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REVIEW ARTICLE

The Use of Biochemical Cardiac Markers in Acute Coronary Syndrome

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ABSTRACT

Every year, acute coronary syndrome (ACS), one of the main causes of death worldwide, is getting more prevalent. Reduced myocardial blood flow is the hallmark of the recently identified medical illness known as acute coronary syndrome. Biochemical cardiac indicators in blood serum are essential for people's early syndrome detection and risk assessment, in addition to an ECG, ECG, and coronary angiography. Numerous biochemical cardiac indicators, such as myoglobin, creatine kinase-MB, aspartate aminotransferase (AST) activity, lactate dehydrogenase (LDH), and cardiac troponin (cTnT and cTnI), are used to detect acute coronary syndrome. However, it is believed that amino-terminal proBNP, B-type natriuretic peptide (BNP), and high-sensitivity cardiac troponin (hs-cTn) are the best markers for identifying those with acute coronary syndrome. They have the highest specificities and sensitivity, which explains why. This review paper covers almost all biochemical cardiac markers and discusses current research on acute coronary syndrome.

1. Introduction:

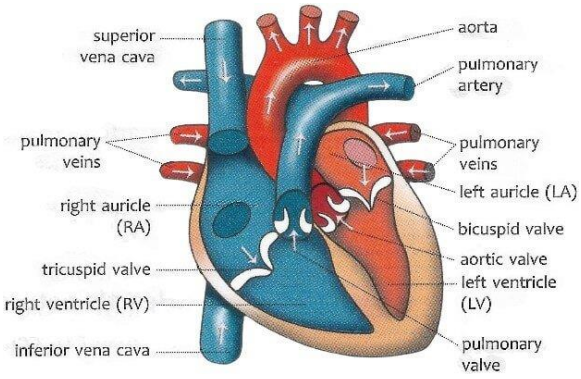
The Human Heart: Structure and Function

The human heart is a remarkable organ that pumps blood flowing through the human body. This page provides a brief overview of the anatomy and physiology of the heart with relevant sources.

Structure of the Heart: The human heart is a cone-shaped muscular organ located in the thoracic cavity, directly beneath the sternum, or breastbone, and slightly to the left of the midline. It is roughly the size of a clenched fist and has four chambers: two atria and two ventricles. These

chambers, which deliver and pump blood to different body parts, divided into septa [1].

Figure 1: Shown the structure of the Heart



Blood Circulation:

• The right atrium contracted, which pushed blood into the right ventricle. Deoxygenated blood from the body returns to the right atrium through the superior and inferior vena cava.

• The right ventricle pumps blood to the lungs via the pulmonary artery.

• Blood receives oxygenation in the lungs and is transported back to the left atrium via the pulmonary veins.

• Blood is forced into the left ventricle by the left atrium's contraction.

• The left ventricle uses the aorta to pump oxygenated blood to the body's other organs.

Cardiac Conduction System:

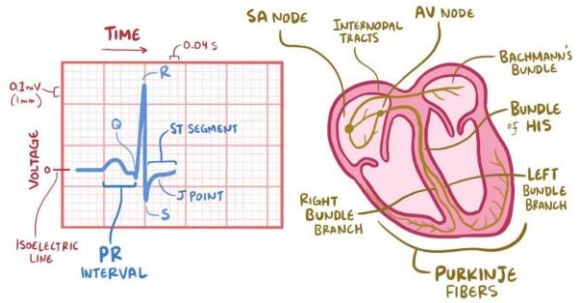
The heart's electrical conduction system regulates its rhythm and ensures that its contractions occur simultaneously. The atrioventricular (AV) node, a bundle of His, and the sinoatrial (SA) node make up this structure [2]. The human heart is an amazing organ with intricate internal workings crucial to preserving circulatory equilibrium. It is essential to fully comprehend its composition and operation to fully grasp the complexities of cardiovascular health and illness.

What is Acute Coronary Syndrome?

The following conditions are collectively referred to as acute coronary syndrome and are marked by acute myocardial ischemia:

1. Unstable angina
2. Myocardial infarction with non-ST segment elevation (NSTEMI)
3. Myocardial infarction with ST-segment elevation (STEMI).

