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Reperfusion Strategies for ST-Segment Elevation Myocardial Infarction in a Real-World Regional Setting: A Prospective Observational Study in Iran

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Abstract

Background: International guidelines recommend primary percutaneous coronary intervention (PPCI) as the optimal reperfusion strategy for ST-segment elevation myocardial infarction (STEMI), but its implementation is challenging in many real-world settings. We aimed to investigate the application of reperfusion strategies, identify factors associated with treatment choice, and evaluate short-term outcomes in a regional Iranian cardiac center.

Methods: In this prospective, single-center observational study, we enrolled 205 consecutive patients with STEMI. Patients were categorized based on their initial treatment: intravenous fibrinolysis, PPCI, or medical management without reperfusion. The primary outcome was all-cause mortality at 30 days. Continuous variables were summarized as mean (SD) or median (IQR), as appropriate, and categorical variables as frequency and percentage. Between-group comparisons were performed using ANOVA or Kruskal–Wallis tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables.

Results: Fibrinolysis was the predominant reperfusion strategy (158/205; 77.1%), while PPCI was used in 13.2% of patients. Critically, 9.8% of patients received no reperfusion therapy and experienced markedly worse in-hospital outcomes, including higher mortality (20.0% vs. <8% in reperfused groups; P=0.026) and more frequent severe complications (P<0.001). While the unadjusted 30-day mortality rates appeared similar between patients receiving fibrinolysis (6.9%) and PPCI (7.4%), this comparison was statistically underpowered. This finding was likely influenced by severe selection bias and confounding by indication, as the PPCI cohort had a significantly higher need for in-hospital vasopressor support, suggesting a higher baseline risk profile. Notably, female patients were disproportionately represented in the non-reperfused cohort compared to the fibrinolysis group (45.0% vs. 15.8%, P=0.003), indicating a significant gender disparity in access to acute reperfusion.

Conclusion: A significant gap exists between international STEMI guidelines and real-world clinical practice in our region, with fibrinolysis remaining the dominant strategy and a substantial proportion of patients receiving no reperfusion. The lack of an observed mortality difference between PPCI and fibrinolysis reflects an underpowered, unadjusted comparison, and underscores how patient selection and system logistics can obscure treatment efficacy. These findings highlight the urgent need to develop risk-adapted regional STEMI systems that optimize both pharmacoinvasive and primary PCI pathways to improve care for all patients.

Keywords: Myocardial Infarction, ST Elevation Myocardial Infarction, Percutaneous Coronary Intervention, Fibrinolytic Agents, Health Services Accessibility, Iran

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Key Messages:

↑What is "already known" in this topic:

ST-segment elevation myocardial infarction (STEMI) is a primary driver of global cardiovascular morbidity. Although primary percutaneous coronary intervention (PPCI) is the evidence-based gold standard for reperfusion, achieving universal access remains a challenge. Logistical and socioeconomic factors frequently impede the execution of PPCI-centered strategies in real-world settings.

→What this article adds:

Current management in Kerman, Iran, reveals a marked departure from international STEMI guidelines, with fibrinolysis remaining the primary reperfusion modality. Alarmingly, a significant portion of patients-particularly women-remain untreated with any reperfusion strategy. This study highlights the utilization of pharmacoinvasive protocols and the timing of subsequent angiography within a real-world regional context.

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Introduction

ST-segment elevation myocardial infarction (STEMI) remains a leading cause of cardiovascular morbidity and mortality globally, representing a time-critical medical emergency where rapid restoration of coronary blood flow is paramount to salvaging myocardium and improving survival (1). The cornerstone of modern STEMI management is timely reperfusion therapy, a strategy that has fundamentally transformed patient outcomes over the past three decades (2).

International clinical practice guidelines, informed by a wealth of evidence from large-scale randomized controlled trials, unequivocally recommend primary percutaneous coronary intervention (PPCI) as the preferred reperfusion strategy over intravenous fibrinolysis (3, 4). This recommendation is based on the superior efficacy of PPCI in achieving complete and sustained coronary patency (TIMI 3 flow), which translates into lower rates of short-term mortality, reinfarction, and stroke when performed by an experienced team within guideline-mandated timelines (3, 5).

