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Clinical and Angiographic Profile of Failed Thrombolysis in STEMI Patients

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ABSTRACT

Background: Failed thrombolysis remains an important clinical problem in patients with ST-segment elevation myocardial infarction (STEMI), particularly where fibrinolysis is used as the initial reperfusion strategy. This study evaluated the clinical and coronary angiographic profile of patients with failed thrombolysis.

Methods: This observational study included 196 consecutive patients with STEMI and failed thrombolysis who underwent coronary angiography during the index hospitalization. Failed thrombolysis was defined as <50% resolution of maximal baseline ST-segment elevation at 90 minutes after fibrinolytic therapy with persistent or recurrent ischemic chest pain. Demographic and clinical characteristics, cardiovascular risk factors, ischemic window period, fibrinolytic therapy, angiographic findings, revascularization strategy, and in-hospital mortality were assessed.

Results: The mean age was 53.2 ± 11.8 years, and 158 (80.6%) patients were male. Smoking (45.4%) and diabetes mellitus (44.6%) were the most prevalent cardiovascular risk factors. The mean ischemic window period was 6.3 ± 2.3 hours. Streptokinase was the predominant fibrinolytic agent (91.8%). The left anterior descending artery was the most frequent infarct-related artery (53.6%), while single-vessel disease was present in 55.1% of patients. TIMI grade 0/1 flow was observed in 151 (77.0%) patients, whereas TIMI grade 3 flow was present in only 11 (5.6%). Rescue or subsequent PCI was performed in 166 (84.7%) patients. In-hospital mortality occurred in 7 (3.6%) patients.

Conclusion: Failed thrombolysis was associated with a prolonged ischemic window and severe residual epicardial coronary obstruction. Most patients underwent rescue or subsequent PCI, with a relatively low in-hospital mortality. Early recognition of failed reperfusion and timely angiographic assessment with appropriate revascularization remain important in this setting.

Keywords: Acute myocardial infarction; angiography, coronary; fibrinolytic agents; percutaneous coronary intervention; ST elevation myocardial infarction; thrombolytic therapy; treatment failure

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is a time-critical cardiovascular emergency requiring prompt restoration of

coronary blood flow to limit myocardial injury and improve outcomes. Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy when timely access is available. However, fibrinolytic therapy remains an important alternative for patients who cannot undergo primary PCI within the recommended time frame, particularly in settings with limited access to PCI-capable centres [1,2].

Despite its benefits, fibrinolysis fails to achieve adequate reperfusion in approximately 30–40% of patients [3,4]. Persistent coronary occlusion can lead to larger infarct size, left ventricular dysfunction, and adverse clinical outcomes [5]. Inadequate ST-segment resolution (<50% at 60–90 minutes) is a key marker of failed reperfusion and helps identify patients requiring further intervention [3,6].

Failed fibrinolysis requires early recognition and prompt angiographic assessment, with rescue PCI recommended when reperfusion is unsuccessful or ischemia persists [1,2]. Rescue PCI has been associated with improved clinical outcomes, including reduced recurrent ischemia and heart failure, compared with conservative management [7,8]. Coronary angiography further allows assessment of the infarct-related artery, TIMI flow, and extent of coronary artery disease, providing insight into the anatomical profile of failed reperfusion [3,9].

The present study therefore aimed to characterize patients with failed thrombolysis by evaluating their clinical and coronary angiographic findings.

MATERIALS AND METHODS

Study Design and Population

This was an observational study conducted in the Department of Cardiology, at tertiary care hospital, over a period of one year in India. A total of 196 patients with failed thrombolysis were included in the final analysis.

Consecutive patients presenting with acute ST-segment elevation myocardial infarction (STEMI) within 12 hours of symptom onset, or with stuttering symptoms or ongoing ischemia, who received fibrinolytic therapy as the initial reperfusion strategy and subsequently underwent coronary angiography during the index hospitalization were considered for inclusion. Patients with failed thrombolysis, defined according to prespecified clinical and electrocardiographic criteria, constituted the study population. Patients with contraindications to fibrinolytic therapy or coronary angiography, death before coronary angiography, or incomplete clinical or angiographic data were excluded. Patients with a history of prior percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), rheumatic or congenital heart disease, pulmonary embolism, chronic kidney disease, cor pulmonale, or an active pacemaker were also excluded.

