Cardiac Troponin: Current Status and Future Promise

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Disclosures

• Honoraria: Siemens Healthcare, Roche Diagnostics, Mitsubushi, Abbott

• Consultant: Siemens Healthcare, Philips Healthcare, Roche Diagnostics

• Research Funding: BG Medicine, Roche Diagnostics, Siemens Healthcare, Beckman-Coulter, Mitsubushi, Abbott Diagnostics, Alere
Objectives

• List the biomarker criteria needed to establish the diagnosis of myocardial infarction

• List four characteristics that are critical to evaluate for determining an appropriate troponin

• Explain criteria and definition of early generation, contemporary and high sensitivity cardiac troponin assays

• Discuss four important criteria for a clinically appropriate point of care troponin system
Organization of Session

- Biomarker(s) used for MI diagnosis.
- Characteristics of assay(s).
  - Antibody configuration
  - Imprecision
  - Cutoffs, 99th %tile of a reference control population
- Focus on Turnaround Time
  - Point of Care vs. Central Laboratory Measurement
- Next Generation Assays
When troponin is increased think heart

Cardiac isoforms in blood
Necrosis Biomarkers Timeline

- 1950: AST in MI
- 1960: LD & CK in MI
- 1970: CK isoenzymes
- 1980: Electrophoresis CK and LD
- 1990: WHO criteria MI
- 2000: CK-MB Mass
- 2010: cTnI in MI

Guidelines sensitive cTn Assays
Pathfast Sensitive cTnI Clears FDA

High-Sensitivity cTn Assays
Single Biomarker Test for MI

2014 AHA/ACC* Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
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<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
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<tr>
<td>Measure cardiac-specific troponin (troponin I or T) at presentation and 3–6 h after symptom onset in all patients with suspected ACS to identify pattern of values</td>
<td>I</td>
<td>A</td>
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<tr>
<td>Obtain additional troponin levels beyond 6 h in patients with initial normal serial troponins with electrocardiographic changes and/or intermediate/high risk clinical features</td>
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<td>Consider time of presentation the time of onset with ambiguous symptom onset for assessing troponin values</td>
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<td>With contemporary troponin assays, CK-MB and myoglobin are not useful for diagnosis of ACS</td>
<td>III: No Benefit</td>
<td>A</td>
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<td><strong>Prognosis</strong></td>
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<td>Troponin elevations are useful for short- and long-term prognosis</td>
<td>I</td>
<td>B</td>
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<td>Remeasurement of troponin value once on d 3 or 4 in patients with MI may be reasonable as an index of infarct size and dynamics of necrosis</td>
<td>IIb</td>
<td>B</td>
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<tr>
<td>BNP may be reasonable for additional prognostic information</td>
<td>IIb</td>
<td>B</td>
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Cardiac Troponin
Elevated Troponin in Patients without ACS or Heart Failure

- **Acute Disease**
  - Cardiac and Vascular
  - Acute Aortic dissection
  - Cerebrovascular accident
  - Ischemic Stroke
  - Intracerebral Hemorrhage
  - Subarachnoid Hemorrhage
  - Medical ICU Patients

- **Chronic Disease**
  - ESRD
  - Cardiac infiltrative disorders
  - Amyloidosis
  - Sarcoidosis
  - Hemochromatosis
  - Scleroderma

- **Heart Specific**
  - Birth Complications in Infants
  - Extreme Low Birth Weight
  - Preterm Delivery
  - Acute Complications of
    - Inherited Disorders
  - Neurofibromatosis
  - Duchenne Muscular Dystrophy
  - Klippel-Feil syndrome
  - Environmental Exposure
  - Carbon Monoxide
  - Hydrogen Sulfide
  - Colchicine exposure

- **Disease Specific**
  - Other Medications
  - **Myocardial Injury**
  - Blunt Chest Injury
  - Endurance athletes
  - Envenomation
  - Snake
  - Jellyfish
  - Spider
  - Centipede
  - Scorpion
Are All Cardiac Troponin Assays Created Equal?

NO x 1000
Cardiac biomarker assays must be characterized with respect to potential interferences, including rheumatoid factors, human anti-mouse antibodies, and heterophile antibodies.

