Cardiac biomarkers: present and the future

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IFCC- Task Force-Young Scientists
Cardiac biomarkers: what we have now!

- Cardiac Necrosis
- Remodeling
- Inflammatory response
- Myocyte Injury/Stress-Myocardial ischemia
- Plaque destabilisation
# Cardiac Necrosis and Ischemia Biomarkers

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Molecular Weight (kDa)</th>
<th>Initial Elevation in blood</th>
<th>Time to peak</th>
<th>Return to normal</th>
<th>Type of Marker</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-FABP</td>
<td>15kDa</td>
<td>1-2 hrs</td>
<td>6-8 hrs</td>
<td>24 hrs</td>
<td>Ischemic</td>
<td>Early rise Highly specific</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>17kDa</td>
<td>1-3 hrs</td>
<td>5-8 hrs</td>
<td>16-24 hrs</td>
<td>Ischemic</td>
<td>Early rise Highly unspecific</td>
</tr>
<tr>
<td>Troponin I (TnI)</td>
<td>22kDa</td>
<td>3-6 hrs</td>
<td>14-18 hrs</td>
<td>5-10 days</td>
<td>Necrotic</td>
<td>Late rise Very Highly specific</td>
</tr>
<tr>
<td>Troponin T (TnT)</td>
<td>33kDa</td>
<td>3-6 hrs</td>
<td>10-48 hrs</td>
<td>10-15 days</td>
<td>Necrotic</td>
<td>Late rise Very Highly specific</td>
</tr>
<tr>
<td>CK-MB</td>
<td>86kDa</td>
<td>3-8 hrs</td>
<td>9-24 hrs</td>
<td>48-72 hrs</td>
<td>Necrotic</td>
<td>Late rise Relatively specific</td>
</tr>
</tbody>
</table>
Cardiac Necrosis biomarkers

Troponins I and T

- The biochemical « gold standard »
- Specific of AMI
- I : completely specific for heart
- T: released small amounts by skeletal muscles
- Increase with cardiac insufficiency, angina…
- Elevated levels can persist for weeks; retrospective diagnosis of infraction.

- CKD
- New highly sensitive: good or more false positive: is what really necessary?
Ischemia biomarkers

*H-FABP* (heart-type fatty acid binding protein)
Ischemia biomarkers

H-FABP (heart-type fatty acid binding protein)

- Early rise marker of ACS (30 min following the onset of an ischemic episode)
- Marker for re-infarction
- Combination with Tn improve the diagnostic sensitivity for MI/ACS
- Not widely use in practice
Myocyte injury/Stress

- Natriuretic peptide
- BNP, NT-proBNP, ANP

Especially useful in ruling out heart failure as cause of dyspnea given its excellent negative predictive value.

- BNP and NT-proBNP: more specific of cardiac dysfunction ➔ clinical interest+++
Myocyte Injury/Stress

**Copeptin**

- *Endogenous stress*
- Elevated after AMI and associated with LV dysfunction and remodeling and clinical HF post-AMI
- In acute and chronic HF → elevation of it → predicts disease severity and poor outcome
- 99.7% NPV
- May obviate the need of prolonged monitoring and serial blood sampling
- Has been said to and an additive to BNP
- Best single predictor of mortality in patients with NYHA functional class II and III
Myocyte injury/Stress

GDF 15

- Only detectable in liver and placenta can induced in the heart by MI and pressure overload
- Strong predictor of mortality in some patients
- Similar prognostic as NT=proBNP
- Role to play in diagnosis and risk stratification in HF
- The exact pathophysiological mechanisms of GDF-15 in the cardiovascular system and in acute ST-elevation myocardial infarction (STEMI) are not well defined.
- Not widely use in practice
Remodeling biomarker

Matrix metalloproteinase (MMP9):
- The main cause of fibrous cap disruption in plaque rupture
- Associated with higher mortality rates in HF --> Prognosis in HF
Galectin 3
- Link between inflammation and fibrosis
- Early marker of potential myocyte dysfunction and it may be a marker of early remodeling
- Increased in HF
- Diagnostic role (<NT-proBNP)
- Prognosis (>to NT-proBNP in short term)
Inflammatory response

Highly sensitive CRP
- Plasma levels can increase rapidly in response to acute inflammation
- Risk factor or risk marker?

MPO
- Activated leukocytes
- Predicts cardiac risk independently of other markers of inflammation
- IL (1,2,18)
  → NOT specific
## Clinical advantages and disadvantages of more interesting biomarkers

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponins HS</td>
<td>Elevated after 8h</td>
<td>Elevated in non-MI cases</td>
</tr>
<tr>
<td></td>
<td>Elevated for 7-10 days</td>
<td>Need 2nd test if 1st too early</td>
</tr>
<tr>
<td></td>
<td>Cardiac specific</td>
<td>Some TNT in skeletal muscle</td>
</tr>
<tr>
<td></td>
<td>Very sensitive</td>
<td>Incomplete understanding of elevation post cardiac and non</td>
</tr>
<tr>
<td></td>
<td>Stratifies short and long terms risk in AMI</td>
<td>cardiac surgery</td>
</tr>
<tr>
<td></td>
<td>Detects reinfarction</td>
<td>Baseline higher in CRF</td>
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<tr>
<td></td>
<td>Correlates to MI</td>
<td></td>
</tr>
<tr>
<td>Myoglobin</td>
<td>Theoretically rapid detection</td>
<td>Lack of specificity</td>
</tr>
<tr>
<td>CRP HS</td>
<td>Marker of inflammation</td>
<td>Not specific</td>
</tr>
<tr>
<td>Copeptin</td>
<td>If level low--&gt; rules out MI</td>
<td>Not specific</td>
</tr>
<tr>
<td>H-FABP</td>
<td>Early marker of ischaemia</td>
<td>Disappointing in studies</td>
</tr>
<tr>
<td>BNP (NT-pro)</td>
<td>Prognistication in AMI</td>
<td>Difficult to interpret in critical ill</td>
</tr>
<tr>
<td>MPO</td>
<td>Elevated in inflammation</td>
<td>Not superior</td>
</tr>
</tbody>
</table>
The dream biomarker: what we wish...

- Specificity
- Sensitivity
- Predictibility
- Durability
- Fiability
- Simplicity
- Quickly
- Cost
The future....

- Multiple biomarkers approach show a best choice....
- TnThs...
- Metabolomic and proteomic