CHOOSING WISELY®: THINGS WE DO FOR NO REASON

Creatine Kinase-Myocardial Band for Chest Pain and Suspected Acute Coronary Syndrome

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The “Things We Do for No Reason” (TWDFNR) series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent “black and white” conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CASE PRESENTATION

A 45-year-old man with medically controlled hypertension and a 40-pack-year smoking history presents to the emergency room complaining of intermittent chest pain for several days. He first noticed a “sharp, knifelike” sensation in the center of his chest when he reached for a glass in his kitchen a few days ago. The pain lasted for 30 seconds and resolved spontaneously. Since this time, he has had 2 subsequent episodes unrelated to exertion or rest. His physical exam is unremarkable, except for a body mass index of 29. An initial electrocardiogram shows no ischemic changes and no evidence of prior myocardial infarction.

He is currently chest-pain-free and admitted to the inpatient telemetry floor. Is ordering serial sets of creatine kinase (CK), creatine kinase-myocardial band (CK-MB), and troponin the most high-value method to evaluate him for acute coronary syndrome (ACS)?

WHY YOU MIGHT THINK CK-MB TESTING IS HELPFUL

CK-MB has been used for 4 decades in the diagnostic evaluation of patients with chest pain and suspected ACS. Despite the advent of a more sensitive and specific test for myocardial injury—the cardiac troponin—nearly 3 decades ago, 75% of US clinical pathology laboratories perform both CK-MB and troponin assays, suggesting that many US physicians continue to order both tests in evaluating patients with chest pain.1 There are several clinical scenarios in which physicians generally regard CK-MB testing as useful in addition to troponin. These scenarios include CK-MB testing (1) for the diagnosis of ACS in special patient populations, like those with acute or chronic renal disease, who are thought to have chronically elevated troponins as a function of their renal disease and not myocardial disease; (2) for additional prognostic information in the setting of a minimally elevated troponin; (3) for the detection of reinfarction, in which troponin is thought to be inferior to CK-MB; and (4) for estimation of infarct size.

WHY CK-MB TESTING ADDS NO ADDITIONAL VALUE TO TROPONIN TESTING IN DIAGNOSIS OF ACS

Is CK-MB More Accurate Than Troponin in the Diagnosis of ACS?

Numerous studies have established that CK-MB is not as specific as troponin for detecting myocardial injury and will result in more false-positive tests.2,3 CK-MB can be elevated in the setting of acute muscle injury (in 60% of patients), as well as chronic muscle disease (in 80% of patients). In contrast, troponin (I or T), a protein exclusively found in cardiac myocytes, is only elevated due to myocardial injury and is therefore more specific for ACS than CK-MB.2 In a study of patients with both skeletal muscle injury and suspected ACS, the respective specificities of troponin and CK-MB were 94% and 63%, respectively.3 In special patient populations, like those with chronic renal disease, both troponin and CK-MB can be elevated in the absence of ACS; the mechanism for cardiac enzyme elevation is unclear. Importantly, there is no evidence to support the incremental value of CK-MB over troponin alone in this population.4,5 Despite chronic troponin and CK-MB elevations in some patients with chronic renal failure, it is still possible for these patients to have acute changes from baseline that represent myocardial injury. In these patients, cardiac biomarker results must be considered in the context of other clinical features (ie, the patient history, physical exam, and electrocardiogram findings) in making or excluding the diagnosis of ACS.

Does CK-MB Diagnose ACS More Rapidly Than Troponin?

In patients with myocardial injury, both troponin and CK-MB typically are detectable in the bloodstream...
within 2 to 4 hours of symptom onset and peak within 12 to 18 hours; neither has been established as a more rapid biomarker for the detection of myocardial infarction. Furthermore, a systemic review of point-of-care cardiac enzyme testing reported that troponin and CK-MB had similar positive and negative predictive values for diagnosing acute myocardial infarction (AMI) within the first 6 hours of symptom onset.

**Does CK-MB Add Prognostic Information in Addition to Troponin in Patients With ACS?**

If CK-MB adds additional prognostic information in patients with suspected ACS and normal troponin values, then we should continue using it. Based on several large registries of patients with chest pain and/or ACS, approximately 8% to 28% of patients have discordant CK-MB and troponin values, where 1 value is normal while the other value is abnormal. Several studies have examined whether an abnormal CK-MB, in the setting of a normal troponin, offers additional prognostic information in comparison with normal values of both biomarkers.

In the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress AVerage outcomes with Early implementation of the American College of Cardiology/American Heart Association guidelines) registry, a cohort of 29,357 patients with ACS was retrospectively divided into 4 groups: (1) patients with abnormal CK-MB (CK-MB+) and troponin (Tn+) values (ie, “double-positive” group); (2) patients with normal CK-MB (CK-MB−) and troponin (Tn−) values (ie, “double-negative” group); (3) patients with CK-MB+/Tn−; and (4) patients with CK-MB−/Tn+. Among the 4 groups, the rate of in-hospital mortality was not significantly different between CK-MB+/Tn− (group 3) and patients with double-negative (ie, normal) values. However, the presence of an abnormal troponin, regardless of CK-MB status, was associated with an increased risk of in-hospital death. The authors concluded that “in clinical practice, there is little advantage of simultaneous CK-MB and cTn testing for risk stratification in patients with high-risk ACS presentations.”