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.

Stability (over time and across temperature ranges) for each acceptable specimen type.
Analytical False Positive

cTnI

Heterophile Antibody
Identification of antibody/epitope recognition sites for each biomarker.

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

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

Stability (over time and across temperature ranges) for each acceptable specimen type
Six commercial (Hytest) mAbs evaluated for use in a 1 x 1 “reference “immunoassay

Epitope 1

Epitope 2

mAb M18
mAb 3C7
mAb 19C7
mAb MF4
mAb 267
mAb 560

mAb M18

mAb 3C7

mAb 19C7

mAb MF4

mAb 267

mAb 560

mAb M18

mAb 3C7

mAb 19C7

mAb MF4

mAb 267

mAb 560

mAb M18

mAb 3C7

mAb 19C7

mAb MF4

mAb 267

mAb 560

mAb M18

mAb 3C7

mAb 19C7

mAb MF4

mAb 267

mAb 560

mAb M18

mAb 3C7

mAb 19C7

mAb MF4

mAb 267

mAb 560

mAb M18

mAb 3C7

mAb 19C7

mAb MF4

mAb 267

mAb 560

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<tr>
<th>Commercially available assays - Company/ platform(s)</th>
<th>assay</th>
<th>LoB * (ng/L)</th>
<th>LoD b (ng/L)</th>
<th>99 th % (ng/L)</th>
<th>% CV at 99 th %</th>
<th>10 % CV (ng/L)</th>
<th>Reference population N: age range (y)</th>
<th>Epitopes recognised by Antibodies</th>
<th>Detection Antibody Tag</th>
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<td>0.7 – 1.3</td>
<td>1.1 – 1.9</td>
<td>26.2</td>
<td>4.0</td>
<td>1531: 21 - 75</td>
<td>M: 766 21 - 73; F: 765 21 - 75</td>
<td>C: 24-9; D 59-49</td>
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<td>22</td>
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<td>(50% &gt; 40 y)</td>
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<td>27.7</td>
<td>747: 20 - 81</td>
<td>C: 79-91, 22-29; D: 87-91, 7B9</td>
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<td>Ortho VITROS Troponin I ES</td>
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<td>7</td>
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<td>23</td>
<td>12.3</td>
<td>27</td>
<td>231 (M:125; F:106)</td>
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<td>Response Biomedical RAMP</td>
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<td>180: 18 - 80 (M: 84; F: 96)</td>
<td>C: 85-92; D: 26-38</td>
<td>Fluorophor</td>
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* LoB: Lower limit of blank
b LoD: Lower limit of detection

**Notes:**
- Siemens ADVIA Centaur® Tnl-Ultra™
- Siemens Dimension® Rxl CTNI
- Siemens Dimension® EXL™ TNI
- Siemens Dimension® VISTA® CTNI
- Siemens IMMULITE® 1000 Turbo e
- Siemens IMMULITE® 1000 e
- Siemens IMMULITE® 2000 XPl e
- Siemens IMMULITE®1000 Turbo f
- Siemens Stratus® CS cTnl
- Tosoh ST AIA-PACK cTnl (2nd gen)
<table>
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<tr>
<th>Commercially available assays - Company/platform(s)/assay</th>
<th>LoB* (ng/L)</th>
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<td>C: 49; 85: D: 28-39, 62-78, 87-91, 7B9</td>
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<td>40</td>
<td>14.0</td>
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<td>1000: &gt; 40</td>
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<td>bioMerieux Vidas Ultra</td>
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<td>27.7</td>
<td>110</td>
<td>747: 20 – 81</td>
<td>527: 18 – 94 (50% &gt; 40 y)</td>
<td>C: 7B9; D: 163-209</td>
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<td>5.2</td>
<td>3.1</td>
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<td>231 (M:125; F:106)</td>
<td>C: 4; D: 190-196; D: 137-149</td>
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<td>Fluorophor</td>
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Cardiac Biomarkers and the Definition of Acute Myocardial Infarction (AMI)

Cardiac biomarkers should be used in clinical settings consistent with acute cardiac ischemia

