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Original Article

Impact of Failed Thrombolysis: Clinical Outcomes in a PCI-Capable Setting

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Abstract

Background: Streptokinase remains the primary mode of reperfusion therapy in many centers, including some with percutaneous coronary intervention (PCI) capabilities. According to the pharmacoinvasive strategy, all ST-elevation myocardial infarction (STEMI) patients who receive thrombolysis should undergo routine angiography, while those with failed thrombolysis must undergo urgent rescue PCI. However, the rate of complications following unsuccessful thrombolysis and the frequency of rescue PCI are not well studied in our setting.

Objective: To determine the frequency of rescue PCI and compare the rates of in-hospital complications between successfully and unsuccessfully thrombolysed STEMI patients.

Methodology: Patients receiving intravenous streptokinase for their first STEMI were enrolled 90 minutes post-infusion. Patients with cardiogenic shock, third-degree heart block, acute left ventricular failure, or left bundle branch block before thrombolysis, and those with contraindications to thrombolysis or who declined participation, were excluded. Patients were followed until discharge to assess the incidence of cardiogenic shock, left ventricular failure, left ventricular dysfunction, acute kidney injury, and in-hospital death. Outcomes were compared between patients with successful versus unsuccessful thrombolysis. The frequency of rescue PCI was also recorded.

Results: A total of 391 patients were included, with males comprising 75% of the sample. The most prevalent comorbidities were diabetes (54%) and hypertension (32%). Anterior and inferior wall STEMI each accounted for 36% of cases. Thrombolysis was successful in 73% and unsuccessful in 27% of patients. Mortality was 7.3% in successfully thrombolysed patients and 14% in the unsuccessful group. All pre-specified complications were significantly more common in the failed thrombolysis group. Only 19% of patients underwent rescue PCI.

Conclusion: Streptokinase-based thrombolysis results in suboptimal reperfusion in a significant proportion of STEMI patients. Furthermore, the rate of rescue PCI among these high-risk individuals remains low. There is a critical need to enhance reperfusion strategies in PCI-capable settings.

Keywords: Rescue PCI, Streptokinase, ST-segment elevation myocardial infarction, Unsuccessful thrombolysis.

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Introduction

Timely reperfusion remains the cornerstone of effective management in ST-elevation myocardial infarction (STEMI) [1]. This can be achieved through either primary percutaneous coronary intervention (PCI) or thrombolysis. While studies consistently demonstrate the superiority of primary PCI when performed promptly [2], implementation requires the development of robust, resource-intensive systems, including trained personnel, dedicated facilities, and efficient referral networks [3]. Due to cost-effectiveness and accessibility, streptokinase remains the most widely used thrombolytic agent in many hospitals across the country [4].

However, thrombolysis fails to achieve reperfusion in a considerable proportion of patients, leading to adverse clinical outcomes such as acute left ventricular failure and in-hospital mortality [5]. Despite these concerns, there is a dearth of national data regarding the clinical consequences of failed thrombolysis, particularly in PCI-capable centers like ours, where thrombolysis continues to be the default reperfusion strategy.

It is important to understand that thrombolysis should not be viewed as a standalone intervention. As per the pharmacoinvasive approach, all STEMI patients receiving thrombolysis should undergo coronary angiography within 2 to 24 hours, regardless of initial reperfusion success. Moreover, patients with failed thrombolysis require immediate rescue PCI [1]. While several studies from PCI-capable centers in Pakistan have addressed the rates of successful and unsuccessful thrombolysis, very few have explored the outcomes and management of patients experiencing failed reperfusion.

For example, Shah Zeb et al. described their experience with STEMI management at Lady Reading Hospital, where only 5.4% of patients underwent either primary or rescue PCI; however, the study did not report on the success rate of thrombolysis [6]. Other investigations have documented ST-segment resolution rates following streptokinase use, but they did not analyze the complications or downstream treatment strategies associated with failed thrombolysis [7,8]. Imad M et al. reported a 20.7% failure rate of thrombolysis but did not address the clinical outcomes or whether these patients underwent rescue PCI [9]. Similarly, Baber MZ et al. noted a 24% failure rate based on TIMI flow assessment but lacked information regarding adverse outcomes and interventional management [10].

