High-Sensitivity Troponin T: What you need to know

Last Edits: 4/23/19
Case Study to Consider

• 75yo man postop for a lap chole with a history of HTN and paroxysmal AF develops Afib with RVR
• Denies any chest pain or shortness of breath
• ECG shows AF RVR without ischemic changes
• Rate was controlled with PO beta-blocker
• A hs-Trop T reveals an initial value of 26 and the 4 hour follow up was 36

What do you do?
• High-sensitivity Troponin (hs-Trop) assays have been introduced in an effort to improve detection of myocardial infarction.

• These assays are able to detect much lower concentrations of the troponin protein, thereby shortening the time interval required to identify myocardial injury.

• Although kinetics are different for Trop T and Trop I, an hs-Trop T measurement of 30 pg/ml roughly correlates with the initial detectable level of our current Trop I assay (just above 0.1 ng/ml). An hs-Trop T of 140 pg/ml roughly correlates with a current Trop I value of 1.0 ng/ml.

• Because of their increased sensitivity, up to 50% of patients without Acute Coronary Syndrome (ACS) will have a detectable (but not abnormal) hs-Trop.

• Since hs-Trop T will result in more detectable Trops, it is critical that we learn how to interpret these values.
Elevated troponins constitute myocardial injury

Myocardial infarction (MI) is one cause of myocardial injury

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.

Kristian Thygesen et al. JACC 2018; j.jacc.2018.08.1038
Elevated Troponin Levels & Outcomes

Any level of Troponin whether due to myocardial injury or infarction is worse than no Troponin.

Higher Troponin is worse than lower Troponin.

CENTRAL ILLUSTRATION: Elevated Troponin Levels and Outcomes: Cumulative Mortality

Clinical context critical to interpretation

The enhanced sensitivity of hs-Trop T means the assay may come back with more “positive results”. It is important to put clinical context into decision making. Do not rely on the interpretation of the test alone.

- Are the troponins chronically elevated?
- Is there any acute rise and fall?
- Does the patient have a suspicious history for ACS?
- Is there evidence of ischemia?
Troponin: acute from chronic injury?

Troponin is a marker of myocardial injury, **it does not differentiate acute from chronic injury.**

- Acute injury such as that seen in Acute Coronary Syndrome (ACS) should display a rise in Troponin over time. For rule in and rule out on the floor, samples drawn 2 hours apart are used and a difference or delta value of 6 pg/mL is considered consistent with acute injury.

- A decrease in hs-Trop T over time can indicate an acute injury that occurred days ago, but is less specific for ACS and **more often associated with non-ACS conditions.**

- Chronic conditions that can produce an elevation of hs-Trop T rarely show an increase over time intervals of 2 to 6 hours.
Timing Matters and Serial Sampling is Important

Cardiac Troponin (cTn)

- Very early sampling: Rising cTn values from below to >99th percentile. Delta is detectable.
- Early sampling: cTn values >99th percentile. Delta may not be seen over a short period.
- Later sampling: Declining delta.
- Very late sampling: Acute myocardial infarction. Chronic myocardial injury.

Time from onset of symptoms (hours)
Troponin Interpretation for workup of suspected ACS

High Sensitivity Troponin T Interpretation For Inpatients

1st Troponin T=0h
- 0h ≥ 53 pg/mL
- 19 pg/mL < 0h < 53 pg/mL
- 0h ≤ 19 pg/mL

2nd Troponin T=2h
- 2h increment ≥ 6 pg/mL
- 2h increment < 6 pg/mL

3rd Troponin T=2h after 2nd troponin
- 4h increment ≥ 6 pg/mL
- 4h increment < 6 pg/mL

Result Interpretation
- Rule-In
- Rule-In
- Rule-In
- Rule-In
- Rule-Out

Rule-In means ruled-in for myocardial injury. Clinical content must be taken into consideration to determine if this constitutes myocardial infarction. If you have a strong suspicion for ACS, then do not delay proper treatment until the hs-trop results come back from the lab.

*Patients should be considered for the possibility of known CKD (GFR < 30), CHF w/ LVH or known CAD w/ LVH. A repeat troponin for with these conditions should be demonstrated by a stable follow up troponin level with a delta of less than 6; however, in some instances this could still be suggestive of a recent MI depending on level of suspicion. If suspicion is high, consider downstream stress or CTCA testing to further assess patient condition, else consider other etiology.

Biotin Notice: If a patient has taken greater or equal to 10 mg of Biotin in the last 6-hours at time of blood draw, the troponin values may present falsely lower.
When do abnormal trops constitute an Acute Myocardial Infarction (AMI)?

**Fourth Universal Definition of Myocardial Infarction:**

- Detection of a rise and/or fall of a biomarker (preferably cardiac troponin) in serial samples, with at least one value above the 99%ile reference limit (19ng/ml) and at least one of the following:
  - Symptoms of acute myocardial ischemia
  - New ischemic ECG changes
  - Development of pathologic Q waves
  - Imaging evidence of new myocardial viability loss or new regional wall motion abnormality
  - Identify coronary thrombus by angiography

This is particularly important for patients with declining value between 1\textsuperscript{st} and 2\textsuperscript{nd} hs Trop T!

