e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(6); 2268-2274

Original Research Article

Feasibility and Clinical Efficacy of a Delayed Pharmacoinvasive Approach for ST-Elevation Myocardial Infarction

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Received: 27-04-2026 / Revised: 26-05-2026 / Accepted: 28-06-2026
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Conflict of interest: Nil

Abstract:

Background: Primary PCI is the preferred reperfusion strategy for ST-elevation myocardial infarction (STEMI), but timely intervention is frequently limited in resource-constrained settings. Pharmacoinvasive therapy is recommended when primary PCI is not feasible; however, evidence regarding PCI performed 24–72 hours after thrombolysis remains scarce. This study evaluated the feasibility and clinical efficacy of delayed pharmacoinvasive PCI compared with routine pharmacoinvasive therapy.

Methods: This prospective single-center study included 152 thrombolyzed STEMI patients undergoing PCI between January and December 2024. Patients were categorized into routine (PCI within 24 hours; n=84) and delayed (PCI between 24 and 72 hours; n=68) pharmacoinvasive groups. Thirty-day major adverse cardiac and cerebrovascular events (MACCE) and secondary clinical outcomes were compared between the groups.

Results: Baseline demographic and clinical characteristics were comparable between the two groups, except for a modestly lower left ventricular ejection fraction in the delayed group (45.6 ± 4.6% vs. 47.1 ± 4.8%, *P*=0.041). Thirty-day MACCE occurred in 8.3% of the routine group and 13.2% of the delayed group (*P*=0.187). No significant differences were observed in death, reinfarction, congestive heart failure, target vessel revascularization, or major bleeding (all *P*>0.05). Subgroup analysis of patients undergoing PCI within 24–48 hours and 48–72 hours also demonstrated comparable clinical outcomes.

Conclusion: Delayed pharmacoinvasive PCI performed up to 72 hours after successful thrombolysis appears to be a feasible and clinically effective alternative when timely PCI is not possible, particularly in resource-limited settings.

Keywords: ST-elevation myocardial infarction (STEMI); Pharmacoinvasive therapy; Percutaneous coronary intervention (PCI); Delayed PCI; Thrombolysis.

DOI: 10.25258/ijcpr.18.6.357

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Introduction

ST-elevation myocardial infarction (STEMI) remains a leading cause of cardiovascular death, characterized by acute coronary occlusion, myocardial ischemic symptoms, ST-segment elevation on electrocardiography, and elevated cardiac biomarkers [1]. Primary percutaneous coronary intervention (PPCI) is currently the preferred reperfusion therapy for patients presenting with acute STEMI when it can be performed by an experienced team in a timely fashion [2]. However, achieving this timely window remains difficult in practice: a substantial segment of patients are managed at hospitals lacking PPCI capability, and even in well-resourced health systems a majority of transferred patients fail to meet guideline-recommended door-to-balloon time metrics [3]. Pharmacoinvasive strategy — fibrinolysis combined with rescue PCI in case of failed lysis, or a routine early invasive strategy within 3–24 hours in case of successful lysis — has therefore been proposed as a therapeutic option for STEMI patients when timely PPCI is not feasible [4], a concept substantiated by randomized evidence from the STREAM trial [5]. Delay in performing PCI is especially common in low- and middle-income countries, where PPCI is not universally available [6], and the Occluded Artery Trial (OAT) further complicated decision-making by failing to show benefit of late PCI (beyond 72 h–28 d) of a totally occluded infarct-related artery over medical therapy alone in stable post-STEMI patients [7].

