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Emerging Biomarkers in Acute Coronary Syndrome

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Abstract: Acute coronary syndrome (ACS) remains one of the leading causes of morbidity and mortality worldwide despite significant advances in cardiovascular diagnosis and treatment. Early recognition of myocardial ischemia and rapid risk stratification are essential for improving clinical outcomes. Cardiac troponins remain the gold standard biomarkers for diagnosing myocardial injury; however, they have limitations in detecting very early ischemia and predicting long-term prognosis. Recent research has identified several novel biomarkers reflecting myocardial injury, inflammation, plaque instability, thrombosis, endothelial dysfunction, oxidative stress, and cardiac remodeling. Biomarkers such as copeptin, heart-type fatty acid-binding protein (H-FABP), growth differentiation factor-15 (GDF-15), soluble suppression of tumorigenicity-2 (sST2), galectin-3, microRNAs, and circulating extracellular vesicles have shown promising diagnostic and prognostic value. Contemporary strategies increasingly combine multiple biomarkers with clinical assessment, electrocardiography, and cardiac imaging to improve early diagnosis and personalized management. This review summarizes current evidence regarding established and emerging biomarkers in acute coronary syndrome and discusses their potential clinical applications.

Keywords: Acute coronary syndrome; Cardiac biomarkers; Troponin; Copeptin; Heart-type fatty acid-binding protein; Precision cardiology.

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INTRODUCTION

Acute coronary syndrome (ACS) encompasses a spectrum of clinical conditions resulting from sudden reduction in coronary blood flow caused by plaque rupture, plaque erosion, or coronary thrombosis. The syndrome includes ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina. Despite substantial improvements in reperfusion therapy and secondary prevention, ACS remains a major cause of cardiovascular mortality and long-term disability worldwide [1].

Rapid diagnosis is essential because early reperfusion therapy significantly reduces myocardial damage and improves survival. Clinical assessment, electrocardiography (ECG), and measurement of cardiac biomarkers constitute the cornerstone of ACS diagnosis. Among available biomarkers, cardiac troponins have become the international standard because of their excellent sensitivity and specificity for myocardial injury. Nevertheless, troponin concentrations may remain normal during the initial hours following symptom onset and provide limited information regarding plaque instability, inflammation, or future cardiovascular risk.

The complex pathophysiology of ACS involves multiple biological processes including endothelial dysfunction, inflammation, oxidative stress, thrombosis, myocardial necrosis, ventricular remodeling, and neurohormonal activation. Consequently, increasing attention has focused on identifying novel biomarkers that reflect these diverse pathological mechanisms and complement conventional troponin testing.

Recent advances in molecular biology, proteomics, metabolomics, and genomics have identified several promising biomarkers with potential applications in early diagnosis, prognosis, therapeutic monitoring, and precision cardiovascular medicine. These emerging biomarkers may improve identification of high-risk patients and facilitate individualized treatment strategies.

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Pathophysiology of Acute Coronary Syndrome and Biomarker Release

Acute coronary syndrome usually develops following rupture or erosion of an atherosclerotic plaque within a coronary artery. Exposure of thrombogenic material activates platelets and the coagulation cascade, resulting in thrombus formation and partial or complete coronary artery occlusion. Reduced myocardial perfusion produces ischemia followed by progressive myocardial necrosis if blood flow is not rapidly restored [2].

Cellular injury triggers release of intracellular proteins into the circulation. Cardiac troponins I and T are structural proteins unique to cardiac myocytes and are released following irreversible myocardial injury. Although highly specific, measurable elevation generally occurs several hours after symptom onset.

In addition to myocardial necrosis, ACS activates inflammatory pathways, endothelial dysfunction, neurohormonal responses, oxidative stress, extracellular matrix remodeling, and myocardial fibrosis. Each of these biological processes produces specific circulating biomarkers that may provide complementary information beyond conventional cardiac troponins.

