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Introduction: Approximately 8 million patients present to the ED with complaints of chest pain each year. Because of the delay between onset of cardiac ischemia and elevation of cardiac biomarkers greater than 50% of these patients are admitted or placed into observation units. However, less than 10% are eventually diagnosed with an acute coronary syndrome. Despite this "pervasive no-miss approach" 2-5% of patients with acute myocardial infarction (MI) go undiagnosed and are discharged home. In order to minimize both the resource cost of ruling out acute MI as well as the morbidity-mortality of missed diagnosis, higher sensitivity cardiac biomarker tests have been developed, the superiority of which have yet to be established.

Clinical Question: Can a single High-Sensitivity Troponin Assay accurately exclude acute myocardial infarction?

Methods: A multi-database search identified 3,071 potential studies, of which 141 were selected for full text review. 40 of these studies were further independently reviewed for inclusion criterion with 23 ultimately being chosen for meta-analysis. Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. Studies chosen used a composite reference standard for diagnosis of acute MI including a variety of troponin assays including High-Sensitivity Troponin Assays with pre-specified diagnostic thresholds. 9,428 total patients were included in the meta-analysis with age range of 54 to 71 years and time of symptom onset to presentation of 3.5 to 5.6 hours. Of note, the median prevalence of acute MI was 21%, ranging from 8% to 56%.

Result: Diagnostic accuracy of High-Sensitivity Troponin Assays based on meta-analysis was as follows. For a higher predetermined threshold of 14 ng/L, pooled sensitivity and specificity were 90% and 77% respectively, with positive LR of 3.9 and negative LR 0.14. Lower thresholds of 3 or 5 ng/L showed sensitivity of 97% with drop in specificity to 42% and positive LR 1.7 and negative LR of 0.06.

Discussion: The authors concluded that it may be possible to exclude acute MI using a single High-Sensitivity Troponin Assay when low cut off values of 3 to 5 ng/L are used. However major limitations to this study exist. The prevalence of MI in the pooled study population was significantly higher than the approximately 4 to 6% reported in US emergency departments. Additionally, time of symptom onset has well established impact on sensitivity of known cardiac biomarker assays. The broad range of 3.5 to 5.6 hours between symptom onset and presentation seen in this study raises concern for optimal timing and diagnostic utility of early negative assays.

Take Home Point: It may soon be possible to rule out acute MI after a single High-Sensitivity Troponin Assay, however additional research is necessary to explore the utility of this tool in the average ED as well as its optimal diagnostic threshold and timing.