Despite this body of evidence, a definitive consensus on the safest and most effective timing of the pharmacoinvasive strategy remains elusive, with existing trials largely excluding patients who receive PCI beyond roughly 18–24 hours post-fibrinolysis — precisely the window most frequently encountered in resource-limited settings due to

logistic, financial, and infrastructural delays. To our knowledge, the only study to have specifically addressed this 24–72-hour "delayed pharmacoinvasive" window in STEMI patients with partially occluded coronary arteries is the prospective registry by Sethi et al, which demonstrated comparable 30-day MACCE, bleeding, and symptom outcomes between routine (3–24 h) and delayed (24–72 h) pharmacoinvasive groups, concluding that "delayed PCI pharmacoinvasive strategy in a critical diseased but not completely occluded artery beyond 24 h in patients who have been timely thrombolyzed seems a reasonable strategy" [8]. However, this remains a single-center study with a comparatively short follow-up duration, and the authors themselves called for further prospective registries to corroborate these preliminary findings. Building on and seeking to strengthen this existing evidence base, the present study was carried out to further evaluate the feasibility and efficacy of delayed pharmacoinvasive therapy in acute STEMI patients with partially occluded coronary vasculature, with the aim of generating additional real-world data to support or refine its role as a practical reperfusion strategy in low-resource, high-burden clinical settings.

Methods

Study Design and Setting: This was a physician-initiated, single-center prospective study conducted at a tertiary care center over a period of one year, between January 2024 and December 2024. Written informed consent was obtained from all patients, or from their designees, prior to enrollment.

Study Population: The study enrolled acute STEMI patients who were thrombolyzed within 12 hours of symptom onset and subsequently underwent percutaneous coronary intervention (PCI). Patients were either admitted to peripheral hospitals, thrombolyzed, and then referred to our center; or were directly admitted to our hospital but, being unable to undergo primary PCI in a timely manner, received thrombolysis as the initial reperfusion strategy. A total of 152 patients meeting these criteria were enrolled and analyzed.

Study Groups: For various nonspecific reasons — most commonly financial constraints and a mismatch between patient load and the availability of round-the-clock catheterization laboratory services, even at tertiary care centers — a subset of patients could not undergo PCI within the recommended 3–24 h window following initiation of thrombolytic therapy. The 24–72 h period, though considered a grey area in the literature for the timing of post-thrombolysis PCI, remains a commonly encountered real-world strategy in low-resource settings and is used at many centers when the infarct-related vessel is still found to be occluded on angiography. This subset was designated the delayed pharmacoinvasive group.

To evaluate the effectiveness of this strategy, outcomes in this group were compared with those of a cohort undergoing routine pharmacoinvasive therapy (thrombolysis within 12 h of symptom onset followed by PCI within 3–24 h of thrombolysis initiation). The two groups were not randomized. Stated simply, Group 1 (routine) comprised patients undergoing PCI within 24 h of thrombolysis, and Group 2 (delayed) comprised patients undergoing PCI between 24 and 72 h of thrombolysis.

Inclusion and Exclusion Criteria: Patients who underwent primary PCI were excluded from the study. Additional exclusion criteria included contraindication to thrombolysis, presentation beyond the eligible window for thrombolytic therapy, and evidence of a totally occluded infarct-related artery on angiogram performed within the 24–72 h window.

Data Collection: Baseline demographic and clinical data were recorded for all enrolled patients at the time of admission, including age, gender, and conventional cardiovascular risk factors such as diabetes mellitus, hypertension, and smoking status. Killip class at presentation, infarct territory (anterior wall vs non-anterior wall STEMI), and left ventricular ejection fraction on transthoracic echocardiography were also documented. Coronary angiographic findings were recorded and patients were further classified based on the extent of coronary artery disease as single-vessel or multi-vessel disease. Time intervals — symptom onset to needle (thrombolysis) time and thrombolysis to PCI time — were captured for each patient to characterize the reperfusion timeline in both groups.

Procedural Details: All patients received standard-dose thrombolytic therapy as per institutional protocol, along with guideline-directed antiplatelet and anticoagulant therapy at the time of thrombolysis. Coronary angiography was performed via radial or femoral access at the discretion of the treating interventional cardiologist, and PCI, where indicated, was performed using standard technique with drug-eluting stent implantation. Patients found to have complete recanalization of the infarct-related artery on angiography were managed conservatively and deferred from PCI, while those with a totally occluded artery within the 24–72 h window were excluded from the delayed pharmacoinvasive group, as previously stated. All procedures were performed by experienced operators at the same tertiary care center, and periprocedural antithrombotic management followed a uniform institutional protocol across both groups to minimize variability.