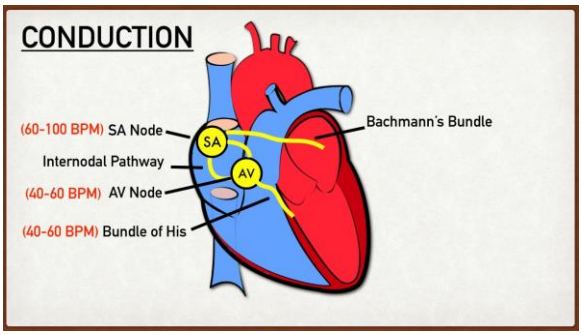
Figure 2: Shown the right ventricle pumps blood to the lungs via the pulmonary artery



Cardiac Output:

The heart adjusts its rhythm and stroke volume to give the body the oxygen and nourishment it needs. It is the output volume of blood pumped by the left ventricle in the 60s; it varies based on activity levels and physiological needs (Figure 3) [3].

Figure 3: **Shown the Cardiac Conduction System**



Atherosclerosis of the coronary arteries is the main cause of acute coronary syndrome, which is triggered by the rupture of an atheromatous plaque and the ensuing increase in thrombosis. Clinically, the degree of ischemia, collateral circulation volume, myocardial oxygen demand, and other patient-specific factors determine it. Early identification of acute coronary syndrome is crucial for prompt and proper therapy to be commenced due to its life-threatening nature. Clinical symptoms, electrocardiographic alterations, and the identification of cardiac biomarkers released into the bloodstream as a result of myocardial injury are crucial diagnostic factors. To differentiate between acute myocardial infarction and unstable angina against chronic stable angina, the phrase acute coronary syndrome was created. The majority of people who suffer from acute coronary syndrome have previously experienced exertion angina or coronary artery disease. Chest discomfort is a common clinical sign of myocardial ischemia. Described in many ways, pain is typically felt as pressure, squeezing, constriction, crushing, tightness, or heaviness. Pain spread to the left arm, shoulder, neck, and jaw. It appears following physical activity, food, or psychological strain [4]. Rest and nitroglycerin can reduce the discomfort associated with angina pectoris. Acute myocardial infarction, or myocardial necrosis owing to ischemia, causes pain akin to this. Still, it is more intense, lasts longer (>30 minutes), and is difficult to ease with rest or nitroglycerin. Additional symptoms of

myocardial infarction, including palpitations, perspiration, nausea, and vomiting, frequently accompany the pain. In 25% of instances, especially in people with diabetes or high blood pressure, an acute myocardial infarction might be clinically quiet [5]. Angina with a severe start, angina when at rest, or a recent rise in the frequency or pattern of angina can all be signs of unstable angina. (Figure 1) Acute myocardial infarction was formally diagnosed in two ways:

- Severe continue ongoing chest pain indicative of myocardial ischemia.
- distinct alterations in an acute myocardial infarction on an ECG (emergence of a Q wave).
- increase in cardiac biochemical markers in blood circulation [6].

Signs and Symptoms:

This syndrome is characterized by abruptly decreased blood flow to the heart and can present various signs and symptoms, depending on the patient's age, sex, and other medical conditions. These symptoms related to age distribution have been reported in **Table 3** and demonstrated in research. **Table 2** lists the distribution of presenting symptoms across various age groups that have been observed.

- Angina or discomfort, frequently with pressure, tension, or burning.
- Pain spreading from the chest to the arms, shoulders, abdomen, back or neck
- Nausea and vomiting
- Indigestion
- Dyspnea
- Diaphoresis
- Unusual fatigue
- Feeling restless [7].

Table 2: Distribution of presenting symptoms

SR	Symptoms	%
1	Chest Pain	94
2	Sweating	78
3	Breathlessness	67
4	Palpitation	58
5	Vomiting	43
6	Giddiness	38
7	Abdominal pain	4

Source: Clinical Profile & Risk Factors in Acute Coronary Syndrome (page 160).

Table 1: Sex and age wise Distribution of cases

S. No	Age groups	Male Percentage	Female Percentage
1	31-40	(8)	(2)
2	41-50	(17)	(4)
3	51-60	(23)	(9)
4	61-70	(19)	(10)
5	71-80	(5)	(3)
Total		(72)	(28)

Source: Clinical Profile & Risk Factors in Acute Coronary Syndrome (page 150).

