Novel Assays for Cardiac Troponin: Diagnosis, Risk Prediction, and Treatment

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Disclosures

• Investigator-initiated grant awards from Novartis Pharmaceuticals, Roche Diagnostics, and the NIH

• Consulting/Advisory Board: Roche Diagnostics
Outline

• Development and definition of high-sensitivity cardiac troponin assays

• The use of these assays for the evaluation of suspected myocardial infarction

• Cardiac troponin as a population screening tool
What is cardiac troponin?
What is a high-sensitivity assay for cardiac troponin?
Diagnostic Criteria for MI
Diagnostic Criteria for MI

ESC/ACCF/AHA/WHF Expert Consensus Document

Third Universal Definition of Myocardial Infarction

Kristian Thygesen, Joseph S. Alpert, Allan S. Jaffe, Maarten L. Simoons, Bernard R. Chaitman, and Harvey D. White: the Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction

Detection of a rise and/or fall of cardiac markers (preferably troponin) with at least one value >99th percentile* of the upper reference limit (URL) together with evidence of myocardial ischemia

*The assay should have a coefficient of variation (CV) is ≤ 10% at the 99th percentile URL

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Novel high-sensitivity troponin assays

- 99% of a healthy population
- 1% of a healthy population
- No myocardial injury
- Myocardial injury

Current Limit of detection (LOD)

URL (upper reference limit)

New LOD

10% CV

Circulating cardiac troponin concentration
High Sensitivity Troponins for MI Diagnosis

The area under the receiver-operating-characteristic curve (AUC) is shown, according to the time since the onset of chest pain, for the four sensitive cardiac troponin assays and the standard assay performed on blood samples. The figure illustrates the performance of these assays in diagnosing myocardial infarction (MI) with high sensitivity.

- **Abbott-Architect Troponin I**
- **Roche High-Sensitive Troponin T**
- **Roche Troponin I Ultra**
- **Siemens Troponin I**
- **Standard assay**

![Graph showing AUC for different troponin assays](image)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>cTnT</th>
<th>hs-cTnT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens</td>
<td>83</td>
<td>95</td>
</tr>
<tr>
<td>Spec</td>
<td>95</td>
<td>80</td>
</tr>
<tr>
<td>NPV</td>
<td>97</td>
<td>99</td>
</tr>
<tr>
<td>PPV</td>
<td>72</td>
<td>50</td>
</tr>
</tbody>
</table>

The graph above shows the area under the ROC curve for different troponin assays as a function of hours since the onset of symptoms. The table indicates the sensitivity (Sens), specificity (Spec), negative predictive value (NPV), and positive predictive value (PPV) for cTnT and hs-cTnT assays.

Accelerated Diagnostic Protocols

- ADAPT Score: Low risk chest pain
  - TIMI risk score = 0 or 1
  - ECG without ischemic changes
  - Hs-cTnl at 0- and 2-hours < (26.2 ng/L)

Acute Chest Pain
N=1635

ADAPT Low risk
TIMI = 0
N=320 (20%)

- 30-day MACE
  N=0 (0%)

- No 30-day MACE
  N=320 (100%)

Sens: 100%
NPV: 100%

ADAPT Low risk
TIMI ≤ 1
N=678 (42%)

- 30-day MACE
  N=2 (0.3%)

- No 30-day MACE
  N=676 (99.7%)

Sens: 99.2%
NPV: 99.7%

Also works with contemporary cTnl

Myocardial Infarction in 2016

Myocardial Injury

Acute Rise in cTn

Plaque Rupture?
Type 1 MI
Follow ACS guidelines

Supply/Demand Mismatch?
Type 2 MI
Correct Underlying Cause

Non ischemic Injury?
PE, HF, myocarditis, subarachnoid hemorrhage, etc.

