Early diagnosis of acute MI: novel strategies

Professor Christian Müller
Disclosures

- Swiss National Science Foundation

- University Hospital Basel

- Abbott

- Alere

- Beckman Coulter

- BG Medicine

- Bülhmann

- Brahms

- Critical Diagnostics

- Roche

- Schiller

- Siemens

- Novartis

- Cardio Rentis
Early diagnosis of AMI: novel strategies

- Background & Case
- Novel strategies
- Medical value for Patients
  Physicians
  Health Care System
Early diagnosis of AMI is critical

- But still an **unmet need** in many patients
- Delayed “rule-in” → morbidity + mortality ↑
- Delayed “rule-out” → time in ED + costs ↑
  patient anxiety ↑
- 3 key tools: **History** incl. chest pain characteristics
  **ECG**
  **cTn**
Early diagnosis of AMI is critical

- But still an **unmet need** in many patients
- Delayed “rule-in” ➔ morbidity + mortality ↑
- Delayed “rule-out” ➔ time in ED + costs ↑
  patient anxiety ↑
- 3 key tools: History incl. chest pain characteristics
  ECG
  hs-cTn
**Presentation:** In the morning (>6h ago) dyspnea + chest pain, 30min, no radiation, no sweating
Never angina during exercise
Asymptomatic at presentation to ED

**History:** stopped anti-hypertensive therapy years ago, no other medical history

**cvRF:** hypertension, former smoking (20 py)

**Vitals:** BP 190/95mmHg, Puls 80/min, Oxy 98%
• **Lab results:**

<table>
<thead>
<tr>
<th></th>
<th>0 h</th>
<th>6 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>TnT4 [&lt;0.01ug/L]</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CK</td>
<td>136 U/L</td>
<td>107 U/L</td>
</tr>
<tr>
<td>CK-MB</td>
<td>4.4</td>
<td>4.2</td>
</tr>
</tbody>
</table>

Completely asymptomatic during 7h in the ED
Normal 2\textsuperscript{nd} ECG
D-dimers negative
Chest x-ray normal
Same Patient presenting 4 (!) days later
Acute chest pain radiating in his left arm and back

STEMI!!!!!
How about hs-cTn at initial presentation 4 days ago??

<table>
<thead>
<tr>
<th></th>
<th>Study blood examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>TnT4 [&lt;0.01 ug/L]</td>
<td>0 h &lt;0.01 1 h &lt;0.01 2 h &lt;0.01 3 h &lt;0.01 6 h &lt;0.01</td>
</tr>
<tr>
<td>CK</td>
<td>136 U/L 120 U/L 107 U/L</td>
</tr>
<tr>
<td>CK-MB</td>
<td>4.4 4.4 4.2</td>
</tr>
<tr>
<td>s-cTnI [Ref. 0.040 ug/L]</td>
<td>0.016 ug/L 0.039 ug/L 0.088 ug/L 0.102 ug/L</td>
</tr>
<tr>
<td>hs-cTnI [Ref. 9 ng/L]</td>
<td>18 ng/L 45 ng/L 67 ng/L 100 ng/L</td>
</tr>
<tr>
<td>hs-cTnT [Ref. 14 ng/L]</td>
<td>11 ng/L 22 ng/L 31 ng/L 32 ng/L</td>
</tr>
</tbody>
</table>

(H)s-cTn improve the early rule-in of AMI
Hs-cTnT
1) Detects AMI earlier
2) Detects small AMI missed with cTn
Hs-cTn improve the early diagnosis of AMI at presentation

Hs-Tn + ECG + History → Rule out ↑ + Rule in ↑

1) Hs-cTn $\neq$ Pregnancy Test

"Troponin-positive"