Statistical Analysis: Categorical variables were expressed as frequency (percentage) and continuous

variables as mean ± standard deviation; comparisons between groups were made using the Chi-square test and independent sample t-test, respectively, with a two-tailed $P < 0.05$ considered statistically significant.

Results

The two study groups were largely comparable at baseline, with no significant difference in mean age (54.8 ± 9.8 years in the routine group vs 53.9 ± 10.7 years in the delayed group, $P = 0.412$) or in the distribution of gender, diabetes, hypertension, and smoking status (all $P > 0.05$). Killip class ≥2 was numerically more frequent in the delayed group (16.2% vs 9.5%), though this difference did not reach statistical significance ($P = 0.209$). Mean left ventricular ejection fraction was modestly but significantly lower in the delayed group compared with the routine group (45.6 ± 4.6% vs 47.1 ± 4.8%, $P = 0.041$). The proportion of anterior wall MI and multi-vessel disease was similar between groups. As expected by study design, the mean thrombolysis-to-PCI time was markedly longer in the delayed group (43.8 ± 15.1 h) compared with the routine group (17.2 ± 5.6 h, $P = 0.001$), while symptom-to-needle time was comparable between the two ($P = 0.132$) (Table 1).

Table 1: Comparison of baseline characteristics of the two study groups (mean ± SD)

Characteristic	Routine (n = 84)	Delayed (n = 68)	P value
Age, years	54.8 ± 9.8	53.9 ± 10.7	0.412
Male, n (%)	73 (86.9)	61 (89.7)	0.567
Diabetes, n (%)	17 (20.2)	15 (22.1)	0.771
Hypertension, n (%)	23 (27.4)	19 (27.9)	0.938
Smoking, n (%)	46 (54.8)	38 (55.9)	0.887
Killip class ≥ 2, n (%)	8 (9.5)	11 (16.2)	0.209
Left ventricular ejection fraction (%)	47.1 ± 4.8	45.6 ± 4.6	0.041
Anterior wall MI, n (%)	45 (53.6)	39 (57.4)	0.523
Multi-vessel disease, n (%)	36 (42.9)	30 (44.1)	0.921
Symptom-to-needle time, h	5.4 ± 3.6	5.9 ± 4.3	0.132
Thrombolysis-to-PCI time, h	17.2 ± 5.6	43.8 ± 15.1	0.001

The primary endpoint of MACCE within 30 days occurred in 9 (13.2%) patients in the delayed group compared with 7 (8.3%) in the routine group, a difference that did not reach statistical significance ($P = 0.187$). Similarly, none of the individual secondary endpoints — death, reinfarction, congestive heart failure, target vessel revascularization, or major bleeding — differed significantly between the two groups (all $P > 0.05$), although reinfarction showed a numerically higher trend in the delayed group (Table 2).

Table 2: Outcomes based on primary and secondary endpoints in the two study groups

Clinical outcome	Routine (n = 84)	Delayed (n = 68)	P value
Primary endpoint			
MACCE, n (%)	7 (8.3%)	9 (13.2%)	0.187
Secondary endpoints			
Death, n (%)	2 (2.4%)	1 (1.5%)	0.744
Reinfarction, n (%)	1 (1.2%)	3 (4.4%)	0.157
Congestive heart failure, n (%)	3 (3.6%)	3 (4.4%)	0.601
Target vessel revascularization, n (%)	1 (1.2%)	1 (1.5%)	0.999
Major bleeding, n (%)	1 (1.2%)	1 (1.5%)	0.999