Chronic Elevation in cTn

Renal disease
LVH
Chronic CAD
Advanced Age
Diabetes

Adapted from de Lemos JA.. JAMA. 2013;309:2262–2269.
High-Sensitivity Troponin Assays in the ED

• The key advantage appears to be the high sensitivity, and the high negative predictive value
• Very low values may be adequate to ROMI within a short time period
• There will be a high prevalence of false positive results
• Unclear whether hs-Tn lead to improved ACS outcomes
Troponin Determines Benefit from an Early Invasive Strategy in ACS

A Cardiac Troponin I (cTnl)

Invasive (n=362) cTnl <0.1 ng/mL
Conservative (n=372)

Event Rate, %

Days

0 30 60 90 120 150 180

Troponin in the General Population
Prevalence of a Detectable hs-cTnT in the General Population

**DHS**
- Age 30-65: 25% Detectable, 75% Undetectable
- Age ≥ 65: 34% Detectable, 66% Undetectable

**WHS**
- Age 51-63: 30% Detectable, 70% Undetectable
- Age 54-74: 33% Detectable, 67% Undetectable

Cardiac Troponin I Concentration in Men and Women Enrolled in JUPITER

<table>
<thead>
<tr>
<th></th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>91.9%</td>
</tr>
<tr>
<td>Women</td>
<td></td>
</tr>
</tbody>
</table>

- **Men**: Median (IQR) 3.6 (2.7-5.3)
- **Women**: Median (IQR) 3.1 (2.3-4.5)

P<0.0001
Key Determinants of Circulating Troponin Concentrations

- Age
- Male sex
- Black race
- LVH
- Hypertension
- Renal dysfunction
- Diabetes
- Existing coronary artery disease
- Congestive heart failure
hsTnT: Primary Prevention in the Elderly

Cardiovascular death

Proportion Without Cardiovascular Death

Follow-up Time, y

Log-rank P<.001

Cardiac troponin T

Category 1

Category 2

Category 3

Category 4

Category 5

0 3 6 9 12 15 18

0 0.2 0.4 0.6 0.8 1.0

<3 ng/L

>13 ng/L

High-Sensitivity cTnT and the Risk of CHD: ARIC

Figure 2. Age-, race-, and gender-adjusted survival curves assessing the time to incident CHD (A), death (B), and HF hospitalization (C) across cardiac troponin T (cTnT) categories. CHD indicates coronary heart disease; hs-cTnT, highly sensitive cTnT assay; and HF, heart failure.

Prediction of Fatal CHD + MI: NRI 10%, IDI 0.032, AUC 0.014
(All significantly improved)

First major cardiovascular event according to baseline tertile of high-sensitivity cardiac troponin I: JUPITER

Adjusted HR for T3 vs. T1: 2.19 (1.56–3.06) P<0.0001
### Adjusted Risk of a first cardiovascular event according to baseline hsTnI: subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Participants</th>
<th>Events</th>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 70+</td>
<td>4085</td>
<td>150</td>
<td>0.87</td>
<td>1.26</td>
<td>2.27</td>
</tr>
<tr>
<td>Age &lt;70</td>
<td>8871</td>
<td>154</td>
<td>0.49</td>
<td>0.72</td>
<td>1.32</td>
</tr>
<tr>
<td>Men</td>
<td>8260</td>
<td>221</td>
<td>0.61</td>
<td>1.07</td>
<td>1.90</td>
</tr>
<tr>
<td>Women</td>
<td>4696</td>
<td>83</td>
<td>0.47</td>
<td>0.60</td>
<td>1.42</td>
</tr>
<tr>
<td>White</td>
<td>10594</td>
<td>264</td>
<td>0.56</td>
<td>0.94</td>
<td>1.75</td>
</tr>
<tr>
<td>Non white</td>
<td>2362</td>
<td>40</td>
<td>0.59</td>
<td>0.64</td>
<td>1.66</td>
</tr>
<tr>
<td>Current smokers</td>
<td>1952</td>
<td>63</td>
<td>0.88</td>
<td>1.31</td>
<td>2.81</td>
</tr>
<tr>
<td>Non smokers</td>
<td>10999</td>
<td>241</td>
<td>0.50</td>
<td>0.85</td>
<td>1.58</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7208</td>
<td>198</td>
<td>0.70</td>
<td>0.95</td>
<td>1.92</td>
</tr>
<tr>
<td>No hypertension</td>
<td>5742</td>
<td>106</td>
<td>0.46</td>
<td>0.85</td>
<td>1.38</td>
</tr>
<tr>
<td>BMI &lt;25</td>
<td>2837</td>
<td>78</td>
<td>0.74</td>
<td>1.14</td>
<td>2.10</td>
</tr>
<tr>
<td>BMI 25 to &lt;30</td>
<td>5220</td>
<td>131</td>
<td>0.60</td>
<td>1.04</td>
<td>1.80</td>
</tr>
<tr>
<td>BMI 30+</td>
<td>4869</td>
<td>94</td>
<td>0.41</td>
<td>0.64</td>
<td>1.48</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>5219</td>
<td>127</td>
<td>0.71</td>
<td>0.72</td>
<td>1.77</td>
</tr>
<tr>
<td>No metabolic syndrome</td>
<td>7626</td>
<td>175</td>
<td>0.48</td>
<td>1.03</td>
<td>1.72</td>
</tr>
<tr>
<td>HDL low</td>
<td>3842</td>
<td>99</td>
<td>0.76</td>
<td>0.87</td>
<td>1.85</td>
</tr>
<tr>
<td>HDL normal</td>
<td>9113</td>
<td>205</td>
<td>0.48</td>
<td>0.92</td>
<td>1.69</td>
</tr>
<tr>
<td>LDL 100+</td>
<td>8806</td>
<td>199</td>
<td>0.45</td>
<td>0.86</td>
<td>1.68</td>
</tr>
<tr>
<td>LDL &lt;100</td>
<td>4148</td>
<td>105</td>
<td>0.76</td>
<td>1.00</td>
<td>1.86</td>
</tr>
<tr>
<td>hsCRP 5+</td>
<td>5092</td>
<td>137</td>
<td>0.53</td>
<td>1.03</td>
<td>2.05</td>
</tr>
<tr>
<td>hsCRP &lt;5</td>
<td>7864</td>
<td>167</td>
<td>0.58</td>
<td>0.83</td>
<td>1.51</td>
</tr>
<tr>
<td>Triglycerides 150+</td>
<td>4152</td>
<td>113</td>
<td>0.93</td>
<td>1.03</td>
<td>1.65</td>
</tr>
<tr>
<td>Triglycerides &lt;150</td>
<td>8803</td>
<td>191</td>
<td>0.39</td>
<td>0.84</td>
<td>1.78</td>
</tr>
<tr>
<td>Summary hsTnI</td>
<td>12956</td>
<td>304</td>
<td>0.56</td>
<td>0.90</td>
<td>1.74</td>
</tr>
</tbody>
</table>

