Elevations of Cardiac Troponin Values Due to Myocardial Injury[4]

Myocardial injury related to acute myocardial ischemia

Atherosclerotic plaque disruption with thrombosis.

Myocardial injury related to acute myocardial ischemia because of oxygen supply/demand imbalance

Reduced myocardial perfusion, e.g.

- Coronary artery spasm, microvascular dysfunction
- Coronary embolism
- Coronary artery dissection
- Sustained bradyarrthythmia
- Hypotension or shock
- Respiratory failure
- Severe anemia

Increased myocardial oxygen demand, e.g.

- Sustained tachyarrhythmia
- Severe hypertension with or without left ventricular hypertrophy

Other causes of myocardial injury

Cardiac conditions, e.g.

- Heart failure
- Myocarditis
- Cardiomyopathy (any type)
- Takotsubo syndrome
- Coronary revascularization procedure
- Cardiac procedure other than revascularization
- Catheter ablation
- Defibrillator shocks
- Cardiac contusion

Systemic conditions, e.g.

- Sepsis, infectious disease
- Chronic kidney disease
- Stroke, subarachnoid hemorrhage
- Pulmonary embolism, pulmonary hypertension
- Infiltrative diseases, e.g. amyloidosis, sarcoidosis
- Chemotherapeutic agents
- Critically ill patients
- Strenuous exercise

References:

1. Roffi M, et al. Eur Heart J. 2016;37:267-315.
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3. Wildi K, et al. Am Heart J. 2016;181:16-25.
4. Thygesen K, et al. Eur Heart J. 2018; 00:1-33.
5. Amsterdam E A, et al. Circulation. 2014;130:e344-426.

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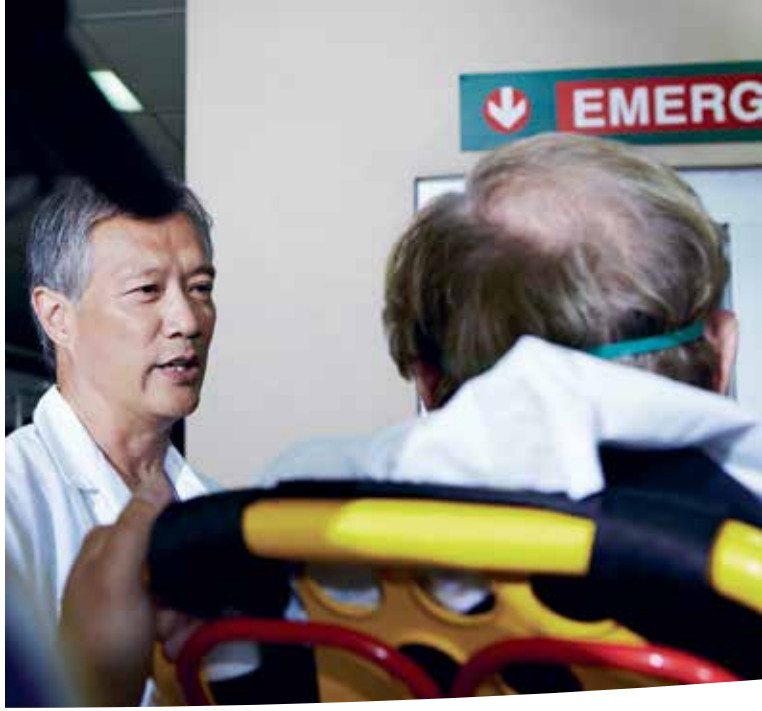

ADVIA Centaur High-Sensitivity Troponin I (TNIH) Assay

0/3-hour Algorithm for Diagnosis of Suspected Acute Myocardial Infarction[1,2,4,5]

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Acute myocardial infarction (AMI) is diagnosed when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia. Necrosis is defined by a significant rise or fall (serial change) of cardiac troponin measured between presentation at 0 hour and 3 hours later, with at least one value above the 99th percentile.[1-4] The 99th percentile is also known as the upper limit of normal (ULN) or the upper reference limit (URL). The ADVIA Centaur® High-Sensitivity Troponin I (TNIH) assay demonstrates analytical imprecision much below 10% CV (coefficient of variation) at the 99th percentile ULN of the reference population.

ADVIA Centaur TNIH Assay 99th Percentile

A reference interval study was conducted using the ADVIA Centaur TNIH assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) Guideline Protocol EP28-A3c. Serum and lithium heparin plasma specimens were collected in the U.S. from 2010 apparently healthy individuals ranging from 22 to 91 years of age.

Inclusion criteria

Each apparently healthy individual who consented to participate in the study was adult, completed a health status questionnaire, and was considered by self-assessment as generally healthy with no symptoms of a heart attack (chest or arm pain).

