

Review Article

Next-Generation Reperfusion Strategies in Acute Myocardial Infarction: A Systematic Review of Emerging Therapies and Technologies

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Abstract

Acute myocardial infarction (AMI) remains a leading cause of global morbidity and mortality, with timely reperfusion therapy forming the cornerstone of contemporary management. Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for ST-segment elevation myocardial infarction (STEMI), demonstrating relative reductions in short-term mortality, reinfarction, and stroke of approximately 20–30% compared with fibrinolysis when performed promptly in high-volume centers. Over the past two decades, system-level initiatives aimed at reducing door-to-balloon (D2B) time have successfully decreased median treatment delays to below 90 minutes in many regions; however, contemporary registry and trial data indicate that incremental reductions in D2B time beyond this threshold are not consistently associated with proportional improvements in survival. Instead, total ischemic time—particularly pre-hospital delay—has emerged as a stronger determinant of infarct size, left ventricular dysfunction, and long-term outcomes. Evolving reperfusion strategies now emphasize complete revascularization in multivessel disease, intravascular imaging-guided PCI, and selective use of mechanical circulatory support in high-risk presentations, each associated with reductions in recurrent ischemic events and heart failure hospitalization in recent randomized trials. Advances in adjunctive pharmacotherapy, including potent P2Y12 inhibitors, optimized anticoagulation strategies, and targeted intracoronary therapies, have further improved thrombus resolution and microvascular perfusion. In parallel, regional STEMI networks and digital health technologies have demonstrated meaningful reductions in first medical contact-to-device time and treatment delays. This narrative review synthesizes contemporary quantitative evidence on modern reperfusion strategies, re-examines the clinical relevance of D2B metrics in the current era, and highlights emerging pharmacologic and system-based innovations aimed at optimizing reperfusion efficacy and improving both short- and long-term outcomes in patients with AMI.

1. Introduction

Acute myocardial infarction (AMI), particularly ST-segment elevation myocardial infarction (STEMI), remains a leading cause of global morbidity and mortality despite significant advances in cardiovascular medicine. The cornerstone of STEMI management is rapid restoration of coronary blood flow to salvage ischemic myocardium, prevent adverse ventricular remodeling, and reduce mortality. Over the past

several decades, reperfusion strategies have evolved from fibrinolytic therapy to primary percutaneous coronary intervention (PCI), which is now regarded as the preferred reperfusion modality when performed in a timely and experienced center [1, 2]. Nevertheless, ongoing challenges related to treatment delays, procedural optimization, and adjunctive pharmacologic therapies continue to drive research and clinical innovation in this field.

Primary PCI has demonstrated superior outcomes compared with thrombolytic therapy, including improved survival, reduced reinfarction rates, and lower incidence of intracranial hemorrhage. Current international guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) strongly recommend primary PCI as the first-line reperfusion strategy when it can be performed within guideline-recommended timeframes [3, 4]. Despite these recommendations, disparities in access to PCI-capable centers, logistical barriers, and system-level inefficiencies remain significant contributors to treatment delays, particularly in low- and middle-income countries. These challenges underscore the importance of revisiting and optimizing primary PCI strategies in contemporary practice.

Door-to-balloon (D2B) time, defined as the interval between hospital arrival and balloon inflation during PCI, has emerged as a critical performance metric and quality indicator in STEMI care. Numerous studies have demonstrated a strong association between shorter D2B times and improved clinical outcomes, including reduced mortality and complications. Menees et al. [5] reported a continuous relationship between shorter D2B times and decreased mortality among patients undergoing primary PCI, reinforcing the concept that “time is myocardium.” Similarly, Butt et al. [6] and Champasri et al. [7] highlighted the prognostic significance of rapid door-to-device times in STEMI management. Efforts to reduce system delays, including prehospital electrocardiogram transmission, catheterization laboratory activation protocols, and regional STEMI networks, have been shown to improve reperfusion times and clinical outcomes [8, 9]. However, recent data suggest that further reductions in D2B time may yield diminishing returns, prompting renewed interest in total ischemic time and prehospital delays as more comprehensive targets for quality improvement.

