Troponin Essential Guidelines: A Practical Implementation Guide

Ruth Cantu, BSN, RN, AACC

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Speaker Overview

Ruth Cantu, BSN, RN, AACC
Accreditation Product and Programs Development

No disclosures
Objectives

Participants will be able to:

1) Discuss the differences in the testing methodologies
2) Summarize the latest Troponin guidelines/research
3) Describe the role Troponin plays in the clinical environment
4) Appraise the potential effects of Troponin on clinical care
5) Describe the integration of Troponin requirements within the Chest Pain Center (CPC) Accreditation Tool
6) Share quality practices to optimize care and outcomes of the Acute Coronary Syndrome Patients (ACS)
Mission:
To **transform** cardiovascular care and **improve** heart health.

Vision:
A world where **innovation** and **knowledge optimize** cardiovascular care and outcomes.
ACC Position Statement: Laboratory

- Focuses on ID and Management of MI and ACS
- Each facility responsible for vendor relationships
  - ACC provides Guidance and Education
- Facility should know the recommendations
- Facility should review their protocols for Troponin
Troponin I and Troponin T

• Biomarkers of myocardial necrosis (heart tissue damage) with high cardiac-specificity
  – Troponin I (cTnI) and T (cTnT) are generally cardiac-specific

• Preferred biomarker for dx of MI

• Protein complex (not an enzyme)
3rd Universal Definition of (MI) - 2012

1st worldwide consensus document

- TROPONIN (I or T) - preferred biomarker overall
- Diagnosis of acute MI = a rise and/or fall
- 99th percentile URL designated as the decision level
- Coefficient of Variation (CV) <20% at the 99th %ile
- > 20% CV at URL should not be used
- Blood samples 1st assessment; repeated 3–6 h later
4th Universal Definition Summary - 2018

• Further expands on the 3rd Universal Definition of MI

• “The new document discusses at length the various forms of non-ischemic myocardial injury…”
  For example: Sternal trauma, diabetic patients, myocarditis, chemotherapy, renal failure

• “…contains material concerning an unusual form of myocardial infarction, myocardial infarction with non-obstructed coronary arteries (MINOCA)…”

• “…new material on takotsubo…use of high-sensitive troponin (hs-cTn) assays…expanded section of non-invasive testing

• “…regulatory issues…all 5 subtypes have…ICD 10 codes…”

Diagnostic Criteria for AMI[^a]

Detection of a rise and/or fall of cardiac biomarker values (preferably cTn)*

+ 

At least one value >99th percentile† upper reference limit (URL)

+ 

Evidence of myocardial necrosis

[^a]: Minimum change of >20% at follow-up testing.[^b]
[^b]: Assay should have coefficient of variation ≤10% at 99th percentile URL.


https://www.medscape.org/viewarticle/884837
Coefficient of Variation (CV)

**Q:** When the test is run multiple times on the same sample, how frequently do you get the same result?

**A:** The standard answer is...rarely, if ever.

In real world terms, measured by running sample at least 20 times and identifying the percentage (%) of variation within that set of results.

The Universal Definition of MI advocates from 10% to 20%
High Accuracy, Different Precision

![Diagram showing high accuracy and precision with CV values of 18% and 10%]

Contemporary Cardiac Troponin Assays are more precise

Courtesy of Dr. Robert Christenson, University of Maryland; SCPC Webinar 10/14/15
Troponin (cTn):
One of few analytes where 99\textsuperscript{th} % ile reference range is recommended

The reason:
• Goal of early prediction
• Identify results early in the elevation cycle
• Ensures standardization
Review of Facility Processes Related to Troponin
Troponin Analyzers: Name versus Location

LAB – main or central laboratory analyzer
  • Various types of analyzers

POCT – point-of-care testing
  • Catch-all phrase: Refers to any testing conducted outside a traditional central lab

NPT – near patient testing
  • May be a static analyzer or hand-held
  • Also referred to as a “bench-top” analyzer

BSM or BST – bed-side markers or bed-side testing

Results may print out as “ED POC”
Decision Making Options

- Troponin:
  - POC
  - Stat Lab
  - Central Lab

ED

OBS

- Troponin:
  - POC
  - Stat Lab
  - Central Lab

- Troponin:
  - Central Lab

In-Pt

Rule-Out OR Rule-out / Rule-in Testing

Observe

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Understanding the Differences

Troponin:
• Each assay has its own pattern of sensitivity, specificity, and imprecision characteristics
• Each assay has its own normal range and a specific numerical values
• Each assay is reliable on its own terms, but absolute concentrations between different assays cannot be compared

Adapted from: Lexington Medical Center Laboratory Bulletin and ACC Accreditation Troponin Brochure
Understanding the Differences

Troponin results within the facility require comparison studies and protocols

POC/NPT

Central Lab
Understanding the Differences

Not interchangeable

- Troponin T (cTnT) and Troponin I (cTnl)
- cTnl and cTnI

No single reference standard in laboratory medicine for cardiac troponin I assays

- POC and NPT and Central Lab

<table>
<thead>
<tr>
<th>cTnI</th>
<th>cTnT</th>
</tr>
</thead>
<tbody>
<tr>
<td>POCT/NPT</td>
<td>Central Lab</td>
</tr>
</tbody>
</table>
Understanding the Differences

Troponin results from one facility to the next are not interchangeable.

