**High Sensitivity Cardiac Troponin T Assay is Coming Soon**

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The use of cardiac troponin (cTn) testing for diagnosing myocardial infarction (MI) has been standard of care for over 20 years because of its absolute specificity for cardiac muscle. For over 5 years, "high sensitivity" cardiac troponin (hscTn) tests have been successfully implemented by healthcare systems across the the world, and they have demonstrated several diagnostic advantages over our coventional cTn assays. Key among these include: (i) permitting the establishment of rapid "rule-out" and "rule-in" protocols for myocardial infarction, (ii) higher diagnostic sensitivity to detect non-ischemic myocardial injury, and (iii) superior ability to assess a patient's future cardiac risk. On March 3rd 2021, the BJC System will standardize from the current cardiac troponin T test to a high sensitivity cardiac troponin T (hs-cTnT) test from Roche Diagnostics.

hs-cTnT assays detect troponin concentrations in blood approximately ten times lower than current methods and accomplish this with superior analytic precision. Upon comparision, the limit of accurate quantification (LOQ) of our current method is 30 ng/L (0.03 ng/mL) while the LOQ of the hs-cTnT method is 6 ng/L (0.006 ng/mL).

By definition, hs-cTnT assays quantify circulating cTn above the LOQ in > 50% of healthy subjects (i.e., those with no history of, or risk factors for, cardiac disease) while having an imprecision of < 10% coefficient of variability (CV) at the 99th% concentration of a healthy population. The 99th% concentration in a healthy population is the upper reference interval (URL) used in the 4th Universal Definition of Myocardial Infarction which states, "*The term acute myocardial infarction should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL.*"

The 99th% URL for the new hs-cTnT was determined in a cohort of 645 healthy males and 656 healthy females. Sex-specific 99th% URLs will be used to improve diagnostic sensitivity for MI in females. Also, note that the units for reporting troponin will change to ng/L to avoid many zeroes in the result field. Analytic characteristics and the 99th% URL of the current method and the new hscTnI method are depicted in **Table 1**.

| Table 1 | Limit of Quantification | 99th% URL | Imprecision (%CV) at 99th% URL |
|---|---|---|---|
| Current Method | 30 ng/L | 10 ng/L - Overall | 20 |
| High Sensitivity Method | 6 ng/L | 14 ng/L - Female<br>22 ng/L - Male | 4 |

The superior sensitivity and precision of hs-cTnT assays has enabled the development of accelerated diagnostic protocols (ADPs) for ruling in or ruling out MI in emergent care settings. These protocols rely on both absolute hs-cTnT values above and below the sex-specific 99th% URL and the detection of changes (i.e., "deltas") at predefined time points in combination with clinical risk factors. Numerous large scale studies have demonstrated that ADPs have exceptional negative predictive values (~ 99.5%). As such, ADPs using hs-cTn assays demonstrated an exceptional capacity to rapidly rule-out myocardial injury and/or infarction. The ADP that will be implemented across BJC is largely based on the algorithm developed at the University of Minnesota, Hennepin County Hospital and the Mayo Clinic **Figure 1**. In this algorithm, patients are considered low risk for MI when symptom duration is greater than 2 hrs is coupled and the hs-cTnT value is less than the LOQ (6 ng/L). At two hours, patients are considered low risk for MI when the 2 hr value remains less than the 99th% sex-specific URL and the delta between the 0 and 2 hr values is < 5 ng/L. In contrast, the accelerated classification defines high risk when hs-cTnT values are above the 99th% URL (when coupled with suggestive clinical characteristics) or when deltas exceed predetermined values, which are purposely set to have high positive predictive values (e.g., >70%). The orderable test for implementing this ADP will be "Troponin T high-sensitivity series (baseline, 2hr, 4hr, 6hr)" which will automatically place orders for baseline, 2, 4 and 6 hour samples. A table of values that will be used for the delta interpretations and a sample of how the Troponin Series will appear in EPIC can be found in **Figure 2**.