2) $cTn_A \neq cTn_B$
Hs-cTn: Quantitative marker of cardiomyocyte injury

<table>
<thead>
<tr>
<th>P/NPV for AMI ug/L</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV &gt;95%</td>
<td>PPV &gt;95%</td>
</tr>
<tr>
<td>10</td>
<td>Very large AMI, myocarditis</td>
</tr>
<tr>
<td>PPV 80%</td>
<td>Large AMI, myocarditis, Tako-tsubo, PE, critical illness</td>
</tr>
<tr>
<td>0.100</td>
<td>Small AMI, early large AMI, myocarditis, Tako-tsubo, PE, shock, CHF, SAB, ...</td>
</tr>
<tr>
<td>PPV 50%</td>
<td>Micro AMI, early large AMI, myocarditis, Tako-tsubo, PE, shock, CHF, hypertensive crisis, SAB, stable CAD, ...</td>
</tr>
<tr>
<td>0.050</td>
<td></td>
</tr>
<tr>
<td>NPV 90%</td>
<td>Stable angina, CHF, LVH, subclinical heart disease, etc</td>
</tr>
<tr>
<td>0.010</td>
<td></td>
</tr>
<tr>
<td>NPV 99%</td>
<td>Healthy individuals</td>
</tr>
<tr>
<td>0.005</td>
<td></td>
</tr>
</tbody>
</table>

Mueller C. Eur Heart J 2014
1. Rule-in
2. Rule-out

<table>
<thead>
<tr>
<th>0h</th>
<th>1h</th>
<th>2h</th>
<th>3h</th>
<th>4h</th>
<th>5h</th>
<th>6h</th>
<th>7h</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td></td>
<td></td>
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<tr>
<td>cTn</td>
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ESC 2011: hs-cTn    hs-cTn

1h-Algo: hs-cTn    hs-cTn
## Diagnostics ≠ Therapeutics

<table>
<thead>
<tr>
<th>Education:</th>
<th>+</th>
<th>+++</th>
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<tbody>
<tr>
<td>Best method:</td>
<td><strong>Diagnostic</strong> (blinded)</td>
<td><strong>RCT</strong> (blinded)</td>
</tr>
<tr>
<td></td>
<td>LOD</td>
<td>+ copeptin</td>
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<td>------------------</td>
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</tr>
<tr>
<td>NPV for AMI</td>
<td>98-100%</td>
<td>98-99%</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Details:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If using hs-cTnT</td>
<td>Hs-cTnT&lt;14 &amp; Copeptin&lt;10 pmol/L</td>
<td>Hs-cTnT&lt;14 &amp; 1h delta&lt;3</td>
</tr>
<tr>
<td></td>
<td>Hs-cTnI&lt;2 &amp; Copeptin&lt;10 pmol/L</td>
<td>Hs-cTnI&lt;26 &amp; 1h delta&lt;2</td>
</tr>
<tr>
<td>Feasibility</td>
<td>+++</td>
<td>+</td>
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<tr>
<td>Also for Rule-in</td>
<td>-</td>
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</table>
Insightful algorithm for hs-cTnT 1h:

- If \( Oh < 12 \) and \( \Delta 1h < 3 \)
  - Rule-out

- Others
  - Observational zone

- If \( Oh \geq 52 \) or \( \Delta 1h \geq 5 \)
  - Rule-in

hs-cTnT 1h-algorithm

- **Oh < 12 and Delta 1h < 3**
  - Rule-out
  - 491 Patients (56%)
  - NPV 100%
  - 95% CI 99-100%

- **Others**
  - Observational zone
  - 212 Patients (24%)
  - Prevalence of AMI 9%

- **Oh ≥ 52 or Delta 1h ≥ 5**
  - Rule-in
  - 169 Patients (19%)
  - PPV 76%
  - 95% CI 69-82%

**However:**
1) Would represent a major change in clinical practice
2) Experts ambivalent
3) NOT used clinically until now
TRAPID-AMI: Methods

12 sites on 3 continents
hs-cTnT 1h-algorithm

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NPV 99.1%, (63%)  TRAPID-AMI n=1282  PPV 77% (14%)

Mueller C et al. Eur Heart J 2015 in revision
hs-cTnT 1h-algorithm

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**NPV**
- 99.1% (63%)
- 99.9% (60%)

**PPV**
- 77% (14%)
- 78% (16%)

---

Medical value for patients

<table>
<thead>
<tr>
<th>Time</th>
<th>ECG</th>
<th>cTn</th>
<th>cTn</th>
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<tbody>
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<td>0h</td>
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ESC 2011: hs-cTn   hs-cTn

1h-Algo: hs-cTn   hs-cTn
Medical value for physicians

0h 1h 2h 3h 4h 5h 6h 7h

ECG
cTn
cTn

ESC 2011: hs-cTn hs-cTn

1h-Algo: hs-cTn hs-cTn
Medical value for health care system

ESC 2011: hs-cTn

1h-Algo: hs-cTn

ECG

cTn

cTn
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