THE SIGNIFICANCE OF EARLY DIAGNOSTIC BIOMARKERS IN ISCHEMIC HEART DISEASE

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Abstract: Ischemic heart disease (IHD) is one of the major cardiovascular disorders and remains an important cause of morbidity and mortality worldwide. Early recognition of myocardial ischemia and myocardial injury is essential for initiating timely treatment and reducing the risk of irreversible cardiac damage. However, the clinical presentation of IHD may be variable, and conventional diagnostic methods may have limitations during the earliest stages of myocardial injury. Therefore, circulating biomarkers have become an important component of the early diagnostic assessment of patients with suspected ischemic heart disease. Among currently available biomarkers, high-sensitivity cardiac troponin I and cardiac troponin T are considered the principal biomarkers for detecting myocardial injury because of their high analytical sensitivity and ability to identify small changes in circulating troponin concentrations. Other biomarkers, including creatine kinase-MB, myoglobin, copeptin, natriuretic peptides, inflammatory mediators, and markers of oxidative stress, may provide complementary diagnostic and prognostic information. The integration of biomarker measurements with clinical assessment, electrocardiography, and cardiac imaging can improve diagnostic accuracy and support early risk stratification. Serial measurements of high-sensitivity cardiac troponin are particularly important because dynamic changes in its concentration may help distinguish acute myocardial injury from chronic elevation. Nevertheless, biomarker interpretation can be challenging because increased cardiac troponin concentrations may occur in various cardiovascular and systemic conditions without acute myocardial infarction. This review summarizes the biological basis, diagnostic

significance, advantages, and limitations of established and emerging biomarkers in ischemic heart disease, with particular emphasis on their role in early detection and clinical decision-making. A better understanding of these biomarkers may contribute to more accurate and timely recognition of myocardial injury and improve strategies for the early assessment of patients with suspected ischemic heart disease.

Keywords: Ischemic heart disease; cardiac biomarkers; high-sensitivity cardiac troponin; myocardial injury; acute coronary syndrome; early diagnosis; cardiovascular disease; risk stratification.

Аннотация: Ишемическая болезнь сердца (ИБС) остается одной из ведущих причин сердечно-сосудистой заболеваемости и смертности. Раннее выявление ишемии и повреждения миокарда имеет важное значение для своевременного лечения и снижения риска осложнений. В настоящее время высокочувствительные сердечные тропонины I и T являются основными биомаркерами повреждения миокарда благодаря высокой аналитической чувствительности. Дополнительные маркеры, включая КФК-МВ, миоглобин, копептин, натрийуретические пептиды, воспалительные и оксидативные показатели, могут предоставлять диагностическую и прогностическую информацию. Последовательное измерение высокочувствительного тропонина позволяет оценивать динамику его концентрации и отличать острое повреждение миокарда от хронического повышения. Однако повышение тропонина возможно и при других сердечно-сосудистых и системных заболеваниях без острого инфаркта миокарда. В данном обзоре рассматриваются современные и перспективные биомаркеры ИБС, их диагностическое значение, преимущества и ограничения, а также роль в раннем выявлении повреждения миокарда и стратификации риска.

Ключевые слова: ишемическая болезнь сердца; сердечные биомаркеры; высокочувствительный сердечный тропонин; повреждение

миокарда; острый коронарный синдром; ранняя диагностика; стратификация риска.

Annotatsiya: Yurak ishemik kasalligi (YIK) yurak-qon tomir kasalliklari va o'limning asosiy sabablaridan biridir. Miokard ishemiyasi va shikastlanishini erta aniqlash o'z vaqtida davolash va asoratlar xavfini kamaytirish uchun muhimdir. Hozirgi vaqtda yuqori sezgirlikdagi yurak troponinlari I va T miokard shikastlanishini aniqlashda asosiy biomarkerlar hisoblanadi. Kreatinkinaza-MB, mioglobin, kopeptin, natriyuretik peptidlar, yallig'lanish va oksidlovchi stress markerlari esa qo'shimcha diagnostik va prognostik ma'lumot berishi mumkin. Troponinni ketma-ket o'lchash uning dinamikasini baholash va o'tkir miokard shikastlanishini surunkali troponin oshishidan farqlashga yordam beradi. Biroq troponin darajasining oshishi o'tkir miokard infarktisiz kechuvchi boshqa yurak-qon tomir va tizimli kasalliklarda ham kuzatilishi mumkin. Ushbu sharhda YIKda qo'llaniladigan zamonaviy va istiqbolli biomarkerlarning diagnostik ahamiyati, afzalliklari va cheklovlari hamda ularning miokard shikastlanishini erta aniqlash va xavfni stratifikatsiya qilishdagi o'rni ko'rib chiqiladi.

