Incorporating High-Sensitivity Troponin into Your ED Workflow
Presenters

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Deborah Diercks, MD
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Mahler Disclosures

• Research funding:
  – NIH: Heart Lung and Blood Institute
  – Donaghue Foundation/ Association of American Medical Colleges
  – AHRQ: Agency for Healthcare Research and Quality
  – Abbott Laboratories
  – Roche Diagnostics
  – Siemens Healthcare
  – Creavo Medical Technologies
  – Ortho Diagnostics

• Author for Up-to-Date

• Chief Medical Officer: Impathiq, Inc.
Baugh, Financial Disclosure Information

**AFFILIATION/FINANCIAL INTEREST — CORPORATE ORGANIZATIONS, MANUFACTURERS, PROVIDERS**

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<th>Category</th>
<th>Organization(s)</th>
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<tr>
<td>Consultant</td>
<td>JANSSEN PHARMACEUTICALS, US DOJ</td>
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<tr>
<td>Grants/Research Support</td>
<td>JANSSEN PHARMACEUTICALS, BOEHRINGER INGELHEIM</td>
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<td>SALIX PHARMACEUTICALS, JANSSEN PHARMACEUTICALS, ROCHE DIAGNOSTICS</td>
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Diercks financial disclosures
2. Simon – can you give us a brief recap of what is different about hs Tn?

Brief summary of hs-cTn vs contemporary cTn
High Sensitivity Troponin Assays Defined

- Measure same cardiac troponin protein
- Are more precise, can detect lower levels; measurable levels in at least 50% of healthy patients

2017 FDA approves hs-cTnT
2018 FDA approves 2 hs-cTnI assays
hs-cTn Units

Contemporary cTn measured in ng/ml
Hs-cTn measured in ng/L

0.006 ng/ml $\rightarrow$ 6 ng/L
0.040 ng/ml $\rightarrow$ 40 ng/L
High Accuracy, Different Precision

Earlier Generation Troponin

High-sensitivity Troponin

15% CV

5% CV
Contemporary vs High-sensitivity Cardiac Troponin Assays

Cardiac Troponin, ng/mL

99th Percentile

Limit of Detection

Cardiac Troponin, ng/mL

99th Percentile

Limit of Detection
Percent of healthy Patients with Detectable Troponin

Slide adapted from A. Jaffe
Detection of more patients with non-AMI cTn elevations

The larger the elevation the more likely it is from MI.
Pattern of Elevation

- AMI differentiated from non-ischemic cTn elevations based on:
  - Pattern of elevation
  - Clinical context
3. a. Great review, thanks Simon. Deb can you tell us about your experience with hsTn at UT Southwestern?

• How to Implement and what are the barriers
hs-cTnT >=52 ng/L is abnormal

Initial hs-cTnT
- <6 ng/L
- >=6 and <52 ng/L

Symptom Duration
- >=3 hours
- <3 hours

Ruled out

Indeterminate

hs-cTnT at 1 hour
- <12 ng/L
- >=12 and <52 ng/L

delta at 1 hour
- <3 ng/L
- >=3 ng/L
- <5 ng/L
- >=5 ng/L

Ruled out

Indeterminate

Abnormal

delta at 3 hours
- <7 ng/L
- >=7 ng/L

Ruled out

Abnormal
Evaluation of a Novel Rule-Out Myocardial Infarction Protocol Incorporating High-Sensitivity Troponin T in a US Hospital, Volume: 138, Issue: 18, Pages: 2061-2063, DOI: (10.1161/CIRCULATIONAHA.118.033861)
Ruled out

Modified Heart Score

By initial cTnT

<=3

Deferred

>3

By 1 hour cTnT

Any

*Outpatient CTA or stress test*

By 3 hour cTnT

<=3

Inpatient CTA or stress test*

>3

Follow up

All patients follow up with their own PCP or else with ARC

*if no stress test, CTA, or cath within the prior 6 months. This may be done in the inpatient setting based on ED attending discretion.
ED Troponin Care Path
Sankey Diagram
Results

<table>
<thead>
<tr>
<th></th>
<th>Care Path n=941</th>
<th>Manual Testing n=205</th>
<th>Difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of Adherence</td>
<td>69%</td>
<td>46%</td>
<td>23% (15-31%)</td>
<td>&lt;0.05</td>
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<tr>
<td>Rate of Excess Phlebotomy</td>
<td>16%</td>
<td>5%</td>
<td>11% (7-15%)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*Limited to those patients with CC: Chest Pain or Analog*
**0/1 Hour, Low Risk:**

**Ruled Out at 0/1 Hour:**
No evidence of myocardial injury. Patient has a Low Risk Heart Score. No additional risk stratification is recommended.

