Comprehensive Review of ST-Elevation Myocardial Infarction: From Pathogenesis to Cutting-Edge Therapies

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ABSTRACT
Background: ST-segment elevation myocardial infarction (STEMI) is a life-threatening cardiovascular emergency resulting from acute coronary artery occlusion. Despite advances in early diagnosis and treatment, STEMI remains a major cause of morbidity and mortality worldwide. Rapid identification and timely reperfusion therapy are critical to reducing myocardial damage and improving clinical outcomes.

Objective: This review aims to provide an updated overview of STEMI pathophysiology, diagnostic strategies, and evolving management approaches, emphasizing novel biomarkers, advanced imaging modalities, and contemporary reperfusion therapies.

Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science using keywords such as "ST-segment elevation myocardial infarction", "primary percutaneous coronary intervention", "reperfusion therapy", "cardiac biomarkers", and "advanced imaging techniques". Recent peer-reviewed articles published in high-impact journals were analyzed, focusing on diagnostic innovations, PCI advancements, and adjunct pharmacological therapies.

Conclusion: Primary PCI remains the gold standard for STEMI management, offering superior outcomes compared to fibrinolysis. The integration of trans-radial intervention, next-generation drug-eluting stents, and tailored antithrombotic strategies has further improved procedural success. Additionally, emerging biomarkers and advanced imaging modalities provide valuable prognostic insights. Future research should focus on optimizing reperfusion strategies, reducing procedural delays, and enhancing risk stratification to improve long-term survival and cardiac function in STEMI patients.

Keywords: STEMI, Primary PCI, Reperfusion Therapy, Cardiac Biomarkers, Advanced Imaging.

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is a life-threatening condition that represents the most severe form of acute coronary syndrome (ACS). It occurs due to a sudden and complete occlusion of a coronary artery, usually caused by a ruptured or eroded atherosclerotic plaque, leading to myocardial ischemia and infarction. Despite significant advances in early diagnosis and treatment, STEMI remains a major cause of morbidity and mortality worldwide. Rapid recognition and timely reperfusion therapy are essential to minimize myocardial damage and improve clinical outcomes. Primary percutaneous coronary intervention (PCI) has become the gold standard treatment, significantly reducing complications and mortality when performed promptly [1]. The pathophysiology of STEMI is complex, involving a cascade of events that include plaque rupture, thrombus formation, and myocardial necrosis. This process leads to the characteristic ST-segment elevation on electrocardiography (ECG), which serves as a crucial diagnostic marker. Alongside ECG, the use of highly sensitive cardiac biomarkers, such as troponins, has further enhanced the early detection and risk stratification of patients. Additionally, novel inflammatory and myocardial necrosis markers, including C-reactive protein, interleukins, and galectin-3, are being investigated for their potential roles in predicting outcomes and guiding treatment strategies [2].

Advancements in STEMI management extend beyond reperfusion therapy to include optimal pharmacological strategies, mechanical circulatory support, and risk factor modification. Innovations in PCI techniques, the development of newer-generation drug-eluting stents, and improvements in antithrombotic therapies have further contributed to better patient survival. Moreover, emerging technologies in cardiac imaging, including echocardiography, cardiac MRI, and intravascular ultrasound, offer valuable insights into myocardial function and viability, aiding in prognostication and personalized treatment approaches [3].

This review aims to provide a comprehensive overview of STEMI, encompassing its pathophysiology, diagnostic modalities, and evolving management strategies. Special emphasis was placed on the role of novel biomarkers, imaging techniques, and recent advancements in reperfusion therapies to improve patient outcomes.

Pathophysiology of STEMI

STEMI represents the most acute and severe manifestation of coronary artery disease (CAD). It is predominantly caused by the complete thrombotic occlusion of a major epicardial coronary artery due to the rupture or erosion of an atherosclerotic plaque. This occlusion leads to rapid myocardial ischemia and infarction, which, if left untreated, results in significant morbidity and mortality. Early diagnosis and timely reperfusion therapy are critical in minimizing myocardial damage and improving survival rates.

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Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy, and if it cannot be performed within 120 minutes of diagnosis, fibrinolysis therapy is recommended to dissolve the thrombus [4].