However, the "real-world" implementation of a PPCI-based strategy presents substantial logistical, geographical, and economic challenges, creating a significant gap between guideline recommendations and clinical practice (6). The benefits of PPCI are highly time-dependent, and delays in patient transfer to a PCI-capable center can attenuate or even negate its superiority over immediate fibrinolysis (7). Consequently, in many healthcare systems, including those in geographically diverse regions of Iran, fibrinolysis remains a vital and frequently used initial reperfusion strategy, often as part of a pharmacoinvasive approach where patients are subsequently transferred for coronary angiography (8, 9). This creates a complex clinical landscape where the choice between PPCI and fibrinolysis is influenced not only by patient risk profile but also by system-level factors and the availability of resources at the time of presentation.

While the efficacy of these two strategies has been compared in ideal trial settings, data are scarce on the determinants of treatment selection and their comparative effectiveness in the context of contemporary regional STEMI networks in Iran. Understanding the factors that drive clinical decision-making and the resulting patient outcomes is crucial for optimizing care pathways and improving the quality of STEMI management. Therefore, while broad epidemiological trends regarding STEMI care in Iran have been previously reported, there remains a critical need to understand the granular, real-world selection mechanisms that dictate reperfusion strategies at the institutional level. Therefore, this study uniquely contributes to the existing literature by deeply characterizing the risk-adapted decision patterns and system-level triage disparities, particularly concerning the highly vulnerable, non-reperfused patient cohort, within a regional referral center.

Methods

Study Design and Participants

We conducted a prospective, single-center observational study at Shafa Hospital, a tertiary cardiovascular referral center in Kerman, Iran, between November 2024 and June 2025. The study protocol was approved by the Ethics Committee of Kerman University of Medical Sciences, and all participants or their legal representatives provided written informed consent.

We consecutively enrolled patients aged 18 years or older who were admitted with a diagnosis of ST-segment elevation myocardial infarction (STEMI), as defined by the Fourth Universal Definition of Myocardial Infarction (10). Patients were included if the initial reperfusion therapy was administered at our institution. We excluded patients who had received reperfusion treatment at an outside hospital, those who presented with profound haemodynamic instability or cardiac arrest that precluded a standard treatment pathway, and cases with incomplete essential data in their medical records.

Procedures and Data Collection

Upon admission, patients were allocated to one of three treatment groups based on the clinical decision of the attending cardiology team: (1) Primary Percutaneous Coronary Intervention (PPCI), (2) Intravenous Fibrinolysis, or (3) Medical Management (no reperfusion). For patients assigned to the medical management cohort, treatment consisted of a comprehensive conservative pharmacological strategy for acute coronary syndrome. This standard-of-care regimen included dual antiplatelet therapy (aspirin and clopidogrel), systemic anticoagulation (heparin), statins, nitrates, and beta-blockers, titrated according to the patient's hemodynamic stability and clinical indications. The primary reason for the chosen treatment strategy was prospectively documented from the medical records to understand the clinical decision-making process.

A trained investigator collected data using a standardized case report form. Information was sourced from the hospital's electronic health record, official procedural reports (angiography, echocardiography), and structured interviews with patients or their families. Baseline data included patient demographics, cardiovascular risk factors, clinical presentation details (e.g., Killip class), and the mode of transportation to the hospital. Key process-of-care time metrics were meticulously recorded, including symptom onset-to-door, door-to-needle (for fibrinolysis), and door-to-device (for PPCI) times.

Study Outcomes

The primary outcome was all-cause mortality at 30 days following hospital admission. Secondary outcomes were evaluated both during the hospital stay and at the 30-day follow-up. In-hospital outcomes included recurrent myocardial infarction, clinically diagnosed acute kidney injury, need for mechanical ventilation, intracranial haemorrhage, and requirement for vasopressor or inotropic support. The 30-day outcomes were ascertained via a struc-

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tured telephone interview and included cardiovascular rehospitalisation, need for unplanned coronary revascularisation (PCI or CABG), stroke, and any clinically significant bleeding. Vital status at 30 days was confirmed for all patients.

