JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2024, VOL 7, NO S8

The Importance of Testing Heart Enzymes

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Abstract:

Approximately 1.7 million people are admitted as the patients of chest pain and the destination is generally the emergency department of a hospital. Only a few of these patients are detected with Acute Coronary Syndrome (ACS), and the remaining are sent back without a diagnosis of cardiac parameters. Such chest pains are may result in sever cardiac arrests and the Cardiac Enzymes must be tested for any such patient. This present study evaluates the scenario with the help of popular and time framed reviews and will present a proper view for the point in question.

Keywords: Heart Enzymes, Cardiac issues, testing, diagnosis.

Introduction:

More than 1.5 million patients are hospitalized each year after presenting to the emergency department (ED) with chest pain. A very small proportion of these presentations have acute coronary syndrome (ACS), and a large proportion are discharged without a cardiac diagnosis. Chest pain is a common and widespread problem among patients. Chest pain is often a symptom of ischemic heart disease, but gender, age, and comorbidities can alter the presentation of coronary artery disease (CAD) in a patient. Severe chest pain can be life-threatening, but it is widely accepted that there are many different diagnoses, many of which are less healthy and more likely to have adverse effects. This is something that is increasing. **Amitava (2021)**

Therefore, it is necessary to evaluate the costs and benefits of a correct diagnosis to determine the best strategy for diagnosing myocardial infarction. Once myocardial infarction (MI) is identified, biomarkers of ischemia or inflammation, exercise electrocardiography (ECG) or computed tomography coronary angiography (CTCA), and anti-inflammatory or cardiovascular intervention are used voluntarily to determine the risk of future adverse events. Reduce the risk of adverse outcomes for those who test positive. ACS is often associated with chest pain and must be distinguished from other causes of chest pain, such as myalgia, abdominal pain, and stress. This distinction is difficult to make because the clinical examination is unreliable and the electrocardiogram may be normal in the presence of ACS. The group of patients suspected of having ACS is large and diverse; they often do not have ACS or CAD but have chest pain from a noncardiac cause. **Zaki et al (2022)** Therefore, ACS and coronary artery disease (CAD) must be

carefully analyzed to plan effective interventions. A good strategic decision must balance the benefit of reducing adverse events with the cost of further investigation and treatment.

Cardiac Enzymes:

Cardiac enzymes, also known as cardiac biomarkers, include myoglobin, troponin, and creatine kinase. Enzymes are proteins produced by the body that enhance chemical reactions. When the heart is injured, it releases certain enzymes. Historically, lactate dehydrogenase (LDH) has also been used, but it is not specific. **Alansari et al (2004); Coli et al (2007)** When myocardial necrosis occurs, as seen in myocardial infarction, cardiac enzymes are released into the blood vessels. Doctors determine if a person has heart disease by measuring cardiac enzymes, including troponin T (TnT) and troponin I (TnI). The most specific enzyme for heart disease. Heart disease occurs when blood flow to the heart is blocked. Blockages are usually caused by fat, cholesterol, and other substances that form plaque in the arteries that supply blood to the heart (coronary arteries). Elevated heart enzymes are an indication that a person is having a heart attack. Heart enzyme tests measure the levels of heart enzymes in a person's blood.

