Direct Comparison of Sensitive and High-Sensitive Cardiac Troponin Assays in the Early Diagnosis of Acute Myocardial Infarction

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Presenter’s Disclosure

- Swiss National Science Foundation
- Swiss Heart Foundation
- University Hospital Basel, Switzerland
- Abbott, Roche, Brahm, Siemens
Background

- **Acute Myocardial Infarction (AMI)** is a major cause of death and disability worldwide.
- Reliable and sensitive **early markers are needed** for the rapid diagnosis or rule out of AMI.
- New **sensitive** cardiac troponin (s-cTn) assays have been invented.

Background

• Substantial **analytical differences** between these sensitive assays

• Terms: **Sensitive vs. High-sensitive cTn Assays**

• **Hypothesis:** hs-cTn are superior to s-cTn assays in the early diagnosis of AMI
APACE – TRIAL

Advantageous Predictors of Acute Coronary Syndrome Evaluation
Methods – Study Design

• Ongoing prospective multicenter study
• 8 international study centers
• n≈1900 patients enrolled

[Map showing locations of study centers]
Methods - Study Design

• Patient presenting to the ED with symptoms suggestive of ACS with onset or peak within the last 12 hours

• Goldstandard Diagnosis
  – 2 independent cardiologists
  – Utilizing all available clinical information from the time of enrolment through 90-day follow-up
Methods - Investigational cTn Assays

Sensitive cardiac Troponin assays

1. Siemens Troponin I Ultra
2. Abbott Architect Troponin I

High-sensitive cardiac Troponin assays

3. Roche high-sensitive Troponin T
Methods - Investigational cTn Assays

Analytical Parameters

- 10% Coefficient of Variation
- 99th Percentile
- Limit of Detection

Cardiac Troponin µg/l

<table>
<thead>
<tr>
<th>Assay</th>
<th>10% CV</th>
<th>99th Percentile</th>
<th>Limit of Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siemens TnI Ultra</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbott Architect TnI</td>
<td></td>
<td></td>
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<tr>
<td>Roche hs TnT</td>
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</tr>
</tbody>
</table>

Sensitive cTn
High-sensitive cTn
### Results - Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n=1106)</th>
<th>AMI (n=174)</th>
<th>No AMI (n=932)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age – yr</strong></td>
<td>64 [51–76]</td>
<td>73 [59–80]</td>
<td>62 [50–74]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Male sex – no. (%)</strong></td>
<td>736 (66)</td>
<td>124 (75)</td>
<td>612 (66)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Risk factors – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>698 (63)</td>
<td>129 (74)</td>
<td>569 (61)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>493 (45)</td>
<td>91 (52)</td>
<td>402 (43)</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>218 (20)</td>
<td>45 (26)</td>
<td>173 (19)</td>
<td>0.02</td>
</tr>
<tr>
<td>Current smoking</td>
<td>267 (24)</td>
<td>51 (29)</td>
<td>215 (23)</td>
<td>0.085</td>
</tr>
<tr>
<td>History of smoking</td>
<td>394 (36)</td>
<td>57 (33)</td>
<td>337 (36)</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>History – no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>404 (37)</td>
<td>77 (44)</td>
<td>327 (35)</td>
<td>0.02</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>272 (25)</td>
<td>54 (31)</td>
<td>218 (23)</td>
<td>0.03</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>275 (24)</td>
<td>49 (28)</td>
<td>249 (27)</td>
<td>0.38</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>78 (37)</td>
<td>20 (11)</td>
<td>58 (6)</td>
<td>0.013</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>64 (6)</td>
<td>21 (12)</td>
<td>43 (5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Results - Goldstandard Diagnosis

- Acute Myocardial Infarction: 16% (174)
- Unstable Angina: 14% (152)
- Non-coronary, cardiac chest pain: 13% (148)
- Extracardiac chest pain: 48% (532)
- Chest pain of unknown origin: 9% (100)

n=1106

STEMI: 24% (42)
NSTEMI: 76% (132)
Results - Distribution of Troponin

- Siemens Troponin I Ultra (s)
- Abbott Architect Troponin I (s)
- Roche high-sensitive Troponin T (hs)
Results - Diagnostic Performance

Assays (s=sensitive, hs=high-sensitive)

- Siemens Troponin I Ultra (s) ROC AUC [95% CI] 0.95 [0.93 - 0.97]
- Abbott Architect Troponin I (s) ROC AUC [95% CI] 0.92 [0.88 - 0.95]
- Roche high-sensitive Troponin T (hs) ROC AUC [95% CI] 0.91 [0.87 - 0.94]

Diagnostic Performance:

All Patients:

- Sensitivity
- Specificity

Chest Pain Onset ≤ 3 hours:

- Sensitivity
- Specificity

n=1106, n=492
Discussion - Limitations

1. **Generalizability** has to be shown

2. Clinical benefit unknown, *interventional studies needed*

3. No patients with **terminal kidney failure**

4. Potential missing of **small AMI’s** with a troponin elevation **below the decision value** of conventional cTnS
Discussion – Major Findings

1. Both s-cTn and hs-cTn had high diagnostic accuracy already at the time of presentation to the ED.

2. The diagnostic accuracy in the early diagnosis of AMI was comparable among s-cTn and hs-cTn.

3. Even in patients presenting very early after chest pain onset, no benefit was apparent for the hs-cTn assay.