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Extended Pharmacoinvasive PCI Compared to Primary PCI: Insights From Madras Medical College STEMI Registry

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In low- and middle-income countries, timely primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) is often limited. When timely PPCI is not feasible, current guidelines recommend a pharmacoinvasive strategy with routine angiography and percutaneous coronary intervention (PCI), if indicated, within 3 - 24 hours after fibrinolysis; however, the role of PCI beyond 24 hours remains uncertain. We compared clinical outcomes of PPCI versus extended pharmacoinvasive PCI (ePIPCI; PCI performed 3 to 48 hours after fibrinolysis) in STEMI. We analyzed the Madras Medical College STEMI Registry (September 2018 to October 2019), comparing patients undergoing PPCI with those receiving ePIPCI, including subgroups treated at 3 to 24 and 24 to 48 hours after fibrinolysis. Outcomes included in-hospital complications, in-hospital mortality, and 1-year all-cause mortality. Of the 2,499 STEMI patients enrolled, 248 underwent PPCI and 210 ePIPCI; among the remainder, 1,091 (43.7%) received fibrinolysis only, 825 (33.0%) had no revascularization, and 125 (5.0%) underwent delayed PCI. In-hospital complications (23.0% vs 21.5%; RR 1.05, 95% CI 0.75 to 1.48; $p = 0.78$), in-hospital mortality (4.4% vs 1.4%; RR 3.11, 95% CI 0.88 to 10.98; $p = 0.07$), and 1-year mortality (8.5% vs 7.4%; RR 1.14, 95% CI 0.59 to 2.19; $p = 0.70$) were similar between PPCI and ePIPCI. Outcomes were comparable between the 3 to 24-hour and 24 to 48-hour post-fibrinolysis subgroups. In multivariable analysis of the full cohort, index-hospitalization PCI was independently associated with lower in-hospital mortality (adjusted OR 0.36, 95% CI 0.21 to 0.62; $p < 0.001$). In conclusion, PCI up to 48 hours after fibrinolysis yielded outcomes comparable to PPCI, supporting an extended pharmacoinvasive strategy in resource-limited settings.

Cardiovascular disease is a major cause of mortality in India, with ST-elevation myocardial infarction (STEMI) representing the most common presentation of acute coronary syndrome.[1-4] Timely primary percutaneous coronary intervention (PPCI) within 120 minutes is the preferred revascularization strategy. When delays to timely PPCI are anticipated, pharmacoinvasive therapy (PIT)- fibrinolysis followed by routine coronary angiography within 3 to 24 hours, with PCI if indicated-is recommended.[5-7] In low-and middle-income countries(LMIC), limited availability of PCI-capable centers, transport delays, financial constraints, and referral barriers, frequently prevent adherence to the recommended 3 to 24-hour pharmacoinvasive window in routine practice.[8,9]

Although emerging evidence suggests that extending the pharmacoinvasive time window beyond 24 hours after fibrinolysis may preserve clinical benefits,[10] its comparative effectiveness versus primary PCI has not been adequately evaluated in the real-world LMIC settings. Therefore, we aimed to compare clinical outcomes of primary PCI with an extended pharmacoinvasive PCI (ePIPCI) strategy (3 to 48 hours after fibrinolysis) in patients enrolled in the Madras Medical College STEMI (M-STEMI) Registry, a prospective registry in a public hospital in India. We also examined overall the revascularization pattern and outcome of the registry patients.

Methods

Study population, study site and data collection

The design and methodology of the Madras Medical College STEMI (M-STEMI) Registry study have been described previously.[11] Briefly, we prospectively enrolled consecutive patients presenting

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Study Summary

What is known

In patients with ST-elevation myocardial infarction (STEMI), catheter-based therapies within a time window of 3 to 24 hours after fibrinolysis offer clinical benefit nearly equivalent to primary PCI.

Key question

In fibrinolysis-treated STEMI patients who subsequently undergo PCI, does extending the interval between fibrinolysis and PCI from the conventional 3 to 24 hours to a broader 3 to 48 hours window results in clinical outcomes comparable to those of primary PCI?

Key finding

In patients with STEMI who undergo fibrinolysis, PCI performed within 3 to 48 hours after fibrinolysis was associated with clinical outcomes comparable with primary PCI.

Clinical implication

Extending the PCI window to 3 to 48 hours after fibrinolysis may represent a pragmatic and safe revascularization strategy in settings with limited timely PCI access, thereby expanding access to catheter-based revascularization in resource-limited and geographically remote regions while maintaining outcomes comparable to primary PCI.

with STEMI within 48 hours of symptom onset, who sought care in our institution between September 2018 and October 2019. Data were collected in real time, using a standardized, STEMI registry case record, with predefined data fields, as described previously.[11] This included time of symptom onset, time of decision to seek medical care, time of first medical contact, mode of transport to the hospital, baseline demographic characteristics, cardiovascular risk factors, comorbidities, clinical findings, and management details.

