Yin and yang
of current troponin assays
- analytical issues

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SKML sectie AC gebruikersdag
3 juni 2010
Hierarchy of Evidence-Based Medicine
Inhoud

I. Inleiding
II. Richtlijnen voor ACS en redefinitie AMI
III. Methode consequenties van de redefinitie van MI?
IV. Know your assay!
   praktijkvoorbeeld
   hs TnT implementatie in het LUMC
V. Landelijke data anno 2009/2010
VI. Conclusies
I. Introduction - cTroponin complex (Tn)

- Globular protein complex present in the thin myofilaments, involved in regulation of muscle contraction
- Different isotypes present in skeletal and cardiac muscle:
  - Yellow: Troponin C binds Calcium - *Identical in heart and skeletal muscle*
  - Blue: Troponin I in absence of Ca++ binds to actin, inhibits actin-myosin ATPase induced contraction - *cardiac specific isoforms*
  - Red: Troponin T links troponin complex to tropomyosin, facilitates contraction - *cardiac specific isoforms*
Lower cutoffs with cardiac troponin

- **Normal individuals**: no injury
- **Stable angina**: no injury
- **Unstable angina**: little to moderate injury
- **Myocardial infarction**: significant injury

**Concentration of cardiac marker** increasing

- **Cutoff specific cardiac marker**
- **Cutoff non-specific cardiac marker**

**hs cTn assays**
cTn allows better categorization and Tx of ACS pts

Acute Coronary Syndrome

ECG

NSTEACS  STEMI

Biomarker of necrosis

cTn normal  cTn positive

UA  NSTEMI  STEMI

confirm
cTn & interpretation

• Increases of cTns are **INDICATIVE** of myocardial injury but do not identify the mechanism of injury. If an ischemic mechanism of injury is unlikely, other etiologies of myocardial injury should be pursued.

• The **degree of the increase** of cTns in ischemia-induced injury patients is related to the patient’s prognosis.
Causes of Elevated Troponin in clinical settings other than ACS or PCI

<table>
<thead>
<tr>
<th>Ischaemic causes other than plaque fissuring or rupture</th>
<th>Myopericarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Coronary embolism (red cell or platelet thrombi, vegetation, atrial myxoma, calcification)</td>
<td>- Rheumatic fever</td>
</tr>
<tr>
<td>- Coronary spasm</td>
<td>- Rheumatoid arthritis</td>
</tr>
<tr>
<td>- Coronary dissection</td>
<td>- Systemic vasculitis</td>
</tr>
<tr>
<td>- Aortic dissection</td>
<td>- Post-viral</td>
</tr>
<tr>
<td>- Transplant vasculopathy</td>
<td><strong>Infiltrative diseases of the myocardium</strong></td>
</tr>
<tr>
<td>- <strong>Cardiac surgery</strong></td>
<td>- Amyloidosis</td>
</tr>
<tr>
<td>- Left ventricular venting</td>
<td>- Sarcoidosis</td>
</tr>
<tr>
<td>- Inadequate cardioplegia</td>
<td><strong>Traumatic</strong></td>
</tr>
<tr>
<td>- Traumatic atrial cannulation</td>
<td>- Atrioventricular ablation</td>
</tr>
<tr>
<td>- Manipulation of the heart</td>
<td>- Defibrillation</td>
</tr>
<tr>
<td>- Ischaemia related causes such as conduit or native vessel occlusion</td>
<td>- Chest wall trauma</td>
</tr>
</tbody>
</table>

**Miscellaneous**

- Tachyarrhythmia
- Hypertension
- Congestive heart failure
- Renal failure
- Drug toxicity (e.g. adriamycin, 5-fluorouracil, etc)
- Hypothyroidism
- Pulmonary embolism with right ventricular infarction
- Sepsis (including sepsis occurring with shock)
- Transient ischaemic attack, stroke or subarachnoid haemorrhage
- Pheochromocytoma
- Rhabdomyolysis with myocyte necrosis
Improved clinical performance with hs cTn assays

• **↑ clinical sensitivity for AMI diagnosis**
  - Rise and fall pattern should be typical
  - Timing of blood specimens: from 6-9 hrs after presentation → 3 hr
  - *Early clinical sensitivity*: > 90% at 3 hr!
  - Lowered specificity

• **↑ clinical sensitivity for risk stratification of adverse cardiac events**
  - Higher % of non-ACS pts with abnormal cTn results!
  - Higher % of chronic elevations (e.g. CRF)!
II. Guidelines for Acute Coronary Syndromes and re-definition of Myocardial Infarction

