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Occam, Hickam, troponin and appropriate use - A commentary on the clinical efficacy of a frequently requested and useful lab test

I recently attended on the cardiology consult service of an academic medical center. It involved working with a talented team of medicine interns, residents, and cardiology fellows in assisting colleagues caring for patients with a variety of cardiovascular issues. These consults were for patients not admitted to a cardiovascular service and came from essentially every medical and surgical specialty. At the presentation of each new patient, it was helpful to know the reason for the consult. For approximately 20% of the consults the reason was that the patient had an elevated troponin level. Most of these patients did not have an acute coronary syndrome. The focus of this commentary is appropriate use of current generation troponin tests. Acute coronary syndromes due to coronary plaque rupture and thrombotic occlusion are a major cause of morbidity and mortality and troponin assays are helpful in detecting them.1 Troponin is a protein in striated muscle that regulates excitation and contraction, and consists of three molecules (C, I, and T.) Troponin I and T are specific to cardiac tissue, and when released in the bloodstream are markers for myocardial injury or stress.1-3 For patients with signs and symptoms of myocardial ischemia, a troponin assay aids in early detection of acute coronary syndromes and saves lives.1-3 Per the Third Universal Definition of Myocardial Infarction global task force, troponin is now the biomarker of choice when evaluating for classic myocardial infarction (type 1) that is due to acute occlusion (partial or full) of a coronary artery.2 First generation troponin assays were highly predictive of acute coronary syndromes and clinicians were conditioned to make that diagnosis with any troponin elevation. This no longer holds true. Now in their fourth or fifth generation, troponin assays yield elevated levels for a number of conditions besides acute coronary syndrome.2-5 In a series of 12,553 hospitalized patients using a current assay, over 40% with an elevated troponin did not have a thrombotic coronary event, and the positive predictive value for diagnosing acute coronary syndrome was 56%; with a troponin level of 1.0 ng/ml or lower it was 48% or less.4 When not due to decreased renal clearance, troponin elevations may be an indication of cardiac myocyte strain or injury without thrombotic coronary occlusion, when the heart is an "innocent bystander" during a severe non-cardiac condition.3,5 This type of acute injury to the myocardial cells is designated as a type 2 myocardial infarction (myocardial necrosis where a condition other than coronary artery disease contributes to an imbalance between myocardial oxygen supply and/or demand 2); it is anticipated that type 2 myocardial infarction will be added as an ICD-10 code in October, 2017. Proposed mechanisms of cardiac injury in these patients include circulating inflammatory cytokines and elevated catecholamines.5 Conditions that may cause troponin detection with current assays include tachycardia (from essentially any cause), hypotension, hypertension, strenuous exercise (e.g. marathon runners), sepsis, renal failure, pulmonary embolus, heart failure, pericarditis, polymyositis, rhabdomyolysis, burns, cardiac trauma, respiratory failure, ventricular hypertrophy, drug toxicity (including cancer chemotherapy) and neurally-mediated sympathetic activation.2-5 Advanced age may be added to this list; one recent study found that 41% of patients over age 70 presenting to the ED in whom both acute coronary syndrome and other known non-thrombotic coronary syndrome causes were ruled out had troponin elevations.6

This relatively new phenomenon of elevated troponin levels in patients not having an acute coronary syndrome may lead to overlooking the appropriate diagnosis and thus inappropriate treatments, increased costs of tests and services, increased length of stay, and unindicated procedures.7 For example, when patients with gastrointestinal bleeding or intracranial hemorrhage have elevated troponin results, treatment for acute coronary syndrome with antiplatelet or anticoagulant medication is antithetical to their primary diagnosis. Likewise, giving a beta blocker for a positive troponin to a hypotensive

patient in septic shock may be detrimental. Clinicians dealing with an abnormal troponin result, even when the patient's presentation is not consistent with coronary thrombosis, often feel compelled to order additional cardiac tests and services, adding to the overall cost of care. Elevated troponin levels in such patients may lead to invasive cardiac procedures. In a study of patients with an elevated troponin and subsequent normal coronary angiograms, 28% had tachycardia, 10% pericarditis, 5% heart failure, 10% strenuous exercise, and 47% had no clear precipitating event.8

