Providence HEALTH CARE
How you want to be treated.

St. Paul's Hospital &
Mount Saint Joseph Hospital

Laboratory Medicine Bulletin

HIGH SENSITIVITY TROPONIN T (hsTnT) TO REPLACE TROPONIN I

January 21, 2016

St Paul's Hospital and Mount Saint Joseph Hospital will have a new test for troponin as of **January 26, 2016**. Important changes in the test performance and result reporting are summarized by topic:

Test Reagents

The Roche high sensitivity cardiac troponin T test (hsTnT) replaces the Siemens Centaur Ultra cardiac troponin I (TnI) test at St Paul's Hospital and the Siemens Stratus TnI test at Mount Saint Joseph Hospital.

Test Performance

The hsTnT test has a higher degree of precision and sensitivity than the current TnI tests. With this improved assay performance, the hsTnT test can accurately measure troponin at lower concentrations. Accordingly, there is now a lower reporting limit (5 ng/L) for the hsTnT test, as compared to 20 ng/L (0.02 µg/L) for the Ultra and 30 ng/L (0.03 µg/L) for the Stratus TnI tests.

Test Units

The hsTnT test will be reported in **ng/L** instead of µg/L (the unit for current TnI tests). This 1000-fold difference (1 µg/L = 1000 ng/L) means that all patients, even healthy individuals, will have results expressed in whole numbers.

Expected Test Results in Health and Disease

Because of the lower reporting limit, more people with an **acute NSTEMI** will have a detectable (> 5 ng/L) hsTnT concentration at baseline (i.e. at presentation to hospital), and/or a detectable rise (**delta hsTnT** concentration) meeting the diagnostic criterion within the first 3 hours of patient observation.

Also, because of the lower reporting limit, **about 50% of healthy people** will have a measurable hsTnT which would have been undetectable with the current TnI tests.

Many people with **cardiac and non-cardiac diseases other than an acute MI** will have abnormal hsTnT results (defined as > 14 ng/L, i.e. > 99th percentile of a healthy population; see causes in appendix A). While there are many causes of chronic myocardial injury leading to an elevated hsTnT, few will result in a significant **delta hsTnT** (see delta hsTnT below). Although not predictive of an acute MI, the magnitude of the baseline value in a patient with chronic hsTnT elevation is **predictive of 30 day cardiac and total mortality**. In acute cardiac injury **of any etiology**, both baseline hsTnT and delta hsTnT are expected to be elevated.

Ordering and Reporting

When investigating an acute MI, order the hsTnT test. If there is no previous hsTnT in the past 12 hours, the test will be considered a **baseline hsTnT**, whereas if a previous hsTnT has been measured within the past 12 hours, the test will be considered a **follow-up hsTnT** (see appendix B). The **baseline hsTnT** result is reported with a comment that is contextualized to the numeric result. The **follow-up hsTnT** result is reported with a

generic comment advising calculation of the delta hsTnT value at 3 hours:

delta hsTnT = follow-up hsTnT – baseline hsTnT

The generic comment will also highlight reference delta hsTnT values, which are strong indicators of the presence or absence of an acute MI, respectively (see delta hsTnT below).

When the pretest probability of disease (based on clinical symptoms and EKG findings) is low, the **baseline hsTnT** may suffice to rule-out an acute MI.[2] However, in most cases, particularly when the baseline sample is collected fewer than 3 hours after the onset of symptoms, a follow-up hsTnT in 3 hours is recommended to utilize the predictive power of a delta hsTnT.

Delta hsTnT (Absolute Delta)

The definition of an acute MI requires a typical rise (positive delta hsTnT early after onset of infarction) and/or fall (negative delta hsTnT late after resolution of the infarction) of a cardiac biomarker such as hsTnT. The best delta hsTnT to discriminate an acute MI from other causes of cardiac injury depends on the time difference between the baseline hsTnT and the follow-up hsTnT. At 3-6 hours post baseline, a delta hsTnT of < 5 ng/L is a sensitive indicator to assist in **ruling-out** a NSTEMI, while a delta hsTnT of ≥ 20 ng/L is a specific indicator for **ruling-in** an acute MI (see appendix C).[3-7] Intermediate delta hsTnT values neither rule-in nor rule-out an acute MI, and must be interpreted in conjunction with the pretest probability of disease, or with a subsequent delta hsTnT.

Considerations in Renal Disease and Aging

eGFR and aging both correlate inversely with the baseline hsTnT value. The average patient over 75 years of age, or with an eGFR < 60 mL/min/1.73 m^2, has a > 70% chance of an abnormal baseline hsTnT (> 14 ng/L), even without obvious cardiac disease on clinical or echocardiographic exam.[8,9] Therefore, in this particular patient population, modest elevations in hsTnT (14 to 150 ng/L) are not specific indicators of an acute MI. However, **delta hsTnT** retains similar sensitivity and specificity for the diagnosis of a NSTEMI in patients with CKD, as it does in patients with normal renal function.

Please contact either of us, or the on-call chemist, for any questions regarding the interpretation of this new troponin test.

