10 Ways to Make the Use of High Sensitivity Cardiac Troponin Values Easier and Better

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Use the proper definition for high sensitivity
## Cardiac Troponin Assay Score Card

<table>
<thead>
<tr>
<th>Acceptance Designation</th>
<th>Total Precision at 99th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Acceptable</td>
<td>\leq 10%</td>
</tr>
<tr>
<td>Clinically Usable</td>
<td>&gt;10 to \leq 20%</td>
</tr>
<tr>
<td>Not Acceptable</td>
<td>&gt; 20%</td>
</tr>
</tbody>
</table>

### Assay Designation

<table>
<thead>
<tr>
<th>Assay Designation</th>
<th>Measurable Normal Values below 99th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 4 3rd gen hs</td>
<td>\geq 95%</td>
</tr>
<tr>
<td>Level 3 2nd gen hs</td>
<td>75 to &lt; 95%</td>
</tr>
<tr>
<td>Level 2 1st gen hs</td>
<td>50 to &lt; 75%</td>
</tr>
<tr>
<td>Level 1 Contemporary</td>
<td>&lt; 50%</td>
</tr>
</tbody>
</table>

*gen = generation; hs = high sensitivity*
Comparison of Normals Detected With Various Assays

99th Percentile Values and Percent of Patients Detected by Various Cardiac Troponin Assays
Implementation of a Sensitive Troponin I Assay and Risk of Recurrent Myocardial Infarction and Death in Patients With Suspected Acute Coronary Syndrome

Nicholas E. Wells, MD, PhD
Antonio D. Corbalis, MD, BS
Tzu-Chieh Lin
Hai-Leong Lu
Stefan J. Kastrati, MD
Michael A. Jacobson, MD
Patric J. De Buyzere, MD
Dominique Thivolet, MD
Mark W. Dehmer, MD
Bruce R. Kurland, MD

Context: Although troponin assays have become routine in the diagnosis of acute myocardial infarction, there are still controversies regarding their use in the early diagnosis of acute coronary syndrome, especially in patients with non-ST-elevation acute coronary syndrome (NSTE-ACS), as they are often considered "non-specific".

Objective: To determine the role of troponin I in the diagnosis of NSTE-ACS in clinical practice.

Design, Setting, and Patients: A prospective cohort study of 1,000 consecutive patients with suspected NSTE-ACS, who underwent a sensitive troponin I assay and had a standard coronary angiography.

Results: In patients with suspected NSTE-ACS, the diagnostic accuracy of troponin I was significantly improved compared to the standard troponin assay. The area under the receiver operating characteristic curve (AUC) for troponin I was 0.74, compared to 0.65 for the standard troponin assay. In patients with acute coronary syndrome, the diagnostic accuracy of troponin I was 0.90, compared to 0.80 for the standard troponin assay. The positive predictive value (PPV) and negative predictive value (NPV) of troponin I were 0.90 and 0.80, respectively.

Conclusions: The implementation of a sensitive troponin I assay in the diagnosis of NSTE-ACS significantly improves the diagnostic accuracy compared to the standard troponin assay. Troponin I is a valuable biomarker for the early diagnosis of NSTE-ACS.
Accuracy by Time of Admission

Area under the ROC curve

99\textsuperscript{th}% value

Mostly same assays but < 99\textsuperscript{th}% value cut off used

- Abbott-architect troponin I
- Roche high-sensitive troponin T
- Roche troponin I
- Siemens troponin I ultra
- Standard assay

Hours since onset of symptoms

NEJM 361:858, 2009
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**Effects of Hemolysis on hscTnT Values**

Reference Range for cTn Assays
(hscTnT – Roche)

99th Percentile Values and Percent of Patients Detected by Various Cardiac Troponin Assays
Clinical Implications of a Recent Adjustment to the High-Sensitivity Cardiac Troponin T Assay: User Beware

To the Editor:

