Biomarkers and ACS

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Disclosures

- Swiss National Science Foundation

- University Hospital Basel

- Abbott

- Alere

- Bühlmann

- Brahms

- Critical Diagnostics

- Nanosphere

- Roche

- Schiller

- Siemens
Biomarkers and ACS

1. Diagnosis of AMI
2. Hs-cTn
3. Copeptin
Chest Pain $\rightarrow$ AMI

History

ECG

No ST $\uparrow$

ST $\uparrow$

Troponin

Diagnosis

Other

ACS

Unstable Angina

NSTEMI

AMI

STEMI

Thygesen K et al, Eur Heart J 2012
Fissure and Rupture of Plaque
Markers of Plaque Instability

Cardiac Troponin

- cTn 0h + cTn 6h
- ECG Monitoring 6-8h
- Time + Ressources
Acute Chest Pain

1. Rule-in


2. Rule-out

0h 1h 2h 3h 4h 5h 6h 7h
ECG 1.Tn
hs-cTn + copeptin hs-cTn

ESC 2011, US 2013


New

Pathologic

Old

likely pathologic

Normal

likely normal

s-cTn, hs-cTn
S-cTn increase diagnostic accuracy at presentation


s-Tn + ECG + Clinical → Rule out ↑ + Rule in ↑
Early risk stratification

1) Knowing the differential Dg of an elevated cTn
2) Use of all available clinical information
3) Use of quantitative hs-cTn levels
4) Use of hs-cTn changes
5) Cardiac work-up

**Absolute levels of hs-cTnT**

Hs-cTnT (ug/l)

<table>
<thead>
<tr>
<th>Level</th>
<th>PPV</th>
<th>NPV</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>&gt;95%</td>
<td></td>
<td>Very large AMI, myocarditis</td>
</tr>
<tr>
<td>1</td>
<td>80%</td>
<td></td>
<td>Ly large AMI, myocarditis, Tako-tsubo, PE, critical illness</td>
</tr>
<tr>
<td>0.100</td>
<td>50%</td>
<td></td>
<td>Ly large AMI, myocarditis, Tako-tsubo, SAB, ...</td>
</tr>
<tr>
<td>0.050</td>
<td></td>
<td></td>
<td>Ly large AMI, myocarditis, Tako-tsubo, hypertensive crisis, SAB, stable CAD...</td>
</tr>
<tr>
<td>0.014</td>
<td>95%</td>
<td></td>
<td>CHF, LVH, subclinical heart disease, etc</td>
</tr>
<tr>
<td>0.010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.005</td>
<td>99%</td>
<td></td>
<td>Individuals</td>
</tr>
</tbody>
</table>

Levels at presentation in pts with acute chest pain

Elderly (>70y)

∅ AMI

→ cut-off Werte ↑

436 Patients with chest pain—validation cohort

- Oh < 12 and Delta 1h < 3
  - Rule-out
    - 259 Patients (60%)
      - Sensitivity: 100%
      - NPV: 100%

- Others
  - Observational zone
    - 101 Patients (23%)
      - Prevalence of AMI: 8%

- Oh ≥ 52 or Delta 1h ≥ 5
  - Rule-in
    - 76 Patients (17%)
      - Specificity: 97%
      - PPV: 84%
AMI versus other Cardiac

295 patients

167 AMI
128 CNCD

13 AMI
5 CNCD

13 AMI
5 CNCD

ST-elevation
No ST-elevation

154 AMI
123 CNCD

presentation value of high-sensitive cardiac Troponin T

<0.012 ug/l

<14 AMI
62 CNCD

0.012 - 0.028 ug/l

31 AMI
30 CNCD

>0.028 ug/l

<109 AMI
31 CNCD

abs. change 0h-1h

<0.003 ug/l

0 AMI
56 CNCD

<0.003 ug/l

6 AMI
22 CNCD

≥0.003 ug/l

14 AMI
6 CNCD

<0.003 ug/l

6 AMI
8 CNCD

≥0.003 ug/l

25 AMI
18 CNCD

abs. change 0h-1h

<0.003 ug/l

18 AMI
13 CNCD

≥0.003 ug/l

91 AMI
18 CNCD

Haaf P et al, Circulation 2012;126:31-40
Hypothesis

Cardiomyocyte ↓

cTn

+ Endogenous Stress Copeptin

Rule-out of AMI

• at presentation (0h)

• without 2.nd cTn after 6h

Incremental Value of Copeptin for Rapid Rule Out of Acute Myocardial Infarction

**Figure 1** Copeptin Levels at Presentation

Incremental Value of Copeptin for Rapid Rule Out of Acute Myocardial Infarction

Figure 2: Copeptin and Troponin T Levels at Presentation in Relation to Time Since Onset of Symptoms

Figure 4: ROC Curves at Presentation for the Diagnosis of AMI

Area under the curve for the combination of troponin T and copeptin: 0.97

hs-cTnT + Copeptin

NPV > 99%

Reichlin 2009
Keller 2010
Chenevier-Gobeaux C 2011
Giavarina 2011
Giannitsis 2011
Charpentier 2012
Ray 2012
Meune 2012
Folli 2012
Potocki 2012
Chopin 2013
.....

Twerenbold R et al. In review.
Mortality Prediction

High-sensitive Troponin

Cutoff-value: 0.014 µg/l

Log-rank p<0.001, HR 10.0

10.3%

1.1%

Copeptin

Cutoff-value: 9 pmol/l

Log-rank p<0.001, HR 7.2

9.0%

1.3%

Twerenbold R et al. In review.
## Results – Mortality Prediction

**Cutoff-values:** hs-cTnT 0.014 µg/l, Copeptin 9 pmol/l

<table>
<thead>
<tr>
<th>Combination</th>
<th>n</th>
<th>Events – n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hs-cTnT + / Copeptin +</td>
<td>266</td>
<td>41 (15.4%)</td>
</tr>
<tr>
<td>Hs-cTnT + / Copeptin –</td>
<td>163</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Hs-cTnT - / Copeptin +</td>
<td>213</td>
<td>3 (0.09%)</td>
</tr>
<tr>
<td>Hs-cTnT - / Copeptin –</td>
<td>528</td>
<td>6 (1.1%)</td>
</tr>
</tbody>
</table>

Log-rank p<0.001, HR 13.7
Acute Chest Pain

1. Rule-in

2. Rule-out

hs-cTn + copeptin
hs-cTn