Summary HR 2.19 (1.56–3.06)

Adjusted Hazard Ratio for Tertile 3 vs. Tertile 1 of hsTnI

Everett BM et al. *Circulation*. 2015;131:1851
## Improvements in Risk Prediction: ARIC

<table>
<thead>
<tr>
<th></th>
<th>Base model</th>
<th>Base model + hsTnT</th>
<th>Base model + hsCRP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHD death and nonfatal MI</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC</td>
<td>0.710</td>
<td>0.724</td>
<td>0.714</td>
</tr>
<tr>
<td>NRI</td>
<td></td>
<td>10.1%</td>
<td>3.0%</td>
</tr>
<tr>
<td><strong>All-cause mortality†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC</td>
<td>0.719</td>
<td>0.740</td>
<td>0.723</td>
</tr>
<tr>
<td>NRI</td>
<td></td>
<td>10.7%</td>
<td>2.5%</td>
</tr>
<tr>
<td><strong>Heart failure†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC</td>
<td>0.749</td>
<td>0.777</td>
<td>0.752</td>
</tr>
<tr>
<td>NRI</td>
<td></td>
<td>15.4%</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

* CHD base model: ARIC coronary risk score  
† Base model for total mortality and heart failure: ARIC Coronary Risk Score + BMI + LVH + creatinine  
- Results from BiomarCaRE, a study of >90,000 patients without preexisting CVD are in submission
Hammers, nails, and personalized medicine

• Are troponins (or other biomarkers) only useful if they improve the performance of existing algorithms?
• Or, are there specific therapies that should be utilized in patients with abnormal troponin?
Absolute and Relative Risk Reductions in the JUPITER Primary Endpoint by hsTnI Category at Baseline

<table>
<thead>
<tr>
<th>Tertile</th>
<th>Incidence Rate per 100 person years</th>
<th>Rosuvastatin</th>
<th>Placebo</th>
<th>RRR</th>
<th>NNT 5yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.42</td>
<td>0.71</td>
<td>0.68</td>
<td>1.13</td>
<td>67</td>
</tr>
<tr>
<td>2</td>
<td>0.68</td>
<td>1.13</td>
<td>1.17</td>
<td>1.74</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>2.29</td>
<td></td>
<td></td>
<td></td>
<td>18</td>
</tr>
</tbody>
</table>

