Stressing the Utility of High-Sensitivity Cardiac Troponin Testing in Patients with Possible Cardiac Ischemia

Peter A. Kavsak

Strategies to rule out myocardial infarction (MI) in the emergency department include stress test echocardiography, electrocardiography, and assessment of cardiac biomarkers such as troponin I and T (1). The potential for new high-sensitivity cardiac troponin testing to simplify and expedite these rule-out protocols is of great interest. Is all the hype justified? Or are we placing unreasonable expectations on a single laboratory test?

There are indeed data indicating that an undetectable or low high-sensitivity cardiac troponin concentration alone at presentation might be useful to rule out MI. Recent data, however, suggest that the addition of other tests may improve the performance and be even more cost-effective compared to high-sensitivity cardiac troponin alone (2, 3). As a laboratory professional, this is welcome news as one has to wonder if the amount of stress placed on a single test, at a single time point, at such low concentrations imposes unrealistic expectations on the test performance (4). Ruling out MI, after all, is only one of the many conditions that physicians are concerned about when patients present with symptoms suggestive of acute coronary syndrome (ACS). In fact, if high-sensitivity cardiac troponin alone is not sufficient for ruling-out MI among patients with ACS, is there any utility for this test in ruling-out or ruling-in cardiac ischemia?

In this issue of JALM, Limkakeng et al. (5) explore this topic by measuring high-sensitivity cardiac troponin T (hs-cTnT) before and 2 h after an exercise stress test in a well-characterized population suspected of having ACS, with cTnT (4th generation) <100 ng/L before the stress test. In their study population of 317 patients, only 26 patients (8%) were positive for ischemia by exercise stress echocardiography, and there were only 8 patients who had a composite cardiac outcome (i.e., any revascularization, MI, or death) within 90 days of the index visit (5). Three major findings from this work are evident: (a) patients with exercise stress-induced cardiac ischemia had higher baseline and 2-h concentrations of cTnT (4th generation) than patients without ischemia, but the majority of patients with ischemia had hs-cTnT concentrations below 14 ng/L (99th percentile cutoff); (b) the change in hs-cTnT concentrations from baseline to 2 h after the stress test was not significant in either group; (c) using the limit of the blank (i.e., hs-cTnT <3 ng/L) at baseline to rule out ischemia would miss 8 patients (or 30% of the 26 patients) who were positive for cardiac ischemia and would miss 2 patients (or 25% of the 8 patients) who had a composite cardiac outcome at 90 days (5).
The findings of Limkakeng et al. add to the growing body of evidence that high-sensitivity cardiac troponin concentrations are higher in patients with stress test–induced cardiac ischemia and that short-term changes in their high-sensitivity cardiac troponin concentration are not necessarily evident after the stress test (6–8). This finding should not be extended to individuals who participate in more vigorous endurance exercise where changes in concentrations for high-sensitivity cardiac troponin and other biomarkers have been observed (9). Rather, these findings support the concept that minor differences in high-sensitivity cardiac troponin concentrations are apparent in individuals positive vs negative for cardiac ischemia alone. Importantly, these concentration differences are for the most part small and may well be within the expected long-term analytical variation of the assay (10). Furthermore, the incorporation of additional variables and tests in conjunction with high-sensitivity cardiac troponin may be required to identify those patients with cardiac ischemia (8).

It would also be inaccurate to state that changes in high-sensitivity cardiac troponin concentrations never occur after cardiac stress tests (6, 11); however, there are larger issues with respect to standardization that may have a more marked influence over the results (e.g., variation in the protocol, blood collection and time for collection, cardiac troponin assay, and/or type of stress test). In fact, different combinations of laboratory tests and blood sampling protocols might be able to identify patients with inducible cardiac ischemia or injury (12, 13).

For laboratories offering high-sensitivity cardiac troponin testing, there are reports of improved utilization of services within the hospital and even a reduction in cardiac stress testing since its implementation (14). These are exciting times, but it is unlikely that serial high-sensitivity cardiac troponin measurements alone will replace all stress testing in low-risk chest pain patients. In this regard, a recent study using biomarkers to characterize a low-risk group of patients in the emergency department identified that stress testing further reduced the rate of cardiac rehospitalization (another important variable when considering preventative actions) (15). High-sensitivity cardiac troponin testing has for the most part reduced laboratory professionals’ anxiety on analytical performance issues; but it is important to stress that no test is perfect or applicable in every setting. We need well-conducted studies to continue defining and refining the role of high-sensitivity cardiac troponin testing outside of MI diagnosis, especially if want to keep the anxiety (stress) low.

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