What is the impact of the new definitions of myocardial infarction?
Universal definition of myocardial infarction

Kristian Thygesen, Joseph S. Alpert and Harvey D. White on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction

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Definition of Myocardial Infarction

Pathology

Acute myocardial infarction is defined as myocardial cell death due to prolonged myocardial ischemia.
Classification of Myocardial Infarction

Type 1  Spontaneous myocardial infarction related to ischemia due to a primary coronary event such as plaque erosion or rupture, fissuring or dissection

Type 2  Myocardial infarction secondary to ischemia due to imbalance between oxygen demand and supply e.g. coronary spasm, anemia, or hypotension

Type 3  Sudden cardiac death with symptoms of ischemia, accompanied by new ST elevation or LBBB, or verified coronary thrombus by angiography or autopsy, but death occurring before blood samples could be obtained

Type 4a Myocardial infarction associated with PCI

Type 4b Myocardial infarction associated with verified stent thrombosis

Type 5  Myocardial infarction associated with CABG
Criteria for Acute Myocardial Infarction
Type 1 and Type 2

Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit together with evidence of ischemia with at least one of the following:

- Symptoms of ischemia
- ECG changes of new ischemia (new ST-T changes or new LBBB)
- Development of pathological Q waves in the ECG
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
Elevations of Troponin in the Absence of Overt Ischemic Heart Disease

- Cardiac contusion, or other trauma including surgery, ablation, pacing etc
- Congestive heart failure – acute and chronic
- Aortic dissection, aortic valve disease
- Hypertrophic cardiomyopathy
- Tachy- or bradyarrhythmias, or heart block
- Apical ballooning syndrome
- Rhabdomyolysis with cardiac injury
- Pulmonary embolism, severe pulmonary hypertension
- Renal failure
- Acute neurological disease, including stroke, or subarachnoid hemorrhage
- Infiltrative diseases, e.g., amyloidosis, hemochromatosis, sarcoidosis or scleroderma
- Inflammatory diseases, e.g., myo/pericarditis or myocardial extension of endocarditis
- Drug toxicity or toxins
- Critically ill patients, especially with respiratory failure, or sepsis
- Burns, especially if affecting > 30% of body surface area
- Extreme exertion
# Cardiac Troponin Assays

<table>
<thead>
<tr>
<th>Assay</th>
<th>LLD</th>
<th>99th Percentile</th>
<th>WHO-ROC Cutoff</th>
<th>10% CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott ARCH</td>
<td>0.009</td>
<td>0.012</td>
<td>0.3</td>
<td>0.032</td>
</tr>
<tr>
<td>AxSYM ADV</td>
<td>0.02</td>
<td>0.04</td>
<td>0.4</td>
<td>0.16</td>
</tr>
<tr>
<td>I-STAT</td>
<td>0.02</td>
<td>0.08 (WB)</td>
<td>ND</td>
<td>0.1</td>
</tr>
<tr>
<td>Bayer Centaur</td>
<td>0.02</td>
<td>0.1</td>
<td>1.0</td>
<td>0.35</td>
</tr>
<tr>
<td>Ultra</td>
<td>0.006</td>
<td>0.04</td>
<td>0.78</td>
<td>0.03</td>
</tr>
<tr>
<td>Beckman Accu</td>
<td>0.01</td>
<td>0.04</td>
<td>0.5</td>
<td>0.06</td>
</tr>
<tr>
<td>Biosite Triage</td>
<td>0.05</td>
<td>&lt;0.05</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Blomerieux Vds</td>
<td>0.001</td>
<td>0.01</td>
<td>0.16</td>
<td>0.11</td>
</tr>
<tr>
<td>Dade RxL CS</td>
<td>0.04</td>
<td>0.07</td>
<td>0.6-1.5</td>
<td>0.14</td>
</tr>
<tr>
<td>DPC Immulite</td>
<td>0.1</td>
<td>0.2</td>
<td>1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>MKI Pathfast</td>
<td>0.006</td>
<td>0.01</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>Ortho Vitros</td>
<td>0.02</td>
<td>0.08</td>
<td>0.4</td>
<td>0.12</td>
</tr>
<tr>
<td>ES (R&amp;D)</td>
<td>0.012</td>
<td>0.032</td>
<td>NA</td>
<td>0.053</td>
</tr>
<tr>
<td>Response</td>
<td>0.03</td>
<td>&lt; 0.03 (WB)</td>
<td>ND</td>
<td>0.21</td>
</tr>
<tr>
<td>Roche Elecsys</td>
<td>0.01</td>
<td>&lt; 0.01</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Reader</td>
<td>0.05</td>
<td>&lt; 0.05 (WB)</td>
<td>0.1</td>
<td>ND</td>
</tr>
<tr>
<td>Tosoh AIA</td>
<td>0.06</td>
<td>0.06</td>
<td>0.31-0.64</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*Per manufacture. WB whole blood, IFCC C-SMCD 2006
Impact of Changing Definitions for Myocardial Infarction: A Report from the AMIS Registry