Understanding the temporal sequence of biomarker release has encouraged development of multimarker strategies combining markers of early ischemia, myocardial necrosis, inflammation, and ventricular remodeling to improve diagnostic accuracy and risk prediction.

Table 1. Biological Processes and Associated Biomarkers in Acute Coronary Syndrome

Pathophysiological Process	Representative Biomarkers
Myocardial necrosis	Cardiac troponin I, Cardiac troponin T
Early myocardial ischemia	Heart-type fatty acid-binding protein (H-FABP), Copeptin
Inflammation	High-sensitivity C-reactive protein, Interleukin-6
Plaque instability	Matrix metalloproteinases, Myeloperoxidase
Cardiac remodeling	sST2, Galectin-3
Oxidative stress	Growth differentiation factor-15 (GDF-15)

Established and Emerging Cardiac Biomarkers

High-sensitivity cardiac troponins remain the reference standard for diagnosing myocardial infarction and have significantly improved early detection of myocardial injury. High-sensitivity assays detect very small concentrations of circulating troponin, enabling earlier diagnosis while facilitating rapid rule-in and rule-out protocols in emergency departments. Nevertheless, elevated troponin concentrations may also occur in myocarditis, heart failure, pulmonary embolism, chronic kidney disease, and other non-ischemic conditions, emphasizing the importance of clinical interpretation.

Copeptin has emerged as one of the most extensively investigated biomarkers for early diagnosis of ACS. Released rapidly following endogenous stress activation, copeptin increases within minutes after symptom onset and complements high-sensitivity troponin during the earliest stages of myocardial infarction. Simultaneous measurement of copeptin and troponin has demonstrated improved sensitivity for excluding acute myocardial infarction shortly after presentation [3].

Heart-type fatty acid-binding protein (H-FABP) is a small cytoplasmic protein rapidly released following myocardial injury, frequently becoming detectable earlier than conventional troponin. Although its specificity is lower than cardiac troponins, H-FABP may improve early diagnosis when incorporated into multimarker strategies.

Growth differentiation factor-15 (GDF-15) reflects oxidative stress, inflammation, and cellular injury. Elevated concentrations are associated with increased mortality, recurrent myocardial infarction, and heart failure following ACS, making GDF-15 a valuable prognostic biomarker. Similarly, soluble suppression of tumorigenicity-2 (sST2) and galectin-3 provide information regarding myocardial fibrosis, ventricular remodeling, and long-term cardiovascular outcomes.

MicroRNAs represent an emerging class of molecular biomarkers. Specific circulating microRNAs released from injured cardiomyocytes demonstrate considerable diagnostic and prognostic potential because of their tissue specificity, biological stability, and involvement in cardiovascular gene regulation. Although routine clinical implementation remains limited, continued advances in molecular diagnostics may facilitate future integration into cardiovascular practice.

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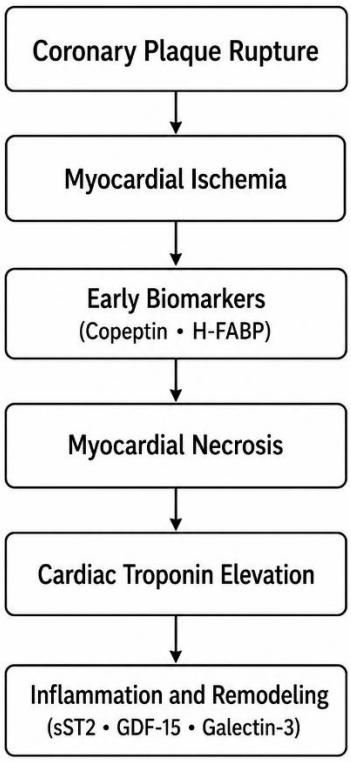

Figure 1. Biomarker Release Following Acute Coronary Syndrome

Clinical Applications, Multimarker Strategies, and Emerging Diagnostic Technologies

The increasing understanding of acute coronary syndrome pathophysiology has encouraged the development of multimarker strategies that integrate biomarkers reflecting different stages of myocardial injury. Rather than relying solely on cardiac troponin concentrations, contemporary clinical practice increasingly combines markers of early ischemia, myocardial necrosis, inflammation, ventricular remodeling, and thrombosis to improve diagnostic accuracy and risk stratification. This integrated approach is particularly valuable during the initial hours following symptom onset when conventional biomarkers may still be within the normal range [4].