Guidelines with analytical focus

• NACB/IFCC working group

Guidelines with clinical focus

• Joint ESC/ACC/AHA/WHF Task Force
  1. Alpert et al. JACC 36:959-69, 2000;
  2. Thygesen et al JACC 50:2173-95, 2007
Criteria for acute MI

The term MI should be used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for myocardial infarction:

- Detection of a rise and/or fall of cardiac biomarkers (preferably cTn) with at least one value above the 99th percentile together with evidence of myocardial ischemia with at least one of the following:
  - Symptoms of ischemia
  - ECG changes indicative of new ischemia (new ST-T changes or new left bundle branch block (LBBB))
  - Development of pathologic Q waves in the ECG
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

- Timing is essential: sampling at admission, 6-9h, 12-24h

Thygesen K et al. EHJ 2007; 28, 2525-33. JACC, 502173-95.
NACB Clinical Guidelines for ACS

2007 Clin Chem and Circulation

Class I Recommendation

In the presence of a clinical history suggestive of ACS, the following are considered indicative of myocardial necrosis consistent with MI (Level of Evidence: C):

- Maximal concentration of cardiac troponin exceeding the 99th percentile of values (with optimal precision defined by total CV ≤ 10%) for a reference control group on at least one occasion during the first 24 hours after the clinical event (Observation of a rise and fall in values is useful in discriminating the timing of injury).
Class I (Level of Evidence C)

Identification of antibody/epitope recognition sites for each biomarker.

Assays for cardiac biomarkers should strive for a total imprecision (%CV) of ≤10% at the 99th percentile reference limit.

Cardiac biomarker assays must be characterized with respect to potential interferences, including rheumatoid factors, human anti-mouse antibodies, and heterophile antibodies.

Stability (over time and across temperature ranges) for each acceptable specimen type
NACB Analytical Guidelines for ACS
2007 Clin Chem and Circulation

Class I (Level of Evidence C)

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Assays for cardiac biomarkers should strive for a total imprecision (%CV) of ≤10% at the 99th percentile reference limit.

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Stability (over time and across temperature ranges) for each acceptable specimen type
Assay specificity (interferences)

• Heterophile antibodies
  • Natural autoimmune rheumatoid factors
  • Incidence: 0.02%
  • False positive if binding to Fc constant domain of Ag-Ab complexes
  • False low if binding to variable regions of the capture antibody

• HAAA
  • Most commonly HAMA
  • Compete with cTn by cross-reacting with reagent antibodies of the same
    species → false high

• Autoantibodies
  • Incidence of falsely negative cTn: 3.5%
  • Major effect when cTn concentration is low
  • Incidence of interference will increase in high sensitive cTn assays
NACB Analytical Guidelines for ACS
2007 Clin Chem and Circulation

Class I (Level of Evidence C)

Identification of antibody/epitope recognition sites for each biomarker.

Assays for cardiac biomarkers should strive for a total imprecision (%CV) of ≤10% at the 99th percentile reference limit.

Cardiac biomarker assays must be characterized with respect to potential interferences, including rheumatoid factors, human anti-mouse antibodies, and heterophile antibodies.

**Stability (over time and across temperature ranges) for each acceptable specimen type**
Where Should Quality Control Be?

- 3.0 µg/L QC level 2
- 0.50 µg/L QC level 1

Risk

Decision Point

0.050 µg/L

0.00
Where Should Quality Control Be?

- 0.25 µg/L QC level 2
- 0.04 µg/L QC level 1
- 0.050 µg/L Decision Point
- 0.00
III. Methodological consequences of the redefinition of MI?

- cTn assays need to be **more sensitive at the low end** → lower cutoff points

- cTn assays need to be **more precise**
History of cTn Cutoffs

cTnI concentration (µg/L)

- 0.01: Assay detection limit (mean+3SD)
- 0.0: Protein-free sample
- 0.05: 95% upper reference limit (NACB)
- 0.06: 99% upper reference limit (ESC/ACC)
- 0.07: 20% CV limit ("functional sensitivity")
- 0.08: 10% CV limit (ESC/ACC)
- 0.20: ROC AMI cutpoint (WHO)
Cutoffs for cardiac markers

• **ROC cutpoint**: separating data from patients with unstable angina vs. confirmed AMI.