Exclusion criteria

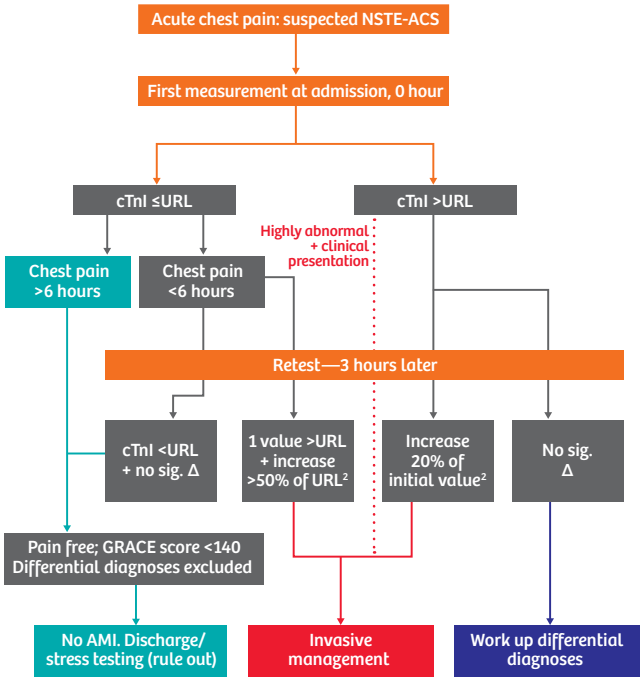
- History of vascular or cardiovascular disease (e.g., atherosclerosis, coronary artery disease, coronary artery bypass surgery, angioplasty or myocardial infarction, congestive heart failure, deep vein thrombosis, pulmonary embolism, etc.).
- History of hypertension.
- Taking cardioactive drugs (aspirin, beta-blockers, diuretics, angiotensin-converting enzyme inhibitors or angiotensin-2 blockers, alpha-blockers, statins, calcium- or potassium-channel blockers, antidysrhythmic drugs, digoxin, inotropes, COUMADIN). The following exceptions did not exclude a subject as long as all other criteria were met:
  - Aspirin (up to 325 mg/day) taken in prophylaxis
  - Statins taken in prophylaxis or for dyslipidemia without a confirmed diagnosis of atherosclerosis
  - History of diabetes mellitus, chronic renal disease, and/or rheumatoid arthritis

Each specimen was frozen, thawed, and assayed once. The 99th percentile values were determined using the nonparametric statistical method described in CLSI Document C28-A3c. Sample type, gender, and age had no statistically significant effect on the 99th percentile.

Table 1. The 99th percentile values for males, females, and combined sex.

Sample Type	Sex	n	99th Percentile (ng/L or pg/mL)	90% CI* (ng/L or pg/mL)
Lithium heparin	Female	1012	37.0	30.2–72.6
	Male	998	57.3	38.6–90.1
	Combined	**2010**	**47.3**	**36.4–64.3**

*CI: confidence interval.



cTnI: cardiac troponin I
URL: upper reference limit (99th percentile)
AMI: acute myocardial infarction

Figure 1. 0/3-hour algorithm for diagnosis of suspected AMI.[1,2,4,5]

0/3-hour Algorithm to Interpret Cardiac Troponin I Values[1-5]

The upper reference limit (URL) referenced in the algorithm refers to the 99th percentile concentration of the cTnI assay (Figure 1).

Chest pain more than 6 hours with a first cardiac troponin I measurement below the URL indicates that myocardial necrosis can be ruled out.

Chest pain less than 6 hours

- **A first measurement below the URL** in patients with suspected AMI requires a second measurement 3 hours later. It may be repeated 6 hours after admission in patients whose 3-hour values are unchanged but for whom AMI is still highly suspected.
  - If the second cardiac troponin I value is above the URL and the increase within 3 hours is above 50% of the URL with evidence of ischemia, AMI diagnosis is highly likely.
  - If the second cardiac troponin I value is unchanged, the patient can be discharged.
- **A first measurement above the URL** in patients suspected of chronic illness requires a second measurement 3 hours later to help differentiate acute from chronic necrosis. The serial change value in the case of chronic necrosis will be below 20% of the initial value at admission.

Cardiac troponin is a marker of myocardial necrosis and not a specific marker of AMI. The latter may only be diagnosed with a rise and/or fall of cardiac troponin together with characteristic symptoms, and/or electrocardiogram changes indicative of ischemia and/or imaging evidence of acute myocardial ischemia. Stable or inconsistently variable cardiac troponin values without significant dynamic changes are likely markers of chronic structural heart disease.