High-sensitivity cardiac troponin remains the cornerstone of diagnostic algorithms for patients presenting with suspected acute coronary syndrome. International guidelines recommend serial high-sensitivity troponin measurements together with clinical assessment and electrocardiographic findings to rapidly confirm or exclude myocardial infarction. Addition of early biomarkers such as copeptin has demonstrated improved diagnostic sensitivity during the first hours after symptom onset and may facilitate earlier discharge of low-risk patients from emergency departments.

Risk stratification represents another important application of emerging biomarkers. While cardiac troponin primarily reflects myocardial necrosis, biomarkers including GDF-15, soluble ST2, galectin-3, and high-sensitivity C-reactive protein provide complementary information regarding inflammation, myocardial remodeling, oxidative stress, and long-term cardiovascular risk. Elevated concentrations of these biomarkers have consistently been associated with increased mortality, recurrent myocardial infarction, heart failure, and adverse cardiovascular events following ACS.

Several studies have demonstrated that combining biomarkers with established clinical risk scores such as the Global Registry of Acute Coronary Events (GRACE) score or the Thrombolysis in Myocardial Infarction (TIMI) score improves prognostic accuracy. This integrated strategy enables clinicians to identify patients who may benefit from early invasive coronary angiography, intensive antithrombotic therapy, prolonged hospitalization, or closer post-discharge follow-up.

Biomarkers are also increasingly used to monitor therapeutic response following acute coronary syndrome. Serial measurements of high-sensitivity troponin help estimate infarct size and assess ongoing myocardial injury, whereas inflammatory and remodeling biomarkers may provide information regarding ventricular recovery and future heart failure risk. Such information supports individualized secondary prevention strategies including optimization of lipid-lowering therapy, antiplatelet treatment, and cardiac rehabilitation.

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Table 2. Clinical Applications of Emerging Biomarkers in Acute Coronary Syndrome

Biomarker	Principal Clinical Application	Major Clinical Value
High-sensitivity Troponin	Diagnosis of myocardial infarction	Highest diagnostic accuracy
Copeptin	Early rule-out of myocardial infarction	Improved early diagnosis
H-FABP	Detection of early myocardial injury	Early biomarker release
GDF-15	Prognostic assessment	Predicts mortality and heart failure
sST2	Ventricular remodeling	Long-term cardiovascular risk
Galectin-3	Cardiac fibrosis	Prognostic evaluation
MicroRNAs	Experimental diagnosis and prognosis	Precision cardiovascular medicine

Molecular diagnostics continue to expand the field of cardiovascular biomarkers. Circulating microRNAs regulate gene expression involved in inflammation, apoptosis, angiogenesis, and myocardial repair. Their remarkable biological stability and tissue specificity make them attractive candidates for future clinical application. Likewise, extracellular vesicles released from activated platelets, endothelial cells, and cardiomyocytes contain proteins, messenger RNA, and microRNAs that may provide novel insight into plaque instability and myocardial injury.

Proteomic and metabolomic technologies have further accelerated biomarker discovery by identifying complex molecular signatures associated with acute coronary syndrome. Rather than relying upon individual biomarkers, future diagnostic platforms may analyze multiple proteins and metabolites simultaneously to generate personalized cardiovascular risk profiles.