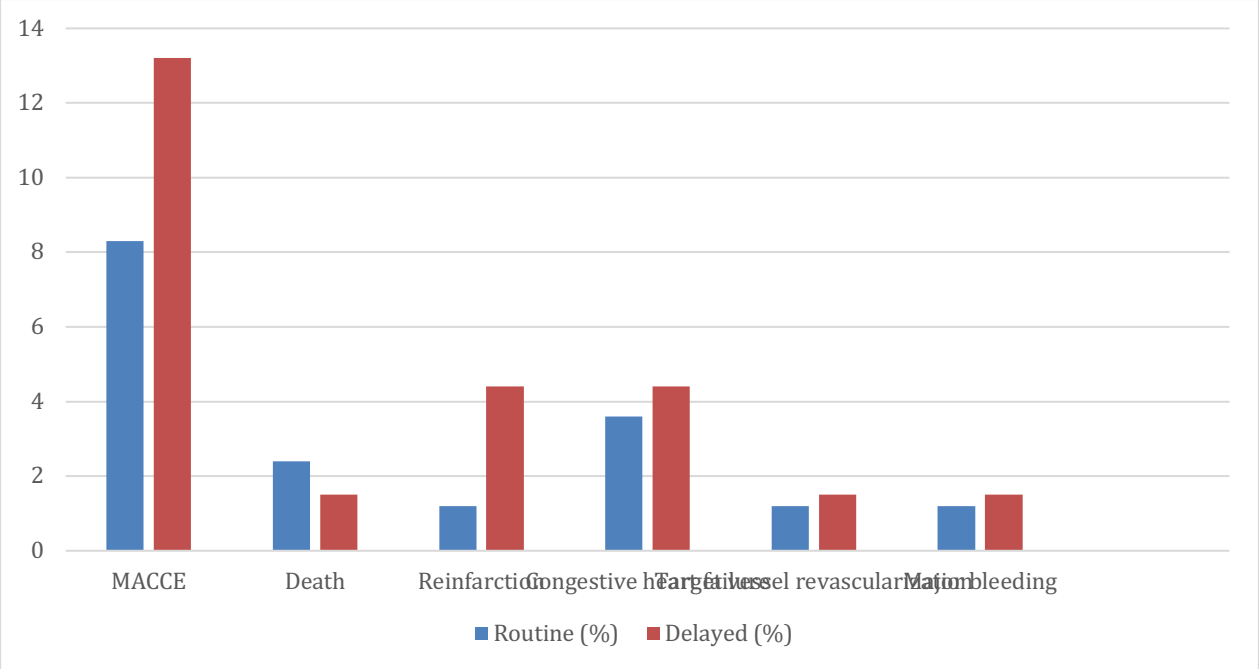

Figure 1: Comparison of Primary and Secondary Clinical Outcomes Between Routine and Delayed Pharmacoinvasive Groups.

When the delayed group was further stratified into 24–48 h (Group B) and 48–72 h (Group C) subgroups and compared with the routine group (Group A, ≤24 h), no statistically significant differences were observed in MACCE or any secondary outcome across the three time windows (all P > 0.05 for A vs B, A vs C, and B vs C comparisons). MACCE occurred in 8.3%, 15.0%, and 10.7% of patients in Groups A, B, and C, respectively, suggesting that outcomes did not worsen progressively with increasing delay from 24 to 72 hours. Reinfarction showed a numerically increasing trend from Group A to Group C (1.2% to 7.1%), but this did not reach statistical significance (P = 0.152 for A vs C) (Table 3).