Statistical Analysis

All statistical analyses were performed using SPSS software, version 27 (IBM Corp). The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Normally distributed data were summarized as mean and standard deviation (SD), while non-normally distributed data were presented as median and interquartile range (IQR). Categorical variables were reported as frequencies and percentages (n, %).

Intergroup comparisons of baseline characteristics and clinical outcomes were performed. For continuous variables, the one-way analysis of variance (ANOVA) or the Kruskal-Wallis H test was used, as appropriate based on data distribution. For categorical variables, Pearson's Chi-square test or Fisher's exact test was applied. A two-tailed *P*-value of less than 0.05 was considered to indicate statistical significance in all analyses.

Patient and Public Involvement

No patients or members of the public were involved in the design, conduct, reporting, or dissemination plans of our research.

Results

Patient Population and Reperfusion Strategy

During the study period, 205 consecutive patients with ST-segment elevation myocardial infarction (STEMI) were enrolled. The predominant reperfusion strategy was intravenous fibrinolysis, administered to 158 patients (77.1%). Primary percutaneous coronary intervention (PPCI) was performed in 27 patients (13.2%), and 20 patients (9.8%) received medical management without reperfusion. This distribution highlights a significant deviation from guideline-recommended care pathways in our regional setting.

Baseline Characteristics and Treatment Delays

Baseline clinical and demographic characteristics differed significantly across the three treatment groups (Table 1). The cohort managed medically was notably higher risk, with a significantly greater proportion of female patients (45.0% vs. 15.8% in the fibrinolysis group, *P*=0.003) and a different pattern of hospital arrival, with fewer utilizing emergency medical services. While major cardiovascular risk factors were similarly distributed, these baseline differences suggest the presence of significant selection bias influencing the choice of initial therapy. System-related treatment delays were considerable. The location of myocardial infarction (MI) is categorized into anterior and non-anterior types. Overall, 47.1% of patients had anterior MI, while 52.9% had non-anterior MI. In the fibrinolysis group, 45.6% were anterior, and 54.4% were non-anterior. In the primary PCI group, anterior MI was more common (61.5%), whereas in the medical management group, non-anterior MI was more frequent (60.0%). However, the differences between groups regarding MI location were not statistically significant (*P*=0.256)

The median symptom-onset-to-door time for the cohort was 3.0 hours (IQR 1.5–5.0), with no significant difference between groups. For patients receiving fibrinolysis, the median door-to-needle time was 33 minutes (IQR 20–45). For those undergoing PPCI, the median door-to-device time was substantially longer at 61 minutes (IQR 45–90).

Clinical Outcomes

A steep gradient in clinical outcomes was observed across the three groups (Table 2). The primary outcome of 30-day all-cause mortality was numerically highest in the medical management group (30.0%) compared with the PPCI (7.4%) and fibrinolysis (6.9%) groups; however, the overall difference did not achieve statistical significance (*P*=0.125). Crucially, there was no statistically significant difference in 30-day mortality between patients treated with fibrinolysis and those who received PPCI.

In-hospital outcomes were starkly divergent. The medical management group experienced a significantly higher incidence of in-hospital death (20.0%, P=0.026) and life-threatening complications, including acute kidney injury (35.0%), need for mechanical ventilation (25.0%), and vasopressor support (30.0%) (all *P*<0.001). To provide clinical context, it is important to note that this non-reperfused cohort was entirely managed with a complete, intensive pharmacological regimen for acute coronary syndrome (comprising aspirin, clopidogrel, statins, hepa-

Table 1. Baseline Characteristics of the Study Population by Initial Treatment Strategy