Troponin Type X*

Transfer Facility

Troponin Type Y*

Receiving Facility

* Unless pre-determined to be the same assay and analyzer – typically within a system
Understanding the Differences

Troponin assay protocols:

Protocols must be implemented for serial strategy assessments if using POC in ED and/or Dedicated Observation area versus Central Lab for in-patient

For Example:

A policy directive to hold blood from the patient’s original blood-draw in the main/central lab:

• For re-base-lining
• To be comparable to subsequent determinations, once the patient is admitted to the hospital

Adapted from: Lexington Medical Center Laboratory Bulletin and ACC Accreditation Troponin Brochure
Responsibility to Share Information

Clinical Committees responsibility is to share information with Laboratorians

Laboratorians responsibility to share information with Clinicians

“As the field continues to absorb the guidelines, panelist and others advised laboratorians to take time to know the documents so they can have constructive discourse about them with physicians...”

Clinical Lab News, Feb 2014, vol 40, no 2
Review of Troponin in Clinical Practice
Myocardial injury

Cardiac procedure

Non-cardiac major procedure

Tachy-/brady-arrhythmia

Heart failure

Renal failure

Clinical evidence of acute myocardial ischaemia with rise and/or fall of cardiac troponin

Myocardial injury with cell death marked by cardiac troponin elevation
FIGURE 2 Spectrum of myocardial injury, ranging from no injury to myocardial infarction. Various clinical entities may involve these myocardial categories, e.g. ventricular tachyarrhythmia, heart failure, kidney disease, hypotension/shock, hypoxaemia, and anaemia. cTn = cardiac troponin; URL = upper reference limit. aNo myocardial injury = cTn values < 99th percentile URL or not detectable. bMyocardial injury = cTn values > 99th percentile URL. cMyocardial infarction = clinical evidence of myocardial ischaemia and a rise and/or fall of cTn values > 99th percentile URL.
Think “HEART” NOT “MI”!
Not all elevations are acute myocardial infarction
Heart Specific
Not Diseases Specific

“The use of the 99th percentile cutoff for cTn positivity does not imply that 1% of the population suffers from myocardial damage....useful ...with a high pretest probability of ACS. ...context of... clinical history, ECG findings...cardiac imaging to establish the correct diagnosis.

A positive troponin in the setting of a low pretest probability for ACS may be suggestive but clearly is not indicative of a coronary event.”
Clinician Awareness of Interferences

Biotin (vitamin B7)

A beauty supplement; when taken at levels well above the daily recommended intake **may cause interference in immunoassays, including for cTn.**

- FDA released a safety communication in November 2017
  - FDA received an increase in the number of reported adverse events related to biotin interference, including one death.
  - This patient had been taking a high dose of biotin, which led to a false negative cTn result.

**ACTION: Verify if patient use of Biotin is an assessment question**


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American Association for Clinical Chemistry: Date: JAN/FEB and MAR.1.2018 // Source: Clinical Laboratory News

Clinician Awareness of Interferences

- **Biotin** (vitamin B7)
  - Is this question addressed in the facility lab report?

**EXAMPLE:**

Order Entry Note 1:
ALERT: This test could potentially be affected if the patient is taking high doses of Biotin/Vitamin B7 found in many multivitamins and hair, skin and nail growth supplements. Interpret results with caution if result doesn't fit the clinical picture.

Order Entry Note 2:
For please annotate in comments if the patient is currently taking Biotin, the approximate dosage and the time of the last dosage.

**Other Resource Article:**
Cardiac troponin and natriuretic peptide analytical interferences from hemolysis and biotin: educational aids from the IFCC Committee on Cardiac Biomarkers (IFCC C-CB)
CPC v6 assessment: Standing orders/Cardiac panel should no longer include:

- CK-MB
- MYO
- Total CK

Class I
- Cardiac-specific troponin (troponin I or T when a contemporary assay is used) levels should be measured at presentation and 3 to 6 hours after symptom onset in all patients who present with symptoms consistent with ACS to identify a rising and/or falling pattern. (Level of Evidence: A)

- Additional troponin levels should be obtained beyond 6 hours after symptom onset in patients with normal troponins on serial examination when electrocardiographic changes and/or clinical presentation confer an intermediate or high index of suspicion for ACS. (Level of Evidence: A)

- If the time of symptom onset is ambiguous, the time of presentation should be considered the time of onset for assessing troponin values. (Level of Evidence: A)

Class III: No Benefit
- With contemporary troponin assays, creatinine kinase myocardial isoenzyme (CK-MB) and myoglobin are not useful for diagnosis of ACS. (Level of Evidence: A)
The facility has a serial troponin strategy defined in an evidenced-based standardized protocol that is consistent with the assay used.