Definition of Failed Thrombolysis

Failed thrombolysis was defined as failure to achieve <50% resolution of the maximal baseline ST-segment elevation on a 12-lead electrocardiogram at 90 minutes following administration of the fibrinolytic agent, accompanied by persistent or recurrent ischemic chest pain. Patients fulfilling these criteria were considered to have failed pharmacological reperfusion and underwent further evaluation for rescue or subsequent revascularization.

Clinical and Risk-factor Assessment

Baseline demographic and clinical characteristics were recorded using a standardized data collection form. Variables included age, sex, presenting symptoms, heart rate, systolic blood pressure, and Killip class at presentation. Traditional cardiovascular risk factors, including diabetes mellitus, hypertension, dyslipidemia, smoking, alcohol use, and family history of coronary artery disease, were documented from the clinical history and available medical records. The ischemic window period was defined as the interval between the definite onset of chest pain or anginal equivalent symptoms and initiation of fibrinolytic therapy. The type of fibrinolytic agent administered, dosage, and

timing of administration were also recorded. The ischemic window period was defined as the interval between the definite onset of chest pain or anginal equivalent symptoms and initiation of fibrinolytic therapy. The type of fibrinolytic agent administered, dosage, and timing of administration were also recorded.

Coronary Angiographic Assessment

Coronary angiography was performed during the index hospitalization according to standard institutional practice. Patients with persistent ischemia, cardiogenic shock, or significant hemodynamic instability underwent early angiographic assessment with the intention of proceeding to rescue PCI when clinically indicated.

The angiographic profile included identification of the infarct-related artery (IRA), extent of coronary artery disease, and TIMI coronary flow grade. The extent of coronary artery disease was categorized as single-vessel disease (SVD), double-vessel disease (DVD), or triple-vessel disease (TVD). The IRA was classified as the left anterior descending artery (LAD), left circumflex artery (LCX), or right coronary artery (RCA). IRA patency was graded according to the Thrombolysis in Myocardial Infarction (TIMI) flow grading system from grade 0 to grade 3.

Revascularization Strategy

The subsequent management strategy following identification of failed thrombolysis was documented. This included rescue or subsequent PCI, percutaneous balloon angioplasty with or without CABG, and other management strategies including optimal medical therapy.

Study Outcomes

The primary outcome was the clinical and angiographic profile of patients experiencing failed thrombolysis. Secondary outcomes included assessment of the relationship of clinical characteristics, particularly ischemic window period and Killip class, with the presentation of failed thrombolysis, and the incidence of in-hospital mortality.

In-hospital mortality was defined as death from any cause occurring during the index hospitalization.

Statistical Analysis

Data were entered into a standardized database and analyzed using IBM SPSS Statistics, version 20.0. Continuous variables were summarized as mean ± standard deviation (SD) when normally distributed and as median with interquartile range when appropriate. Categorical variables were expressed as frequencies and percentages. The demographic, clinical, cardiovascular risk-factor, thrombolytic, angiographic, and revascularization characteristics of the study population were summarized descriptively. The distribution of Killip class, ischemic window period, infarct-related artery, extent of coronary artery disease, and TIMI flow grade was assessed.

RESULTS

A total of 196 patients with failed thrombolysis were included in the final analysis. The mean age was 53.2 ± 11.8 years, with a predominance of males (n=158, 80.6%). Chest pain was the most common presenting symptom in 171patients (87.2%), and most patients presented in Killip class I (n=127, 64.8%). Smoking (n=89, 45.4%) and diabetes mellitus (n=87/195, 44.6%) were the most prevalent cardiovascular risk factors, followed by dyslipidemia (n=76/195, 39.0%) and hypertension (n=69/195, 35.4%) **(Table 1)**.

Table 1: Baseline demographic, clinical, and cardiovascular risk-factor characteristics of the study population

Variable	N=196 patients
Age, years	53.2 ± 11.8
Male	158 (80.6)
Female	38 (19.4)
Heart Rate, bpm	92 ± 5
Presenting symptoms	
Chest pain	171 (87.2)
Dyspnea	13 (6.6)
Chest pain + dyspnea	12 (6.1)
Killip class	
I	127 (64.8)
II	41 (20.9)
III	18 (9.2)
IV	10 (5.1)
Traditional cardiovascular risk factors	
Diabetes mellitus	87/195 (44.6)
Hypertension	69/195 (35.4)
Dyslipidemia	76/195 (39.0)
Smoking	89 (45.4)
Alcohol use	57 (29.1)
Family history of CAD	16 (8.2)

Data are presented as mean ± SD or n (%), as appropriate. CAD: coronary artery disease; SD: standard deviation.