Several other studies also report on thrombolysis success and failure [11,12], but fail to document whether patients with unsuccessful thrombolysis received rescue PCI. This lack of data likely reflects the infrequent practice of rescue PCI in thrombolysis-driven centers. A transition from a thrombolysis-first to a PCI-first strategy could be better justified if well-designed studies demonstrate that thrombolysis-based strategies yield suboptimal results.

To date, no study from our center has assessed the frequency of failed thrombolysis, its associated complications, or the extent to which rescue PCI is implemented. Furthermore, the survival outcomes and rates of left ventricular dysfunction in patients with failed thrombolysis remain unknown in our context. Understanding these variables is crucial for assessing whether our current practice aligns with evidence-based standards and whether a shift toward primary PCI is warranted.

Therefore, our primary objective was to evaluate the in-hospital incidence of cardiogenic shock, acute heart failure, left ventricular dysfunction, acute kidney injury, and death among patients with failed thrombolysis. We also aimed to determine the frequency of rescue PCI in these patients and identify associated predictive factors.

Methodology

Study Design, Ethics, and Setting

This descriptive cross-sectional study was conducted in a tertiary care hospital and aimed to evaluate the success rate and clinical outcomes of thrombolysis in patients presenting with ST-elevation myocardial infarction (STEMI). Ethical

approval was obtained prior to the commencement of the study from the hospital's research ethics committee on 15th March 2024 (Approval Code/Ref. No. RC-EA-2024/054). The study was conducted over a two-month period from 20th March 2024 to 20th May 2024.

Participants

A total of 391 patients diagnosed with STEMI and eligible for thrombolysis were recruited. Patients aged between 18 and 80 years who survived at least 90 minutes post-thrombolysis and had interpretable post-thrombolysis electrocardiograms (ECGs) were included. Exclusion criteria encompassed patients presenting with poor prognosis at admission (e.g., cardiogenic shock or acute left ventricular failure prior to thrombolysis), those with ECG findings that rendered ST-segment interpretation difficult (e.g., left bundle branch block, paced rhythm, complete heart block with wide complex escape rhythm, prior STEMI in the same territory), and patients with silent myocardial infarctions.

Variables

The primary exposure variable was the success or failure of thrombolysis. Unsuccessful thrombolysis was defined as less than 50% resolution in ST-segment elevation in the lead with maximum elevation and/or persistent chest pain rated greater than 5 on the Numeric Pain Measurement Scale (NPMS) at 90 minutes post-infusion. Clinical outcomes compared between groups included cardiogenic shock (CS), acute left ventricular failure (ALVF), left ventricular dysfunction, acute kidney injury, and in-hospital mortality. Definitions of comorbidities and conditions were standardized. Acute heart failure was defined as new-onset dyspnea or orthopnea with inspiratory rales or the need for intravenous diuretics. Cardiogenic shock was defined as systolic blood pressure < 90 mmHg accompanied by signs of hypoperfusion, including cold extremities, low-volume pulse, or delayed capillary refill (>3 seconds). Diabetes mellitus was defined by a previous diagnosis, use of oral hypoglycemics/insulin, or documented fasting glucose >126 mg/dL or random glucose ≥200 mg/dL. Hypertension was defined as systolic/diastolic blood pressure ≥140/90 mmHg or the use of antihypertensive medications. Smoking status included current smokers and those who had smoked within the past six months.

Data Sources/Measurement

Data on baseline demographics, medical history, and risk factors were collected through patient interviews and review of medical records. The Numeric Pain Measurement Scale (0–10) was used to quantify chest pain, with scores categorized as: 0 (no pain), 1–3 (mild), 4–6 (moderate), and 7–10 (severe). ECGs were recorded at baseline and repeated 90 minutes after thrombolysis. STEMI was defined as ST-segment elevation ≥2 mm in two contiguous leads in men, ≥1.5 mm in anterior leads in women, or ≥1 mm in other leads. Thrombolysis was standardized using an infusion of 1.5 million units of Streptokinase in 100 mL of normal saline over one hour. Rescue angioplasty was defined as a percutaneous coronary intervention (PCI) undertaken following a diagnosis of failed thrombolysis.

