Early Diagnosis of Acute Myocardial Infarction (Heart Attack): Immunoassay for Serum Troponin Marker

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ABSTRACT

Background: Heart disease is a common and debilitating condition that affects millions of patients globally. Measurement of troponin assays has been a tremendous boon to clinical diagnosis. Objective: To evaluate the clinical utility and the biochemical characteristics of serum troponin as an early and accurate cardiac marker for diagnosis of acute myocardial infarction. Method: a review of serum troponin as choice biomarker for diagnosis of Acute Myocardial Infarction (AMI). Result: Troponin T allows for early and late diagnosis of AMI. Troponin is only found in the myocardium in adults making it extremely specific for cardiac disease. Troponin I or T is replacing total CK and CK-MB detection as the marker of choice for cardiac dysfunction as seen in AMI. Conclusion:
There is value in detection myocardial damage early after its onset. Clinical laboratories should move rapidly to implement the new cardiac troponin standard for the early and accurate diagnosis of AMI.

Key Words: AMI, Troponin, Cardiac Marker, Early diagnosis.

INTRODUCTION

Cardiovascular diseases are the leading cause of death globally. Cardiovascular disease includes coronary artery disease (CAD) such as angina and myocardial infarction commonly known as a heart attack. The World Health Organization has established three criteria for the diagnosis of acute myocardial infarction (AMI) including a history of chest pain, evolutionary changes on the ECG, and elevations of serial cardiac markers [2] however it was rare for a diagnosis of AMI to be made in the absence of biochemical evidence of myocardial injury. [3]. Numerous biomarkers have been monitored to assess myocardial injury. Most are myocardial proteins and differ in their location within the myocyte, release kinetics after damage and clearance from the circulation [4]. The European Society of Cardiology/American College of Cardiology of Cardiology (ESC/ACC) has published consensus guidelines for the diagnosis of AMI [5,6,7]. A cornerstone of the consensus document is predicated on cardiac biomarker especially cTnI or CTnT [8,9]. Because of its dire consequence, great efforts have been made to determine the best tools for the early and accurate diagnosis of AMI. Therefore, this article aimed at assessing some cardiac markers that could provide an early and accurate diagnosis for acute myocardial infarction.

Myocardial infarction (MI)

Acute myocardial infarction is one of the largest killers globally. Its diagnosis is usually made on the clinical presentation and electrocardiographic (ECG) findings and confirmed by the characteristic changes in plasma enzyme activities or troponin levels. Symptoms and ECG abnormalities however may be absent or non-specific. Thus, the diagnosis of an acute MI has increasingly depended upon evaluation of Cardiac biomarkers particularly troponins [10,11]. Acute myocardial infarction is defined as an imbalance between myocardial oxygen supply and demand resulting in injury and the eventual death of myocyte. When the blood supply to the heart is interrupted, gross necrosis of myocardium results. Such extensive necrosis is most often associated with a thrombotic occlusion superimposed on coronary atherosclerosis. Myocardial infarction is seen as a spectrum of disease ranging from angina pectoris through to acute myocardial infarction; this stratification is based upon cardiac markers reflecting ischemic damage. [12,13]. Myocardial ischemia and infarction are usually segmental diseases. The American College of Cardiology and European Society of Cardiology have defined acute myocardial infarction as a typical rise and fall of biochemical marker, for example plasma creatine kinase isoenzyme MB.
(CK-MB) or troponin, with at least one of the following: Ischemic symptoms, new pathological Q waves, on electrocardiogram (ECG), ischemic ECG changes (ST depression or elevation) and coronary artery intervention [14]

The patients previously classified as having unstable angina or minor myocardial injury are now reclassified as having non-ST segment elevation myocardial infarction (NSTEMI), therefore myocardial infarction is now regarded as a spectrum of disease ranging from angina pectoris through to acute myocardial infarction. Acute myocardial infarction and NSTEMI have a common pathophysiological pathway (15)

**Cardiac markers**

Cardiac markers are biomarkers measured to evaluate heart function. They are clinical laboratory tests useful for detecting AMI or minor myocardial injury. They are most useful when patients have non-diagnostic ECG tracings.

Most efforts to date have been placed on the development of an ideal cardiac marker for the early and accurate diagnosis of AMI. Many factors must be considered in the selection of the most clinically diagnostic effective, cost effective and cost efficient laboratory tests for patients with chest pain which include:

1. the time that has elapsed after onset of chest pain;
2. Any concomitant diseases;
3. The possibility of skeletal muscle injury
4. The ease of measurement and turn around time for results.
5. Assay specificity, sensitivity and interferences. (17, 18)

Serum enzymes such as aspartate aminotransferase (AST), Creatine Kinase (CK), Lactate dehydrogenase (LD) and their iso enzymes have all been used as biomarkers of AMI. Decades ago they were thought to be sensitive indicators of myocardial necrosis and could be used to correlate with other signs and symptoms such as abnormalities in ECG pattern [19,20] All three of these enzymes, however are found in other tissues as well, making them less specific to myocardial damage. AST for example is also found in skeletal muscle, liver parenchyma cells, and erythrocytes, while CK is found in skeletal muscles, brain tissue and embryonic and malignant tissue. LD is the least specific of these three enzymes in that it is found in virtually all tissues and is associated with damage to liver, skeletal muscle, cardiac muscle, erythrocytes renal cells and many other tissues as well as ovarian and testicular tumors. [21] Historically myocardial infarction was detected by looking for the CK Iso enzyme CK-MB. This marker is released into circulation from necrotic heart muscle. As the heart muscle becomes damaged this CK Isoenzyme is released into the blood stream and may be detected.
Cardiac proteins

