Cardiac Troponins T and I: Reproducible Discrepancies in the Clinical Setting

To the Editor:

The universal definition of myocardial infarction includes the increase and/or decrease in cardiac biomarkers, with at least 1 value greater than the 99th-percentile upper reference limit, concurrently with evidence of myocardial ischemia and corresponding clinical symptoms, electrocardiographic changes, or imaging evidence (1). Among cardiac biomarkers, cardiac troponins, including cardiac troponin I (cTnI) and cTnT, have become the gold standard. Several noncardiac etiologies for increases in cardiac troponins have been described, however (2), and discordant values for cTnT and cTnI have been encountered in the clinical setting. The aim of our study was to systematically compare a cTnT assay and a cTnI assay with regard to discrepant results. This study was conducted in accord with the World Medical Association Declaration of Helsinki (3).

We used the Architect cTnI assay (Abbott Diagnostics) and the new high sensitive Troponin T (hsTnT) assay on the Modular Analytics system (Roche Diagnostics) to make 9004 simultaneous cTnI and cTnT measurements on 3995 patients and then analyzed the data.

Because we were concerned about major discrepancies, we used 0.032 µg/L as the cutoff value for both the cTnI and hsTnT measurements. After applying this cutoff to our samples, we found that 1037 samples from 664 patients had inconsistent cTnI and hsTnT results. The majority of the discrepant results were explained by minor differences near the cutoff or by differences in cardiac troponin kinetics.

To exclude minor inconsistencies, we filtered our database to retain only entries in which a result for one of the cardiac troponin assays was below the 0.032-µg/L cutoff value and the result for the other assay was >0.096 µg/L (i.e., 3 times the cutoff value). This filtering produced 128 discrepant pairs of results, from 83 cases. To minimize the possibility of measurement discordance attributable to dynamic differences or sampling errors, we examined only cases of discrepant results that were confirmed by at least one additional measurement from a separate blood sample collected during the same hospital stay. This second filtering step produced 18 cases, which we evaluated in detail.

Nine of the 18 cases had cTnI concentrations above and hsTnT concentrations below our cutoffs (Table 1, case nos. 1–9). The primary clinical diagnoses in this group were acute coronary syndrome (ACS) (n = 2), coronary artery disease without ACS (n = 4), hypertension (n = 5), atrial fibrillation (n = 1), respiratory diseases (n = 4), muscular damage (n = 2), inflammatory diseases (n = 2), type 2 diabetes mellitus (n = 3), and renal failure (n = 1). Four patients underwent coronary angiography, but discordant values had already been observed before the procedure.

Nine patients had hsTnT concentrations above the threshold and cTnI concentrations below the threshold (Table 1, case nos. 10–18). None of these patients had received an ACS diagnosis. The primary clinical diagnoses in this group were coronary artery disease (n = 3), atrial fibrillation (n = 2), renal failure (n = 5), respiratory diseases (n = 7), inflammatory disorders (n = 3), type 2 diabetes mellitus (n = 4), chest trauma (n = 1), malignancy (n = 1), and dermatomyositis (n = 1). Coronary angiography was performed in 2 patients who had marked differences in cardiac troponin values before the intervention. Two patients in this group died during the hospital stay, from respiratory failure and cardiorespiratory failure. One individual was healthy with no sign of illness. Thus, diagnoses of coronary artery disease, with or without ACS, tended to be more frequent in the high-cTnI group, whereas diagnoses of renal insufficiency tended to be more common in the high-hsTnT group, but these differences were not statistically significant (P > 0.05). When we used the 99th percentiles provided by the manufacturers (0.022, 0.009, and 0.014 µg/L for cTnI males, cTnI females, and hsTnT males and females, respectively), the cTnI values for 7 individuals in the high-hsTnT group and the hsTnT values for 2 individuals in the high-cTnI group were below this cutoff.

Increases of cardiac troponins in conditions other than ACS have been well established (2); however, the discrepancies between cTnT and cTnI are less well documented and understood. Differences in cTnT and cTnI kinetics due to variations in clearance rates, especially in patients with renal failure, can be a possible cause (4). Furthermore, the degradation of cardiac troponins to antigenic structures that alter analytical detection also may play a role. Recently, autoantibodies against cardiac troponins with possible negative (interfering) or positive (stabilizing) effects on troponin measurements have been described. In one study, 11% of individuals with cardiac troponin antibodies had antibodies directed against both cTnT and cTnI (5). Hence, such autoantibodies can affect cTnT measurements, cTnI measurements, or both. Because

1 Nonstandard abbreviations: cTnI, cardiac troponin I; hsTnT, high sensitive Troponin T; ACS, acute coronary syndrome.
we were unable to identify a common clinical denominator in the high-hsTnT group or the high-cTnI group, we suspect that autoantibodies directed against cardiac troponins contributed to the severely discrepant cTnI and hsTnT measurements in our patients, but we cannot prove this hypothesis owing to the retrospective study design. Irrespective of the mechanisms involved and despite their rare occurrence, the differences in cTnI and hsTnT values of this magnitude that we obtained with these reliable assays were unexpected. It therefore might be helpful to confirm clinically equivocal increases or unexpectedly typical results obtained for one cardiac troponin by measuring the other.

**Author Contributions:** All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

**Authors’ Disclosures of Potential Conflicts of Interest:** No authors declared any potential conflicts of interest.

**Role of Sponsor:** The funding organizations played no role in the design of study, choice of enrolled patients, review and interpretation of data, or preparation or approval of manuscript.

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Previously published online at DOI: 10.1373/clinchem.2010.151241