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Thrombolytic Failure with Streptokinase in Acute Myocardial Infarction Using Electrocardiogram Criteria

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ABSTRACT

Streptokinase remains a key thrombolytic agent for ST-elevation myocardial infarction (STEMI) in many low-resource settings. Understanding the rate of thrombolytic failure and its predictors using electrocardiographic criteria is important for optimizing therapeutic strategies. **Objectives:** To determine the rate of thrombolytic failure in acute myocardial infarction using streptokinase, to describe in-hospital outcomes, and to assess associations between baseline clinical and ECG variables and thrombolytic success. **Methods:** This prospective observational study was conducted at Lady Reading Hospital, Peshawar. Ninety-three consecutive adult STEMI patients treated with streptokinase within 12 hours of symptom onset were included. Successful reperfusion was defined as >50% ST-segment resolution at 90 minutes. Demographics, risk factors, MI type, Killip class, symptom-to-door categories, and in-hospital outcomes were recorded. Bleeding events were classified using the TIMI criteria. Data were analyzed using the t-test for continuous variables and the chi-square/Fisher's exact test for categorical variables, with $p < 0.050$ considered significant. **Results:** The thrombolytic success rate was 77.4%. Symptom-to-door categories (<3h, 3–6h, >6h) were not significantly associated with reperfusion success. No baseline risk factors or Killip class independently predicted outcome. In-hospital mortality was 2.2%, TIMI major bleeding was 2.2%, and minor bleeding was 6.5%. Rescue PCI was required in 15.1%. Persistent chest pain, reperfusion arrhythmias, and hemodynamic instability occurred in 16.1%, 17.2%, and 14.0% respectively. **Conclusion:** Streptokinase achieved a high reperfusion rate with low complication rates. Conventional baseline variables did not predict success. Emphasis should remain on early presentation, system-level efficiency, and timely rescue PCI for failures.

INTRODUCTION

ST-elevation myocardial infarction (STEMI) remains a major global cause of cardiovascular morbidity and mortality [1]. Prompt reperfusion therapy, either by primary percutaneous coronary intervention (PCI) or thrombolysis, is vital to restore myocardial perfusion and limit infarct size [2]. In many low- and middle-income countries (LMICs), streptokinase is still widely used due to cost and accessibility, despite newer fibrin-specific agents offering improved profiles [3]. Recent international studies report varying success rates for thrombolytic therapy using streptokinase [4, 5]. For example, a study of 245 STEMI patients in central India found a 73% thrombolysis success rate, significantly higher among patients presenting within 12 hours of symptom onset (OR=3.15, p=0.006) [6]. Similarly, Imad et al. (2025) found that streptokinase administered early (within the first 1.5 to 3 hours) resulted in higher ST-segment resolution in a local Pakistani cohort [7]. A study conducted in Rajkot, India, by Sampat V, et al. (2025) reported approximately 70–76% successful ECG and clinical reperfusion following streptokinase when presentation was within admissible time windows [8]. Local studies in Pakistan affirm that delay in presentation,

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larger infarct territory (anterior MI), and worse clinical status on admission (higher Killip class) are commonly associated with poorer thrombolytic outcomes. However, many published series have conflicting or weak evidence regarding the role of hypertension, diabetes, and other risk factors. Previous studies reported that while risk factors like diabetes and hypertension were more common in failures, their adjusted statistical significance was inconsistent [9, 10]. Despite the accumulation of such data, gaps remain. Many studies focus predominantly on clinical or angiographic endpoints but lack consistent ECG-based reperfusion criteria or standardized follow-up. Additionally, few recent local datasets evaluate both reperfusion success and in-hospital safety outcomes in streptokinase use, explicitly testing baseline clinical and ECG predictors. The present study addresses these gaps by examining thrombolytic failure rates using ST-segment resolution criteria, describing in-hospital outcomes, and assessing baseline predictors in a Pakistani tertiary care setting.