Several proteins may be monitored in suspected cases of AMI to give significant diagnostic information. Myoglobin, an oxygen-binding protein, is rapidly released from striated muscles (both skeletal and cardiac muscle) when damaged. However, because of its small size, myoglobin is rapidly cleared by the kidney, making it an unreliable long-term marker of cardiac damage. Myoglobin is significantly more sensitive than CK and CK-MB activities during the first hours after chest pain onset. It starts to rise within 1-4 hrs and is detectable in essentially all AMI patients between 6 and 9 hours from chest pain onset, returning to baseline levels within 18-24 hours. If myoglobin concentration remains within the reference range 8 hours after onset of chest pain, AMI can essentially be ruled out. Myoglobin is released into circulation with any damage to muscle tissue, including myocardial necrosis. Since skeletal muscle contains myoglobin, this measurement is quite non-specific for myocardial infarctions. The benefit lies in the fact that a detectable increase is seen only 30 minutes after injury occurs, unlike troponin and creatine Kinase which can take 3-4 hours. Troponin I and troponin T are normal proteins important in the contractile apparatus of the cardiac myocyte. They are released into the circulation about 3-4 hours after myocardial infarction and are still detectable for 10 days afterwards. The long half-life allows for the late diagnosis of myocardial infarction. All of the initial cardiac markers were enzymes, so the earliest techniques measured the catalytic activity of the marker. Immunoassay techniques measure the mass of a marker and they are the predominant methodology used in clinical laboratory practice today. Analytically, they offer lower limits of detection, improved precision, and faster assay time on both highly automated central laboratory Platforms and Point of Care Testing (POCT). Over the past 15 years, numerous manufacturers have described the development of monoclonal antibody-based diagnostic immunoassays for the measurement of troponins (CTnI and CTnT) in serum. Troponin assays have been a tremendous boon to clinical diagnosis. Troponins released from heart muscle remain in the bloodstream for up to 10-14 days after onset of AMI, making them preferred marker for detection of an AMI. Troponins as cardiac markers appear to have many advantages primarily due to their quick release following heart muscle damage.

Recommendations

The National Academy of clinical Biochemistry recommends that two biochemical markers be used for routine diagnosis of AMI: an early marker that is reliably increased within 6 hours after onset of symptoms and a definitive marker that remains increased after 6-9 hours but has high sensitivity and specificity for myocardial injury and remains abnormal for several days. To assist in differentiating patients with AMI from non-AMI, the European Society of
cardiology/American College of cardiology (ESC/ACC) has published consensus guidelines for redefinition of AMI [34]. A cornerstone of this is predicated on cardiac biomarkers, especially CTnI or CTnT. The cardiology recommendations imply that for clinical laboratories that cannot move as rapidly as others to implement the new cardiac troponin standard, CK-MB (Preferable mass should be used. Although it is suggested that CK-MB be used together with cardiac troponin for assisting in timing the onset of myocardial injury, infarct sizing or determination of reinfarction at present there is no strong evidence to support dual testing for cTn and CK-MB.

Conclusion

The diagnosis of acute myocardial infarction can be difficult, but it is important to make prompt diagnosis as thrombolysis needs to be given early. The diagnosis of an acute myocardial infarction has increasingly depended upon evaluation of cardiac biomarker particularly troponins. Troponins are more specific cardiac marker than the CK. Also, plasma troponin stays elevated for longer than CK after an infarct. Troponins are therefore useful for the late diagnosis of myocardial infarction. Clinical Laboratories should move rapidly to implement the new cardiac troponin standard for the early and accurate diagnosis of myocardial infarction.

Table I. The time sequence of changes in plasma cardiac markers after myocardial infarction

<table>
<thead>
<tr>
<th>Cardiac marker</th>
<th>Starts to rise (hours)</th>
<th>Time after Infarction for peak rise (hours)</th>
<th>Duration of rise (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK (total)</td>
<td>4-6</td>
<td>24-48</td>
<td>3-5</td>
</tr>
<tr>
<td>AST</td>
<td>6-8</td>
<td>24-48</td>
<td>4-6</td>
</tr>
<tr>
<td>LDH/HBD</td>
<td>12-24</td>
<td>48-72</td>
<td>7-12</td>
</tr>
<tr>
<td>MYOGLOBIN</td>
<td>2-4</td>
<td>12-24</td>
<td>2-4</td>
</tr>
<tr>
<td>TROPONIN</td>
<td>4-6</td>
<td>12-24</td>
<td>7-10</td>
</tr>
</tbody>
</table>

CK= Creatine kinase; AST= aspartate transaminase

LDH= lactate dehydrogenase; HBD= Hydroxybutyrate dehydrogenase

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