality benefit decreases as the time delay occurs with an increase in the

incidence of myocardial rupture.<sup>21,22</sup> The Fibrinolytic Therapy Trialists (FTT) observed a slightly greater relative reduction in mortality in the younger patients with STEMI as compared to the elderly with 26% reduction in mortality in patients <55 years of age and only a 15% reduction in mortality >75 years of age.<sup>23</sup>

Angeja et al. examined data from the National Registry of Myocardial Infarction-2 and found that, compared with patients receiving no reperfusion therapy, those who were treated with t-PA had lower rates of in-hospital mortality and composite of in-hospital death or CVA in <85 years of age, but no similar benefits were observed above 85 years of age.<sup>24</sup> Soumerai et al. evaluated the patients ≥ 65 years who presented with STEMI, fibrinolysis was associated with low in-hospital mortality in patients <80 years of age, however there was a 1.4 fold increase in mortality among patients aged 80 and above.<sup>25</sup> But in present study advantage of thrombolytic therapy was found in up to 85 years of age.

Toleva et al. randomised patients ≥75 years with STEMI into 3 groups: those who underwent primary percutaneous coronary intervention (PCI), fibrinolysis group and those who received neither fibrinolysis nor primary PCI. In-hospital mortality was 13.3%, 9.4% and 19.7% (p=0.018) in the respective groups. Also the composite of death, reinfarction, cardiogenic shock and congestive heart failure (CHF) was 28%, 20% and 33.2% (p=0.022) respectively.<sup>26</sup> In present study in-hospital mortality was similarly less in subgroup B (76-85 years) (12.50% versus 21.62%) with thrombolytic therapy group as compared to control group.

Limitations of the study was an observational single centre study and Sample size was small which may have been the reason for statistical insignificance.

## CONCLUSION

Despite the higher prevalence of co-morbidities and high risk features in elderly patients of acute STEMI, timely thrombolysis is beneficial. A mortality benefit was seen in all groups suggesting net benefit regardless of increasing age up to the age of 85 years. In developing countries like India where primary PCI may not be feasible, timely thrombolysis should be given to the elderly patients also.

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