Kalit so'zlar: yurak ishemik kasalligi; yurak biomarkerlari; yuqori sezgirlikdagi yurak troponini; miokard shikastlanishi; o'tkir koronar sindrom; erta diagnostika; xavfni stratifikatsiya qilish.

Introduction: Serial biomarker measurements are often more informative than a single measurement because biomarker concentrations change over time following myocardial injury. The development of high-sensitivity cardiac troponin assays has improved the detection of small amounts of myocardial injury and enabled earlier diagnosis using rapid rule-in and rule-out algorithms for suspected acute coronary syndrome [2,3].Importantly, myocardial injury and myocardial infarction are not synonymous. Elevated cardiac troponin indicates myocardial injury, whereas myocardial infarction requires evidence of acute injury together with

clinical evidence of myocardial ischemia. Troponin elevation may also occur in heart failure, myocarditis, pulmonary embolism, renal dysfunction, severe hypertension, tachyarrhythmias, and other systemic conditions [1,3].Different biomarkers reflect distinct biological processes. CK-MB and myoglobin indicate tissue injury but have limitations in specificity and timing. Natriuretic peptides reflect myocardial wall stress, while inflammatory biomarkers indicate inflammatory activity. Copeptin reflects systemic stress and may complement troponin during the early phase of myocardial injury [4]. Novel markers, including cardiac myosin-binding protein C, are also being investigated, although their routine clinical role remains under evaluation [5].

Therefore, biomarker results should be interpreted according to their biological characteristics and temporal changes and integrated with symptoms, electrocardiography, and other evidence of myocardial ischemia to improve diagnostic accuracy.

Disease

The identification of circulating biomarkers has substantially improved the diagnostic assessment of patients with suspected ischemic heart disease. Biomarkers can provide objective evidence of myocardial injury and may become detectable before some clinical or structural manifestations are fully established. Among the available biomarkers, cardiac troponins have the greatest diagnostic importance, while other markers such as creatine kinase-MB and myoglobin have historically contributed to the evaluation of myocardial injury. Their diagnostic characteristics, however, differ considerably in terms of cardiac specificity, sensitivity, release kinetics, and clinical applicability.

High-Sensitivity Cardiac Troponin I

Cardiac troponin I (cTnI) is a regulatory protein that forms part of the cardiac contractile apparatus. Because the cardiac isoform differs structurally from skeletal

muscle isoforms, its detection in peripheral blood provides highly specific evidence of myocardial injury. The development of high-sensitivity cardiac troponin I (hs-cTnI) assays has enabled clinicians to detect very low circulating concentrations of cTnI and identify myocardial injury at an earlier stage than was possible with conventional assays.The diagnostic interpretation of hs-cTnI is based primarily on the assay-specific 99th percentile upper reference limit. A concentration above this threshold indicates myocardial injury, while evidence of a rise and/or fall in troponin concentration supports the presence of an acute process. However, an elevated hs-cTnI concentration alone does not establish the diagnosis of myocardial infarction. Clinical evidence of myocardial ischemia must also be present [1,2].One of the major advantages of hs-cTnI is its high sensitivity for myocardial injury. Serial measurements can detect relatively small changes in concentration and therefore contribute to accelerated diagnostic pathways for patients presenting with suspected acute coronary syndrome. The clinical interpretation of hs-cTnI should nevertheless take into account the timing of symptom onset, the patient's baseline cardiovascular condition, and possible non-ischemic causes of myocardial injury.

High-Sensitivity Cardiac Troponin T

Cardiac troponin T (cTnT) is another highly specific cardiac biomarker that is structurally associated with the myocardial contractile apparatus. High-sensitivity cardiac troponin T (hs-cTnT) assays allow the detection of low concentrations of circulating cTnT and have become an important component of contemporary acute coronary syndrome assessment.Similar to hs-cTnI, hs-cTnT should be interpreted using an assay-specific reference limit and in conjunction with the clinical presentation. A dynamic change in hs-cTnT concentration may provide evidence of acute myocardial injury, whereas persistently elevated concentrations may occur in patients with chronic structural or systemic cardiovascular conditions. This distinction is particularly relevant in patients with chronic kidney disease, heart failure, or other disorders associated with persistent myocardial stress or injury [1,3].The principal clinical value of hs-cTnT is its ability to contribute to rapid

diagnostic algorithms. Baseline measurement followed by repeat testing after an appropriate interval can help clinicians determine whether acute myocardial injury is likely, unlikely, or requires further investigation. Thus, hs-cTnT has an important role in both early diagnosis and clinical risk assessment.