Beyond mechanical reperfusion, adjunctive pharmacologic therapies play a pivotal role in optimizing outcomes in patients undergoing primary PCI. Antiplatelet agents, anticoagulants, glycoprotein IIb/IIIa inhibitors, and novel antithrombotic strategies have been extensively investigated to enhance microvascular perfusion and prevent thrombotic complications. Routine use of glycoprotein IIb/IIIa inhibitors has been associated with improved angiographic and clinical outcomes in selected high-risk patients, although their role in contemporary practice has evolved with the advent of potent oral P2Y₁₂ inhibitors [10]. Comparative studies of anticoagulation strategies, including bivalirudin versus heparin-based regimens, have further refined procedural pharmacotherapy during primary PCI [11]. Additionally, mechanical adjuncts such as aspiration thrombectomy have been evaluated for their potential to improve myocardial reperfusion, although results have been mixed and remain controversial [12, 13].

Emerging paradigms in reperfusion therapy increasingly emphasize a systems-based and technology-driven approach to reducing ischemic time and improving patient outcomes. Digital health innovations, including smartphone-based applications and telemedicine platforms, have demonstrated promising potential to streamline STEMI triage, enhance inter-hospital communication, and reduce reperfusion delays [14]. These innovations represent a shift toward integrated STEMI networks that leverage real-time data sharing and artificial intelligence-driven decision support to optimize clinical workflows.

Despite significant progress, several knowledge gaps remain in the optimal management of STEMI. The relative importance of procedural strategies versus pharmacologic adjuncts, the evolving role of thrombectomy and potent antithrombotic therapies, and the clinical relevance of increasingly stringent time-based metrics continue to be debated. Furthermore, real-world implementation of guideline-recommended practices varies widely across regions and healthcare systems, highlighting the need for contextualized strategies tailored to resource availability and patient populations.

In this context, revisiting contemporary primary PCI strategies, re-evaluating the clinical relevance of door-to-balloon metrics, and exploring adjunctive pharmacologic innovations are essential for advancing STEMI care. This review aims to synthesize current evidence on emerging paradigms in AMI reperfusion therapy, focusing on evolving mechanical and pharmacologic strategies, system-level interventions to reduce reperfusion delays, and novel technological innovations that may shape the future of acute coronary syndrome management.

2. Methods

This narrative review was conducted to critically synthesize contemporary evidence on reperfusion therapy in acute myocardial infarction (AMI), with emphasis on evolving primary percutaneous coronary intervention (PCI) strategies, system-level delays including total ischemia time, and adjunctive pharmacologic and device-based innovations. The methodological approach followed established best-practice recommendations for narrative clinical reviews, with predefined objectives, transparent search strategies, and structured evidence synthesis.

2.1. Literature Search Strategy

A comprehensive literature search was performed across four electronic databases: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search covered publications from January 2000 through December 2025, enabling inclusion of both foundational trials and recent studies that have influenced contemporary clinical guidelines and practice patterns.

Search terms were developed using a combination of Medical Subject Headings (MeSH) and free-text keywords. Core concepts included:

- Acute myocardial infarction
- ST-elevation myocardial infarction
- Primary percutaneous coronary intervention
- Reperfusion therapy
- System delay” and “total ischemia time
- Door-to-balloon time
- Aspiration thrombectomy and manual thrombectomy
- Adjunctive pharmacologic therapy

Boolean operators were used to refine searches, and reference lists of key articles and guidelines were manually screened to identify additional relevant studies.

2.2. Eligibility Criteria

Eligible sources included randomized controlled trials, observational cohort studies, registry analyses, systematic reviews, meta-analyses, and international clinical practice guidelines that evaluated reperfusion strategies in adult patients with AMI, particularly ST-elevation myocardial infarction (STEMI).

Studies were excluded if they:

- Focused on pediatric populations or non-human models
- Addressed non-ischemic cardiac conditions
- Lacked full-text availability
- Were published in languages other than English

No restrictions were placed on geographic region or healthcare setting to ensure broad applicability of findings.

2.3. Study Selection and Data Extraction

Study selection was performed through title and abstract screening, followed by full-text review of potentially eligible articles. Data extraction was conducted using a predefined framework to enhance consistency and reproducibility.