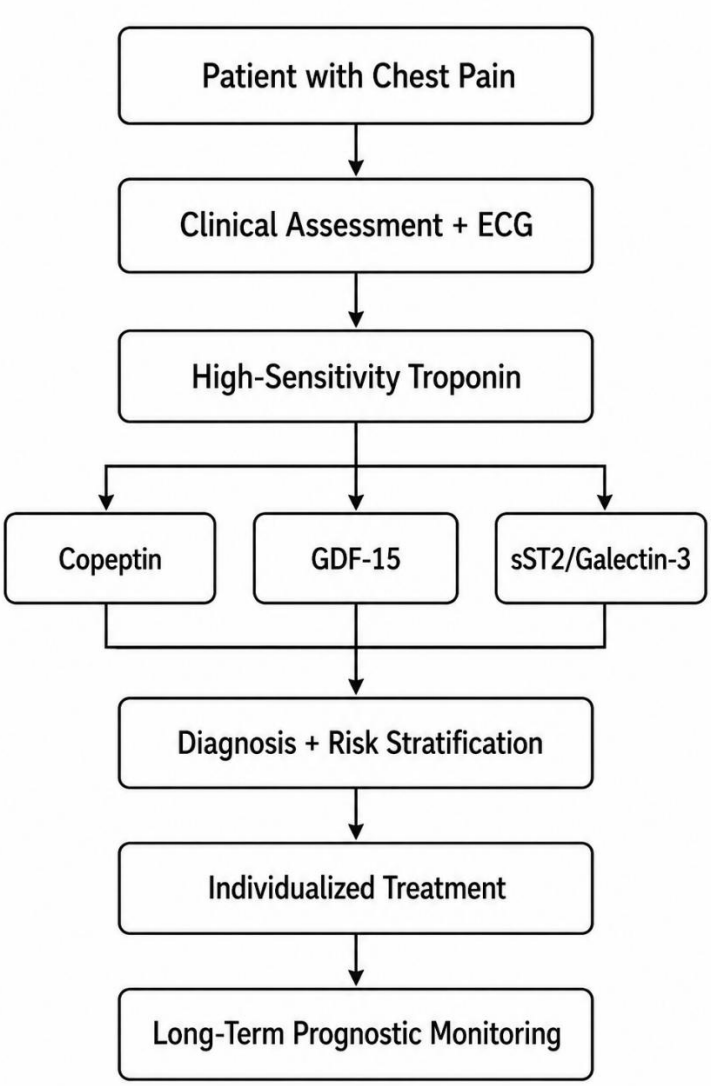

Figure 2. Multimarker Strategy in Acute Coronary Syndrome

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Table 3. Emerging Technologies Supporting Biomarker-Based Diagnosis

Innovation	Current Status	Potential Clinical Benefit
High-sensitivity troponin assays	Routine clinical practice	Earlier myocardial infarction diagnosis
Point-of-care biomarker testing	Increasing implementation	Rapid emergency department assessment
Multiplex biomarker panels	Clinical investigation	Simultaneous measurement of multiple biomarkers
MicroRNA profiling	Experimental	Precision cardiovascular diagnosis
Proteomic and metabolomic analysis	Ongoing research	Personalized cardiovascular risk prediction
Artificial intelligence-assisted biomarker interpretation	Early clinical application	Improved diagnostic accuracy and risk prediction

Artificial intelligence is expected to play an increasingly important role by integrating biomarker profiles with clinical characteristics, electrocardiographic findings, imaging data, and electronic health records. Machine learning algorithms may improve early diagnosis, predict adverse cardiovascular events, and support personalized therapeutic decision-making more accurately than conventional risk assessment models alone.

DISCUSSION

The diagnosis and management of acute coronary syndrome have undergone remarkable transformation with the introduction of high-sensitivity cardiac biomarkers and advances in molecular medicine. Although high-sensitivity cardiac troponins remain the cornerstone of myocardial infarction diagnosis, growing evidence indicates that myocardial ischemia involves multiple biological processes extending beyond cardiomyocyte necrosis. Consequently, reliance on a single biomarker may not fully reflect disease complexity or accurately predict long-term clinical outcomes. Emerging biomarkers therefore provide important complementary information regarding inflammation, plaque instability, endothelial dysfunction, thrombosis, oxidative stress, and ventricular remodeling [1].

