value of hs-cTnT to rule out myocardial infarction in chest pain patients in the emergency department. After investigating 14,636 patients who sought medical attention for chest pain, the investigators concluded that patients with chest pain who have an initial hs-cTnT level of <5 ng/l and no signs of ischemia on an electrocardiogram (ECG) can be safely discharged directly from the emergency department. This work is very meaningful for relieving medical burden.

However, the original study did not mention a very common issue—the duration of the onset of chest pain. Although the time of the first detectable low-level elevation of hs-cTnT has become shorter compared with conventional troponin T, it still needs 90 to 180 min after the onset (3). This means that within about 1.5 to 3 h after the onset of chest pain, the hs-cTnT level may be undetectable even if the patient is having a myocardial infarction. Correspondingly, in the original study, 15 patients with undetectable hs-cTnT and no signs of ischemia on the ECG had a final diagnosis of myocardial infarction, of which 13 patients had hs-cTnT <5 ng/l within 3 h after the onset of chest pain, and 11 of the 13 patients were found to have hs-cTnT elevation after 3 h (2). Therefore, we presumed that the negative predictive value for myocardial infarction with undetectable hs-cTnT within 3 h after the onset of chest pain was much lower than what the original study reported. Given a lot of patients with chest pain are going to the emergency department within 3 h (4), the low negative predictive value of hs-cTnT might render a number of missed diagnoses. As a consequence, we considered that the conclusion of the original study was too arbitrary, which might inadvertently mislead clinicians into making mistakes.

Besides, a diurnal hs-cTnT rhythm was detected by Klinkenberg et al. (5). The diurnal variation of hs-cTnT was characterized by peak concentrations during the morning hours (by 08:30 h), gradually decreasing values during the daytime (until 20:30 h), and rising concentrations during the nighttime (until 08:30 h the next day) (5), which might also affect the accuracy of hs-cTnT on predicting myocardial infarction.

In conclusion, we think the utilization of hs-cTnT should be combined with the duration of the events and the diurnal hs-cTnT rhythm.

We read with great interest the recent publication by Bandstein et al. (1), and congratulate the authors on their thought-provoking results. If the findings are substantiated, then such an approach could have a major impact on the resources and time required to investigate patients with possible cardiac chest pain. The conclusion is emphatically worded: “All patients with chest pain who have an initial hs-cTnT level of <5 ng/l and no signs of ischemia on ECG [electrocardiogram] have a minimal risk of MI [myocardial infarction] or death within 30 days and can be safely discharged directly from the ED [emergency department].” We therefore ask the authors whether they believe that such an investigative approach is ready for widespread international uptake without further external validation using robust recruitment and follow-up processes? The impressive size of the study was achievable only by making a number of methodological compromises that we shall discuss in the following text.

First, this was an observational trial, and no patients were actually discharged by virtue of their findings. In fact, at least 21% were hospitalized using...
unknown criteria, many for as long as 4 to 5 days (mean length of stay was 1.5 days), where it’s likely that they underwent further investigation and risk modification despite an initial single negative troponin test. One must assume hospitalization resulted in at least some element of risk mitigation.

Furthermore, Bandstein et al. (1) report that 89% (n = 1,704) of those with an initial troponin <5 ng/l had a second test. The total “low-risk population” who had serial troponin tests was 1,917 patients. Thus, of the 8,907 with an initial troponin <5 ng/l, only 19% (n = 1,704) had serial troponin testing? If correct, this practice is inconsistent with either the European Society of Cardiology or American Heart Association/American College of Cardiology guidelines. Were many of the initial troponins ordered inappropriately for clinical scenarios later not considered to be consistent with acute coronary syndrome?

Of patients with a second troponin test performed, 3% (44 of 1,704) of levels were elevated. If not an acute MI (AMI), what were their diagnoses? And, if the 3% elevated second troponin rate was applied to the single troponin low-risk cohort, an additional 210 patients may have had an elevated second troponin. Without a second troponin level, how can it be claimed that an elevation wasn’t present? By not using a standard AMI evaluation, is it possible that missed AMI occurred and were not found upon follow-up simply because the patient didn’t die? Further, 39 patients were diagnosed with MI by 30 days, implying a 2% (39 of 1,917) event rate. If this event rate is also applied to the low-risk population with a single troponin level, it is possible that as many as 140 Mls were missed simply because the patients weren’t tested nor dead in 1 year.

Ultimately, the suggested approach needs the further support of an interventional trial with accurate follow-up and in which data are collected to measure the effect of the investigators’ recommendation. Until this consideration is validated, the “one and done” troponin strategy should only be considered as hypothesis generating.

*Louise Cullen, MB, BS  
Martin Than, MB, BS  
W. Frank Peacock, MD

*Emergency Medicine  
Royal Brisbane and Women’s Hospital  
Herston  
Brisbane, Queensland 4029  
Australia  
E-mail: louise-cullen@bigpond.com

http://dx.doi.org/10.1016/j.jacc.2014.04.061

REFERENCE

REPLY: High Sensitivity Cardiac Troponin T: Testing Time Is Also a Learning Time

We would like to express our gratitude to Dr. Liu and colleagues and Dr. Cullen and colleagues for their letters regarding our recently published paper (1). Firstly, we do agree that our findings need to be validated in other settings than a university hospital, with a different diversity of ethnicity, socioeconomic status, and prevalence of cardiovascular disease.

All patients who were included in our study had chest pain, an electrocardiogram (ECG) recorded, and at least 1 troponin level measured (1). To our knowledge, troponins are not used for any other reasons than to confirm or to exclude myocardial ischemia. In addition, all patients had a clinical assessment made, which we believe is common practice. Occasionally, patients were assessed clinically after the troponin level was available, and an explanation for the chest pain other than a myocardial infarction (MI) would lead to a discharge home. We believe that this is in line with how patients with chest pain are assessed in most emergency departments (ED).

Seventy-seven percent of admitted patients went home the same or the next day. Naturally, diagnoses such as pneumonia, pulmonary embolism, or atrial fibrillation may have necessitated longer hospital stays. Our primary aim was not to investigate risk mitigation in admitted versus discharged patients. We believe that exercise tests, stress echocardiograms, or coronary angiograms by themselves have no impact on prognosis. We do acknowledge that there may have been patients discharged who may have had a second troponin >14 ng/l if measured. However, the risk of all-cause mortality was not higher in patients discharged versus admitted, and there were only 2 cardiovascular deaths within 12 months in 8,907 patients with troponins <5 ng/l, which indicates an excellent long-term prognosis.

In a random sample of 100 patients, the mean time to measurement of troponins was 2.5 h. Thus, most patients had their first troponin level evaluated...