



# Clinical Cardiac Markers for Acute Myocardial Infarction Diagnostic

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## Abstract

Cardiac biomarkers are biological macromolecules that can be used in laboratory routine and clinical as confirmatory evidence for diagnostic of the Acute Myocardial Infarction (AMI). Several cardiac biomarkers, such as cardiac enzymes and specific cardio proteins, have been traditionally used in the AMI diagnostic. However, the difference between the sensitivity and specificity of the biomarker of clinical choice can be assistance of in the early diagnosis and the evaluation prognosis of the infarcted patient. The purpose of this review is to summarize an update of the clinical cardiac biomarker used in the diagnostic of AMI, specifying the criterion of sensitivity, tissue performance and its correlation regarding the diagnosis.

**Keywords:** Cardiovascular Diseases, Acute Myocardial Infarction, Cardiac Biomarkers, Diagnosis

## Introduction

Cardiovascular Diseases (CVDs) represent 31% of the world mortality rate, according to the World Health Organization, with an estimated 17.9 million deaths per year [1]. CVDs are associated with numerous non-modifiable risk factors such as age, sex, race, and family genetics and modifiable, such as unbalanced diet, alcoholism, smoking, stress, and sedentary lifestyle [2]. The CVDs include coronary heart disease (such as acute coronary syndromes and heart failure), cerebrovascular disease, rheumatic heart disease and other conditions. Among the acute coronary syndromes, Acute Myocardial Infarction (AMI) is classified as one of the main causes of hospitalizations and deaths in the world [3].

AMI refers to acute focal myocardial necrosis caused by prolonged and severe ischemia, which can progress by reducing oxygen consumption in the myocardium [4]. The most deaths from AMI occur during the first 4h of myocardial necrosis. If the patient is diagnosed and treated effectively within the first few h, mortality

can be reduced from 9% to 3%, but if diagnosed within 3-4h, the mortality rate can be five times higher [5]. Therefore, agility in the diagnosis is essential for the therapeutic conduct and survival of the infarcted patient.

According with the Universal Definition of Myocardial Infarction [4], the diagnosis of the AMI requires the clinical history of the patient associated with clinical symptoms, electrocardiogram (ECG) tracing and cardiac markers. The ECG is the main diagnostic method used in the screening; it must be performed in less than 10 min from presentation to the emergency. However, a negative percentage of infarcted patients do not present changes in the ST segment of the ECG, reducing their sensitivity to 50-60% for AMI diagnostic [6,7]. A rapid and accurate diagnosis is essential for effective medical management and revascularization of the infarcted patients. In this sense, the use elevation in serum concentration of cardiac biomarkers is of paramount importance for stratifying risk and prognosis of the AMI.

Cardiac markers are described as protein molecules of the cellular structure detectable in the bloodstream when damage to cardiac cells occurs. The release kinetics of the cardiac markers in AMI depends on several factors, such as size of molecules, clearance rate of the marker, analytical method used for its measurement and, above all, of its sensitivity. There are numerous cardiac biomarkers, it is useful to classify biomarkers into various pathophysiological groups, such as myocardial ischemia or necrosis, inflammation, hemodynamics, angiogenesis, atherosclerosis, or plaque instability [8]. Traditionally, some cytosolic enzymes were measured as indicators of the cardiac ischemia and infarction. Currently, other constituent biochemical markers muscle cell proteins without enzyme function have also been used for this purpose.

The ideal biomarker for detecting myocardial injury needs to be expressed at relatively high levels within cardiac tissue, with high clinical sensitivity and specificity that is detectable in the blood early after the onset of symptoms, such as chest pain [8,9]. The choice of the cardiac biomarkers associated with point-of-care testing technology demonstrate a potential strategy for the rapid and practical management and cost reduction of the AMI diagnostic. The current article shows an integrative review about of the sensibility and specificity of mainly cardiac biomarkers used for AMI diagnostic and its use of the in clinical practice. The main molecular markers used in clinical practice for the diagnosis of AMI are enzyme Creatine Kinase (CK), Myoglobin (Mb), Cardiac Fatty Acid Binding Protein (H-FABP), Brain Natriuretic Peptide (BNP) and Cardiac Troponins T and I (cTnT and cTnI).