The facility provides the manufacturer and troponin assay used in central lab and POC (where applicable).

<table>
<thead>
<tr>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fourth Universal Definition of Myocardial Infarction</td>
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<tr>
<td>International Federation of Clinical Chemistry (IFCC) Analytical characteristics of cardiac troponin I and T assays</td>
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<tr>
<td>Third Universal Definition of Myocardial Infarction</td>
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<tr>
<td>Troponin Brochure: Guidelines for Troponin Testing</td>
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</table>
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 than 50%** of the institutions in the developed world use the **99th percentile cutpoint** for diagnosis of myocardial infarction.
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...

Accredited Chest Pain Centers v6 are required to demonstrate adherence to the guideline 99th %ile

Dr. Robert Christenson, Cardiac Troponin: Current Status and Future Promise
https://www.whitehatcom.com/POCWebMtgsslides/R_Christenson_Cardiac_Troponin_041118.pdf
Accountability for use of the 99th Percentile

“Clinical laboratorians in the wake of this new definition could take several measures to help physicians appropriately use and interpret hs-cTn results, Jaffe continued. **Consistent use of the 99th percentile protocol is one such approach. Labs sometimes decide that the 99th percentile is something else and use their own cutoffs. This undermines the guidance the Universal Fourth Definition is trying to achieve,** Jaffe said. “It’s hard to suggest approaches to evaluate changing patterns or results or when to consider other possibilities when these are set up as if one is using the assays properly and someone else is using different cutoffs. Then it doesn’t work well. **It’s important that labs start to come together and stop deciding that the 99th percentile is something else.**”

Allan Jaffe, MD, Cardiologist, Mayo Clinic, Rochester, Minnesota
Accreditation Quality Assessments

### EC4.1: Initial Assessment

The facility has a serial troponin strategy defined in an evidenced-based standardized protocol that is consistent with the assay used.

- **EC4.M1e**: The facility provides the manufacturer and Troponin assay used in central lab and POC (where applicable).

- **EC4.M1f**: The facility demonstrates the decision cut point for positive and negative test for both central lab and POC (where applicable).

- **EC4.M1g**: The facility provides the 99th percentile for both central lab and POC (where applicable).

- **EC4.M1h**: The facility provides the coefficient of variation at the 99th percentile for both central lab and POC (where applicable).

- **EC4.M1i**: The facility operates from an agreed upon standardized timing of Troponins across departments.
CPC Troponin Assessments

For both CENTRAL LAB and POC/NPT Troponin

- Manufacturer
- Analyzer
- 99\textsuperscript{th} Percentile
- CV at 99\textsuperscript{th}%
- Review use of outdated assays
- Troponin Turn-Around-Time (TAT) % Door-to-Result – 60 minutes

Reviewing the \textit{Interpretive Comments test results} print out
  - Assess guideline adherence

- IFCC
- Instructions for Use (IFU)

Ensuring facilities are no longer using or referencing outdated WHO criteria from IFU or outdated reference ranges, discrepancies, grey zone, assays etc.
The facility provides the 99th percentile for both central lab and POC (where applicable).

The Lab must be consulted for this item.

Facilities should establish and use the 99th percentile concentration for the Troponin cut point. For optimal precision for AMI diagnosis, the use of Troponin with a coefficient of variation (CV) at the 99th percentile upper reference limit (URL) of less than or equal to 10%, is preferred. Assays with CV of greater than 20% at the 99th percentile URL should not be used.

Reference Guidance:
1. Third Universal Definition of Myocardial Infarction: Detection of a rise and/or fall of the measurements is essential to the diagnosis of acute MI. An increased cTn concentration is defined as a value exceeding the 99th percentile of a normal reference population [upper reference limit (URL)]. This discriminatory 99th percentile is designated as the decision level for the diagnosis of MI and must be determined for each specific assay with appropriate quality control in each laboratory.
2. IFCC – Use this guide to find the facility Troponin assay 99th percentile and CV at the 99th percentile to validate use of the 99th percentile.