- Rise and/or fall of cardiac biomarker values
  - Preferably cardiac troponin (cTn)
- At least one value above the 99\textsuperscript{th} percentile upper reference limit (URL)
- Precision (CV) of \leq 10\% at the 99 percentile URL
**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***
More Sensitive Troponin

High Accuracy, Different Precision

- High accuracy, low precision (15% CV)
- High accuracy, high precision (5% CV)
Timing of sampling?
Evolution of Serial Blood Sample Timing

1. Rule-out

2. Rule-in

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High Sensitivity: cTnI cTnI
### Table. Analytical characteristics of commercial and research cardiac troponin I and T assays declared by the manufacturer.

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<th>Assay Details</th>
<th>% CV at 99th %</th>
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<td>Beckman Coulter Access Accu</td>
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<td>bioMerieux Vidas Ultra</td>
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<td>Tosoh ST AIA-PACK</td>
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Definition of Myocardial Infarction

“Small heart attacks are so common; they are almost within normal range.”

Paul Dudley White, 1957
The Father of American Cardiology
4th Universal Definition of Myocardial Infarction


- cTnI and cTnT are the preferred biomarkers recommended to both rule in and rule out myocardial injury, and thus to define MI and each specific subtype of MI.
- Detection of a rise and/or fall of cTn values is essential, and a key early component along with other elements of the clinical evaluation to establish the diagnosis of acute MI.
Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin] with at least one value above the 99th percentile upper reference limit ...

• Less than 50% of institutions in the USA use the recommended 99th percentile cutpoint for diagnosis of myocardial infarction.

• Less that 50% of the institutions in the developed world use the 99th percentile cutpoint for diagnosis of myocardial infarction.
Does improved precision at 99\textsuperscript{th} percentile result in better outcomes?
Implementation of a Sensitive Troponin I Assay and Risk of Recurrent Myocardial Infarction and Death in Patients With Suspected Acute Coronary Syndrome

Mills et al. JAMA. 2011;305(12):1210-1216
Management of patients with suspected acute coronary syndrome before (validation phase) and after (implementation phase) the introduction of a sensitive Troponin Assay

<table>
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<tr>
<th>No. (%) of Patients</th>
<th>Stratified by Peak Troponin Concentration, ng/mL</th>
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<td></td>
<td>All &lt;0.05 0.05-0.19 ≥0.20 P Value</td>
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<tr>
<td><strong>Validation phase</strong></td>
<td>(N = 1038) (n = 657) (n = 90) (n = 291)</td>
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<tr>
<td>Cardiology referral</td>
<td>506 (49) 197 (30) 40 (44) 271 (93) &lt;.001</td>
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<tr>
<td>Coronary angiography</td>
<td>257 (25) 39 (6) 18 (20) 203 (69) &lt;.001</td>
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<tr>
<td>PCI</td>
<td>187 (18) 13 (2) 14 (16) 160 (55) &lt;.001</td>
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<tr>
<td>CABG surgery</td>
<td>16 (2) 3 (0) 1 (1) 12 (4) &lt;.001</td>
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<tr>
<td><strong>Medication on discharge</strong></td>
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<tr>
<td>Aspirin</td>
<td>712 (69) 376 (57) 67 (75) 269 (92) &lt;.001</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>393 (38) 118 (18) 28 (31) 247 (85) &lt;.001</td>
</tr>
<tr>
<td>Dual-antiplatelet therapy</td>
<td>336 (32) 79 (12) 24 (27) 233 (80) &lt;.001</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>473 (46) 239 (36) 42 (47) 192 (66) &lt;.001</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>477 (46) 217 (33) 39 (43) 221 (76) &lt;.001</td>
</tr>
<tr>
<td>Statins</td>
<td>685 (66) 374 (57) 52 (58) 259 (89) &lt;.001</td>
</tr>
<tr>
<td><strong>Implementation phase</strong></td>
<td>(N = 1054) n = (683) n = (80) n = (291)</td>
</tr>
<tr>
<td>Cardiology referral</td>
<td>573 (54) 242 (35) 59 (74) 272 (93) &lt;.001</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>302 (29) 44 (5) 37 (46) 221 (76) &lt;.001</td>
</tr>
<tr>
<td>PCI</td>
<td>212 (20) 23 (3) 16 (20) 173 (59) &lt;.001</td>
</tr>
<tr>
<td>CABG surgery</td>
<td>21 (2) 3 (0) 3 (4) 15 (5) &lt;.001</td>
</tr>
<tr>
<td><strong>Medication on discharge</strong></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>707 (67) 376 (55) 66 (83) 265 (91) &lt;.001</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>403 (38) 89 (13) 49 (61) 266 (91) &lt;.001</td>
</tr>
<tr>
<td>Dual-antiplatelet therapy</td>
<td>348 (33) 55 (8) 46 (58) 247 (85) &lt;.001</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>468 (44) 232 (34) 50 (62) 186 (64) &lt;.001</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>514 (49) 246 (36) 47 (59) 221 (76) &lt;.001</td>
</tr>
<tr>
<td>Statins</td>
<td>695 (66) 369 (54) 64 (80) 262 (90) &lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