Bias

Selection bias was minimized by using a clear set of inclusion and exclusion criteria. However, the use of a non-probability sampling technique may have introduced some selection bias. Information bias was mitigated by using standardized definitions for all clinical conditions and outcomes. Observer bias was reduced through the objective use of pain scores and ECG readings assessed by trained staff.

Study Size

The sample size was calculated using OpenEpi version 3.01 (Open-Source Epidemiologic Statistics for Public Health, www.OpenEpi.com). Assuming a 25% rate of unsuccessful thrombolysis and targeting a 95% confidence level for estimating associated complications, a minimum of 288 participants was required. A total of 391 patients were ultimately enrolled to ensure adequate power and compensate for possible data loss.

Quantitative Variables

Continuous variables such as age and pain scores were recorded as means and standard deviations. Categorical variables including gender, smoking

status, diabetes, hypertension, and clinical outcomes were expressed as frequencies and percentages. ECG ST-segment elevations were measured in millimeters and documented from the leads showing the highest elevation.

Statistical Methods

Statistical analysis was conducted using SPSS version 22. Continuous variables were compared between groups using the independent samples t-test, while categorical variables were analyzed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant. Subgroup analyses were performed for various baseline risk factors to assess their association with thrombolysis outcomes.

Results

Participants

A total of 391 patients with ST-elevation myocardial infarction (STEMI) underwent thrombolysis during the study period. Of these, 294 (75.2%) were males and 97 (24.8%) were females. The majority of patients (90%) were over 40 years of age, with 209 (53.5%) aged between 41–60 years and 165 (42.2%) aged between 61–80 years. Only 4.3% of the participants were in the 18–40 age group. All patients received thrombolytic therapy with streptokinase according to the study protocol, and ECG as well as pain scores were documented at baseline and 90 minutes post-thrombolysis for assessment of success or failure.

Descriptive Data

Baseline clinical and demographic characteristics of the study population are presented in Table 01. Hypertension was the most prevalent comorbidity, affecting 212 patients (54.2%), followed by diabetes mellitus in 125 patients (32%). A history of ischemic heart disease (IHD) was reported in 67 (17.1%) patients, and 86 (22%) were smokers. Dyslipidemia was infrequent, seen in only 1.5% of the sample. A family history of IHD was noted in 15% of patients. Previous cardiac interventions such as PCI or CABG were rare.

Regarding STEMI localization, anterior wall MI and inferior wall MI were the most common, collectively accounting for over 72% of cases. The time from onset of chest pain to thrombolysis was also recorded: 9.7% of patients received thrombolysis within 3 hours, 41.7% within 3–6 hours, 39.6% within 7–12 hours, and 8.9% after more than 12 hours of symptom onset.

Outcome Data

Overall, 286 (73%) patients experienced successful thrombolysis based on ST-segment resolution and pain reduction criteria, while 105 (27%) had unsuccessful thrombolysis. The in-hospital mortality rate was 9%, with a total of 36 deaths recorded. Clinical outcomes differed significantly between the two groups (Table 02). Mortality was higher in the unsuccessful thrombolysis group (14.3%) compared to the successful group (7.34%). Acute left ventricular failure occurred in 49.5% of patients with unsuccessful thrombolysis, compared to 18.2% among those with successful outcomes.

Similarly, left ventricular (LV) dysfunction without overt heart failure was present in 60% of the unsuccessful group versus 39.2% in the successful group. Cardiogenic shock was more prevalent among the unsuccessful group (33.3%) than in the successful group (22.7%). Acute kidney injury occurred in 22.9% of patients with failed thrombolysis and in 17.1% of those with successful thrombolysis. Inpatient coronary angiography was performed in 19.4% of patients with unsuccessful thrombolysis compared to 7.7% in the successful group. Survival to discharge was achieved in 92.7% of successfully thrombolysed patients, compared to 85.7% in those with unsuccessful thrombolysis.

