Lown Right Care: *Reducing Overuse and Underuse*

The Overdiagnosis of Myocardial Infarction

Andy Lazris, MD, and Alan Roth, DO
Patient perspective by Helen Haskell and John James

CASE SCENARIO

A 72-year-old man with a history of well-controlled hypertension, stage 3a chronic kidney disease, supraventricular tachycardia, and gout went to the emergency department (ED) after nearly fainting while mowing his lawn. After a long wait, the ED staff took blood, started intravenous fluids, and obtained an electrocardiogram (ECG). A few hours later, the ED physician informed the patient that results of the blood test showed a slightly elevated troponin level, which could suggest a heart attack. The patient told the physician that he felt fine other than still being a bit dizzy; he asked why the blood test was done and what was going to be done about his dizziness. The physician explained that the laboratory tests were routine for someone his age after a near-fainting spell. The physician also told the patient that he would need to stay in the hospital for two more troponin tests and an echocardiogram. Several hours later, a cardiologist informed the patient that he may have had a small heart attack based on the troponin levels but that the ECG and echocardiogram results were normal. The patient was admitted to the hospital overnight for further testing. He was relieved that the heart attack was discovered, but when he asked about the cause of his dizziness, he did not receive any answers.

CLINICAL COMMENTARY

In her book *The Danger Within Us,* medical journalist Jeanne Lenzer discussed the introduction of highly sensitive blood tests in the late 1970s to detect even very small myocardial infarctions (MIs).[1] Previously, MIs were diagnosed by a combination of symptoms, ECG changes, and elevations in creatine kinase. With the new, more sensitive tests, MIs could be diagnosed in patients without any classic symptoms or ECG abnormalities. The case fatality rate of MIs declined markedly at that time, but the mortality rate remained consistent. This was due to clinicians diagnosing more MIs, thus increasing the denominator (total MIs) without changing the numerator (MI deaths).

Today, many EDs measure troponin levels even in patients without signs or symptoms of MIs, thus increasing the number of patients with an MI diagnosis.[2] In one study, 27% of patients admitted to the ED received troponin testing, most of whom did not present with symptoms suggesting a cardiac diagnosis.[3]

Diagnosis of MI

Researchers and cardiologists previously thought that evaluation using only clinical and ECG criteria, followed by confirmatory echocardiography or cardiac catheterization, missed some MIs, leading to increased mortality and morbidity.[2] Troponin is a highly sensitive laboratory assay that measures myocardial injury. The introduction of troponin testing in the 1990s increased the ability of physicians to identify myocardial damage. Normal troponin values are defined as falling

ANDY LAZRIS, MD, CMD, Personal Physician Care, Columbia, Maryland

ALAN ROTH, DO, FAAFP, FAAHPM, Jamaica Hospital Medical Center, Jamaica, New York

Author disclosure: No relevant financial relationships.

Address correspondence to Andy Lazris, MD, at alazris50@gmail.com.

Lown Institute Right Care Alliance is a grassroots coalition of clinicians, patients, and community members organizing to make health care institutions accountable to communities and to put patients, not profits, at the heart of health care.

A collection of Lown Right Care published in *AFP* is available at https://www.aafp.org/afp/rightcare.

TAKE-HOME MESSAGES FOR RIGHT CARE

- Troponin levels can be elevated in the setting of chronic conditions, such as inflammatory disease, autoimmune disease, and chronic renal insufficiency, and age older than 70 years. Increased levels can also be a result of noncardiac triggers that lead to insufficient myocardial blood flow, such as pulmonary emboli, infection, low oxygen states, and running a marathon.
- When checked indiscriminately in patients without classic cardiac symptoms, the positive predictive value of troponin testing for type 1 myocardial infarction is low.
- Overdiagnosis of type 2 myocardial infarction, which is defined as reduced cardiac blood flow without coronary artery occlusion, can lead to overtreatment and unnecessary testing without improved health outcomes.

into the 99th percentile for young, healthy patients.[4] Troponin elevations in conjunction with other abnormal findings (eg, clinical, ECG, echocardiographic) are considered diagnostic of MI. Sequential increases in troponin levels over time can also help diagnose MI in the absence of other parameters.[5]

Although troponin levels are highly sensitive, they are not specific for type 1 MI, in which closure of myocardial vessels results in cardiac damage, and have very low positive predictive value in the absence of other criteria. The positive predictive value is much lower in the United States compared with the United Kingdom (16.4% vs 59.7%) due to the higher rate of troponin testing in the United States and the low pretest probability of MI in patients for whom troponin tests are ordered.[6] In fact, approximately one-fifth of patients admitted to EDs have elevated troponin levels, and most are not having a type 1 MI.[7] A type 2 MI is diagnosed in patients who meet troponin criteria for an MI but do not have obstructive coronary artery disease. The prevalence of type 2 MI diagnoses has increased with the use of troponin testing.[8]

