References

1. Morrow DA, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical characteristics and utilization of biochemical markers in acute coronary syndromes. Clin Chem. 2007;53:552-74.
2. Bodor GS, et al. Development of monoclonal antibodies for an assay of cardiac troponin-I and preliminary results in suspected cases of myocardial infarction. Clin Chem. 1992;38:2203-14.
3. Cummins B, et al. Cardiac-specific troponin-I radioimmunoassay in the diagnosis of acute myocardial infarction. Am Heart J. 1987;113:1333-44.
4. Cullen L, et al. Performance of risk stratification for acute coronary syndrome with two-hour sensitive troponin assay results. Heart Lung Circ. 2014;23:428-34.
5. Druey S, et al. Early rule-out and rule-in of myocardial infarction using sensitive cardiac Troponin I. Int J Cardiol. 2015;195:163-70.
6. Reichlin T, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. N Engl J Med.
7. Amsterdam EA, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:e344-426.
8. Anderson JL, et al. 2012 ACCF/AHA focused update incorporated into the ACCF/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61:e179-347.
9. Roffi M, et al./Task Force. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2015;37:267-315.
10. Hamm CW, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2011;32:2999-3054.
11. Thygesen K, et al. Third universal definition of myocardial infarction. Eur Heart J. 2012;33:2551-67.
12. Thygesen K, et al. Universal definition of myocardial infarction. Eur Heart J. 2007;28:2525-38.
13. Casals G, et al. Evaluation of a new ultrasensitive assay for cardiac troponin I. Clin Biochem. 2007;40:1406-13.
14. Siemens ADVIA Centaur® TnI Ultra Assay (directional insert 10629901_EN Rev. L, 2014-08. Siemens Healthcare Diagnostics Inc, Tarrytown, NY, USA.
15. Apple FS. A new season for cardiac troponin assays: it's time to keep a scorecard. Clin Chem. 2009;55:1303-6.
16. Apple FS, et al. IFCC educational materials on selected analytical and clinical applications of high sensitivity cardiac troponin assays. Clin Biochem. 2015;48:201-3.
17. Keller T, et al. Sensitive troponin I assay in early diagnosis of acute myocardial infarction. N Engl J Med. 2009;361:868-77.
18. Melanson SE, et al. Earlier detection of myocardial injury in a preliminary evaluation using a new troponin I assay with improved sensitivity. Am J Clin Pathol. 2007;128:282-6.
19. Wu AH, et al. Short- and long-term biological variation in cardiac troponin I measured with a high-sensitivity assay: implications for clinical practice. Clin Chem. 2009;55:52-8.
20. Anderson JL, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;123:e426-579.
21. Jaffe AS, et al. Biomarkers in acute cardiac disease: the present and the future. J Am Coll Cardiol. 2006;48:1-11.
22. Thygesen K, et al. How to use high-sensitivity cardiac troponins in acute cardiac care. Eur Heart J. 2012;33:2252-7.
23. Wildi K, et al. How acute changes in cardiac troponin concentrations help to handle the challenges posed by troponin elevations in non-ACS-patients. Clin Biochem.
24. Wu AH, et al. Growing pains with the use of high-sensitivity cardiac troponin assays. J Am Coll Cardiol. 2013;62:1250-1.
25. Druey S, et al. Early rule-out and rule-in of myocardial infarction with comparision of a 1-hour, 2-hour and 3-hour algorithm using sensitive cardiac Troponin Ultra. Unpublished manuscript with 3 hour data (in addition to the 1 and 2 hour data presented in Druey et al. Int J Cardiol 2015;195:163-70. 2014).

Global Business Area
Siemens Healthcare
Laboratory Diagnostics
511 Benedict Avenue
Tarrytown, NY 10591-5005
USA
Telephone: +1 914-631-8000
siemens.com/healthcare

Siemens Healthcare Headquarters
Siemens Healthcare GmbH
Henkestrasse 127
91052 Erlangen
Germany
Telephone: +49 9131 84-0
siemens.com/healthcare

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The ADVIA Centaur Cardiac Troponin I Assay User Guide

Achieve Accurate Diagnosis of AMI

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Using the ADVIA Centaur Cardiac Troponin I Assay for Accurate Early Diagnosis of AMI

On the basis of sensitivity and myocardial specificity, cardiac troponin (cTn) is the preferred biomarker for diagnosis of acute myocardial infarction (AMI).[1] Conventional cardiac troponin assays require 4–8 hours (h) for levels to become abnormal, peaking at 12–16 h and declining over the subsequent 5–9 days.[2,3] Newer, more sensitive cardiac troponin assays allow earlier detection, supporting more rapid triage of chest-pain patients. Use of a sensitive cardiac troponin I assay facilitates expeditious detection and assessment of a change—important in the differentiation of an AMI related to myocardial ischemia from other causes of myocardial necrosis.[4-6]

3-hour algorithm

Diagnosis of Acute Myocardial Infarction[7-12]

Acute myocardial infarction (AMI) is diagnosed when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Necrosis has been defined by a significant rise or fall (serial change) of cardiac troponin, with at least one value above the 99th percentile upper limit of normal (ULN). Diagnosis also requires at least one other well-defined hallmark of AMI (evidence of ischemia, ECG and/or imaging abnormalities).

Cardiac troponin assays should strive for total imprecision of ≤10% coefficient of variation (CV) at the 99th percentile ULN of the reference population.