Philip Urban, MD, Dragana Radovanovic, MD, Paul Erne, MD, Jean-Christophe Stauffer, MD, Giovanni Pedrazzini, MD, Stephan Windecker, MD, Osmund Bertel, MD; For the AMIS Plus investigators
Cardiovascular Department, La Tour Hospital, Geneva, Switzerland.

ABSTRACT

BACKGROUND: To assess the impact of the new definitions of myocardial infarction, we retrospectively analyzed 9190 patients from 63 hospitals with reported peak troponin values included between 2001 and 2007 in the Swiss AMIS (Acute Myocardial Infarction in Switzerland) Plus registry.

METHODS: Patients were classified as belonging to the “classic” myocardial infarction group (peak total CK or CK-MB above the upper limit of normal, or troponin T [TnT] >0.1 μg/L or troponin I [TnI] >0.1-0.8 μg/L [depending on the assay]) or “new” myocardial infarction group (TnT >0.01 μg/L or TnI >0.01-0.07 μg/L).

RESULTS: There were 489 patients in the “new” group who were similar to the 8701 “classic” patients in terms of age, sex, and prevalence of both diabetes and renal failure, but more frequently had a history of prior coronary artery disease, hypertension, and hyperlipidemia. At admission, they less frequently had ST elevation on their electrocardiogram, were more frequently in Killip class I, and received less primary percutaneous coronary intervention. Hospital mortality was 3.5% in the “new” and 6.7% in the “classic” myocardial infarction group (P = .004). In a subset of patients with a longer follow-up, mortality at 3 and 12 months was 1% and 5.6%, respectively, for “new” and 1.6% and 4%, respectively, for “classic” myocardial infarction (NS).

CONCLUSIONS: Patients with minimal elevation of serum troponin have smaller infarctions, less aggressive treatment, less early complications, and a better early prognosis than patients with higher serum biomarker levels. After discharge, however, their prognosis currently appears no different from that of patients with a “classic” myocardial infarction event.
Who are the new MI patients?

- Analysis of in-hospital course of 9188 AMIS patients with ACS (2001-2007) and a peak troponin value reported
- Follow-up at 3 and 12 months for 2218 patients from 44 hospitals (2005-2007)
- Definition of 3 groups
  - « classic » MI
  - « new » MI
  - unstable angina

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Who are the new MI patients?

- Compatible clinical presentation and/or ECG changes, together with
  - "classic" MI
    - Peak CK/CKMB > ULN, or
    - TnT > 0.1 ug/l, or
    - TnI > 0.1-0.8 ug/l (depending on assay used)
  - "new" MI
    - Biomarkers < cutoff for "classic" MI, and
    - TnT > 0.01 ug/l, or
    - TnI > 0.01-0.07 ug/l (depending on assay used),
- unstable angina
  - All others (no biomarker elevation)

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New MI represent 5.6% of all MI patients