Extracted variables included:

- Study design and year of publication
- Population characteristics and sample size
- Reperfusion modality and timing metrics (including door-to-balloon time, symptom-to-device time, and total ischemia time)
- Pharmacologic and device-based adjuncts
- Clinical outcomes such as mortality, reinfarction, heart failure, stroke, and bleeding complications
- Key conclusions relevant to evolving reperfusion paradigms

Particular attention was given to studies examining the relationship between cumulative ischemic delay and clinical outcomes, as well as trials and meta-analyses evaluating thrombectomy strategies and their impact on mortality, microvascular perfusion, and stroke risk.

2.4. Guideline and Evidence Prioritization

Contemporary international guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) were included to contextualize evidence within current clinical recommendations. Greater weight was assigned to guideline updates, large randomized trials, and high-quality meta-analyses published in the past decade, especially those that informed changes in recommendations regarding thrombectomy use and system-of-care optimization.

2.5. Quality Appraisal and Synthesis

The methodological quality of included studies was appraised based on study design, sample size, risk of bias, outcome relevance, and consistency with other evidence. Randomized controlled trials and guideline documents were prioritized, while observational studies and registry data were used to complement randomized evidence and provide real-world insights.

Given the narrative nature of the review, no formal meta-analysis was performed. Instead, a structured qualitative synthesis was employed to integrate findings and identify converging trends across studies.

The synthesis focused on three principal domains:

1. Optimization of primary PCI and reperfusion workflows
2. Transition from isolated door-to-balloon metrics toward total ischemia time as a prognostic and system-level indicator
3. The evolving role of adjunctive pharmacologic and device-based strategies, including thrombectomy, in contemporary AMI management

2.6. Reporting Standards

References were formatted according to the American Psychological Association (APA) 7th edition guidelines. The review methodology was designed to ensure transparency, reproducibility, and clinical relevance for clinicians, researchers, and policymakers involved in acute cardiovascular care.

3. Results

Reperfusion therapy remains the cornerstone of acute ST-segment elevation myocardial infarction (STEMI) management, with primary percutaneous coronary intervention (PCI) recognized as the preferred reperfusion strategy when timely access is available. Contemporary evidence continues to demonstrate that rapid restoration of coronary blood flow significantly reduces myocardial necrosis, preserves left ventricular function, and improves survival outcomes [1]. Over the past decades, improvements in catheterization laboratory infrastructure, interventional techniques, and pharmacologic adjuncts have contributed to substantial reductions in morbidity and mortality associated with STEMI. Key components and emerging paradigms in reperfusion therapy, including system-level and pharmacologic innovations, are summarized in Table 1.

Door-to-balloon (D2B) time has emerged as a critical quality metric for STEMI care, with multiple studies demonstrating a strong inverse relationship between treatment delays and patient survival. Menees et al. [5] reported that shorter D2B times were associated with reduced in-hospital mortality among patients undergoing primary PCI, reinforcing the importance of rapid reperfusion. Similarly, Butt et al. [6] highlighted that minimizing D2B time remains a pivotal determinant of clinical outcomes, particularly in healthcare systems with evolving emergency cardiac care pathways. Recent registry-based analyses further confirmed that door-to-device time is independently associated with mortality, emphasizing the need for continuous system-level improvements in STEMI networks and emergency medical services coordination [7]. System delays, including pre-hospital delays and inter-hospital transfer times, have also been shown to contribute significantly to adverse outcomes, underscoring the necessity of comprehensive regional STEMI systems of care [8]. Comparative performance metrics and system delay factors are outlined in Table 2.

Guideline recommendations from major cardiovascular societies reinforce the priority of rapid reperfusion and standardized care pathways. The European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) recommend primary PCI within 90 minutes of first medical contact, or within 120 minutes when inter-hospital transfer is required [2, 4]. Updated ESC guidelines further emphasize integrated networks, early diagnosis, and pre-hospital activation of catheterization laboratories to reduce treatment delays and optimize outcomes [3]. Achieving sustainable D2B targets has been demonstrated in structured quality improvement initiatives, highlighting the role of multidisciplinary collaboration and continuous performance feedback in improving STEMI outcomes [9]. These system-based strategies and benchmarks are summarized in Tables 1 and 2.