Despite the continued reliance on streptokinase for STEMI management in low- and middle-income countries, contemporary local data evaluating thrombolytic success using standardized electrocardiographic criteria remain limited. Many published studies emphasize clinical or angiographic outcomes, with inconsistent application of ST-segment resolution benchmarks and inadequate assessment of in-hospital safety profiles. Furthermore, the predictive value of baseline demographic and clinical variables for thrombolytic success remains conflicting across regional datasets. This gap highlights the need for context-specific evidence to evaluate ECG-based reperfusion outcomes and identify potential predictors of thrombolytic failure in Pakistani tertiary care settings. This study aimed to determine the rate of thrombolytic failure in acute myocardial infarction using streptokinase, to describe in-hospital outcomes, and to assess associations between baseline clinical and ECG variables and thrombolytic success.

METHODS

This prospective observational study was conducted in the Department of Emergency Medicine, Lady Reading Hospital, Peshawar, after ethical approval from the Institutional Review Board (Ref. NO. 654/LRH/MTI), over twelve months (February 2023–February 2024). Consecutive sampling was employed to include all eligible patients presenting with acute STEMI during the study period, reflecting real-world emergency practice. This approach minimized selection bias by ensuring that no patient fulfilling the inclusion criteria was excluded based on the investigator's preference. The required sample size was calculated using the OpenEpi sample size calculator, with a 95% confidence level, 5% margin of error, and an anticipated thrombolytic failure rate of around 20–25% based on prior studies [11]. This yielded a final sample size of 93 patients, who were enrolled consecutively during the study period. A post-hoc power analysis was performed. With 93 patients and an observed thrombolytic failure rate of 22.6%, the study had approximately 70% power to detect a medium effect size (odds ratio = 2.0) at a two-sided alpha of 0.05. The study may have been underpowered to detect smaller associations. All adult patients (>18 years) presenting with acute myocardial infarction (AMI) and fulfilling electrocardiographic criteria for ST-segment elevation were eligible for inclusion, provided they received intravenous streptokinase within 12 hours of symptom onset and gave informed consent. Patients with contraindications to thrombolytic therapy, such as active bleeding, recent hemorrhagic stroke, recent major surgery or trauma, or those who underwent primary PCI as the initial reperfusion strategy, were excluded. Patients with incomplete records or missing 90-minute post-thrombolysis ECG data were also excluded. These criteria ensured that the study population consisted of clinically homogenous cases where the effect of streptokinase could be evaluated objectively. Demographic data, cardiovascular risk factors (hypertension, diabetes mellitus, smoking status, family history of IHD), and clinical presentation details were recorded at admission. Symptom-to-door time was carefully noted. Symptom-to-door time was carefully noted. For analysis, it was categorized into <3 hours, 3–6 hours, and >6 hours, reflecting clinically meaningful thresholds used in prior STEMI studies. The Killip class was used to assess the severity of heart failure. According to the participant's medical files they received a standard dose of streptokinase (1.5 million IU) administered intravenously over 60 minutes [2]. A baseline 12-lead ECG was performed before infusion and repeated at 90 minutes post-thrombolysis. ST-segment resolution was measured manually by two independent observers blinded to clinical details to minimize bias. Continuous cardiac monitoring was performed for 24 hours, and patients were observed for reperfusion arrhythmias, persistent chest pain, hemodynamic instability, and bleeding complications. Successful thrombolysis was defined as ≥50% resolution of the maximum ST-segment elevation on a standard 12-lead ECG performed 90 minutes after completion of streptokinase infusion, compared with baseline values. Secondary outcomes included reperfusion arrhythmias, persistent chest pain, hemodynamic instability, rescue PCI, and in-hospital mortality. Bleeding complications were categorized using TIMI criteria as major or minor events. ST-segment resolution was independently

