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Evolving Acute Coronary Syndrome (ACS) Diagnosis: Role of Emerging Biomarkers

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ABSTRACT

The future of Acute Coronary Syndrome (ACS) diagnosis lies in combining traditional and emerging biomarkers to optimize patient outcomes and improve efficiency in emergency settings. To minimize the negative consequences of this potentially fatal illness, has to be identified and treated quickly in the Emergency Department (ED). Although cardiac troponins, myoglobin, CKMB, and electrocardiograms (ECGs) constitute the golden standard for diagnosing ACS, their shortcomings in early identification underscore the need for further biomarkers. Copeptin, microRNAs (miRNAs), inflammatory indicators, Heart-type Fatty Acid-Binding Peptin (H-FABP), and Glycogen Phosphorylase Isoenzyme BB (GPBB) are among the new biomarkers examined in this article. These biomarkers have the potential to enhance early ACS identification by enhancing conventional diagnostic techniques. Extensive validation through large-scale research is necessary to evaluate the cost-effectiveness and reliability of integrating these new biomarkers into clinical practice.

KEYWORDS

• Emerging Biomarkers • Acute coronary syndrome • Copeptin • miRNAs • Inflammatory Markers

INTRODUCTION

Unstable angina, non-ST-segment Elevation Myocardial Infarction (NSTEMI), and ST-segment Elevation Myocardial Infarction (STEMI) are among the diseases linked to myocardial ischemia that are together referred

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to as acute coronary syndrome (ACS). It is a major global source of morbidity and mortality, and to avoid serious consequences and enhance patient outcomes, emergency departments (EDs) must recognize and treat it as quickly as possible.[1] Clinical examination, Electrocardiogram (ECG), and Cardiac biomarker analysis are necessary for the diagnosis of ACS. Among these, cardiac troponins (cTnI and cTnT), myoglobin, and CKMBs are commonly acknowledged as unmistakable indicators of myocardial damage. But in the few hours after symptom onset, their sensitivity is low, which causes delays in diagnosis and therapy.[2,3] Early ACS detection is further complicated by the possibility that ECG abnormalities are not always evident or definitive.[4]

In light of these drawbacks, scientists are looking for other biomarkers to increase the precision and speed of ACS detection. Heart-type fatty acid - binding protein (H-FABP), copeptin, microRNAs miR-208a and miR-499, inflammatory markers, and glycogen phosphorylase isoenzyme BB (GPBB) are examples of emerging biomarkers that have demonstrated promise in improving risk stratification and identification.[5] These indicators shed light on a number of physiological and pathological processes, including inflammation, stress response, and metabolic alterations, that are linked to myocardial damage. The management of ACS in EDs may be greatly enhanced by the combination of these new biomarkers with traditional diagnostic techniques. The present state of ACS diagnostics is examined in this review, with a focus on the contribution of new biomarkers to improving early detection.

Current Diagnostic Modalities

ECGs, Cardiac troponin testing, and clinical examinations have historically been used to diagnose ACS. Cardiac troponins are precise indicators of myocardial damage, such as troponin I (cTnI) and troponin T (cTnT). They might not be noticeable right away once symptoms appear, though, which could cause a delay in diagnosis and treatment 6. To circumvent this constraint, high-sensitivity troponin tests have been created; nevertheless, they are still unable to detect myocardial damage in its early stages. This emphasizes how important it is to use new biomarkers in order to enhance early diagnosis.

Emerging Biomarkers in ACS Diagnosis

a. **Copeptin**: Acute stress events, such as myocardial infarction, cause the fast release of copeptin, a peptide that is produced from the precursor of vasopressin. Following cardiac injury, its levels rapidly increase, enhancing the diagnostic accuracy of troponin assays. According to studies done M Kankra, Copeptin and troponin tests together enhance early ACS identification, facilitating more effective ED patient triage.[7,8]

b. **MicroRNAs (miRNAs)**: Small, non-coding RNA molecules called miRNAs have been identified as possible biomarkers for ACS and other disorders. They are involved in the control of genes. After myocardial damage, some miRNAs, such miR-208a and miR-499, are released into the circulation and show high sensitivity and specificity that are on pair with conventional biomarkers. The quick circulation of miRNAs in blood makes potential for early ACS diagnosis, although more study is needed to confirm their clinical use.[9]

c. **Inflammatory Biomarkers**: An important part of the pathogenesis of ACS and atherosclerosis is inflammation. The inflammatory biomarker known as high-sensitivity C-reactive protein (hs-CRP) has been thoroughly investigated for its potential use in diagnosis and prognosis. A higher risk of subsequent cardiovascular events is correlated with elevated (hs-CRP) levels. Early risk assessment may be enhanced by including hs-CRP in the ACS diagnostic procedure, especially for individuals with non-specific symptoms.[10,11]

d. **Heart-Type Fatty Acid-Binding Protein (H-FABP)**: Following cardiac damage, the tiny cytoplasmic protein H-FABP, which is present in cardiomyocytes, is released into the circulation. It is a useful biomarker for early ACS identification since it shows an earlier release profile than troponins. H-FABP can improve diagnosis accuracy in emergency departments by aiding in the differentiation of cardiac from noncardiac causes of chest discomfort.[12]

e. **Glycogen Phosphorylase Isoenzyme BB (GPBB)**: An enzyme called GPBB is involved in the metabolism of glycogen in cardiac cells. It enters the bloodstream soon after ischemic episodes, before troponin levels rise. According to research, GPBB may be an early biomarker for myocardial damage, which would speed up the identification of ACS.[13]