Serial cTn testing is essential for diagnosing acute MI, particularly when index troponin concentrations are above the 99th% URL but < 100 ng/L. Patients with chronic comorbidities that cause non-ischemic cardiac injury (e.g., cardiomyopathy, end-stage renal failure, etc.) will often have hs-cTn values falling within this range. Thus, the initial differential for hs-cTnT concentrations within this range must be kept broad, including non-ischemic conditions responsible for insidious (e.g., chronic kidney disease, cardiac amyloidosis, dilated cardiomyopathy) and acute (e.g., acute heart failure exacerbation, myocarditis, pulmonary embolism, sepsis, drug cardiotoxicity) myocardial injury. Unlike acute MI, myocardial injury due to non-ischemic etiologies will not ordinarily result in significant deltas when serial hscTn testing is performed over several hours, unless their onset is acute.

The Washington University Department of Pathology and Immunology worked with the Division of Cardiology, the Department of Emergency Medicine, the BJH laboratory, the Christian Hospital Laboratory, and all BJC laboratory medical directors to prepare educational materials posted on a website that will promote the best utilization of hs-cTnT testing https://nrl.testcatalog.org/show/hsTrop. Please contact either Chris Farnsworth (cwfarnsworth@wustl.edu) of Washington University Pathology and Immunology or your local laboratory medical director if you have any questions.