• **99\textsuperscript{th} percentile with acceptable precision (≤10\%)**: established by ESC/ACC in 2000/2007 redefinition of AMI.

• **10\% CV surrogate cutoff** in absence of assays with acceptable sensitivity to determine 99\textsuperscript{th} percentile.
### Analytical characteristics of commercial and research high sensitivity cardiac troponin I and T assays per manufacturer.

<table>
<thead>
<tr>
<th>Company/Platform/assay</th>
<th>LoD µg/L</th>
<th>99th % µg/L</th>
<th>99th CV µg/L</th>
<th>10th CV µg/L</th>
<th>Risk Stratification</th>
<th>Epitopes recognized by antibodies</th>
<th>Detection Antibody Tag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott AxSYM ADV</td>
<td>0.02</td>
<td>0.04</td>
<td>15.0</td>
<td>0.16</td>
<td>Yes</td>
<td>C, 87-91, 41-69; D, 24-40</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Abbott ARCHITECT</td>
<td>&lt;0.01</td>
<td>0.028</td>
<td>15.0</td>
<td>0.032</td>
<td>No</td>
<td>C, 87-91, 24-40; D, 41-49</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Abbott i-STAT</td>
<td>0.02</td>
<td>0.084</td>
<td>16.5</td>
<td>0.10</td>
<td>Yes</td>
<td>C, 41-49, 88-91; D, 28-39, 62-78</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Beckman Coulter Access Accu</td>
<td>0.01</td>
<td>0.04</td>
<td>14.0</td>
<td>0.06</td>
<td>No</td>
<td>C, 41-49, 22-29; D, 87-91, 7B9</td>
<td>Acriflavine</td>
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<tr>
<td>bioMérieux Vidas Ultra</td>
<td>0.01</td>
<td>0.01</td>
<td>27.7</td>
<td>0.11</td>
<td>No</td>
<td>C, 41-49, 22-29; D, 87-91, 7B9</td>
<td>Acriflavine</td>
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<tr>
<td>Inverness BioSite Triage</td>
<td>0.05</td>
<td>&lt;0.05</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
<td>C, NA, D, 27-40</td>
<td>Fluorophor</td>
</tr>
<tr>
<td>Inverness BioSite Triage (r)</td>
<td>0.01</td>
<td>0.056</td>
<td>17.0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Fluorophor</td>
</tr>
<tr>
<td>Mitsubishi Chemical PATHFAST</td>
<td>0.008</td>
<td>0.029</td>
<td>10.0</td>
<td>0.014</td>
<td>No</td>
<td>C, 41-49, D, 116, 163-209</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Ortho Viron ECi ES</td>
<td>0.012</td>
<td>0.034</td>
<td>17.7</td>
<td>0.039</td>
<td>No</td>
<td>NA</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Radiometer AQT90</td>
<td>0.0095</td>
<td>0.032</td>
<td>17.7</td>
<td>0.039</td>
<td>No</td>
<td>C, 41-49, 180-190; D, 137-149</td>
<td>Acriflavine</td>
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<tr>
<td>Response Biomedical RAMP</td>
<td>0.03</td>
<td>&lt;0.1</td>
<td>18.5</td>
<td>0.21</td>
<td>No</td>
<td>C, 25-92; D, 26-38</td>
<td>Acriflavine</td>
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<tr>
<td>Roche Elecsys 2000</td>
<td>0.01</td>
<td>&lt;0.01</td>
<td>18.0</td>
<td>0.03</td>
<td>Yes</td>
<td>C, 125-131; D, 136-147</td>
<td>Gold nanoparticles</td>
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<tr>
<td>Roche Elecsys 2010</td>
<td>0.01</td>
<td>&lt;0.01</td>
<td>18.0</td>
<td>0.03</td>
<td>Yes</td>
<td>C, 125-131; D, 136-147</td>
<td>Gold nanoparticles</td>
</tr>
<tr>
<td>Roche Elecsys Reader</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
<td>C, 125-131; D, 136-147</td>
<td>Gold nanoparticles</td>
</tr>
<tr>
<td>Siemens Centria CR</td>
<td>0.008</td>
<td>0.04</td>
<td>10.0</td>
<td>0.03</td>
<td>No</td>
<td>C, 41-49, 87-91; D, 27-40</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Siemens Dimension Ql</td>
<td>0.04</td>
<td>0.07</td>
<td>10.0</td>
<td>0.14</td>
<td>Yes</td>
<td>C, 27-32; D, 41-56</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Siemens Immulite 2500 STAT</td>
<td>0.1</td>
<td>0.2</td>
<td>10.0</td>
<td>0.14</td>
<td>Yes</td>
<td>C, 87-91; D, 27-40</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Siemens Immulite 1000 Turbo</td>
<td>0.15</td>
<td>NA</td>
<td>NA</td>
<td>0.64</td>
<td>No</td>
<td>C, 87-91; D, 27-40</td>
<td>Acriflavine</td>
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<tr>
<td>Siemens Statham CS</td>
<td>0.03</td>
<td>0.07</td>
<td>10.0</td>
<td>0.06</td>
<td>Yes</td>
<td>C, 27-32; D, 41-56</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Siemens VISTA</td>
<td>0.015</td>
<td>0.045</td>
<td>10.0</td>
<td>0.04</td>
<td>Yes</td>
<td>C, 27-32; D, 41-56</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Tosoh AIA II</td>
<td>0.06</td>
<td>&lt;0.06</td>
<td>8.5</td>
<td>0.09</td>
<td>No</td>
<td>C, 41-49, 87-91</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Research High Sensitive Assays</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beckman Coulter Access hs-cTnT</td>
<td>0.0020</td>
<td>0.0086</td>
<td>10.0</td>
<td>0.0086</td>
<td>NA</td>
<td>C, 41-49, D, 24-40</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Beckman Coulter Access hs-cTnI</td>
<td>0.0001</td>
<td>0.0013</td>
<td>8.0</td>
<td>0.012</td>
<td>NA</td>
<td>C, 125-131; D, 136-147</td>
<td>Acriflavine</td>
</tr>
<tr>
<td>Roche Elecsys hs-cTnT</td>
<td>0.0002</td>
<td>0.0026</td>
<td>9.5</td>
<td>0.0005</td>
<td>NA</td>
<td>C, 136-147; D, 49-52, 70-73, 88, 169</td>
<td>Gold nanoparticles</td>
</tr>
<tr>
<td>Roche Elecsys hs-cTnI</td>
<td>0.00009</td>
<td>0.00101</td>
<td>9.0</td>
<td>0.00008</td>
<td>NA</td>
<td>C, 41-49, D, 27-41</td>
<td>Gold nanoparticles</td>
</tr>
</tbody>
</table>

