Exercise stress testing is associated with an increase in cardiac troponin T levels in patients with suspected coronary artery disease

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Disclosures

- R. Røysland: none
- G. Kravdal: none
- A. D. Høiseth: none
- P. Badr: none
- T. Omland: speaker’s honoraria from Roche
- H. Røsjø: none
Introduction

• Troponin – biomarker of myocardial injury

![Figure 2. Incidence of Cardiovascular Death According to Quartile of High-Sensitivity Cardiac Troponin T Level.](image)
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- Used to diagnose acute myocardial infarction
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- Associated with adverse prognosis in:
  - ACS
  - stable CAD
  - General population

Figure 2. Incidence of Cardiovascular Death According to Quartile of High-Sensitivity Cardiac Troponin T Level.

Introduction

• Troponin – biomarker of myocardial injury
• Used to diagnose acute myocardial infarction
• Associated with adverse prognosis in:
  ▫ ACS
  ▫ stable CAD
  ▫ General population
• Detectable in 98% of patients with stable CAD with a high sensitive assay (PEACE)

Mechanism of troponin release in stable CAD is not established

- Reversible myocardial ischemia?

Figure 1 Cardiac troponin I levels (median and interquartile range) measured using the ultrasensitive assay in patients with none (blue circles), mild (green triangles), and moderate-to-severe (red squares) ischaemia at baseline (samples available in 44, 30, and 34 patients, respectively), immediately after stress testing (37, 26, and 27 patients), 2 h after stress testing (20, 15, and 16 patients), and 4 h after stress testing (44, 28, and 36 patients). P-values are for trend across ischaemic categories at each timepoint.

Sabatine et al. Eur Heart J 2009
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Mechanism of troponin release in stable CAD is not established

- Reversible myocardial ischemia?
- Left ventricular hypertrophy?
- Increased cardiomyocyte apoptosis?
- Increased myocardial stress?
Identifying chest pain patients with CAD and stable CAD patients in need of intensified therapy can be challenging

- Only a subset of chest pain patients has significant CAD
- Only a subset of patients with stable CAD requires intensified therapy i.e. active CAD
- ECG changes on exercise stress testing has low sensitivity and specificity for diagnosing active CAD
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- ECG changes on exercise stress testing has low sensitivity and specificity for diagnosing active CAD

We hypothesised that troponin T measured by a sensitive assay could improve diagnostic accuracy in patients with suspected active CAD
Methods

- 200 patients with suspected CAD referred to an outpatient clinic at Akershus University Hospital, Norway

- Referred to exercise stress testing and SPECT

- Consecutive inclusion into three risk strata (low, intermediate, high) based on cardiologist pre-test assessment

- 2 excluded due to invasive cancer discovered shortly after inclusion

- For myocardial perfusion (SPECT) a stress-rest imaging protocol was used.

- Troponin T measured with a high sensitive assay, at 4 different time points, before, immediately after, 1.5 hours after and 4.5 hours after exercise.
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- For myocardial perfusion (SPECT) a stress-rest imaging protocol was used.
- Troponin T measured with a high sensitive assay, at 4 different time points, before, immediately after, 1.5 hours after and 4.5 hours after exercise testing.
Endpoint

- Three patient categories:
  1. **Active CAD**
     - Positive SPECT
     - Positive angiography
     - Coronary event
     - New or crescendo angina requiring medical intervention
  2. **History of CAD**
  3. **No CAD**