a Variables analyzed using χ² test with post hoc Fisher exact testing between individual groups.
b P < .05 for validation phase vs implementation phase.
c P < .001 for validation phase vs implementation phase.
Major Focus on Troponin TAT

- Society of Cardiovascular Patient Care (SCPC): Requiring POCT 60 minutes or less TAT (90%) for accreditation
- CAP: Established Q-Monitor that measures TAT
- National Academy of Clinical Biochemistry and International Federation of Clinical Chemistry: Recommend 60 minutes or less TAT
- American College of Cardiology & American Heart Assoc.: Recommends 60 minute TAT with preference at 30 minutes

- Time is Critical (but Not Everything)
Demonstrating the value of lab tests on health outcomes is reliant on linking the test with processes that directly impact outcomes.
Point of Care
Troponin Assays
do NOT get a
Pass on Quality!
SnOut:
- Sensitivity (TP/TP+FN) describes the ability of a test to identify true disease
  - A high sensitivity test has few false negatives and is effective at ruling conditions “out” (SnOut)

SpIn:
- Specificity (TN/TN+FP) describes the ability of an IVD test to correctly identify the absence of disease
  - A high specificity test has few false positives and is effective at ruling conditions “in” (SpIn).
Point-of-care troponin values may provide initial diagnostic information, although their sensitivity is substantially below that of central laboratory methods (refs). In addition, the rigorous quantitative assay standardization needed for routine diagnosis favors central laboratory testing.

Accrediting Organizations will likely state something akin: Laboratory Based Assays* and the 99th% URL.”

*PATHFAST, Stratus CS and …. Cardiac Biomarker Analyzers are equivalent.
Randomised Assessment of Treatment using Panel Assay of Cardiac markers: A randomised controlled trial of point-of-care cardiac markers in the emergency department

P. O. Collinson¹, Steve Goodacr², Mike Bradburn², Patrick Fitzgerald², Liz Cross², Alasdair Gray³, Alistair Hall⁴ on behalf of the RATPAC investigators.
Randomized Design

N= 2263 across 6 sites

Patients With Suspected ACS Enrolled

Randomize

POC, cTn

Data collection

Outcomes

Usual Biomarker Strategy

Data collection

Outcomes

OUTCOMES

• Proportion of patients successfully discharged home or to in-patient ward after ED assessment by 4 hours.
• Discharge with no adverse event during the subsequent three months = Success.
Duration from arrival to discharge from hospital

- **Point of Care**
- **Standard Care**

**Time to discharge (hours)**

- Proportion in hospital
  - 0.00
  - 0.25
  - 0.50
  - 0.75
  - 1.00

Duration from arrival to discharge from hospital.
**Successful discharge at 4 hrs?**

<table>
<thead>
<tr>
<th></th>
<th>Point of care</th>
<th>Standard Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yes</strong></td>
<td>358 (32%)</td>
<td>146 (13%)</td>
</tr>
<tr>
<td><strong>Discharged but re-admitted</strong></td>
<td>4 (&lt;1%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td><strong>In hospital at 4 hours, decision to discharge</strong></td>
<td>43 (4%)</td>
<td>13 (1%)</td>
</tr>
</tbody>
</table>
## Major adverse events within 90 days