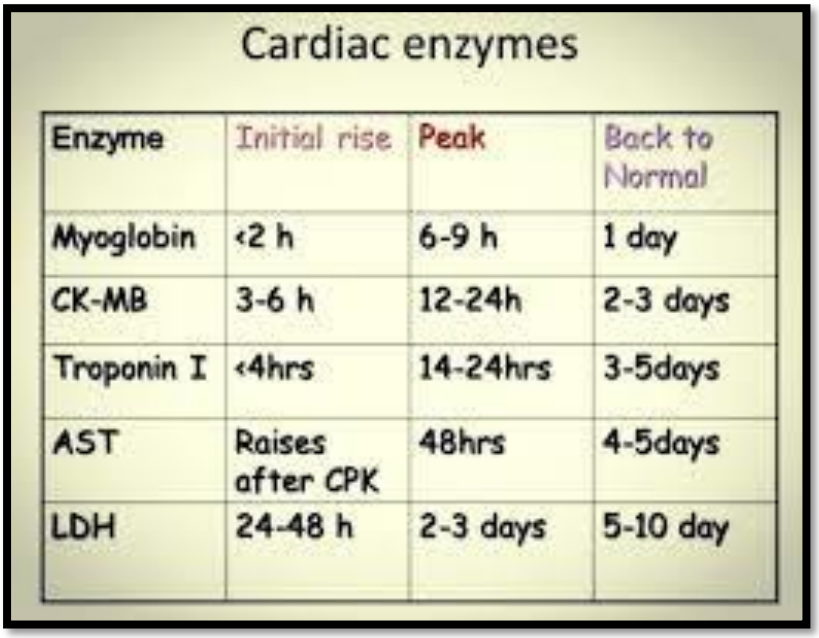

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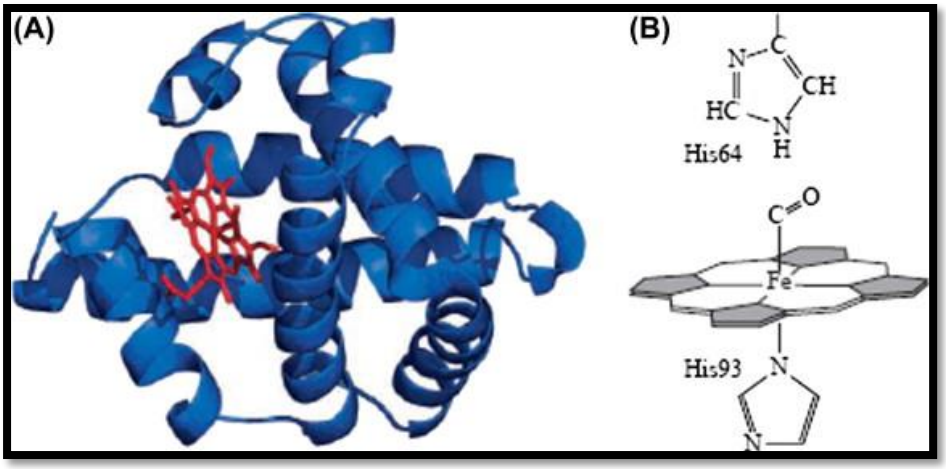
Figure 1: Flow of Cardiac Enzymes

Types of Cardiac Enzymes:

Myoglobin:

When muscle tissue is injured, including myocardial necrosis, myoglobin is released into the bloodstream. This test is not specific for MI because skeletal muscle contains myoglobin. The advantage of myoglobin is that the increase can be seen as early as 30 minutes after injury, while it takes 3 to 4 hours for troponin and creatine kinase. It is a naturally occurring protein that is important for muscle cell function. **Collinson et al (2003); Eggers et al (2004)**

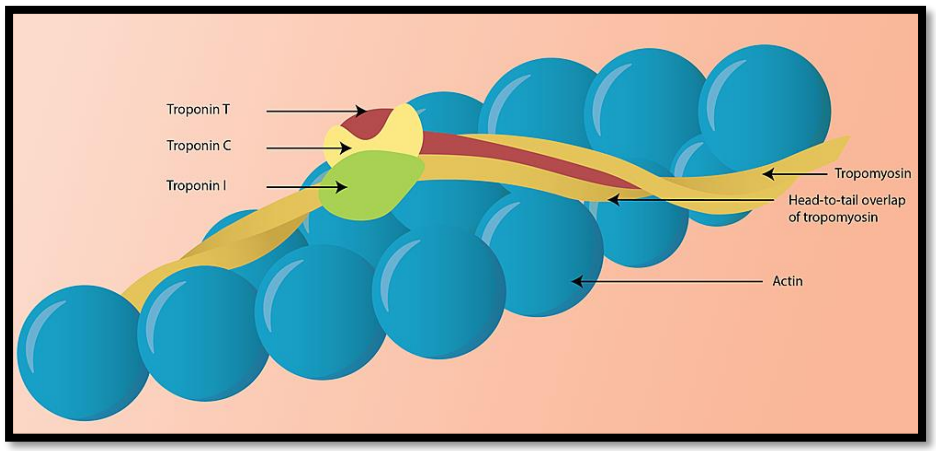


Source: Dasgupta (2021)

Figure 2: Myoglobin

Troponin:

It is a naturally occurring protein that is important for muscle cell function. These proteins are released into the bloodstream within 3 to 4 hours of a myocardial infarction and can still be detected for up to 10 days afterward. This long half-life allows for late diagnosis of myocardial infarction, but makes it difficult to detect reinfarction, such as stent thrombosis after percutaneous coronary intervention (PCI). There are many causes of elevated troponin that are not related to myocardial infarction, but elevated troponin, myoglobin, and even creatine kinase is more common than muscle enzymes.