NNT 5 yrs = 67  NNT 5yrs = 45  NNT 5yrs = 18

RRR 0.6 (0.3-1.0)  RRR 0.6 (0.4-0.9)  RRR 0.5 (0.4-0.7)

P for interaction between rosvastatin and hsTnI tertile = 0.53

Sex-specific High-Sensitivity Cardiac Troponin I Tertile

Everett BM et al. Circulation. 2015;131:1851
Absolute and Relative Risk Reductions in the JUPITER Primary Endpoint by Framingham Risk Score at Baseline

<table>
<thead>
<tr>
<th>Framingham Risk Score</th>
<th>Rosuvastatin RRR (95% CI)</th>
<th>Placebo RRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5%</td>
<td>0.60 (0.3-1.4)</td>
<td>0.49</td>
</tr>
<tr>
<td>&gt;5 to ≤10%</td>
<td>0.70 (0.4-1.1)</td>
<td>0.94</td>
</tr>
<tr>
<td>&gt;10%</td>
<td>0.50 (0.4-0.7)</td>
<td>1.05</td>
</tr>
</tbody>
</table>

NNT 5 yrs = 103, NNT 5yrs = 59, NNT 5 yrs = 20

P for interaction between rosuvastatin and FRS = 0.40

Everett BM et al. Circulation. 2015;131:1851
Troponin in the General Population

• Troponin is a strong marker of increased risk for major cardiovascular events and mortality

• Troponin is a non-specific marker of myocardial injury

• Troponin could be used to identify a high risk group for higher risk or more expensive therapy
Troponin and Specific Therapies

• Troponins identify patients with acute coronary syndromes who benefit from coronary revascularization

• Could troponin also identify a group of patients with stable ischemic heart disease who would benefit coronary revascularization?
Stable Ischemic Heart Disease
Stable Ischemic Heart Disease

- Patients with stable ischemic heart disease and diabetes frequently have abnormal cardiac troponin levels

- Elevated cardiac troponin concentrations are a strong predictor of major CV events and death

- Could these markers be used to identify patients who would benefit from coronary revascularization, just as they have in patients with ACS?
Troponin Determines Benefit from an Early Invasive Strategy in ACS

**Troponin and Cardiac Events in Stable Ischemic Heart Disease and Diabetes**

Brendan M. Everett, M.D., M.P.H., Maria Mori Brooks, Ph.D., Helen E.A. Vlachos, M.S., Bernard R. Chaitman, M.D., Robert L. Frye, M.D., and Deepak L. Bhatt, M.D., M.P.H., for the BARI 2D Study Group*

**ABSTRACT**

**BACKGROUND**
Cardiac troponin concentrations are used to identify patients who would benefit from urgent revascularization for acute coronary syndromes. We hypothesized that they might be used in patients with stable ischemic heart disease to identify those at high risk for cardiovascular events who might also benefit from prompt coronary revascularization.
BARI 2D: Trial Schema

Type 2 diabetes and stable ischemic heart disease

PCI most appropriate
N=1605

CABG most appropriate
N=763

Randomization

Prompt revascularization plus intensive medical therapy
N=1176

Intensive medical therapy Alone
N=1192

MI, stroke, CV death: HR 0.98 (0.80 to 1.19)

BARI 2D Study Group, Frye RL. NEJM 2009;360:2503
Baseline Cardiac Troponin Concentration (ng/L) - BARI 2D

Normal (hsTnT < 14)
N = 1388 (60.7%)

Abnormal (hsTnT ≥ 14)
N = 897 (39.3%)

2277/2285 (99.6%) ≥ 3 ng/L
hsTnT 95th percentile: 60.6 ng/L
hsTnT 99th percentile: 309.4 ng/L
hsTnT maximum: 3308.0 ng/L

High Sensitivity Cardiac Troponin T (ng/L)
Five-Year Rate of Myocardial Infarction, Stroke, or Cardiovascular Death Stratified by Baseline Cardiac Troponin T

