High Sensitive Troponin T (hsTnT): A New 5th Generation Assay

Introduction

Troponin T (TnT) is a component of the contractive apparatus of the striated musculature. The cardiac isoform of TnT originates exclusively from the myocardium and is cardio-specific. As a result of its high tissue specificity, cardiac TnT is also a highly sensitive marker for myocardial damage and increases rapidly after acute myocardial infarction, which may persist up to 2 weeks thereafter.[1]

The newest high sensitive 5th generation cardiac TnT assay (hsTnT) detects an elevation in TnT levels within 1 hour of the onset of myocardial infarction.[1] It also measures low levels of TnT that were undetectable in prior assay generations, in subjects that do not have myocardial infarction. The new hsTnT assay is reported to be able to detect low TnT levels in more than 55% of healthy subjects. Chronic TnT elevations now can be detected in patients with ischemic or non-ischemic conditions, such as, but not limited to: clinically stable patients with heart failure, different forms of cardiomyopathy, renal failure, sepsis, diabetes, myocarditis, heart contusion, pulmonary embolism, and drug-induced cardiotoxicity.[1]

In order to distinguish between acute and chronic TnT elevations, the Universal Definition of Myocardial Infarction stresses the need for serial sampling to observe a rise and/or fall of TnT levels with at least one serial sample above the 99th percentile upper reference limit that is consistent with the clinical assessment, including symptoms, electrocardiographic changes or imaging results.[1] Different protocols were described and are in use by acute care facilities and hospitals depending on desired sensitivity and specificity of time intervals between serial hsTnT sampling and chosen admission/discharge practices.[2] However, in the reference laboratory setting, it is unlikely that those protocols will be practically useful due to limitations in turnaround time and lack of proximity to acute care units. On the other hand, the use of new hsTnT assay allows for the outpatient monitoring and risk stratification of patients with non-acute conditions that was never considered in clinical practice prior to the introduction of this modern technology.[2]

The manufacturer of hsTnT assay, Roche Diagnostics, lists the factors associated with the values of TnT that may be detectable and even considered as elevated in its instructions for use, such as, but not limited to, unstable angina, heart failure, myocarditis, pulmonary embolism, pericarditis, arrhythmias, cardiac contusions, cardiac transplants, rhabdomyolysis, polymyositis, acute aortic syndrome, hypertensive crisis, and Takotsubo cardiomyopathy.[1]

Use in Outpatient Settings

TnT is released during cardiomyocyte necrosis. It is cardiac specific, but not myocardial infarction-specific, and detectable levels using hsTnT assay may be seen in other diseases that involve the heart muscle.[2]

The most recent 2017 American Heart Association Scientific Statement on the role of biomarkers for the prevention, assessment, and management of heart failure points out that older adults with initially low TnT levels that demonstrated a rise of TnT greater than 50% with time were found to be at greater risk for systolic dysfunction, heart failure events, and cardiovascular death, and that serial measurements of TnT may improve risk classification and should be included in the initial evaluation as part of early risk assessment. The same guideline reports that decreases in TnT levels with time and treatment is associated with a better prognosis, and that in stable patients with chronic heart failure without overt evidence of myocardial infarction, detectable TnT levels were associated with increased risk of death [Hazard ratio (HR) of 2.08] and first hospitalization for heart failure (HR of 1.55) at 2 years. In addition, measurement of biomarkers like TnT can be used as indicators of safety in clinical trials.[3]

The 2019 American College of Cardiology and American Heart Association Antihypertensive Medication Assessment guidelines include recommendations for the use of the hsTnT assay in the stratification of indication for the antihypertensive medications. Patients with stage 1 or stage 2 hypertension and hsTnT levels greater than 6 ng/L (just above the detectable level) doubled the 10-year risk for development of cardiovascular events (incidence rate of 15.1%) versus patients without an elevated TnT (incidence rate of 7.9%).[4]

