

# HS-TROPONIN: TWELVE MONTHS ON

by Dr Bevan Hokin

## INTRODUCTION

The Troponins are a group of proteins that form part of the regulatory mechanism for muscle contraction. In Cardiac muscle the Cardiac Troponins (cTn) comprise three distinct molecules that work in together to effect contractility - Troponin C (cTnC), Troponin T (cTnT), and Troponin I (cTnI) (Figure 1).

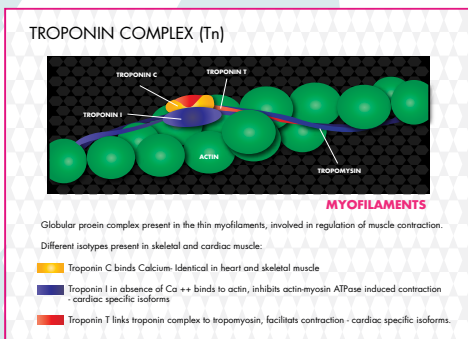


Figure 1

## UNIVERSAL DEFINITION OF MI<sup>1</sup>

- Detection of rise and/or fall of cardiac biomarkers (preferably cTn) with at least one value >99th percentile with better than 10% CV together with at least one of the following:
  - Ischaemia
  - ECG changes of new ischaemia
  - ECG Q-wave development
  - Imaging evidence of **new** loss of viable myocardium or new regional wall motion abnormality
- Sudden, unexpected cardiac death (no bloods taken)
- For Percutaneous Coronary Interventions:
  - x3 increase of the reference range for cTn (Reference range is 14 ng/L , thus > 52 ng/L)
  - For CABG- x5 increase of the reference range for cTn (> 70 ng/L)
- Pathological findings of AMI

Use of this definition<sup>1</sup> in the management of patients with UA and NSTEMI highlights several important points:

- The redefined criteria establish Troponin elevation as the predicate marker to classify ACS patients presenting with ischemic symptoms in ACS patients with Ischemic discomfort.
- An increased cTn value establishes the diagnosis of NSTEMI, where a normal cardiac troponin value establishes the diagnosis of unstable angina.
- Any amount of detectable cTn release is associated with risk of adverse clinical events.
- An abnormal troponin-T is now reported as >14 ng/L (0.014 µg/mL). Older 4th generation Troponin assays lower limit of detection was 0.03 µg/mL. Unless a laboratory is using the new 5th generation cTn assay (hs-cTn), compliance with the current guidelines is impossible.

## CLINICAL APPLICATION OF HS-CTN

- There is support for the more sensitive hs-cTn assay in spite of the trade-off – superior clinical sensitivity for diminished specificity for diagnosis of MI.<sup>2,3</sup>
- The increased number of cTn positive results does not affect the specificity of cTn for cardiac tissue, but highlights that myocardial injury may result from a variety of mechanisms.
- A rising or falling pattern of cTn values is helpful in discriminating acute cardiac injury from chronic causes.
- For the clinical diagnosis of MI it is essential to use both the clinical data and the elevated (changing) levels of cTn.

## LIMITATIONS OF THE HS-CTN ASSAY

- Increases of cTn are indicative of myocardial injury but do not identify the mechanism of injury. If an ischemic mechanism of injury is unlikely, other aetiologies of myocardial injury should be pursued.
- Increases in cTn are likely to reflect irreversible rather than reversible injury, although there is divided opinion on this issue.
- The degree of increase of cTn in ischaemia induced injury is related to the patient's prognosis.
- Table 1 overleaf lists examples of conditions where cTn may be elevated in the absence of MI<sup>4</sup>

## USING HS-TROPONIN RESULTS

A rising or falling pattern of cTn values is helpful in discriminating between acute cardiac injury and chronic causes. For the clinical diagnosis of MI it is essential to use both the clinical data and the elevated (changing) levels of cTn. Several sites across Australia, in commissioning the 5th generation hs-cTn assay, have established flowcharts to assist clinicians integrate Troponin results and clinical data. San Pathology has adopted a flowchart similar to and consistent with Royal North Shore Hospital and associated NSAHS hospitals. (Figure 2 overleaf).