Roche Diagnostics recently issued a technical bulletin calling for an adjustment to the calibration curve for the Elecsys Troponin T hs and Elecsys Troponin T hs STAT assays. Although this bulletin was disseminated widely in some countries, it was less widely distributed in others. The Roche high-sensitivity (hs) assays are in clinical use worldwide except within the US, where they are used for research but have not yet been cleared by the Food and Drug Administration. A 99th percentile value of 14 ng/L that has consistently been reported in the literature? Second, what percentage increase in detectable results will be seen among patients presenting for emergency care? Third, how does this change affect findings from the hundreds of published studies that have used both the 99th percentile value and changes over time to examine diagnostic accuracy, and how does it change the findings for risk stratification of acute coronary syndrome patients and apparently healthy patients? Fourth, what mechanisms are in place to alleviate customers’ concerns that similar product adjustments for this hs assay that have substantial downstream implications for patient triage? This percentage fell even further, with only 25% above this limit in a community-based study (4). In addition, the original diagnostic study (1) found that the hs assay for cardiac troponin T did not detect more myocardial infarctions than conventional assays (5). Was this decrease due to the change now reported by Roche, or did some other change occur very early in the assay?

We believe that these findings have major implications for patient care. We urge that in addition to correcting the lot issues it has defined, Roche reevaluate (at a minimum) subsets of the key research sample sets to ensure that: (a) there is no need to recalculate the 99th percentile value that is the...
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# Demographic Characteristics, Cardiovascular Risk Factors, and Cardiac Phenotypes Across Increasing Categories of Cardiac Troponin T Level

<table>
<thead>
<tr>
<th>Variable</th>
<th>cTnT Category, ng/mL(^a)</th>
<th>(n = 2589)</th>
<th>(n = 278)</th>
<th>(n = 279)</th>
<th>(n = 278)</th>
<th>(n = 122)</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTnT ≥ 0.01 ng/mL with standard assay, No/total (%)</td>
<td>&lt;0.003</td>
<td>0/2589</td>
<td>0/278</td>
<td>0/279</td>
<td>1/277 (0.4)</td>
<td>40/120 (33.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age, median (QR), y</td>
<td>0.003–0.00440</td>
<td>41 (35-49)</td>
<td>47 (39-55)</td>
<td>49 (41-55)</td>
<td>52 (45-58)</td>
<td>53 (44-68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Men, No./total, (%)</td>
<td>0.0066–&lt;0.014</td>
<td>175/278 (62.9)</td>
<td>196/279 (70.3)</td>
<td>214/278 (77.0)</td>
<td>85/122 (69.7)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity, No./total (%)</td>
<td>≥ 0.014</td>
<td>1229/2589 (47.5)</td>
<td>150/278 (54.0)</td>
<td>173/279 (62.0)</td>
<td>182/278 (65.5)</td>
<td>94/122 (77.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Black</td>
<td>P for Trend</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)P-values for trends.
99th Percentile Values in Normal Subjects Measured By Contemporary, Sensitive and High-Sensitivity Cardiac Troponin Assays

<table>
<thead>
<tr>
<th></th>
<th>99th Percentile</th>
<th>Percent Measurable</th>
<th>Male 99th Percentile</th>
<th>Female 99th Percentile</th>
<th>LoD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Sensitivity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbott ARCHITECT</td>
<td>23.4</td>
<td>95.0</td>
<td>35.8</td>
<td>15.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Beckman Access</td>
<td>32.2</td>
<td>87.4</td>
<td>52.2</td>
<td>23.1</td>
<td>3.0</td>
</tr>
<tr>
<td>Siemens Dimension</td>
<td>57.5</td>
<td>85.3</td>
<td>81.0</td>
<td>42.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Vista</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singulex Erenna</td>
<td>31.4</td>
<td>100.0</td>
<td>36.3</td>
<td>30.3</td>
<td>0.009</td>
</tr>
<tr>
<td>Roche cTnT</td>
<td>14.5</td>
<td>25.4</td>
<td>20.3</td>
<td>12.9</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Apple et al: CLINCHEM/2012/186874
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Low-End Comparability

Troponin T, Elecsys® 4th gen (pg/mL)

Difference with TnThs (%)
TACTICS (TIMI 18) Subgroups

Cardiac troponin T

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>Conservative treatment</th>
<th>Invasive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1 ng/mL</td>
<td>840</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.0</td>
</tr>
<tr>
<td>0.1 - &lt;0.4</td>
<td>137</td>
<td>16.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.7</td>
</tr>
<tr>
<td>0.4 - &lt;1.5</td>
<td>101</td>
<td>12.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.9</td>
</tr>
<tr>
<td>≥1.5</td>
<td>748</td>
<td>16.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.3</td>
</tr>
</tbody>
</table>