**0/1 Hour, Not Low Risk:**

**Rule Out at 0/1 Hour:**
No evidence of myocardial injury. Patient has Moderate/High Risk Heart Score. Early outpatient stress test or CTA Coronary is recommended. Consider referral to Chest Pain Clinic: ###-####-####

**3 Hour, Low Risk:**

**Rule Out at 3 Hours:**
No evidence of myocardial injury. Patient has Low Risk Heart Score. Early outpatient stress test or CTA Coronary recommended. Consider referral to Chest Pain Clinic: ###-####-####

**3 Hour, High Risk:**

**Rule Out at 3 Hours:**
No evidence of myocardial injury. Patient has Moderate/High Risk Heart Score. Stress test or CTA Coronary is recommended prior to discharge.
3. b. Thanks Deb, that was fantastic! Let’s move on to Chris. Chris, can you tell us about your experience with implementing hsTn at Brigham?
Brigham and Women’s Hospital

• Academic, urban tertiary care hospital in Boston, MA
• ~62,000 annual adult visits
• 750 inpatient beds, 39 ED beds, 20 ED observation beds
• Launched high-sensitivity troponin in April, 2018
Four Settings to Consider

- Emergency
- Perioperative
- Inpatient
- Clinic
ADPs: Focus on Type 1 MI

Plaque rupture with thrombus

Vasospasm or endothelial dysfunction

Fixed atherosclerosis and supply-demand imbalance

Supply-demand imbalance alone

MI Type 1

MI Type 2

MI Type 2

MI Type 2
Typical Recommendations for 99th Percentile cutoffs

• Europe: 14 ng/L for both males and females
• US: variable, some use FDA value of 19 ng/L, others use lower and gender-specific values
• For example:
  • Females: 10 ng/L
  • Males: 15 ng/L

THE ELECTRONIC MEDICAL RECORD WILL FLAG AS “ABNORMAL” AT THESE VALUES AND ABOVE; DOES NOT NECESSARILY DEFINE AMI
Partners Healthcare ADP: hsTnT

**TROPOIN**

- ANY troponin ≥52 ng/L
  - OR
  - ∆ >5 ng/L

- Neither “Rule in” nor “Rule out” Order 3hr troponin

- ALL troponins <10 ng/L (female) or <12 ng/L (male) with ∆ <3 ng/L² if arrival >3hr after symptom onset

**RISK SCORE**

- Rule In Zone
  - HEART 7-10: High probability
  - HEART 0-6: Low & Intermediate probability

- Gray Zone
  - HEART 7-10: High probability
  - HEART 0-6: Low & Intermediate probability

- Rule Out Zone
  - HEART 0-6: Low & Intermediate probability

**DISPOSITION**

- Admit to Cardiology
- Admit to Medicine
- Gray Zone Supplement
- Discharge Home
3hr Δ troponin

ANY troponin ≥52 ng/L
OR
Δ ≥7 ng/L

Δ = 5-7 ng/L

Δ < 5 ng/L

CONCERN FOR ACS

Moderate

Low

Moderate

Low

Admit to Cardiology

Same-visit stress test or cardiac imaging

Discharge Home, 72h follow up scheduled

Discharge Home
Unstable Angina – Lower Prevalence

Effect of use of hsTn instead of cTn on prevalence of UA in the PLATO trial

Findings of Coronary Angiography

Impact on ED LOS

- 20% reduction of ED LOS
- Change in trend
- 15% more out-patients

-79 minutes
3.c. That was very interesting Chris, thanks. Simon, how does Wake Forest plan on modifying the HEART Pathway based on hs-cTn
Current HEART Pathway with contemporary cTnI

ADP version of the HEART score
- No ischemic ECG changes
- No known CAD
  (prior AMI, revascularization, >70% coronary stenosis)
- Low risk = HEAR(t) score: 0-3
- Negative serial troponins

Mahler et al, Crit Path Cardiol, 2011
Mahler et al, Int J Cardiol, 2013
Mahler et al, Circ CVQO J, 2015
Mahler et al, Circulation, 2018
Proposed HEART Pathway with hs-cTnI

Patients with Acute Chest Pain

- ECG
  - Non-Ischemic
    - Known CAD
      - No
        - HEAR Score
          - 0-3
            - hs-cTnI 0/2hr
              - Negative <47 ng/L & Δ < 5 ng/L
                - Discharge
              - Intermediate 47-99 ng/L or Δ 5-14 ng/L
                - Observation
              - Elevated ≥100 ng/L or Δ≥15 ng/L
                - Cardiology Consult & Admission
          - ≥4
            - hs-cTnI 0 hr
              - <99 ng/L
                - Observation
              - ≥100 ng/L
                - Cardiology Consult & Admission

- Ischemic
  - STEMI Guidelines
    - STEMI
  - Observation
  - Cardiology Consult & Admission

Outpatient pathway for HEAR 4-6 with negative serial hs-cTnI
4. Thank you Deb, Chris, and Simon for sharing your experience and protocols. Simon you recently co-authored a paper in JACC on how to implement hsTn and what are the barriers. It is a great reference to use. Can you provide a synopsis of that paper.
Where to Start?

