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Newsletter

PATHOLOGISTS LANCET Kenya

HIGH SENSITIVITY CARDIAC TROPONIN I (hs-cTnI)

Acute Myocardial Infarction (AMI) is the major cause of death and disability worldwide with an increasing incidence. The risk of death is highest within the first few hours of AMI onset. Rapid identification of AMI is critical for the initiation of medical treatment and management. Fortunately, most patients presenting at emergency clinics with chest pain do not have AMI.

The 12-lead ECG and Cardiac Troponin are the diagnostic cornerstones and complement clinical evaluation. For patients with ST- elevation AMI, clinical evaluation and ECG provide a straightforward diagnosis and allow early initiation of therapy. However, about 95% of patients have non-ST elevation AMI (NSTEMI) leading to uncertainty after ECG and clinical evaluation. Cardiac Troponins play a prominent role in these patients. Cardiac Troponins are structural proteins unique to the heart. Detection of Cardiac Troponins in the blood indicates as well as quantifies the degree of cardiomyocyte necrosis.

Acute Myocardial Infarction = Myocardial cell death due to prolonged myocardial ischemia.

Cardiac troponin assays (Contemporary cardiac troponin assays versus highly sensitive assays

The major limitations of contemporary Cardiac Troponin assays (i.e., non-hs-cTnI assays) is lack of sensitivity (i.e., failure to detect low troponin levels in blood) within the first few hours of AMI. Contemporary assays require time for more cardiomyocyte damage to occur to release enough cardiac troponin to reach levels detectable by these assays.

The hs-cTnI assay represents a significant advance in assay technology that allows early diagnosis of AMI i.e., saving time and cardiac muscle. Hs-cTnI assay is defined as an assay that can detect as well as quantify troponin levels in at least 50% of healthy individuals. Unlike conventional troponin assays, hs-cTnI assay achieves the required analytical performance of 10% CV below the 99th percentile (26 ng/l), which has become the hallmark for the diagnosis of AMI.

To achieve the best clinical use, hs-cTnI should be interpreted as a quantitative variable. The previous terms used for contemporary Troponin I assays, such as 'Troponin-positive' and 'Troponin-negative' should now be avoided. Detectable troponin has now become the norm and has to be interpreted according to different concentration levels.

The differential diagnosis of a small amount of cardiomyocyte necrosis and therefore low levels of hs-cTnI is broad and includes acute and chronic cardiac disorders. The differential diagnosis of a large amount of cardiomyocyte necrosis and therefore higher levels of hs-cTnI is much smaller and includes AMI, myocarditis and takotsubo cardiomyopathy.

High-sensitivity cardiac troponins are the preferred biomarkers for the evaluation of myocardial injury; other biomarkers, for example, (CK-MB), are less sensitive and less specific.

DEFINITION OF AN ACUTE MYOCARDIAL INFARCTION (FOURTH UNIVERSAL DEFINITION OF MYOCARDIAL INFARCTION-2018 ESC/ACC/AHA/WHF EXPERT CONSENSUS DOCUMENT)

Presence of acute myocardial injury with clinical evidence of acute myocardial ischemia and detection of a rise and/or fall of cTn values with at least 1 value above the 99th percentile upper reference limit (URL) and at least 1 of the following:

- Symptoms of myocardial infarction
- New ischemic ECG changes
- Development of pathological Q waves
- Imaging evidence of loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with ischemic etiology.
- Identification of a coronary thrombus by angiography or autopsy

DISTINCTION OF ACUTE FROM CHRONIC CAUSES OF CARDIO MYOCYTE NECROSIS

An elevated hs-cTnI is any level > 26 ng/L and indicates as well as quantifies cardiomyocyte necrosis. A rise in hs-cTnI cannot differentiate acute from chronic or ischaemic from non- ischaemic causes of necrosis. The most important cause of elevated hs-cTnI is AMI. An elevated cTn above the 99th percentile URL is considered cardiac injury but not all cardiac injury is AMI.

Acute myocardial injury is defined as newly detected, dynamic rising and / or falling troponin values above the 99th percentile URL. Chronic cardiac injury is characterized by persistently elevated cTn values above the 99th percentile URL.

ISCHEMIC AND NON -ISCHEMIC CAUSES OF ELEVATED CARDIAC TROPONINS

Cardiac troponins may arise in myocardial injury but do not indicate the underlying pathophysiological mechanisms and may arise in physiological stresses from otherwise normal hearts. Demonstration of a rise and /or fall in cTn values with at least 1 value above the 99th percentile URL and caused by myocardial ischemia is designated Myocardial infarction. Other causes of elevated cardiac injury should be considered in persistently elevated cardiac troponin (See table 1).

TROPONIN I VERSUS TROPONIN T

Studies have shown no difference between Troponin I and Troponin T in diagnosis and prognostication. In this regard, consensus guidelines do not recommend one over the other. Cardiac troponin testing must be carried out serially and reviewed within the clinical context.