Death or MI

<table>
<thead>
<tr>
<th></th>
<th>Conservative treatment</th>
<th>Invasive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1 ng/mL</td>
<td>810</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.9</td>
</tr>
<tr>
<td>0.1 - &lt;0.4</td>
<td>137</td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>0.4 - &lt;1.5</td>
<td>101</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.9</td>
</tr>
<tr>
<td>≥1.5</td>
<td>748</td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.5</td>
</tr>
</tbody>
</table>

JAMA 286:2405, 2001
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Recognize there will be more elevations
# Prevalence of Detectable cTnT & levels ≥ 99<sup>th</sup> Percentile URL

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample Size, No.</th>
<th>cTnT Level, ng/mL</th>
<th>Prevalence, % (95% CI)</th>
<th>Sample Weight-Adjusted Prevalence, % (95% CI)</th>
<th>No. (%)</th>
<th>95&lt;sup&gt;%&lt;/sup&gt; Cl</th>
<th>No. (%)</th>
<th>95&lt;sup&gt;%&lt;/sup&gt; Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population</td>
<td>3546</td>
<td>957 (27.0)</td>
<td>25.0 (22.7 – 27.4)</td>
<td>122 (3.4)</td>
<td>2.0</td>
<td>(1.5 – 2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restricted population</td>
<td>3428</td>
<td>891 (26.0)</td>
<td>24.2 (21.8 – 26.5)</td>
<td>103 (3.0)</td>
<td>1.8</td>
<td>(1.2 – 2.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without CHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without cardiovascular disease</td>
<td>3277</td>
<td>813 (24.8)</td>
<td>23.7 (21.3 – 26.1)</td>
<td>82 (2.5)</td>
<td>1.9</td>
<td>(1.0 – 2.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without cardiovascular disease or CKD&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3222</td>
<td>773 (24.0)</td>
<td>23.1 (20.7 – 25.5)</td>
<td>65 (2.3)</td>
<td>1.2</td>
<td>(0.8 – 1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without cardiovascular disease, CKD, subclinical heart disease, diabetes, or hypertension&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2554</td>
<td>510 (20.0)</td>
<td>19.3 (16.8 – 21.8)</td>
<td>43 (1.7)</td>
<td>1.1</td>
<td>(0.6 – 1.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> CKD: Chronic kidney disease

<sup>b</sup> Subclinical heart disease, diabetes, or hypertension
Risk of CV Death or Heart Failure by hscTnI (Abbott) in PEACE

P<0.001

Omland et al: JACC, 2013
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Recognize there will be more elevations

Recognize that more patients will be diagnosed with AMI
Detection of cTnI in Patients with Unstable Angina

Current Generation cTnI (ng/ml)

- >=0.1
- 0.07-0.1
- 0.04-0.07

Nano-cTnI (ng/ml)

- >=0.008
- 0.002-0.008
- 0.0005-0.002

Wilson and Morrow, AHJ September 2009
<table>
<thead>
<tr>
<th>Change criteria</th>
<th>Myocardial injury present&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Myocardial injury absent&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Earliest pair (median interval 1 h; IQR 1-3 h)</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hs-cTnl change positive</td>
<td>88 [44.0 ng/L (19.0-153)]</td>
<td>75 [15.4 ng/L (6.3-34.7)]</td>
</tr>
<tr>
<td>hs-cTnl change negative</td>
<td>20 [13.4 ng/L (5.9-54.5)]</td>
<td>107 [5.4 ng/L (4.0-9.7)]</td>
</tr>
<tr>
<td>AccuTnl change positive</td>
<td>67 [0.06 µg/L 0.02-0.21]</td>
<td>7 [0.00 µg/L (0.00-0.01)]</td>
</tr>
<tr>
<td>AccuTnl change negative</td>
<td>41 [0.05 µg/L 0.02-0.16]</td>
<td>175 [0.00 µg/L (0.00-0.01)]</td>
</tr>
<tr>
<td><strong>Any specimen pair (median 4 specimens/subject; IQR 2-6)</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hs-cTnl change positive</td>
<td>107 [323 ng/L (77.0-4099)]</td>
<td>104 [31.9 ng/L (15.7-101)]</td>
</tr>
<tr>
<td>hs-cTnl change negative</td>
<td>1</td>
<td>78 [6.2 ng/L (4.8-9.4)]</td>
</tr>
<tr>
<td>AccuTnl change positive</td>
<td>95 [0.55 µg/L (0.11-5.5)]</td>
<td>13 [0.03 µg/L (0.03-0.04)]</td>
</tr>
<tr>
<td>AccuTnl change negative</td>
<td>13 [0.09 µg/L 0.05-0.18]</td>
<td>169 [0.01 µg/L (0.01-0.02)]</td>
</tr>
</tbody>
</table>