The Prognosis for MI With High Troponin Levels

Recent evidence points to an overall reduction in mortality from MIs in the United States.[9] However, many diagnosed MIs have no associated coronary obstruction. Studies indicate that patients who present with a high baseline troponin level or with a dynamic troponin level that increases with time, but who have no obstructive disease, are not at an increased risk for poor cardiac outcomes. The overall cardiac mortality rate of these patients is no different than their matched population cohort, and outcomes are not improved with regular cardiac testing or use of drugs prescribed for secondary prevention (eg, aspirin, statins, clopidogrel).[10]

Causes of High Troponin Levels

Various conditions can cause the production of heterophile antibodies that falsely elevate troponin levels (eg, autoimmune conditions, such as systemic lupus erythematosus or rheumatoid arthritis; elevated alkaline phosphatase or bilirubin levels; hemolysis; and immune complex formation).[11,12] However, as one researcher states, the absence of obstructive coronary artery disease in the setting of high troponin levels is not a false-positive because it does represent cardiac injury.[13] But is it appropriate to label such an injury as an MI? Sepsis, pulmonary embolism, myocardial irritation, rapid heart rhythms, acute congestive heart failure, and even running a marathon can trigger dynamic changes in troponin levels and likely cause some degree of myocardial injury, without representing MI.[12,13]

Similarly, conditions such as chronic obstructive pulmonary disease, chronic renal insufficiency, and some inflammatory conditions (eg, gout, infections, cancer) can increase troponin levels.[14,15] Factors such as age older than 70 years and male sex are also associated with higher baseline troponin values, and most studies of type 2 MIs exclude people who are older or who have comorbid conditions.[16]

There is less knowledge about how medicines and medical interventions can affect troponin levels. In all such cases, patients can present to the ED with noncardiac symptoms, undergo troponin tests, and then be told they may have had an MI.

The Danger of Overdiagnosis

The use of a single troponin measurement with other criteria for diagnosis—so-called universal definition of MI criteria—can overdiagnose MIs because of the high prevalence of elevated troponin levels in patients who are older or who have comorbidities.[2,5] Similarly, dynamic troponin level increases can occur from benign or noncardiac conditions. This could lead to further laboratory testing to establish the stability of troponin levels, echocardiography, and sometimes catheterization. It could also lead to a diagnosis of type 2 MI, prompting a cascade of further testing and adverse emotional and physical repercussions without any proven benefit.[5]

One study found that in patients with high troponin levels, a diagnosis of type 2 MI leads to higher use of cardiac angiography (39% vs 5%) and secondary prevention, with no mortality benefit over 5 years.[8] These patients live with the burden of an MI diagnosis, which can lead to depression, insurance and job instability, unnecessary testing and treatment, increased costs, and potentially physical harm without improved outcomes.[6,12,17]

How to Address Overdiagnosis

Routine troponin measurement should be performed in the ED only as part of a clinical and ECG diagnostic process when subjective reports or objective findings suggest MI. In addition, it is important for physicians to understand that mild troponin elevations that do not increase with time in older patients or those with comorbid conditions should not be labeled as an MI. Finally, it is crucial to recognize that dynamic increases in troponin levels can result from causes as benign as intense exercise and as worrisome as a pulmonary embolism and should not all be ascribed to MIs. Physicians should avoid overdiagnosing type 2 MI when other factors that could elevate troponin levels are present, thus preventing the cascade of unnecessary testing, overtreatment, and mental and physical risk in the absence of meaningful clinical benefit.

PATIENT PERSPECTIVE

To us, this seems to be a case where the primary symptom reported by the patient (near-syncope under stress) was ignored in favor of a biased interpretation of the laboratory findings. The patient should have been told that the slight elevation in troponin level could be due to other causes besides an MI, since the ECG and echocardiogram results were normal and he had numerous medical conditions that could have contributed to such a finding. Treating this patient's evaluation as routine for someone of his age with a "fainting spell" seems to be misapplied, cookie-cutter medicine. The patient was right to ask about the cause of his dizziness.