Table 3: Outcomes based on time from thrombolysis to PCI among study groups

Outcome	Group A (≤24 h), n = 84	Group B (24–48 h), n = 40	Group C (48–72 h), n = 28	P value (A vs B)	P value (A vs C)	P value (B vs C)
MACCE, n (%)	7 (8.3%)	6 (15.0%)	3 (10.7%)	0.226	0.601	0.712
Death, n (%)	2 (2.4%)	1 (2.5%)	0 (0%)	0.999	0.999	0.999
Reinfarction, n (%)	1 (1.2%)	1 (2.5%)	2 (7.1%)	0.999	0.152	0.421
Congestive heart failure, n (%)	3 (3.6%)	2 (5.0%)	1 (3.6%)	0.732	0.999	0.999
Major bleeding[1], n (%)	1 (1.2%)	0 (0%)	1 (3.6%)	0.999	0.412	0.418

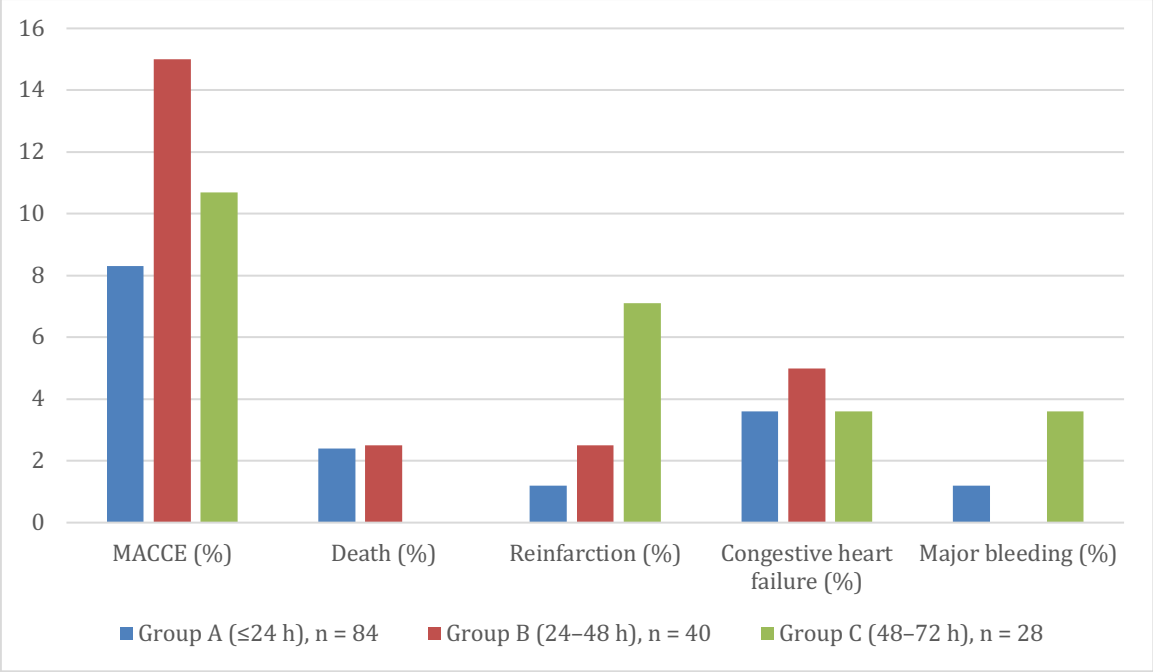

Figure 2: Comparison of 30-Day Clinical Outcomes According to Timing of PCI After Thrombolysis

Discussion

Primary percutaneous coronary intervention (PPCI) remains the preferred reperfusion strategy for patients presenting with acute ST-elevation myocardial infarction (STEMI), provided it can be performed within the recommended time frame by an experienced team [2,3]. However, timely PPCI is frequently unattainable in routine clinical practice, particularly in low- and middle-income countries where catheterization laboratory availability, inter-hospital transfers, financial constraints, and delayed patient presentation remain significant barriers [10]. Consequently, current guidelines recommend a pharmacoinvasive approach consisting of timely fibrinolysis followed by routine PCI within 3–24 hours when PPCI cannot be achieved promptly [11]. Despite these recommendations, the optimal management of patients who undergo PCI beyond the conventional 24-hour window following successful thrombolysis remains uncertain because evidence supporting delayed pharmacoinvasive intervention is limited. In the present study, patients undergoing PCI between 24 and 72 hours after thrombolysis demonstrated clinical outcomes comparable to those receiving routine pharmacoinvasive therapy within 24 hours, with no statistically significant differences in 30-day major adverse cardiac and cerebrovascular events (MACCE) or individual secondary outcomes. These findings suggest that delayed pharmacoinvasive PCI may represent a reasonable alternative when early intervention is not feasible.