Fibrinolysis was the predominant reperfusion strategy during the study period. Primary and pharmacoinvasive PCI were offered predominantly during the regular office hours. Patients presenting outside the thrombolytic window or with contraindications to fibrinolysis were often unable to undergo definitive catheter-based revascularization, particularly when arriving outside routine working hours. Although many patients underwent coronary angiography, timely PCI was not always feasible because of coordination challenges between health insurance approval processes and treatment providers. Details regarding the use of various reperfusion modalities—including fibrinolysis and percutaneous coronary intervention (PCI)—were documented, along with any in-hospital complications such as mechanical, arrhythmic, or thromboembolic events.

Adjunctive pharmacotherapy and periprocedural care

All patients were discharged on guideline-directed medical therapy comprising aspirin 150 mg, clopidogrel 75 mg, and atorvastatin 80 mg, unless contraindicated. Beta-blockers and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers were prescribed as clinically indicated. Use of glycoprotein IIb/IIIa inhibitors, thrombus aspiration, vasopressors and mechanical ventilation was at the discretion of the treating physician.

Study definitions and clinical end points

STEMI was diagnosed based on characteristic chest pain and electrocardiographic ST-segment elevation in accordance with standard guidelines.[12] Primary percutaneous coronary intervention (PPCI) was defined as coronary angiography and angioplasty (with or without stent implantation) of the culprit lesion within 12 to 24 hours' time window in patients who have not received fibrinolysis.[13] We defined extended pharmacoinvasive PCI (ePIPCI) as PCI performed between 3 to 48 hours after fibrinolysis. This group included both conventional pharmacoinvasive PCI (PIPCI), defined as PCI between 3 to 24 hours, and delayed pharmacoinvasive PCI (dPIPCI), defined as PCI between 24 to 48 hours following fibrinolysis. IRA patency was assessed using the Thrombolysis in Myocardial Infarction (TIMI) flow grading system.[14] The IRA patency was defined as the presence of TIMI 2 or 3 flow.

Outcomes

The primary outcome of the study was in-hospital mortality. Secondary outcomes included in-hospital complications, cardiac hospitalizations during follow-up, and all-cause mortality at 1 year.

Discharge and follow-up

All patients were scheduled for follow-up at 1 year after discharge. However, follow-up for ~75% of patients occurred during the COVID-19 pandemic, limiting in-person visits and ascertainment of nonfatal events. Thus, only all-cause mortality was reliably captured as the 1-year secondary outcome.

Analysis

We analyzed overall revascularization patterns and associated clinical outcomes. While all data were collected prospectively with prespecified analysis plans from the registry's planning phase, analyses were performed later. Baseline characteristics and outcomes were compared between patients undergoing ePIPCI and PPCI. Categorical variables were summarized as frequencies and percentages and compared using Pearson's Chi-squared test or Fisher's exact test, as appropriate. Continuous variables were reported as means with standard deviations (SD) or medians with interquartile ranges (IQR), and compared using the Student's t-test or Mann–Whitney U test based on data distribution. Variables with $p < 0.10$ in univariable analysis were entered into multivariable logistic regression to identify independent predictors of in-hospital mortality. All statistical analyses were performed using SPSS version 2025 (IBM Corp., Armonk, NY), with a 2-sided p-value < 0.05 considered statistically significant.

Results

Between September 2018 and October 2019, 2,499 adults with acute STEMI were enrolled in the M-STEMI registry (mean age 56.2 ± 12.3 years; range: 22 to 86). Women constituted 23% of the cohort. Most patients (75%; 1,874) presented in Killip class I; 51.7% (1,292) arrived within 6 hours of symptom onset, whereas 12.4% (309) presented beyond 24 hours. Baseline demographic and clinical characteristics are summarized in Table 1 and Figure 1.

Revascularization strategies used

Fibrinolysis was the dominant revascularization strategy, (52.1%; 1301/2499). Among those undergoing angiography 24 to 48 hours

Table 1
Baseline features of the study cohort (n = 2,499)

Parameters	Baseline values
Age (years)	56.2 ± 12.336*
Women	582 (23.3%)
Risk factors/comorbidities	
Type II diabetes	996 (39.9%)
Hypertension	870 (34.8%)
Current smoking/tobacco use	873 (34.9%)
Ex tobacco use	167 (6.7%)
Prior coronary artery disease	120 (4.8%)
Chronic kidney disease	30 (1.2%)
Cerebrovascular accident	50 (2%)
Time window from symptom onset (hours)	13.3 ± 7.5*
Preinfarction angina	1,526 (61.1%)
Myocardial infarction-location	
Anterior wall	1,437 (57.5%)
Inferior wall	982 (39.3%)
ECG findings	
Complete atrio-ventricular block	88 (3.5%)
Right bundle branch block	164 (6.6%)
Left bundle branch block	11 (0.6%)
Ventricular tachycardia/fibrillation	58 (2.3%)
Cardiogenic shock	248 (9.9%)
Echocardiography	
Left ventricular systolic dysfunction (EF ≤40%)	731 (29.3%)
Right ventricular dysfunction	324 (17%)
Left ventricular thrombus	33 (1.3%)
Ventricular septal rupture	37 (1.5%)
Free wall rupture	7 (0.3%)
Left ventricular ejection fraction (%)	45.9 ± 18.8*
Tricuspid annular plane excursion (mm)	17.8 ± 2.5*