Table 1: Baseline Characteristics

Parameter (N= 391)	Number (%)
Males	294 (75.20)
Females	97 (24.80)
18-40 years	17 (4.34)
41-60 years	209 (53.45)
61-80 years	165 (42.20)
Diabetes Mellitus	125 (31.97)
Hypertension	212 (54.20)
Ischeamic Heart disease (IHD)	67 (17.14)
Smokers	86 (21.99)
Dyslipidemia	6 (1.53)
Family History of IHD	59 (15.09)
Previous PCI	10 (2.56)
Previous CABG	1 (0.26)
Anterior wall	142(36.32)
Anterolateral wall	64(16.37)
High lateral wall	14(3.58)
Inferior wall	141(36.06)
Infroposterior wall	22(5.63)
Inferolateral wall	6(1.53)
Posterior wall	1(0.26)
Posterolateral wall	1(0.26)
Pain to Thrombolysis <3 hours	38(9.72)
Pain to Thrombolysis 3-6 hours	163(41.69)
Pain to Thrombolysis 7-12 hours	155(39.64)
Pain to Thrombolysis >12 hours	35(8.95)

IHD: Ischeamic Heart Disease, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft surgery.

Table 2: Outcomes of Successful vs Unsuccessful patients undergoing thrombolysis.

Parameters	Unsuccessful thrombolysis (n=105) No.(%)	Successful thrombolysis(n=286) No.(%)	P value
Deaths	15(14.3%)	21(7.34%)	0.015
Acute LVF	52(49.5%)	52(18.2%)	<0.001
LV dysfunction	63(60%)	112(39.2%)	<0.001
Shock	35(33.3%)	65(22.7%)	<0.001
AKI	24(22.9%)	49(17.1%)	<0.001
Referred	7(6.67%)	20(7%)	0.125
Inpatient angio	20(19.4%)	22(7.69%)	0.001
Survival to discharge	90(85.7%)	265(92.7%)	0.001

LV: Left Ventricular, LVF: Left ventricular failure, AKI: Acute Kidney injury.

Table 3: Results of Thrombolysis in Prespecified Subgroups

Subgroup	Unsuccessful Thrombolysis Num (%)	Successful Thrombolysis Num (%)	P Value
DM	45(42.9%)	80(27.9%)	0.001
Smoker	18(17.1%)	68(23.8%)	0.166
AWMI	48(45 7%)	94(32.9%)	0.001
ALWMI	12(11.4%)	52(18.2%)	0.003
IWMI	37(35.2%)	104(36.3%)	0.794
IPWMI	6(5.71%)	16(5.59%)	0.051
ILWMI	2(1.9%)	4(1.39%)	0.526
HLWMI	0	14(4.89%)	0.037
PWMI	0	1(0.35%)	0.344
PLWMI	0	1(0.35%)	0.344
MALES	218 (74)	76 (26)	0.073
FEMALES	68 (70)	29 (30)	
< 3 HOURS	12 (32)	26 (68)	0.001
3-6 HOURS	12 (17)	135 (83)	
7-12 HOURS	48 (31)	107 (69)	
> 12 HOURS	17 (49)	18 (51)	

DM: Diabetes Mellitus, AWMI: Anterior wall myocardial infarction, ALWMI: Anterolateral wall myocardial infarction, IWMI: Inferior wall myocardial infarction, IPWMI: Inferoposterior wall myocardial infarction, ILWMI: Inferolateral wall myocardial infarction, HLWMI: High lateral wall myocardial infarction, PWMI: Posterior wall myocardial infarction, PLWMI: Posterolateral wall myocardial infarction.