• Stakeholder Involvement
• Developing Institutional Algorithm
• Process Changes
• Timeline
• Defining Success
• Anticipating Pain Points
• Education
Engagement

• Define key leadership team
• Begin weekly meetings months prior to rollout
• Involve key stakeholders from around the hospital/health system
Stakeholders

- **Clinical Administration** – are health system leaders supportive?
- **Laboratory** – how will the new assay impact laboratory processes?
- **IT** – does IT have the expertise and time to build an algorithm into the EHR?
- **ED** – is ED leadership on board? Are they committed to the rollout and change in processes in the ED?
- **Outpatient Clinics** – is outpatient leadership willing to help with clinic access for ED patients?
- **Inpatient Services** – Are the cardiology services and hospital medicine involved and aware of changes in patient flow?
ED preparation

• How will hs-cTn results be integrated into clinical work flow, pathways, and protocols?
  – Which cut-offs will be used?
  – What time points?
  – Combined with decision aids?
• Follow-up plans in place
• Integration with the electronic health record?
• Educate clinicians regarding the transition

Januzzi, Mahler, Christenson, Rymer, Newby, Body, Morrow, Jaffe. JACC 2019
Lab preparation

• Is the lab ready to provide necessary analytical education?
• Has an assay been selected?
• Is assay performance acceptable in the local Clinical Laboratory?
• Is the Lab able to process samples within a reasonable time-frame?
• How are results reported in the EHR?

Januzzi, Mahler, Christenson, Rymer, Newby, Body, Morrow, Jaffe. JACC 2019
• 4. a. Excellent overview. A common concern is a sudden onslaught of new positive results. Relative to contemporary Tn, how many new positives can one expect and are do they represent true positives?
  • Deb
Item 4b

• 4. b. Chris, how did you manage this change at your hospital?
  • Change management, hospital staff education
Convene Multidisciplinary Workgroup

• Required: EM, Cards, Pathology/Lab, IM, RN, APP, IS/project management
Required Work: The Punch List

- Set go-live date
- Which metrics will you use (collect baseline and post-launch)
- Create new pathway
  - Define 99th percentile for troponin
  - Delta strategy/sampling frame
  - Risk stratification tool
  - Use of ED observation unit
  - Role of consultants
  - Follow up guidance and resources
- IS compatibility; review order sets
- Provider education/messaging
- Go-live
- Post-go-live support
- Post-go-live data monitoring and QA
<table>
<thead>
<tr>
<th>Phase 1</th>
<th>AQUIRE DATA &amp; SECURE LEADERSHIP</th>
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<tbody>
<tr>
<td>Define quality &amp; operational metrics</td>
<td>1-3</td>
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<tr>
<td>Obtain baseline data</td>
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<tr>
<td>Make a clinical &amp; business case for protocol to key leaders (e.g., Cardiology Leadership, Nurse Director, CMO)</td>
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<tr>
<td>Create project plan (include deliverables, roles, clinical charter plans)</td>
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<td>Identify executive sponsors (who can assist with funding, challenge escalations problem solving)</td>
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<td>Develop timeline</td>
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<td>Obtain access to resources, (e.g., data analysts, admin. &amp; IT support, educators)</td>
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<td>Evaluate feasibility a follow-up clinic</td>
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<td>Phase 2</td>
<td>PLAN FOR PROTOCOL DEVELOPMENT</td>
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<tr>
<td>Perform literature search (start with ACEP-provided references)</td>
<td>1-3</td>
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<td>Review protocols from peer institutions</td>
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<tr>
<td>Establish a interdisciplinary workgroup and assign roles</td>
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<td>Identify &amp; engage supportive key opinion leaders</td>
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<td>Identify &amp; engage staff likely to oppose pathway</td>
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<td>Phase 3</td>
<td>DEVELOP PROTOCOL &amp; KEY COMPONENTS</td>
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<tr>
<td>Define inclusion &amp; exclusion criteria</td>
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<tr>
<td>Determine expected interventions</td>
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<td>Phase 4</td>
<td>VERIFY &amp; LAUNCH PROTOCOL</td>
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<tr>
<td>Present protocol to relevant stakeholder groups</td>
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<tr>
<td>Revise based on feedback</td>
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<tr>
<td>Pilot the protocol (if multiple sites available, select the most challenging)</td>
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<tr>
<td>Revise for gaps &amp; barriers</td>
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<tr>
<td>Rollout protocol; publicize “go-live” event</td>
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<td>Phase 5</td>
<td>MAINTAIN PROTOCOL</td>
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<tr>
<td>Monitor data to ensure appropriate adherence</td>
<td>1-3</td>
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<tr>
<td>Report metrics to frontline staff &amp; leadership</td>
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<tr>
<td>Integrate protocol maintenance activities into standing meetings</td>
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<tr>
<td>Revisit literature to ensure alignment with most recent scientific evidence</td>
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<tr>
<td>Perform annual revisions</td>
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Summary: Putting it all Together