Creatine Kinase-MB

Creatine kinase-MB (CK-MB) is an isoenzyme of creatine kinase that is relatively enriched in cardiac muscle. Before the widespread implementation of cardiac troponin assays, CK-MB was commonly used as a principal laboratory marker for myocardial infarction. It typically increases following myocardial injury and subsequently returns toward baseline over a shorter period than cardiac troponin.The relatively rapid decline of CK-MB can be useful when evaluating possible recurrent myocardial infarction occurring shortly after an initial event. However, CK-MB is less cardiac-specific than cardiac troponin because it can also be elevated in skeletal muscle injury and other conditions. Consequently, current diagnostic strategies generally favor cardiac troponins over CK-MB for the routine diagnosis of acute myocardial injury [2,4].

Despite its reduced role in contemporary practice, understanding CK-MB remains relevant because it illustrates the historical development of cardiac biomarker diagnostics and may still have limited clinical applications in selected circumstances.

Myoglobin

Myoglobin is a small oxygen-binding protein present in both cardiac and skeletal muscle. Following muscle injury, it can enter the circulation relatively rapidly, making it one of the earliest proteins historically investigated for the detection of myocardial injury. Its early appearance in blood was considered a potential advantage in patients presenting shortly after symptom onset.However, the major limitation of myoglobin is its poor cardiac specificity. Skeletal muscle injury, physical trauma, strenuous exercise, and several other conditions can increase circulating myoglobin concentrations. Therefore, an elevated myoglobin

concentration cannot reliably distinguish myocardial injury from non-cardiac muscle damage. With the development of high-sensitivity cardiac troponin assays, the clinical importance of myoglobin in the routine diagnosis of acute myocardial infarction has consequently declined [2,4].

Comparative Diagnostic Significance

The established biomarkers differ in their biological characteristics and diagnostic performance. High-sensitivity cardiac troponins provide the greatest combination of cardiac specificity and analytical sensitivity and therefore represent the central biomarkers for contemporary myocardial injury assessment. CK-MB may retain a limited role in specific clinical circumstances, whereas myoglobin has substantially less diagnostic value because of its limited tissue specificity.Importantly, the diagnostic usefulness of any biomarker depends not only on its absolute concentration but also on the timing of measurement and the clinical context. A biomarker obtained very early after symptom onset may remain below the diagnostic threshold despite ongoing myocardial injury. Conversely, an elevated biomarker concentration obtained later may reflect an injury that has already occurred. For this reason, serial testing and assessment of temporal changes are fundamental components of modern biomarker-based diagnostic strategies.

Overall, the transition from conventional biomarkers toward high-sensitivity cardiac troponin assays represents a major development in the early diagnosis of ischemic heart disease. Nevertheless, biomarker results should always be interpreted alongside the patient's clinical presentation, electrocardiographic findings, and other diagnostic evidence rather than being considered in isolation.

Biomarker	Main biological source	Early diagnostic potential	Cardiac specificity	Major advantage	Main limitation	Current clinical role
hs-cTnI	Cardiac myocytes	High	High	Very high analytical sensitivity; detects small myocardial injury	May be elevated in non-ischemic myocardial injury	**Primary biomarker** for myocardial injury assessment
hs-cTnT	Cardiac myocytes	High	High	High sensitivity and useful for serial measurements	Chronic elevations may occur in several conditions	**Primary biomarker** in acute coronary syndrome assessment
CK-MB	Mainly cardiac and skeletal muscle	Moderate	Moderate	Relatively short duration of elevation; may assist in suspected recurrent injury	Less cardiac-specific than troponin	Limited/selective use; generally not preferred over hs-cTn
Myoglobin	Cardiac and	Relatively early	Low	Rapid release following	Poor cardiac	Limited role in contemporary myocardial

Biomarker	Main biological source	Early diagnostic potential	Cardiac specificity	Major advantage	Main limitation	Current clinical role
	skeletal muscle			muscle injury	specificity	infarction diagnosis

Overall, the comparison demonstrates that high-sensitivity cardiac troponins have become central to contemporary biomarker-based assessment because they combine high analytical sensitivity with cardiac specificity. CK-MB and myoglobin retain historical and limited complementary relevance, but their lower specificity reduces their usefulness compared with high-sensitivity cardiac troponin assays. Importantly, no biomarker should be interpreted independently of clinical presentation, electrocardiographic findings, and the temporal pattern of biomarker change.

Emerging and Complementary Biomarkers in Ischemic Heart Disease

Although high-sensitivity cardiac troponins remain the principal biomarkers for detecting myocardial injury, several complementary biomarkers have been investigated to improve early diagnosis and provide additional information about the underlying cardiovascular processes.

Copeptin is a stress-related biomarker that can increase rapidly during acute cardiovascular events. Its potential value is mainly related to the very early phase of suspected acute myocardial infarction, when cardiac troponin concentrations may still be low. However, because copeptin is not specific to myocardial ischemia, it is generally considered a complementary rather than a primary biomarker [1].