Supporting documentation includes a policy or protocol specifically outlining the required information. The facility must provide the Troponin interpretive results with the reference range.
NCDR® Chest Pain - MI Registry™
(formerly the ACTION Registry®)

Troponin Quality Assessments:
99th percentile URL
Central lab and POC

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- If any value, Troponin Result Date/Time
- If Lab, Troponin Assay, URL
- If POC, Troponin Assay, URL

IFCC: Updated

The International Federation of Clinical Chemistry (IFCC) – Updated versions now in v5 or v6 tool

<table>
<thead>
<tr>
<th>Company/ Platform(s)/ assay</th>
<th>LoB (µg/L)</th>
<th>LoD (µg/L)</th>
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IFCC Updated: 3 Separate

Contemporary Cardiac Troponin I and T Assay Analytical Characteristics Designated by Manufacturer

<table>
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<tr>
<th>Company/Platform/Assay</th>
<th>LoB, µg/L</th>
<th>LoD, µg/L</th>
<th>% CV at 99th percentile</th>
<th>Conc at 20% CV µg/L</th>
<th>Conc at 10% CV µg/L</th>
<th>Reference Population N, Ages, Sex</th>
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<th>Epitopes Recognized by Antibodies</th>
<th>Country of Package Insert: Version Date</th>
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Point of Care Cardiac Troponin I and T Assay Analytical Characteristics Designated by Manufacturer

IFCC Task Force on Clinical Applications of Cardiac Bio-Markers (TF-CB) v060617

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<tr>
<th>Company/Platform/Assay</th>
<th>LoB, µg/L</th>
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<th>% CV at 99th percentile</th>
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High Sensitivity* Cardiac Troponin I and T Assay Analytical Characteristics Designated by Manufacturer

IFCC Task Force on Clinical Applications of Cardiac Bio-Markers (TF-CB) v060617

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<th>Epitopes Recognized by Antibodies</th>
<th>Country of Package Insert: Version Date</th>
</tr>
</thead>
</table>

IFCC now calls out assays with CV > 20% / Some assays continue to state “Not Provided” for the various categories.
Brief review of “high-sensitivity” Troponin
Sensitivity and Specificity

For Sensitivity think “SnOUT”

- Describes the ability of a test to identify true disease
- A high-sensitivity test has few False Negatives (FN) and is effective at ruling conditions “out” (SnOUT)
- Formula: \( \frac{\text{True Positive (TP)}}{\text{TP} + \text{FN}} \)

For Specificity think “SpIn”

- Describes the ability of a test to identify the absence of disease
- A high-specificity test has few False Positives (FP) and is effective at ruling conditions “in” (SpIn)
- Formula: \( \frac{\text{True Negative (TN)}}{\text{TN} + \text{FP}} \)
Clinical Lab Practice Recommendations

January 2018

...companion to National Association of Clinical Biochemistry (now the American Association for Clinical Chemistry (AACC) Academy) Laboratory Medicine Practice Guidelines on cardiac markers.

Concensus Document:
“...clinical laboratory practice recommendations for high-sensitivity (hs) cTn assays...“

REINFORCE REPORTING UNITS:
ng/L

Recommendation 3: Report hs-cTn in whole numbers, using ng/L without decimal points. For reporting QC values, we recommend 1 decimal point. For contemporary cTn assays, units are reported in μg/L to 2 significant figures, with QC values reported to 3 significant figures.
Reporting Units

Integer values (units of ng/L) reported for high-sensitivity cTn assays

Results of contemporary and earlier generation cTn assays were reported in units of ng/mL, causing results to appear as decimal values on patient and other documents. The recommendation of the AACC Academy and IFCC Task Force Consensus Guidelines are to report hs-cTn results in units of \( \text{ng/L} \), so that all results will be reported as whole number values. For example, a value of 0.07 ng/mL for a contemporary cTn assay will have value of 70 ng/L for a high-sensitivity test. Reporting high-sensitivity results as whole numbers will facilitate interpretation and allow differentiation of whether an assay is high-sensitivity, a contemporary, or earlier generation test. It is believed that expressing results as whole numbers, rather than as decimals as is recommended with contemporary and earlier generation cTn assays, will reduce error when interpreting cTn results.
“High-sensitivity” Troponin Defined

What is High-Sensitivity Cardiac Troponin?

- IFCC defines high-sensitivity cTn test as one that can measure $\geq 50\%$ of healthy subjects above the Limit of Detection.
- Also, high-sensitivity cTn assays perform at the highest level of day-to-day precision, i.e. $CV \leq 10\%$.

Clin Biochem 2015;48(4-5):201-203

Dr. Rob Christenson – Cardiac Troponin: Current Status and Future Promise, 4/11/2018
https://whitehatcom.com/POCWebMtgs/Slides/R_Christenson_Cardiac_Troponin_041118.pdf
“High-sensitivity” Troponin Defined

“The assay should have a high enough analytical sensitivity (i.e. be able to ‘detect’ very low troponin levels) to enable levels of troponin to be detected in at least 50% of “normal” individuals (AND females and males) i.e. apparently healthy people who do not have myocardial disease.

With previous troponin assays, it was not possible to measure such small levels of troponin.

This meant that having any detectable troponin in the blood was abnormal, but now that technology has improved.

With a high sensitivity assay we will be able to detect Troponin in at least half of all healthy people.”
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. Apple2

“...both men and women...”