Adjunctive pharmacologic therapies have also evolved as integral components of primary PCI strategies. Antiplatelet and anticoagulant therapies are essential for preventing thrombus propagation and procedural complications. Glycoprotein IIb/IIIa inhibitors have been widely investigated, with routine use demonstrating improved angiographic outcomes in select high-risk populations, although bleeding risks remain a concern [10]. Comparative studies evaluating anticoagulation strategies during primary PCI revealed that treatment timing influences the relative efficacy of bivalirudin versus heparin and glycoprotein IIb/IIIa inhibitors, highlighting the importance of individualized therapy based on clinical context and procedural timing [11]. Earlier investigations into adjunctive pharmacologic and mechanical devices also emphasized the role of combination therapies in optimizing reperfusion and reducing infarct size [15], as detailed in Table 1.

Table 1: Key components and emerging paradigms in reperfusion therapy for acute ST-segment elevation myocardial infarction

| Domain | Key Findings / Paradigms | Clinical Implications | Representative Evidence |
|---------------------------------------|--|--|--|
| Primary reperfusion strategy | Primary PCI remains the preferred reperfusion modality when timely access is available | Improves myocardial salvage, left ventricular function, and survival | Akbar et al., [1] |
| Door-to-balloon (D2B) time | Shorter D2B time is strongly associated with reduced mortality | Emphasizes rapid catheterization lab activation and streamlined emergency pathways | Menees et al., [5] Butt et al., [6] |
| Door-to-device/system delays | System and transfer delays independently mortality risk | Necessitates regional STEMI networks and coordinated EMS systems | Champasri et al., [7] Terkelsen et al., [8] |
| Guideline-recommended timelines | PCI within 90 min (direct) or 120 min (transfer) from first medical contact | Benchmark for quality metrics and hospital performance evaluation | Ibanez et al., [2] O'Gara et al., [4] |
| Integrated systems of care | Pre-hospital ECG diagnosis and cath lab pre-activation reduce delays | Multidisciplinary collaboration improves outcomes | Collet et al., [3] Wilson et al., [9] |
| Antiplatelet therapy | GP IIb/IIIa inhibitors improve angiographic outcomes but increase bleeding risk | Selective use in high thrombus burden or bailout scenarios | Karathanos et al., [10] |
| Anticoagulation strategies | Bivalirudin vs. heparin outcomes influenced by timing and clinical context | Personalized anticoagulation approach recommended | Schoos et al., [11] |
| Combination pharmacologic strategies | Combined pharmacologic and mechanical therapies may reduce infarct size | Tailored therapy beneficial in complex STEMI cases | Chiam et al., [15] |
| Thrombectomy devices | Improves myocardial perfusion but inconsistent mortality benefit | Selective rather than routine use recommended | Mongeon et al., [12] |
| Thrombectomy + GP IIb/IIIa inhibitors | Enhanced reperfusion in high thrombus burden patients | Potential targeted strategy in selected STEMI populations | Niu et al., [13] |
| Digital health innovations | Smartphone applications reduce reperfusion delays | Integration of telemedicine may transform STEMI workflows | Piazza et al., [14] |
| Emerging system-level interventions | Digital triage and real-time communication improve care coordination | Future paradigm shift toward technology-driven STEMI care | Piazza et al., [14] |
| Quality improvement initiatives | Continuous monitoring improves sustainable D2B performance | Institutional benchmarking improves clinical outcomes | Wilson et al., [9] |
| Multidisciplinary collaboration | Team-based STEMI protocols enhance efficiency | Essential for achieving guideline targets | Collet et al., [3] |
| Future research directions | Optimization of pharmacologic adjuncts and digital systems | Potential to further reduce mortality and morbidity | Akbar et al., [1], Collet et al., [3] |

Table 2: Comparative overview of reperfusion strategies, system metrics, and adjunctive innovations in STEMI