Integration of Novel Biomarkers into Clinical Practice: Test standardization, cost-effectiveness, and clinical application must be carefully considered when integrating new biomarkers into ED procedures. The early diagnosis of ACS may be greatly improved by combining established biomarkers with newer ones, such as copeptin, miRNAs, inflammatory markers, H-FABP, and GPBB.[14] Before these 4 biomarkers are widely used, however, more prospective research is needed to validate their clinical usefulness and effect on patient outcomes. *Table 1 and 2* shows the biomarkers' functions, advantages, time of release in blood, and clinical uses.

Table 1: Emerging biomarkers, Functions, and Advantages

S. No.	Biomarkers	Functions	Advantages
1.	Copeptin	Released during acute stress, complements troponin testing	Enhances early ACS diagnosis, rapid evaluation post-myocardial infarction.[15]
2.	MicroRNAs	Regulate gene expression, released upon myocardial injury	High sensitivity and specificity for cardiac injury detection.[16]
3.	Inflammatory biomarkers (hs-CRP)	Indicates systemic inflammation linked to cardiovascular events. Values above 2.0 mg/L may increase the risk of heart attacks or risk of a repeat heart attack.	Helps access ACS risk, particularly in nonspecific cases.[17]
4.	Heart-type fatty acid binding protein (H-FABP)	Cytoplasmic protein released after myocardial injury	An early release profile compared to troponins aids in cardiac vs noncardiac differentiation.[18]
5.	Glycogen phosphorylase Isoenzyme BB (GPBB)	Enzyme involved in myocardial glycogen metabolism	Released early post-ischemic event, potential early biomarker.[19]

Table 2: Time of appearance and peak of the biomarkers in blood after the onset of Myocardial Infarction (MI) or Acute Coronary Syndrome (ACS)

S.No.	Biomarkers	Time of Appearance in Blood	Peak Time	Clinical Use
1.	Copeptin	Immediately (within minutes)	1-2 hours	An identical marker of MI is useful in early rule-out when combined with troponin.[20]
2.	MicroRNAs (e.g., miR-1, miR-133a, etc.)	1-3 hours	3-6 hours	Emerging early diagnostic markers of myocardial injury.[21]
3.	hs-CRP (High-sensitivity C-Reactive Protein)	6-12 hours	24-48 hours	Not specific to MI reflects inflammation useful for risk stratification levels of <1.0 mg/L considered low risk, 1.0-3.0 mg/L average risk, and >3.0 mg/L high risk.[22]
4.	H-FABP (Heart-type Fatty Acid Binding Protein)	3 hours	8 hours	An early marker of myocardial injury rises before troponin.[23]
5.	Glycogen phosphorylase Isoenzyme BB (GPBB)	4 hours	12 hours	Early marker released due to ischemia stress especially useful <6 hours.[24]

Future Directions: It is anticipated that cutting-edge research, technological integration, and the creation of more accurate diagnostic instruments will shape the future of ACS diagnosis. There are the following certain areas that need more research:

Validation of Novel Biomarkers: To confirm the diagnostic precision, specificity, and economic possibility of new biomarkers such as copeptin miRNAs, H-FABP, and GPBB, extensive clinical studies are necessary.[25]

Integration of Multi-Biomarker Panels: To enhance early ACS diagnosis and lower false positives, future studies should concentrate on improving multi-biomarker panels by integrating existing and novel bio-markers.[26]

Artificial Intelligence and Machine Learning: By evaluating intricate bio-marker profiles and ECG data, Artificial Intelligence(AI)-driven diagnostic algorithms and machine learning models can improve ACS risk classification and help physicians make data-driven decisions.[27]

Point-of-Care Testing (POCT) Advancements: ACS diagnosis will be transformed by the creation of quick, portable, and affordable PCOT devices that can identify several biomarkers at once, especially in environments with limited resources.[28]

P**ersonalized Medicine Approaches –** Future research should look into how biomarker profiles might be utilized to customize treatment plans, enhancing therapeutic results and patient-specific care.[25]

Longitudinal Studies on Biomarker Efficacy – It is necessary to carry out prospective cohort studies to ascertain how these new biomarkers function over time and how they affect long-term patient outcomes.

It is necessary to carry out prospective cohort studies to ascertain how these new biomarkers function over time and how they affect long-term patient outcomes.By concentrating on these aspects, ACS diagnosis can advance towards more accurate, prompt, and customized management plans, which will eventually enhance patient outcome and healthcare effectiveness.

CONCLUSION

Optimizing patient outcomes in emergency departments requires prompt and precise ACS diagnosis. Emerging biomarkers have encouraging opportunities for enhancing risk assessment and early detection, even though conventional diagnostic methods are still useful. Hence, more research is needed in emerging bio markers validation and successful application in clinical practice to reduce morbidity and mortality related to Acute coronary syndrome.

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