Biochemical Cardiac Marker Studies:

Damage to the membranes caused by cardiac cell necrosis allows intracellular macromolecules from the cells or tissues to be released into the bloodstream. Myocardial infarction can be diagnosed when significant biochemical cardiac markers are found in the bloodstream in the proper clinical context. It is also possible to differentiate between an acute myocardial infarction and unstable angina by measuring these biochemical cardiac markers [8]. The following are a few biochemical cardiac indicators indicating myocardial injury:

- **Creatine kinase (CK)**
  - Total CK
  - Isoenzymes
  - CK-MB (activity)
  - CK-MB (mass)
- **Aspartate aminotransferase (AST) activity**
- **Lactate dehydrogenase (LDH)**
  - LDH activity
  - Isoenzymes)
- **Cardiac troponins (cTn)**
  - cTnT
  - cTnI
- **Myoglobin**
- **Natriuretic peptide test (BNP and NT-proBNP)**

Myocardial infarction was formerly diagnosed using total Creatine Kinase, lactate dehydrogenase, and aspartate aminotransferase. However, these enzymes are rarely tested these days due to their limited specificity.

These days, cardiac markers such as myoglobin and cardiac troponin are advised for the myocardial infarction diagnosis, while the 2nd best option is CK-MB (mass).

The duration of specimen collection following myocardial infarction determines the usefulness of a cardiac marker. A combination of indicators and serial changes is used for a more accurate diagnosis. An optimal cardiac marker should be highly specific, highly sensitive, cost-effective, and contribute to better patient outcomes. There isn't yet a cardiac sign like that.

Timeline of Biochemical Cardiac Markers after Acute Myocardial Infarction (Table 1)

- Myocardial infarction: Myoglobin levels rise and are discovered 1-2 hours after symptoms appear, peak 9 hours later, and return to normal range after 24 hours.
- between 3-6 hours of the beginning of symptoms, CK-MB increases and is identified; it peaks between 12-24 hours and recovers to normal within 48-72 hours.
- Troponin increases and is discovered 4–8 hours after symptoms appear, peaks 12–24 hours later, and levels recover to normal in 5–10 days.
- After symptoms appear, aspartate aminotransferase increases and is discovered 6–12 hours later. It peaks 30 hours later and recovers to normal levels in 2–6 days.

- Within 24 to 72 hours following the beginning of symptoms, lactate dehydrogenase is found, peaks in 3–4 days, and is elevated for 8–14 days [9].

Role of Biochemical Cardiac Markers in Acute Coronary Syndrome

Measurement of biochemical cardiac markers does not provide enough information for initial management in the presence of typical history and electrocardiogram findings with acute myocardial infarction to confirm or refute the diagnosis of acute myocardial infarction in patients with sudden chest pain. Therefore, patients require thrombolytic therapy, angioplasty, or both as an immediate treatment. When a diagnosis cannot be made in an emergency based only on clinical and ECG symptoms, biochemical cardiac markers might help rule out myocardial infarction. It is advised to do serial assessments on the first arrival of the patients for admission, and they should be examined six hours after admission and after twelve hours and twenty-four hours for confirmation. It is advised to use cardiac troponin and CK-MB (mass) for diagnosis.

- Using cardiac troponin to identify previous myocardial infarction
- To diagnose reinfarction (CK-MB mass) and assess the efficacy of percutaneous coronary intervention or thrombolysis as urgent reperfusion treatment for STEMI patients.
- Using risk stratification to estimate the chances of an acute coronary syndrome.

Creatine kinase

It shows the highest activity in the striated muscle, the brain, and the heart.

The causes of increased Creatine kinase are the following:

- Skeletal muscle disorders, such as muscular dystrophy, dermatomyositis, intramuscular injection, trauma, and exercise
- Heart conditions such as myocarditis and myocardial infarction
- Central nervous system disorders, such as strokes, brain traumas, and generalized convulsions

There are three isoenzymes of creatine kinase: CK-BB, CK-MB, and CK-MM. In the heart and skeletal muscle, CK-MM is more prevalent than CK-BB, whereas CK-MB is more prevalent in cardiac muscle. Since CK-MB is a crucial cardiac-specific CK isoenzyme, measuring its mass is advised.