<sup>a</sup>Peak AccuTnl concentration was used to define if myocardial injury was present (>99<sup>th</sup> percentile) or absent (≤99<sup>th</sup> percentile)

<sup>b</sup>Data are n [median cTnl concentration at presentation (IQR)]

<sup>c</sup>Data are n [median cTnl concentration at peak (IQR)]

Survival by hscTnI Values - Preface

P<0.01

Days to death

Kavsak, Clin Chem, 2009
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99th% value

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Abbott-architect troponin I
Roche high-sensitive troponin T
Roche troponin I
Siemens troponin I ultra
Standard assay

Hours since onset of symptoms

NEJM 361:858, 2009
Time to Diagnosis with hscTnT
Based on The Gold Standard

Minutes

0 10% CV 99th % hscTnT

300 229

-68 -11 +61

TUSCA
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New strategies will reduce the time to rule out AMI in many patients.
DIAGNOSTIC PERFORMANCE OF THREE MODELS INCORPORATING hsTnT AND ECG FINDINGS FOR EARLY EXCLUSION OF AMI

<table>
<thead>
<tr>
<th>Model</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>100.0 (97.1 – 100.0)</td>
<td>30.1 (26.3 – 34.0)</td>
<td>23.7 (20.2 – 27.6)</td>
<td>100.0 (97.9 – 100.0)</td>
</tr>
<tr>
<td>B</td>
<td>95.2 (89.9 – 98.2)</td>
<td>69.4 (65.5 – 73.2)</td>
<td>40.4 (34.8 – 46.2)</td>
<td>98.5 (96.8 – 99.5)</td>
</tr>
<tr>
<td>C</td>
<td>100.0 (97.1 – 100.0)</td>
<td>66.4 (63.1 – 69.5)</td>
<td>30.3 (25.9 – 35.0)</td>
<td>100.0 (99.4 – 100.0)</td>
</tr>
</tbody>
</table>

Model A: hsTnT <3 ng/L and no ECG ischaemia;
Model B: hsTnT <14 ng/L and no ECG ischaemia;
Model C: (hsTnT <3 ng/L and no ECG ischaemia) OR (hsTnT <14 ng/L and no ECG ischaemia and symptom onset <6h)
Reference: Body
Accelerated Diagnostic Protocols with hscTnl (Abbott) – 30 Day MACE Rates

**ADAPT**

- Eligible patients with informed consent \( N = 1976 \)
- Excluded: 
  - \( N = 231 \)
  - TIMI score incomplete
  - No serial stored bloods

- Index test ADP \( N = 1695 \)
  - ADP positive “not low risk” \( N = 957 \)
  - ADP negative “low risk” \( N = 678 \)

- MACE: \( N = 245 \)
  - No MACE \( N = 721 \)

- MACE: \( N = 2 \)
  - No MACE \( N = 676 \)

**APACE**

- Eligible patients with informed consent \( N = 1616 \)
- Excluded: 
  - Chest pain of unknown origin and/or hscTnl above cut off \( N = 46 \)
  - No serial samples \( N = 655 \)
  - No ECG available \( N = 6 \)

- Index test ADP \( N = 909 \)
  - ADP positive “not low risk” \( N = 558 \)
  - ADP negative “low risk” \( N = 351 \)