Due to differences in reference ranges, patients initially evaluated with a particular troponin (for example hsTnI), should be followed up on the same. Similarly, due to differences in instrument performances and laboratory conditions, it is recommended that follow up testing be carried out in the same laboratory and on the same instrument

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following initial evaluation. This approach aids in determining the clinical significance of the delta change in serial cardiac troponins taken from the patient.

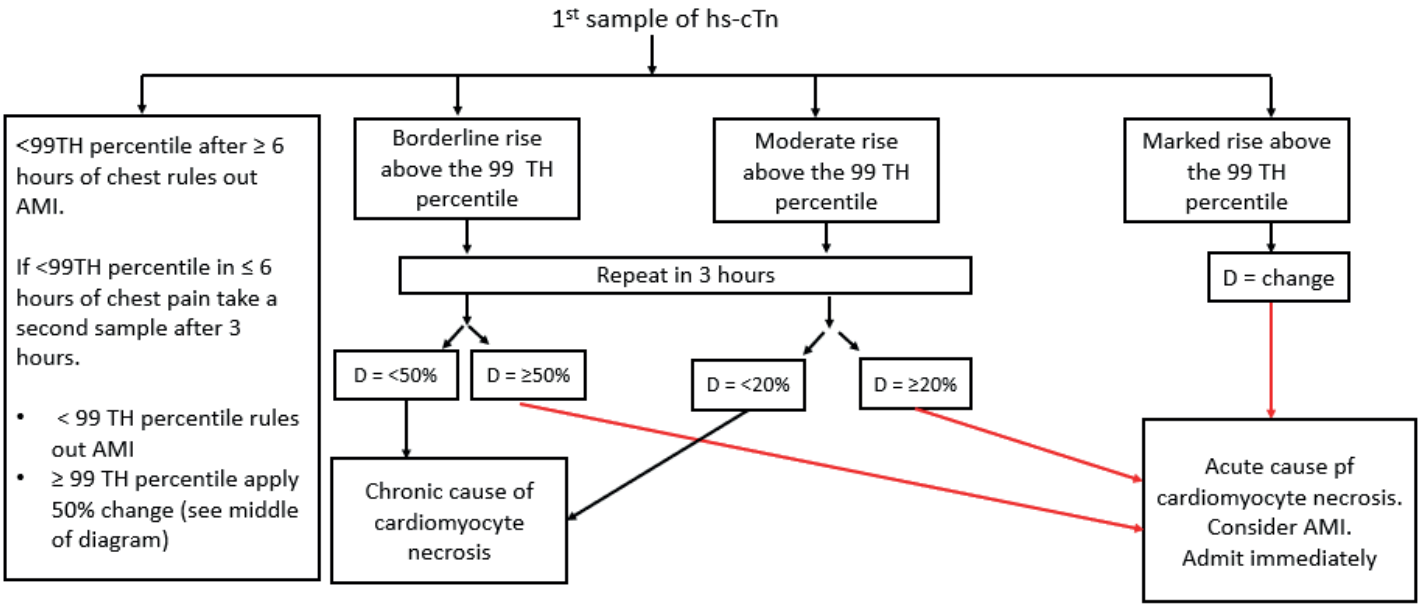
Biochemical data indicate that injured skeletal muscle expresses proteins that are detected by the cTnT assay. Elevations in hs-cTnT may therefore occur in myositis and other skeletal muscle disorders.

Table 1: ISCHEMIC AND NON-ISCHEMIC CAUSES OF ELEVATED CARDIAC TROPONIN LEVELS

Myocardial injury related to myocardial ischemia	**Other causes of myocardial injury**
Atherosclerotic plaque disruption with thrombosis	**Cardiac conditions** - Heart failure - Myocarditis - Cardiomyopathy - Takotsubo syndrome - Coronary revascularization procedure - Cardiac procedure other than revascularization - Catheter ablation - Defibrillator shocks - Cardiac contusion
Myocardial injury related to myocardial ischemia because of oxygen supply / demand imbalance	
Reduced myocardial perfusion - Coronary artery spasm, microvascular dysfunction - Coronary embolism - Coronary artery dissection - Sustained bradyarrhythmia - Hypotension or shock - Respiratory failure - Severe anemia **Increased myocardial oxygen demand** - Sustained tachyarrhythmia - Severe hypertension with or without left ventricular hypertrophy	**Systemic conditions** - Sepsis - Chronic kidney disease - Stroke and subarachnoid hemorrhage - Pulmonary embolism and pulmonary hypertension - Infiltrative diseases such as Amyloidosis sarcoidosis - Chemotherapeutic agents - Critically ill patients - Strenuous exercise

ALGORITHM FOR TROPONIN

Clinical symptoms consistent with myocardial ischemia in an acute care setting.



D – Delta change

Fig 1: High sensitivity cardiac Troponin algorithm (Adapted from SAHA guidelines 2012)

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