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Review article

Myocardial Infarction: A Review of Laboratory Biomarkers

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Abstract

Myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide, necessitating rapid and accurate diagnostic and prognostic tools. Laboratory biomarkers have become indispensable in the management of acute coronary syndromes, offering a window into the dynamic pathophysiological processes of myocardial ischemia, injury, and repair. This review provides a comprehensive evaluation of the spectrum of cardiac biomarkers, from the established gold standard of high-sensitivity cardiac troponin (hs-cTn) to conventional enzymes like creatine kinase-MB (CK-MB) and myoglobin, as well as emerging novel markers. We discuss the clinical utility, diagnostic accuracy, prognostic value, and limitations of each biomarker within the context of current international guidelines. Additionally, this article explores the evolving landscape of biomarker research, including the potential of microRNAs, cardiac myosin-binding protein C (cMyC), and multimarker panels to use in an era of personalized medicine in cardiovascular care.

The future of MI biomarker utilization lies in integration. No single biomarker is likely to capture the full complexity of the disease. Multimarker panels that combine markers of myocyte necrosis (e.g., hs-cTn), hemodynamic stress (e.g., BNP/NT-proBNP), inflammation (e.g., GDF-15, hs-CRP), and fibrosis (e.g., galectin-3, sST2) are being developed to provide a comprehensive picture of a patient's risk profile and guide personalized treatment strategies

Keywords: high-sensitivity cardiac troponin, CK-MB, cMyC, BNP/NT-proBNP, galectin-3.

1. Introduction

Acute myocardial infarction remains a significant global health concern, necessitating prompt and accurate diagnosis for effective patient management and improved outcomes (1). The evolution of diagnostic approaches for myocardial infarction has significantly benefited from the development of cardiac circulating biomarkers, which have become integral to clinical evaluation alongside symptomatic presentation and electrocardiographic assessment (2,3). These biomarkers aid in detecting disease onset, progression, and therapeutic responses, providing insights into molecular mechanisms (4). Early and accurate identification of myocardial injury via these markers is crucial for timely intervention and appropriate treatment strategies, ultimately reducing morbidity and mortality associated with cardiovascular disease (5). Clinical biochemistry plays a fundamental role in this process, employing cardiac markers as essential tools to confirm myocardial damage (6,7). The clinical laboratory, through its rapid and accurate

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quantification of these cardiac biomarkers, is therefore crucial not only for diagnosing myocardial injury but also for assessing its size, establishing prognoses, and estimating reinfarction risk (8). Traditionally, the diagnosis of acute myocardial infarction relied on a triad of clinical symptoms, electrocardiogram changes, and serum markers (9). However, with advancements in medical laboratories, the incorporation of highly sensitive and specific biochemical markers, particularly cardiac troponins, has revolutionized diagnostic algorithms and redefined myocardial infarction (10). This review comprehensively examines the historical evolution and current landscape of various serum enzyme profiles and other biochemical biomarkers, discussing their diagnostic kinetics, clinical significance, and integration into multi-marker strategies for acute myocardial infarction (11). Initially, cardiac biomarker assessment was constrained by the poor cardiac specificity and unsuitable release kinetics of available tests for early diagnosis of irreversible myocardial injury (12).

2. The Gold Standard: High-Sensitivity Cardiac Troponin (hs-cTn)

Cardiac troponins I and T (cTnI and cTnT) are integral components of the sarcomere, regulating excitation-contraction coupling in cardiomyocytes (13). Following myocardial injury, these proteins are released into the circulation. Traditionally, this release was attributed solely to irreversible necrosis; however, it is now understood that reversible ischemia, apoptosis, and even physiological cardiomyocyte turnover can contribute to detectable levels, particularly with high-sensitivity assays. (13, 14)

High-sensitivity cardiac troponin (hs-cTn) assays have displaced conventional markers as the preferred biomarker for MI diagnosis. These assays can detect minute concentrations of troponin with high precision, allowing for the implementation of rapid rule-in and rule-out algorithms. The Fourth Universal Definition of Myocardial Infarction and major guidelines from the European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) endorse the use of hs-cTn, with the 99th percentile upper reference limit of a healthy population serving as the diagnostic threshold for myocardial injury (15-17).

The diagnostic performance of hs-cTnI and hs-cTnT, while both excellent, is not identical. The APACE study demonstrated that hs-cTnI may offer superior diagnostic accuracy for MI, whereas hs-cTnT provides better prognostic accuracy for long-term all-cause and cardiovascular mortality (16, 17). Furthermore, assay choice significantly impacts clinical decision-making; one study found that an hs-cTnI assay identified more low-risk patients for emergency department discharge compared to hs-cTnT, although the latter was associated with lower rates of adverse one-year outcomes. Despite these differences, both assays perform exceptionally well when applied within standardized triage algorithms, such as the ESC 0/1-hour protocol (18).

Emerging evidence suggests that the standard abnormal baseline cutoff of 52 ng/L may not be optimal. A 2025 study proposed increasing the cutoff to 82 ng/L for hs-cTnT and 122 ng/L for hs-cTnI to reduce false positives, unnecessary testing, and emergency department overcrowding, without compromising diagnostic sensitivity (19).

3. Conventional Cardiac Enzymes:

3.1. Creatine Kinase-MB (CK-MB):

Before the widespread adoption of troponin, CK-MB was the primary biomarker for MI. It is more cardiac-specific than total creatine kinase (CK) and rises 4 to 6 hours after symptom onset. However, CK-MB is now largely considered a secondary marker. Current guidelines indicate that CK-MB testing is not routinely indicated for the diagnosis of acute MI or reinfarction, as troponin is the preferred marker. CK-MB may still have a role in detecting early reinfarction or estimating infarct size in certain settings, but its utility is limited by its relatively short

window of detection (1–2 days) and lack of cardiac specificity (16, 20,21).