I. USE hs-TROPONIN
   - IMPROVES RULE-OUT
   - IMPROVES RULE-IN

II. IN THE RIGHT CONTEXT
   - SUSPECTED AMI
   - NOT A SCREENING TOOL
   - CONSIDER TIMING OF SYMPTOM ONSET

III. WITH AN ADP
   - BASELINE TROPONIN LEVEL AND DELTA
   - CONSIDERS RISK SCORE
   - USES OBSERVATION UNIT
4.b. With such a rapid protocol, does the new timing pose any issues?

Deb - Throughput issues - 0/1 hr protocol with an 3 hr Xray TAT - Deb - 2 min
Item 4c

• Besides timing, were there any other system level issues?
  • Chris - Administrative issues - I.T. etc.
Beware of IT Delays
Item 4d

• 4.d. Okay so, how do you handle those slightly elevated (over 99th percentile) hsTn
  • Chris -
The Multiple Causes of Troponin Elevation

- Cardiac contusion
- Heart failure
- Aortic dissection
- HOCM
- Takotsubo
- Renal failure
- SAH
- Burns
- Extreme exertion
- Type 1 myocardial infarction
- Type 2 myocardial infarction
- Normal biological variation

50% of patients with suspected cardiac chest pain and a positive hs-cTnT actually have AMI.

From Body et al, JACC 2021; 78: 1320-9
Delta Troponin Useful

• Definition: change in value between serial measurements

• Use combination of specific troponin values at 2 time points and an absolute difference between time points to confirm NSTEMI

• Absolute change better than relative percentage change
Outcomes in Patients with Undetectable Contemporary Troponin Values (<0.01µg/L)

Special Populations: Renal Disease

High-Sensitivity Cardiac Troponin and the Risk Stratification of Patients With Renal Impairment Presenting With Suspected Acute Coronary Syndrome

Eve Miller-Hodges, MBChB, PhD*
Atul Anand, MBChB*
Anoop S.V. Shah, MBChB, PhD
Andrew R. Chapman, MBChB
Peter Gallacher, MBChB
Kuan Ken Lee, MBChB
Tariq Farrah, MBChB
Nynke Halbesma, MBChB
James P. Blackmur, MBChB
David E. Newby, MBChB, PhD
Nicholas L. Mills, MBChB, PhD
Neeraj Dhaun, MBChB, PhD

4,726 patients; 904 (19%) with renal dysfunction (GFR <60 mL/min)

17% with renal dysfunction had a hsTnI <5 ng/L vs 56% of the patients without renal dysfunction

Specificity at the 99th percentile cutoff was 70.9% versus 92.1%

Hazard ratio 2.19 at 1 year for death or MI for values >99th percentile (24% versus 10%)
Item 4d

4.d. Okay so, how do you handle those slightly elevated (over 99th percentile) hsTn
  Deb – what do you do at UT?
Item 5a

• 5. a. Very interesting! You know, the question that this begs, is do we really need an observation unit anymore with the advent of hsTn? Is this test so good that we can either discharge from the ED or cath everybody? Chris, what impact has this had on your practice and on your observation unit or observation admissions?
ED Observation Units

• Previous convention dictated that patients with “positive” troponin were always admitted.

• Adoption of high-sensitivity troponin assay shifts patient cohorts to less resource-intensive settings; allows for higher-risk patients to receive observation care and reduces avoidable inpatient admissions.
Downstream Impacts

- Consults
- Admissions
- Clinic Referrals

Cardiology Consult Attending
The Brigham Experience: 6 Months Later

- Total tests and encounters
- Disposition changes
- ED length of stay
- Cardiology consult volume
- Stress testing
- MACE volume
Item 5a

5. a. Great information Chris, thanks!
   • Deb, what impact has this had on your practice?
Challenges

• Time delay in starting
• Overall decrease in length of stay
Open forum
For More Information

- E-QUAL Website
  - www.acep.org/equal
  - equal@acep.org

- Contacts:
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    - ntarrant@acep.org
  - Dhruv Sharma: (Project Manager)
    - dsharma@acep.org