Serial high-sensitivity troponin-I and long-term risk of myocardial infarction and coronary revascularization in subjects with suspected acute coronary syndrome

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Funding Acknowledgements: Type of funding sources: Foundation. Main funding source(s): Danish Cardiovascular Academy funded by the Novo Nordisk Foundation and the Danish Heart Foundation

Background: Serial high-sensitivity troponin-I (hsTnI) concentrations are associated with mortality in individuals with suspected acute coronary syndrome. However, their relation to myocardial infarction and revascularization events is unknown.

Purpose: To determine short- and long-term risks of myocardial infarction and revascularization (PCI or CABG) according to hsTnI concentrations and their changes from baseline, in patients with suspected acute coronary syndrome.

Methods: Through Danish national registries, we identified subjects who underwent two hsTnI measurements (Siemens TnI Flex® Reagent, 99th percentile upper reference limit, 45 ng/l) separated by 1-7 hours, during hospitalization for myocardial infarction, unstable angina, observation for suspected myocardial infarction, or chest pain from 2012 through 2019. Individuals were stratified according to their hsTnI concentration pattern (main groups: normal, rising, persistently elevated, or falling) and the magnitude of hsTnI concentration change (secondary groups: <20%, >20 to 50%, or >50% in either direction). We calculated standardized absolute and relative risks of myocardial infarction and coronary revascularization using multivariable logistic regression with average treatment effect modeling, a method that ensures equal distribution of factors that may affect the risk of outcomes across the various groups of interest.

Results: A total of 20,609 individuals were included of whom 22.4% were discharged with a diagnosis of myocardial infarction, 4.8% with unstable angina, and 72.8% with observation for suspected myocardial infarction or chest pain. Median age was 63.2 years, and 53.1% were male. Considering known cardiovascular disease, 21.3% had coronary artery disease, 7.0% had undergone prior PCI or CABG, 8.1% had heart failure, and 10.7% had atrial fibrillation or flutter. The standardized risk of being diagnosed with myocardial infarction was lowest in subjects with two normal hsTnI values and highest in those with persistently elevated concentrations. Within each main group, the likelihood of being diagnosed with myocardial infarction generally appeared to increase with more pronounced hsTnI changes. The standardized risk of undergoing coronary revascularization mimicked this pattern, although among persons with two elevated hsTnI levels, the long-term-risk was not influenced by relative concentration changes. The findings are summarized in the Figure.

Conclusions: Among individuals with suspected acute coronary syndrome, those with a persistently elevated hsTnI concentration consistently had the highest risk of being diagnosed with myocardial infarction and undergoing coronary revascularization. The risk of these outcomes was, for the most part, also positively associated with the magnitude of hsTnI change.
Figure

<table>
<thead>
<tr>
<th>Days 0-30</th>
<th>Normal: 1st hsTnI normal 2nd hsTnI normal</th>
<th>Rising: 1st hsTnI normal 2nd hsTnI elevated</th>
<th>Persistently elevated: 1st hsTnI elevated 2nd hsTnI elevated</th>
<th>Falling: 1st hsTnI elevated 2nd hsTnI normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>Intermediate/high risk</td>
<td>High risk</td>
<td>Intermediate/high risk</td>
<td>Intermediate/high risk</td>
</tr>
</tbody>
</table>

| Days 31-365 | Low risk | Intermediate/high risk | High risk | Intermediate/high risk |

Two hsTnI measurements 1-7 hours apart