Total serum CK and CK-MB levels are consistently raised after myocardial infarction. Furthermore, tissues other than the heart may cause an elevation in serum CK and CK-MB. After the beginning of symptoms, CK-MB increases three to six hours after myocardial infarction, peaks twelve to twenty-four hours later, and falls to normal level by forty-eight to seventy-two hours later [10].

One might utilize the relative index (CK-MB/total CK × 100) to distinguish between cardiac and skeletal muscle injury. It is more than 5% is very suggestive of an acute myocardial infarction. Obtaining sequential samples is advised, one at the time of presentation and one every eight hours for a total of twenty-four hours.

Aspartate aminotransferase

The first widely used biochemical marker of the heart is aspartate aminotransferase (AST), also known as serum glutamic oxidaloacetic transaminase (SGOT). The brain, liver, heart, kidney, and skeletal muscles are the main locations of AST. It is no longer utilized to diagnose myocardial infarction because of its low selectivity to cardiac cells [11]. After a myocardial infarction, the anti-acute serum troponin (AST) increases and is detectable 6–12 hours after the beginning of symptoms. It peaks 30 hours later and recovers to normal levels in 2–6 days.

Lactate Dehydrogenase

In the past, lactate dehydrogenase (LDH) was widely used to diagnose myocardial infarction; however, because troponin tests are now available, LDH is no longer often utilized in the clinical setting for this purpose [12]. its levels increase for 24 to 72 hours before peaking in concentration in 4-6 days. As a late cardiac marker for myocardial infarction, the levels stay elevated for 8–14 days.

Myoglobin

Low molecular weight myoglobin (oxygen-binding protein) is found in cardiac and skeletal muscle. The most helpful sign at this time is myoglobin, which rises one to three hours after myocardial infarction. Both skeletal and cardiac muscles have the same amount of myoglobin. Following myocardial infarction, cardiac surgery, muscular damage, muscular dystrophy, renal failure, shock, and trauma, myoglobin levels rise. Consequently, myoglobin that rises quickly after a myocardial infarction is not exclusive to the heart. Furthermore, in patients who arrived with chest discomfort, non-elevation of myoglobin (in two successive samples taken two to four hours apart) helps rule out an early myocardial infarction [13].

Troponins (Tn)

A biochemical cardiac indicator of myocardial necrosis that is known as cardiac troponin T (cTnT) and cardiac troponin I (cTnI), which are observed as the best markers for concluding diagnosis (either cTnT or cTnI). Actin and myosin filament contact during cardiac contraction is regulated by troponins. Troponins rise in the blood 4–8 hours after myocardial infarction. A troponin's diagnostic sensitivity is 100% if it is elevated for twelve hours or longer after the beginning of chest pain [14]. Since tnI is exclusively present in the heart muscle, it is highly cardio-specific. After damage to the skeletal muscles, it is not raised. TnI increases 4-8 hours after the start of chest pain, peaks 12-24 hours later, and stays increased for five to ten days following myocardial injury. A significant advancement in the verdict of myocardial infarction has been made with the development of tests for TnI and TnT. Troponin is helpful when the patient presents later since it stays high for five to ten days. Only troponin is advised if the beginning of chest discomfort occurs nine to twelve hours before admission [15].

Review of literature:

According to estimates from Wu et al. [16], myocardial infarction is the highest mortality syndrome in the world, and its incidence rises annually. Along with electrocardiograms, echocardiograms, coronary

angiography, and other diagnostic and therapeutic tools, biochemical cardiac markers in circulating blood are critical to the diagnosis and prognosis. Furthermore, because the high sensitivity of cardiac troponin is a particular creation of heart tissue injury, it is the ideal biochemical cardiac marker. Furthermore, for prognosis, treatment impact monitoring, and prevention, additional biochemical cardiac indicators are equally crucial.

According to Mueller, [17], biochemical cardiac indicators are important for the diagnosis, risk assessment, triage, and handling of individuals who may have acute coronary syndrome (ACS). Dekker et al. [18] Concluded that because cardiac troponin (cTn) does not consistently grow in the first few hours following the beginning of symptoms, early diagnosis of acute coronary syndrome (ACS) is critical. He claimed that the 73 papers that were identified on the early biochemical cardiac markers myoglobin, ischemia modified albumin (IMA), glycogen phosphorylase isoenzyme BB, pregnancy-associated plasma protein A, heart-type fatty acid binding protein (H-FABP), and myeloid-related protein 8/14 frequently lacked accurate measures of clinical utility. Furthermore, it appears that heart-type fatty acid binding protein (H-FABP) and ischemia modified albumin (IMA) are effective biochemical makers in the initial diagnosis of acute coronary syndrome (ACS).