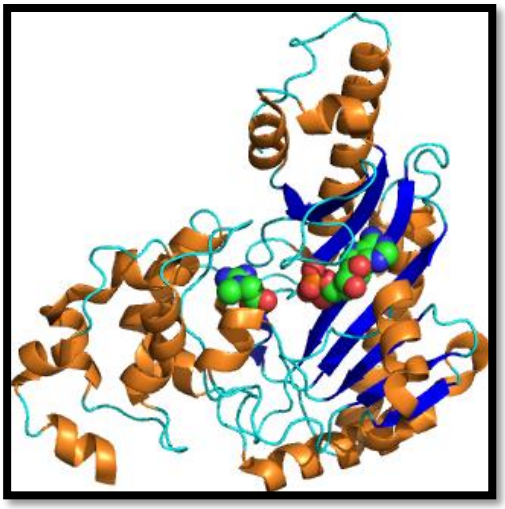


Source: Zaki et al (2022)

Figure 3: Elevated Troponin

Creatine kinase (CK):

The MB type is specific for cardiomyocytes, while the MM and BB are specific for skeletal muscle and brain, respectively. CK levels rise approximately 3 to 4 hours after MI and remain elevated for 3 to 4 days. This makes it useful for detecting recurrence within 4 to 10 days after the initial injury, when troponin remains elevated for 10 days, making it less useful for this purpose.



Source: https://en.wikipedia.org/wiki/Creatine_kinase

Figure 3: Creatine kinase

Research Process:

This present study is the review of various studies conducted in the past 5-10 years and analysis of the same in review form. Mostly the results are suited from the period of 2010-2021. We searched for relevant analyses by contacting experts to identify studies and studies comparing appropriate criteria [MI by definition, invasive coronary angiography (ICA) of CAD] or assessment methods (biomarkers, CTCA or exercise electrocardiography) for major negative adverse cardiovascular events (MACE) in patients with suspected ACS]. We divide our study into two parts. They include early biomarkers and sensitive biomarkers.

Discussion:

Early risk biomarkers:

Several systematic reviews have been conducted to investigate the diagnostic value and accuracy of troponin testing in suspected ACS. Other analyses were also performed to determine the accuracy of troponin, CK, CK-MB, and myoglobin. The results showed that troponin had the highest accuracy for MI. The diagnostic criterion for suspected ACS is measurement of troponin levels 10–12 hours after symptom onset. Alternative and valid biomarkers are available that may improve the diagnostic accuracy of cardiac troponin determinations and develop reference models. However, other biomarkers may have a role to play in overcoming two limitations of troponin measurement. First, because troponin has limited rapid sensitivity, there is potential for biomarkers that will improve the understanding of early myocardial infarction and improve care. Second, although a negative 10- to 12-hour troponin test indicates that a patient is at low risk for a negative outcome, it does not imply uncertainty. **Collinson et al (2013); Christ et al (2010)**

Therefore, surrogate biomarkers may play an important role in identifying additional risk factors for patients. The relative insensitivity of early cardiac troponin testing suggests that more information about patients with heart failure may be obtained by detecting small cytoplasmic proteins that leak across the membrane of ischemic myocytes. Myoglobin is a single-chain globular protein that may be an early marker of myocardial infarction. It has a prosthetic group

and is the main oxygen storage protein in muscle. One form of human serum albumin is ischemia-modified albumin, in which ischemia affects the N-terminal amino acid, thereby binding to iron transport. **Okrainec et al (2004); Alreshidan et al (2014)** Fatty acid-binding proteins are small proteins, 126–137 amino acids long. These proteins are found in tissues with active fatty acid metabolism, such as the heart, intestine, and liver. Heart-type fatty acid binding protein (H-FABP) is a myocardial isoform found predominantly in the heart, but is also found in other tissues such as skeletal muscle and kidney distal fallopian tube cells.

Myoglobin:

Myoglobin (molecular weight 16.7 KDa) is a single-stranded globular protein composed of heme prosthetic groups. Myoglobin is the main oxygen-carrying pigment in muscle tissue. It is also found in the cytoplasm and, due to its molecular weight, may be released earlier than other cytoplasmic biomarkers after cardiomyocyte necrosis. Some studies suggest that measurement of myoglobin may be an early marker of AMI. The kinetics of myoglobin measurement and comparison of its cardiac specificity with other markers suggest that measurement of myoglobin may be used in the early diagnosis of AMI, particularly in conjunction with other cardiac parameters. **Abid et al (2009); Hussain et al (2008)**

Creatine kinase MB isoenzyme:

Creatine kinase-MB (CK-MB) isoenzyme is a cardiac-specific isoenzyme of CK. It is found in the cytoplasm and accounts for 5-50% of myocardial CK, one of the earliest cardiac biomarkers. It is used for biochemical investigation of AMI. **Marzban et al (2008); Schwann et al (2007)** The well-designed and developed test for CK-MB is automated and forms the basis of the current method. One of the most established biomarkers of AMI is the measurement of CK-MB quality and is also accepted in the definition of MI. The advantage of this method is the earlier increase of CK-MB compared to cardiac troponin.

