Comparison of conventional and high-sensitivity troponin in patients with chest pain: A collaborative meta-analysis

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Background Multiple studies have evaluated the diagnostic and prognostic performance of conventional troponin (cTn) and high-sensitivity troponin (hs-cTn). We performed a collaborative meta-analysis comparing cTn and hs-cTn for diagnosis of acute myocardial infarction (AMI) and assessment of prognosis in patients with chest pain.

Methods MEDLINE/PubMed, Cochrane CENTRAL, and EMBASE were searched for studies assessing both cTn and hs-cTn in patients with chest pain. Study authors were contacted and many provided previously unpublished data.

Results From 17 included studies, there were 8,644 patients. Compared with baseline cTn, baseline hs-cTn had significantly greater sensitivity (0.884 vs 0.749, $P < .001$) and negative predictive value (NPV; 0.964 vs 0.935, $P < .001$), whereas specificity (0.816 vs 0.938, $P < .001$) and positive predictive value (0.558 vs 0.759, $P < .001$) were significantly reduced. Based on summary receiver operating characteristic curves, test performance for the diagnosis of AMI was not significantly different between baseline cTn and hs-cTn (0.90 [95% CI 0.85-0.95] vs 0.92 [95% CI 0.90-0.94]). In a subanalysis of 6 studies that alternatively defined AMI based on hs-cTn, cTn had lower sensitivity (0.666, $P < .001$) and NPV (0.906, $P < .001$). Elevation of baseline hs-cTn, but negative baseline cTn, was associated with increased risk of death or nonfatal myocardial infarction during follow-up ($P < .001$) compared with both negative.

Conclusion High-sensitivity troponin has significantly greater early sensitivity and NPV for the diagnosis of AMI at the cost of specificity and positive predictive value, which may enable early rule in/out of AMI in patients with chest pain. Baseline hs-cTn elevation in the setting of negative cTn is also associated with increased nonfatal myocardial infarction or death during follow-up. (Am Heart J 2014;169:6-16.e6.)

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Funding: None.

Submitted March 17, 2014; accepted October 10, 2014.

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0002-8703

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http://dx.doi.org/10.1016/j.ahj.2014.10.007

More than 7 million patients present annually to the emergency department (ED) with chest pain,[1] and >1 million patients are hospitalized each year in the United States with acute myocardial infarction (AMI).[2] The ability to rapidly exclude AMI through high-sensitivity troponin (hs-cTn) in combination with clinical evaluation may reduce ED length of stay, reduce financial cost, and improve outcomes in these challenging patients. Evidence suggests that even minimal elevations of conventional troponin (cTn) are associated with worse clinical outcome and that these patients may benefit from initiation of appropriate medical intervention.[3,4] Furthermore, use of a very low cut-point for hs-cTn has been suggested as a tool to rule out AMI due to the resulting high negative predictive value (NPV).[5] However, the introduction of hs-cTn may significantly decrease specificity and can prompt a costly cardiovascular workup in patients in which cTn is elevated due to nonischemic causes for cTn release. Although multiple studies have compared the diagnostic and prognostic test characteristics of cTn and hs-cTn, the results of these data are mixed. Therefore, we performed a diagnostic and prognostic collaborative meta-analysis to assess cTn values and hs-cTn values in patients with chest pain.

Methods

Data sources and searches

Two independent reviewers (M.J.L. and N.C.B.) systematically searched (November 2013) Cochrane CENTRAL, EMBASE, and MEDLINE/PubMed for studies that assessed both cTn and hs-cTn in patients with nontraumatic chest pain. Search criteria included "high sensitivity troponin" AND ("chest pain" OR "acute coronary syndromes" [ACS] OR "myocardial infarction"). We limited our search to studies published in peer-reviewed journals; trials presented in abstract-only form were excluded. Our meta-analysis was performed in accordance with the Meta-Analysis Of Observational Studies in Epidemiology guidelines.[6] After obtaining full reports, eligibility was assessed from the full-text articles with divergences resolved after consensus. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

Study selection

Prespecified inclusion and exclusion criteria were established at study onset. We included any study that (*a*) assessed patients with nontraumatic chest pain and (*b*) measured both cTn and hs-cTn levels. We excluded any study that (*a*) limited patients to only those with myocardial infarction (MI) or a specific subgroup of patients, (*b*) excluded patients with a baseline positive troponin, and (*c*) used a case-control format. We included studies regardless of whether patients with ST-segment elevation MI (STEMI) were included or excluded, whether the criterion standard diagnosis was made centrally or locally, and regardless of the cTn criteria used for diagnosis of AMI.

Data extraction and quality assessment

Data were abstracted by the same 2 investigators (M.J.L. and N.C.B.). An attempt was made to contact the corresponding authors of included studies to obtain complete data. Study quality was appraised in accordance with QUality Assessment of Diagnostic Accuracy Studies (QUADAS)-2.[7] We accepted the authors' definitions of conventional and hs-cTn.

Data synthesis and analysis

Dichotomous variables are reported as proportions (percentages), whereas continuous variables are reported as mean (SD) or median. Sensitivity, specificity, positive predictive values (PPV), NPVs, positive and negative likelihood ratios (LRs), and diagnostic odds ratios (ORs) were computed. Pooling was performed using random-effects methods. Measures of test performance are reported as point estimates (with 95% CIs). These were calculated for the baseline cTn at presentation, baseline hs-cTn at presentation, cTn at the second serial sampling (second cTn), and hs-cTn at the second serial sampling (second hs-cTn). Adjudication of AMI was typically defined by cTn. Given that authors used their own cut-points and delta changes in troponin with different times for sampling, we were unable to assess for value of serial sampling in this meta-analysis.

We generated weighted symmetric summary receiver operating characteristic (SROC) plots using the Moses-Shapiro-Littenberg method.[8] Area under the ROC curves of individual studies were pooled using a random effect generic-inverse variance method. Sources of clinical and statistical heterogeneity were explored by means of subgroup analyses and meta-regression with unrestricted maximum-likelihood meta-regression (inverse variance-weighted regression) on diagnostic ORs.

Binary outcomes from individual studies were combined with random-effect models, leading to computations of ORs with 95% CIs. Between-study statistical heterogeneity was assessed using the Cochran Q χ^2 test. I^2 was calculated as a measure of statistical heterogeneity; I^2 values of 25%, 50%, and 75% represented mild, moderate, and severe inconsistency, respectively. Small study or publication bias was explored with funnel plots and Peters test.[9] Statistical analysis was performed using Review Manager (RevMan) 5 version 5.1.7 freeware package (The Nordic Cochrane Centre, The Cochrane Collaboration, 2008, Copenhagen, Denmark), Meta-DiSc software,[10] and NCSS 2007 (Kaysville, UT), with statistical significance for hypothesis testing set at the .05 two-tailed level and for heterogeneity testing at the .10 two-tailed level.

Results

Of the 824 citations we identified, we assessed 177 abstracts from which we performed detailed review of 91

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