One of the most important developments has been the implementation of high-sensitivity cardiac troponin assays, which enable detection of myocardial injury at much lower concentrations than previous assays. These tests have significantly shortened diagnostic pathways and facilitated rapid rule-in and rule-out algorithms in emergency departments. Nevertheless, elevated troponin concentrations are not exclusive to acute coronary syndrome and may occur in myocarditis, heart failure, pulmonary embolism, chronic kidney disease, and sepsis. Careful interpretation within the appropriate clinical context therefore remains essential.

Biomarkers released during the earliest phases of myocardial ischemia, particularly copeptin and heart-type fatty acid-binding protein, have demonstrated considerable value when combined with high-sensitivity troponin. Several studies have shown that multimarker strategies improve early diagnostic sensitivity, especially during the first hours after symptom onset when troponin concentrations may still be below diagnostic thresholds. Such approaches may reduce unnecessary hospital admissions while enabling earlier treatment for patients with acute myocardial infarction [3].

Beyond diagnosis, emerging biomarkers provide valuable prognostic information. Growth differentiation factor-15, soluble ST2, galectin-3, and inflammatory biomarkers such as high-sensitivity C-reactive protein reflect biological pathways associated with ventricular remodeling, fibrosis, oxidative stress, and systemic inflammation. Elevated concentrations consistently predict recurrent myocardial infarction, heart failure, and cardiovascular mortality, thereby assisting clinicians in identifying patients requiring intensive monitoring and aggressive secondary prevention.

Recent advances in molecular biology have expanded the search for highly specific biomarkers. Circulating microRNAs, extracellular vesicles, metabolomic signatures, and proteomic profiles offer promising opportunities for precision cardiology because they reflect complex cellular responses to myocardial injury. Although these technologies remain primarily investigational, ongoing clinical research suggests they may substantially improve individualized diagnosis and therapeutic decision-making in the future.

Artificial intelligence is expected to further enhance biomarker interpretation by integrating laboratory data with clinical history, electrocardiography, imaging findings, and electronic health records. Machine learning algorithms have demonstrated encouraging accuracy in predicting acute myocardial infarction, identifying high-risk patients, and estimating long-term cardiovascular outcomes. Such integrated diagnostic models may eventually outperform conventional single-biomarker approaches.

Despite these encouraging developments, several challenges remain before widespread clinical implementation of novel biomarkers. Many promising biomarkers require further external validation, standardized laboratory methods, cost-

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effectiveness evaluation, and demonstration of clinical benefit across diverse patient populations. Future studies should determine how these biomarkers can be optimally integrated into existing diagnostic pathways without increasing unnecessary testing or healthcare costs.