* Mean and Standard deviation.
Abbreviation: EF = ejection fraction.

after fibrinolysis, TIMI 2/3 flow was present in 70% (145/210). Overall 23.3% (583/2499) of patients underwent PCI during the index hospitalization, including primary PCI in 9.9% (248), pharmacoinvasive PCI within 3 to 24 hours in 4.7% (118), and delayed pharmacoinvasive PCI at 24 to 48 hours in 3.7% (92); thus, 8.4% (210 /2499) underwent extended pharmacoinvasive PCI (ePIPCI). Baseline characteristics according to the revascularization strategy are presented in the Table Supplementary Table. Older patients, women, individuals with hypertension, diabetes, admission Killip Class >1, LVEF <40%, or cardiogenic shock were less likely to undergo PCI.

Outcome

In-hospital mortality in the overall cohort was 11.3% (283/2499). Left ventricular systolic dysfunction (LVEF ≤40%) occurred in 29.3% (731) and Right ventricular dysfunction (TAPSE <17) in 17% (324) of patients. Overall in-hospital complications were observed in 34.4% (859) of the cohort.

Extended pharmacoinvasive PCI

We compared 248 patients undergoing primary PCI with 210 undergoing ePIPCI. Baseline demographic, clinical, echocardiographic characteristics and use of guideline-directed medical therapy were similar between groups (Table 2). Compared with the primary PCI cohort, the ePIPCI group had higher preprocedure TIMI 2/3 flow rates (70% vs 21.4%; RR 2.62; 95% CI 2.11 to 3.27; p <0.001) and lower prevalence of left main or 3-vessel disease (1.4% vs 6.7%; RR 0.21, 95% CI 0.06 to 0.73; p = 0.008). In-hospital complications (23% vs 21.5%; RR 1.05; 95% CI 0.75 to 1.48; p = 0.78), in-hospital mortality (4.4% vs 1.4%; RR 3.11; 95% CI 0.88 to 10.98; p = 0.07), and 1-year mortality (8.5% vs 7.4%; RR 1.14; 95% CI 0.59 to 2.19; p = 0.70) were not significantly different between PPCI and ePIPCI (Central Illustration).

In multivariable logistic regression analysis adjusting for baseline demographic, clinical, echocardiographic, and angiographic variables, cardiogenic shock was the only independent predictor of in-hospital mortality (OR 10.30, 95% CI 1.04 to 102.47; p = 0.05). All other covariates, including preprocedure TIMI 2/3 flow and extent of coronary

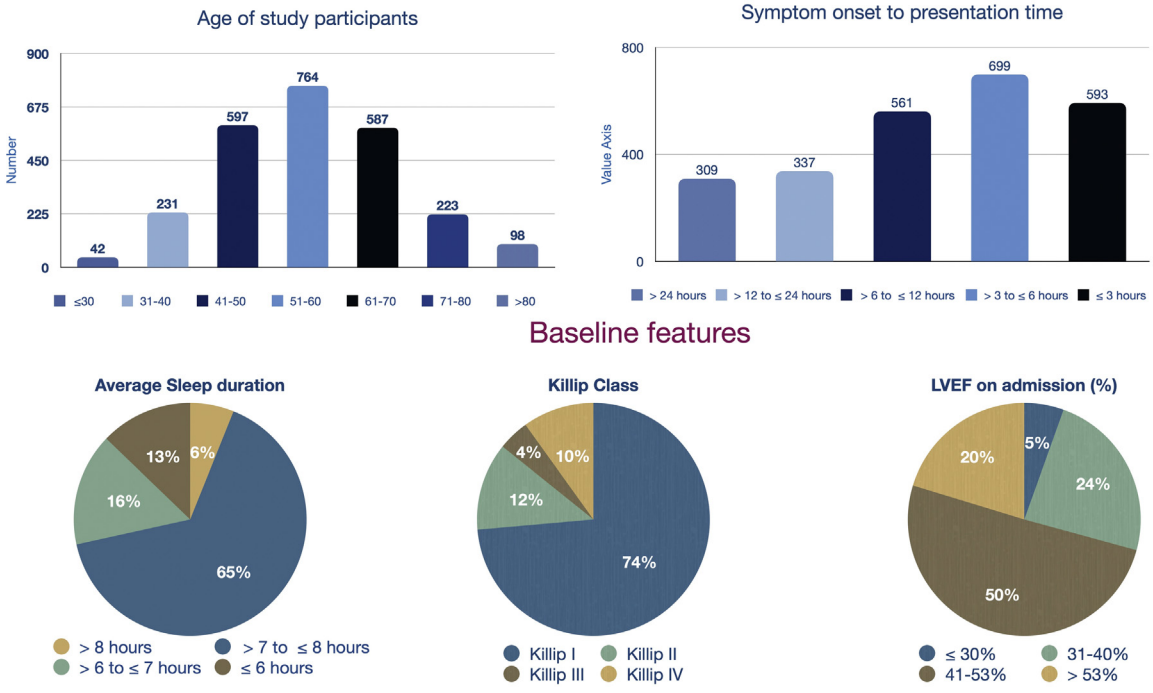
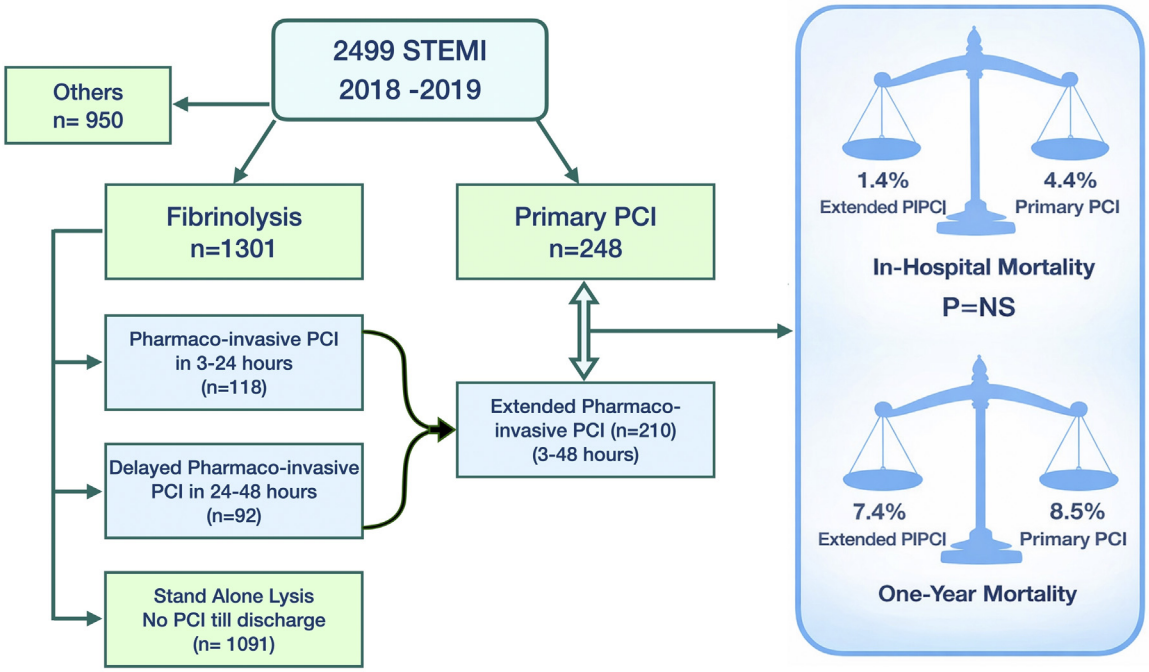