| Category | Strategy / Metric | Description | Advantages | Limitations / Challenges | Key References |
|-----------------------|--|--|---|---|--|
| Reperfusion modality | Primary percutaneous coronary intervention (PCI) | Mechanical reopening of occluded coronary artery via catheter-based intervention | Superior reperfusion rates, reduced mortality, improved LV function | Requires specialized centers and rapid access | Akbar et al., [1] Ibanez et al., [2] |
| Reperfusion modality | Fibrinolytic therapy | Pharmacologic thrombolysis when PCI unavailable | Widely available, rapid initiation | Lower efficacy, bleeding | O'Gara et al., [4] |
| Performance metric | Door-to-balloon (D2B) time | Time from hospital arrival to coronary balloon inflation | Strong predictor of survival and quality of care | Influenced by system delays and logistics | Menees et al., [5] Butt et al., [6] |
| Performance metric | Door-to-device time | Broader system measure including pre-hospital delays | Reflects system-wide efficiency | Requires integrated EMS and hospital coordination | Champasri et al., [7] |
| System delay factors | Pre-hospital delay | Time from symptom onset to first medical contact | Early EMS activation improves survival | Patient awareness and transport limitations | Terkelsen et al., [8] |
| Guideline benchmark | PCI ≤ 90 min (direct) or ≤ 120 min (transfer) | Recommended timelines from first medical contact | Standardizes quality benchmarks | Difficult in low-resource settings | Ibanez et al., [2] O'Gara et al., [4] |
| Systems of care | Integrated STEMI networks | Coordinated EMS, ED, and cath lab protocols | Reduces delays and improves outcomes | Requires institutional collaboration | Collet et al., [3] Wilson et al., [9] |
| Pharmacologic adjunct | Glycoprotein IIb/IIIa inhibitors | Potent antiplatelet therapy during PCI | Improves angiographic outcomes | Increased bleeding risk | Karathanos et al., [10] |
| Pharmacologic adjunct | Anticoagulants (heparin, bivalirudin) | Prevent thrombus propagation during PCI | Essential for procedural success | Timing-dependent efficacy | Schoos et al., [11] |
| Combined therapy | Pharmacologic + mechanical strategies | Use of drugs plus devices to enhance reperfusion | Potential reduction in infarct size | Limited consistent mortality benefit | Chiam et al., [15] |
| Mechanical adjunct | Thrombectomy devices | Removal of intracoronary thrombus | Improves microvascular perfusion | Mixed clinical outcome evidence | Mongeon et al., [12] |
| Hybrid adjunct | Thrombectomy + GP IIb/IIIa inhibitors | Combined mechanical and pharmacologic reperfusion | Enhanced reperfusion in high thrombus burden | Risk of bleeding and procedural complexity | Niu et al., [13] |
| Digital innovation | Smartphone-based STEMI apps | Real-time diagnosis and cath lab activation | Reduces reperfusion delays | Requires digital infrastructure | Piazza et al., [14] |
| Telemedicine | Digital triage and remote ECG transmission | Early diagnosis and system activation | Improves pre-hospital decision-making | Variable adoption globally | Piazza et al., [14] |
| Future paradigm | Technology-driven STEMI systems | Integration of AI, telehealth, and EMS networks | Potential to further reduce mortality | Implementation and cost barriers | Collet et al., [3] Akbar et al., [1] |

Mechanical adjuncts such as thrombectomy have been extensively studied as methods to improve microvascular reperfusion and reduce thrombus burden during PCI. Meta-analyses have shown that adjunctive thrombectomy can enhance angiographic outcomes and myocardial perfusion, although its routine use has been debated due to inconsistent clinical benefit and procedural risks [12]. Combined approaches incorporating thrombectomy with intracoronary glycoprotein IIb/IIIa inhibitors have demonstrated improved reperfusion parameters in STEMI patients, suggesting potential benefits in selected patient populations with high thrombus burden [13]. These adjunctive mechanical and hybrid strategies are summarized in Table 2.

Emerging innovations in STEMI systems of care increasingly incorporate digital health technologies and system-level interventions. Recent studies suggest that smartphone-based applications and digital platforms can reduce reperfusion delays by facilitating rapid diagnosis, catheterization laboratory activation, and communication among healthcare providers [14]. Such technologies represent a paradigm shift in STEMI management, integrating telemedicine and digital triage systems into traditional reperfusion workflows to further reduce treatment delays and improve outcomes, as highlighted in Table 2.

Overall, the results of contemporary studies and guideline-based evidence highlight the multifaceted nature of reperfusion therapy in acute myocardial infarction. Primary PCI remains the gold standard for STEMI management, with door-to-balloon time serving as a crucial performance metric. Adjunctive pharmacologic and mechanical therapies continue to evolve, offering potential benefits when applied selectively. Furthermore, system-level innovations and digital health strategies are emerging as important tools to enhance reperfusion efficiency and clinical outcomes. Continued research and implementation of integrated STEMI care networks are essential to further reduce delays, optimize therapeutic strategies, and improve survival in patients with acute myocardial infarction.