Clinicians' use of biochemical cardiac indicators in the treatment of acute coronary syndromes (ACS) has reportedly become more sophisticated, according to estimates made by Morrow & Braunwald [19]. The first reports of serum proteins generated by necrotic cardiac myocytes and their potential use in the diagnosis of acute myocardial infarction (AMI) date back to clinical researchers in the 1950s. In the next forty years, indicators of myocardial necrosis will become more specific to cardiac tissue, which will lead to improvements in their clinical sensitivity and specificity when used to diagnose acute myocardial infarction. Clinical decision-making for individuals with acute coronary syndrome (ACS) has greatly enhanced the integration of biochemical cardiac indicators over the last 10 years due to the discovery of compelling data supporting the usefulness of cardiac troponin (cTn) in guiding therapy. The development of new biochemical cardiac markers has been prompted by developments in our understanding of the pathophysiology and values of acute coronary atherothrombosis. This has also opened up the possibility of utilizing multiple biochemical cardiac markers in the arrangement and customization of treatment for acute coronary syndrome (ACS).

Tilea et al. [20] highlighted that despite advancements in managing acute myocardial infarction (AMI), it remains the leading cause of global mortality. Swift and accurate diagnosis of AMI can significantly decrease fatalities within this high-risk demographic. Traditionally, AMI diagnosis has relied on evaluating cardiac markers, notably troponins (cTn), which elevate shortly after the onset of AMI but still lag behind the initial ischemic event. This delay hampers early intervention strategies. The advent of high-sensitivity cTn tests allows for ultra-sensitive detection of cardiac cell death, preceding troponin elevation. Moreover, newer biochemical indicators, reflecting processes like neurohormonal activation, inflammation, or myocardial stress, emerge earlier than cTn elevation or cell necrosis. Researchers, driven by a deeper understanding of AMI's complex pathophysiology, are exploring novel cardiac markers through multi-biomarker approaches to overcome these diagnostic limitations.

Chandhry & Herzog, [21] Acknowledged that one of the most significant indicators of coronary artery disease is an acute coronary syndrome, which is defined as an abrupt decrease in blood flow to the heart and can range from unstable angina to acute myocardial infarction MI. Furthermore, the core cause of mortality in the US is coronary artery disease. Two main objectives of the first evaluation of individuals with suspected ACS should be addressed. First, accurately and promptly diagnose the patient as having acute coronary syndrome (ACS), then consider other diagnoses and appropriate treatment. Reporting findings and diagnoses both during the hospital stay and afterward is the second objective. This objective is especially crucial in light of improved reperfusion techniques and lower primary event mortality. People at high risk might require more stringent monitoring techniques and follow-up.

According to Mendonça da Silva Correia [22], biochemical cardiac markers are biological macromolecules that are utilized as confirmatory indicators for the diagnosis of acute myocardial infarction (AMI) in clinical and laboratory settings. Acute myocardial infarction (AMI) is often diagnosed using several biochemical cardiac markers, including cardio proteins and cardiac enzymes. However, the distinction between the biochemical cardiac indicators of clinical choice's sensitivity and specificity might aid in the patient's early diagnosis and prognostic assessment.

Garg et al. [23] While various biochemical markers exist for diagnosing acute coronary syndrome (ACS), cardiac troponins are a firmly established indicator of myocardial damage within ACS scenarios. The evolution from initial to fifth-generation high-sensitivity cardiac troponin (hs-cTn) assays has seen extensive adoption. However, its clinical implementation preceded the establishment of best practices and guidelines. Despite the usefulness of all biochemical cardiac indicators, the most advantageous marker for identifying ACS appears to be high-sensitivity cardiac troponin (hs-cTn). Serving as a measurable sign of cardiomyocyte damage, hs-cTn facilitates distinguishing coronary diseases from non-coronary conditions.