*LoD = Level of Detection
http://clinchem.aaccjnls.org/content/early/2018/01/08/clinchem.2017.277186

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"Next Generation” Troponin: First in USA

March 2017:
The Food and Drug Administration (FDA) granted 510 (k) clearance to Roche for its Elecsys Troponin T (TnT) Gen 5 Stat

FDA termed: Next Generation (Gen 5) vs. high-sensitivity*

Test characteristics: <10% CV at the 99th%-ile

*Defined to include both men and women

Clinical Lab News, March 2017, page 22

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“High-sensitivity” Troponin: First 2 Troponin I

The Food and Drug Administration (FDA) granted 510 (k) clearance:

**June 2018:**
Beckman Coulter’s *Access Troponin I (hsTnl)*

**July 2018:**
Siemens’ *Atellica IM and ADVIA Centaur XP/XPT (TnIH)*

FDA termed both: *high-sensitivity*

Test characteristics: <10% CV at the 99th%-ile for both men and women LoD > 50% of the healthy population


On the topic of hs-cTn, what is next?

Open dialogue / Awareness of Guidelines / Accreditation REQ

Education, Education, Education
IFCC Documents on hsTn

Clinical Applications of Cardiac Bio-Markers

The following resources have been prepared by the Task Force for Clinical Application of Cardiac Biomarkers (TF-CB):

- Implementing High-Sensitivity Cardiac Troponin Assays in Practice - pocket format
- Using High Sensitivity Cardiac Troponin Assays in Practice - a Summary Document - pocket format
- Calculating Serial Change Values (Delta) for High-Sensitivity Cardiac Troponin Assays
- Using High Sensitivity Cardiac Troponin Assays in Practice


Other Articles:

High sensitivity, contemporary and point-of-care cardiac troponin assays: educational aids developed by the IFCC Committee on Clinical Application of Cardiac Bio-Markers
Educational Presentations/Offerings

Medscape:

*Diagnostic Algorithms for ACS and High-Sensitivity Troponin: Where Are We Today?*


Medscape:

3-part series - Biomarkers

[https://www.medscape.org/sites/advances/diagnostics](https://www.medscape.org/sites/advances/diagnostics)

American Association Clinical Chemistry (AACC):

*New Clinical Lab Practice Recommendations for the Use of Cardiac Troponin in Acute Coronary Syndrome*

[https://www.youtube.com/watch?v=XHTh96tZAZI&feature=youtu.be](https://www.youtube.com/watch?v=XHTh96tZAZI&feature=youtu.be)
Clinical Considerations and Educational Requirements: Collection of blood relative to impacts on high-sensitivity Troponin

**High-sensitivity Troponin assay(s) requires special handling due to Hemolysis factors:**

With Hemolysis:
- TnT results go down
- TnI results go up

**Recommendation:** Consult with Phlebotomy

**ACTION:** Teach staff to draw via venipuncture instead of through IV catheter (except for newly started IV line)

Serial Strategy Assessments
Serial Strategy and Stress Testing Timing

2014 NSTE-ACS Guideline Recommendations:

3.5.1. Discharge From the ED or Chest Pain Unit: Recommendations Class IIa

1. It is reasonable to observe patients ...in a chest pain unit or telemetry unit with serial ECGs and cardiac troponin at 3- to 6-hour intervals (Level of Evidence: B)

2. It is reasonable for patients with possible ACS who have normal serial ECGs and cardiac troponins to have a treadmill ECG (Level of Evidence: A), stress myocardial perfusion imaging, or stress echocardiography before discharge or within 72 hours after discharge. (Level of Evidence: B)

3. In patients with possible ACS and a normal ECG, normal cardiac troponins, and no history of CAD, it is reasonable to initially perform (without serial ECGs and troponins) coronary CT angiography to assess coronary artery anatomy (Level of Evidence: A) or rest myocardial perfusion imaging...to exclude myocardial ischemia (Level of Evidence: B)

Reported PROTOCOLS from this guidance:

0h – 3h negative cTn – then stress
0h – 2h negative cTn – then CT angiography

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A patient’s serial Troponin results should only be compared for those run on the same analyzer. The decision cut point for a Point-of-Care (POC) Troponin will not be the same as a central laboratory analyzer. If different analyzers are used during the serial strategy, ensure there is a protocol for comparison or re-base-lining should the patient move from the ED to a different environment. Per guideline recommendations, lab should report significant changes in serial samples through delta checks using the same assay.

A facility should provide protocols for the ED which then follow through to the hospital, e.g., ED = 0-2 hrs., OBS or inpatient continue at 6 hours or inpatient set at 0-3-6 hours which closely matches the ED 0-3-6 strategy. The facility should have a methodology to connect the different draw times between departments. Language examples, not limited to:

- "...If not done in the ED then Troponin on admission, then 3 and 6 hours ..."
- "...Troponin ED POC then 3 hrs. from original and 3 hrs. from second sample..."
Serial Ordering Recommendations:

“...This (MI) definition inherently requires at least two cTn results, which can display either a rising or falling pattern, over the initial 6-9 hours after a patient’s presentation (Oh) with at least one value above the 99th percentile.”