Fatty Acid-binding Protein (FABP) and other early:

The corresponding proteins, FABPs, are small proteins (15 DKa) containing 126–137 amino acids. These proteins are found in tissues involved in fatty acid metabolism, such as the heart, liver, and intestine. **Lehrke et al (2004); Soylu et al (2014)** They reversibly bind long-chain fatty acids, thereby increasing their intracellular translocation. Nine types of FABPs have been identified, each with unique tissue distribution patterns and half-lives of 2–3 days. H-FABP is a myocardial isoform found primarily in the heart but also in other tissues such as skeletal muscle and renal arteries. Several studies have investigated the role of H-FABP in the diagnosis of MI. H-FABP may be an early cytoplasmic marker of myocardial ischemia and myocardial injury.

In addition to measuring cardiac troponins, other markers of the atherothrombotic process can be measured to allow early diagnosis. Markers of atherosclerotic plaque instability or rupture have been suggested and are presumed to be related to the plaque itself [myeloperoxidase (MPO), matrix metalloproteinases, and pregnancy-associated plasma protein A (PAPP-A)]. (BNP) N-terminal pro-B-type natriuretic peptide (NT-pro-BNP), copeptin, and adrenomedullin are also used. A systematic review of 22 novel biomarkers, including CRP, MOP, BNP, and H-FABP, showed that there is insufficient evidence to support the usefulness of these biomarkers in the ED assessment of ACS. In addition to this review, additional studies have been conducted to evaluate the diagnostic and predictive validity of other biomarkers. **Nesher et al (2008); Croal et al (2006)**

Therefore; The purpose of this study was to investigate the role of early biomarkers in identifying MI 10–12 hours earlier and the role of surrogate biomarkers in assigning additional risk to troponin-negative patients with suspected ACS. High-sensitivity troponins and surrogate biomarkers are cardiac troponins derived from the troponin-tropomyosin complex, which is part of the cardiac contractile apparatus and includes three troponins [troponin C, troponin I (TnI), and troponin T (TnT)] and tropomin. Preliminary studies suggest that measurement of cardiac troponin is more sensitive and specific for myocardial injury than previously used biomarkers. The currently recommended biomarkers for MI are TnT or TnI. **Ramsay et al (2005)**

The initial redefinition of acute myocardial infarction suggested that the diagnostic uncertainty of the test should allow for measurements with lower analytical uncertainty in its recent use. Surveillance over the past few years has not followed this established pattern, and this has led to continued improvements in the quality of surveillance until the current generation of highly sensitive troponin assays. **Shams et al (2014); Rosalki et al (2016)**

High-sensitivity troponin assays can measure troponin in healthy individuals, but the assay has a high sensitivity, typically less than 10% in 99% of users. In addition to the quality features listed in the quality specification, the new sensitive detection method can detect myocardial injury earlier than previous-generation detection methods based on the definition of acute myocardial infarction. Improvements in the diagnostic performance of troponin assays suggest that second- and third-order assays are beginning to outperform other markers of myocardial injury, such as myoglobin and CK-MB. In addition, studies of the new tests have shown that they are more effective than other markers of myocardial damage.

Troponin:

Troponin should be measured at least 10-12 hours after the onset of symptoms using the 99 high-risk threshold test. It helps identify true myocardial infarction and identify patients at high risk for adverse outcomes. It can also help patients benefit from hospital treatment. However, patients who expect delayed diagnosis are now being admitted to hospital 10-12 hours after the onset of symptoms. This delay increases the cost of healthcare and harms patients. Early diagnosis may reduce costs by allowing patients to be discharged earlier, but the benefit of treating myocardial infarction will be lost when the prognosis is best. A sensitive troponin test alone or in combination with other biomarkers can detect MI 10–12 hours earlier.

However, the cost savings of this approach should be weighed against its benefits; in other words, the additional benefits of 10–12-hour troponin sampling should be weighed against the additional costs. Given that the risk is not negligible, it would be useful to evaluate other biomarkers that may predict increases in troponin levels. Troponin-negative patients can also be screened with exercise electrocardiography or CTCA to identify patients with CAD, and patients at high risk for adverse outcomes may benefit from coronary intervention and treatment. Therefore, in selecting patients who require hospitalization, it is necessary to evaluate the accuracy of exercise ECG and CTCA for CAD, the accuracy of exercise ECG and CTCA for MACE, and the utility of exercise ECG or CTCA.