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### Baseline demographics

<table>
<thead>
<tr>
<th></th>
<th>« Classic » (n= 8701)</th>
<th>« New » (n=489)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>70.6 %</td>
<td>71.8 %</td>
<td>ns</td>
</tr>
<tr>
<td>Mean age</td>
<td>66.4 + 13.7</td>
<td>67.2 + 13.7</td>
<td>ns</td>
</tr>
<tr>
<td>Chest pain</td>
<td>83.4 %</td>
<td>82.3 %</td>
<td>ns</td>
</tr>
<tr>
<td>Short of breath</td>
<td>28 %</td>
<td>29.3 %</td>
<td>ns</td>
</tr>
<tr>
<td>Pain to door (median)</td>
<td>240 min</td>
<td>210 min</td>
<td>ns</td>
</tr>
<tr>
<td>Pre-hosp CPR</td>
<td>3.4 %</td>
<td>0.2 %</td>
<td>P&lt;0.0001</td>
</tr>
</tbody>
</table>

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CV risk factor profile

Acute Myocardial Infarction in Switzerland

<table>
<thead>
<tr>
<th>Factor</th>
<th>Classic</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known CAD</td>
<td>38.1%</td>
<td>56.8%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>20.2%</td>
<td>23.6%</td>
</tr>
<tr>
<td>High BP</td>
<td>60.4%</td>
<td>69.9%</td>
</tr>
<tr>
<td>Lipids</td>
<td>56.6%</td>
<td>66.7%</td>
</tr>
<tr>
<td>Smoking</td>
<td>37.5%</td>
<td>32%</td>
</tr>
<tr>
<td>Obese</td>
<td>19.6%</td>
<td>22.6%</td>
</tr>
<tr>
<td>Creatinine &gt;160 ug/l</td>
<td>7.8%</td>
<td>10.1%</td>
</tr>
</tbody>
</table>

* p < 0.0001      + p < 0.02

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Killip class at admission

Acute Myocardial Infarction in Switzerland

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Admission ECG

Acute Myocardial Infarction in Switzerland

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In-hospital management

Acute Myocardial Infarction in Switzerland

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LVEF and in-hospital events

- LVEF <35-40%
  - "classic": 7.3%
  - "new": 15.1%
- re-MI: 1.6%
- CVA: 1.0%
- shock: 5.2%
- MACE: 8.4%
- mortality: 6.7%

* p< 0.001     # p=0.004     + p=0.02

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Treatment at discharge

Acute Myocardial Infarction in Switzerland

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Acute Myocardial Infarction in Switzerland

Mortality

<table>
<thead>
<tr>
<th></th>
<th>&quot;classic&quot;</th>
<th>&quot;new&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>in-hospital</td>
<td>6.7%</td>
<td>3.5%</td>
</tr>
<tr>
<td>3 months</td>
<td>1.6%</td>
<td>1.0%</td>
</tr>
<tr>
<td>12 months</td>
<td>4.0%</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

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Re-MI after discharge

Acute Myocardial Infarction in Switzerland

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Hospital readmission

Acute Myocardial Infarction in Switzerland

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Any MACE (cardiovascular death, MI or CVA)

Acute Myocardial Infarction in Switzerland

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>'classic'</td>
<td>13.3%</td>
<td>11.8%</td>
</tr>
<tr>
<td>'new'</td>
<td>14.1%</td>
<td>13.4%</td>
</tr>
</tbody>
</table>

N = 2218

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Conclusions (1)

• Patients with ACS and minimal elevation of serum troponin (="new" MI) represent ca. 6% of all MI patients.
• They have smaller MI’s, less aggressive treatment, less early complications, and a better in-hospital prognosis than patients with higher serum biomarker levels.
• After discharge, however, their prognosis currently appears no different from that of patients with a "classic" MI event.

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Conclusions (2)

Wide implementation of the new definition:
- Will « increase » the incidence of MI
- Will « increase » the prevalence of CAD
- Will require more resources
- Will modify patient perception of event
- May alter insurability
- May impact on obtention of driving/flying licences
- Will markedly increase the rate of procedure-related MI
- Will profoundly influence clinical trials results
- Etc…

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Have we opened Pandora’s box?

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Hyperinflation for MI ???

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Conclusions (3)

✓ We most certainly need an international consensus,

but

✓ We will have to learn how to better qualify « MI » since the meaning of the word is rapidly changing…

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