- MACE: \( N = 155 \)
  - No MACE \( N = 403 \)

- MACE: \( N = 1 \)
  - No MACE \( N = 350 \)

Submitted – Cullen, Than et al
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New strategies will reduce the time to rule out AMI in many patients

Use changing values to diagnose AMI
Criteria for Acute Myocardial Infarction

- Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin (cTn)) with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:
  - Ischaemic symptoms
  - ECG changes of new ischaemia (new ST-T changes or new LBBB)
  - Development of pathologic Q waves in the ECG
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
  - Identification of an intracoronary thrombus by angiography or autopsy

Third Universal Definition of Myocardial Infarction
Changes in cTnT in Dialysis Patients with ACS

Nephron Clin Prac 98:c87, 2004
## Determining Assay Values are Different

<table>
<thead>
<tr>
<th>Assay</th>
<th>Range</th>
<th>Value</th>
<th>Date</th>
<th>Delta</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (Bld Urea Nitr.)</td>
<td>8-24 mg/dL</td>
<td>48</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>100-108 mmol/L</td>
<td>110</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bicarbonate, P/S</td>
<td>22-29 mmol/L</td>
<td>22</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anion Gap</td>
<td>7-15</td>
<td>10</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CARDIAC CHEMIS...</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T, S..........</td>
<td>&lt;0.01 ng/mL</td>
<td>0.11</td>
<td>23 Jan 08</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>3H Troponin T, S.......</td>
<td>&lt;0.01 ng/mL</td>
<td>0.12</td>
<td>23 Jan 08</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>6H Troponin T, S.......</td>
<td>&lt;0.01 ng/mL</td>
<td>0.15</td>
<td>23 Jan 08</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>3H Delta..............</td>
<td>ng/mL</td>
<td>Not Sig @</td>
<td>23 Jan 08</td>
<td>Not Sig @</td>
<td></td>
</tr>
<tr>
<td>6H Delta..............</td>
<td>ng/mL</td>
<td>Sig Delta @</td>
<td>23 Jan 08</td>
<td>Sig Delta @</td>
<td></td>
</tr>
<tr>
<td><strong>LIPIDS 63 AG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LIPIDS 1 AG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL Subfractionation</td>
<td>100-200 g/dL</td>
<td>.@b0</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta LDL Cholesterol</td>
<td>100-200 g/dL</td>
<td>.@b1</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentile Rank........</td>
<td>100-200 g/dL</td>
<td>1.01 @h3</td>
<td>23 Jan 08</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Short-Term Analytical and Biological Variation by hs-cTnI Assays

<table>
<thead>
<tr>
<th></th>
<th>Abbott&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Beckman&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Roche (E170)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Siemens&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Singulex&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV-A (%)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>13.8</td>
<td>14.5</td>
<td>7.8</td>
<td>13.0</td>
<td>8.3</td>
</tr>
<tr>
<td>CV-I (%)</td>
<td>15.2</td>
<td>6.1</td>
<td>15.0</td>
<td>12.9</td>
<td>9.7</td>
</tr>
<tr>
<td>CV-G (%)</td>
<td>70.5</td>
<td>34.8</td>
<td>NA</td>
<td>12.3</td>
<td>57.0</td>
</tr>
<tr>
<td>Index of individuality</td>
<td>0.22</td>
<td>0.46</td>
<td>NA</td>
<td>0.11</td>
<td>0.21</td>
</tr>
<tr>
<td>RCV (%)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>NA</td>
<td>NA</td>
<td>47.0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>RCV increase (%)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>69.3</td>
<td>63.8</td>
<td>NA</td>
<td>57.5</td>
<td>46.0</td>
</tr>
<tr>
<td>RCV decrease (%)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>-40.9</td>
<td>-38.9</td>
<td>NA</td>
<td>-36.5</td>
<td>-32.0</td>
</tr>
<tr>
<td>Within-individual mean (ng/L)</td>
<td>3.5</td>
<td>4.9</td>
<td>NA</td>
<td>5.5</td>
<td>2.8</td>
</tr>
</tbody>
</table>

<sup>a</sup> Apple et al (38); <sup>b</sup> Vasile et al (36); <sup>c</sup> Wu et al (35)