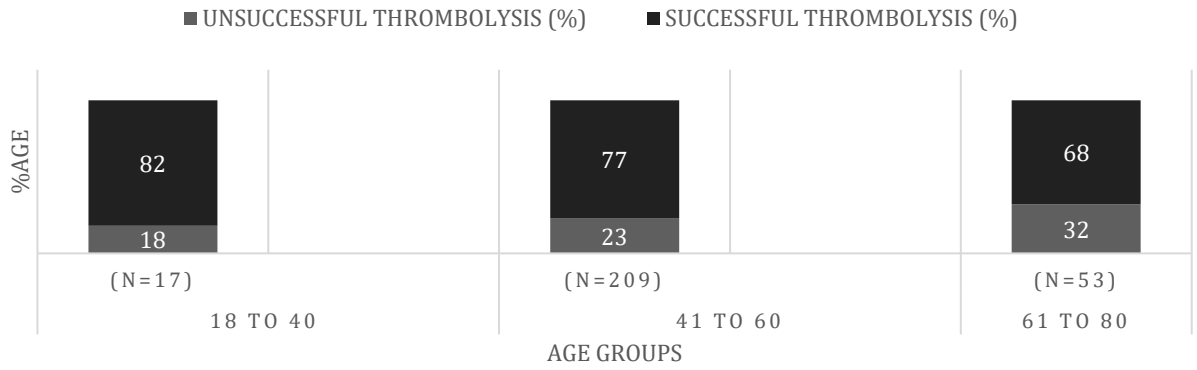


Figure 1: Frequency of successful vs unsuccessful thrombolysis in different age group.

Main Results

The success of thrombolysis varied significantly across prespecified subgroups (Table 03). Diabetic patients had a significantly higher rate of unsuccessful thrombolysis (42.9%) compared to non-diabetics (27.9%, p=0.001). Smoking status did not significantly affect thrombolysis outcomes (p=0.166). Anterior wall myocardial infarction (AWMI) was significantly associated with a higher rate of unsuccessful thrombolysis (45.7% vs. 32.9%,

p=0.001), while inferior wall MI (IWMI) outcomes did not differ significantly between groups. Interestingly, high lateral wall MI (HLWMI) patients showed a significantly better response to thrombolysis, with no unsuccessful cases recorded in this subgroup (p=0.037).

Time from chest pain onset to thrombolysis was a critical determinant of thrombolysis outcome. Patients thrombolysed between 3–6 hours after symptom onset had the highest success rate (83%), while those treated after more than 12 hours had nearly equal proportions of successful (51%) and unsuccessful (49%) outcomes. This finding strongly supports the importance of early reperfusion therapy. A visual representation of thrombolysis success across age groups (Figure 01) indicated a trend toward increased rates of unsuccessful thrombolysis with advancing age, although these differences did not reach statistical significance.

Gender was not significantly associated with thrombolysis outcomes (p=0.073). Among males, the success rate was 74%, and among females, 70%, suggesting that sex did not independently influence thrombolysis efficacy.

Discussion

In this study, the overall rate of successful thrombolysis was 73%, while 27% of patients experienced unsuccessful thrombolysis. Among those with failed reperfusion, the majority received conservative management, with only 19% undergoing inpatient angiography. This low rate of rescue percutaneous coronary intervention (PCI) highlights a significant gap in the optimal care pathway for such high-risk patients.

The reported incidence of unsuccessful thrombolysis with streptokinase in the literature is highly variable. Koh HP et al. reported a failure rate of just 6.4% in patients who received streptokinase, which contrasts sharply with the 55% failure rate reported by Singh et al. [17,18]. Our findings fall in between these two extremes. Notably, Singh et al. also identified anterior STEMI, longer delays from symptom onset to thrombolysis, and diabetes mellitus as predictors of unsuccessful thrombolysis, which aligns with our results. One explanation for the lower failure rate in the Koh HP et al. study may lie in the earlier administration of streptokinase, with a median symptom-to-needle time of just 3 hours. Moreover, in their study, the post-thrombolysis ECG was assessed later (between 90 and 180 minutes), potentially allowing more time for ST-segment resolution, which could have inflated their success rate [17].