Diagnostic studies troponin:

This study identified diagnostic studies for TnI and TnT. Different inclusion and exclusion methods were used in both studies assessing TnI and TnT, and many studies excluded patients with

electrocardiograms. The prevalence of MI ranged from 5% to 73% and was very high, suggesting that patients may have been affected by inappropriate selection criteria. The time from symptom onset ranged from 1.2 hours (mean) to 6 hours (median). The data show that many studies used different measurements for assessment; however, the data in this study are based on the 99th percentile, 10% coefficient of variation (CV), and limit of detection (LoD). In all these studies, the standard definition of MI was used and, in most studies, the results of the troponin test were also used. In cases where troponin was used as a reference standard, the standard (i.e. less sensitive) test using the 10% CV or 99% pain test was used.

However, in the study by Jesus et al., the standard based on high-sensitivity TnT (HsTnT) was used together with the standard test (30). The data in this study were collected using standard test methods. These studies are generally well performed and our selection does not include lower quality studies. Troponin expression is clearly not independent of the troponin-based standard, so the negative test is focused on whether the troponin standard and the troponin standard are measured differently in the same standard. There is some uncertainty about whether the scale and reference standards are blind. This does not seem to have an impact on the publication of the index, as this is usually done by a mechanical process that produces a lot of values.

Description of diagnostic studies of other biomarkers:

This study also identified other biomarkers for diagnostic studies. The prevalence of MI was lower in troponin, H-FABP, and myoglobin studies, ranging from 5% to 29%. The median time from onset of symptoms to 2 to 4.5 hours. Most studies use routine troponin tests with acceptable standards. Research studies using biomarkers in combination with troponin: Many studies have compared the sensitivity and specificity of biomarkers alone in combination with troponin. Since no combination was evaluated in our study, we did not use any analysis. If both tests are positive, troponin and the surrogate biomarker are combined and classified as positive. However, the combination is considered positive only if both tests are positive.

Therefore, in most studies, the specificity of the combination is higher and the specificity lower than troponin alone, while the combination has lower sensitivity and higher specificity than troponin alone. The results of these studies suggest that the combination of troponin and another biomarker may lead to an increase in sensitivity, with elevation of the biomarker leading to a positive diagnosis, but may lead to a decrease in specificity. None of these analyses used high troponin levels. Results from a troponin meta-analysis suggest that similar conversion rates can be achieved at the expense of specificity if a lower troponin positivity threshold is used. Studies have evaluated the accuracy of troponin in diagnosing MI at the onset of symptoms and compared it with the recommended method based on delayed troponin testing.

Several studies have evaluated the accuracy of troponin in diagnosing MI and have provided results comparable to commonly used criteria based on delayed troponin testing. Many of these studies have used troponin as an indicator or standard, and data from different studies are difficult to compare and synthesize due to the initial values and specificity varies between the study and the population, but it can be concluded that using lower and higher tests may lead to a better understanding of specificity.

It is unclear whether the loss of specificity reflects the need for specificity, as demonstrated by reduced positivity for a negative test, or whether the false positive rate (FP) is of true quality (TP) due to inadequate handling of samples and they are misclassified. This study provides additional

data to help determine whether troponin is an inferior predictor of presentation compared with high-sensitivity standards. The majority of post-MI complications are identified by the standard 10-hour troponin test, but these estimates are not completely reliable, and troponin tests are frequently missed for MI complications. The decision to perform 10-hour troponin testing will depend on the costs and benefits of additional data testing, which can be analyzed in detail in the financial analysis.

Conclusion:

The cause of heart failure and sudden death in stroke patients is often problematic. Plaque rupture due to concurrent coronary artery disease and stroke-related factors may also be a cause. The ultimate goal is to clearly distinguish neurogenic from cardiogenic effects using serologic markers. Our study resolves this issue by demonstrating that CK-MB is not suited for this role. Dr. Kasap and Dr. Parsons outlined directions for future research in this area. We agree with everyone, but we would like to add that other cardiac enzymes such as troponin should also be checked. In addition, these studies should be able to identify high levels of enzymes with more accurate golden criteria for neurogenic heart damage. Finally, they should not only find patients with systemic disease, but also unselected patients with multiple infarct patterns, because the significance of their results will be more meaningful for stroke patients.

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