Figure 1. Baseline features of the patients enrolled.

Table 2
Primary PCI versus extended pharmaco-invasive PCI–univariable analysis

Parameters (n = 458)	Total (n = 458)	PPCI (n = 248)	EPIPCI (n = 210)	p value
Age	53.37 ± 10.16*	52.98 ± 10.15*	53.83 ± 10.17*	0.373
Female sex	78 (17.0%)	41 (16.5%)	37 (17.6%)	0.758
Lower socioeconomic status	449 (98.0%)	241 (97.2%)	208 (99.0%)	0.151
Cardio-vascular history				
Diabetes mellitus	154 (33.6%)	78 (31.5%)	76 (36.2%)	0.285
Hypertension	141 (30.8%)	72 (29.0%)	69 (32.9%)	0.377
Cerebrovascular accident	8 (1.7%)	5 (2.0%)	3 (1.4%)	0.632
Past tobacco user	36 (7.9%)	14 (5.6%)	22 (10.5%)	0.056
Current tobacco user	190 (41.5%)	107 (43.1%)	83 (39.5%)	0.433
Prior CAD	13 (2.8%)	3 (1.4%)	10 (4.0%)	0.095
Alcohol use	175 (38.2%)	91 (36.7%)	84 (40.4%)	0.468
Sleep duration hours	7.66 ± 0.81	7.73 ± 0.78	7.58 ± 0.84	0.044
Alcohol use	175 (38.2%)	91 (36.7%)	84 (40.4%)	0.468
Anterior myocardial infarction	261 (57.0%)	139 (56.0%)	122 (58.1%)	0.659
Time to first medical contact	6.03 ± 6.62*	5.51 ± 4.40*	6.64 ± 8.45*	0.082
Killip class >1	61 (13.3%)	27 (10.9%)	34 (16.2%)	0.160
Right ventricular dysfunction	45 (9.8%)	23 (9.3%)	22 (10.5%)	0.667
TAPSE	18.07 ± 1.93	18.15 ± 1.73	17.98 ± 2.14	0.365
LV ejection fraction (%)	47.51 ± 7.56*	47.82 ± 7.30*	47.15 ± 7.83*	0.347
Cardiac drugs use				
Clopidogrel	454 (99.1%)	247 (99.6%)	207 (98.6%)	0.337
Aspirin	452 (98.7%)	245 (98.8%)	207 (98.6%)	0.837
ACEI/ARB	244 (53.3%)	128 (51.6%)	116 (55.2%)	0.438
Beta blocker	328 (71.6%)	174 (70.2%)	154 (73.3%)	0.453
MRA	119 (26.0%)	61 (24.6%)	58 (27.6%)	0.462
Pre-PCI TIMI 2/3 flow (n = 436)	194 (44.5%)	49 (21.4%)	145 (70%)	<0.001
Single vessel disease	351 (78.7%)	178 (74.8%)	173 (83.2%)	0.031
Single/two vessel disease	427 (95.7%)	222 (93.3%)	205 (98.6%)	0.008
Complications	103 (22.5%)	57 (23.0%)	46 (21.9%)	0.783
Arrhythmia	97 (21.2%)	54 (21.8%)	43 (20.5%)	0.735
In hospital mortality	14 (3.1%)	11 (4.4%)	3 (1.4%)	0.063
1 year mortality (n = 424)	34 (8.0%)	20 (8.5%)	14 (7.4%)	0.699