Version updated September 12, 2009: LoD = limit of detection; 99th % = 99th percentile concentration; 10th CV = lowest concentration that has been shown to have a 10% CV (total imprecision); risk stratification claim per FDA; Epitopes were supplied by manufacturers; (r) = revised assay submitted to FDA per Inverness; hs = high sensitivity designation per manufacturers.
## Guideline acceptable troponin assays

<table>
<thead>
<tr>
<th>Method</th>
<th>99th P µg/L</th>
<th>10% CV µg/L</th>
<th>10%CV/ 99th P ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Troponin I</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitsubishi PATHFAST</td>
<td>0.029</td>
<td>0.014</td>
<td>0.48</td>
</tr>
<tr>
<td>ORTHO Vitros</td>
<td>0.034</td>
<td>0.034</td>
<td>1.00</td>
</tr>
<tr>
<td>Siemens Centaur</td>
<td>0.04</td>
<td>0.03</td>
<td>0.75</td>
</tr>
<tr>
<td>Siemens stratus</td>
<td>0.07</td>
<td>0.06</td>
<td>0.86</td>
</tr>
<tr>
<td>Siemens Vista</td>
<td>0.045</td>
<td>0.04</td>
<td>0.89</td>
</tr>
<tr>
<td>Beckman Access</td>
<td>0.0086</td>
<td>0.0086</td>
<td>1.00</td>
</tr>
<tr>
<td>Nanosphere</td>
<td>0.0028</td>
<td>0.0005</td>
<td>0.170</td>
</tr>
<tr>
<td>Singulex</td>
<td>0.0101</td>
<td>0.00088</td>
<td>0.087</td>
</tr>
<tr>
<td><strong>Troponin T</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roche hs TnT</td>
<td>0.013</td>
<td>0.012</td>
<td>0.92</td>
</tr>
</tbody>
</table>
IV. Know your assay!

