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Review Article

# Time to shift from contemporary to high-sensitivity cardiac troponin in diagnosis of acute coronary syndromes

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ABSTRACT

Early rule-in and rule-out of non-ST-segment elevation myocardial infarction (NSTEMI) is a challenge. In patients with inconclusive findings on ECG, cardiac biomarkers play a crucial role in the diagnosis. The introduction of the new high-sensitive cardiac troponin test (hs-TnI assay) has changed the landscape of NSTEMI diagnosis.

The new hs-TnI assay can detect troponin values at a lower level compared with a contemporary cardiac troponin (cTn) assay. The hs-cTnI assay has a coefficient of variation of ≤10%, well below the 99th percentile value. It reduces the time to diagnose acute myocardial infarction from 6 h to 3 h. A recent study has demonstrated that hs-cTnI can further reduce the time to 1 h in 70% of all patients with chest pain.

The European Society of Cardiology 2015 guidelines recommend including a second sample of hs-cTnI within 3 h of presentation This increases the sensitivity of the hs-TnI assay from 82.3% (at admission) to 98.2% and negative predictive value from 94.7% (at admission) to 99.4%. Combining the 99th percentile at admission with serial changes

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in troponin increases the positive predictive value to rule in acute coronary syndrome from 75.1% at admission to 95.8% after 3 h.

The 2015 ESC Guidelines recommend the use of a rapid rule out protocol (0 h and 1 h) when hs-cTnI with a validated 0 to1 h algorithm is available.

Training and displaying the clinical algorithm depicting the role of hs-TnI assay in acute cardiac care units and in EDs are an efficient way to deliver the new standard of care to patients. Compared with contemporary troponin assays, the hs-cTn assay accelerates the diagnostic pathway to 0–1 h, thus reducing the time for diagnosis of NSTEMI and hence, its management.



## 1. Challenges in diagnosing NSTEMI

Acute coronary syndrome (ACS), comprising ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina, is the most common cause of mortality in patients with CAD.[1] Studies from India and China have reported that STEMI remains more frequent than NSTEMI.[2–4] According to the CREATE registry, the incidence of STEMI (60.6%) was greater than that of NSTEMI (39.4%) in India, which is in contrast to data from the developed countries.[5] A recent study by Sharma et al.[6] also reported that the incidence of STEMI (63.7%) was higher than that of NSTEMI (11.3%). This study, conducted in ACS patients of south Indian population, noted that ACS occurred 10 years earlier among Indians compared with western population. The discrepancies in the incidence of STEMI and NSTEMI can be partly attributed to factors such as more subtle or atypical symptoms of NSTEMI in older patients and in women and non-availability of more sensitive cardiac biomarkers, thereby reduced the number of NSTEMI cases diagnosed.[7] In this background, cardiac biomarkers have emerged as integral components in the diagnosis of NSTEMI.

## 2. Implications of early diagnosis of NSTEMI

Despite advances in therapeutic strategies, the rate of acute myocardial infarction (AMI) and consequent mortality remain high in patients with ACS. Therefore, timely diagnosis, especially early ruling in or ruling out of MI is of utmost importance.[7] Early rule-in of AMI prevents the mistaken discharge of patients with AMI with normal findings on initial ECG and also helps in early initiation of effective evidence-based therapy.[8,9] An early rule-out of AMI prevents inadvertent admission of patients without ACS and facilitates early discharge of patients and thereby decreases the unwarranted healthcare burden.[10] Moreover, a delay in rule-in of AMI may increase the risk of complications and mortality, particularly in patients with pre-existing CAD. Similarly, a delay in rule-out of AMI may contribute to prolonged assessments, unnecessary investigations, increased patient anxiety, as well as overcrowding in the emergency department.[11]

## 3. Role of cardiac biomarkers in patients with nondiagnostic ECGs

Cardiac biomarkers are crucial to establish the diagnosis of ACS, especially in patients with nondiagnostic findings on ECG.[12] Cardiac biomarkers used include creatinine kinase, myoglobin, cardiac troponin (cTn), brain natriuretic peptide, lactate dehydrogenase, aspartate aminotransferases, and heart fatty acid binding protein.[13] Cardiac troponin: Cardiac troponins T and I (cTnT and cTnI) are the most sensitive and cardiac specific biomarkers currently available to diagnose non-STACS,[10,11] owing to the tissue-specific expression of cTnT and cTnI in the myocardium.[14] However, in patients with chronic renal failure, cTnI has greater specificity for myocardial injury than cTnT.[15] A diagnosis of AMI is based on the detection of a rise and/or fall of cTn along with the presence of characteristic symptoms, and/or ECG or imaging evidence of acute myocardial ischemia.[13,16] The cut-off value of cTn to diagnose MI is defined as a concentration exceeding the 99th percentile of a normal reference population (i.e. upper reference limit [URL]) using an assay with an imprecision (coefficient of variation, CV) ≤10% at the URL.[16] However, the contemporary cTn assays cannot measure cTn levels at low concentrations corresponding to the 99th percentile value of a normal reference population.[17] Thus, they lack the precision criteria to diagnose AMI. Consequently, the high-sensitivity cardiac troponin (hs-cTn) assays were developed to meet the requirements of analytical precision and overcome the shortcomings associated with contemporary cTn assays.[18]

## 4. Entry of high-sensitive cardiac troponin has changed the landscape of NSTEMI

According to the International Federation of Clinical Chemistry (IFCC) Task Force Recommendation on Analytical Characteristics, an assay is considered high sensitive if the total imprecision (i.e. CV) at the 99th percentile value is ≤10%, and measurable concentrations below the 99th percentile can be attained at a concentration value above the assay's limit of detection (LOD) in at least 50% (and ideally >95%) of healthy individuals.[19] The hs-cTn assays are capable of measuring cTn in single digit ranges of nanograms per liter; some research

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