* Mean and Standard deviation.
Abbreviations: ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; LV = left ventricle; MRA = mineralocorticoid receptor antagonist; PCI = percutaneous coronary intervention; TAPSE = tricuspid annular plane systolic excursion.



Central Illustration. PCI = percutaneous coronary intervention; PIPCI = pharmacoinvasive PCI.

Table 3
Conventional pharmaco-invasive PCI versus delayed pharmaco-invasive PCI

Parameters (n = 210)	Conventional PIPCI (n = 118)	Delayed PIPCI (n = 92)	p value
Age ≥60 years	32 (27.1%)	32 (34.8%)	0.513
Female sex	19 (16.1%)	18 (19.6%)	0.513
Diabetes mellitus	43 (36.4%)	33 (35.9%)	0.932
Hypertension	43 (36.4%)	26 (28.3%)	0.211
Current tobacco user	50 (42.4%)	33 (35.9%)	0.339
Alcohol use	53 (44.9%)	31 (33.7%)	0.100
Sleep duration hours	7.58 ± 0.85	7.57 ± 0.82	0.858
Anterior myocardial infarction	67 (56.8%)	55 (59.8%)	0.662
FMC ≤12 hours	108 (91.5%)	85 (92.4%)	0.819
Killip class I	102 (86.3%)	74 (84.4%)	0.318
Right ventricular dysfunction	12 (10.2%)	10 (10.9%)	0.809
LV ejection fraction (%)	48.19 ± 8.24*	45.82 ± 8.02*	0.029
Pre-PCI TIMI 2/3 flow	80 (69.5%)	65 (70.6%)	0.353
Complications	28 (23.7%)	18 (19.8%)	0.469
Arrhythmia	26 (22.5%)	17 (18.5%)	0.525
In-hospital mortality	3 (2.5%)	0 (0%)	0.258
1-year mortality (n = 188)	8 (7.7)	6 (7.3)	0.140

* Mean and Standard deviation.
FMC = first medical contact; PCI = percutaneous coronary intervention.

artery disease, were not independently associated with mortality in this cohort.

Within the extended pharmacoinvasive PCI (ePIPCI) group, outcomes were compared between conventional pharmacoinvasive PCI (3 to 24 hours) and delayed pharmacoinvasive PCI (24 to 48 hours). Baseline demographic, clinical, and angiographic characteristics, including time from symptom onset to presentation, hemodynamic status and the preprocedure TIMI 2/3 flow, were similar between the groups (Table 3). In-hospital complications (23.7% vs 19.8%; RR 1.21; 95% CI 0.71 to 2.05; p = 0.47), in-hospital mortality (2.5% vs 0%; p = 0.26), and 1-year mortality (7.7% vs 7.3%; RR 0.59; 95% CI 0.19 to 1.87; p = 0.14) were not significantly different. However, the left ventricular ejection fraction was modestly higher in the conventional pharmacoinvasive PCI group (48.19 ± 8.24 vs 45.82 ± 8.02; 95% CI 0.24 to 4.50; p = 0.03).

Mortality predictors

In the overall cohort, older age, female sex, diabetes, hypertension, chronic kidney disease, Killip class >1, greater cumulative ST elevation, LVEF ≤40%, TAPSE ≤17 mm, cardiogenic shock, arrhythmic complications and stand-alone fibrinolysis were associated with increased in-hospital mortality on univariable analysis (Table 4). Time to presentation, preinfarction angina, and anterior wall myocardial infarction were not significantly associated with in-hospital mortality on univariable analysis. On multivariable analysis, age ≥60, Killip Class >1, LV ejection fraction ≤40%, TAPSE ≤17 mm, cardiogenic shock, and RBBB remained independent predictors of in-hospital mortality. Performance of PCI at any time during index admission was independently associated with improved in-hospital survival (OR 0.36, 95% CI 0.21 to 0.62; p <0.001) (Figure 2).

Follow-up outcome

Of the 458 patients who underwent PPCI or ePIPCI, 1-year follow-up was available for 92.6% (424/458). During the follow-up, an additional 20 deaths occurred, resulting in an overall 1-year mortality of 8.0% (34/424) in this subgroup. 1-year mortality did not differ between the PPCI and ePIPCI groups (8.5% vs 7.4%; RR 1.06; 95% CI 0.79 to 1.43; p = 0.70). In the full cohort, among 85.5% (2137/2499) of patients with available 1-year follow-up (including in-hospital deaths), the overall 1-year mortality was 23.1% (494/2137), comprising 283 in-hospital deaths and 211 additional deaths during follow-up.

