Cost-effectiveness of high-sensitive troponin assays for the early rule-out or diagnosis of acute myocardial infarction (AMI) in people with acute chest pain: a NICE diagnostic assessment

Rameakers BLT1, Armstrong NA2, Joore MA1, Westwood ME1, Whiting P1, Thokala P1, Ross J3, Kleijnen J4, Severens JL5, van Asselt ADH1,6,7
1 Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, the Netherlands 2 Kleijnen Systematic Reviews Ltd, York, UK 3 School of Health and Related Research (ScHARR), University of Sheffield, UK 4 School for Public Health and Primary Care (CAPPH), Maastricht University, The Netherlands 5 Institute of Health Policy and Management, Erasmus University, The Netherlands 6 Department of Epidemiology, University Medical Center Groningen, The Netherlands 7 Unit of Pharmacoeconomics and Pharmacoepidemiology, University of Groningen, The Netherlands

The analysis took the perspective of the NHS in England and Wales. Estimates for the model input parameters were retrieved from the literature and by consulting experts for unpublished data. Accuracy estimates were derived from the systematic review which preceded the economic evaluation in this diagnostic assessment.

In the base case, it was assumed that standard troponin testing had perfect sensitivity and specificity (reference case) for diagnosingAMI and that only patients testing positive on the reference standard troponin (preferably standard troponin), were at increased risk for adverse events and would benefit from immediate treatment.

In a secondary analysis, hs-tnt assays were assigned some additional predictive power beyond that of the standard troponin test, in the sense that a proportion of patients testing negative on standard troponin but positive on an hs-tnt test were assumed to be at increased risk for events, and treated accordingly in case of hs-tnt testing but left untreated in case of standard troponin testing. In addition, a number of subgroup and sensitivity analyses were performed, as well as a probabilistic sensitivity analysis (PSA) with 10,000 replications.

Results

Results of the PSA are summarized in the table (only base case analysis) and in the cost effectiveness acceptability curve (CEAC, see figure). In the base case analysis, standard troponin testing was both most effective and most costly. Strategies were considered effective if the ICER thresholds were below the cost effectiveness acceptability curve (CEAC, see figure).

Conclusion

The economic model does not provide strong evidence to prefer one hs-tnt testing strategy over another. Results do, however, indicate that hs-tnt testing in general may be cost-effective compared to standard troponin testing given that hs-tnt testing leads to cost-saving at a QALY loss. Hs-tnt testing dominates standard troponin if one assumes that hs-tnt testing detects some patients who require treatment despite their testing negative with standard troponin, as shown in the secondary analysis. The main issue, if implementation of an hs-tnt testing strategy is considered, is the balance between the likely reduction in cost and the risk of a reduction in effectiveness, albeit possibly small.

Background

People presenting at the Emergency Department (ED) with acute chest pain suspected to be of cardiac origin, but with an electrocardiogram negative for a persistent ST-Segment elevation, may be suffering from a Non-ST Segment Elevation Myocardial Infarction (NSTEMI). Further diagnostic workup of these patients is performed by testing for cardiac biomarkers (preferably troponin) to assess cardiac muscle damage. Since troponin sensitivity is suboptimal in the initial hours after symptom onset, clinical guidelines recommend to perform repeat troponin testing, at respectively 10-12 hours after symptom onset and 6-9 hours after initial assessment. The waiting time for the repeat testing is burdensome for patients, and it requires a hospital admission which incurs additional costs.

High-sensitivity troponin (hs-tnt) assays have shown promise in that they have better sensitivity at presentation and could rule out NSTEMI within the four hour NHS emergency department target. However, hs-tnt assays do not have perfect accuracy either and using them for decision making will inevitably also lead to discharging patients that should have been treated. At present, it is not clear whether the benefits of an early rule-out strategy outweigh the negative consequences. The aim of this study, which was performed within a NICE diagnostic assessment (NIHR HTA Programme project no. 13/51/01), was to assess the cost-effectiveness of high-sensitivity troponin assays for the management of adults presenting with acute chest pain, in particular for the early rule-out of AMI.

Methods

We considered the long-term costs and quality-adjusted life years (QALYs) associated with different troponin testing methods, to diagnose or rule-out NSTEMI, for patients presenting at the ED with suspected non-ST-segment elevation acute coronary syndrome (NSTE-ACS). The model consisted of a decision tree and a Markov model. The decision tree was used to model the 30 day outcomes after presentation, based on test results and the accompanying treatment decision. The outcome of the short term model defined the mix of health states in which the cohort would enter the long term model. The long-term consequences in terms of costs and QALYs were estimated using a Markov cohort model (see figure) with a lifetime time horizon (60 years).

The following strategies were included in the analysis:

- Standard troponin at presentation and at 10-12 hours (reference standard)
- Roche Elecsys hs-tnt 99th centile threshold at presentation
- Roche Elecsys hs-tnt optimal strategy: LoD threshold at presentation followed by 99th centile threshold peak within three hours and/or ≥200% (compared to presentation test) at 1-3 hours
- Abbott ARCHITECT hs-tnt 99th centile threshold at presentation
- Abbott ARCHITECT hs-tnt optimal strategy: LoD threshold at presentation, followed by 99th centile threshold at three hours

No ACS, no UA = No Acute Coronary Syndrome
UA = Unstable Angina

ACS = Acute Coronary Syndrome

Cost Effectiveness Acceptability Curve

Hs-tnt testing dominates standard troponin if one assumes that hs-tnt testing detects some patients who require treatment despite their testing negative with standard troponin, as shown in the secondary analysis. The main issue, if implementation of an hs-tnt testing strategy is considered, is the balance between the likely reduction in cost and the risk of a reduction in effectiveness, albeit possibly small.

Strategy   Costs (95% CI) QALYs (95% CI) Compared to delta C delta Q ICER

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Costs (95% CI)</th>
<th>QALYs (95% CI)</th>
<th>Compared to</th>
<th>delta C</th>
<th>delta Q</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>No testing</td>
<td>£1675 (£1233 - £2182)</td>
<td>11.637 (10.334 - 13.179)</td>
<td>Abbott strategy</td>
<td>£206</td>
<td>0.002</td>
<td>£90.725</td>
</tr>
<tr>
<td>Standard troponin</td>
<td>£2697 (£2113 - £3359)</td>
<td>11.73 (10.334 - 13.179)</td>
<td>Abbott strategy</td>
<td>£206</td>
<td>0.002</td>
<td>£90.725</td>
</tr>
<tr>
<td>Roche ARCHITECT hs-tnt 99th centile</td>
<td>£2343 (£1846 - £3077)</td>
<td>11.73 (10.334 - 13.179)</td>
<td>Abbott strategy</td>
<td>£206</td>
<td>0.002</td>
<td>£90.725</td>
</tr>
<tr>
<td>Abbott ARCHITECT hs-tnt 99th centile</td>
<td>£2253 (£1702 - £2914)</td>
<td>11.73 (10.334 - 13.179)</td>
<td>Abbott strategy</td>
<td>£206</td>
<td>0.002</td>
<td>£90.725</td>
</tr>
</tbody>
</table>

In the secondary analysis, standard troponin testing was dominated, i.e. it was both less effective and more costly than another strategy. Sensitivity analyses showed main drivers to be the difference in outcomes between treated and untreated patients, and treatment costs for patients testing false-positive. As for subgroups, hs-tnt testing is more cost-effective in younger, pre-existing coronary artery disease, and symptom onset <3hrs ago. No testing is only cost-effective when pre-test prevalence is ≤ 1%.