According to del Val Martin et al. [24] biochemical cardiac markers are crucial for the identification and risk assessment of individuals suffering from acute coronary syndrome. The biomarker of choice for acute coronary syndrome diagnosis these days is cardiac troponin. However, a few other biochemical cardiac indicators are also crucial for enhancing prognostic data and sensitivity [24].

Christenson and Christenson [25] recognized myocardial infarction (MI) as a leading global cause of mortality. Within clinical settings, the use of biochemical cardiac markers holds significant importance in diagnosing, evaluating risks, determining treatment, and making clinical

decisions for patients displaying MI symptoms. When MI symptoms manifest, cardiac troponin (cTn) stands out as the foremost biochemical cardiac marker. The recent diagnostic criteria for MI involve observing an increase or decrease in cardiac troponin (cTn) levels, with at least one measurement exceeding the upper reference limit. Besides, in prognosticating and guiding treatments, the role of natriuretic peptides like amino-terminal proBNP (NT-proBNP) and B-type natriuretic peptide (BNP) is also noteworthy. Advancements in cardiac troponin (cTn) tests have enabled the detection of progressively lower protein levels in the blood. With the evolution of more sensitive cardiac troponin (cTn) assays, amino-terminal pro-BNP (NT-proBNP), and natriuretic peptides such as B-type natriuretic peptide (BNP), the diagnosis of myocardial infarction (MI) has become potentially faster through these novel techniques.

As per Chacko [26] , acute coronary syndrome (ACS) leads to heart muscle damage due to insufficient blood supply, potentially causing reversible or irreversible harm, and remains a leading cause of global mortality. Timely identification of ACS is crucial for appropriate therapy to prevent heart failure and myocardial necrosis. While conventional biochemical cardiac markers like cardiac troponins and creatine kinase play significant roles in diagnosing and treating ACS, they cannot detect myocardial ischemia without necrosis. This raises uncertainty regarding the optimal timing for diagnosing ischemia in ACS patients. Notably, high-sensitivity cardiac troponin (hs-cTn) stands out as a crucial biochemical marker in this context, aiding in diagnosis and treatment. Furthermore, these cardiac indicators contribute to understanding the disease process, while analyzing multiple markers helps categorize risks.

Azzazy & Christenson [27] utilized point-of-care testing (POCT) to identify acute coronary syndrome (ACS) indicators. Their study focused on assessing how point-of-care (POC) biochemical cardiac marker testing might influence clinical treatment and recommendations for ACS patients. Their findings highlighted cardiac troponins (cTn) as the most effective biochemical cardiac marker in this scenario. They also emphasized that quick multi-analyte point-of-care (POC) tests, some of which align with central laboratory assays, have simplified the use of biochemical cardiac indicators in clinical management and therapeutic recommendations. In summary, the use of biochemical cardiac marker point-of-care testing (POCT) could hold significant importance in treating patients with acute coronary syndrome (ACS).

As per Amodio et al. [28], early detection is pivotal in treating acute coronary syndrome (ACS) effectively. Among biochemical cardiac markers, cardiac troponin (both I and T) stands out as the most crucial for early ACS detection. Following troponin, B-type natriuretic peptide (BNP) and N-terminal proB-type natriuretic peptide (NT-proBNP) emerge as valuable markers for diagnosing ACS patients. Furthermore, the introduction of point-of-care testing aims to expedite the verification of results after blood draws, reducing the time taken for confirmation.

As per Al-Hadi & Fox [29], chest discomfort, a non-specific complaint, prompts most patients to seek emergency care, often associated with acute coronary syndromes (ACS). However, diagnosing ACS solely based on electrocardiograms and clinical history proves insufficient. This inadequacy results in some patients receiving incorrect diagnoses, being admitted to inappropriate units, or receiving unsuitable care, therapies, and investigations. Delayed diagnoses further delay the onset of treatment for certain individuals affected by ACS. Moreover, premature discharge from the emergency room can have adverse health consequences for ACS patients. Consequently, a considerable number of individuals without ACS end up needlessly hospitalized due to these shortcomings in the healthcare system.