Classification and ECG Characteristics

CAD, a leading cause of cardiovascular disease, typically involves progressive atherosclerosis that narrows the coronary arteries, leading to ischemic heart disease. ACS encompass three major conditions: unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and STEMI. Myocardial infarction (MI) is defined by cardiomyocyte death due to a prolonged imbalance between oxygen supply and demand. ECG findings differentiate between STEMI, which involves full-thickness myocardial ischemia and exhibits ST-segment elevation, and NSTEMI, which does not show ST elevation but may have ST depressions or T-wave inversions [5].

Diagnosis and Role of ECG

Early and accurate diagnosis of STEMI is essential, as time to treatment directly impacts patient outcomes. The hallmark of STEMI diagnosis is persistent ST-segment elevation on a 12-lead ECG, typically obtained within 10 minutes of first medical contact. Symptoms include crushing chest pain, shortness of breath, and atypical presentations, such as nausea or jaw pain, more common in women. In ambiguous cases, additional ECG criteria are required, particularly in the presence of left bundle branch block (LBBB) or right bundle branch block (RBBB). Pre-hospital ECG transmission improves time to reperfusion and clinical outcomes, enabling rapid triage and transport to PCI-capable facilities [6].

Biomarkers in STEMI Diagnosis

Although ECG remains the primary diagnostic tool, cardiac biomarkers play a crucial role in confirming myocardial necrosis. Troponins, particularly high-sensitivity troponin I and T, are the gold standard for detecting myocardial injury due to their high specificity for cardiac tissue. Additional biomarkers such as creatine kinase-MB (CK-MB) and myoglobin provide supplementary diagnostic information. Emerging biomarkers, including inflammatory markers like C-reactive protein (CRP) and interleukin-6, as well as markers of plaque instability like myeloperoxidase and TNF-α, are being explored for their prognostic value in STEMI [5].

Advances in Imaging and Risk Stratification

Imaging techniques complement ECG and biomarkers in STEMI assessment, particularly in complex cases. Transthoracic echocardiography (TTE) is used to evaluate left ventricular function, detect wall motion abnormalities, and rule out mechanical complications. Cardiac MRI provides detailed myocardial characterization and is useful in distinguishing STEMI from other conditions such as myocarditis. Risk stratification models, including the GRACE and TIMI scores, aid in predicting patient outcomes and guiding management decisions. Additionally, coronary artery calcium scoring with CT imaging is gaining traction for identifying individuals at high cardiovascular risk [7].

The management of STEMI has evolved significantly over the years, with a strong emphasis on rapid diagnosis, early reperfusion therapy, and adjunct pharmacological treatments. PCI remains the gold standard for reperfusion, while newer advancements such as trans-radial access, drug-eluting stents, and hemodynamic support devices have improved patient outcomes. Additionally, anticoagulation and antiplatelet therapies play a crucial role in reducing thrombotic complications and enhancing procedural success. The following table provides a structured summary of the key components of STEMI management, including interventional and pharmacological strategies based on current clinical guidelines [6].

Table 1: Summary of Key Components in the Management of STEMI [6]

Category	
Primary Reperfusion Strategy	Primary PCI is the preferred reperfusion strategy if performed within 120 minutes of STEMI diagnosis.
Reperfusion Therapy	In-hospital mortality reduced to <10% with early reperfusion. PCI is preferred over fibrinolysis when feasible.
Trans-radial Intervention	Trans-radial intervention (TRI) is a safer alternative to femoral access, reducing bleeding complications.
Stent Technology	New-generation drug-eluting stents (DES) improve outcomes by reducing thrombotic events and restenosis.
Hemodynamic Support	In high-risk PCI and cardiogenic shock, intra-aortic balloon pumps and LV assist devices provide support.
Aspiration Thrombectomy	Routine aspiration thrombectomy is not recommended due to an increased stroke risk.
Distal Protection Devices	Used selectively in large thrombus burden to prevent distal embolization.
Anticoagulation Therapy	Heparin, enoxaparin, and bivalirudin used for thrombin inhibition during PCI.
Antiplatelet Therapy	Dual antiplatelet therapy with aspirin and P2Y12 inhibitors is recommended post-STEMI.