Andre Mattman, MD FRCPC
Medical Biochemist, SPH

Sophia Wong, MD FRCPC
Medical Biochemist, SPH

REFERENCES

[1] Sara JD, Holmes DR Jr, Jaffe AS. Fundamental concepts of effective troponin use: important principles for internists. Am J Med 2015;128:111-9.
[2] Carlton EW, Cullen L, Than M, et al. A novel diagnostic protocol to identify patients suitable for discharge after a single high-sensitivity troponin. Heart 2015;101:1041-6.
[3] Mueller M, Biener M, Vafaie M, et al. Absolute and relative kinetic changes of high-sensitivity cardiac troponin T in acute coronary syndrome and in patients with increased troponin in the absence of acute coronary syndrome. Clin Chem 2012;58:209-18.
[4] Reichlin T, Twerenbold R, Wildi K, et al. Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay. CMAJ 2015;187:E243-52.
[5] Biener M, Mueller M, Vafaie M, et al. Comparison of a 3-hour versus a 6-hour sampling-protocol using high-sensitivity cardiac troponin T for rule-out and rule-in of non-STEMI in an unselected emergency department population. Int J Cardiol 2013;167:1134-40.
[6] Bahrmann P, Christ M, Bahrmann A, et al. A 3-hour diagnostic algorithm for non-ST-elevation myocardial infarction using high-sensitivity cardiac troponin T in unselected older patients presenting to the emergency department. J Am Med Dir Assoc 2013;14:409-16.
[7] Biener M, Mueller M, Vafaie M, et al. Impact of leading presenting symptoms on the diagnostic performance of high-sensitivity cardiac troponin T and on outcomes in patients with suspected acute coronary syndrome. Clin Chem 2015;61:744-51.
[8] Twerenbold R, Wildi K, Jaeger C, et al. Optimal Cutoff Levels of More Sensitive Cardiac Troponin Assays for the Early Diagnosis of Myocardial Infarction in Patients with Renal Dysfunction. Circulation 2015;131:2041-50.
[9] Olivieri F, Galeazzi R, Giavarina D, et al. Aged-related increase of high sensitive Troponin T and its implication in acute myocardial infarction diagnosis of elderly patients. Mech Ageing Dev 2012;133:300-5.

APPENDIX A: REASONS FOR AN INCREASED TROPONIN (modified from [1])

Table 1. Causes of an *Acute* Troponin Elevation

CARDIAC	NON-CARDIAC
▪ Thrombotic acute coronary syndrome ▪ Spontaneous coronary artery dissection ▪ Acute heart failure ▪ Myocarditis, pericarditis ▪ Aortic dissection (Stanford A) ▪ Cardiac procedures (coronary angioplasty, electrophysiologic ablations, electrical cardioversions, open heart surgery) ▪ Defibrillator shocks ▪ Heart transplantation ▪ Cardiotoxic drugs ▪ Cardiac contusion after blunt chest wall trauma	▪ Pulmonary embolism ▪ Septic shock/critically ill patients ▪ Strenuous exercise ▪ Rhabdomyolysis

Table 2. Causes of a *Chronic* Troponin Elevation

CARDIAC	NON-CARDIAC
▪ Chronic ischemic heart disease ▪ Chronic heart failure ▪ Left ventricular hypertrophy ▪ Cardiac infiltrative disorders (amyloidosis, sarcoidosis, etc.)	▪ End-stage renal disease

APPENDIX B: INTERPRETIVE COMMENTS TO BE APPENDED TO hsTnT RESULTS

hsTnT Reference Interval (males and females, age >1 year) <14 ng/L
*Any result above the reference range will be flagged.

For a ***baseline hsTnT*** (i.e. no troponin testing in the past 12 hours):

hsTnT Result	Interpretive Comment
< 14 ng/L	Normal TnT level indicates a low risk for acute myocardial injury. To confirm this low risk, repeat at 3 hours and evaluate the delta value.
14 to 149 ng/L	Abnormal result consistent with acute or chronic myocardial injury. To clarify, repeat at 3 hours and evaluate the delta value. The positive predictive value for acute myocardial injury rises with increasing baseline and delta troponin values.
≥ 150 ng/L	Suggestive of acute myocardial injury (e.g. acute MI, myocarditis, pulmonary embolism, acute heart failure). To confirm acute myocardial injury, repeat at 3 hours and evaluate the delta value.

For a ***follow-up hsTnT*** (i.e. troponin testing was performed in the past 12 hours), the following generic comment will be added:

Relative to the baseline sample, expected TnT delta values at 3 hours are:

Delta < 5 ng/L	Acute myocardial injury absent
Delta 5 to 19 ng/L	Consistent with acute myocardial injury but low positive predictive value. Consider a further delta TnT
Delta ≥ 20 ng/L	Specific indicator of acute myocardial injury (applicable to any follow-up period under 6 hours)

APPENDIX C: SENSITIVITY, SPECIFICITY & LIKELIHOOD RATIOS FOR hsTnT ABSOLUTE DELTA VALUES

Table 1. Sensitivity, specificity, and likelihood ratios for NSTEMI associated with absolute delta values for hsTnT at 3 and 6 hours.[3-7]

hsTnT Delta Cutoff	Delta Time Period	Sensitivity (%)	Specificity (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
5 ng/L	3 Hours	85 (77-91)	65 (59-70)	2.4	0.23
20 ng/L	3 Hours	65 (55-74)	87 (minimum)	5.0	0.40
5 ng/L	6 Hours	95 (90-100)	57.5 (55-60)	2.2	0.09
9 ng/L	6 Hours	87 (84-90)	74 (73-75)	3.3	0.18
20 ng/L	6 Hours	68.5 (64-73)	87.5 (87-88)	5.5	0.36

Note: most of the data is derived from cohorts of patients presenting to the emergency department with acute onset chest pain. The sensitivity and specificity values are lower in patients presenting with other symptoms, such as atypical chest pain or dyspnea.[7]