Outlined by Searle et al. [30], the universal definition of myocardial infarction underlines the pivotal role of biochemical cardiac indicators in diagnosing acute coronary syndrome (ACS). This shift has led to a more focused and personalized treatment approach for individuals with ACS, albeit with further potential for improvement. They recognize natriuretic peptides (NPs), cardiac troponin (cTn), highly sensitive cardiac troponin (hs-cTn), and copeptin as presently valuable biochemical markers in diagnosing ACS patients. Additionally, potential future biomarkers such as choline, copeptin, and lipoprotein-associated phospholipase A2 (LP-PLA2) are being considered. However, extensive diagnostic clinical studies are necessary to evaluate their impact on ACS patients within clinical settings. Furthermore, brain-type natriuretic peptide (BNP) and its amino-terminal fragment NT-proBNP provide significant analytical information for patients undergoing ACS treatment. Microalbuminuria, particularly in non-diabetic individuals, appears to indicate vascular system issues, specifically related to endothelial problems. Elevated levels of myeloperoxidase in plasma, neopterin, cystatin C, and pregnancy-associated proteins are associated with cardiovascular disease, cerebrovascular illness, and both cardiovascular and non-cardiovascular mortality. Recent research highlights the significant impact of blood levels of the CD40-CD40L pathway on the development of acute coronary syndrome [31].

Per Moe & Wong [32], biochemical cardiac markers play a pivotal role in diagnosing acute coronary syndrome (ACS), especially concerning unstable angina, ST-segment elevated myocardial infarction and non-ST-segment elevation myocardial infarction. The approach to diagnosing and treating ACS patients has significantly evolved over the past decade. While several cardiac-related biochemical indicators exist—including myoglobin, aspartate aminotransferase, lactate dehydrogenase, and creatine kinase—the most precise and sensitive markers for myocardial damage are believed to be cardiac troponin and creatine kinase. Recent research has introduced novel biochemical cardiac indicators, although identifying the optimal markers for early identification, risk assessment, therapy selection, disease progression monitoring, and treatment effectiveness remains unclear. Studies highlight associations between higher levels of interleukin-6 and C-reactive protein and increased mortality rates among acute coronary syndrome patients. The quest for determining the

most effective biochemical cardiac markers for various aspects of ACS management continues.

Panteghini et al. [33] examined the use of biochemical cardiac markers for swiftly diagnosing acute coronary syndromes (ACS). They emphasized the necessity of having access to both early and definitive biochemical indicators of myocardial injury within an hour or less. Currently, cardiac troponin stands as the definitive biochemical cardiac marker, while myoglobin serves as the early indicator. These markers play a crucial role in identifying individuals with acute coronary syndrome, especially when an electrocardiogram may not be immediately indicative—given the initial ECG's 50% sensitivity in identifying myocardial infarction early on. Moreover, the rising importance of novel molecular markers like cardiac troponins is highlighted in detecting even mild myocardial cell injury. Conventional standards dictate that a lower abnormal value of cardiac troponin signifies the presence of myocardial injury, while a higher value indicates a diagnosis of myocardial infarction. These markers have become pivotal in efficiently diagnosing and categorizing various degrees of myocardial damage [33].

Apple et al. [34] investigated the challenges associated with evaluating individuals experiencing chest pain or symptoms suggestive of acute coronary syndrome (ACS), noting the time-consuming and costly nature of such assessments. Recent research has identified biochemical markers related to ischemia, myocardial stretch, plaque destabilization, and rupture occurring earlier in the cascade than markers of necrosis like cardiac troponins I and T. These upstream markers hold potential in aiding earlier diagnosis of acute coronary syndrome. Several promising biochemical markers have emerged, showing potential for diagnosing ACS earlier. These markers present an avenue for potentially enhancing the early identification and diagnosis of acute coronary syndrome, warranting continued exploration and validation in clinical settings.

