Correspondence

Reply to Letter Regarding Article, “High-Sensitivity Troponin T Concentrations in Acute Chest Pain Patients Evaluated With Cardiac Computed Tomography”

We appreciate the very insightful comments by Drs Lippi and Cervellin regarding our study and agree that the exceptional analytic sensitivity of the novel high-sensitivity (hs) troponin (hsTn) assays raises several important questions about their optimal use in the evaluation of patients with suspected or proven acute coronary syndrome (ACS), including those with acute myocardial infarction (MI).

The tension created today by the hsTn assays is rather reminiscent of that when original cardiac troponin (cTn) methods were released nearly 20 years ago. Indeed, with the initial use of first-generation cardiac-specific cTnT or cTnI assays, it was immediately evident that these tests were more sensitive for acute MI than creatine kinase-MB (CK-MB); this led to confusion about the correct nomenclature of a cTn-positive/CK-MB–negative event. Subsequent studies demonstrated patients with such a syndrome had a risk comparable to that of an acute MI, and the biochemical redefinition of acute MI was changed to a cTn standard.

We are now poised to experience a similar transition as the hsTn methods are released and applied clinically. It is increasingly clear that although already adopted in concept by recent position papers, the use of the 99th troponin percentile (essentially achievable by hsTn assays only) must be accompanied by a parallel evolution in clinician understanding of troponin biology in health and disease. In point of fact, clinicians will need to learn exactly what an elevated hsTn means.

Our data and those of others suggest the hsTn assays tell us much more about the patient than the mere presence or absence of “acute MI.” Indeed, even in the absence of an ACS, we found the hsTn assay identified patients with significant underlying heart disease, including more extensive coronary artery disease, whereas other studies have found that elevated hsTn in “apparently well” patients predicts future heart failure. These findings, together with the observation that elevation above the 99th percentile is prognostically meaningful irrespective of ACS presence, all argue that an elevated hsTn result must not be viewed necessarily as a test for “heart attack.”

We do agree with Drs Lippi and Cervellin that a negative hsTn result has outstanding negative predictive value to “rule out” ACS. On the other hand, many ACS patients previously diagnosed with unstable angina pectoris (by definition, cTnT or cTnI negative) will be reclassified to a diagnosis of acute MI by the hsTn assays; as with cTn-positive/CK-MB–negative events, we now recognize that hsTn-positive/non–hsTn-negative ACS has a higher risk, which validates the use of the 99th percentile for this indication. Thus, although the positive predictive value of hsTn is lower than its negative predictive value, clinicians will need to accept the veracity of an elevated hsTn result when measured in the correct clinical context.

To this point, however, we believe more than ever—as Lippi and Cervellin point out as well—that context and clinical judgment are everything when the hsTn assays are used. In our report, we cautioned the reader that “elevation of either hsTnT or hsTnI likely identifies a patient with significant heart disease, at higher risk for adverse outcome, irrespective of the presence or absence of ACS”; however, we also emphasized the crucial need to consider each patient not only as a function of their hsTn value but also with respect to their clinical presentation.

However, it is well recognized that a biomarker with a high negative predictive value for ACS early on, ie, at the time of presentation at the emergency department, may result in a tremendous improvement of the management of the many patients who present with acute chest pain every day. The primary effect could be seen in relieving overcrowded emergency departments from patients who can be sent home safely and lowering costs of current rule-out MI protocols, which typically include serial troponin measurements and an ECG, as well as some form of stress testing, during a 24-hour hospitalization. Whether the hsTn assays will ultimately be best used as a rule-out test (on the basis of their excellent negative predictive value) or as a rule-in test conjoined with clinical judgment, correct context, and supplemental testing, such as with other biomarkers or imaging (such as computed tomography coronary angiography), remains to be determined.

Disclosures

None.

James L. Januzzi, Jr, MD
Quyhn A. Truong, MD, MPH
Asim A. Mohammed, MD
Division of Cardiology
Fabian Bamberg, MD, MPH
John H. Nichols, BA
Christopher L. Schlett, BS
Udo Hoffmann, MD, MPH
Cardiac MR PET CT Program
Department of Radiology
Hang Lee, PhD
Biosatistics Center
John T. Nagurney, MD
Emergency Medicine
Massachusetts General Hospital
Boston, MA

Mahir Karakas, MD
Wolfgang Koenig, MD, PhD
Department of Internal Medicine II and Cardiology
University of Ulm Medical Center
Ulm, Germany

References


Reply to Letter Regarding Article, "High-Sensitivity Troponin T Concentrations in Acute Chest Pain Patients Evaluated With Cardiac Computed Tomography"

James L. Januzzi, Jr, Quynh A. Truong, Asim A. Mohammed, Fabian Bamberg, John H. Nichols, Christopher L. Schlett, Udo Hoffmann, Hang Lee, John T. Nagurney, Mahir Karakas and Wolfgang Koenig

_Circulation_. 2011;123:e4
doi: 10.1161/CIRCULATIONAHA.110.967224

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circ.ahajournals.org/content/123/1/e4

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/