If a Troponin Falls in a Forest but No One Measures It, Does It Really Matter?

A recent morbidity and mortality conference at my institution discussed the care of an elderly patient with multiple comorbidities for a noncardiac surgical procedure. Unfortunately, despite excellent perioperative care, the patient died of a perioperative myocardial infarction (PMI) in the postanesthesia care unit. Hypotension and marked ST segment elevation on the postoperative electrocardiogram left no doubt about the etiology of the patient’s death. However, for the vast majority of patients, the diagnosis of myocardial injury and infarction is not so obvious, and the role of minor elevations in cardiac biomarkers is unclear. In this issue of Anesthesiology, Levy et al. examine the value of creatine kinase MB-fraction and cardiac troponin (cTn) as independent predictors of all-cause mortality or a major cardiovascular event over the year after surgery. The meta-analysis focuses on patients undergoing noncardiac surgery with outcomes assessed by adjudicators blinded to cardiac biomarker values. They show that an increased postoperative creatine kinase MB-fraction or cTn is associated with a six-fold increased risk of death in the first year after surgery. Complicating the matter, however, is that only 14% of patients who experience a PMI will have chest pain, and only 53% of patients will have clinical signs or symptoms. That leaves a large group of patients with asymptomatic PMI who are at an increased risk of earlier mortality.

This lack of symptoms in the postoperative patient is the crux of the problem and begs the important questions: Should we be testing asymptomatic postoperative patients for cardiac biomarker release? If the answer is no, then is there a patient risk index that indicates when such a level of increased vigilance is warranted? What level of biomarker release warrants patient intervention? What investigations or therapies should be initiated if there is an abnormal result? And, even more problematic, what should we tell the patient and family about a normal or abnormal result? The Joint Task Force of the European Society of Cardiology/American College of Cardiology for the Redefinition of Myocardial Infarction still defines PMI as a combination of symptoms, electrocardiogram changes, and biomarker elevation. Yet, most patients with increased postoperative cardiac biomarkers experience myocardial infarction, regardless of electrocardiogram changes or symptomatology, which, in the presence of residual anesthesia, analgesics, and possible intubation with sedation, is not surprising. More important, state-of-the-art biomarkers are able to detect muscle damage earlier and with sensitivity down to the detection of a single molecule of troponin.

**Should We Be Testing Asymptomatic Postoperative Patients for Cardiac Biomarker Release?**

The answer most likely lies in specific groups of patients, rather than the population as a whole. A wide variability exists in the release of biomarkers, depending on factors such as patient comorbidities, type of surgery, preexisting cardiovascular disease, and genetics. A possible scenario, well elaborated on in a recent commentary by Archan et al., could be to come up with a risk score that determines, according to a pretest probability, (1) whether a patient needs to have a cardiac biomarker tested and (2) what biomarkers (such as a natriuretic peptide, C-reactive protein, interleukin-6, or cTn) or genetic tests should be included in the risk score.

**What Level of Biomarker Release Warrants Patient Intervention?**

Currently, the technology does not exist to differentiate between myocardial ischemia (i.e., membrane instability or release of cardiac biomarkers from the cytosol) and myocardial infarction (i.e., cell necrosis) in real time. Kim et al. showed a dose-response relationship between cTn concentration and mortality—the more cTn released, the more likely a patient will do poorly. Understanding the release of cardiac biomarkers on a continuous scale is important from a mechanistic point of view, but for a clinician, it is more important to know when to intervene.

This makes establishing a threshold problematic, which was already highlighted in this issue’s study; table 2 shows 17 studies with 13 different thresholds at which troponin predicts an increased risk of early mortality. However, with more and more sensitive biomarkers, at what point do we reach a threshold above which a patient is not adversely affected?
What Investigations or Therapies Should Be Initiated If There Is an Abnormal Result?

Levy et al. suggest in-hospital management strategies for patients with PMI (e.g., increased vigilance, monitoring, and specialized care units) and prophylactic interventions for patients once discharged from the hospital (e.g., aspirin, ACE inhibitors, β blockers, and statins). The investigators are currently conducting a large, prospective, multicenter study with the aim of enrolling 40,000 patients to examine the predictive value of cTn on mortality and, more important, to determine thresholds at which patients are at increased risk of adverse events. They are to be commended for this extraordinary undertaking, but what we still need are prospective studies to ascertain whether any intervention in the perioperative period can reduce the incidence and severity of PMI and the consequences of the myocardial infarction.

In conclusion, Levy et al. presented convincing data to support the value of postoperative cardiac-biomarker measurement in predicting 1-yr all-cause mortality. In addition, their metaanalysis shows that cTn is a more sensitive, specific biomarker than creatine kinase MB-fraction for predicting myocardial injury in patients undergoing noncardiac surgery. Future studies are needed to examine whether interventions could be successful in reducing the amount of myocardial damage, thereby reducing early and late mortality.

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References