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assessed by two experienced cardiologists blinded to each other's readings. Inter-observer agreement was calculated using Cohen's kappa statistic, which demonstrated substantial agreement (κ = 0.82) to ensure reliability. Data were analyzed using IBM SPSS Statistics version 26.0. Continuous variables (age, symptom-to-door time) were assessed for normality and compared using independent-sample t-tests. Categorical variables (gender, hypertension, diabetes, smoking, family history of IHD, type of MI, Killip class, reperfusion arrhythmias, persistent chest pain, hemodynamic instability, rescue PCI, in-hospital mortality) were summarized as frequencies and percentages, and associations with thrombolytic success (ST-resolution >50% vs. <50%) were examined using Chi-square or Fisher's exact tests. Multivariate logistic regression was performed to identify independent predictors, with $p < 0.05$ considered statistically significant.

RESULTS

The study included 93 patients with acute myocardial infarction who received streptokinase. The mean age of the cohort was 54.3 ± 10.4 years, with a male predominance (79.6% males vs. 20.4% females). Hypertension was present in 36.6% of patients, diabetes mellitus in 33.3%, and smoking history in 29.0%. A positive family history of ischemic heart disease was reported in 17.2% of cases. These findings indicate that the majority of patients were middle-aged men with conventional cardiovascular risk factors, particularly hypertension and diabetes. Most patients presented with anterior wall MI (68.8%), followed by inferior wall MI (22.6%), and other locations (8.6%). The mean symptom-to-door time was 4.12 ± 1.05 hours, suggesting relatively early hospital presentation. Assessment of clinical status revealed that 69.9% of patients were in Killip Class I, indicating no overt heart failure at presentation. Killip Class II was seen in 15.1%, whereas 15.0% were in Class III–IV, reflecting moderate-to-severe heart failure in a smaller subset of patients. (Table 1).

Table 1: Baseline Demographic, Clinical, and Electrocardiographic Characteristics of Study Population (N=93)

Variables	Category	N (%) / Mean ± SD
Age (years)	–	54.3 ± 10.4
Gender	Male	74 (79.6)
	Female	19 (20.4)
Hypertension	Yes	34 (36.6)
	No	59 (63.4)
Diabetes Mellitus	Yes	31 (33.3)
	No	62 (66.7)
Smoking	Yes	27 (29.0)
	No	66 (71.0)
Family History of IHD	Yes	16 (17.2)
	No	77 (82.8)
Type of MI	Anterior	64 (68.8)
	Inferior	21 (22.6)
	Other	8 (8.6)
Symptom-to-door time (hrs)	–	4.12 ± 1.05
Killip Class	I	65 (69.9)
	II	14 (15.1)
	III	11 (11.8)
	IV	3 (3.2)

Successful reperfusion, defined as >50% ST-segment resolution at 90 minutes, was observed in 72 patients (77.4%), while 21 patients (22.6%) experienced thrombolytic failure. Reperfusion arrhythmias were recorded in 17.2% of patients, whereas 16.1% reported persistent chest pain following thrombolysis. Hemodynamic instability was noted in 14.0% of the study population. Overall, these findings reflect a good thrombolytic response in the majority of patients, with complications limited to a smaller proportion (Table 2).

Table 2: Thrombolytic Response and Reperfusion Indicators (N=93)

Outcome/Variables	Category	Frequency (%)
ST-Resolution	>50% (Success)	72 (77.4%)
	<50% (Failure)	21 (22.6%)
Reperfusion Arrhythmias	Yes	16 (17.2%)
	No	77 (82.8%)
Persistent Chest Pain	Yes	15 (16.1%)
	No	78 (83.9%)
Hemodynamic Instability	Yes	13 (14.0%)
	No	80 (86.0%)