Discussion

In this large real-world STEMI registry from a resource-limited public-sector setting, extending the pharmacoinvasive PCI window up to 48 hours after fibrinolysis was feasible and associated with clinical outcomes comparable to primary PCI. Despite predominant use of streptokinase, a substantial proportion (70%) of patients achieved TIMI 2/3 flow prior to PCI, supporting the feasibility of a flexible pharmacoinvasive strategy in this setting. Collectively, these findings suggest that, in health systems where timely primary PCI is frequently not achievable, such an approach may represent a pragmatic alternative.

Current guidelines recommend routine angiography and PCI within 3 to 24 hours after successful fibrinolysis; however, this time window is often difficult to achieve in low- and middle-income countries because of delays related to referral pathways, patient transport, and financial authorization. Our observations suggest that extending the pharmacoinvasive window up to 48 hours may remain clinically reasonable in selected patients, particularly when early fibrinolysis has likely established infarct-related artery patency. Although myocardial salvage declines significantly beyond 12 hours from symptom onset,[15] prior smaller studies have suggested that revascularization up to 72 hours may still confer benefit, especially in the presence of a patent infarct-related artery ,[16] while systematic real-world comparisons with primary PCI remain limited. Accordingly, our findings provide supportive observational evidence that an extended pharmacoinvasive strategy may retain clinical effectiveness when early guideline-recommended PCI is not feasible, although causal inference cannot be established and prospective randomized evaluation is needed.

The relatively high rate of preprocedural TIMI 2/3 flow in the extended pharmacoinvasive cohort suggests that early fibrinolysis may have contributed to sustained infarct-related artery patency, thereby permitting deferral of PCI beyond the conventional 24-hour window in selected patients. Notably, these patency rates were achieved despite predominant use of streptokinase, underscoring its continued pragmatic role in many low- and middle-income settings. The angiographic patency rate of approximately 70% with streptokinase in this real-world cohort is broadly comparable to rates reported with fibrin-specific agents in contemporary pharmacoinvasive trials such as

Table 4
Predictors of in hospital mortality-univariable analysis

Variable	Total (n = 2,499)	Death (283; 11.32%)	Alive (2,216; 88.68%)	p value
Age (mean age ± SD)	56.2 ± 12.33	63.1 ± 11.76	55.31 ± 12.12	<0.001
Age <60 years	1,459 (58.4%)	92 (32.5%)	1,367 (61.7%)	<0.001
Female sex	582 (23.3%)	102 (36.0%)	480 (21.7%)	<0.001
Hypertension	870 (34.8%)	129 (45.6%)	741 (33.4)	<0.001
Diabetes	996 (39.9%)	142 (50.2%)	854 (38.5%)	<0.001
Current tobacco user	900 (36%)	62 (21.9%)	838 (37.8%)	<0.001
Alcohol	889 (35.6%)	58 (20.5%)	831 (37.5%)	<0.001
Preinfarction angina	1,526 (61.1%)	179 (63.3%)	1,347 (60.8%)	0.423
Sleep duration per day (hours)	7.64 ± 0.888	7.6 ± 0.854	7.65 ± 0.893	0.435
Chronic Kidney Disease	30 (1.2%)	10 (3.5%)	20 (0.9%)	0.001
Cerebro-vascular accident	51 (2.0%)	6 (2.1%)	45 (2.0%)	0.920
Prior coronary artery disease	120 (4.8%)	18 (6.4%)	102 (4.6%)	0.193
Time window ≤6 hours	1,292 (51.7%)	138 (48.8%)	1,154 (52.1%)	0.171
Time window ≤12 hours	1,853 (74.1%)	208 (73.5%)	1,645 (74.2%)	0.790
Killip class >I	660 (26.4%)	201 (71%)	459 (20.7%)	<0.001
AWMI	1,437 (57.5%)	174 (61.5%)	1,263 (57%)	0.150
Sigma ST elevation	11.09 ± 7.79	13.035 ± 8.6	10.84 ± 7.6	<0.001
Sigma ST deviation	15.12 ± 9.57	17.63 ± 10.38	14.86 ± 9.42	<0.001
LVEF ≤40%	731 (29.3%)	156 (55.1%)	575 (25.9%)	<0.001
TAPSE <17 mm	324 (13.0%)	71 (25.1%)	253 (11.4%)	<0.001
Complications	859 (34.4%)	216 (76.3%)	643 (29%)	<0.001
Cardiogenic shock	248 (9.9%)	139 (49.1%)	109 (4.9%)	<0.001
Mechanical complications	46 (1.8%)	28 (9.9%)	18 (0.8%)	<0.001
Arrhythmic complications	709 (28.4%)	148 (52.3%)	561 (25.3%)	<0.001
Revascularization modes				
Primary PCI	248 (9.9%)	11 (3.9%)	237 (10.7%)	
PIPCI	118 (4.7%)	3 (1.1%)	115 (5.2%)	<0.001
Delayed PCI	217 (8.6%)	2 (0.7%)	215 (9.7%)	
Stand-alone fibrinolysis	1,091 (43.7%)	164 (58%)	927 (41.8%)	
No revascularization	825 (33%)	103 (36.4%)	722 (32.6%)	
PPCI + PIPCI	366 (14.6%)	14 (4.9%)	352 (15.9%)	<0.001
Extended PIPCI	210 (8.6%)	3 (1.1%)	207 (9.3%)	<0.001
Any PCI	583 (23.3%)	16 (5.7%)	567 (25.6%)	<0.001
Fibrinolysis	1,301 (52.1)	167 (59%)	1,134 (45.4%)	<0.001
Streptokinase	1,147 (45.9%)	152 (53.7%)	995 (44.9%)	
TNK tPA	130 (5.2%)	12 (4.2%)	118 (5.3%)	
Reteplase	24 (1.0%)	3 (1.1%)	21 (10.7%)	