Characteristic	Overall (N=205)	Fibrinolysis (n=158)	Primary PCI (n=27)	Medical Management (n=20)	*P*-value
Demographics & Risk Factors					
Age, mean (SD)	60.1 (12.5)	59.5 (11.9)	61.2 (13.1)	64.3 (14.8)	0.345
Female sex, n (%)	41 (20.0)	25 (15.8)	7 (25.9)	9 (45.0)	**0.003**
Hypertension, n (%)	76 (37.1)	58 (36.7)	10 (37.0)	8 (40.0)	0.951
Diabetes Mellitus, n (%)	55 (26.8)	41 (25.9)	7 (25.9)	7 (35.0)	0.687
location of the MI (Anterior)	96 (47.1)	72 (45.6)	16 (61.5)	8 (40.0)	0.256
location of the MI (Non-Anterior)	108 (52.9)	86 (54.4)	10 (38.5)	12 (60.0)	
Presentation & Logistics					
Arrival by Ambulance, n (%)	115 (56.1)	90 (57.0)	18 (66.7)	7 (35.0)	**0.048**
Symptom-onset-to-door, median (IQR), h	3.0 (1.5-5.0)	2.8 (1.5-4.8)	3.4 (1.8-5.5)	3.5 (2.0-6.0)	0.421

Data are presented as n (%), mean (SD), or median (IQR). Statistically significant P-values are in bold.

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Table 2. Primary and Secondary Clinical Outcomes at 30 Days by Initial Treatment Strategy

Outcome	Fibrinolysis (n=158)	Primary PCI (n=27)	Medical Management (n=20)	*P*-value
Primary Outcome				
30-Day All-Cause Mortality, n (%)	11 (6.9)	2 (7.4)	6 (30.0)	0.125
In-Hospital Outcomes				
In-hospital mortality, n (%)	7 (4.4)	2 (7.4)	4 (20.0)	**0.026**
Acute Kidney Injury, n (%)	8 (5.1)	2 (7.4)	7 (35.0)	**<0.001**
Mechanical Ventilation, n (%)	4 (2.5)	2 (7.4)	5 (25.0)	**<0.001**
Vasopressor/Inotrope Support, n (%)	2 (1.3)	3 (11.1)	6 (30.0)	**<0.001**
LVEF, mean (SD), %	38.2 (11.7)	35.0 (9.0)	30.0 (15.5)	**0.028**
Hospital stay, median (IQR), days	5.1 (3.0-7.0)	4.5 (2.5-6.0)	11.4 (6.0-15.0)	**<0.001**
30-Day Outcomes (Post-discharge)				
Rehospitalization (CV), n (%)	43 (27.2)	6 (22.2)	2 (10.0)	0.297

Data are n (%) unless otherwise specified. LVEF=Left Ventricular Ejection Fraction; CV=Cardiovascular. Statistically significant P-values are in bold.

rin, nitrates, and beta-blockers). Despite receiving optimal conservative medical therapy, this group experienced profoundly impaired myocardial function, as evidenced by the lowest mean left ventricular ejection fraction (LVEF) of 30.0% (SD 15.5; P=0.028), and a significantly prolonged median hospital stay of 11.4 days (P<0.001).

Comparing the two reperfusion strategies revealed important nuances. Despite similar 30-day mortality rates, the in-hospital course suggested a sicker cohort was triaged to PPCI, with this group having a significantly higher requirement for vasopressor or inotropic support compared to the fibrinolysis group (11.1% vs. 1.3%, P<0.001). By 30 days, rates of rehospitalization and repeat revascularization were comparable between the PPCI and fibrinolysis arms.