Previous evidence regarding delayed coronary intervention after STEMI has been inconsistent. The Occluded Artery Trial (OAT) demonstrated no clinical benefit of PCI performed between 3 and 28 days after myocardial infarction in stable patients with persistently occluded infarct-related arteries and even suggested a possible increase in recurrent infarction, leading to recommendations against routine late PCI in completely occluded vessels beyond 72 hours [12,13]. Similarly, observational data have reported that PCI performed during the index hospitalization after the first 24 hours does not adversely affect mortality, although the precise timing of intervention has varied across studies [14]. Importantly, the current study differs from these investigations because patients with totally occluded infarct-related arteries were excluded, and only those with patent or partially recanalized vessels after successful thrombolysis were evaluated. This distinction is clinically relevant, as preservation of residual coronary flow may allow delayed revascularization without exposing patients to the potential risks associated with intervention on chronically occluded arteries. The present findings therefore reinforce the limited but growing evidence supporting delayed pharmacoinvasive PCI in carefully selected STEMI patients [8,15].

An important observation in the present study was that delaying PCI from 24 to 72 hours did not result in a progressive increase in adverse clinical outcomes. The incidence of MACCE remained similar across patients undergoing PCI within 24 hours, between 24–48 hours, and between 48–72 hours after thrombolysis, while no significant differences were observed in mortality, congestive heart failure, target vessel revascularization, or major bleeding. Although reinfarction demonstrated a numerically increasing trend with longer delays, this difference did not achieve statistical significance, likely because of the relatively modest

sample size. Furthermore, baseline clinical characteristics were largely balanced between study groups, with the exception of a slightly lower left ventricular ejection fraction in the delayed group, indicating that delayed intervention did not substantially compromise short-term outcomes despite the presence of somewhat poorer ventricular function. These findings suggest that, within the first 72 hours after successful thrombolysis, delayed PCI may remain clinically acceptable when unavoidable logistical constraints prevent earlier intervention.

The findings of this study have particular relevance for healthcare systems in resource-constrained settings, where delays in referral and definitive revascularization are frequently unavoidable. Factors such as delayed recognition of symptoms, limited access to electrocardiography and catheterization facilities, transportation challenges, and financial barriers continue to prolong reperfusion timelines despite successful thrombolysis. Under such circumstances, insisting on routine PCI within the recommended 24-hour window may not always be practical. The comparable short-term outcomes observed in this support the feasibility of extending the pharmacoinvasive window to 72 hours in selected patients when timely PCI cannot be achieved. Nevertheless, the study should be interpreted in light of its limitations, including its single-center, non-randomized design, relatively small sample size, and short 30-day follow-up period. Larger multicenter randomized studies with longer follow-up are warranted to confirm these findings and further define the role of delayed pharmacoinvasive PCI in contemporary STEMI management.

Conclusion

In this prospective study, delayed pharmacoinvasive PCI performed between 24 and 72 hours after successful thrombolysis demonstrated comparable 30-day clinical outcomes to routine pharmacoinvasive PCI performed within 24 hours. Although the delayed group showed a numerically higher incidence of MACCE and reinfarction, these differences were not statistically significant, and no increase in mortality, heart failure, target vessel revascularization, or major bleeding was observed. Furthermore, outcomes remained consistent across the 24–48-hour and 48–72-hour subgroups, suggesting that extending the pharmacoinvasive window up to 72 hours may be a feasible and safe alternative when timely PCI cannot be achieved. These findings support the practical role of delayed pharmacoinvasive therapy in resource-constrained settings, while emphasizing the need for larger multicenter randomized studies with longer follow-up to validate these observations.

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