Cardiac Troponin

Myocardial Infarction and More

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KEYWORDS

• Cardiac troponin • High-sensitivity troponin • Myocardial necrosis
• Myocardial ischemia • Myocardial infarction

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Cardiac troponin (cTn) is a component of the myocyte contractile apparatus that is released into the circulation in the setting of myocardial necrosis.
2. cTnI and cTnT are protein subunits of the larger troponin molecule, and assays for their measurement perform similarly for most clinical indications.
3. Sequential generations of cTn assays are characterized by lower limits of detection and improved precision profiles, with more frequent detection in healthy populations.
4. cTn is specific for the presence but not the mechanism of myocardial necrosis. Positive levels must be interpreted in a clinical context and never in isolation.
5. The diagnosis of acute myocardial infarction (MI) requires an elevated cTn concentration as well as a temporal increase and/or decrease in levels.
6. Both the magnitude and the pattern of cTn elevation provide prognostic information in the setting of an acute MI, and patients with greater elevations likely benefit from a more aggressive treatment strategy.
7. cTn is useful in the identification of nonischemic causes of myocardial necrosis, with an increase and/or decrease in levels supportive of an acute process causing myocardial injury.
8. Elevated cTn is predictive of mortality in acute decompensated HF, acute pulmonary embolism, and chronic kidney disease (CKD); it is reasonable to use cTn for risk stratification and prognostication in these conditions.
9. cTn should not be checked in the asymptomatic patient.
10. Despite frequent baseline elevation in patients with CKD, cTn is still the preferred biomarker for the diagnosis of myocardial infarction in this setting.

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BACKGROUND

What is troponin?

Troponin is an intracellular regulatory protein complex associated with the contractile apparatus of skeletal and cardiac myocytes. It is composed of 3 protein subunits: troponin I (cTnI), troponin T (cTnT), and troponin C. Cardiac myocytes express structurally unique isoforms of cTnI and cTnT as compared with skeletal myocytes.[1] Irreversible injury of cardiac myocytes leading to cell death (myocardial necrosis) results in the release of cTnI and cTnT into the circulation.[2,3] Highly specific immunoassays have been developed for the detection of these cardiac-specific proteins in peripheral blood (with minimal cross-reactivity to skeletal troponin).[4] In prior decades, consensus opinion held that an elevation in cardiac troponins (cTns) exclusively signified irreversible myocardial cell death.[2,5] However, the potential for release of cTns in the setting of reversible myocyte injury is now a topic of considerable debate.[6,7] This issue is made even more controversial by the advent of increasingly sensitive assays that can reliably detect low levels of cTn in a majority of apparently disease-free individuals.[8,9] Although this debate is ongoing, cTn remains the preferred biomarker of myocardial necrosis due to its superior performance in the diagnosis and prognosis of cardiac conditions.[10–12]

What are the differences between assays for cardiac troponin I and troponin T?

Following release from cardiac myocytes, cTnI exists in different forms (free or bound to other types of cTn) in the circulation as well as in multiple isoforms (oxidized, reduced, or phosphorylated).[13] In the development of immunoassays for cTnI detection, various manufacturers have used detection antibodies directed against different epitopes of the multiple cTnI forms. As a result, there is a lack of standardization between cTnI assays from different manufacturers, and absolute concentrations of cTnI cannot be compared between different assays.[7] Because of the existence of an international patent, cTnT assays in widespread use have been produced by a single manufacturer.[14] As a result, the uniform use of a single current generation cTnT assay across clinical care centers allows for direct comparison of absolute concentrations. Of note, all cTnI and cTnT assays meet the same performance specifications, and no distinction is made in terms of their diagnostic and prognostic utility when used for the clinical indications discussed later.[12]

What is the difference between sequential generations of cardiac troponin assays?

The US Food and Drug Administration (FDA) first approved the use of a cTn assay for clinical care in 1994. Since that time, manufacturers have produced successive assay generations with progressive improvement in analytical performance. This improvement is characterized by the ability to detect increasingly lower concentrations of circulating cTn while maintaining similar test accuracy and precision.[15] Accordingly, each improvement in assay performance has led to earlier detection of increasing cTn levels following the onset of myocardial necrosis.[16] Furthermore, the most recently developed assays can detect circulating cTn levels in up to 90% of healthy individuals as compared with less than 50% for earlier generation assays.[17,18]

There is currently no widely accepted classification scheme for the multitude of cTn assays. As a result, manufacturers describe their commercial assays using terms that do not have standardized meanings according to analytical performance. For example, newer-generation assays with lower limits of detection have generally