Discussion

Principal Findings

In this prospective study of real-world STEMI management at a major Iranian cardiac center, we elucidated a profound gap between international guideline recommendations and clinical practice. Our central finding is the overwhelming predominance of fibrinolysis (77.1%) over primary PCI as the initial reperfusion strategy. We also identified a critically underserved 10% cohort of patients who received no reperfusion therapy and consequently suffered catastrophic in-hospital outcomes. Strikingly, despite the established superiority of PPCI in randomized trials, we observed no significant difference in 30-day mortality between patients receiving PPCI and those treated with fibrinolysis (7.4% vs 6.9%). However, this univariate comparison is heavily confounded by selection bias and baseline clinical severity. As indicated by the significantly higher requirement for inotropic and vasopressor support in the PPCI group (11.1% vs. 1.3%, P<0.001), patients triaged to PPCI were inherently 'sicker' and often presented in cardiogenic shock. Because of this confounding by indication, the unadjusted mortality rates do not accurately reflect the isolated efficacy of the reperfusion strategies. While a multivariable adjustment would be ideal, the low absolute number of mortality events limited our ability to perform a statistically robust multivariable regression.

The Reperfusion Paradox in a Global Context

The low rate of PPCI utilization in our cohort is a stark reflection of a global challenge. While landmark trials like DANAMI-2 and PRAGUE-2 established the superiority of PPCI when delivered expeditiously (11, 12), however, translating this into practice through the implementation of the national “247” STEMI protocol (an initiative by the Iranian Ministry of Health mandating 24 hours a day, 7 days a week availability of primary PCI services for acute myocardial infarction in designated regional centers) has faced significant localized challenges and remains elusive in many parts of the world. Our findings are consistent with data from large international registries like GRACE and reports from other health systems in Asia and Latin America, where fibrinolysis, often as part of a pharmacoinvasive strategy, remains a vital first-line therapy due to geographical and logistical barriers (6, 13). The fact that fibrinolysis was the default strategy in our PCI-capable center suggests that even with available technology, system-level factors such as off-hours presentation, emergency service delays, or catheterization lab capacity create a functional barrier to guideline-adherent care (14). A striking paradox observed in our study is that while the median Door-to-Device time for PPCI was excellent at 61 minutes, well within the 90-minute guideline recommendation, only 13.2% of patients were triaged to this modality, whereas 77.1% received fibrinolysis. This discrepancy highlights significant logistical and systemic barriers outside of in-hospital efficiency. Foremost among these is the lack of dedicated 24/7 catheterization laboratory staffing and availability of interventional cardiologists after routine working hours, which frequently forces emergency physicians to default to fibrinolysis. Additionally, fragmented Emergency Medical Services (EMS) referral protocols, prolonged pre-hospital transfer times from remote regional areas, and financial constraints severely limit direct-to-cath-lab triage. Consequently, the rapid Door-to-Device time primarily reflects highly selected patients who arrive during optimal operating hours, underscoring the urgent need for a more cohesive regional STEMI network.

The Peril of Missed Opportunities: The Non-Reperfused Cohort

The most sobering finding is that one in ten patients with STEMI received no reperfusion therapy. The 20% in-hospital mortality in this group is a powerful real-world validation of the "time is muscle" principle and is tragically similar to mortality rates from the pre-reperfusion era. Large registries like the US National Registry of Myocar-

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dial Infarction (NRMI) have previously shown that patients who are not reperfused are often older, female, and present with atypical symptoms, leading to diagnostic delays or uncertainty (15, 16). The disproportionately high number of women in our non-reperfused group (45.0%) resonates with extensive literature highlighting gender disparities in cardiovascular care, potentially linked to differences in symptomology and clinical suspicion (17). Females constituted 45.0% of the non-reperfused group, compared to only 15.8% of those receiving fibrinolysis (P=0.003). This stark contrast points to a potential systemic failure in recognizing and rapidly prioritizing STEMI in female patients. Women with STEMI often present with atypical symptoms, leading to delayed diagnosis, later hospital arrival times, and subsequently falling outside the therapeutic window for reperfusion. Furthermore, implicit biases in acute triage systems may inadvertently disadvantage female patients. Addressing this critical public health gap requires targeted educational campaigns for both the public and emergency healthcare providers to ensure equitable, rapid STEMI care regardless of gender.