On the basis of imprecision and other performance characteristics, the ADVIA Centaur® TnI-Ultra™ assay is a contemporary-sensitive assay[13] which is guideline acceptable.[14-16]

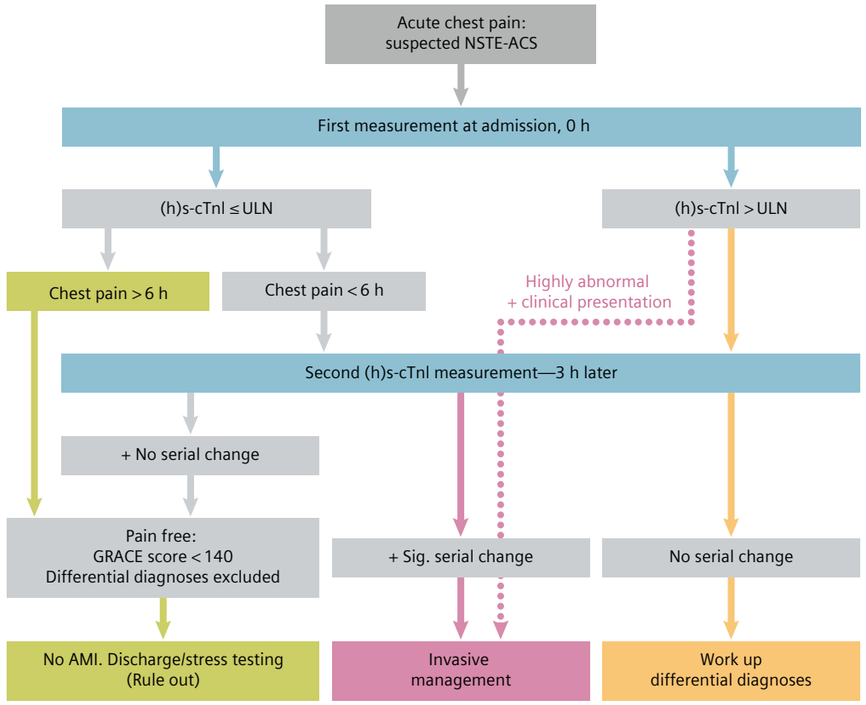
Clinical introduction of the sensitive cardiac troponin assays significantly increases the number of chest pain patients presenting with values exceeding the 99th percentile ULN as a result of causes other than AMI (see table).[6,17-19]

In the appropriate clinical setting, serial testing can differentiate between increased troponin levels due to AMI and increased levels due to non-ischemic causes. Rising or falling patterns indicate AMI;[7,9-12,20] whereas, unchanged levels are found in chronic diseases.

However, changes in cardiac troponin concentrations are also observed in patients with atrial fibrillation non-coronary artery disease patients; and, for other acute cardiac situations such as tachyarrythmias, myocarditis, hypertensive crisis, and Takotsubo cardiomyopathy.[21-24]

It is important to remember that interpretation of cardiac troponin values must always accompany clinical assessment, including evidence of ischemia by clinical symptoms, ECG, and imaging.

Example algorithm for the diagnosis of AMI and risk stratification of patients with suspected NSTE-ACS using sensitive (s) and high-sensitivity (hs) assays.[9,10,17]



ADVIA Centaur TnI-Ultra Assay Decision Cutoffs:

ULN = upper limit of normal
= 99th percentile of a healthy population
= 40 ng/L (40 pg/mL, 0.040 µg/L)[14]

Example significant serial change
3 h = >16 ng/L (16 pg/mL, 0.016 µg/L)[5,25*]

The significant serial change must be determined for each assay, and may be determined independently by each institution.[11]

*Data derived based on adjudicated samples (n=700) from the APACE (Advantageous Predictors of Acute Coronary Syndromes Evaluation) study, a prospective international multi-center study, University Hospital, Basel, Switzerland.

Elevations of Cardiac Troponin Values Due to Myocardial Injury[11,23]

Injury Related to Primary Myocardial Ischemia[11,23]

- Plaque rupture
- Intraluminal coronary artery thrombus formation

Injury Related to Supply/ Demand Imbalance of Myocardial Ischemia

- Tachy-/bradyarrhythmias
- Aortic dissection or severe aortic valve disease
- Hypertrophic cardiomyopathy
- Cardiogenic, hypovolemic, or septic shock
- Severe respiratory failure
- Severe anemia
- Hypertension, with or without LVH
- Coronary spasm
- Coronary embolism or vasculitis
- Coronary endothelial dysfunction without significant CAD
- Injury not related to myocardial ischemia
- Cardiac contusion, surgery, ablation, pacing, or defibrillator shocks
- Rhabdomyolysis with cardiac involvement
- Myocarditis
- Cardiotoxic agents

Multifactorial or Indeterminate Myocardial Injury

- Congestive heart failure: acute and chronic
- Stress cardiomyopathy
- Severe pulmonary embolism or pulmonary hypertension
- Sepsis and critical illness
- Renal failure
- Acute neurological disease, including stroke, or subarachnoid hemorrhage
- Infiltrative diseases (amyloidosis, hemochromatosis, sarcoidosis, and scleroderma)
- Strenuous exercise

Abbreviations: LVH: left ventricular hypertrophy; CAD: Coronary artery disease; GRACE score: Global Registry of Acute Coronary Events Risk Score; NSTE-ACS: Non-ST-elevation acute coronary syndrome; NSTEMI: non-ST-elevation myocardial infarction; ECG: electrocardiograph.