Clinical Practice Assessment

Use of Troponin to Rule Out a Myocardial Infarction

Clinical Question:
What is the minimal amount of time to rule out Myocardial Infarction using serial troponin I measurements?

Bottom Line:
An undetectable highly sensitive troponin I (below the level of detection of the assay) on admission in patients presenting with chest pain is effective in ruling out myocardial infarction (MI).

When any detectable troponin is noted on admission, then serial measurements of a highly sensitive Troponin I (hsTnI) or contemporary/standard Troponin I (cTnI) on admission and three hours later had a Negative Predictive Value of 99% (rule out MI).

Synopsis:
Symptoms of myocardial ischemia are non-specific. To accurately diagnose acute myocardial infarction a combination of symptoms, EKG changes and biomarkers are used.

Cardiac troponins (I and T) are structural proteins specific to the heart. They are sensitive and specific markers of myocardial damage. In addition to cardiac ischemia, however, troponin levels can be elevated in conditions such as myocarditis and heart failure and hence continued clinical assessment and serial changes in the level of troponin I are required to diagnose myocardial infarction and to rule out other causes of troponin elevation.

Unstable angina by definition is not associated with troponin elevation. A value of troponin greater than the 99th percentile of a normal population is labeled high. This level of detection needs to be determined for each specific type of assay with appropriate controls. A coefficient of variation <10 % is considered optimal. Troponins (I and T) have also been shown to be superior to other markers of cardiac ischemia, such as Creatine Kinase (CK) and Creatine Kinase – MB (CK-MB).

The early diagnosis of acute myocardial ischemia is critical in initiating appropriate therapy to limit myocardial damage and decrease mortality and morbidity. Ruling out myocardial ischemia early could help with appropriate risk stratification of the patient and avoid unnecessary testing and treatment and the exposure to potential side effects from these tests and treatments.
Current recommendations are to obtain cardiac markers on patients presenting with symptoms suggestive of myocardial ischemia on admission and repeating levels 6-9 hours later. If initial levels are not high, but there remains a strong clinical suspicion, levels could be repeated between 12-24 hours (1). In this prospective study 1818 patients (between the ages of 18-85 years) were enrolled between January 2007 and December 2008 at three centers in Germany (2).

Exclusion criteria were:
1. Pregnancy
2. Recent trauma or surgery (within four weeks)
3. Anemia (hemoglobin less than 10 g/dl) or
4. Intravenous drug use.

Evaluation and diagnosis of myocardial ischemia was determined by review of all available data by two cardiologists who were blinded to the investigational biomarkers. A third cardiologist acted as referee if there was disagreement between the two primary cardiologists. Myocardial ischemia was diagnosed based on the clinical symptoms, electrocardiographic changes, imaging evidence of myocardial ischemia or identification of a culprit lesion on coronary angiography. In addition there had to be at least one troponin elevation above the 10% imprecision cutoff of the in-house troponin assay (which was different at the three centers). Blood was drawn for measurement of hsTnI and cTnI on patients presenting with chest pain at all three centers. The technicians processing the samples were blinded to the results.

A negative highly sensitive troponin I (below the level of detection of the assay) had negative predictive value of 100% at admission in patients presenting with symptoms of chest pain. In other words an undetectable highly sensitive troponin I on presentation ruled out myocardial infarction. While any detectable level of hsTnI had a sensitivity (positive in disease) of 100% on admission, the specificity was only 35% (meaning that using this result alone as criteria for diagnosis of MI, then 65% of patients would be falsely diagnosed with MI).

If a value greater than the 99th percentile of a normal population was used to define troponin elevation (abnormal result), then the serial measurements of hsTnI and cTnI on admission and at three hours were comparable in ruling out MI.
### Use of Troponin Assays to Rule Out a Myocardial Infarction

<table>
<thead>
<tr>
<th>Assay</th>
<th>cTnI</th>
<th>cTnI</th>
<th>cTnI</th>
<th>cTnI</th>
<th>hsTnI</th>
<th>hsTnI</th>
<th>hsTnI</th>
<th>hsTnI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>ADM</td>
<td>ADM</td>
<td>3H</td>
<td>3H</td>
<td>ADM</td>
<td>ADM</td>
<td>3H</td>
<td>3H</td>
</tr>
<tr>
<td>Test cut off</td>
<td>&gt;LOD</td>
<td>&gt;99&lt;sup&gt;th&lt;/sup&gt; P</td>
<td>&gt;LOD</td>
<td>&gt;99&lt;sup&gt;th&lt;/sup&gt; P</td>
<td>&gt;LOD</td>
<td>&gt;99&lt;sup&gt;th&lt;/sup&gt; P</td>
<td>&gt;LOD</td>
<td>&gt;99&lt;sup&gt;th&lt;/sup&gt; P</td>
</tr>
<tr>
<td>SENSITIVITY</td>
<td>87.4  (83.3-90.8)</td>
<td>79.4  (74.6-83.7)</td>
<td>98.8  (96.9-99.7)</td>
<td>98.2  (96-99.3)</td>
<td>100   (98-100)</td>
<td>82.3  (77.3-86.5)</td>
<td>100   (98-100)</td>
<td>98.2  (95.9-99.4)</td>
</tr>
<tr>
<td>SPECIFICITY</td>
<td>88.6  (86.6-90.4)</td>
<td>94.5  (93-95.7)</td>
<td>78.9  (76.4-81.3)</td>
<td>89.8  (87.8-91.5)</td>
<td>35.3  (32.3-38.4)</td>
<td>92.1  (90.3-93.7)</td>
<td>1.9   (1.2-3)</td>
<td>90.4  (88.4-92.2)</td>
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<tr>
<td>PPV</td>
<td>69.3  (64.6-73.8)</td>
<td>80.9  (76.2-85.1)</td>
<td>58    (53.8-62.2)</td>
<td>73.9  (69.5-78)</td>
<td>30.8  (27.8-33.9)</td>
<td>75.1  (69.9-79.8)</td>
<td>22.7  (20.4-25.2)</td>
<td>74.7  (69.9-79)</td>
</tr>
<tr>
<td>NPV</td>
<td>96    (94.6-97.1)</td>
<td>94    (92.4-95.3)</td>
<td>99.5  (98.8-99.9)</td>
<td>99.4  (98.7-99.8)</td>
<td>100   (98.4-100)</td>
<td>94.7  (93.1-96.1)</td>
<td>100   (75.1-100)</td>
<td>99.4  (99.4-99.8)</td>
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<tr>
<td>No pos/total</td>
<td>411/1430</td>
<td>302/1430</td>
<td>555/1430</td>
<td>433/1430</td>
<td>915/1260</td>
<td>309/1260</td>
<td>1241/1260</td>
<td>371/1260</td>
</tr>
</tbody>
</table>

**ABBREVIATIONS:**
ADM: Admission.
LOD: Level Of Detection.
99<sup>th</sup> P: 99<sup>th</sup> percentile.
PPV: Positive predictive value.
NPV: Negative predictive value.

**References:**
   Level: 2.

Originated: 5/12/12