BNP and NT-proBNP primarily reflect myocardial wall stress and ventricular dysfunction. Although they are not specific markers of acute myocardial infarction, elevated concentrations may provide useful information about cardiac function and prognosis in patients with ischemic heart disease [2].

Inflammatory and oxidative-stress biomarkers have also received increasing research attention because inflammation, endothelial dysfunction, and oxidative imbalance contribute to atherosclerotic plaque progression and cardiovascular injury. High-sensitivity C-reactive protein (hs-CRP), oxidized low-density lipoprotein, and other oxidative-stress-related markers may provide information about vascular inflammation and cardiovascular risk. However, their limited specificity currently prevents them from replacing cardiac troponins in routine diagnosis [3].

Overall, emerging biomarkers may complement high-sensitivity cardiac troponin by reflecting different aspects of cardiovascular pathology. Their clinical value is likely to depend on whether they can provide additional diagnostic or prognostic information beyond established troponin-based strategies.

Biomarker	Main biological source	Early diagnostic potential	Cardiac specificity	Major advantage	Main limitation	Current clinical role
hs-cTnI	Cardiac myocytes	High	High	Very high analytical sensitivity; detects small myocardial injury	May be elevated in non-ischemic myocardial injury	**Primary biomarker** for myocardial injury assessment
hs-cTnT	Cardiac myocytes	High	High	High sensitivity and useful for serial measurements	Chronic elevations may occur in several	**Primary biomarker** in acute coronary syndrome assessment

Biomarker	Main biological source	Early diagnostic potential	Cardiac specificity	Major advantage	Main limitation	Current clinical role
					conditions	
CK-MB	Mainly cardiac and skeletal muscle	Moderate	Moderate	Relatively short duration of elevation; may assist in suspected recurrent injury	Less cardiac-specific than troponin	Limited/selective use; generally not preferred over hs-cTn
Myoglobin	Cardiac and skeletal muscle	Relatively early	Low	Rapid release following muscle injury	Poor cardiac specificity	Limited role in contemporary myocardial infarction diagnosis

Overall, the comparison demonstrates that high-sensitivity cardiac troponins have become central to contemporary biomarker-based assessment because they combine high analytical sensitivity with cardiac specificity. CK-MB and myoglobin retain historical and limited complementary relevance, but their lower specificity reduces their usefulness compared with high-sensitivity cardiac troponin assays. Importantly, no biomarker should be interpreted independently of clinical presentation, electrocardiographic findings, and the temporal pattern of biomarker change.

Conclusion: Early identification of myocardial injury is essential for the timely diagnosis and management of patients with suspected ischemic heart disease. High-sensitivity cardiac troponin I and T have become the principal biomarkers for detecting myocardial injury because of their high analytical sensitivity and ability to identify small changes in circulating troponin concentrations. Serial measurements further improve diagnostic interpretation by demonstrating dynamic changes that may indicate an acute process.Other biomarkers, including CK-MB, myoglobin, copeptin, natriuretic peptides, inflammatory markers, and oxidative-stress-related biomarkers, may provide complementary information about different aspects of cardiovascular pathology. However, their diagnostic value is generally limited by lower specificity, biological variability, or insufficient evidence of additional clinical benefit beyond established hs-cTn-based strategies.The clinical interpretation of biomarkers should therefore be integrated with patient symptoms, ECG findings, serial biomarker measurements, and appropriate cardiac imaging. This multimodal approach helps distinguish acute ischemic myocardial injury from non-ischemic causes of biomarker elevation and supports more accurate risk assessment and clinical decision-making.This review has several limitations. First, the available evidence for emerging biomarkers is heterogeneous, with differences in study populations, assay methods, diagnostic thresholds, and clinical endpoints. Second, many novel biomarkers have been investigated primarily in observational or relatively small studies, limiting the ability to determine their independent clinical value. Finally, differences in laboratory platforms and patient characteristics may affect the generalizability of reported biomarker performance. These limitations highlight the need for larger prospective, multicenter studies and standardized analytical approaches.Future research should focus on validating novel biomarkers, improving assay standardization, and developing integrated diagnostic models that combine biomarkers with advanced imaging and artificial intelligence. The clinical relevance of emerging biomarkers will ultimately depend on their ability to provide reliable and actionable information that improves diagnosis or patient outcomes

beyond current diagnostic strategies.In conclusion, biomarkers represent a fundamental component of modern ischemic heart disease assessment. Their greatest clinical value is achieved not through isolated measurement, but through timely, serial, and context-dependent interpretation within a comprehensive diagnostic framework.

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