## CONCLUSIONS

- Hs-cTn are reported in nanograms per litre (ng/L) (rather than µg/L so that units are whole numbers e.g. Cut off value for normal is 14 ng/L.
- New reference interval is 0-14 ng/L. The 99th percentile is 14 ng/L. Results 15 ng/L and above are marked as abnormal.
- There will be more patients identified with an abnormal hs-cTn due to the non-ACS elevations, but most would have been admitted (or referred for follow up) on the basis of clinical signs irrespective of the Troponin result.
  - o Patients with AMI history will have an elevated hs-cTn rise and/or fall pattern (depending on the timing of the test from the onset of symptoms) termed a "delta" or change in troponin level.
    - o Good AMI history and a hs-cTn > 100 ng/L = AMI
    - o Smaller infarcts will require a delta hs-cTn
      - ◆ Delta >30% (3-12 hours), at least one value >14 ng/L is supportive of AMI
      - ◆ Delta <30% indicates a more stable (chronic) condition.



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## ELEVATIONS OF CARDIAC TROPONIN IN THE ABSENCE OF OVERT ISCHAEMIC HEART DISEASE.<sup>4</sup>

Damage related to secondary myocardial ischaemia (MI Type 2)	Damage not related to myocardial ischaemia	Indeterminate or multifactorial causes
Tachy- or bradyarrhythmias	Cardiac contusion	Apical ballooning syndrome
Aortic dissection and severe aortic valve disease	Cardiac incisions with surgery	Severe pulmonary embolism or pulmonary hypertension
Hypo- or hypertension e.g. haemorrhagic shock, hypertensive emergency	Radiofrequency or cryoablation therapy	Peripartum cardiomyopathy
Acute and chronic heart failure without significant concomitant coronary artery disease	Rhabdomyolysis with cardiac involvement	Renal failure
Hypertrophic cardiomyopathy	Myocarditis	Severe acute neurological disease e.g. stroke, trauma
Coronary vasculitis e.g. systemic lupus, Kawasaki syndrome	Cardio toxic agents e.g. anthracyclines, herceptin, CO poisoning	Extreme exertion
Coronary endothelial dysfunction without significant CAD e.g. cocaine abuse	Severe burns affecting >30% of the body surface	Sepsis
-	-	Frequent defibrillator shocks (?? impact of repeated Taser shocks)

- Rule out time for AMI: If after 4-6 hours at presentation, or 6-8 hours after onset of pain, hs-cTn has not risen >14 ng/L.

- Kidney disease: hs-cTn will be elevated in ESRD but delta will be <30%.

- Hs-cTn findings >15 ng/L (but without a delta >30%) have significant prognostic value in a range of diseases including:

- o Stable coronary artery disease
- o Heart failure
- o Pulmonary embolism.

*San Pathology provides the hs-cTn test.*

### ACKNOWLEDGEMENT

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### REFERENCES

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3. Reclin T et al., NEJM 361, 2009
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Table 1

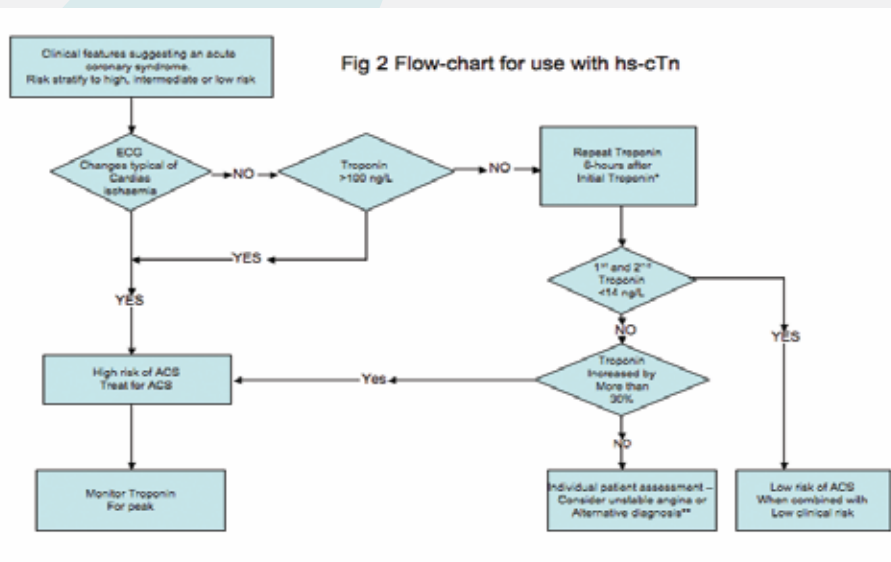


Figure 2