In addition to the CRUSADE registry, 2 smaller registries, involving different patient populations, have reported similar results. An analysis of the Global Registry of Acute Coronary Events (GRACE) registry of 10,719 patients with ACS reported no difference between CK-MB+/Tn− patients and double-negative patients with respect to in-hospital mortality, as well as 6-month mortality. In the Internet Tracking Registry of Acute Coronary Syndromes (ITRACS) registry, 8769 patients presenting to emergency rooms with chest pain were analyzed. A minority (18.4%) were ultimately diagnosed with ACS. The authors found that an abnormal troponin, irrespective of CK-MB status, was associated with an increased in-hospital mortality rate. In-hospital death rates were similar between CK-MB+/Tn− and double-negative patients.

In summary, troponin offers important prognostic information regardless of the CK-MB result.

**Is CK-MB More Accurate for Diagnosing Reinfarction (Repeat Infarction in Patients With Recent Acute Myocardial Infarction)?**

Whereas CK-MB typically returns to normal within 2 to 3 days, troponin can be elevated for up to 5 to 14 days. Consequently, some have argued that CK-MB may be more accurate in detecting reinfarction. In the only study to date comparing CK-MB and troponin patterns in 9 patients with reinfarction, the rise and fall of both biomarkers were similar. Furthermore, those patients with persistently elevated troponin values from baseline (after the initial infarction) experienced a significant rise in troponin with reinfarction.

**Is CK-MB More Accurate for Estimating Infarct Size?**

Some have argued that a peak CK-MB value is more accurate than a peak troponin value for estimating infarct size. However, 2 comparative studies have reported that troponin is as good as and possibly superior to CK-MB for estimating infarct size. In a study of 65 patients with AMI, a single troponin T measurement obtained 72 hours after coronary care unit admission significantly correlated with peak CK-MB in estimating infarct size (r = 0.76, P < 0.001), using single-photon emission computed tomography imaging as the gold standard. In a similar study of 37 patients with AMI, a single troponin T value had a significantly higher correlation with infarct size than serial and peak CK-MB. Unlike CK-MB, the ability of troponin T to predict infarct size was independent of coronary reperfusion.

**What do Guidelines and Thought Leaders Say About Using CK-MB?**

The most recent Third Universal Definition of Myocardial Infarction states that troponin is the “preferred (cardiac) biomarker-overall and for each specific category of MI,” and that CK-MB should be considered an “alternative” if troponin is not available. Several national guidelines endorse troponin as the primary cardiac biomarker for diagnosis of ACS. Finally, several groups have called for the elimination of CK-MB. In 2008, 2 experts in the field of cardiovascular laboratory medicine argued that CK-MB test adds “little to no incremental information” but does add “cost and...confusion.” Their institution, the Mayo Clinic, removed CK-MB from their cardiac biomarker panel without any “discernible negative effects on clinical care.” In a more recent publication, a group of authors from the departments of pathology and laboratory medicine of 7 major US academic medical...
centers identified CK-MB as part of a “top 10” list of antiquated tests that “no longer provide value.”

WHAT YOU SHOULD DO INSTEAD: ORDER TROPI NON IN ALONE

In all cases where a patient presents with chest pain and/or symptoms concerning for ACS, we recommend that troponin be ordered alone. CK-MB is no longer necessary as an additional test. As healthcare providers, we aim to provide the highest healthcare value—defined as clinical benefit divided by cost. Routine ordering of CK-MB offers essentially no benefit but does come at a significant cost. Each CK-MB costs roughly $40 to $50 a test. If CK-MB is used in approximately 2 million patients annually diagnosed with ACS and a proportion of the 17 million patients annually evaluated for chest pain, the potential cost, without clear benefit, is substantial.

RECOMMENDATIONS

1. In patients suspected of having ACS, troponin should be measured in lieu of CK-MB and serial CK testing to evaluate for myocardial injury.
2. CK-MB tests should not be ordered routinely for patients suspected of having ACS. Hospitals should remove CK-MB from pathology lab catalogs or require specific permission to order it.

CONCLUSION

Because CK-MB, as compared to troponin, is detectable in the bloodstream in a similar timeframe, adds no additional prognostic information, estimates infarct size no differently, and appears to diagnose reinfarction no differently (Table 1), the authors believe that CK-MB should no longer be ordered for patients with suspected ACS, unless ordering troponin is not an option. Ordering CK-MB and serial CK for the evaluation of ACS is a “Things We Do for No Reason.”

Disclosures: Nothing to report.

Do you think this is a low-value practice? Is this truly a “Things We Do for No Reason?” Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other “Things We Do for No Reason” topics by emailing TWDFNR@hospitalmedicine.org.

References