According to Romić et al. [35], myocardial ischemia primarily underlies acute coronary syndrome (ACS), and the varying subtypes, such as unstable angina, are classified based on the degree of myocardial ischemia. The determination of blood biochemical cardiac markers significantly influences the diagnosis of acute myocardial infarction. Older biochemical markers like aspartate transaminase, lactate dehydrogenase, and creatine kinase, once utilized, are no longer considered due to their lack of specificity and sensitivity for cardiac-related issues. The National Academy of Clinical Biochemistry (NACB) recommends investigating two specific types of biochemical cardiac markers for diagnosing acute coronary syndrome: one that rises in serum within six hours after chest pain and another that elevates between six to nine hours after chest pain and remains elevated for several days. Current measurements often include myoglobin, CK-MB mass, and cardiac troponins, each having distinct characteristics. CK-MB mass, while unique to cardiomyopathy, can also rise due to skeletal muscle injury, posing challenges for specificity. Myoglobin, although initially sensitive, lacks exclusivity to cardiac-related issues. Cardiac troponins (cTn), recognized as late biochemical cardiac indicators, play a significant role in diagnosing ACS. However, researchers are exploring novel biochemical indicators specific to myocardial ischemia, aiming to enhance diagnostic accuracy and specificity in identifying acute coronary syndrome [35].

According to Raguz et al. [36] acute coronary syndrome (ACS) stands as a significant global socioeconomic concern. Of the 6-7 million people seeking emergency care in the US annually for chest pain or similar ACS-related symptoms, approximately 20–25% truly present with acute coronary syndrome. The primary indicator remains chest discomfort, categorizing ACS patients into two groups: ST-elevation acute coronary syndrome and non-ST elevation acute coronary syndrome, discernible by electrocardiogram (ECG) changes. Within these groups, subsets include unstable angina and non-ST elevation myocardial infarction. The differentiation between unstable angina and non-ST elevation myocardial infarction often relies on a biochemical cardiac marker—elevated cardiac troponin. Diagnostic procedures in emergency services and coronary wards encompass various methods such as clinical history and state assessment, EKG, laboratory testing for biochemical cardiac markers, cardiac and pulmonary x-rays, cardiac ultrasounds, and risk level evaluations (risk scores). Among these, biochemical cardiac markers are predominantly pivotal in acute coronary syndrome diagnosis. The Thrombolysis in Myocardial Infarction risk score, commonly utilized for risk assessment due to its simplicity, is used alongside other diagnostic tools, despite its comparatively lower predictive accuracy [36].

Table 1: Timeline of Biochemical Cardiac Markers after Acute Myocardial infarction

Markers	Time of detection	Peak	Return to Normal
Myoglobin	1-3 hours	6-9 hours	24 hours
CK-MB	3-6 hours	12-24 hours	2-3 days
Troponin	4-8 hours	12-24 hours	5-10 days
AST	6-12 hours	30 hours	2-6 days
LDH	24-72 hours	3-4 days	8-14 days

Discussion:

Biochemical cardiac markers play a crucial role in diagnosing and categorizing patients with acute coronary syndrome (ACS) and distinguishing them from those with abrupt heart failure, pulmonary embolism, and other conditions. These markers encompass indicators of myocardial necrosis (myoglobin, cardiac troponins I and T, and creatine kinase-MB [CK-MB] fraction), ischemia (ischemia-modified albumin), myocardial stress (natriuretic peptides), and prognostic or inflammatory markers (C-reactive protein [CRP], soluble CD40 ligand [sCD40L], and homocysteine). The consensus criteria of the American

College of Cardiology (ACC) and the European Society of Cardiology (ESC) largely define acute myocardial infarction (MI) by cardiac troponin levels. However, cardiac troponin markers are unable to detect myocardial ischemia in the absence of necrosis, leaving room for improvement in the early detection of acute coronary syndrome. Current recommendations emphasize examining biochemical cardiac markers when there's suspicion of myocardial infarction. B-type natriuretic peptide, amino-terminal proBNP, and high-sensitivity cardiac troponin are suggested markers aiding in the diagnosis and prognosis of patients with myocardial necrosis, ischemia, and stress related to acute coronary syndrome. However, ongoing research is essential to identify more reliable biochemical cardiac markers for enhanced diagnostic accuracy and prognostic value.

Conclusion:

Acute coronary syndrome (ACS) diagnosis made quickly is crucial for clinical decision-making on appropriate therapies that might enhance a patient's prognosis. Over the past ten years, biochemical cardiac markers for the diagnosis of acute coronary syndrome have grown increasingly sensitive. The most useful indicators for ruling in and ruling out acute coronary syndrome at this time are amino terminal proBNP. New biochemical markers must be found to supplement electrocardiograms and x-rays and offer more precise and sensitive techniques for detecting, classifying, and treating cardiovascular disorders.

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Authorship contribution statement:
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