<table>
<thead>
<tr>
<th>Event</th>
<th>Point of care</th>
<th>Standard Care</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>6 (1%)</td>
<td>2 (&lt;1%)</td>
<td>3.4 (0.7 to 17.3)</td>
<td>0.142</td>
</tr>
<tr>
<td>Non-fatal AMI</td>
<td>5 (&lt;1%)</td>
<td>5 (&lt;1%)</td>
<td>0.9 (0.3 to 3.2)</td>
<td>0.903</td>
</tr>
<tr>
<td>Hospitalisation for ACS</td>
<td>18 (2%)</td>
<td>9 (1%)</td>
<td>1.8 (0.8 to 4.1)</td>
<td>0.149</td>
</tr>
<tr>
<td>Life threatening arrhythmia</td>
<td>6 (1%)</td>
<td>2 (&lt;1%)</td>
<td>3.2 (0.6 to 15.9)</td>
<td>0.160</td>
</tr>
<tr>
<td>Emergency revascularisation</td>
<td>10 (1%)</td>
<td>14 (1%)</td>
<td>0.7 (0.3 to 1.5)</td>
<td>0.324</td>
</tr>
</tbody>
</table>
The Next Generation

Prior Gen commercial TnI
Limit of detect ~ 0.1 ng/ml
10% CV = 0.4 ng/ml

Current commercial TnI
Limit of detect ~ 0.005 ng/ml
10% CV = 0.02 - 0.04 ng/ml

Next Gen Ultrasensitive
Limit of detect ~ 0.0001 ng/ml
10% CV < 0.001 ng/ml

From: Contemporary Cardiology: Cardiovascular Biomarkers: Pathophysiology and Disease Management
Edited by: David A. Morrow © Humana Press Inc., Totowa, NJ
“...when troponin was a lousy assay it was a great test, but now that it's becoming a great assay, it's getting to be a lousy test.”
High-sensitivity Cardiac Troponin Assays

Definition is Analytical, Benefit is Clinical

- **High-Sensitivity’** is an analytical term
- **hsTn assays **DO NOT measure a different analyte
Clinical Laboratory Practice Recommendations for the Use of Cardiac Troponin in Acute Coronary Syndrome: Expert Opinion from the Academy of the American Association for Clinical Chemistry and the Task Force on Clinical Applications of Cardiac Bio-Markers of the International Federation of Clinical Chemistry and Laboratory Medicine

Alan H.B. Wu,¹* Robert H. Christenson,² Dina N. Greene,³ Allan S. Jaffe,⁴ Peter A. Kavsak,⁵ Jordi Ordonez-Llanos,⁶ and Fred S. Apple⁷
What is High-Sensitivity Cardiac Troponin?
Clinical Chemistry 64:4;645–655 (2018)

AACC Academy and IFCC Task Force defines a high-sensitivity cTn as:

• an assay that can measure $\geq 50\%$ of healthy men and healthy women, i.e. values above the Limit of Detection.

• Also, hs-cTn assays are precise, i.e. day-to-day Total CV $\leq 10\%$.

AACC: American Association for Clinical Chemistry
IFCC: International Federation for Clinical Chemistry
Recommendation 5: We recommend that assays unable to detect cTn at concentrations at or above the LoD in at least 50% of healthy men and women be labeled as contemporary cTn assays.
# AACC Universal Sample Bank

Demographic and Clinical Laboratory Data For Enrolled Healthy Individuals

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Caucasian</th>
<th>African-American</th>
<th>Asian</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>406</td>
<td>402</td>
<td>481</td>
<td>212</td>
<td>91</td>
<td>24</td>
</tr>
<tr>
<td>Age, years</td>
<td>39 (13)(^a)</td>
<td>39 (13)</td>
<td>41 (13)</td>
<td>36 (13)</td>
<td>37 (11)</td>
<td>38 (13)</td>
</tr>
<tr>
<td>Hb A(_1c), %</td>
<td>5.5 (0.33)</td>
<td>5.5 (0.30)</td>
<td>5.4 (0.28)</td>
<td>5.6 (0.37)</td>
<td>5.6 (0.30)</td>
<td>5.7 (0.25)</td>
</tr>
<tr>
<td>NT-proBNP, ng/L</td>
<td>27 (39)</td>
<td>56 (52)</td>
<td>49 (52)</td>
<td>31 (53)</td>
<td>26 (26)</td>
<td>40 (48)</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73 m(^2)</td>
<td>89 (17)</td>
<td>89 (18)</td>
<td>86 (16)</td>
<td>90 (12)</td>
<td>90 (11)</td>
<td>85 (12)</td>
</tr>
</tbody>
</table>