**Figure 1**

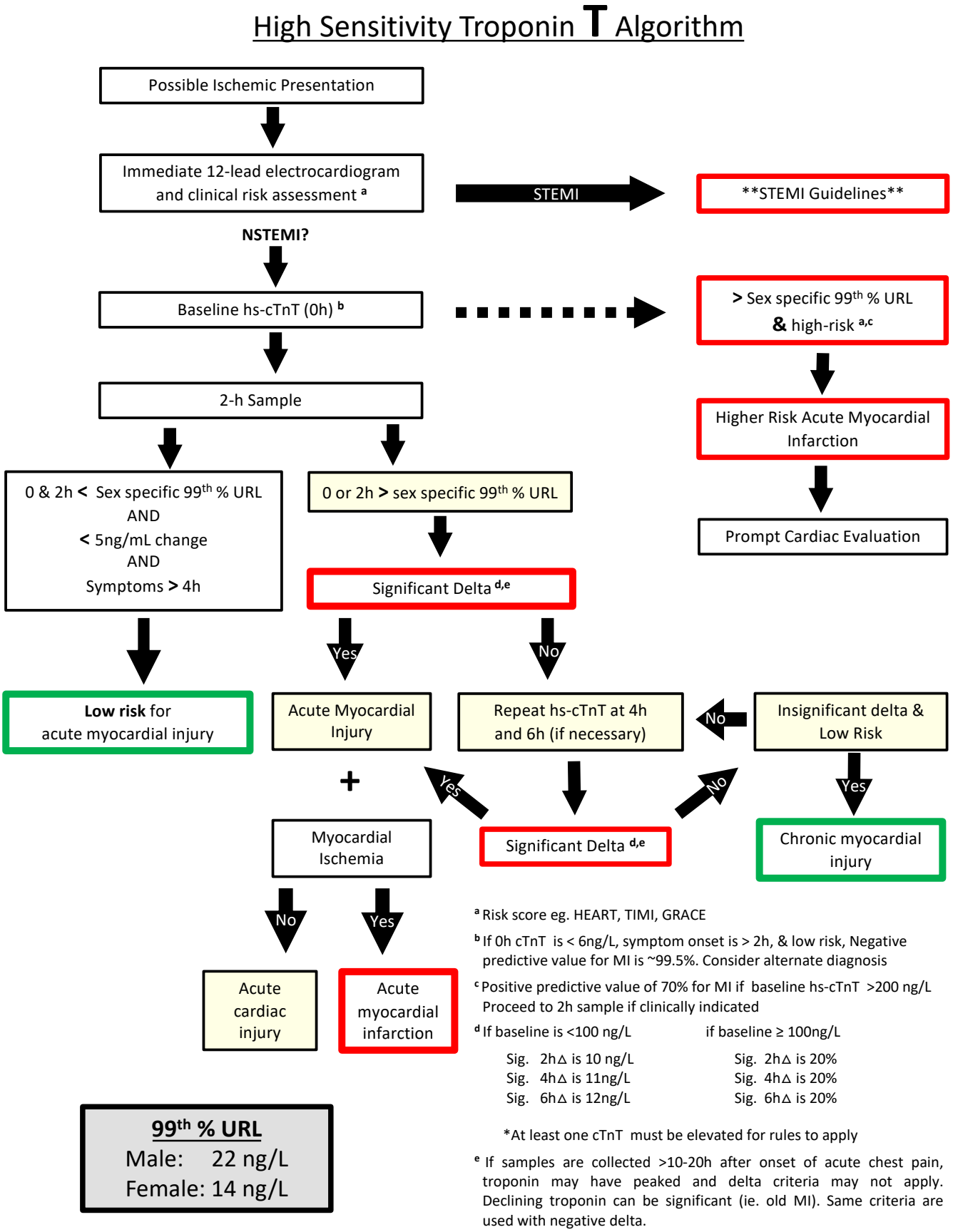
High Sensitivity Troponin T Algorithm
Possible Ischemic Presentation
Immediate 12-lead electrocardiogram and clinical risk assessment [a]
STEMI
**STEMI Guidelines**
NSTEMI?
Baseline hs-cTnT (0h) [b]
> Sex specific 99th % URL & high-risk [a,c]
2-h Sample
Higher Risk Acute Myocardial Infarction
Prompt Cardiac Evaluation
0 & 2h < Sex specific 99th % URL AND < 5ng/mL change AND Symptoms > 4h
0 or 2h > sex specific 99th % URL
Significant Delta [d,e]
Yes
No
Low risk for acute myocardial injury
Acute Myocardial Injury
Repeat hs-cTnT at 4h and 6h (if necessary)
No
Insignificant delta & Low Risk
+
Yes
No
Yes
Myocardial Ischemia
Significant Delta [d,e]
Chronic myocardial injury
No
Yes
Acute cardiac injury
Acute myocardial infarction
99th % URL
Male: 22 ng/L
Female: 14 ng/L
[a] Risk score eg. HEART, TIMI, GRACE
[b] If 0h cTnT is < 6ng/L, symptom onset is > 2h, & low risk, Negative predictive value for MI is ~99.5%. Consider alternate diagnosis
[c] Positive predictive value of 70% for MI if baseline hs-cTnT >200 ng/L Proceed to 2h sample if clinically indicated
[d] If baseline is <100 ng/L
Sig. 2hΔ is 10 ng/L
Sig. 4hΔ is 11ng/L
Sig. 6hΔ is 12ng/L
if baseline ≥ 100ng/L
Sig. 2hΔ is 20%
Sig. 4hΔ is 20%
Sig. 6hΔ is 20%
*At least one cTnT must be elevated for rules to apply
[e] If samples are collected >10-20h after onset of acute chest pain, troponin may have peaked and delta criteria may not apply. Declining troponin can be significant (ie. old MI). Same criteria are used with negative delta.

**Figure 2**

## Rules for Calculating the Troponin T Delta

| cTnT at 0h (baseline) | Interval (h) | Insignificant | Equivocal | Significant |
|---|---|---|---|---|
| < 100 | 2 | <5ng/L | 5-9 ng/L | ≥ 10 ng/L |
| | 4 | | 5-10 ng/L | ≥ 11 ng/L |
| | 6 | | 5-11 ng/L | ≥ 12 ng/L |
| delta = change in absolute concentration | | | | |
| cTnT at 0h (baseline) | Interval (h) | Insignificant | Equivocal | Significant |
| ≥ 100 | 2 | <5% | 5-19% | ≥20% |
| | 4 | | | |
| | 6 | | | |
| delta = % change in concentration | | | | |

*The delta is automatically calculated, and the interpretation (insignificant, equivocal, or significant) will appear in EPIC.

**The delta criteria used for Troponin T differ from troponin I, and they should not be used interchangably

## How Results will appear in EPIC