PCI: Percutaneous Coronary Intervention, STEMI: ST-segment Elevation Myocardial Infarction, LV Assist Device: Left Ventricular Assist Device.

❖ Primary PCI in CAD

Introduction and Anatomy

CAD remains a leading cause of mortality globally, with PCI emerging as a critical non-surgical technique to restore myocardial perfusion. PCI involves catheter-based interventions to relieve arterial narrowing and occlusion, thereby improving blood flow to ischemic myocardium. The procedure is performed by accessing the bloodstream via the femoral or radial artery, utilizing real-time X-ray fluoroscopy for guidance. Catheters are maneuvered into the coronary arteries, and contrast dye is introduced to delineate vascular anatomy, allowing for precise visualization of stenotic segments [8].

Pathophysiology and Clinical Benefits of PCI

STEMI typically results from the acute thrombotic occlusion of a coronary artery, often triggered by plaque rupture, erosion, or fissuring. This sudden obstruction leads to severe myocardial ischemia, requiring urgent reperfusion. Primary PCI, involving balloon angioplasty with or without stenting, directly restores blood flow in the occluded artery, achieving normal perfusion in over 90% of cases, significantly outperforming thrombolytic therapy, which has a success rate of only 50–60%. Early intervention minimizes myocardial damage, reducing infarct size and improving long-term cardiac function [9].

Evolution of PCI and Current Standards

The first catheter-based reperfusion for STEMI was introduced in 1979 using balloon angioplasty. Since then, PCI has evolved significantly with advancements such as antiplatelet therapy, bare-metal and DES, and thrombectomy devices. Current clinical guidelines recommend PCI as the preferred reperfusion strategy in STEMI patients, provided it can be performed within 90 minutes of first medical contact. Patients presenting at non-PCI-capable hospitals should undergo rapid transfer to an interventional facility to optimize outcomes [6].

Door-to-Balloon Time and Access Approaches

The door-to-balloon (D2B) time, measuring the interval between hospital arrival and balloon inflation during PCI, is a crucial performance metric. Studies from the NRMI-3 and 4 registries highlight that prolonged D2B times are linked to increased in-hospital mortality, emphasizing the need for rapid intervention. Additionally, access site selection plays a key role in procedural success. While femoral artery access is more commonly used, the radial approach is preferred due to its lower risk of bleeding and vascular complications. A meta-analysis of major trials (RIVAL, MATRIX, RIFLE-STEACS, STEMI-RADIAL) demonstrated reduced bleeding, mortality, and major adverse cardiovascular events in patients undergoing trans-radial PCI [10].

Technical Considerations and Future Directions

PCI involves precise catheter manipulation to cross stenotic lesions and deploy stents. Advances in procedural techniques include the use of guidewires, improved stents, and distal protection devices to minimize embolization risk. However, technical challenges such as large thrombus burden, no-reflow phenomenon, and multivessel disease persist. Emerging therapies, including cell-based myocardial repair and novel pharmacological adjuncts, are under investigation to enhance post-PCI myocardial salvage [11].

❖ Left Ventricular Diastolic Dysfunction (LVDD) and Heart Failure with Preserved Ejection Fraction (HFpEF)

Introduction and Relationship to Heart Failure

LVDD has long been recognized as a significant contributor to HF, particularly heart failure with preserved ejection fraction (HFpEF). However, its diagnosis, pathophysiology, and treatment remain complex and controversial. LVDD can occur in asymptomatic individuals, in those with preserved ejection fraction (EF), and even in heart failure with reduced ejection fraction (HFrEF). Not all cases of HFpEF or HFrEF are associated with diastolic dysfunction, further complicating its clinical characterization. Diastolic HF is a subset of HFpEF, but diastolic dysfunction can exist in HFrEF as well [12].