- Determined by an endpoint committee of two cardiologists, concordant in >90% of cases.
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total N = 198</th>
<th>Active CAD N = 44</th>
<th>Hx CAD N = 41</th>
<th>No CAD N = 113</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>100 (50.5%)</td>
<td>13 (29.5%)</td>
<td>18 (43.9%)</td>
<td>69 (61.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age 60 ±11</td>
<td>13 (29.5%)</td>
<td>65 ±10</td>
<td>63 ±9</td>
<td>56 ±12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>73 (36.9%)</td>
<td>21 (47.7%)</td>
<td>16 (40.0%)</td>
<td>36 (32.4%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Diabetes</td>
<td>26 (13.1%)</td>
<td>7 (15.9%)</td>
<td>9 (22.0%)</td>
<td>10 (8.8%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>55 (27.8%)</td>
<td>13 (29.5%)</td>
<td>8 (19.5%)</td>
<td>34 (30.1%)</td>
<td>0.41</td>
</tr>
<tr>
<td>eGFR 101 ±30</td>
<td>100 ±33</td>
<td>92 ±28</td>
<td>125 ±29</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td><strong>Previous CAD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doc MI</td>
<td>44 (22.4%)</td>
<td>20 (45.5%)</td>
<td>23 (56.3%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hx PCI</td>
<td>55 (29.8%)</td>
<td>26 (60.5%)</td>
<td>29 (72.5%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hx ACB</td>
<td>20 (10.1%)</td>
<td>13 (29.5%)</td>
<td>7 (17.5%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet aggr. inhib.</td>
<td>118 (59.6%)</td>
<td>39 (88.6%)</td>
<td>35 (85.4%)</td>
<td>44 (35.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin</td>
<td>111 (56.1%)</td>
<td>38 (86.4%)</td>
<td>41 (100%)</td>
<td>32 (28.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>92 (46.5%)</td>
<td>34 (77.3%)</td>
<td>34 (82.9%)</td>
<td>24 (21.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Clinical Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive ECG</td>
<td>61 (30.8%)</td>
<td>16 (36.4%)</td>
<td>8 (19.5%)</td>
<td>37 (32.7%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Positive SPECT</td>
<td>19 (9.6%)</td>
<td>19 (43.2%)</td>
<td>0</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Positive angiography</td>
<td>23 (11.6%)</td>
<td>23 (52.3%)</td>
<td>0</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Troponin T at baseline
Troponin T at baseline

![Graph showing troponin T levels over time with labels for different conditions: No CAD, Active CAD, and Hx of CAD. The graph indicates a significant difference (p<0.001) between the groups.](image-url)
Troponin T at baseline

- Time
- Troponin T (ng/L)
- Baseline
- Time

- p<0.001
- p=0.43

Legend:
- No CAD
- Active CAD
- Hx of CAD
Troponin T increases from baseline to 4.5 hours after exercise

We did not observe a difference in release characteristics of TnT after stress testing in patients with active CAD vs. patients with history of CAD or no CAD.
Variables associated with active CAD

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<tr>
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<th>Univariable analysis</th>
<th>Multivariable analysis</th>
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<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% C.I.</td>
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<tr>
<td>Baseline logTnT</td>
<td>2.89</td>
<td>1.72</td>
</tr>
<tr>
<td>Age</td>
<td>1.03</td>
<td>1.00</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>3.10</td>
<td>1.51</td>
</tr>
<tr>
<td>BMI</td>
<td>1.04</td>
<td>0.96</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.03</td>
<td>1.01</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.97</td>
<td>0.94</td>
</tr>
<tr>
<td>Hx of CAD</td>
<td>12.40</td>
<td>5.33</td>
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<td>1.33</td>
<td>0.52</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.74</td>
<td>0.88</td>
</tr>
<tr>
<td>Use of statin</td>
<td>6.94</td>
<td>2.77</td>
</tr>
<tr>
<td>Pre-test probability</td>
<td>1.04</td>
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Does troponin T add diagnostic information?

- Cardiologist pre-test probability of active CAD:
  - AUC: 0.70; 95% CI: 0.61-0.78
Does troponin T add diagnostic information?

- Cardiologist pre-test probability of active CAD:
  - AUC: 0.70; 95% CI: 0.61-0.78
- baseline troponin T:
  - AUC: 0.68; 95% CI: 0.58-0.77
Does troponin T add diagnostic information?

- Cardiologist pre-test probability of active CAD:
  - AUC: 0.70; 95% CI: 0.61-0.78
- Baseline troponin T:
  - AUC: 0.68; 95% CI: 0.58-0.77
- Pre-test probability + baseline troponin T:
  - AUC: 0.75; 95% CI: 0.67-0.83; p=0.049
Conclusion

- Troponin T increases from baseline to 4.5 hours after stress testing, regardless of patient group.
- Mechanisms other than reversible myocardial ischemia may play a role for this increase.
- Troponin T levels at rest are associated with active CAD independently of risk factors.
- Troponin T adds to the cardiologist's pre-test assessment of probability of active CAD.
Acknowledgement

- Participating patients
- Supportive Staff
- The Regional Health Authority - Helse Sør-Øst
Troponin T and ischemia

Figure 3: Median Levels of cTnT Measured by the hs-cTnT Assay From the CS Following Pacing Stress Stratified by the Presence or Absence of CAD and Lactate Elution

At baseline, there were significant differences in cTnT concentrations, which diminished over time following pacing. The p values refer to changes in biomarker levels across time points for each group. *p < 0.05 for the comparison with CAD−/lactate− group. #p < 0.05 for comparison with the CAD+/lactate− group. CAD = coronary artery disease; other abbreviations as in Figure 2.
SPECT

- Troponin T measured at 4 time points

Active CAD, n=44
Hx of CAD, n=41
No CAD, n=113