Praktijkvoorbeeld
- Validatie van de hs cTnT assay in het LUMC
<table>
<thead>
<tr>
<th>Generation</th>
<th>Year</th>
<th>Test Name</th>
<th>Specificity</th>
<th>Sensitivity/Interferences</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>1989</td>
<td>ELISA Troponin T</td>
<td>1 cardio-specific monoclonal Ab</td>
<td></td>
</tr>
<tr>
<td>2nd</td>
<td>1993</td>
<td>Enzymun Troponin T, Elecsys Troponin T</td>
<td>2 cardio-specific monoclonal Ab cal: bovine cTnT</td>
<td></td>
</tr>
<tr>
<td>3rd</td>
<td>1996</td>
<td>Elecsys Troponin T</td>
<td>2 cardio-specific monoclonal Ab cal: human recombinant cTnT</td>
<td></td>
</tr>
<tr>
<td>4th</td>
<td>2005</td>
<td>Elecsys Troponin T</td>
<td>No interferences with heparin</td>
<td></td>
</tr>
<tr>
<td>5th</td>
<td>2009</td>
<td>High sensitive Elecsys cardiac Troponin T</td>
<td>Min. detectable conc: 0.003 µg/L * 99th percentile: 0.014 µg/L * 10% CV: 0.014 µg/L *</td>
<td></td>
</tr>
</tbody>
</table>

* ng/mL = µg/L
Development of a high sensitive TnT assay

Strategy:

1. Increase of sample volume from 15 µl to 50 µl
2. Signal amplification by use of highly optimized antibody-Ru conjugates
3. Increase of signal-to-noise ratio by lowering of background signal
4. Use of same antibodies as in 4th gen Troponin T assay
Chimeric anti Troponin T Antibodies
constructed from IgG from 2 different species (mouse / human)
Higher sensitivity, new guidelines means many more “false positives” !?
Dr Lefevre:

“With the 99th P cut-off value, cTn tests are not used anymore for their diagnostic value but rather for their prognostic value. This is why the 99th P cut-off value doesn’t meet the needs of ER & interventional cardiologists.

The initial IFCC objective was to force the manufacturers to standardize test accuracy and sensitivity, and not to define an ACS cut-off.

The side effect of an increased sensitivity has always been a specificity decrease. Clinicians should know this”.
LUMC nieuwsbrief en beslisgrenzen

hs cTnT test

- WHO Criteria > 0.1 µg/L
- 5th generation: > 0.05 µg/L
- Observational zone
  - Request additional sampling (T 3h, T 6h)
- 99th P at 0.014 µg/L

Voorstel: rekening houden met pos. bias in lage gebied; cutpoint evenredig verhogen!
V. SKML data hartmerkers anno 2009/2010

I. cTnI/T Combi data; cTnI histogram en interlab CVs

II. Klinische effectiviteit vigerende cTn assays: is de klinische interpretatie identiek?
Hartmerker rondzending vlg Combi Nieuwe Stijl

cTroponine Combi 2010.1:
gemiddelde van de meetbare resultaten (in \(\text{ug/L}\))

<table>
<thead>
<tr>
<th>Methode</th>
<th>n</th>
<th>A</th>
<th>B*</th>
<th>E</th>
<th>D</th>
<th>F</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Architect</td>
<td>8</td>
<td>0.017</td>
<td>0.051</td>
<td>0.211</td>
<td>0.312</td>
<td>0.608</td>
<td>1.234</td>
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<tr>
<td>Beckman Access Dxl</td>
<td>11</td>
<td>0.029</td>
<td>0.070</td>
<td>0.250</td>
<td>0.360</td>
<td>0.755</td>
<td>1.388</td>
</tr>
<tr>
<td>Beckman UniCel DxC</td>
<td>8</td>
<td>0.017</td>
<td>0.059</td>
<td>0.254</td>
<td>0.362</td>
<td>0.770</td>
<td>1.430</td>
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<tr>
<td>Siemens ADVIA</td>
<td>4</td>
<td>0.027</td>
<td>0.095</td>
<td>0.382</td>
<td>0.555</td>
<td>1.192</td>
<td>2.403</td>
</tr>
<tr>
<td>Siemens Dimension RxL</td>
<td>4</td>
<td>&lt;0.020</td>
<td>0.072</td>
<td>0.250</td>
<td>0.357</td>
<td>0.755</td>
<td>1.260</td>
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<tr>
<td>Siemens Dimension Vista</td>
<td>7</td>
<td>0.010</td>
<td>0.077</td>
<td>0.423</td>
<td>0.539</td>
<td>1.142</td>
<td>2.034</td>
</tr>
<tr>
<td>Siemens DPC Immulite</td>
<td>5</td>
<td>&lt;0.20</td>
<td>0.210</td>
<td>0.606</td>
<td>0.830</td>
<td>1.837</td>
<td>3.030</td>
</tr>
<tr>
<td>BioMerieux VIDAS</td>
<td>5</td>
<td>0.030</td>
<td>0.017</td>
<td>0.264</td>
<td>0.344</td>
<td>0.680</td>
<td>0.825</td>
</tr>
<tr>
<td>Totaal cTnI</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Roche Conventioneel</td>
<td>75</td>
<td>0.010</td>
<td>0.012</td>
<td>0.046</td>
<td>0.067</td>
<td>0.138</td>
<td>0.231</td>
</tr>
<tr>
<td>Hs-cTnT</td>
<td>4</td>
<td>0.008</td>
<td>0.019</td>
<td>0.065</td>
<td>0.086</td>
<td>0.160</td>
<td>0.250</td>
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<tr>
<td>Totaal cTnI</td>
<td>79</td>
<td></td>
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<tr>
<td>Doelstelling cTnI</td>
<td>79</td>
<td>0.010</td>
<td>0.015</td>
<td>0.050</td>
<td>0.070</td>
<td>0.140</td>
<td>0.240</td>
</tr>
</tbody>
</table>

