Update on the use and reporting of high-sensitivity cardiac troponins

The pivotal role of cardiac troponins in the diagnosis of acute myocardial infarction (AMI) was established in 2000 with the redefined MI definition of the joint panel of the European Society of Cardiology (ESC), American College of Cardiologists (ACC) and the American Heart Association (AHA). High-sensitivity cardiac troponin (hsTn) assays now comply with the prerequisite imprecision (percentage coefficient of variation or %CV) of ≤ 10% at the 99th percentile of a healthy population.

While the increased sensitivity of the newer assays enables an earlier diagnosis of MI, a more reliable rule-out of MI and a shortening of chest pain triage (to 4 hours), it is associated with decreased specificity (increased number of false positives) for MI, as hsTn levels may be mildly increased in a number of other clinical settings.

The Ethics and Guidelines Standing Committee of the South African Heart Association convened a meeting in May 2012 to provide guidelines for the use and standardised reporting of hsTn assays. Even though the currently available troponin I methods do not comply with all the specifications for “high-sensitivity” assays, they nevertheless provide adequate sensitivity and reproducibility with a %CV <20% at the 99th percentile, and therefore have been included in the guidelines for the use of hsTn’s.

Main recommendations and changes to be implemented:

- High-sensitivity cardiac troponin (TnI/TnT) is the preferred biochemical marker for the diagnosis of AMI, replacing previously used biomarkers such as myoglobin, CK-MB and troponin assays with an imprecision of >20% at the 99th percentile, and therefore have been included in the guidelines for the use of hsTn’s.
- Troponins should never be seen in isolation, but interpreted in the clinical setting of chest pain and accurate ECG interpretation. The use of risk algorithms, e.g. Thrombolysis in Myocardial Infarction (TIMI) or Global Registry of Acute Coronary Events (GRACE), are encouraged.
- The diagnosis of ST elevation myocardial infarction (STEMI) is made by typical ECG findings in patients with a suggestive clinical presentation, and not by the elevation of troponins. Treatment must be initiated immediately and should not be delayed until Tn results are available.
- The diagnosis of non-ST elevation myocardial infarction (NSTEMI) is confirmed by a troponin above the MI rule-in level (according to WHO criteria) i.e. >100 ng/l for hsTnT – please refer to Table 1 and Troponin algorithms. Apart from MI, the following causes of acute myocardial damage can also cause Tn elevation above this level: pulmonary embolism, myocarditis, Takotsubo cardiomyopathy, shock, congestive cardiac failure (CCF) and subarachnoid haemorrhage.
- Troponin results above the 99th percentile but below the MI rule-in level (15-100 ng/l for hsTnT) should be repeated after three hours to show a significant change for the diagnosis of acute myocardial damage/AMI.
- A significant change is regarded as a 50% change in a follow-up hsTnT sample for values from 15 to 52 ng/l or 20% change for values from 53 to 100 ng/l. A 50% change should be regarded as significant in the case of troponin I.
- A stable increase in troponin level (hsTnT 15–100 ng/l with insignificant percentage of change) occur in chronic cardiomyocyte damage, e.g. due to CCF.

Table 1: List of contemporary sensitivity troponin assays with relevant cut-off values (ng/L):

<table>
<thead>
<tr>
<th>Assay</th>
<th>99th percentile (upper limit of normal)</th>
<th>MI rule-in level (using WHO criteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche hs TnT</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Abbott ARCHITECT TnI</td>
<td>28</td>
<td>300</td>
</tr>
<tr>
<td>Beckman AccuTnI</td>
<td>40</td>
<td>500</td>
</tr>
<tr>
<td>Siemens Centaur Ultra TnI</td>
<td>40</td>
<td>600</td>
</tr>
<tr>
<td>Siemens Dimension RxL TnI</td>
<td>70</td>
<td>600</td>
</tr>
<tr>
<td>Siemens Stratus CS TnI</td>
<td>70</td>
<td>600</td>
</tr>
</tbody>
</table>

Please contact your local pathologist for more information.
severe hypertension, atrial fibrillation, hypertrophic cardiomyopathy, chronic renal failure, hypothyroidism and diabetes, as well as in the elderly.

- **NSTEMI is excluded** after two measurements taken at least three hours apart that remain negative or show an insignificant change or if a value reliably six hours following the onset of chest pain is negative.
- **Unstable angina** may require admission, even though hsTn levels remain normal.
- The previous 4th-generation troponin T was replaced by the currently available hsTnT method during November 2010 in Ampath laboratories. The new hsTnT assay reads 23 ng/l higher for values below 100 ng/l, and it was therefore initially decided to use a 50 ng/l cut-off for hsTnT which was equivalent to the previously reported cut-off of 30 ng/l, to minimise confusion due to false positive results. Consensus guidelines on the interpretation of borderline results (15–50 ng/l) were not available at that time.
- The **high-sensitivity (quantitative/laboratory) TnT method** should be distinguished from the semi-quantitative/point-of-care method for TnT, which only provides quantitative/absolute values above 100 ng/l. A semi-quantitative result of 50–100 ng/l is reported for values below 100 ng/l and a value of < 50 ng/l for lower values.
- **Troponin I** is not standardised among different manufacturers, and therefore the cut-offs are different for different methods (refer to Table 1 and troponin I algorithm). The listed troponin I methods comply with the minimum requirement of a < 20% CV at the 99th percentile of a reference population and provide comparable clinical accuracy to hsTnT in the acute coronary syndrome (ACS) setting and can be used instead of hsTnT.

**Proposed algorithm for workup of suspected acute coronary syndrome (ACS):**

For **Troponin I:**

1. **1st sample**
   - Tnl<99th percentile
   - Tnl value between 99th percentile and MI cut-off
   - Tnl above MI cut-off

   - Pain duration > 6 hr
     - Discharge
   - Pain duration < 6 hr
     - Follow up sample after 3 hr
       - <50% change
         - Discharge
       - >50% change
         - Admit

   - Follow up sample after 3 hr
     - <50% change
       - Discharge
     - >50% change
       - Admit

For **hsTroponin T:**

1. **1st sample**
   - hsTnT <15 ng/l
   - hsTnT 15–52 ng/l
   - hsTnT 53–100 ng/l
   - hsTnT >100 (MI cut-off)

   - Pain duration > 6 hr
     - Admit
   - Pain duration < 6 hr
     - Follow up sample after 3 hr
       - <50% change
         - Discharge
       - >50% change
         - Admit
       - >20% change
         - Discharge

• **Change** is defined as a rise or fall.
• **Admit**: Admit and treat for ACS.
• **Discharge**: May include symptomatic treatment, stress test or investigations for other causes of chest pain.

**References:**