Epidemiology and Risk Factors

Heart failure remains a significant public health burden, affecting over 5.1 million patients in the United States and more than 23 million worldwide. The incidence of LVDD increases with age, and key risk factors include hypertension, diabetes mellitus, and left ventricular hypertrophy (LVH). Studies show that approximately 34% of diabetic patients exhibit diastolic dysfunction due to increased LV mass, wall thickness, and arterial stiffness. Although risk factors overlap between HFpEF and HFrEF, the pathophysiological mechanisms differ. HFpEF is more prevalent in older patients and females, with concentric remodeling and a preserved LV end-diastolic volume. In contrast, HFrEF is characterized by LV dilation and eccentric remodeling [13].

Progression from Diastolic Dysfunction to Diastolic Heart Failure

Epidemiological data suggest a latent phase in which LVDD progresses before symptomatic HF develops. Mild LVDD is found in approximately 21% of individuals, while moderate to severe dysfunction is present in 7%, both of which significantly increase the risk of symptomatic HF and mortality. This asymptomatic phase offers an opportunity for early intervention to prevent heart failure progression. Early LVDD manifests as increased LV stiffness and impaired diastolic filling, yet exercise tolerance remains normal. As the disease advances, pulmonary pressures rise abnormally during exertion, leading to reduced exercise capacity and HF symptoms. Notably, a high prevalence of atrial fibrillation in diastolic HF patients suggests a shared pathophysiology, as atrial fibrillation exacerbates diastolic dysfunction by increasing LV filling pressures [14].

Mechanisms Underlying Diastolic Dysfunction

Several mechanisms contribute to LVDD, including oxidative stress, impaired calcium handling, fibrosis, and changes in sarcomere function. Increased cardiac reactive oxygen species (ROS) have been implicated in altering calcium homeostasis and myofilament sensitivity. A prolonged calcium transient results in increased intracellular Ca^{2+} during diastole, impairing both relaxation and passive stiffness. Dysregulation of key calcium-handling proteins, including the sarcoplasmic reticulum (SR) Ca^{2+} pump (SERCA2A), sodium-calcium exchanger (NCX), and ryanodine receptor (RyR), leads to impaired relaxation. Additionally, oxidative stress-mediated modifications of RyR and SERCA2A further disrupt calcium balance [15].

Structural Changes: Fibrosis and Extracellular Matrix Remodeling

Cardiac fibrosis plays a crucial role in LVDD, particularly in hypertensive and aging populations. Fibrosis increases LV stiffness, impairing diastolic filling and ventricular compliance. Upregulation of transforming growth factor-β (TGF-β) and connective tissue growth factor (CTGF) promotes collagen deposition and extracellular matrix. Dysregulation of matrix metalloproteases (MMPs) and their inhibitors (TIMPs) also alters collagen turnover, with increased MMP-2 and MMP-9 levels being linked to diastolic dysfunction severity. Additionally, increased fibrosis correlates with impaired myocardial relaxation and elevated LV filling pressures [16].

Advancements in Diagnosis: Imaging and Biomarkers

Echocardiography remains the gold standard for diagnosing LVDD, utilizing Doppler-derived parameters such as mitral inflow velocity (E/A ratio), tissue Doppler imaging (TDI), and pulmonary vein flow assessment. Speckle tracking echocardiography (STE) and cardiac magnetic resonance (CMR) imaging have emerged as promising tools for evaluating myocardial deformation and strain analysis. Novel biomarkers, including B-type natriuretic peptide (BNP) and cardiac myosin binding protein C (cMyBP-C), have shown potential in detecting diastolic dysfunction. Notably, oxidative stress-induced S-glutathionylation of cMyBP-C has been associated with impaired relaxation and may serve as a circulating biomarker of disease progression [17].

Future Therapeutic Strategies

Despite advances in understanding LVDD, no specific treatment has been proven to reverse diastolic dysfunction or improve long-term outcomes in HFpEF. Current research focuses on targeting oxidative stress, calcium handling abnormalities, and extracellular matrix remodeling. Ranolazine, an anti-anginal agent, has shown promise in improving myocardial relaxation by reducing intracellular Na^{+} and Ca^{2+} levels. Tetrahydrobiopterin (BH4) supplementation has been explored as a strategy to restore nitric oxide synthase (NOS) function and improve LV relaxation. Additionally, mitochondria-targeted antioxidants, such as mitoTEMPO and MitoQ10, have demonstrated potential in preventing diastolic dysfunction in animal models [18]. As research advances, these novel therapeutic approaches may pave the way for targeted interventions to mitigate the burden of LVDD and HFpEF.