### Creatine Kinase in the AMI Diagnostic

CK is a cytoplasmic protein that catalyzes the reversible phosphorylation of creatine to phosphocreatine, generating anaerobic muscle contraction, common in ischemic events. It consists of two subunits (M and B), forming three isomers (CK-BB, CK-MB and CK-MM). The CK-MM isoenzyme is more abundant in the heart and skeletal muscle tissue; CK-BB derived from the brain, lungs, and smooth tissues; CK-MB originating predominantly in the myocardium [10]. Serum CK-MB levels rise 3-6h after precordial chest pain, reaching a peak in 24h and normalizing within 48-72h. The CK-MB has a sensitivity of 50% after 3h of onset of symptoms and 80% after 6h [11]. Therefore, its increasing level during trauma and inflammation reduces its specificity due to the false-positive correlation with non-cardiac tissues [10,11]. Additionally, the levels of CK-MB concentrations can not detect minor damage in myocardial tissue, due to the high molecular weight.

### Myoglobin in the AMI Diagnostic

Mb is a cytoplasmic hemoprotein of low molecular weight (17 kDa) with a structure like that of hemoglobin. Mb is the earliest cardiac marker that changes and normalizes in the bloodstream

after an ischemic injury. The serum MB levels rise rapidly after myocardial injury, their elevation occurs between 30min after the onset of ischemia, reaching its maximum around 6-10h and normalizing between 12-24h [12,13]. The Mb can be used for evaluation of the infarct size and reperfusion [14]. Mb has low specificity for cardiac tissue, especially in patients with renal failure and trauma to the skeletal muscles, chronic insufficiency, exposure to drugs and toxins. However, it should be noted that it is useful in evaluating infarct size and reperfusion.

### Cardiac Troponins in the AMI Diagnostic

Currently, cardiac troponins are the "gold standard" markers for diagnosis of ischemic myocardial lesions. Due to its high specificity and sensitivity became a consensus since the first redefinition of the AMI proposed by a committee by the European Society of Cardiology and the American College of Cardiology [4]. Recent revisions of the committee considered the importance of serial dosing of troponins in the AMI, reiterating its position as a differential and first-choice marker. The cTnT and cTnI are expressed as isoforms specific to cardiac muscle. These become measurable within a period of 2 to 4h after the onset of symptoms clinical and remains elevated for about 4 to 7 days for cTnI, and 10 to 14 days for cTnT [15,16]. Some authors attribute to cTnI and cTnT the same specificity and importance in the evaluation of cardiac damage [17]. However, the cTnT has a wider diagnostic window and compared to cTnI, allowing the assessment of both the acute and chronic phases of AMI.

### Other Cardiac Proteins in the AMI Diagnostic

Recently, others cardiac biomarkers have been described in the literature with the aim of improving the diagnostic specificity of the infarction and the prognostic of the myocardial damage. Among them, the H-FABP and BNP serum concentrations and have shown potential application to improve the accuracy and sensitivity of infarction diagnosis in emergency departments.

The H-FABP protein is released from 20min after the beginning of the necrosis process and reaches its peak concentration after 4-6h. This allows the use of H-FABP as a cardiac marker within the first hours of the infarction [18]. In this sense, it is important to be evaluated in association with other markers, improving the accuracy of the diagnosis. The H-FABP provides increase in the sensitivity and negative predictive value for patients with chest pain and no cTn elevations, showing a higher sensitivity in the diagnosis of AMI with a positive rate of 55% [19].

However, the high sensibility of the cTn blood levels in the AMI diagnostic, its concentration on admission of the patients was weakly associated with the infarct size estimation [20]. The BNP blood concentration can be used as an important predictor for left

ventricular dysfunction after the onset of AMI and a good indicator of infarct size and monitoring of the damage tissue. The BNP is a cardiac neurohormone released from ventricles in response to myocardial dysfunction [21]. In this sense, the BNP serum concentration associated with cTn showed a good correlation for immediate infarct severity estimation and risk stratification of the ventricular dysfunction [22].

## Conclusion

The rapid diagnosis of infarction is crucial for clinical decision the appropriate therapeutic treatment that can be improve the patient prognostic. Serum measurement of cardiac biomarkers helps clinical practice, especially when other decision-making events such as characteristic symptoms and ECG changes are inconclusive. Although there are many cardiac biomarkers, their use in clinical practice depends on their specificity/sensitivity to detect myocardial damage, reproducibility, precision, and discriminatory limits to distinguish between pathological and physiological levels.

## Conflict of Interest

The authors declare no conflict of interest.

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