* Monster met borderline cTroponine dat doorloopt in 2011 en 2012
Landelijke cTroponine I data

SKML rondzending 2009.2C

Concentratie in µg/L
### cTroponine I methodegroepen in Nederland

*interlaboratorium VC in monster 2009.3C*

<table>
<thead>
<tr>
<th>Methode</th>
<th>N</th>
<th>Gemiddelde (µg/L)</th>
<th>Interlab CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Architect</td>
<td>10</td>
<td>0.19</td>
<td>17%</td>
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<tr>
<td>Beckman</td>
<td>15</td>
<td>0.23</td>
<td>26%</td>
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<tr>
<td>VIDAS</td>
<td>4</td>
<td>0.22</td>
<td>28%</td>
</tr>
<tr>
<td>Siemens ADVIA</td>
<td>5</td>
<td>0.32</td>
<td>10%</td>
</tr>
<tr>
<td>Siemens Dimension</td>
<td>8</td>
<td>0.25</td>
<td>26%</td>
</tr>
<tr>
<td>Siemens Immulite</td>
<td>7</td>
<td>0.49</td>
<td>9%</td>
</tr>
</tbody>
</table>
Comparative Clinical Effectiveness of current cTn assays in the Netherlands

Hierarchy of Evidence-Based Medicine

- Decisions
- Cost Effectiveness
- Clinical Impact
- Diagnostic Performance
- Preanalytical Variables
- Technical Performance
Comparative Clinical Effectiveness of current cTn assays in the Netherlands

DOEL:

• Onderzoek naar de impact van de cTn analysekwaliteit op de klinische interpretatie: diagnose MI [ja/nee]

• Gebruik makend
  – van landelijke SKML rondzenddata (2010)
  – IFCC tabel met cTn beslisgrenzen (99e P, 10% CV) EN CVₐ

• Kleurcoderen: aan een getal hangt een klinische interpretatie vast die is aangegeven met een kleurcode
Klinische interpretatie cTn methoden anno 2010

• Verschilt ngl. methode, generatie en fabrikant

• Meest gevoelige assays momenteel, zowel in termen van betrouwbaar positief en betrouwbaar negatief meten zijn:

  • Siemens Advia cTnI
  • Siemens Dimenstion Vista cTnI
  • Roche hs cTnT
Conclusies bij (hs) cTn bepalingen: 1/2

Keys to Analytical Quality

• Know your cardiac troponin assay

• Harmony with other troponin assays?

• Imprecision (95% CI) at low levels ≤10%?

• Quality control monitoring at low (~99th percentile) troponin levels
Conclusies:

- **Troponin-omics:** cardiac troponin is niet meer weg te denken...
  - CK-MB and Mb geen rol meer
  - Seriele testing c.q. delta criterium vergt meer onderzoek
  - Reviseer tijdsinterval tussen opeenvolgende bloedafnames.

- Langzame beweging naar hs cTn I/T assays in Nederland

- Educatieve worsteling teneinde hs cTn begrijpelijk en hanteerbaar weg te zetten voor zowel lab als kliniek.

- Partnerships tussen kliniek en lab zijn essentieel.

- SKML rondzendmonsters: 12 paren per 2010, CNS concept, alsook levels in het referentiegebied en rond de 99° P!