Another study from 2019 reported that in the general population, cardiac TnT at concentrations above 3 ng/L is strongly associated with risk of non-cardiovascular disease mortality, and to a lesser degree with heart failure and cardiovascular death.[5] A study from 2011 by Sauders et al. reported that even minimally elevated hsTnT assay levels (greater than 3 ng/L) were associated with increased risk of mortality and heart failure in individuals from a general population without known coronary heart disease or stroke.[6] Those observations were in complete agreement with earlier large-scale population studies from the Dallas Heart Study and the Cardiovascular Health Study (when in both studies the hsTnT tests were able to stratify patients at high risk for incident heart failure, cardiovascular death, structural heart disease, and all-cause mortality). Among individuals with initially detectable hsTnT, a subsequent increase of more than 50% was associated with an HR for heart failure of 1.61, and an HR for cardiovascular death of

1.65. A decrease from baseline hsTnT of more than 50% was associated with a lower risk for heart failure (HR of 0.73) and cardiovascular death (HR of 0.71) compared with participants with less than 50% changes. Moreover, higher TnT levels demonstrated a graded association with all-cause cardiovascular disease mortality independent of traditional risk factors, renal function, and levels of other biomarkers such as high-sensitivity CRP and NT-proBNP.[7,8]

In 2017, reported results from the Vascular Events in Noncardiac Surgery Patients Cohort Evaluation (VISION) Study showed that an absolute hsTnT change of 5 ng/L or higher in patients undergoing noncardiac surgery was associated with an increased risk of 30-day mortality (HR of 4.69).[9]

Serial measurements of cardiac troponins also have a major potential in monitoring the impact of therapeutic interventions and assessment of future coronary risk independent of cholesterol lowering.[10]

The diagnostic and prognostic role of TnT measurements in cardiac amyloidosis was shown in the number of reports and clinical guidelines. A staging system for cardiac amyloidosis relies solely on the measurements of two biomarkers: troponins (T or I) and NT-proBNP. Serum hsTnT levels were significantly higher in patients with cardiac amyloidosis than those with cardiac hypertrophy who were free of amyloidosis (cutoff value of 31 ng/L had a sensitivity and specificity of 74% and 76%, respectively). Measurements of TnT together with NT-proBNP and free light chains were shown to be useful in determining the prognosis among newly diagnosed patients with Light-Chain (AL) amyloidosis.[11-13]

In general, chronic, stable elevations of hsTnT at or above 99th percentile without a significant rise or fall are common in patients with structural heart disease, but not in acute coronary events (see table on the following page).[2]

Test Name	Test No.
Troponin T (Highly Sensitive)	140150
For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.LabCorp.com.	

References

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Etiology Category	Cause of Myofilament Damage	
Oxygen Demand Mismatch (in the absence of Acute Myocardial Infarction)	Tachy/Brady Arrythmias	
	Hypertensive Crisis	
	Anemia	
	Hypovolemia or Hypotension	
	Aortic Dissection or Aortic Valve Disease	
	Hypertrophic Cardiomyopathy	
	Strenuous Exercise	
Direct Myocardial Damage	Cardiac Contusion	
	Cardiac Procedures	Cardioversion
		Pacing
		Ablation
		Endomyocardial Biopsy
	Cardiac Infiltrative Disorders	Amyloidosis
		Haemochromatosis
		Sarcoidosis
		Scleroderma
	Chemotherapy	Adriamycin
		5-Fluoroacil
		Trastuzumab
	Myocarditis	
	Pericarditis	
	Cardiac Transplantation	
	Other Innumo-Mediated Reactions	
Myocardial Strain	Severe Congestive Heart Failure (Acute or Chronic)	
	Pulmonary Embolism	
	Pulmonary Hypertension	
	Chronic Obstructive Pulmonary Disease	
Accumulation of Troponin in Plasma	Renal Dysfunction (Acute or Chronic)	
Systemic Processes	Sepsis	
	Systemic Inflammatory Processes	
	Burns (if Affecting >30% of Body Area)	
	Hypothyroidism	
	Snake Venoms	
Neurological Disorders	Intracerebral Hemorrhage	
	Stroke	
	Seizures	