Our study demonstrated a clear association between failed thrombolysis and adverse in-hospital outcomes. Death, acute left ventricular failure (ALVF), asymptomatic LV dysfunction, acute kidney injury (AKI), and cardiogenic shock were all significantly more frequent in patients with unsuccessful reperfusion. These findings are consistent with prior studies, where failed thrombolysis has been a strong predictor of mortality and poor clinical outcomes [19]. Conversely, successful thrombolysis was associated with significantly better survival to discharge in our cohort.

The mortality rate among patients with failed thrombolysis in our study was 14.3%, compared to 7.34% in those with successful reperfusion. This overall in-hospital mortality rate of 9.2% is concerning, especially considering that we excluded patients with severely unstable conditions (e.g., cardiogenic shock or ALVF prior to thrombolysis). This rate is comparable to mortality reported in early thrombolytic-era trials, prior to the widespread use of dual antiplatelet therapy. For instance, the GISSI-2 trial reported a 7.3% mortality rate among patients with failed thrombolysis [20], which is nearly half the rate observed in our cohort.

The current gold standard for STEMI patients undergoing thrombolysis is the pharmacoinvasive approach, which recommends coronary angiography within 2 to 24 hours of thrombolytic therapy. In cases of failed thrombolysis, immediate or "rescue" PCI is advised [1]. Despite these guidelines, only 19.4% of our patients with unsuccessful thrombolysis underwent rescue PCI. The low uptake of this critical intervention is troubling and likely multifactorial.

Multiple challenges hinder timely rescue PCI. First, failed thrombolysis is often recognized late, by which time the opportunity for effective reperfusion may be diminished. Second, rescue PCI may require cath lab activation during off-hours, contributing to delays [21]. In some cases, clinicians may hesitate, hoping that delayed thrombolysis might eventually work, or fearing futility in patients with extensive myocardial damage. This delay in decision-making may result in missed opportunities for improved outcomes.

Moreover, clinical instability may further complicate the logistics of performing rescue PCI. Hemodynamic compromise, shock, and ALVF may necessitate mechanical ventilation and hemodynamic support, adding complexity to the procedure. These high-risk features paradoxically reduce the likelihood of invasive intervention—a phenomenon described in literature as the "treatment-risk paradox," wherein the patients who are most likely to benefit from guideline-directed interventions are least likely to receive them [23]. Even though some patients in our study may have had legitimate contraindications to angiography, it is probable that reluctance to intervene in high-risk individuals also contributed to the low rescue PCI rates. As noted by others, clinicians may more readily accept errors of omission than errors of commission in critically ill patients [24].

Our findings emphasize the urgent need to re-evaluate reperfusion strategies in our institution. Given the modest success rates and complications associated with streptokinase thrombolysis, and the logistical and clinical barriers to implementing pharmacoinvasive therapy, transitioning to primary PCI as the preferred reperfusion strategy appears essential. As advocated by the European Stent for Life initiative, resource allocation—both human and financial—should prioritize prognostically significant interventions like primary PCI over elective procedures such as those for chronic stable angina [25].

Limitations

One notable limitation of our study is that it did not collect detailed data on the reasons for deferring rescue PCI. Such information would have added valuable insight into barriers to optimal care and should be addressed in future research.

Conclusion

Thrombolysis with streptokinase results in suboptimal outcomes in a significant proportion of STEMI patients. Failed thrombolysis is associated with increased in-hospital mortality, cardiogenic shock, acute heart failure, and acute kidney injury. Predictors of failed thrombolysis include anterior infarct location, diabetes mellitus, and prolonged time from symptom onset to reperfusion. Despite guideline recommendations, the frequency of rescue PCI in our center remains low. These findings underscore the need for enhanced reperfusion strategies, including increased use of primary PCI and better implementation of the pharmacoinvasive approach, to improve outcomes for STEMI patients in our setting.

Authors' Contributions

All authors meet the ICMJE criteria for authorship. They have reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Author 1: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 2: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 3: Analysis and interpretation of data, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 4: Analysis and interpretation of data, critical revision, final approval, agreed to be accountable for all the work.
Author 5: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 6: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.

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