<sup>d</sup> CV-A, analytical CV; CV-I, within-individual CV; CV-G, between individual CV; NA, not available;

RCV, relative change value; <sup>e</sup> REC percentage applies to parametric data

<sup>f</sup> RCV increase and decrease percentages refer to nonparametric data and are log-transformed

### PERCENTILES OF CHANGE IN cTnT CONCENTRATION IN CORONARY CARE UNIT PATIENTS WITHOUT MI

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Relative change, %</th>
<th>Absolute change, ng/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50th (95% CI)</td>
<td>97.5th (95% CI)</td>
</tr>
<tr>
<td>All diagnoses</td>
<td>10 (10 - 11)</td>
<td>59 (48 - 71)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>10 (9 - 12)</td>
<td>51 (38 - 65)</td>
</tr>
<tr>
<td>Stable angina pectoris</td>
<td>10 (9 - 12)</td>
<td>67 (34 - 99)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>9 (6 - 12)</td>
<td>66 (29 - 104)</td>
</tr>
<tr>
<td>Noncardiac chest pain</td>
<td>12 (10 - 15)</td>
<td>64 (46 - 82)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Number of cTnT measurements included in calculations.

<sup>b</sup> NA, not applicable, because the absolute change in cTnT concentration differed among diagnosis groups (heart failure vs atrial fibrillation, stable angina pectoris, and noncardiac chest pain, all P < 0.02, and atrial fibrillation vs stable angina pectoris, P = 0.017, for difference in medians.

Reference: Clin Chem 2012;58(3)
Use of High Sensitivity Troponin T to Diagnose Myocardial Infarction

Clinical setting consistent with myocardial ischemia

Baseline

- **<14 ng/L**
  - Retest hsTnT 3 hours after symptom onset or if timing of symptom onset is unclear at 6 hours after presentation
  - ≤14 ng/L rules out MI with >90% probability
  - If ≥14 ng/L then proceed to middle part of algorithm

- **≥14-52 ng/L**
  - Change <50%
  - Change ≥50%
  - Adverse prognosis
  - Retest hsTnT at 6, 12 hr

- **≥53 ng/L**
  - Change <20%
  - Change ≥20%
  - Myocardial infarction
  - Evidence-based treatments

White HD; AHJ 2010
Absolute and Relative Changes in Patients with AMI, Unstable Angina and “Non-Cardiac Chest Pain”

Defining the Optimal Delta: The Tension Between Sensitivity and Specificity

Data from Keller et al (JAMA 2012)
Delta for the Diagnosis of AMI with hscTnT Based on The Gold Standard (T0-T3hr)

Mean increase in hscTnT (ng/L)

- 10% CV: 1136 ng/L
- 99th %: 604 ng/L
- hscTnT: 452 ng/L

TUSCA, AJM in press
Delta Guidance

MUST USE FIXED TIMING

Near 99\textsuperscript{th}\% URL value

The greater the change, the more likely AMI

The lesser the change, the less likely AMI

Percentages and absolute values may provide similar information

At higher levels

Absolute values may be better
Delta Guidance

MUST USE FIXED TIMING

Near 99th% URL value

- The greater the change, the more likely AMI
- The lesser the change, the less likely AMI
- Percentages and absolute values may provide similar information

At higher levels

- Absolute values may be better

Avoid

Extrapolating the data from one assay to another assay

The idea that release is continuous so that one can use a one or 2 hour delta by dividing by the delta found at 5 or 6 hours.
10 Ways to Make the Use of High Sensitivity Cardiac Troponin Values Easier and Better

Use the proper definition for high sensitivity

Be aware that hs assays will be more sensitive to pre-analytical and analytical confounds

Use whole numbers and gender specific cut off values

Use anchor values from previous assays to gauge differences

Recognize there will be more elevations

Recognize that more patients will be diagnosed with AMI

Recognize that the time to rule in will be shortened for many but, despite the hype may not be shortened overall

New strategies will reduce the time to rule out AMI in many patients

Use changing values to diagnose AMI

Remember it is the clinician who makes the diagnosis of AMI and not the laboratory results
It is not the Data but How You Interpret it that is Important

"Your labwork is back, Don. It appears you're a squirrel."