The practice of obtaining a troponin level before assessment of the patient deserves special mention. It runs counter to what most of us learned in our training, and contrary to good medical practice. It remains advisable to take a history, perform a physical examination, and then order appropriate studies. Indiscriminate troponin testing is an international finding: in a study from the U.K. at a National Health Service hospital, 28% of the troponin requests were deemed "completely irrelevant." 7 These were ascribed to "tick box" practice in the triage setting prior to a clinical assessment. When educational interventions were done on how to improve troponin requests and when to do so, this percentage decreased to 15%. In a busy emergency department, with its mandates to both turn patient census over quickly, and to not miss a patient having an acute myocardial infarction or unstable angina, it is understandable why indiscriminate ordering of a troponin level may be favoured. Also, in intensive care units a troponin may be requested for a sick patient who is poorly communicative.3 Yet in our pursuit of quickly recognizing acute coronary syndrome, giving patients that diagnosis when they do not have it is an undesired outcome. The routine practice of requesting a troponin as part of a bundled lab set should be re-examined.

A strategy for improved troponin use is to perform a history (with attention to cardiac risk factors), a physical exam, and a review of the ecg in order to put abnormal troponin results in the appropriate clinical context and avoid diagnostic confusion and malfeasance.2-5 In some cases an echocardiogram to detect left ventricular wall motion abnormalities adds additional value. I offer three examples of patients with positive troponin results due to non-thrombotic causes where this strategy was helpful: 1) a 55 year old man with colon cancer presented to the emergency department with dizziness after two days of severe bleeding per rectum. He had sinus tachycardia, hypotension, and his hematocrit was 16%; 2) A 36 year old woman being treated for acute myelogenous leukemia on the oncology service developed atrial fibrillation with a fast ventricular response; her platelet count was severely low; the electrocardiogram did not suggest infarction or ischemia; 3) An 86 year old man was admitted to the intensive care unit with a temperature of 400 Celsius, septic shock, and renal failure. Cardiology consultation in such cases, if desired, may indeed aid the referring caregivers in sorting out the cause of the troponin elevation and can provide not only a clinical but also an educational service. It is recognized that an elevated troponin level in patients not having an acute coronary syndrome is an indication of illness severity and predicts mortality. This is an ongoing area of research.2-5

In clinical medicine we often like to refer to Occam's razor and the utility in finding one cause or diagnosis that accounts for the patient's presenting signs and symptoms. There will always be dynamic tension between Occam and Hickam, who stated "patients can have as many diseases as they……please."9 The concern here is indiscriminant ordering of today's highly sensitive troponin assays dulls Occam's razor and renders it sorely in need of sharpening. We should avoid "check the box" or "click on the test" ordering of troponin levels without first doing an assessment of the patient. If however an indiscriminate troponin assay is abnormal it behooves us to put it in clinical context before ordering unnecessary tests, medicines, and procedures. When elevated troponin levels are present in patients admitted for non-cardiac reasons, and the probability of myocardial ischemia due to coronary thrombosis is low, evaluation and treatment should be directed towards the primary diagnosis. We, and our patients, can ill afford to do otherwise.

Speaker Biography

Gregory D. Chapman, MD, FACC is a Professor of Medicine/Cardiovascular Disease at the University of Alabama at Birmingham. He has published commentaries and research papers in The New England Journal of Medicine, Circulation, the American Journal of Cardiology, and the American Journal of Medicine. He is now in his third decade of practice as a cardiologist, with experience in academic and private practice settings. His interests include STEMI recognition and treatment, as well as the diagnosis of acute coronary syndromes and their mimics. In addition to an active clinical role, he enjoys teaching residents in internal medicine, emergency medicine, and cardiology.

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