Elevations of Cardiac Troponin Values Due to Myocardial Injury

Related to primary myocardial ischemia
• Plaque rupture
• Intraluminal coronary artery thrombus formation

Injury related to supply/demand imbalance of myocardial ischemia
• Tachy-brady arrhythmias
• 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 (HERCEPTIN, anthracyclines)

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

References:

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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. 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.23. 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, antiarrhythmic 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>
<thead>
<tr>
<th>Sample Type</th>
<th>Sex</th>
<th>n</th>
<th>99th percentile (ng/L or pg/mL)</th>
<th>90% CI* (ng/L or pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium heparin</td>
<td>Female</td>
<td>1012</td>
<td>37.0</td>
<td>30.2–72.6</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>998</td>
<td>57.3</td>
<td>38.6–90.1</td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td>2010</td>
<td>47.3</td>
<td>36.4–64.3</td>
</tr>
</tbody>
</table>

*CI: confidence interval.

0–3 Hour Algorithm to Interpret ADVIA Centaur TNIH Assay Values

The algorithm uses the 99th percentile concentration of the healthy individual as the ADVIA Centaur TNIH assay’s upper reference limit (URL).

**Chest pain more 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 ischaemia and/or imaging evidence of acute myocardial ischaemia. Stable or inconsistently variable cardiac troponin values without significant dynamic changes are likely markers of chronic structural heart disease.