The mean ischemic window period was 6.3 ± 2.3 hours. Streptokinase was the predominant fibrinolytic agent, administered to 180 patients (91.8%), while full-dose fibrinolysis was used in 185 patients (94.4%). The left anterior descending artery was the most frequent infarct-related artery (n=105, 53.6%), followed by the right coronary artery (n=66, 33.7%). Single-vessel coronary disease was present in 108 patients (55.1%), whereas double-vessel and triple-vessel disease were observed in 56 (28.6%) and 32 (16.3%) patients, respectively. The mean left ventricular ejection fraction was 45% ± 15%. Angiography demonstrated TIMI grade 0 flow in 99 patients (50.5%), while TIMI grades 1, 2, and 3 were observed in 52 (26.5%), 34 (17.3%), and 11 (5.6%) patients, respectively **(Table 2)**.

Table 2: Thrombolytic therapy and coronary angiographic characteristics of the study population

Variable	N=196 Patients
Ischemic window period, hours	6.3 ± 2.3
Fibrinolytic agent	
Streptokinase	180 (91.8)
Reteplase	1 (0.5)
Tenecteplase	15 (7.7)
Dose	
Full dose	185 (94.4)
Half dose	11 (5.6)
Infarct-related artery	
LAD	105 (53.6)
LCX	25 (12.8)
RCA	66 (33.7)
Extent of coronary artery disease	
SVD	108 (55.1)
DVD	56 (28.6)
TVD	32 (16.3)
Troponin T	3.2 ± 1.2

LVEF	45 ± 15
TIMI flow grade	
Grade 0	99 (50.5)
Grade 1	52 (26.5)
Grade 2	34 (17.3)
Grade 3	11 (5.6)

Data are presented as mean ± SD or n (%), as appropriate. CABG: coronary artery bypass grafting; DVD: double-vessel disease; LAD: left anterior descending artery; LCX: left circumflex artery; LVEF: left ventricular ejection fraction; RCA: right coronary artery; SD: standard deviation; SVD: single-vessel disease; TIMI: Thrombolysis in Myocardial Infarction; TVD: triple-vessel disease

Following failed thrombolysis, rescue or subsequent PCI was performed in 166 patients (84.7%). POBA with or without CABG was performed in 11 patients (5.6%), whereas 19 patients (9.7%) received other management, including OMT. In-hospital mortality was observed in 7 patients (3.6%) **(Table 3)**.

Table 3: Revascularization strategy and in-hospital outcome

Variable	N=196 Patients
Rescue/subsequent PCI	166 (84.7)
POBA ± CABG	11 (5.6)
Other management/OMT	19 (9.7)
In-hospital mortality	7 (3.6)

Data are presented as n (%). CABG: coronary artery bypass grafting; OMT: optimal medical therapy; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty

DISCUSSION

This study provides a real-world description of patients with STEMI and failed thrombolysis in an Indian setting where fibrinolysis remains an important reperfusion strategy. The cohort was relatively young (53.2 ± 11.8 years) and predominantly male (80.6%), with smoking (45.4%) and diabetes (44.6%) being the most frequent cardiovascular risk factors. Fibrinolysis was initiated after a mean ischemic window of 6.3 ± 2.3 hours, and angiography demonstrated severe residual epicardial obstruction, with TIMI 0/1 flow in 77.0% of patients and TIMI 3 flow in only 5.6%. Despite this adverse angiographic profile, 84.7% underwent rescue or subsequent PCI, and in-hospital mortality was 3.6%. These findings highlight the clinical burden of failed pharmacological reperfusion and the potential importance of rapid recognition followed by timely invasive revascularization in settings where primary PCI is not universally available.

The demographic profile is broadly consistent with previous Indian and Asian STEMI cohorts. Study by Koh et al.[10] reported a mean age of 53.0 ± 12.2 years among 941 thrombolysed STEMI patients, with 89.9% being men; the corresponding values in the present cohort were 53.2 ± 11.8 years and 80.6%, respectively. The high prevalence of smoking and diabetes in the present study is also consistent with the substantial cardiometabolic risk burden described in Indian STEMI populations. Notably, Mishra et al. [11] reported diabetes in 55.3% of patients with failed thrombolysis, compared with 44.6% in the present cohort, while dyslipidemia and obesity were reported in 60.6% and 77.7%, respectively, in their study. Although differences in study populations and definitions limit direct comparison, the consistently high prevalence of modifiable risk factors emphasizes the importance of prevention alongside improvements in acute STEMI care.