4. Discussion

Acute myocardial infarction (AMI), particularly ST-segment elevation myocardial infarction (STEMI), remains a leading cause of morbidity and mortality worldwide despite major advances in reperfusion therapy and systems of care. Primary percutaneous coronary intervention (PCI) has emerged as the preferred reperfusion strategy when timely access is feasible, owing to its superior efficacy in restoring coronary patency, reducing infarct size, and improving survival compared with fibrinolytic therapy. Contemporary guidelines consistently emphasize rapid reperfusion, comprehensive antithrombotic therapy, and system-level optimization as central pillars in the management of AMI [2–4].

Primary PCI has transformed outcomes in STEMI through direct mechanical restoration of coronary blood flow, minimizing ischemic time and myocardial necrosis. Advances in catheter technology, stent design, imaging guidance, and adjunctive pharmacotherapy have further enhanced procedural success and reduced complications. However, the effectiveness of primary PCI is critically dependent on minimizing delays from symptom onset to reperfusion, with door-to-balloon (D2B) and door-to-device times serving as key quality metrics. Early observational studies demonstrated a continuous relationship between D2B time and mortality, highlighting that even incremental delays can adversely affect survival outcomes [5]. Similarly, system-level delays, including prehospital transport and inter-hospital transfers, have been associated with increased mortality, reinforcing the need for coordinated regional STEMI networks [8].

Despite widespread adoption of guideline-recommended targets, achieving optimal D2B times remains challenging, particularly in resource-limited settings. Butt et al. [6] highlighted persistent delays in real-world clinical practice, underscoring the need for ongoing quality improvement initiatives. Wilson et al. [9] demonstrated that structured institutional strategies, including multidisciplinary protocols and real-time performance feedback, can achieve sustainable D2B times below the recommended 90-minute benchmark. More recent evidence has extended these concepts to door-to-device metrics, with Champasri et al. [7] showing a significant association between shorter reperfusion times and reduced mortality, reinforcing the clinical importance of rapid catheterization laboratory activation and streamlined patient flow.

Emerging paradigms in AMI management increasingly focus on optimizing prehospital and in-hospital systems of care through technological and organizational innovations. Digital health tools, such as smartphone applications and telemedicine platforms, have shown promise in reducing reperfusion delays by facilitating early diagnosis, direct catheterization laboratory activation, and improved communication between emergency medical services and interventional teams. Piazza et al. (2025) demonstrated that smartphone-based systems could significantly shorten reperfusion times and improve clinical outcomes, highlighting the potential of digital solutions to transform AMI care pathways.

Adjunctive pharmacologic therapies remain a cornerstone of primary PCI, targeting thrombosis, platelet aggregation, and inflammation to improve procedural success and reduce adverse events. Antiplatelet therapy with aspirin and P2Y₁₂ inhibitors, along with anticoagulation using heparin or bivalirudin, is standard of care, while glycoprotein IIb/IIIa inhibitors and other agents are selectively used in high-risk patients. Karathanos et al. [10] reported that routine glycoprotein IIb/IIIa inhibitor therapy in STEMI treated with primary PCI may improve angiographic outcomes but must be balanced against bleeding risks. Similarly, Schoos et al. [11] highlighted the importance of time-to-treatment in determining the relative benefits of anticoagulation strategies, emphasizing that pharmacologic efficacy is closely linked to timely administration.

Mechanical adjunctive strategies, such as thrombectomy devices, have also been investigated as methods to improve myocardial reperfusion. Early studies suggested that aspiration thrombectomy could reduce thrombus burden and improve microvascular perfusion, though subsequent trials yielded mixed results. Mongeon et al. [12] demonstrated that adjunctive thrombectomy could improve procedural outcomes, while later meta-analyses and randomized trials tempered enthusiasm due to limited impact on long-term clinical endpoints. Combining thrombectomy with intracoronary glycoprotein IIb/IIIa inhibitors has been explored as a strategy to enhance reperfusion, with Niu et al. [13] reporting potential benefits in selected patient populations. These findings underscore the evolving role of mechanical and pharmacologic adjuncts and the need for individualized therapy based on thrombotic burden and patient risk profiles.

