High-Sensitivity Cardiac Troponin (hs-cTn)

Frequently Asked Questions

What is cardiac troponin (cTn)?

Cardiac troponin is the preferred biomarker for diagnosis of acute myocardial infarction (AMI) on the basis of sensitivity and myocardial specificity.[1]

How is AMI diagnosed?

Patients presenting to the emergency department with chest pain are evaluated clinically and by electrocardiogram (ECG).[2] Patients with ST elevation upon ECG are immediately treated; those without ST elevation may be experiencing non-ST elevation myocardial infarction (NSTEMI), unstable angina, another cardiac or noncardiac cause, or are normal. Repeat testing for a cardiac marker such as cTn will differentiate NSTEMI patients from those with other causes of chest pain. Depending on the clinical assessment, NSTEMI patients are among those who will demonstrate a significant serial change in cTn.[2]

What is the definition of a high-sensitivity cardiac troponin (hs-cTn) assay?

The International Federation of Clinical Chemistry (IFCC) task force on cardiac biomarkers defines hs-cTn assays as assays that reliably detect cTn below the 99th percentile and above the limit of detection (LoD) in at least 50% of healthy subjects.[2-4]

Total imprecision (coefficient of variation [CV]), should be <10% at the 99th percentile of healthy subjects.[2-4]

Why is precision at the low end of the hs-cTn assay range important?

Precision at the low end is important to minimize analytic variation that could confound assessment of a clinically significant change. This is important for standard 0 hour (h) and 3 h testing algorithms a well as accelerated 0 h and 1 h to 2 h strategies. Shorter protocols will have smaller serial change values that may be lower than analytical variation.[4]

What are the most recent European Society of Cardiology (ESC) guidelines for hs-cTn testing in those with non-ST elevation acute coronary syndrome (NSTE-ACS)?

Current 2015 ESC Guidelines describe several options for hs-cTn testing:

1. 0 h and 3 h or longer testing strategy uses the 99th percentile cutoff. Patients presenting are assessed for chest pain if <6 h or >6 h. If chest pain is >6 h and the first cTn result is <99th percentile, rule out. If chest pain is <6 h, repeat cTn test after 3 h. If result shows a significant serial change, further investigate, and/or rule in; if result shows no change, rule out.[2,3,5,6]
2. Shorter 0 h and 1 h,[7-11] and 0 h and 2 h,[7,12,13] rule-out and rule-in algorithms.
   a. Rule-out is based on either <LoD (limit of detection), or low cutoff value combined with low 1 h or 2 h serial change value, respectively; otherwise, patients are further investigated.[7,8,10-13] The LoD as sole cutoff has been rejected.[14-18]
   b. Rule-in is based on a high cutoff value (3- to 10-fold greater than the 99th percentile) at admission and/or high 1 h or 2 h serial change, respectively.[7,8,10-13] The 99th percentile is not used in this algorithm.
3. 99th percentile combined with a 2 h serial change and the Thrombolysis in Myocardial Infarction (TIMI) risk score.[19-21] This option is a compromise of Option 1 using TIMI instead of GRACE score and a 2 h serial change instead of 3 h (used in Australia and New Zealand). The GRACE score is generally preferred.
4. A dual-marker strategy combines measurement of cTn and the stress marker copeptin.[22-28]

A single-value rule-out is not currently recommended.[2] In all these algorithms, ECG is part of the diagnosis. Cutoff levels and delta change values are assay-specific and should be applied for all the algorithms.

Is there value for hs-cTn outside of an acute setting?

A growing body of evidence suggests that low levels of cTn are prognostic.[29-35] This may have utility in aiding assessment and management of patients at risk of an adverse cardiac event.[29-35] Cardiac troponin detected with hs-cTn assays may find utility in other non-acute coronary syndrome scenarios.[36-40]

Are there other clinical conditions that may result in elevated levels of cTn ?

Other causes of cardiac necrosis include myocarditis, sepsis-related damage, renal failure, arrhythmias, cardiotoxicity of anticancer treatments, pulmonary embolism, chronic renal disease, and congestive heart failure. Patients may show elevated (and even changing) levels of cTn. Notably, cTn is a marker of cardiac damage and not specific for AMI.[2,3,6,41-44]

Will all patients be triaged within standard 0 h and 3 h or 0 h and 1 h to 2 h protocols using hs-cTn?

Not all patients will rule in or rule out in a 0 h and 1 h testing algorithm. Patients with hs-cTn levels above the 99th percentile at presentation may require repeat testing to detect a significant serial change—generally 3 h or longer after presentation. Some patients for whom suspicion remains high for AMI are observed longer.[2] Alternatively, the 1 h to 2 h rule-in/rule-out algorithms triage about 75% of patients using specific cutoff values and/or significant serial change values. Only 25% remain in the observation zone needing further investigation such as imaging (e.g., CT for 20%).[2]

NSTEMI patients presenting early (within less than 2 h of chest pain onset) or late after chest pain onset may not demonstrate a significant serial change between 0 h and 1 h to 2 h after presentation. Those presenting early require further testing. Imaging, serial ECGs, and additional hs-cTn testing can aid in triage of these patients, along with signs and symptoms.[2]

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