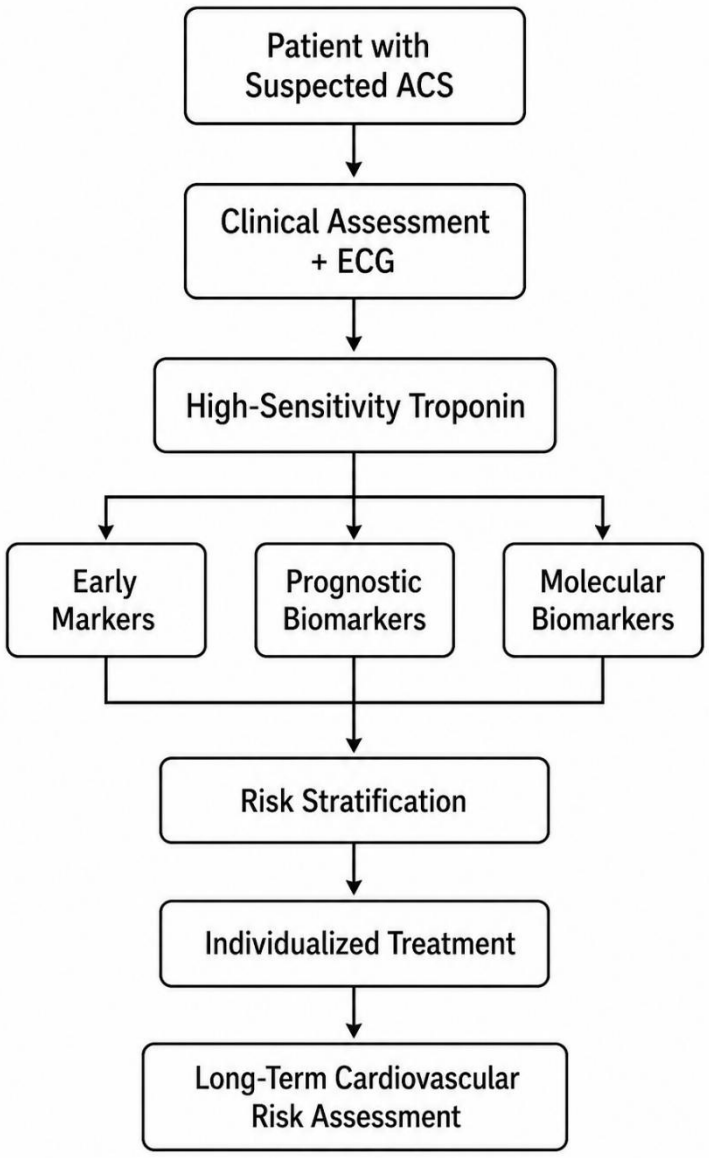

Figure 3. Clinical Integration of Emerging Biomarkers in Acute Coronary Syndrome

Future Perspectives

Future cardiovascular diagnostics are expected to move from single-marker assessment toward comprehensive multimarker platforms integrating proteomics, metabolomics, transcriptomics, and genomic profiling. These technologies may enable clinicians to characterize individual biological pathways involved in plaque instability, myocardial injury, inflammation, and ventricular remodeling.

Artificial intelligence-assisted interpretation of biomarker profiles is likely to improve diagnostic accuracy by combining laboratory findings with electrocardiography, cardiac imaging, demographic characteristics, and electronic health records. Point-of-care multiplex biomarker assays capable of simultaneously measuring several biomarkers within minutes may further accelerate emergency department decision-making.

Continued research into circulating microRNAs, extracellular vesicles, inflammatory mediators, and metabolomic signatures may provide novel diagnostic and therapeutic targets. Precision medicine approaches based on individualized molecular profiles are expected to optimize risk stratification, therapeutic selection, and secondary prevention following acute coronary syndrome.

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CONCLUSION

Acute coronary syndrome remains a leading cause of cardiovascular morbidity and mortality worldwide, making early diagnosis and accurate risk stratification essential for improving patient outcomes. High-sensitivity cardiac troponins continue to represent the reference standard for diagnosing myocardial infarction, while emerging biomarkers provide valuable complementary information regarding inflammation, plaque instability, myocardial remodeling, and long-term prognosis.

Multimarker strategies combining conventional biomarkers with novel molecular markers have demonstrated improved diagnostic sensitivity and prognostic accuracy compared with single-marker approaches. Advances in molecular diagnostics, proteomics, metabolomics, artificial intelligence, and precision cardiology are expected to further enhance individualized management of patients with acute coronary syndrome.

Future clinical practice will likely integrate these innovative biomarkers into comprehensive diagnostic algorithms, supporting earlier intervention, personalized treatment selection, and improved long-term cardiovascular outcomes.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this review.

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Author Contributions

All authors contributed to the literature review, manuscript preparation, critical revision, and approval of the final version.

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