

Elevations of Cardiac Troponin Values Due to Myocardial Injury¹⁻⁴

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 bradyarrhythmia
- 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

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Atellica IM

High-Sensitivity Troponin I (TnIH) Assay

0/3-Hour Algorithm for Diagnosis of Suspected Acute Myocardial Infarction

[siemens-healthineers.com/troponin](https://www.siemens-healthineers.com/troponin)

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 (cTn) measured between presentation at 0 hour (h) and 3h 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 Atellica® IM High-Sensitivity Troponin I (TnI) Assay demonstrates analytical imprecision much below 10% CV (coefficient of variation) at the 99th percentile ULN of the reference population.

Atellica IM TnI Assay 99th Percentile

A reference interval study was conducted using the Atellica IM TnI 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 2007 apparently healthy individuals ranging from 22 to 91 years of age (Table 1).

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

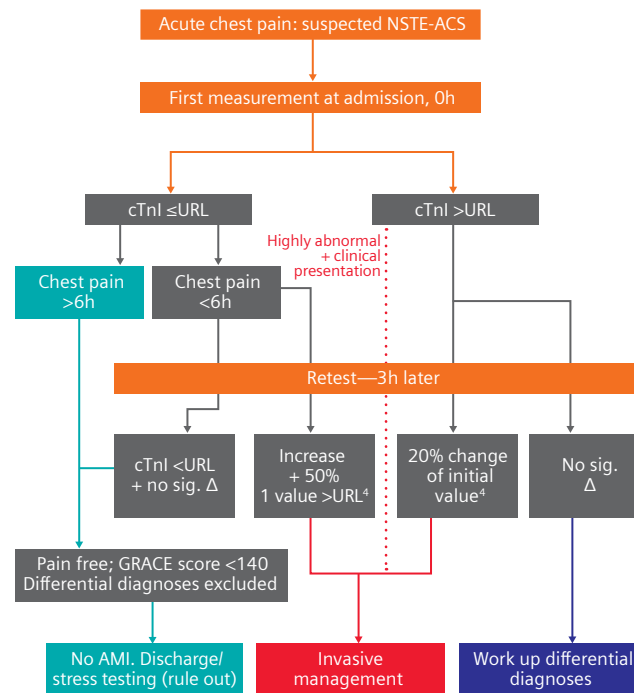
- History of vascular or cardiovascular disease (e.g., atherosclerosis, coronary artery disease, coronary artery bypass surgery, angioplasty or myocardial infarction, congestive heart failure, deep vein thrombosis, pulmonary embolism, etc.).
- History of hypertension.
- Taking cardioactive drugs (aspirin, 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. There was no difference in results between lithium heparin plasma and serum samples ($y = 1.01x + 5.433$, $n=8588$, $r=0.998$).

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 plasma	Female	1007	34.0	27–66
	Male	1000	53.5	39–80
	Combined	2007	45.0	33–64

*CI: confidence interval.



cTnI: cardiac troponin I
 URL: upper reference limit (99th percentile)
 AMI: acute myocardial infarction
 No sig Δ: no significant delta

Figure 1. 0/3h algorithm considerations for diagnosis of suspected AMI.¹⁻⁵

Considerations for Example 0/3h Interpretation of Atellica IM TnI Values

The upper reference limit referenced in the algorithm refers to the 99th percentile concentration of the cTnI assay (Figure 1). Significantly lower values are observed among women compared to men, and therefore sex-specific 99th percentile URLs are recommended for high-sensitivity cardiac troponin assays.⁴

Chest pain more than 6h with a first cTnI measurement below the URL indicates that myocardial necrosis can likely be ruled out.

Chest pain less than 6h

- **A first measurement below the URL** in patients with suspected AMI requires a second measurement 3h later. It may be repeated 6h after admission in patients whose 3h values are unchanged but for whom AMI is still highly suspected.
 - If the second cTnI value is above the URL and the increase within 3h is above 50% of the initial value with evidence of ischemia, AMI diagnosis is highly likely.
 - Troponin results that remain below the 99th percentile URL most likely suggest that the patient does not have AMI and can be discharged, with follow up as appropriate.

- **A first measurement above the URL** in patients suspected of chronic illness requires a second measurement 3h 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. In the Fourth Universal Definition Myocardial Infarction consensus document, experts recommended use of a relative change of greater than 20% rise or fall when the initial concentration was >99th percentile URL.⁶

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 cTn together with characteristic symptoms, and/or electrocardiogram changes indicative of ischemia and/or imaging evidence of acute myocardial ischemia. Stable or inconsistently variable cTn values without significant dynamic changes are likely markers of chronic structural heart disease.