We both have had family members who underwent this sort of cardiac testing in the ED when the undiscovered and uninvestigated

cause of their syncope was something entirely different. We presume that the ED physician in this case was exercising caution to not miss a diagnosis by ordering additional tests, but the cardiologist should have been more reassuring to the patient that the weight of evidence did not indicate that he had an MI. We both live in places where summer heat is high and prolonged. If this incident took place with that sort of backdrop, then an electrolyte imbalance or dehydration could also have been suspected. Presumably, the former possibility was ruled out by the blood tests. We also wonder if the patient's medications had anything to do with the dizziness. Did he accidentally take two doses of the antihypertensive medications? If we were accompanying this patient to the ED, we would have asked such questions.

RESOLUTION OF CASE

The patient went to his primary care physician after hospitalization. Together, they discussed the lack of prognostic value of the tests performed at the hospital and that the patient most likely did not have a heart attack or coronary artery disease. The chronic renal insufficiency, inflammatory gout, and supraventricular tachycardia, along with his age, could have accounted for the increased troponin level. The primary care physician informed the patient that the high troponin level was unrelated to the near-syncopal episode and that he may just have been dehydrated. Together, the physician and patient approached the ED director to discuss avoiding the use of troponin tests in the absence of chest pain or other relevant symptoms.

REFERENCES

1. Lenzer J. *The Danger Within Us: America's Untested, Unregulated Medical Device Industry and One Man's Battle to Survive It*. Little, Brown and Company; 2017:254-256.
2. McCarthy CP, Wasfy JH, Januzzi JL Jr. Is myocardial infarction overdiagnosed? *JAMA*. 2024;331(19):1623-1624.
3. Furmaga J, McDonald SA, Hall HM, et al. Impact of high-sensitivity troponin testing on operational characteristics of an urban emergency department. *Acad Emerg Med*. 2021;28(1):114-116.
4. McEvoy JW, Wang D, Brady T, et al. Myocardial injury thresholds for 4 high-sensitivity troponin assays in a population-based sample of US children and adolescents. *Circulation*. 2023;148(1):7-16.
5. Eggers KM, Lind L, Venge P, et al. Will the universal definition of myocardial infarction criteria result in an overdiagnosis of myocardial infarction? *Am J Cardiol*. 2009;103(5):588-591.
6. Shah ASV, Sandoval Y, Noaman A, et al. Patient selection for high sensitivity cardiac troponin testing and diagnosis of myocardial infarction: prospective cohort study. *BMJ*. 2017;359:j4788.
7. Giannitsis E, Katus HA. Cardiac troponin level elevations not related to acute coronary syndromes. *Nat Rev Cardiol*. 2013;10(11):623-634.
8. Gard A, Lindahl B, Baron T. Impact of clinical diagnosis of myocardial infarction in patients with elevated cardiac troponin. *Heart*. 2023; 109(20):1533-1541.
9. Yeh RW, Sidney S, Chandra M, et al. Population trends in the incidence and outcomes of acute myocardial infarction. *N Engl J Med*. 2010; 362(23):2155-2165.
10. Planer D, Mehran R, Ohman EM, et al. Prognosis of patients with non-ST-segment-elevation myocardial infarction and nonobstructive coronary artery disease: propensity-matched analysis from the Acute Catheterization and Urgent Intervention Triage Strategy trial. *Circ Cardiovasc Interv*. 2014;7(3):285-293.
11. Lum G, Solarz DE, Farney L. False positive cardiac troponin results in patients without acute myocardial infarction. *Lab Med*. 2006;37(9): 546-550.
12. Chaulin AM. Some common causes of false positive increases in serum levels of cardiac troponins. *Curr Cardiol Rev*. 2022;18(6): e130422203527.
13. Januzzi JL Jr, McCarthy CP. Cardiac troponin and the true false positive. *JACC Case Rep*. 2020;2(3):461-463.
14. Berger M, Emir M, Brünnler T, et al. Non-coronary predictors of elevated high-sensitive cardiac troponin T (hs-cTnT) levels in an unselected emergency patient cohort. *Clin Cardiol*. 2018;41(8): 1055-1061.
15. Akwe J, Halford B, Kim E, et al. A review of cardiac and non-cardiac causes of troponin elevation and clinical relevance part II: non cardiac causes. *J Cardiol Curr Res*. 2018;11(1):00364.
16. Wu W, Li DX, Wang Q, et al. Relationship between high-sensitivity cardiac troponin T and the prognosis of elderly inpatients with non-acute coronary syndromes. *Clin Interv Aging*. 2018;13:1091-1098.
17. Warraich HJ, Kaltenbach LA, Fonarow GC, et al. Adverse change in employment status after acute myocardial infarction: analysis from the TRANSLATE-ACS Study. *Circ Cardiovasc Qual Outcomes*. 2018; 11(6):e004528. ■