A 5-Yr Rate of Primary Composite End Point

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>Troponin T &lt;14 ng/liter</th>
<th>Troponin T ≥14 ng/liter</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>0.4%</td>
<td>12.9%</td>
</tr>
<tr>
<td>24</td>
<td>2.2%</td>
<td>27.1%</td>
</tr>
<tr>
<td>36</td>
<td>5.9%</td>
<td>31.2%</td>
</tr>
<tr>
<td>48</td>
<td>9.8%</td>
<td>35.7%</td>
</tr>
<tr>
<td>60</td>
<td>13.7%</td>
<td>40.2%</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th>Troponin T ≥14 ng/liter</th>
<th>897</th>
<th>737</th>
<th>684</th>
<th>620</th>
<th>455</th>
<th>255</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>1388</td>
<td>1281</td>
<td>1229</td>
<td>1124</td>
<td>892</td>
<td>529</td>
</tr>
</tbody>
</table>

P<0.001
Five-Year Rate of Myocardial Infarction, Stroke, Heart Failure, or Death Stratified by Baseline Cardiac Troponin T

Figure S6. Unadjusted Kaplan-Meier estimates of 5-year death/myocardial infarction (MI)/stroke/congestive heart failure (CHF) rates for BARI 2D subjects with an abnormal high sensitivity cardiac troponin T (hsTnT ≥ 14 ng/L) at baseline compared to those with a normal hsTnT (<14 ng/L) at baseline.

P-value = 0.0001

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>hsTnT ≥14</th>
<th>hsTnT &lt;14</th>
</tr>
</thead>
<tbody>
<tr>
<td>hsTnT ≥14</td>
<td>895</td>
<td>718</td>
</tr>
<tr>
<td>hsTnT &lt;14</td>
<td>1388</td>
<td>1272</td>
</tr>
</tbody>
</table>
Random Allocation to Prompt Coronary Revascularization Does Not Benefit Patients with Abnormal Troponin T

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Revascularization Group</th>
<th>Medical-Therapy Group</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from cardiovascular causes, myocardial infarction, or stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>11.8</td>
<td>14.0</td>
<td>0.96 (0.71–1.30)</td>
<td>0.99</td>
</tr>
<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>26.5</td>
<td>27.6</td>
<td>0.96 (0.74–1.25)</td>
<td></td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>2.6</td>
<td>4.4</td>
<td>0.63 (0.34–1.14)</td>
<td>0.05</td>
</tr>
<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>11.7</td>
<td>10.1</td>
<td>1.27 (0.85–1.91)</td>
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<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>8.2</td>
<td>10.1</td>
<td>0.94 (0.66–1.35)</td>
<td>0.28</td>
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<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>15.6</td>
<td>21.7</td>
<td>0.72 (0.52–1.00)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>2.1</td>
<td>2.5</td>
<td>0.87 (0.43–1.77)</td>
<td>0.75</td>
</tr>
<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>4.6</td>
<td>4.2</td>
<td>1.03 (0.51–2.05)</td>
<td></td>
</tr>
</tbody>
</table>
# Random Allocation to Prompt Coronary Revascularization Does Not Benefit Patients with Abnormal Troponin T

## Table: Subgroups and Event Rates

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Revascularization Group</th>
<th>Medical-Therapy Group</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>6.4</td>
<td>7.7</td>
<td>0.77 (0.53–1.14)</td>
<td>0.20</td>
</tr>
<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>19.4</td>
<td>19.8</td>
<td>1.06 (0.80–1.39)</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>11.5</td>
<td>10.7</td>
<td>1.07 (0.78–1.47)</td>
<td>0.32</td>
</tr>
<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>23.8</td>
<td>27.6</td>
<td>0.87 (0.67–1.13)</td>
<td></td>
</tr>
<tr>
<td>Death from any cause, myocardial infarction, stroke, or heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troponin T &lt;14 ng/liter</td>
<td>22.3</td>
<td>22.2</td>
<td>1.03 (0.83–1.29)</td>
<td>0.24</td>
</tr>
<tr>
<td>Troponin T ≥14 ng/liter</td>
<td>42.2</td>
<td>47.8</td>
<td>0.87 (0.71–1.05)</td>
<td></td>
</tr>
</tbody>
</table>

*Note: The hazard ratio and confidence interval are shown for each subgroup.*

*Figure: Comparison of event rates between revascularization and medical therapy groups.*
Summary: Troponin in Stable Heart Disease

• Troponin is a strong predictor of major cardiovascular events and mortality

• A substantial proportion of patients with stable heart disease and diabetes have values that are high enough to meet the “MI threshold”

• Revascularization does not appear to mitigate the CV risk associated with an elevated troponin
Summary and Conclusions (1)

- High sensitivity assays for cardiac troponin are in routine clinical use in Europe and Asia, and are likely to be approved for use in the US soon.

