Faster diagnosis of Acute Myocardial Infarction
Pocket guide for Elecsys® Troponin T-high sensitive

Based on the 2015 NSTE-ACS Guidelines of the European Society of Cardiology

Test early. Treat right. Save lives.
The first algorithm to rule-in or rule-out AMI within 0 to 1 hour
New in the 2015 European Society of Cardiology (ESC) guidelines

The 0 h / 1 h algorithm complemented with ESC cut-offs for cTnT-hs

<table>
<thead>
<tr>
<th>cTnT-hs values in patients presenting to the emergency department</th>
</tr>
</thead>
<tbody>
<tr>
<td>0h &lt; 5ng/L*</td>
</tr>
<tr>
<td>0h &lt; 12ng/L and ∆1h &lt; 3ng/L</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>0h ≥ 52ng/L or ∆1h ≥ 5ng/L</td>
</tr>
</tbody>
</table>

- **Rule-out**
- **Observational zone** (retest later, e.g. 3h)
- **Rule-in**

* Applicable for chest pain patients with onset longer than 3 hours
Performance to rule-out AMI at admission (0 hour)
Applicable for chest pain patients with onset longer than 3 hours

- In combination with electrocardiogram (ECG) and clinical symptoms, non-ST-segment elevation myocardial infarction (NSTEMI) can be reliably ruled-out with a single value of cTnT-hs < 5 ng/L for chest pain patients with onset longer than 3 hours.
- The results of this approach, tested with 18,453 patients, certify a high negative predictive value (NPV) and a low 30-day mortality.

<table>
<thead>
<tr>
<th>Reference</th>
<th>N (patients)</th>
<th>Patients ruled-out (%)</th>
<th>NPV</th>
<th>Events in ruled-out patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bandstein, N. et al., <em>J Am Coll Cardiol</em> 2014</td>
<td>14,636</td>
<td>61.0%</td>
<td>99.8%</td>
<td>0.02% (30-day mortality)</td>
</tr>
<tr>
<td>Body, R. et al., <em>Clin Chem</em> 2015</td>
<td>463</td>
<td>17.3%</td>
<td>100%</td>
<td>0% (30-day MACE)</td>
</tr>
<tr>
<td>Body, R. et al., <em>Acad Emerg Med</em> 2016</td>
<td>1,282</td>
<td>36.7%*</td>
<td>99.6%*</td>
<td>1.3% (30-day MACE)*</td>
</tr>
<tr>
<td>Rubini Gimenez, M. et al., <em>Int J Cardiol</em> 2013</td>
<td>2,072</td>
<td>26.5%</td>
<td>98.4%</td>
<td>0% (30-day mortality)</td>
</tr>
</tbody>
</table>

* cTnT-hs < 5 ng/L and limit of detection (LOD) and negative ECG
## Performance of cTnT-hs 0h/1h algorithm

Validated by three multicenter trials in over 3,038 patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Pain Onset</th>
<th>Patients</th>
<th>Rule-out</th>
<th>Observational Zone</th>
<th>Rule-in</th>
</tr>
</thead>
<tbody>
<tr>
<td>APACE-2012&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Pain onset &lt; 12 h</td>
<td>n = 436</td>
<td>60% of patients</td>
<td>23% of patients (to be retested later, e.g. 3h)</td>
<td>17% of patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NPV: 100%</td>
<td></td>
<td>PPV: 84%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sensitivity: 100%</td>
<td></td>
<td>Specificity: 97%</td>
</tr>
<tr>
<td>APACE-2015&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Pain onset &lt; 12 h</td>
<td>n = 1,320</td>
<td>60% of patients</td>
<td>24% of patients (to be retested later, e.g. 3h)</td>
<td>16% of patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NPV: 99.9%</td>
<td></td>
<td>PPV: 78.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sensitivity: 99.6%</td>
<td></td>
<td>Specificity: 95.7%</td>
</tr>
<tr>
<td>TRAPID-AMI&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Pain onset &lt; 6 h</td>
<td>n = 1,282</td>
<td>64% of patients</td>
<td>22% of patients (to be retested later, e.g. 3h)</td>
<td>14% of patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NPV: 99.1%</td>
<td></td>
<td>PPV: 77.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sensitivity: 96.7%</td>
<td></td>
<td>Specificity: 96.1%</td>
</tr>
</tbody>
</table>

NPV: Negative predictive value  
PPV: Positive predictive value
Early and effective diagnosis of AMI within 0 to 1 hour

More than 75% of suspected AMI patients triaged within 1 hour\textsuperscript{6–8}

Adopting the novel 0 h / 1 h algorithm has the potential to:

- Reduce time to diagnosis and improve patient care\textsuperscript{9}
- Lower the need for cardiac stress testing by more than 30\%\textsuperscript{10}
- Shorten the length of stay in the emergency department by nearly 80 minutes and contribute to cost savings\textsuperscript{10,11}
When every minute counts
*Early diagnosis saves lives in AMI*

**Test early**
- Number 1 cause of death in the Western world is coronary heart disease\(^{12}\)
- An early and accurate diagnosis of AMI is critical

**Treat right**
- In the 2015 NSTE-ACS ESC guidelines, hs-cTn is now the biomarker test preferred by the ESC. Troponin testing is mandatory in all patients with suspected NSTE-ACS. A rise and/or fall in troponin concentration, in complement with clinical symptoms and ECG, defines AMI\(^{1}\)
- The time interval to the second cardiac troponin assessment can be shortened to 0 to 1 hour with the use of hs-cTn assays

**Save lives**
- Every 30 minute delay between symptoms and treatment increases 1-year mortality by 7.5\(\%\)^{13}

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The 0h / 1h algorithm using cTnT-hs is endorsed by the 2015 ESC guidelines and allows a highly accurate rapid rule-out and rule-in of AMI, when applied in combination with clinical assessment and 12-lead ECG\(^{1,6-8}\).
Safety aspects of the 0h/1h algorithm
High negative predictive value and low 30-day mortality rate

The high NPV (99.1 – 100 %) and the low 30-day mortality (0.0 – 0.2 %) in the rule-out zone confirm the safety of this approach for early discharge and support the recommendation of the 2015 ESC guidelines1,6–8.
The 0 to 3 hours alternative algorithm to rule-in or rule-out AMI
Confirmed by the 2015 ESC guidelines and based on studies investigating cTnT-hs

This algorithm has been established based on studies which mainly investigated cTnT-hs

- This approach requires the use of high sensitivity troponin tests and reduces the observation time from 6 to 3 hours as compared to conventional cTn tests
- It can also be used for patients remaining in the observational zone of the 0 h/1 h algorithm

The recommended cut-off values and minimum $\Delta$ change between 0 and 3 hours: $^{14,15}$

- 7 ng/L (= 50% of the ULN) for values $\leq$ 14 ng/L (the upper limit of normal [ULN], 99th percentile of healthy controls corresponding to 14 ng/L for cTnT-hs) $^{14}$
- 20% for values $>$ 14 ng/L
- Highly abnormal cTnT-hs value defined as $>$ 70 ng/L (>5-fold of the ULN)$^1$
The 0 h/3 h algorithm, complemented with ESC cut-offs for cTnT-hs

Acute Chest Pain

- cTnT-hs < 14 ng/L
  - Pain > 6 h
  - Pain < 6 h

- Retest cTnT-hs: 3 h
  - cTnT-hs no change
    - Painfree, GRACE < 140, Differential diagnosis excluded
    - Discharge / Stress testing
  - Δ change (1 value > 14 ng/L)
    - Invasive management

- cTnT-hs > 14 ng/L
  - cTnT-hs no change
  - Work-up differential diagnosis

GRACE = Global Registry of Acute Coronary Events score; cTnT-hs = Elecsys® cardiac Troponin T high-sensitive; ULN = upper limit of normal, 99th percentile of healthy controls. Delta change dependent on assay.
Point Of Care option with Roche cobas® h 232 system
Immediate rule-in for high-risk AMI patients with initial sample

- Easy to use even in mobile situations and ensures fast turn-around time with results available in just 12 minutes\textsuperscript{16,17}

- POC cTnT ≥ 50 ng/L can be used to identify patients with a high risk of long-term mortality for accelerated medical investigation and appropriate treatment\textsuperscript{16}

- Pre-hospital patients with suspected AMI with Roche CARDIAC POC Troponin T ≥ 50 ng/L have a 3-10 times higher long-term mortality risk\textsuperscript{16}

- Specificity for the diagnosis of AMI (POC cTnT ≥ 50 ng/L); 95\%, PPV: 68\%\textsuperscript{16}

\textbf{Roche CARDIAC POC Troponin T test ≥ 50 ng/L allows fast triaging in every setting}
Point Of Care option with Roche cobas® h 232 system

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Standardized Troponin T results among all locations
From pre-hospital and emergency rooms to laboratories

Comparable cardiac Troponin T results with immediate rule-in cut-offs
(≈ 50 ng / L) among any cobas® integrated platforms.

GP Setting
Health Clinic
Ambulance
Point-of-care testing
1 heparinized tube
Laboratory
Satellite Laboratory
Emergency Laboratory
Central Laboratory

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