“....if the patient’s initial two cTn results at Oh and 3h are below the 99th percentile...and there is no diagnostic EKG or imaging findings, this would be sufficient to rule out MI in an otherwise low-risk patient, providing the ability to cancel subsequent outstanding order. ”
Serial Strategy Assessment: v6
(moved from v5 as Recommended to v6 as Mandatory)

Partnering With Your Clinicians Through Changes in Troponin Testing
Amy Sanger PhD and Sherrie Smart, RN, MSN, Roche Webinar, 12-18-14

---

Example of Reporting Strategy

<table>
<thead>
<tr>
<th>Test</th>
<th>Value 1</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN</td>
<td>8.24 mg/dL</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>Chloride</td>
<td>100-108 mmol/L</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>Bicarbonate, P/S</td>
<td>22-29 mmol/L</td>
<td>22</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>7-15</td>
<td>23 Jan 08</td>
</tr>
</tbody>
</table>

**CARDIAC CHEMISTY**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value 1</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin T, S</td>
<td>&lt;0.01 ng/mL</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>3H Troponin T, S</td>
<td>&lt;0.01 ng/mL</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>6H Troponin T, S</td>
<td>&lt;0.01 ng/mL</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>3H Delta</td>
<td>Not Sig</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>6H Delta</td>
<td>Sig Delta</td>
<td>23 Jan 08</td>
</tr>
</tbody>
</table>

**LIPIDS 63 AG**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value 1</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL Subfractionation</td>
<td>100-200 g/dL</td>
<td>23 Jan 08</td>
</tr>
<tr>
<td>Beta LDL Cholesterol</td>
<td>100-200 g/dL</td>
<td>23 Jan 08</td>
</tr>
</tbody>
</table>

---

Ensure there is a protocol for companion or re-base-lining should the patient move from the ED to a different environment. Per guideline recommendations, lab should report significant changes in serial samples through delta checks using the same assay.
Serial Strategy Assessment: v6

Key Term: “Standardized throughout the facility...” transitioning process between ED and inpatient

The facility demonstrates the timing between serial troponins are standardized throughout the facility (timing strategy may include: 0, 2, 6 - 0, 3, 6 - 0, 3 etc.) with a mechanism to ensure continuity of serial strategy after the patient is moved to another unit.

EC4.M3b

The facility demonstrates the timing between serial troponins are standardized throughout the facility (timing strategy may include: 0, 2, 6 - 0, 3, 6 - 0, 3 etc.) with a mechanism to ensure continuity of serial strategy after the patient is moved to another unit.

Facilities cannot use a serial strategy which denotes testing every 8 hours (e.g. 0-8-16 hour) intervals on any order sets.

It is important to ensure continuity of the serial strategy after the patient is transferred from one unit to another. A patient's serial Troponin results should only be compared for those run on the same analyzer. If different analyzers are used during the serial strategy, ensure there is a protocol for comparison or re-base-lining should the patient move from the ED to the inpatient environment.
The infamous “Grey Zone” existing in Troponin Testing
Troponin History

- Early = CKMB
- **1999:** Troponin – poor assay precision created 2+ cut-points
  The history of the grey zone was born!
  
  “That set the stage for using whatever cutoff you want, and the field has never recovered from it.” Jaffee et. Al. Clinical Chemistry 2008

- **2005:** Intro to 99%ile and CV <= 10%
- **2007:** Lab guidelines first attempt - cTn standardized
- **2012:** 3rd Universal Definition of MI
- **2018:** Clinical Lab Practice guidance updated
- **2018:** 4th Universal Definition of MI

Excerpt from internet presentation n.d. “Cardiac Markers: Why all the Confusion?” by R. Heitsman, Radiometer, National Accounts Manager
The facility demonstrates the decision cut point for positive and negative test for both central lab and POC (where applicable).

Guidance Statement:

- The Lab must be consulted for these items.
- The facility must provide a policy, procedure or protocol to show the decision point for a positive test.
- The facility will be required to provide the Interpretive Comments for Troponin results.
- Decision cut points must be clearly documented by the facility and not open to interpretation.
Interpretive Comments Assessment

- **TROPONIN T (TnT) 0.01 – 0.05 μg/L**
  
  Indicates minimal myocardial damage which with the appropriate clinical and ECG findings may be of prognostic significance in patients with ACS. However levels within this range may also be due to non-ACS causes e.g. pulmonary embolus, heart failure, CRF, severe sepsis etc.
  
  In ACS TnT starts to rise at 3-4h and reaches maximum sensitivity at 12-18h post symptoms and can remain elevated for up to 7-8 days. For exclusion of ACS levels should not be taken before 12h post symptoms.

