



Danbury Hospital  
Department of Pathology & Laboratory Medicine  
*Technically Speaking*

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## **New Assay for Cardiac Troponin I**

Effective November 29, 2007, the Laboratory is introducing a new test for **cardiac troponin I (cTnI)**. The Siemens TnI Ultra assay will be performed on our new Centaur XP immunoassay systems. This test will replace the current cardiac troponin T (cTnT) test to assess patients with suspected acute coronary syndrome (ACS).

### **What is the difference between cardiac troponin I and cardiac troponin T?**

cTnI and cTnT are subunits of the cardiac troponin complex with different amino acid sequences and molecular weights (24,000 for cTnI, 37,000 for cTnT) and are encoded by unique, heart-specific genes. Following myocardial injury, both cTnI and cTnT are released from injured myocytes into the circulation in free and complexed forms - the troponin TIC ternary complex, troponin IC binary complex, free troponin I and free troponin T. Assays for cTnI and cTnT measure both the free and complexed forms of these subunits in plasma or serum.

### **Release kinetics**

The early release kinetics of both cTnI and cTnT after myocardial injury are similar to those of CK-MB. Increases above the upper reference limit can be observed as early as 3-6 hours after the onset of symptoms; however, the clinical sensitivity in this time frame is only 50-65%, making cardiac troponins insufficient for effective early diagnosis of AMI. For most patients, it is recommended that blood samples be obtained at time of hospital presentation and at 6-9 hours after presentation in order to provide adequate sensitivity for detecting AMI. For patients in whom both of these early samples are negative and for whom there is an intermediate or high clinical index of suspicion, a third sample should be obtained at 12-24 hours. As opposed to CK-MB, which returns to normal levels by 48-72 hours, cTnI and cTnT remain elevated considerably longer (4-7 days for cTnI and 10-14 days for cTnT), giving the cardiac troponins a distinct advantage over CK-MB in detecting AMI in late-presenting patients.

### **What is the upper reference limit (upper limit of normal) for the cTnI assay?**

The American College of Cardiology and European Society of Cardiology consensus guidelines recommend using the 99<sup>th</sup> percentile of cardiac troponin values measured in a healthy reference population as the clinical decision limit. Most healthy individuals have undetectable cTnI (<0.01 ng/mL) with the Centaur TnI Ultra assay with a 99<sup>th</sup> percentile value of 0.04 ng/mL. Therefore, any cTnI value >0.04 ng/mL is considered to be an elevated level indicative of myocardial injury; however, the mechanism may or may not be due to ischemic heart disease (see below).

### **Are the numerical results for cTnI different from cTnT results?**

Yes. As stated above, cTnI and cTnT are unique molecular species with different molecular weights and clearance rates; therefore, the circulating concentrations of these species following myocardial injury are expected to be different. Although cTnI and cTnT values are of similar magnitude at low levels and the recommended cTnI cutoff of 0.04 ng/mL is very close to the 0.03 ng/mL cutoff we have used for cTnT, cTnI and cTnT values diverge rapidly as they increase, with cTnI values becoming appreciably higher than cTnT values on the same patient sample. It is not possible to predict the cTnI level from the cTnT level or vice-versa in an individual patient.

### **What are the clinical consequences of the new cTnI assay?**

Since the TnI Ultra assay is a more sensitive “3<sup>rd</sup> generation” assay capable of measuring low levels of cTnI with high precision, a consequence of this improved low-end detection is that lower level elevations can be detected more reliably. Clinically, this translates into detection of smaller infarcts and earlier detection of myocardial injury in patients presenting soon after onset of symptoms. It also means detection of mild cTnI elevations that may or may not have obvious clinical significance, although mild troponin elevations and even measurable levels of troponin below the 99%ile cutoff have been found in several studies to be prognostic for poor outcomes (see references).

### **Important points to keep in mind when interpreting troponin results:**

- The new cardiac troponin I assay is more sensitive than the current troponin T assay and is capable of detecting elevations earlier after myocardial injury.
- As with cTnT, the tissue specificity of cTnI should not be confused with specificity for the mechanism of cardiac injury, i.e., an elevated cardiac troponin is not always due to ACS or ischemic coronary heart disease. Troponin elevations (both cTnI and cTnT) in the absence of overt ischemic heart disease have been documented in patients with conditions such as sepsis, hypovolemia, atrial fibrillation, coronary vasospasm, myocarditis, cardiac trauma (contusion, cardioversion) heart failure, pulmonary embolism, drug cardiotoxicity (adriamycin, 5-FU, herceptin), rhabdomyolysis with cardiac injury, and renal failure. Elevated troponin levels have been found to be highly prognostic for both short-term and long-term outcomes in many of these disorders.
- Serial levels of cTnI are frequently helpful in assessing patients with a mild troponin elevation on presentation and a low pre-test probability of MI. If serial levels do not change appreciably, acute MI is unlikely.
- Elevations of cTnI and cTnT in patients with chronic renal insufficiency but without ACS are well documented and have been found to have prognostic value, although the exact underlying mechanisms are unclear. cTnT is more frequently elevated than cTnI in these patients; this may be related to the relatively higher concentrations of unbound cTnT in the cytosol of the myocyte and its higher molecular weight.

### **When will the transition from cTnT to cTnI occur?**

Beginning on November 27, we will perform both cTnI and cTnT on all samples and report both results to provide continuity of patient care for patients being admitted and monitored during the transition and to enable clinicians to become accustomed to the new values. Beginning on November 29, we will perform only the cTnI assay.

### **Questions?**

Please contact Dr. Sal Sena at ext. 7622, pager 289-1885.

### **References**

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