Beyond procedural considerations, evolving paradigms in AMI reperfusion therapy emphasize a holistic approach that integrates rapid diagnosis, timely reperfusion, optimized pharmacotherapy, and comprehensive post-PCI care. StatPearls reviews and contemporary clinical guidelines highlight the importance of early recognition of STEMI, rapid triage, and adherence to evidence-based treatment protocols to improve outcomes [1, 3]. The integration of multidisciplinary teams, continuous quality improvement programs, and regional STEMI networks has been shown to reduce treatment delays and improve survival.

5. Conclusion

Despite significant progress, several challenges persist. Disparities in access to primary PCI remain a major global issue, particularly in low- and middle-income countries where infrastructure, trained personnel, and catheterization facilities are limited. In such settings, delayed reperfusion and reliance on fibrinolytic therapy continue to contribute to higher mortality rates. Additionally, patient-related delays, including delayed presentation due to lack of awareness or socioeconomic barriers, remain substantial contributors to total ischemic time. Addressing these challenges requires public health initiatives, education campaigns, and investments in healthcare infrastructure to ensure equitable access to timely reperfusion therapy.

Future directions in AMI reperfusion therapy are likely to focus on precision medicine approaches, integrating patient-specific risk stratification, imaging modalities, and biomarker-guided therapy to tailor reperfusion strategies. Advances in intracoronary imaging, such as optical coherence tomography and intravascular ultrasound, may further optimize PCI outcomes by guiding stent selection and deployment. Novel pharmacologic agents targeting inflammation, thrombosis, and myocardial reperfusion injury are also under investigation, potentially expanding the therapeutic armamentarium beyond traditional antithrombotic therapies.

Article Information

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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References

- [1] H. Akbar and S. Sharma. *Acute ST-segment elevation myocardial infarction (STEMI)*. StatPearls Publishing, 2024.
- [2] B. Ibanez, S. James, S. Agewall, M. J. Antunes, C. Bucciarelli-Ducci, H. Bueno, A. L. P. Caforio, F. Crea, J. A. Goudevenos, S. Halvorsen, G. Hindricks, A. Kastrati, M. J. Lenzen, E. Prescott, M. Roffi, M. Valgimigli, C. Varenhorst, P. Vranckx, and P. Widimsky. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal*, 39(2):119–177, 2018. doi: 10.1093/eurheartj/ehx393.
- [3] J.-P. Collet, H. Thiele, E. Barbato, O. Barthélémy, J. Bauersachs, D. L. Bhatt, and M. Valgimigli. 2023 ESC guidelines for the management of acute coronary syndromes. *European Heart Journal*, 2023.
- [4] P. T. O’Gara, F. G. Kushner, D. D. Ascheim, D. E. Casey, M. K. Chung, J. A. de Lemos, S. M. Ettinger, J. C. Fang, F. M. Fesmire, B. A. Franklin, C. B. Granger, H. M. Krumholz, J. A. Linderbaum, D. A. Morrow, L. K. Newby, J. P. Ornato, N. Ou, M. J. Radford, J. E. Tamis-Holland, C. L. Tommaso, C. M. Tracy, Y. J. Woo, D. X. Zhao, J. L. Anderson, A. K. Jacobs, J. L. Halperin, N. M. Albert, R. G. Brindis, M. A. Creager, D. DeMets, R. A. Guyton, J. S. Hochman, R. J. Kovacs, F. G. Kushner, E. M. Ohman, W. G. Stevenson, and C. W. Yancy. 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction: Executive Summary: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*, 61(4):e78–e140, 2023.
- [5] D. S. Menees, E. D. Peterson, Y. Wang, J. P. Curtis, J. C. Messenger, J. S. Rumsfeld, and H. S. Gurm. Door-to-balloon time and mortality among patients undergoing primary PCI. *Journal of the American College of Cardiology*, 61(12):1231–1238, 2023.
- [6] T. S. Butt, E. Bashtawi, B. Bououn, B. Wagley, B. Albarrak, H. E. Sergani, S. Mujtaba, and J. Buraiki. Door-to-balloon time in the treatment of st segment elevation myocardial infarction in a tertiary care center in saudi arabia. *Annals of Saudi Medicine*, 40(4): 281–289, 2020. URL <https://doi.org/10.5144/0256-4947.2020.281>.
- [7] K. Champasri, S. Srimahachota, M. Chandavimol, W. Udayachalerm, A. Thakkinstian, B. Sookananchai, W. Phatharajaree, S. Kitchoosakun, and N. Sansanayudh. Door-to-device Time and Mortality in Patients with ST-Elevation Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention: Insight from Real World Data of Thai PCI Registry. *Cardiovascular Diagnosis and Therapy*, 13(5):843–854, 2023. URL <https://doi.org/10.21037/cdt-22-611>. pmid 37941842, pmcid PMC10628423.
- [8] C. J. Terkelsen, J. T. Sørensen, M. Maeng, L. O. Jensen, H. Tilsted, S. Trautner, W. Vach, S. P. Johnsen, L. Thuesen, and J. F. Lassen. System delay and mortality among patients with ST-segment elevation myocardial infarction treated with primary PCI. *JAMA*, 304(7): 763–771, 2024.
- [9] B. H. Wilson, A. D. Humphrey, J. C. Cedarholm, W. E. Downey, S. J. Ratcliffe, S. A. Murphy, C. G. Pietras, D. M. Kolansky, H. C. Herrmann, J. E. Bavaria, and J. S. Giri. Achieving sustainable first door-to-balloon times of 90 minutes for regional transfer st-segment elevation myocardial infarction. *JACC: Cardiovascular Interventions*, 6(10):1064–1071, 2013. URL <https://doi.org/10.1016/j.jcin.2013.05.018>. pmid 24156970.
- [10] A. Karathanos, Y. Lin, L. Dannenberg, C. Parco, V. Schulze, M. Brockmeyer, C. Jung, Y. Heinen, S. Perings, U. Zeymer, M. Kelm, A. Polzin, and G. Wolff. Routine glycoprotein iib/iiia inhibitor therapy in st-segment elevation myocardial infarction: A meta-analysis. *Canadian Journal of Cardiology*, 35(11):1576–1588, 2019. URL <https://doi.org/10.1016/j.cjca.2019.05.003>. pmid 31542257.

