Troponins: Current Status in Coronary Artery Disease

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Abstract

The acute coronary syndromes (ACS) represent a pathological, diagnostic and risk continuum from unstable angina (UA) through myocardial infarction (MI) with or without ST segment elevation. The past 12 years have seen extensive investigations into the use of various cardiac markers to establish the diagnosis and prognosis in ACS and to evaluate perfusion after thrombolysis. The Troponins comprise a group of three proteins (C, I and T) which interact with tropomyosin to form a troponin-tropomyosin complex. Troponin-T is a structural component of the troponin complex and is known to exist in three isoforms. Troponins have both diagnostic, post-event risk stratification and prognostic significance. Apart from myocardial infarction however they are raised in several conditions like Myocarditis, dilated Cardiomyopathy, Severe congestive cardiac failure, severe pulmonary embolism with right ventricular strain and Preterm infants with respiratory distress. False positives have been reported with Angioplasty, cardiac surgery, RF ablation, Allograft rejection following cardiac transplant and seropositive rheumatoid arthritis. False negatives have been reported with early sampling, early reading, use of wrong anticoagulant, clotted blood, careless storage of kits. Significantly, lower troponin values have been reported in heparinised plasma than in serum.

The acute coronary syndromes (ACS) represent a pathological, diagnostic and risk continuum from unstable angina (UA) through myocardial infarction (MI) with or without ST segment elevation. The management strategies and outcomes of patients who present with symptoms of acute coronary ischemia depends upon where they fall in this spectrum.

The past 12 years have seen extensive investigations into the use of various cardiac markers to establish the diagnosis and prognosis in ACS and to evaluate perfusion after thrombolysis. The following part of this communication deals with such a cardiac marker namely, the cardiac troponins.

The troponins comprise a group of three proteins (C, I and T) which interact with tropomyosin to form a troponin-tropomyosin complex. Troponin-T is a structural component of the troponin complex and is known to exist in three isoforms. The biochemical differences are highlighted in Table 1.

Table 1: Characteristics of troponins

<table>
<thead>
<tr>
<th>Feature</th>
<th>cTnT</th>
<th>cTnI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (kDa)</td>
<td>33</td>
<td>23.5</td>
</tr>
<tr>
<td>Cardiac Specific</td>
<td>+++*</td>
<td>+++</td>
</tr>
<tr>
<td>Affected by renal function</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Initial detection</td>
<td>4 - 6 hrs</td>
<td>4 - 6 hrs</td>
</tr>
<tr>
<td>Duration of elevation</td>
<td>10 - 14 days</td>
<td>7 - 10 days</td>
</tr>
<tr>
<td>Cytoplasmic pool</td>
<td>6%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Rapid laboratory assay</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bedside assay</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Extremely specific

**Noninvasive detection of reperfusion after thrombolytic therapy**

Abe et al.6 studied the ability of cTnT and CK-MB to predict patency in patients undergoing reperfusion therapy with either angioplasty / thrombolytic therapy within seven hours of symptom onset. Reperfusion status was determined by comparing angiograms done pre and postprocedurally. 100% sensitivity, specificity
Diagnosis of non ST-segment elevation MI

cTnT is reported to have a lower specificity for acute MI in UA populations. A number of studies have evaluated cTnT as a diagnostic tool for MI in ACS. In a meta analysis the cumulative sensitivities for cTnT and CK-MB were similar. The diagnostic specificity of cTnT compared with CK-MB was however, significantly lower. Since CK-MB is the gold standard for diagnosis of MI, cTnT may appear less specific as it picks up minor infarctions that manifest as minimal/no rise in CK-MB levels. These patients would be classified as having acute MI.

Risk stratification in non ST-segment elevation ACS

cTnT provides important prognostic information in the UA, non Q MI cohorts. In a meta analysis the cumulative sensitivities for cTnT and CK-MB were similar. The diagnostic specificity of cTnT compared with CK-MB was however, significantly lower. Since CK-MB is the gold standard for diagnosis of MI, cTnT may appear less specific as it picks up minor infarctions that manifest as minimal/no rise in CK-MB levels. These patients would be classified as having acute MI.

Troponins as guide to therapeutic decision making

Fractionated heparins/low molecular weight heparins - FRISC trial demonstrated a greater reduction in mortality/MI for patients receiving Dalteparin in cTnT positive subgroups. This was corroborated in a sub study of FRISC II trial.

Glycoprotein IIb/IIIa antagonists - In PRISM study cTnT positivity in ACS was associated with benefits from use of Tirofiban. Similarly, in CAPTURE trial the cTnT positive subgroups fared better in terms of treatment benefits with Abciximab while the treatment benefits with Lamifiban are being explored in a sub study of PARAGON-B trial.

Angiographic correlates

cTnT and cTnI positivity is associated with greater propensity for multivessel involvement, presence of thrombus and presence of significant coronary artery disease.
REFERENCES