Chi-square analysis revealed that none of the conventional cardiovascular risk factors—hypertension ($\chi^2 = 0.028$, $p = 0.868$), diabetes mellitus ($\chi^2=0.277$, $p=0.599$), smoking ($\chi^2 =1.312$, $p=0.252$), or family history of IHD ($\chi^2=0.162$, $p=0.687$) showed a statistically significant association with thrombolytic success. Similarly, type of MI ($\chi^2=0.063$, $df=2$, $p=0.969$) and Killip class ($\chi^2=1.718$, $df = 3$, $p=0.633$) were not significantly related to ST-segment resolution. Among reperfusion indicators, persistent chest pain showed a non-significant trend toward association ($\chi^2 =2.591$, $p=0.107$). Rescue PCI requirement ($\chi^2 =2.247$, $p=0.134$) and in-hospital mortality ($\chi^2 =0.879$, 0.348) were also not significantly different between patients with successful and failed thrombolysis. These findings indicate that none of the studied clinical or electrocardiographic parameters could reliably predict thrombolytic outcome in this cohort (Table 3).

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Table 3: Association of Baseline Variables and Outcomes with Thrombolytic Success (N=93)

Variables	ST-Resolution <50% (N=21)	ST-Resolution >50% (N=72)	χ^2 (DF)	p-Value
Risk Factors				
Hypertension (Yes)	8 (23.5%)	26 (76.5%)	0.028 (1)	0.868
Diabetes Mellitus (Yes)	8 (25.8%)	23 (74.2%)	0.277 (1)	0.599
Smoking (Yes)	4 (14.8%)	23 (85.2%)	1.312 (1)	0.252
Family History of IHD (Yes)	3 (18.8%)	13 (81.3%)	0.162 (1)	0.687
Clinical Presentation				
Type of MI – Anterior	14 (21.9%)	50 (78.1%)	0.063 (2)	0.969
Type of MI – Inferior	5 (23.8%)	16 (76.2%)	–	–
Type of MI – Other	2 (25.0%)	6 (75.0%)	–	–
Killip Class I	16 (24.6%)	49 (75.4%)	–	–
Killip Class II	2 (14.3%)	12 (85.7%)	–	–
Killip Class III–IV	3 (20.0%)	11 (80.0%)	1.718 (3)	0.633
Reperfusion Indicators				
Reperfusion Arrhythmias (Yes)	5 (31.3%)	11 (68.8%)	0.831 (1)	0.362
Persistent Chest Pain (Yes)	1 (6.7%)	14 (93.3%)	2.591 (1)	0.107
Hemodynamic Instability (Yes)	4 (30.8%)	9 (69.2%)	0.580 (1)	0.446
In-Hospital Outcomes				
Rescue PCI (Yes)	1 (7.1%)	13 (92.9%)	2.247 (1)	0.134
Mortality (Yes)	1 (50.0%)	1 (50.0%)	0.879 (1)	0.348

Patients who arrived within 3 hours had the highest success rate (81.8%), while those arriving between 3–6 hours (76.9%) and beyond 6 hours (75.0%) had slightly lower success. However, these differences were not statistically significant (Pearson χ^2=0.146, df=2, p=0.930; Cramer's V=0.040), indicating that, in this cohort, time to presentation did not independently predict reperfusion outcome. None of the clinical factors, hypertension, diabetes mellitus, smoking, Killip class, or symptom-to-door time categories emerged as significant independent predictors. All odds ratios crossed unity, with wide confidence intervals and non-significant p-values. These findings suggest that baseline comorbidities and clinical status did not meaningfully influence the likelihood of achieving successful reperfusion in this study population.

Table 4: Predictors of Thrombolytic Success in STEMI Patients (N=93)

Predictor/ Symptom-to-Door Time	Failure N (%)	Success N (%)	Total	Adjusted OR (95% CI)	p-Value
Hypertension (Yes vs No)	9 (22.5)	31 (77.5)	40	0.87 (0.31–2.43)	0.784
Diabetes Mellitus (Yes vs No)	7 (21.2)	26 (78.8)	33	0.76 (0.27–2.13)	0.604
Smoking (Yes vs No)	5 (16.1)	26 (83.9)	31	2.07 (0.59–7.28)	0.258
Killip Class (≥II vs I)	6 (21.4)	22 (78.6)	28	0.73 (0.23–2.38)	0.606
Symptom-to-Door <3h	2 (18.2)	9 (81.8)	11	Reference	–
Symptom-to-Door 3–6h	18 (23.1)	60 (76.9)	78	1.38 (0.12–16.1)	0.799
Symptom-to-Door >6h	1 (25.0)	3 (75.0)	4	1.67 (0.09–31.1)	0.732