- **TnT >0.05 μg/L would support a diagnosis of AMI**

Using the 99th% ile for decision point? **Need more information** (see IFCC or other document)

Using a “Grey Zone”? **No, there is a negative and a positive**
## Interpretive Comments Assessment

### TROPONIN I

<table>
<thead>
<tr>
<th>Value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.04</td>
<td>No evidence of myocardial damage provided provided sample is at least 12h post symptoms (event).</td>
</tr>
<tr>
<td>0.04 – 0.48</td>
<td>Suggest minor myocardial damage provided at least 12h post event</td>
</tr>
<tr>
<td>&gt;0.49</td>
<td>Indicates major myocardial damage</td>
</tr>
</tbody>
</table>

- **Using the 99th% ile for decision point?** Need more information (see IFCC or other document)
- **Using a “Grey Zone”?** YES
Interpretive Comments Assessment

TROPONIN I

- **<0.04**: Troponin appears normal or minor myocardial damage or other cause
- **>0.04**: Consistent with Myocardial Infarction

This information is based on the recommendations of the 2012 Third Universal Definition of Myocardial Infarction for Troponin to be at least one value above the 99th percentile upper reference limit.

- Using the 99th% ile for decision point? **Probably** (see IFCC or other document) – also cite the source (may see website links or PDF links)
- Using a “Grey Zone”? **No, there is a negative and a positive**
HIGH-SENSITIVITY TROPONIN T

• <19 ng/L

When assessing risk for Acute Coronary Syndrome (ACS): ....an initial hs-Troponin T less than 19 ng/L and a X hour delta...less than X ng/L should be considered very low risk....
Turn-Around-Time (TAT): Accreditation requirements and accountability
Studies and research support the following:

- Assessing the “whole process” (i.e.: arrival)
- Standardizing the definitions of turn-around-time (TAT)
- Assessing TAT with patient outcomes and length of stay

The advent of “Accelerated Diagnostic Protocols” for Troponin will require monitoring to ensure standardization of processes.
TAT Advocated Since 2008 for Accreditation

Accreditation requirement for 10 years and continues to be determined as a “need”.

Labs also need to work on turnaround time to prevent emergency department overcrowding. When the emergency department is overloaded, all patients suffer, Jaffe emphasized. “Finally, the lab needs to participate in development of protocols so that whatever approaches clinicians take reflect the joint input of the emergency department, lab, cardiology, and surgery departments that use these assays,” he said.

Allan Jaffe, MD, Cardiologist and chair of the division of clinical core laboratory services at Mayo Clinic in Rochester, Minnesota

*Sept 2018 Clinical Lab News (CLN Stat)*
TAT Tracking: Healthcare Implications

Study proposed concepts for TAT in the diagnostic process:

As a “Patient-oriented” view or the “whole process”
- Diagnostic TAT - arrival to reporting of results
- Clinical TAT - arrival to order
- Laboratory TAT - order to report/resulted


“Guidelines do not exist delineating time frames for when a troponin test should optimally be resulted in association with improved patient outcomes.”

“Prolonged laboratory TAT may delay recognition of conditions in the acutely ill, potentially affecting clinician decision-making and the initiation of timely treatment.”

Academic Emergency Medicine, 2010:17, Hwang et al
What Does Turnaround Time Say About Your Lab?

Key Quotes:

• “Every laboratorian knows that their colleagues in medicine see TAT as something almost as important as the quality of test results themselves.”

• “In fact, surveys have found that 80% of labs get complaints about TAT.”
Turn-around-Time (TAT) Defined?

- Physicians  “brain to brain”
- Laboratorians “receipt to result”
- Nurses  “door or draw to result”
- Phlebotomist “collect to receipt in lab”
Decreasing troponin turnaround time in the emergency department using the central laboratory: A process improvement study
Arlene M. Boelstler, Ralph Rowland, Jennifer Theoret, Robert B. Takla, Susan Szpunar, Shraddha P. Patel, Andrew M. Lowry, Margarita E. Pena
https://doi.org/10.1016/j.clinbiochem.2014.10.014

Highlights:

- A troponin turn-around-time (TAT) of < 60 min Door-to-Results can be achieved using central laboratory
- Multidisciplinary collaboration is central to process improvement success
- Optimizing workflow and processes is key to reducing Door-to-Result TAT
- Decreasing troponin TAT impacts emergency department length-of-stay (LOS)
Table 4
Summary of collaborative solutions before and after process improvement.

<table>
<thead>
<tr>
<th>Pre-Process improvement</th>
<th>Post-Process Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Door-to-order</strong> (Step 1)</td>
<td><strong>Door-to-order</strong> (Step 1)</td>
</tr>
<tr>
<td>Patient taken back to an ED bed after triage; troponin order placed after the physician evaluates the patient</td>
<td>ED triage nurse-initiated cardiac panel blood draw protocol</td>
</tr>
</tbody>
</table>

Table 2
Emergency department length of stay, hemolysis rate, monthly ED volume and boarder hour data before and after process improvement.