3.2. Myoglobin

Myoglobin is a small heme protein that appears in the blood very early after myocardial injury, often within 2–3 hours of symptom onset. Its rapid rise makes it a sensitive early marker for ruling out MI. However, myoglobin is highly non-specific, as it is also abundant in skeletal muscle and can be elevated in renal failure, trauma, and strenuous exercise. Consequently, its use has been largely supplanted by hs-cTn, which offers superior specificity and a longer diagnostic window (16, 17).

4. Natriuretic Peptides: BNP and NT-proBNP

B-type natriuretic peptide (BNP) and its N-terminal prohormone (NT-proBNP) are established biomarkers for the diagnosis and management of heart failure. In the context of MI, they serve as powerful prognostic indicators. Elevated levels of BNP and NT-proBNP reflect myocardial stretch and hemodynamic stress, which are common after large infarcts. Both markers are consistent, independent predictors of mortality and other adverse cardiac outcomes in patients with known coronary artery disease, including those who have suffered an MI. The measurement of natriuretic peptides is particularly valuable for risk stratification, helping to identify patients at high risk for subsequent heart failure or death (22, 23).

5. Emerging and Novel Biomarkers

The quest for improved diagnostic accuracy, particularly in the early "troponin-blind" period, and enhanced risk stratification has spurred research into numerous novel biomarkers.

5.1. Copeptin

Copeptin, the C-terminal portion of the vasopressin prohormone, is released during the acute phase of stress. It has been proposed as an adjunct to hs-cTn for the early rule-out of MI. Because copeptin levels rise very rapidly after symptom onset, a combination of a negative hs-cTn and a low copeptin level at presentation has shown a high negative predictive value for MI, potentially allowing for earlier discharge of low-risk patients (24).

5.2. Growth Differentiation Factor-15 (GDF-15)

GDF-15 is a stress-responsive cytokine that is upregulated in response to inflammation, oxidative stress, and mechanical stretch. It has emerged as a robust prognostic marker in cardiovascular disease. In post-MI patients, GDF-15 provides prognostic information beyond that of clinical factors and NT-proBNP, particularly in predicting death and the development of heart failure (25).

5.3. Heart-Type Fatty Acid-Binding Protein (H-FABP)

H-FABP is a small cytosolic protein abundant in cardiomyocytes. Due to its low molecular weight, it is released very early after myocardial injury, making it a sensitive marker for the very early stages of MI. Some research suggests it may be a superior biomarker for diagnosing MI within the first three hours of symptom onset. Elevated H-FABP levels are also associated with worse outcomes and increased long-term risk of death and recurrent MI (26).

5.4. MicroRNAs (miRNAs)

MicroRNAs are small, non-coding RNA molecules that regulate gene expression. Cardiac-enriched miRNAs, such as miR-1, miR-133a, miR-208, and miR-499, are rapidly released into the bloodstream following cardiomyocyte injury. Their high stability in blood and tissue-specific expression patterns make them promising candidates for early MI detection. For instance, circulating miR-499 levels can increase up to 300-fold in MI patients. The development of point-of-care biosensors for miRNA detection holds significant promise for rapid, decentralized MI diagnosis (27,28).

5.5. Other Novel Markers

Several other biomarkers are under investigation, each reflecting different aspects of MI pathophysiology. Galectin-3, a mediator of

inflammation and fibrosis, predicts adverse ventricular remodeling and heart failure post-MI. Soluble suppression of tumorigenicity-2 (sST2) is a marker of biomechanical stress and cardiac fibrosis, providing independent prognostic value for mortality in MI patients. Ischemia-modified albumin (IMA) is a marker of ischemia that rises within minutes of an ischemic event, potentially filling a gap where troponin is not yet elevated. Myeloperoxidase (MPO), an enzyme released by activated leukocytes, reflects plaque instability and has been proposed as a marker for identifying vulnerable plaques at risk of rupture. **Cardiac myosin-binding protein C (cMyC)** is another emerging biomarker with rapid release kinetics, offering potential for even earlier diagnosis than hs-cTn (29).

6. Future Directions: Personalized and Multimarker Strategies

The future of MI biomarker utilization lies in integration. No single biomarker is likely to capture the full complexity of the disease. Multimarker panels that combine markers of myocyte necrosis (e.g., hs-cTn), hemodynamic stress (e.g., BNP/NT-proBNP), inflammation (e.g., GDF-15, hs-CRP), and fibrosis (e.g., galectin-3, sST2) are being developed to provide a comprehensive picture of a patient's risk profile and guide personalized treatment strategies (30).

Artificial intelligence (AI) and machine learning models that integrate multiple biomarker concentrations with clinical variables, ECG findings, and imaging results are poised to further refine diagnostic and prognostic accuracy. Additionally, the continued development of point-of-care technologies, including paper-based biosensors for miRNAs and other novel markers, promises to bring advanced diagnostics directly to the patient's bedside, enabling faster clinical decision-making (31).

7. Conclusion

Cardiac biomarkers are integral to the modern management of myocardial infarction. High-sensitivity cardiac troponin remains the undisputed gold standard for diagnosis, while natriuretic peptides provide critical prognostic information. Conventional enzymes like CK-MB and myoglobin have a diminishing role, largely relegated to specific niche applications. The landscape is rapidly evolving with the emergence of novel markers that target distinct pathophysiological pathways, from early ischemia (IMA, H-FABP) to long-term remodeling (GDF-15, galectin-3, sST2). The integration of these diverse markers into multimarker panels, guided by AI-driven algorithms, holds the promise of delivering truly personalized care and improving outcomes for patients with this devastating disease.

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