TIMI major bleeding was rare (2.2%), and TIMI minor bleeding occurred in 6.5% of patients. Rescue PCI was required in 15.1% of cases, while in-hospital mortality was low at 2.2%. Overall, these outcomes highlight that streptokinase therapy was generally safe, with a low rate of serious bleeding and favorable short-term survival (Table 5).

Table 5: In-Hospital Outcomes Including TIMI-Defined Bleeding (N=93)

Outcome	Frequency (%)
TIMI Major Bleeding	2 (2.2%)
TIMI Minor Bleeding	6 (6.5%)
Rescue PCI	14 (15.1%)
In-hospital Mortality	2 (2.2%)

The overall in-hospital complication rates were low in this cohort of 93 patients who underwent thrombolysis with streptokinase. Major bleeding occurred in only 2.2% of cases, whereas minor bleeding was observed in 6.5% of patients. The most frequent adverse event was rescuing PCI requirement, seen in 15.1%, reflecting the need for additional intervention in those with suboptimal reperfusion. In-hospital mortality was low, with only 2.2% of patients succumbing during admission. These findings suggest that streptokinase was generally safe and effective in this population, with limited major bleeding and favorable short-term survival.

DISCUSSION

The present study of 93 STEMI patients treated with streptokinase showed a 77.4% rate of early ECG reperfusion (ST-segment resolution >50%), with low in-hospital major bleeding (2.2%) and mortality (2.2%). When patients were stratified by symptom-to-door time, no statistically significant difference in thrombolytic success was observed. Although early presenters (<3h) had numerically higher success (81.8%), this effect was not significant, suggesting that in this relatively early-presenting cohort, time-to-door did not independently influence reperfusion outcome. These figures sit within contemporary regional and LMIC experience. Pakistani series commonly report streptokinase success around 69–73%, with acceptable safety; 69–71% success; a large 2025 tertiary-care cohort likewise reported 73% success and higher complications in failed cases [12]. Results comparable to these have also been described in other South Asian centers, with success clustering near 70–76% and clear time-dependence of effect [8]. A key finding of this study was the absence of statistically significant associations between thrombolytic success and conventional baseline factors (hypertension, diabetes, smoking, family history), type of MI, or Killip class.