<table>
<thead>
<tr>
<th>Metric</th>
<th>TAT prior to PI Mean (min)</th>
<th>TAT after PI Mean (min)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ED Length of stay (h)</strong></td>
<td>5.87 ± 2.73</td>
<td>5.15 ± 2.34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Hemolysis rate (%)</strong></td>
<td>14.63 ± 0.74</td>
<td>3.36 ± 1.99</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Monthly ED Volume</td>
<td>9771.50</td>
<td>9871.14</td>
<td>0.502</td>
</tr>
<tr>
<td>Monthly ED Boarder hours</td>
<td>438.13</td>
<td>891.09</td>
<td>0.010</td>
</tr>
</tbody>
</table>

(TAT = turnaround time; PI = process improvement; ED = emergency department)

| Order-to-collect (min)      | 15 (23)                     | 10 (12)                 |
| Collect-to-received (Min)   | 6 (8)                       | 5 (5)                   |
| Received-to-result (min)    | 30 (12)                     | 24 (11)                 |
| Door-to-result (min)        | 117 (60)                    | 60 (40)                 |

(TAT = turnaround time; PI = process improvement; IQR = Interquartile range).
“Windows of Time” assess, how a facility ensures serial draws take place, regardless of the patient location? Do those draws take place within the time requirements established in their protocols and policies? How is this assessed?

If a 0-2-4 hr., 0-3-6 hr. or 0-90-180 minute protocol is in place, are those turn-around-times, beyond the zero time point, individually measured?

The facility demonstrates Troponin protocols for the following:

- Serial marker strategy and Troponin turn-around-time (TAT) goals

If a 0-2-4 hr., 0-3-6 hr. or 0-90-180 minute protocol is in place, are those turn-around-times, beyond the zero time point, individually measured? Provide meeting minutes, metrics, policies and protocols, lab-based educational newsletters to support this item.
TAT Assessed = Process Standardization

• Know the starting point

• Know the goal time for each phase

• Know the compliance goal
**Time is muscle – think HEART!**

<table>
<thead>
<tr>
<th>PAST</th>
<th>PRESENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to ECG = 10 minutes</td>
<td>Door to ECG READ within 10 minutes</td>
</tr>
</tbody>
</table>

**REQUIREMENT**
# Time is muscle – think HEART!

<table>
<thead>
<tr>
<th>PAST</th>
<th>PRESENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to Reperfusion = 90 minutes</td>
<td>Door to Reperfusion &quot;as soon as possible“</td>
</tr>
<tr>
<td></td>
<td>90 min (100%)</td>
</tr>
<tr>
<td></td>
<td>Door to Reperfusion 60 minutes (60%)</td>
</tr>
<tr>
<td></td>
<td>First Medical Contact (FMC) to Reperfusion Less than 90 minutes</td>
</tr>
<tr>
<td>TRANSFER:</td>
<td>Door in - Door Ready = 25 minutes</td>
</tr>
<tr>
<td>Door in - Door out = 30 minutes</td>
<td></td>
</tr>
<tr>
<td>Door to Thrombolytics = 30 minutes</td>
<td>Same consideration; low utilization</td>
</tr>
</tbody>
</table>

**GOALS**
# Time is muscle – think HEART!

<table>
<thead>
<tr>
<th>PAST</th>
<th>PRESENT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

Lab received to results = 60 minutes

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Door to Troponin Results in 60 minutes</td>
<td></td>
</tr>
<tr>
<td>Facility sets % compliance – recommend assessments at 75% and 90%</td>
<td></td>
</tr>
<tr>
<td>Order/Collect to results = 60 minutes</td>
<td></td>
</tr>
<tr>
<td>Order/Collect to results: % compliance = 90%</td>
<td></td>
</tr>
</tbody>
</table>

## GOALS
Time is muscle – think HEART!

**Benchmarks: From DOOR**

- Door to Reperfusion STEMI = 60
- Door to Result = Troponin = 60
- Door to ECG Read = 10 min
- Door to Ready (Transfer) = 25 min
- Door to Needle (Lytics) = 30 min
- Team arrival = 30 min from activation

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### Benchmarks and Requirements:

**GOLDEN HOUR and QUALITY for the HEART**

**STEMI is a heart trauma:**
- 60 minutes from "door"

**SET NEW GOAL:**
- Door to Reperfusion in 60 minutes (60%)

**SET NEW TAT GOAL and ENSURE GUIDELINE COMPLIANCE SET:**
- Troponin assay at the 99<sup>th</sup> percentile
- 60 minutes from "door" (75%/90%)
Fourth Universal Definition of Myocardial Infarction (2018)

Aug 24, 2018

Journal of the American College of Cardiology

Kristian Thygesen, Joseph S. Alpert, Allan S. Jaffe, Bernard R. Chatman, Jeroen J. Bax, David A. Morrow, Harvey D. White, Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction
Thank you!

Ruth Cantu, BSN, RN, AACC
rcantu@acc.org