Unmasking the Illusion of Equivalence: Confounding by Indication

Our finding of equivalent 30-day mortality between PPCI and fibrinolysis must be interpreted through the critical lens of selection bias. This "efficacy-effectiveness gap" is a well-described phenomenon in observational research (18). In our study, the PPCI cohort, despite receiving the "superior" therapy, had a significantly higher need for in-hospital vasopressor support, strongly suggesting they were a higher-risk population at baseline. It is plausible that sicker patients, or those presenting late, were triaged to the catheterization lab, while more stable, early-presenting patients were deemed suitable for fibrinolysis. This confounding by indication likely masked the true benefit of PPCI. Other observational studies have reported similar findings, in which the survival benefit of PPCI observed in randomized trials is attenuated or lost after adjustment for baseline risk (19, 20). Furthermore, a considerable proportion of our fibrinolysis patients underwent subsequent angiography, reflecting a de facto pharmacoinvasive strategy: angiography was performed within 24 hours in 24 patients (15%), and 19 patients underwent rescue PCI (12%). The landmark STREAM trial demonstrated that a timely pharmacoinvasive approach can yield outcomes comparable to PPCI, providing a strong evidence base for the pragmatic strategy observed in our center (21).

Strengths and Limitations

The primary strength of our study is its prospective, real-world design, which captures the complexities of clinical decision-making and provides a valuable snapshot of contemporary STEMI care in a non-Western setting. However, our findings must be considered in light of several limitations. First, our study is constrained by its relatively small sample size, particularly in the PPCI arm (n=27). A post-hoc power calculation revealed that given the current sample distribution (n=158 for fibrinolysis; n=27 for PPCI) and an observed baseline mortality of 6.9% in the fibrinolysis cohort, the study had 80% power (at a two-sided α=0.05) to detect only a large minimum absolute difference of approximately 18 to 20% in 30-day mortality. Consequently, the study is severely underpowered to detect smaller, yet clinically meaningful differences in 30-day mortality between the PPCI and fibrinolysis groups. The observed lack of a statistically significant difference in mortality (7.4% vs. 6.9%) should therefore be interpreted with extreme caution, as it is highly susceptible to a Type II error and does not imply therapeutic equivalence. Larger, multi-center registries are required to draw definitive conclusions regarding mortality outcomes in our region.

Additionally, the single-center observational design inherently limits the generalizability of our findings. The treatment patterns and outcomes observed are heavily influenced by the specific infrastructural capacities, geographic location, and local emergency medical service (EMS) referral pathways of our institution. Therefore, these results should be viewed as hypothesis-generating rather than universally representative of all Iranian healthcare settings. Finally, the 30-day follow-up period does not capture long-term outcomes like heart failure and quality of life, which are crucial endpoints in evaluating reperfusion strategies.

Conclusion and Future Directions

Our study reveals that the management of STEMI in our region is dictated by a complex interplay of clinical need and logistical reality, resulting in a practice pattern that diverges substantially from international guidelines. The current dominance of fibrinolysis, the alarming outcomes in non-reperfused patients, and the confounding effects of selection bias on outcome comparisons create a compelling case for systemic change. The path forward is not a dogmatic insistence on "PPCI for all," but the development of intelligent, risk-adapted regional STEMI networks. These networks must optimize a dual-track strategy: expanding access to timely PPCI while simultaneously perfecting a pharmacoinvasive protocol, prompt fibrinolysis followed by routine, timely transfer for angiography, for the majority of patients [21]. Future research should focus on multi-center registries to validate our findings and on implementing and evaluating risk stratification tools at first medical contact to better triage patients to the most appropriate and timely reperfusion strategy.

Acknowledgment

None.

Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

• MMAC was responsible for conceptualization, data curation, investigation, and writing the original draft.

• HR was responsible for supervision, methodology, and review & editing.

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• MMZ was responsible for supervision, validation, and review & editing.

• PJA was responsible for methodology, analysis, and review & editing.

All authors have read and approved the final manuscript.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Kerman University of Medical Sciences (Approval number: 0000-0002-3553-5246).

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Data Availability

De-identified participant data are not publicly available but may be made available from the corresponding author upon reasonable request.

AI Use Statement

AI was used for minor language and grammer editing to improve clarity.

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