The prolonged ischemic window is an important finding. In the present study, fibrinolysis was administered at a mean of 6.3 ± 2.3 hours after symptom onset, closely resembling the 6.58 ± 1.42 hours window reported by Mishra et al.[11] among patients with failed thrombolysis. In a comparative study of successful and failed thrombolysis Jain P. et al. [12] reported a higher frequency of failed thrombolysis among patients presenting after 9 hours, with longer symptom-to first-medical-contact time also observed in the failed-thrombolysis group. Karthikeyan G. et al. [13] highlighted that patients with STEMI in India frequently

present beyond 5-6 hours after symptom onset, with delays in symptom recognition, transportation and referral contributing to prolonged prehospital time. This delay is clinically relevant because the probability of successful myocardial reperfusion declines with increasing ischemic time. The Cardiological Society of India has similarly emphasized the time-dependent benefit of reperfusion and the substantial symptom-to-first-medical contact delays observed in Indian STEMI populations [14]. Delayed presentation may reflect a combination of poor symptom recognition, transportation barriers, referral delays, and treatment delays rather than failure of the fibrinolytic agent alone [10,15]. Thus, reducing total ischemic time through public awareness, prehospital ECG acquisition, early STEMI activation, and streamlined transfer pathways may be critical to improve the effectiveness of fibrinolysis in resource-constrained settings.

The angiographic findings provide direct anatomical evidence of the severity of failed reperfusion. The LAD was the infarct-related artery in 53.6% of patients, consistent with the predominance of anterior STEMI reported in previous cohorts; Koh et al., [10] reported anterior STEMI in 57.4% of their overall thrombolysed population. This finding is also consistent with the comparative observations of Jain et al.,[12] who reported a higher frequency of failed thrombolysis among patients with anterior-wall MI and a lower proportion of successful thrombolysis when the LAD was the infarct-related artery. Saravanan et al. [16] similarly reported a predominance of anterior-wall infarction among patients with failed thrombolysis, providing further context for the anterior LAD predominance observed in the present cohort. Although single-vessel disease was common in the present study (55.1%), most of the patients had markedly impaired epicardial flow at angiography. TIMI 0/1 flow was present in 77.0%, compared with 73.4% reported by Mishra et al. [11] in a prospective Indian cohort of failed thrombolysis. In contrast, only 5.6% of patients in the present study achieved TIMI 3 flow, underscoring the severity of persistent epicardial obstruction in this population. These findings also support the clinical importance of regarding TIMI 2 flow as incomplete rather than equivalent reperfusion, given the possibility of residual thrombus and flow-limiting stenosis.

The ECG-based definition of failed thrombolysis used in this study is clinically pragmatic, particularly in settings where immediate angiographic assessment is not readily available. The Cardiological Society of India position statement defines failed thrombolysis by persistent or worsening chest pain <50% ST-segment resolution 90 minutes after thrombolysis and recommends prompt transfer to rescue PCI when these criteria are present [14]. The use of persistent ischemic symptoms together with <50% ST-segment resolution at 90 minutes is supported by evidence linking the extent of ST-segment resolution with infarct-related artery patency and TIMI 3 flow. In TIMI 14 trial, limited ST-segment resolution was associated with lower infarct-related artery patency and higher 30-day mortality [17].Other clinical studies have similarly demonstrated that ST-segment resolution is a useful marker of successful thrombolysis and is associated with a more favorable in-hospital course[18,19]. Nevertheless, ST-segment nonresolution is not synonymous with persistent epicardial occlusion and may also reflect microvascular obstruction or extensive myocardial injury despite an angiographically patent artery [17]. Therefore, ECG assessment is best regarded as an early clinical trigger for angiographic evaluation and escalation of treatment rather than a substitute for anatomical assessment.