- [11] M.M. Schoos, G. De Luca, G. D. Dangas, P. Clemmensen, G. M. Ayele, R. Mehran, and G. W. Stone. Impact of time to treatment on the effects of bivalirudin vs. glycoprotein iib/iiia inhibitors and heparin in patients undergoing primary percutaneous coronary intervention: Insights from the horizons-ami trial. *EuroIntervention*, 12(9):1144–1153, 2016. URL <https://doi.org/10.4244/EIJV12I9A186>. pmid 27548527.
- [12] F.-P. Mongeon, P. Bélisle, L. Joseph, M. J. Eisenberg, and S. Rinfret. Adjunctive thrombectomy for acute myocardial infarction: A meta-analysis. *Circulation: Cardiovascular Interventions*, 3(1):6–16, 2024.
- [13] X. Niu, J. Zhang, M. Bai, Y. Peng, and Z. Zhang. Combined thrombectomy and intracoronary administration of glycoprotein iib/iiia inhibitors improves myocardial reperfusion in patients undergoing primary percutaneous coronary intervention: A meta-analysis. *Journal of Geriatric Cardiology*, 14(10):614–623, 2017. doi: 10.11909/j.issn.1671-5411.2017.10.002. pmid 29118838, pmcid PMC5668154.
- [14] N. Piazza, W. Gibson, D. Al Kindi, E. Akl, K. B. Dandona, J. P. Pelletier, A. Zgheib, G. Martucci, and M. Spaziano. Impact of smartphone apps on reperfusion times and clinical outcomes in acute st-segment elevation myocardial infarction: Systematic review and meta-analysis. *JMIR mHealth and uHealth*, 13:e66605, 2025. doi: 10.2196/66605. URL <https://doi.org/10.2196/66605>.
- [15] P. T. L. Chiam and R. Liew. Adjunctive pharmacologic agents and mechanical devices in primary percutaneous coronary intervention. *Annals of the Academy of Medicine, Singapore*, 39(3):230–236, 2010.