- **You need to have one of these findings to make a diagnosis of acute coronary syndrome/AMI.**

Once a diagnosis of myocardial infarction (MI) is made, it is further classified into type based on the etiology:

- **Type 1 MI** is acute coronary syndrome (ACS) due to plaque rupture with thrombus.
- **Type 2 MI** is due to supply-demand mismatch:
  - Supply-demand imbalance alone
  - Fixed atherosclerosis and supply-demand imbalance
  - Vasospasm or endothelial dysfunction

Third Universal Definition of Myocardial Infarction 2012
Troponin elevations and myocardial infarction/injury

Elevated troponin value(s) > 99th percentile URL

Myocardial injury with necrosis

Overt ischemia

Thrombosis
- T1M1 Examples:
  - Atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus

Oxygen imbalance
- T2M1 Examples:
  - Severe anemia, Severe respiratory failure, Tachyarrhythmia, Cardiogenic or hypovolemic shock, Severe hypertension, Coronary embolism, Coronary endothelial dysfunction, or spasm

Troponin rise/fall

Myocardial infarction

Cardiac
- Examples:
  - CHF, Cardiomyopathy, Myocarditis, Cardiac trauma, Cardiac surgery, Defibrillator shocks, Hypertension, Tachycardia, Stress-induced cardiomyopathy, Myopericarditis, Infiltrative cardiac disease

Systemic
- Examples:
  - Sepsis/infection, Critically ill patients, Renal failure, Stroke, Pulmonary embolism, Toxic agents, Subarachnoid hemorrhage, CVA, Rhabdomyolysis, Strenuous exercise

Without overt ischemia

Troponin rise/fall or chronic elevation

Myocardial injury condition
What do we call these different causes of trop elevation in MiChart?

Elevated troponin value(s) > 99th percentile URL

Myocardial injury with necrosis

- Overt ischemia
  - Troponin rise/fall
  - Myocardial infarction
    - Thrombosis
      - TIMI Examples: Atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus
    - Oxygen imbalance
      - T2MI Examples: Severe anemia, Severe respiratory failure, Tachyarrhythmia, Cardiogenic or hypovolemic shock, Severe hypertension, Coronary embolism, Coronary endothelial dysfunction, or spasm

- Without overt ischemia
  - Troponin rise/fall or chronic elevation
  - Myocardial injury condition
    - Cardiac
      - Examples: CHF, Cardiomyopathy, Myocarditis, Cardiac trauma, Cardiac surgery, Defibrillator shocks, Hypertension, Tachycardia, Stress-induced cardiomyopathy, Myopericarditis, Infiltrative cardiac disease
    - Systemic
      - Examples: Sepsis/Infection, Critically ill patients, Renal failure, Stroke, Pulmonary embolism, Toxic agents, Subarachnoid hemorrhage, CVA, Rhabdomyolysis, Strenuous exercise

STEMI
NSTEMI
Type 2 myocardial infarction
Myocardial injury due to_______

MiChart terminology

If NSTEMI is not the final diagnosis associated with elevated hs-trop T value, but you initially stated that you were “evaluating for NSTEMI”, then you should clarify in your later notes that you have “ruled-out for NSTEMI” and specify the final diagnosis as “type 2 myocardial infarction” or “myocardial injury due to_______”.

DOI: 10.1373/clinchem.2016.255521 Published December 2016
Rapid and substantial increases in hs-trop T enhance the likelihood of acute MI.

A broader differential diagnosis associated with lower-range elevations of hs-cTn begins to narrow as concentrations are higher. HF = heart failure; LVH = left ventricular hypertrophy; MI = myocardial infarction; PE = pulmonary embolism. Modified with permission from Mueller (21).
When is it safe to do a stress test?

It would usually be safe to perform a stress test in the following situations:

<table>
<thead>
<tr>
<th>Active Chest Pain</th>
<th>No Active Chest Pain* or Resolved Chest Pain*</th>
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<tbody>
<tr>
<td></td>
<td>*if clinically indicated</td>
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<tr>
<td>• Ruled-out troponins and clinically stable (<em>no aortic dissection, no acute PE, no severe aortic stenosis, etc.</em>)</td>
<td>• Indeterminate troponins</td>
</tr>
<tr>
<td></td>
<td>• Ruled-out troponins</td>
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Cardiology Consultation can be considered for:

- Any patient with a down trending troponin above the normal range of 19 pg/ml, prior to stress
- Unsure what type of stress test is most appropriate
- Active chest pain with unclear cardiovascular stability

Do not perform a stress test on a patient with active chest pain and a rising troponin.
How to Select Imaging:

Stress Test Decision Algorithm:
- **Consider ETT/Echo for:** can exercise/walk on treadmill, BMI < 40
- **Consider Nuc Med Perfusion for:** Prior MI, Obesity, Hx of AF or Arrhythmia
- **Consider Dobutamine Stress for:** Lung Disease, no Arrhythmia, inability to exercise

CTCA Algorithm:
- Renal function (GFR ≥ 30)
- Able to get HR ≤ 65 (w/ or w/o beta-blocker)
- Normal sinus rhythm
- No known CAD
- No IV contrast allergy
Take Home Points:

• Lower level of detection leads to;
  - Higher confidence and quicker rule-outs
  - More “false positives” for ACS evaluation that make clinical assessment critically important

• Acute MI is defined by labs and clinical changes, **not just labs alone**. Serial measurement of hs-trop T is important.

• Do not order hs-tropT routinely unless you have a compelling clinical reason (concern for ACS/NSTEMI) to do so

• Utilize stress testing or imaging in patients with **no active chest pain** and/or **non-rising troponins**

• Proper MiChart documentation of the cause of an elevated hs-trop T (myocardial injury due to ____ , NSTEMI, or type 2 myocardial infarction) is critical.
Back to Our Case Study:

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What do you do?

Given a very low suspicion for ACS (no history or ECG findings c/w ACS), he has myocardial injury due to tachyarrhythmia if otherwise clinically stable. Outpatient Cardiology follow up would be advisable.
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Proper documentation is critical. If this is called an NSTEMI instead of myocardial injury it will be recorded as a post op complication.....

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Please contact the following individuals with any questions or concerns:

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For patient concerns, consult Cardiology.