- These assays can often detect circulating cardiac troponin even in healthy adults.

- Cardiac troponin is a non-specific marker of myocardial injury and adverse prognosis.
Summary and Conclusions (2)

- Hs-cTn assays may shorten the time required to rule out MI, but may have serious downstream consequences in increased testing and cardiology consultation.

- Cardiac troponin is a marker of adverse prognosis regardless of the etiology of its release.
Summary and Conclusions (2)

• Cardiac troponin assays are promising for risk assessment in the ambulatory setting
  – Modest improvement in risk prediction in primary prevention
  – Identify patients at high risk in secondary prevention

• Troponin may provide a novel means of monitoring disease activity

• Identified populations may be amenable to preventive intervention
• Outside of ACS, no intervention that specifically benefits patients with abnormal troponin has been identified.

• Statins and revascularization do not appear to directly target troponin-associated risk.

• Troponin’s lack of pathophysiologic specificity may actually make it a better marker of general cardiovascular risk.
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Robert Frye
Thank you!

Brendan M. Everett, MD, MPH

Director, General Cardiology Inpatient Service
Assistant Professor of Medicine, Harvard Medical School
Cardiac Troponin and Treatment for Conservatively Managed ACS: PLATO Trial

In the PLATO trial, 9946 patients had an entry diagnosis of NSTE-ACS and provided plasma samples for analyses of all biomarkers, allowing inclusion in the present study. Baseline characteristics by randomized treatment and management strategy are shown in the Table. The randomized treatment groups were balanced within the respective in-hospital invasively and noninvasively managed patients, with the exception that there were somewhat more smokers in the clopidogrel group in the in-hospital noninvasive arm. As expected, there were differences in characteristics in relation to the in-hospital invasive or noninvasive treatment. Patients treated invasively were more often male and habitual smokers, and reported less hypertension, diabetes mellitus, previous angina pectoris, MI, heart failure and stroke, but more often previous PCI. At entry, the invasively managed patients less often had ST-segment depression but more often had troponin elevation and higher Thrombolysis in Myocardial Infarction NSTE-ACS risk score.

Biomarkers and Effects of Ticagrelor in the In-Hospital Noninvasive Group

In patients managed without revascularization, hs-TnT levels were significantly related to the rate of the primary composite end point of CV death, MI, and stroke (log-rank \( P < 0.001 \)), driven by associations both with CV death and spontaneous MI (Figures 1 and 2) corresponding mainly to type 1 to 3 MI.

![Graph showing the relationship between hsTnT levels and treatment effect]

No interaction between ticagrelor and troponin for patients managed invasively

Impact of Randomly Allocated Antihyperglycemic Therapy on Glucose, HbA1c, and Cardiac Troponin in LANCET

Percent Change from Baseline

Fasting glucose  |  HbA1c  |  Postprandial glucose  |  Cardiac troponin T

Placebo Versus placebo  |  Insulin glargine  |  Metformin  |  Insulin glargine + Metformin

- Placebo
  - Versus placebo: P=0.91
- Insulin glargine: P=0.43
- Metformin: P=0.43
- Insulin glargine + Metformin: P=0.63

Insulin glargine P=0.74
Metformin P=0.43

Everett et al. AHA Scientific Sessions 2013
Valsartan-Sacubitril vs. Enalapril in HF

Our clinical findings are supported by the effects on the levels of N-terminal pro-BNP and Troponin T. The contrasting effects of LCZ696 on the 2 types of natriuretic peptides represents an important finding, because the levels of the 2 peptides characteristically parallel each other during the course of heart failure.

The advantage of LCZ696 over enalapril is likely to have important ramifications for both quality of life and resource utilization in this disorder.

The study was funded by Novartis.

The effect of LCZ696 to stabilize the course of heart failure is likely to have important ramifications for both quality of life and resource utilization in this disorder.

Furthermore, although differences in the levels of troponin and NTproBNP will reflect the effects of the drug on the heart, the levels of BNP will reflect the action of the drug, whereas levels of NTproBNP will reflect the effects of the drug on the heart.