Letters to the Editor

terpretation of data, or approval of manuscript.

References


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Comment on “High-Sensitivity Cardiac Troponin: Hype, Help, and Reality”

To the Editor:

We thank Jaffe and Apple (1) for their interest in our study. In their perspectives article, they commented on details of our study and the study by Keller et al., which were both published recently in the New England Journal of Medicine (2, 3). Although we fully agree with several of their statements, we strongly disagree with others. It is detrimental to the much-needed interdisciplinary discussion on the best possible clinical use of sensitive cardiac troponin assays when the discussion is based on incorrect statements. Unfortunately, the Jaffe and Apple perspective contains 2 important errors.

First, and of most importance, Jaffe and Apple (1) asked, “How did these studies deal with the problem of increased [cardiac troponin] concentrations produced by diseases other than acute myocardial infarction (AMI)?” and stated, “Not very well. For the most part, the authors . . . used a [cardiac troponin] concentration above the cutoff value as the sole criterion for the diagnosis of acute coronary syndrome (ACS).” They also stated, “The presence of a changing . . . pattern, which is an essential part of the criteria for the diagnosis of AMI in all the guidelines, was used in only a subset of patients in the Reichlin et al. article . . . .” These statements are incorrect in 2 respects. On the one hand, AMI was defined in our study in all patients in full agreement with the current universal definition of AMI (4), which requires evidence of myocardial necrosis with a changing pattern associated with clinical signs of myocardial ischemia, as stated clearly in the Methods section of our report (2). Necrosis was diagnosed on the basis of a rising and/or falling pattern of the cardiac troponin concentration, with at least 1 value above the 99th percentile at a level of precision of <10% (2). On the other hand, noncoronary conditions that increased cardiac troponin concentrations according to conventional cardiac troponin assays were not called “true positives” but were included in the diagnostic group “cardiac symptoms from causes other than coronary artery disease” (2). Ninety-five (13%) of 718 patients were adjudicated in this group, and 16 of these patients had acute cardiac necrosis of an origin other than coronary artery disease (e.g., myocarditis, tachyarhythms, or acute heart failure).

Second, Jaffe and Apple (1) argue that the incidence of ACS is much lower in the US than the incidence reported in the 2 studies published in the New England Journal of Medicine (2, 3) and state that the incidence of ACS was 46% in our study. This statement is incorrect. The incidence of ACS in our study as reported in the Results section of the report was 33% (2). In addition, results from a recently completed multicenter study that included consecutive patients presenting to the emergency department with symptoms suggestive of AMI showed that the difference in the incidence of local emergency department diagnosis of ACS among centers in the US [range, 4%–40%; data on file at FAST-TRAC Data Management Center, San Diego, CA (Dr. Greg Shipp, Nanosphere, personal communication, January 15, 2010)] was greater by far than potential differences between the US and Europe. Therefore, we think that the disease incidence encountered in an individual emergency department is predominantly determined by the details of the local patient flow, such as a competing high-volume catheterization laboratory in a neighboring hospital that receives most high-risk and high-probability ambulance cases, or such as local hospital standards that guide chest pain patients only to the emergency department as long as they are perceived as low risk and low probability and that triage all high-probability patients directly to a coronary care unit.

We hope that these clarifications help to advance the important

1 Nonstandard abbreviations: AMI, acute myocardial infarction; ACS, acute coronary syndrome.
discussion on the best clinical use of sensitive cardiac troponin assays.

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**References**


**In Reply**

We are pleased to have the opportunity to clarify some issues that, due to word count restrictions, were not as clear as would have been ideal.

The issue of the use of a δ (changing pattern) is a good example. Deltas are important for lower cardiac troponin concentrations because most chronic increases (an occasional dialysis patient excepted) are modest. At low concentrations, the δ takes into account the imprecision of the assay and, if possible, biological variation. The δ for the cardiac troponin T (cTnT) assay used for the gold standard diagnosis was unstated. Clinicians think of a changing pattern as any alteration, and that is not the case. At the Mayo Clinic, we require a 0.03 μg/L change at low cTnT concentrations, which is 300% from 0.01 μg/L and 100% from 0.03 μg/L. At higher concentrations, lower δ values are used because the imprecision is less. No criteria were provided for the comparison assays or for the novel high-sensitivity assay (1). Table 3C in the supplementary material for the report of Reichlin et al. (1), where this matter is evaluated, provides no criteria. We have recently established that the conjoint biological and analytical variation with the high-sensitivity cTnT assay is 85% in the short term (2). Kavšak et al. used a 20% change on the basis of an imprecision profile with the Beckman assay (3). It appears that Reichlin et al. (1) allowed clinical judgment rather than criteria to be used, with the consequence varying from embracing a change of 0.01 μg/L (a 20% change at 0.05 μg/L) to something more reasonable. In addition, most cardiac troponin assay results are reported in hundredths, and rounding issues will thus alter percentage changes. It is not clear that these authors understand these issues, which affect clinical classifications and triage decisions.

Who was or was not included in the various diagnostic groups and what criteria were used are also unclear. Even now, how many patients had increases in cTnT is unclear. The authors say that 95 (13%) of 718 patients were in the group, but only 16 had necrosis. If indeed 13% had increases due to noncoronary causes, it would have been important to comment on the specificity of rising and/or falling cTnT concentrations for coronary disease in patients with chest discomfort because noncoronary increases were nearly as prevalent as acute myocardial infarction (AMI). If only 16 patients fit and the others had typical cTnT values but alternative diagnoses, that might be less necessary. The criteria for these decisions are not stated. For example, for patients who present late after AMI and the cardiac troponin concentration is near its peak, a changing pattern might not be seen. Was this possibility taken into account? If patients did not have acute lesions according to the angiography results but had severe coronary artery disease, were they then classified as

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Nonstandard abbreviations: cTnT, cardiac troponin T; AMI, acute myocardial infarction; ACS, acute coronary syndrome; STEMI, ST-elevation myocardial infarction; ROMICAT, Rule Out Myocardial Infarction Using Computer-Assisted Tomography.