Prognostic impact of stepwise 0/1/3h rule-out of myocardial infarction using high-sensitivity troponin T

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**Background:** The European Society of Cardiology (ESC) recommends the application of 0/1h-algorithms for rapid triage of patients with suspected myocardial infarction (MI). These algorithms enable rule-out or rule-in of MI at presentation and after 1 hour (h), depending on absolute high-sensitivity cardiac troponin (hs-cTn) concentrations and changes. Recently, specific cut-offs to allow for additional 3h triage have been derived for hs-cTnT, to reduce the relevant proportion of patients remaining in the observe zone after 1h. However, the prognostic implications of this 3h rule-out option is unclear.

**Objective:** We aimed to evaluate and directly compare the prognostic impact of three rule-out options at 0, 1 and 3h for the composite endpoint of major adverse cardiac events (MACE) and all-cause mortality at 90 days and 3 years.

**Methods:** We prospectively enrolled patients presenting with suspected MI to the emergency department of a tertiary hospital in Germany. Concentrations of hs-cTnT were measured at presentation (0h), after 1h and 3h. Final diagnoses were centrally adjudicated by two physicians independently according to the 4th Universal Definition of MI. Patients were followed-up for 5 years to assess all-cause mortality and major adverse cardiac events (MACE), composed of cardiac rehospitalization, revascularization, MI excluding index events, and death. We triaged patients into three rule-out categories applying the 0/1/3h-algorithm. Kaplan-Meier survival curves were created for the three rule-out groups and compared using the log-rank test. Further, Cox regression analyses comparing the risk of death and MACE at 90 days and 3 years were performed in patients ruled-out after 1h and 3h compared to patients ruled-out at 0h (reference).

**Results:** In 2514 patients, median age was 64 years and 63.6% were men. Application of the 0/1/3h algorithm ruled-out 371 (14.8%) patients at 0h, 961 (38.2%) after 1h, and 179 (7.1%) after 3h. Median follow-up time was 4.59 \([4.51, 4.75]\) years with a total of 732 patients experiencing MACE and 256 patients dying within 3 years. Incidence of MACE increased with later time of rule-out at 90 days (5.0% vs. 7.0% vs. 9.1%, \(p=0.19\)) and 3 years (16.2% vs. 20.8% vs. 32.3%, \(p<0.001\); Figure 1A). The same trend was observed for all-cause mortality, reaching statistical significance at 3 years (2.3% vs. 4.0% vs. 9.5%, \(p<0.001\); Figure 1B). In the Cox regression analyses at 3 years, patients ruled-out after 3h showed a doubled risk for MACE (hazard ratio 2.11 (95%CI: 1.44, 3.08), \(p<0.001\)) and quadrupled risk for death (hazard ratio 4.33 (95% CI: 1.85, 10.12), \(p<0.001\)) compared to patients ruled-out directly at 0h (Table 1).

**Conclusion:** Application of the 0/1/3h algorithm for triage of patients with suspected MI has predictive value regarding short- and long-term prognosis, with patients ruled-out after 3h showing significantly higher risk of MACE and death over three years as compared to rule-out after 0h and 1h.

**Figure 1:** Kaplan-Meier survival curves for the endpoints of A) major adverse cardiac event (defined as cardiac death, incident myocardial infarction, cardiac rehospitalization and revascularization) and B) all-cause mortality over a period of 3 years. Log-rank p-values calculated for 90 days and 3 years for 0h/1h/3h-rule-out with observe group displayed as visual reference. Categories according to 0/1/3h algorithm. MACE = major adverse cardiac event.

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**Figure 1:** Kaplan-Meier survival curves
Table 1

<table>
<thead>
<tr>
<th>Rule-out group</th>
<th>MACE at 3 years</th>
<th>All-cause mortality at 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Rule-out @0h</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>Rule-out @1h</td>
<td>1.33 (0.99, 1.78)</td>
<td>0.062</td>
</tr>
<tr>
<td>Rule-out @3h</td>
<td>2.11 (1.44, 3.08)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Cox regression for the endpoints of major adverse cardiac events (defined as composite of cardiac death, nonfatal myocardial infarction, cardiac rehospitalization and revascularization) and all-cause mortality at 3 years. Rule-out categories according to the 0/1/3h-algorithm. MACE = Major adverse cardiac event; CI = confidence interval.

Table 1 Cox-regression