The in-hospital mortality of 3.6% in the present study is also notable when considered alongside previous real-world cohorts. Koh et al. [10] reported an overall in-hospital mortality of approximately 10% in a large thrombolysis-treated population, with failed thrombolysis associated with adverse outcomes. In another resource-constrained cohort, mortality among patients with failed thrombolysis approached 30%, underscoring

the potential prognostic consequences of persistent, failed reperfusion [15]. Although direct comparisons are limited by differences in patient selection, study design, follow-up duration, and treatment pathways, the relatively low in-hospital mortality observed in the present cohort is encouraging. The high utilization of rescue or subsequent PCI may have contributed to this favorable outcome; however, the observational nature of the study does not permit a causal inference regarding the effect of PCI on mortality.

Overall, the present study demonstrates that failed thrombolysis in STEMI is characterized by a relatively young but high-risk population, a prolonged ischemic window, frequent anterior infarction, and severe residual epicardial coronary obstruction. Importantly, the high use of rescue or subsequent PCI and the relatively low in-hospital mortality observed in this cohort suggest that systematic recognition of failed reperfusion followed by timely invasive management may mitigate the adverse consequences of unsuccessful fibrinolysis. In resource-constrained settings where fibrinolysis remains an important initial reperfusion strategy, improving outcomes will therefore require a coordinated approach that combines reduction of treatment delays, reliable ECG-based recognition of failed reperfusion, rapid angiographic assessment, and efficient rescue PCI pathways, together with sustained efforts to address the substantial burden of modifiable cardiovascular risk factors.

The high rate of rescue or subsequent PCI in the present cohort (84.7%) is particularly noteworthy and may reflect a systematic approach to early recognition of failed reperfusion followed by prompt anatomical assessment. This proportion is higher than the 58.5% rescue PCI rate reported by Mishra et al.[11] in an Indian cohort of failed thrombolysis, potentially reflecting differences in institutional protocols, PCI availability, patient referral, and treatment pathways [11]. The clinical rationale for this strategy is supported by randomized evidence. In trial by Gershlick A et al.[8], rescue PCI resulted in superior event-free survival compared with conservative treatment or repeat thrombolysis after failed fibrinolysis; at 6 months, event-free survival was 84.6% with rescue PCI compared with 70.1% with conservative treatment and 68.7% with repeat thrombolysis. A subsequent pooled analysis of randomized trials similarly demonstrated a reduction in short-term mortality with rescue PCI, although this benefit was accompanied by a potential increase in thromboembolic stroke [20]. Population-based data have also suggested lower long-term adverse outcomes among patients undergoing rescue PCI, while highlighting its substantial underuse in routine practice [3]. These data support an invasive strategy when failed fibrinolysis is recognized, particularly when persistent ischemia or clinical instability is present.

Limitations

Several limitations should be considered when interpreting these findings. This was a single-centre observational study, and the findings therefore reflect the experience of a specific clinical setting in which fibrinolysis remains an important reperfusion strategy. The study was also limited to patients with failed thrombolysis who underwent coronary angiography, and consequently the findings may not capture the full spectrum of patients with unsuccessful fibrinolysis. In the absence of a comparator group, the present study cannot establish whether the clinical or angiographic characteristics observed are distinct from those of patients with successful thrombolysis or primary PCI. In addition, outcomes were limited to the index hospitalization, so the subsequent clinical significance of the marked residual coronary obstruction observed in this cohort remains uncertain. Finally, because most patients received streptokinase, the findings may have limited applicability to contemporary fibrinolytic strategies using fibrin-specific agents.

CONCLUSION

In this study, failed thrombolysis in STEMI was characterized by a relatively young, predominantly male population with a high burden of modifiable cardiovascular risk factors and a prolonged ischemic window. The angiographic profile was marked by severe residual epicardial obstruction, with the LAD being the most frequent infarct-related artery and TIMI 0/1 flow present in the majority of patients. Most patients underwent rescue or subsequent PCI, with a relatively low rate of in-hospital mortality. Overall, these findings highlight the substantial angiographic burden associated with failed fibrinolysis and support early recognition of unsuccessful reperfusion followed by timely angiographic assessment and revascularization.

Authors' contributions

Dr Madhan Baskaran, Dr Chetana Krishnegowda contributed to the design of the work. Dr Chetana Krishnegowda collected the data and, together with Dr Madhan Baskaran performed the analysis. All authors collectively interpreted the data. Dr Chetana Krishnegowda drafted the manuscript. All authors critically commented for intellectual content.

Declaration by Authors

Data availability: Data used to generate results are available on request from the corresponding author.

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