MEDICAL CENTER OF CENTRAL GEORGIA
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CHEMISTRY

New Cardiac Troponin I (TpnI) Assay: The laboratory will implement a new TpnI assay on March 12, 2014. This is an improved assay from the same manufacturer which provides near identical results to the old TpnI assay. The assay improvement is primarily with low concentration (0.00 – 0.10 ng/mL) precision and accuracy. This improved performance permits adoption of the cardiac biomarker recommendation from the recently published Third Universal Definition of Myocardial Infarction (MI). This includes using the 99th percentile upper reference limit for healthy adults with no known diseases of the cardiovascular system or other serious acute or chronic diseases, as the normal range. The 99th percentile upper reference limit (URL) observed for our population is 0.049 ng/mL (manufacturer study claim is 0.03 ng/mL). **MCCG Normal Range is: 0 - 0.049 ng/mL** (old range 0 – 0.09).

Acute MI under the new definition requires only a single troponin biomarker value above the 99th percentile URL (> = 0.05) with TpnI exhibiting a rise and fall pattern, along with additional criteria of ischemia.

TpnI is specific for myocardial injury but not for MI. Lowering the threshold for TpnI increases the potential for positive results from non-MI conditions associated with cardiac biomarker increase. These include cardiac conditions such as angina, atrial fibrillation, cardiomyopathy, carditis, heart failure, severe coronary artery disease, tachycardia; or non-cardiac conditions such as renal failure or pulmonary embolism.

The Third Universal Definition of MI makes the following recommendation for cardiac biomarker criteria:

1. For spontaneous MI – cardiac TpnI rise, or fall, with at least one value above the 99th % URL.
2. After percutaneous coronary intervention (PCI) the threshold for a positive biomarker result is > 5 x the 99th percentile URL with a normal baseline. If the baseline is increased but stable or falling, a rise of > 20% from baseline for troponin is sufficient for a positive result.
3. After coronary artery bypass graft (CABG) the requirement is 10 x the 99th percentile URL with a normal baseline value and within 48 hours.

With a sensitive troponin I assay, clinical judgment is essential for separating true MI from myocardial injury, acute coronary syndrome and demand ischemia. A review of December 2013 & January 2014 EC patient laboratory TpnI data showed lowering the threshold from 0.10 to 0.05 resulted in an increase in the % of patients with a **"positive"** result from 20.7% to 27.3%. 10% of the additional "positive" patients had TpnI changes over time making them of greater concern.

Cardiac Biomarker Utilization: The expert consensus recommendation from the Third Universal Definition of MI is that Troponin is the preferred biomarker for ALL categories of MI. At MCCG the two markers, TpnI and CKMB, are ordered together as part of a "cardiac profile" about 90% of the time (~ 60,000 of each per year). TpnI and CK-MB are both markers of myocardial injury with similar release kinetics post injury. TpnI is expressed exclusively in the heart. CKMB has relative specificity for myocardial tissue, but is present in other muscle types in small concentration which may confound interpretation. **Therefore, the use of two markers does not routinely provide additional information over the use of TpnI alone.**

Laboratory recommendations are:

1. **TpnI** - Serial studies, routinely limit to 3 samples: baseline, at 1 – 3 hours and at 6 – 9 hours. Occasionally an additional sample at 12 – 24 hours is needed. (Note Medicare restricts reimbursement to 3 samples in 24 hours.)
2. **CKMB** – Use only when a rare interference is present in the patient blood that produces a method specific false-positive TpnI result. In this situation typically the TpnI results are extremely elevated (>0.15) and remain consistent over the serial draws. CKMB will not demonstrate the same interference as TpnI and should be negative in the absence of MI or other CKMB releasing process. CKMB can be added to TpnI specimens already in the lab.
3. **PCI (type 4a) and CABG (type 5) related MI** – While controversial there has been a preference for use of CKMB (less sensitive marker) in these settings based on the more consistent correlation with adverse outcomes. The raised thresholds for TpnI cut-off in the Third Universal Definition of MI should reduce these differences and allow the use of the more specific TpnI marker.

References:

1. Thygesen, K. et.al: Third Universal Definition of Myocardial Infarction. *Circulation*. 2012; 126:2020-2035.
2. Tehrani, D., Seto, A.: Third universal definition of myocardial infarction: Update, caveats, differential diagnosis. CCJM.2013; 80:777-785.

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Test Information Guide – New Tests

Troponin I

Specimen: Serum, Heparin (Na or Li) gel tube. Use the same sample type for each sample of a serial TpnI assessment on a patient.
Minimum Volume: 0.5 mL serum or plasma
Alternate test names: TpnI, Cardiac Troponin
Stability: 2 hr room temp, 1 day if refrigerated, 6 months if frozen at < -20' C. Centrifuge within 2 hours of collection.
Availability: Monday – Sunday, 24/7, Stat
Turnaround Time: 45 minutes STAT; 2 hr Routine
Reference Ranges:

0.000 – 0.049 ng/mL - "normal "
99th Percentile Normal Population Upper Reference Limit (URL) = 0.049 ng/mL
Critical Value = > 0.500 ng/mL

Manufacturer 95% Confidence Limits for 99% URL:
0.01 -0.05 ng/mL based on a population of healthy adults with no known diseases of the cardiovascular system (including elevated BP or treatment for elevated BP) or other serious acute or chronic diseases.
Interpretative Information:
Evaluation of weak positive TpnI results (0.050 to 0.099) can be facilitated by looking at the change in serial TpnI results (delta value) within the 6 – 9 hour after presentation window typically used for MI assessment with biomarkers. **A change of > = 30% in these weak positive values represents an analytically statistically significant change in TpnI concentration.** Therefore an initial value of 0.06 ng/mL at initial assessment rising by a value of > = 0.018 (> = 0.078 ng/mL) would be an analytically significant rise.
CPT: 84484
Limitations: Assays using antibodies have the possibility of interference due to heterophile antibodies in the patient sample. Patients who have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies (e.g. HAMA) that interfere. Such interfering antibodies typically produce a false positive result that is markedly elevated and does not change over the time period used for MI assessment. Testing using an alternate TpnI method (e.g. iSTAT) or alternate cardiac biomarker (e.g. CK-MB) is recommended as these will not normally show the same interference.