CONCLUSION

Primary PCI remains the gold standard for STEMI management, offering superior outcomes compared to fibrinolysis. The integration of trans-radial intervention, next-generation drug-eluting stents, and tailored antithrombotic strategies has further improved procedural success. Additionally, emerging biomarkers and advanced imaging modalities provide valuable prognostic insights. Future research should focus on optimizing reperfusion strategies, reducing procedural delays, and enhancing risk stratification to improve long-term survival and cardiac function in STEMI patients.

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REFERENCES

1. Mitsis A, Gragnano F (2021): Myocardial infarction with and without ST-segment elevation: a contemporary reappraisal of similarities and differences. Curr Cardiol Rev., 17:e230421189013.

2. Elendu C, Amaechi D, Elendu T *et al.* (2023): Comprehensive review of ST-segment elevation myocardial infarction: Understanding pathophysiology, diagnostic strategies, and current treatment approaches. Medicine (Baltimore), 102:e35687.

3. Sachdeva P, Kaur K, Fatima S *et al.* (2023): Advancements in myocardial infarction management: exploring novel approaches and strategies. Cureus, 15:e45578.

4. Bolognese L (2021): [Treatment of ST-elevation myocardial infarction: state of the art and new horizons]. G Ital Cardiol (Rome), 22:167-80.

5. Bhatt D, Lopes R, Harrington R (2022): Diagnosis and treatment of acute coronary syndromes: a review. JAMA., 327:662-75.

6. Ibanez B, James S, Agewall S *et al.* (2018): 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, 39:119-77.

7. Briosa E, Hinton J, Sirohi R (2021): Cardiogenic shock due to acute severe ischemic mitral regurgitation. Am J Emerg Med., 43:292.e1-.e3.

8. Capodanno D, Milluzzo R, Angiolillo D (2019): Intravenous antiplatelet therapies (glycoprotein IIb/IIIa receptor inhibitors and cangrelor) in percutaneous coronary intervention: from pharmacology to indications for clinical use. Ther Adv Cardiovasc Dis., 13:1753944719893274.

9. Alex A, Lahiri A, Geevar T *et al.* (2018): Observational study comparing pharmacoinvasive strategy with primary percutaneous coronary intervention in patients presenting with ST elevation myocardial infarction to a tertiary care centre in India. J Postgrad Med., 64:80-5.

10. Chugh Y, Chugh S, Chugh S (2020): Post-the SAFARI STEMI study: Is there still a debate on radial vs. femoral access in STEMI? Indian Heart J., 72:466-8.

11. Alrefai M, Murali D, Paul A *et al.* (2015): Cardiac tissue engineering and regeneration using cell-based therapy. Stem Cells Cloning. 8:81-101.

12. Tah S, Valderrama M, Afzal M *et al.* (2023): Heart failure with preserved ejection fraction: An evolving understanding. Cureus, 15:e46152.

13. Tsao C, Aday A, Almarzooq Z *et al.* (2022): Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. Circulation, 145:e153-e639.

14. Kosmala W, Marwick T (2020): Asymptomatic left ventricular diastolic dysfunction: Predicting progression to symptomatic heart failure. JACC Cardiovasc Imaging, 13:215-27.

15. Eisner D, Caldwell J, Trafford A *et al.* (2020): The control of diastolic calcium in the heart: basic mechanisms and functional implications. Circ Res., 126:395-412.

16. Cabral-Pacheco G, Garza-Veloz I, Castruita-De la Rosa C *et al.* (2020): The roles of matrix metalloproteinases and their inhibitors in human diseases. Int J Mol Sci., 21(24):9739.

17. Berezin A, Berezin A (2023): Biomarkers in heart failure: From research to clinical practice. Ann Lab Med., 43:225-36.

18. Jubaidi F, Zainalabidin S, Mariappan V *et al.* (2020): Mitochondrial dysfunction in diabetic cardiomyopathy: The possible therapeutic roles of phenolic acids. Int J Mol Sci., 21(17):6043.