\(^a\) Data in parentheses are SD.

JALM 2017;1; 711–719 May 2017
First High-Sensitivity Cardiac Troponin I Assay Cleared by the United States Food and Drug Administration: Validation and Implications

PATHFAST cTnI-II cardiac biomarker assay (LSI Medience Corp, Tokyo, Japan)

<table>
<thead>
<tr>
<th>Population and Statistical Modeling Method</th>
<th>Overall cohort</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy populations after eGFR&lt;60 mL/min/1.73 m² AND HbA1c ≥ 6.5% AND NT-proBNP: &gt;125 ng/L if &lt;75 years; NT-proBNP: &gt;450 ng/L if ≥75 years</td>
<td>734</td>
<td>352</td>
<td>382</td>
</tr>
<tr>
<td>Number of subjects (% of specific cohort exceeding the Limit of Detection)</td>
<td>487 (66.3%)</td>
<td>186 (52.8%)</td>
<td>301 (78.8%)</td>
</tr>
</tbody>
</table>

### Section IV. Healthy Population after exclusion for <60 eGFR<60 mL/min/1.73 m² AND HbA1c ≥ 6.5% AND NT-proBNP: >125 ng/L if <75 years; NT-proBNP: >450 ng/L if ≥75 years

#### Non-parametric percentile method (CLSI C28-A3)

- **99th percentile decision point**
  - Overall: 27.9 ng/L
  - Females: 20.3 ng/L
  - Males: 29.7 ng/L
- **90% Confidence Interval**
  - Overall: 90% CI: 20.1 – 29.7
  - Females: 90% CI: 12.8 – 29.7
  - Males: 90% CI: 21.2 – 36.9

#### Robust method (CLSI C28-A3)*

- **99th percentile decision point**
  - Overall: 14.0 ng/L
  - Females: 10.5 ng/L
  - Males: 16.4 ng/L
- **90% Confidence Interval**
  - Overall: 90% CI: 12.7 - 15.3
  - Females: 90% CI: 8.6 - 12.3
  - Males: 90% CI: 14.5 - 18.2

#### Harrell-Davis method

- **99th percentile decision point**
  - Overall: 26.1 ng/L
  - Females: 21.0 ng/L
  - Males: 28.6 ng/L
- **90% Confidence Interval**
  - Overall: 90% CI: 20.7–31.5
  - Females: 90% CI: 13.9 - 28.0
  - Males: 90% CI: 23.9 – 33.3
Cardiac Troponin Units of Measure

ng/mL, Contemporary versus ng/L, High-sensitivity

High-sensitivity • 19 ng/L
Contemporary • 0.03 ng/mL or 30 ng/L
High-sensitivity • 22 ng/L
Contemporary • 0.003 ng/mL or 3 ng/L
Contemporary • 0.30 ng/mL or 300 ng/L
High-sensitivity • 14 ng/L
High-sensitivity • 6 ng/L
Effective Quality Monitoring

- **140 ng/L**
- **34 ng/L**
Summary and Conclusions

• Cardiac Troponin is the biomarker for MI
  – Use 99\textsuperscript{th} percentile as cutoff
  – CV at 99\textsuperscript{th} percentile cutoff
  – Rise and/or fall in cTn

• Target appropriate epitopes, avoid interferences

• No ‘Pass’ for POC. Characteristics for POC must be the same as central lab assays.
  – There are attractive POC technologies, but caution is advised.

• Several generations of assays developed

• Higher Sensitivity Assays have advantages
Thank You!
rchristenson@umn.edu