Abbreviations: LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; SD = standard deviation; ST = segment; TAPSE = tricuspid annular plane systolic excursion; tPA = tissue plasminogen activator.

STREAM (64%) and STREAM-2 (66%)[17,18] although direct comparisons should be interpreted cautiously given differences in patient selection, trial protocols, and timing of angiography. In this context, performing PCI within 48 hours after fibrinolysis may also help mitigate the higher risk of reocclusion associated with non–fibrin-specific agents,[19,20] although this mechanistic explanation remains speculative. The similar outcomes between the 3 to 24-hour and 24 to 48-hour subgroups further suggest that clinically significant reocclusion during this interval may be uncommon, but this observation should be interpreted cautiously given the observational design and limited sample size.

Consistent with this mechanistic plausibility, our results are also aligned with prior studies comparing early (3 to 24 hours) and delayed (24 to 72 hours) pharmacoinvasive strategies that reported no significant differences in clinical outcomes, although these analyses did not include a direct comparison with primary PCI.[10] By providing a head-to-head real-world comparison between an extended pharmacoinvasive approach and primary PCI, our study extends existing evidence and enhances clinical relevance for health systems where timely PPCI is not universally feasible. These findings provide a strong rationale for future prospective and randomised evaluations of delayed pharmacoinvasive strategies in healthcare settings characterised by late presentation, limited access to round the clock PCI, and continued reliance on streptokinase.

We observed that older patients, women, those with higher-risk clinical profiles—including left ventricular dysfunction, higher Killip class, and cardiogenic shock—were less likely to undergo catheter-based revascularization, suggesting potential treatment-selection patterns during the early phase of PPCI program implementation. Despite being conducted in a large metropolitan public-sector hospital, delays in definitive revascularization were observed, reflecting common real-world constraints in high-volume public healthcare settings. Overcrowded emergency services, dependence on interfacility referral pathways, financial authorization processes, and limited round-the-clock catheterization laboratory availability are possible contributors, although these were not formally analyzed. The cohort was socioeconomically relatively homogeneous, with the vast majority of patients belonging to below-poverty-line categories (Table 2), thereby limiting the discriminatory value of including socioeconomic status in multivariable adjustment models. Detailed rural–urban residence and other social determinants were not systematically captured in the registry. Taken together, the phased implementation of PPCI services and pragmatic triaging based on clinical stability and resource availability may still have introduced residual treatment-selection bias.

The relatively high in-hospital mortality observed in our cohort (11.3%) likely reflects delayed presentation, limited access to timely PCI, and the substantial proportion of patients who did not undergo revascularization. This interpretation is supported by the finding that the performance of PCI at any time during hospitalization was independently associated with improved survival. Notably, women were under-represented in the PPCI and ePIPCI groups, constituting only 16% to 17% of these cohorts, despite representing nearly a quarter of the overall population, consistent with previously reported sex-based disparities in access to invasive management.[10,21]