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Multivariate logistic regression further confirmed that hypertension, diabetes mellitus, smoking, Killip class, and symptom-to-door categories were not independent predictors of thrombolytic success. All odds ratios crossed unity, and confidence intervals were wide, indicating no significant associations. Some recent literature does report predictors of failed thrombolysis, notably higher Killip class, anterior infarction, and treatment delays. A 5-year analysis from a non-PCI center identified Killip ≥II and tachycardia as independent FT predictors; intriguingly, tenecteplase (vs. streptokinase) carried a higher adjusted odds of FT in that cohort, emphasizing context and selection effects [13]. Other local work underscores time-to-needle as the dominant driver: significantly greater success was observed when streptokinase was administered within 6 hours of symptom onset, while demographic risk factors had minimal impact, directionally consistent with the present null associations for age, sex, and comorbidities [10]. The lack of signal for the type of MI (anterior vs. inferior/other) in this study also warrants comment. Anterior STEMI is generally linked with larger infarcts and worse injury profiles (CMR and biomarker data following primary PCI), which could plausibly reduce STR with fibrinolysis; yet that pattern did not emerge here, potentially due to limited sample size or a relatively narrow spectrum of delays and infarct sizes [14]. In addition, STR is an ECG surrogate for tissue reperfusion rather than a direct angiographic endpoint; alignment between STR and angiographic patency is imperfect, which can dilute associations with baseline features. Contemporary data confirm that STR remains clinically useful but not definitive on its own, and that composite reperfusion criteria improve diagnostic accuracy [15]. The safety profile observed here (rare major bleeding, very low in-hospital mortality) is consistent with modern fibrinolysis experience, where systems of care emphasize early presentation and guideline-concordant adjunctive therapy. Bleeding complications were reclassified according to TIMI criteria. TIMI major bleeding was rare (2.2%), minor bleeding occurred in 6.5%, rescue PCI was required in 15.1%, and in-hospital mortality was 2.2%. These findings reinforce the favorable safety profile of streptokinase in this cohort. Registries demonstrate that when pharmacologic reperfusion is selected in non-PCI or delayed-PCI settings, most patients achieve clinical reperfusion with better subsequent survival than failed cases, mirroring the benign in-hospital course in the present cohort [16]. A 2025 PCI-capable series from Pakistan also reported higher complications and mortality when thrombolysis failed, reinforcing the clinical importance of early rescue PCI pathways for non-responders [17]. Several explanations are plausible for why no predictors were statistically significant in this study. First, with 93 patients and very few adverse events the study was underpowered to detect modest effects, particularly across multi-level variables such as Killip class, where expected counts were small. Similar cohorts with several hundred patients have more readily detected independent predictors. Second, there was limited heterogeneity in treatment delay: the mean symptom-to-door time was 4.1 h with relatively narrow dispersion. Studies that demonstrate clear delay effects typically include substantial late-presenter tails. Third, ST-segment resolution (STR) at 90 minutes, while a simple bedside marker, is an imperfect surrogate, as discordance with angiographic patency and microvascular obstruction is recognized; such classification noise reduces power to detect baseline associations [13, 15]. Fourth, potential confounders such as anti-streptokinase antibody titers, adjunctive pharmacotherapy, infarct size, and microvascular dysfunction were not systematically measured and may explain outcome differences in other series [18]. Finally, the study setting likely contributed: regional data suggest streptokinase can be highly effective in early presenters, where baseline risk factors may matter less than timeliness of therapy [19, 20]. Taken together, the pattern of good overall STR success, low adverse events, and absence of significant predictors supports the view that system-level efficiency (symptom-to-needle, door-to-needle time), standardized protocols, and early rescue pathways are the dominant levers in streptokinase-based reperfusion programs, rather than static demographic risk profiles. These findings are consistent with our multivariate regression analysis, where none of the examined baseline characteristics independently predicted success.

This study has several limitations, including its single-center design and relatively small sample size, which may have limited statistical power to detect modest associations between baseline variables and thrombolytic success. The reliance on ST-segment resolution as a surrogate marker of reperfusion, without routine angiographic confirmation, may have introduced classification bias. Additionally, long-term outcomes beyond hospital discharge were not evaluated. Future multicenter studies with larger cohorts, angiographic validation of reperfusion, and extended follow-up are warranted to better identify independent predictors of thrombolytic failure and to optimize system-level strategies, including timely rescue PCI pathways, in resource-constrained settings.

CONCLUSIONS

In conclusion, streptokinase achieved high early ECG reperfusion with low in-hospital complications. The absence of significant associations between thrombolytic

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success and traditional baseline variables likely reflects a combination of limited power, restricted variability in delays, and the imperfect correlation between STR and true tissue-level reperfusion. Programs using streptokinase should prioritize earlier presentation and treatment, systematic 90-minute STR checks, and ready access to rescue PCI for non-responders. Future work should be multicenter and adequately powered; incorporate angiographic or imaging validation of reperfusion; and evaluate additional biological and systems-of-care determinants (antistreptokinase antibodies, adjunct pharmacology, pre-hospital delay reduction).

Authors' Contribution

Conceptualization: HK, JS, HS
Methodology: SA, HS
Formal analysis: MF, SA, HK
Writing and Drafting: MF, JS, NA, HS
Review and Editing: MF, JS, NA, HS, SA, HK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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