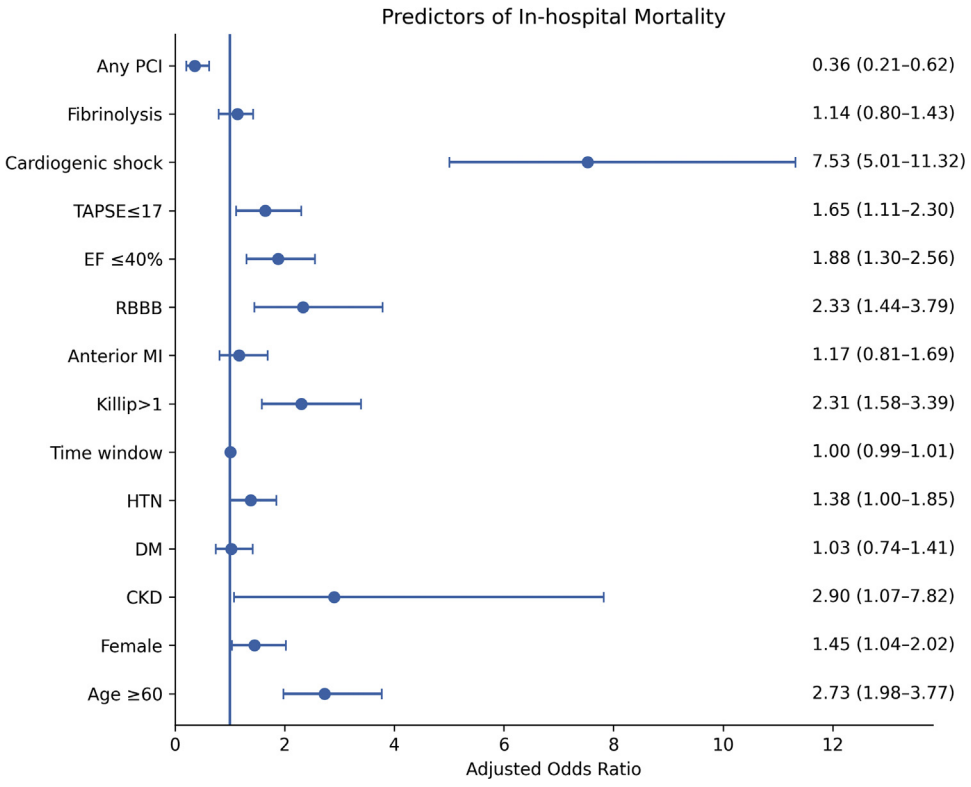


Figure 2. Multivariable analysis of predictors of in-hospital mortality.

Forest plot showing the independent predictors of in-hospital mortality derived from multivariable logistic regression analysis. Points represent adjusted odds ratios (aORs) and horizontal lines indicate 95% confidence intervals (CIs). The vertical reference line at aOR = 1.0 denotes no association with mortality. Variables with CIs not crossing 1.0 were considered statistically significant predictors of in-hospital mortality.

Strengths and Limitations

This study represents one of the largest contemporary real-world STEMI registries from a public sector hospital in a resource-limited setting and uniquely evaluates an extended pharmacoinvasive PCI window (3 to 48 h) in direct comparison with primary PCI. The prospective enrolment of consecutive patients and the availability of detailed angiographic and echocardiographic data strengthen the internal validity of the comparative analyses and support the generalizability of these findings to similar low- and middle-income healthcare settings. However, as a single-center observational study, the results are primarily descriptive and do not permit causal inference.

The phased implementation of primary PCI services, limited availability of PCI outside office hours, and exclusion of patients undergoing angiography without PCI may have introduced treatment-selection bias. In addition, the long-term follow-up was partially incomplete—particularly for nonfatal outcomes—due to the COVID-19 pandemic, restricting reliable 1-year assessment largely to all-cause mortality. Additionally, the cohort was relatively socioeconomically homogeneous, with the vast majority of patients belonging to below-poverty-line status and being referred from metropolitan public and private sectors due to affordability constraints. While this homogeneity strengthened internal comparability, it limited our ability to adjust for rural–urban and socioeconomic factors in the multivariable models. Finally, the small number of patients treated with fibrin-specific agents limited the statistical power for direct comparison of angiographic patency across thrombolytic strategies.

Conclusion

In this observational study from a resource-limited STEMI network, patients undergoing extended pharmacoinvasive PCI within 3-48 hours after fibrinolysis demonstrated outcomes comparable to those treated with primary PCI. Given the observational design and potential for survival and treatment-selection bias, causal inference regarding the safety or effectiveness of delayed intervention beyond 24 hours cannot be made. The findings should therefore be considered exploratory and hypothesis-generating, and require validation in adequately powered prospective studies and randomized trials in low- and middle-income healthcare systems.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Justin Paul Gnanaraj: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Karthika Saaminathan:** Writing – review & editing, Visualization, Methodology, Formal analysis, Data curation. **Anne Princy Steaphen:** Writing – review & editing, Visualization, Formal analysis, Data curation. **Suryakanth Sethupathy:** Writing – review & editing, Methodology, Data curation. **Iliyas Mohammed:** Writing – review & editing, Methodology, Data curation. **Sijoy Kurien:** Writing – review & editing, Methodology, Data curation. **Sabarish Sankaran:** Writing – review & editing, Methodology, Data curation. **Sandeep Srinivas:** Writing – review & editing, Methodology, Data curation. **Salai Sudhan Prabhu:** Writing – review & editing, Methodology, Data curation. **Sivasubramanian S:** Writing – original draft, Methodology, Data curation. **Anurag Polvarappu:**

Writing – review & editing, Methodology, Data curation. **Ravindran Raji:** Writing – review & editing, Data curation. **Kumaran Srinivasan:** Writing – original draft, Supervision, Data curation. **Gnanavelu Ganesan:** Writing – original draft, Supervision, Data curation. **Sangareddi Venkatesan:** Writing – review & editing, Supervision, Methodology. **Kumaresan Kannan:** Writing – review & editing, Supervision.

Ethical Approval

The study adhered to the ethical principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Madras Medical College (Approval No. 01102017). Written informed consent was obtained from all participants or their legally authorized representatives.

Data Availability

The deidentified data underlying this study are available upon reasonable request to the corresponding author, subject to approval by the Institutional Ethics Committee.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2026.02.064.

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