



**BRIEF ANSWERS
TO SPECIFIC
CLINICAL
QUESTIONS**

1-MINUTE CONSULT

Nolan Anderson, MD

Pediatric Residency Program,
University of Washington,
Seattle

Samuel T. Ives, MD

Division of General Internal Medicine,
Hennepin Healthcare, Minneapolis, MN;
Assistant Professor of Medicine,
Department of Medicine, University of
Minnesota, Minneapolis

Michelle D. Carlson, MD

Division of Cardiology, Hennepin
Healthcare, Minneapolis, MN; Assistant
Professor of Medicine, Department of
Medicine, University of Minnesota,
Minneapolis

Fred Apple, PhD, DABCC

Co-Medical Director, Clinical & Forensic
Toxicology Laboratory, Hennepin Health-
care/Hennepin County Medical Center;
Principal Investigator, Cardiac
Biomarkers Trials Laboratory, Hennepin
Healthcare Research Institute; Profes-
sor, Laboratory Medicine & Pathology,
University of Minnesota

Q: Should we monitor troponin up to peak value when evaluating for acute coronary syndrome?

A: No. Once the cardiac troponin concentration is higher than the 99th percentile (the upper reference limit), finding the peak value (before levels start to descend) does not help diagnose the cause of the elevation. Although the peak level has prognostic significance, continuing to follow the level after the initial set of measurements adds cost to the evaluation without providing further insight into cause, and any prognostic information gained would not change the subsequent evaluation or management, which should be driven by guidelines.¹

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DEFINITIONS

Standard practice in evaluating for possible acute coronary syndrome includes following serial cardiac troponin levels.

The Fourth Universal Definition of Acute Myocardial Infarction calls cardiac troponin levels above the 99th percentile *myocardial injury*, which is considered acute if the level rises or falls (or both).² *Acute myocardial infarction* requires acute myocardial injury plus signs or symptoms of acute myocardial ischemia or other findings. There are 5 types of myocardial infarction; here, we are mainly concerned with type 1 (caused by acute coronary occlusion) and type 2 (caused by an acute imbalance of oxygen supply and demand).

Dr. Apple has disclosed membership on advisory committees, review panels, or board of directors for Brava Diagnostics, HyTest, Instrumentation Laboratory, and Siemens.

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DISTINGUISHING THE CAUSE OF TROPONIN ELEVATION

In the workup of acute coronary syndrome, cardiac troponin levels may be elevated, but keep in mind that they can be elevated in many conditions other than type 1 myocardial infarction.

Type 1 vs type 2 myocardial infarction

Distinguishing type 1 from type 2 acute myocardial infarction is important but challenging. No clinical criteria exist to reliably tell them apart,³ and unfortunately, cardiac troponin levels (whether initial, peak, or the trend over time) cannot help to do so either.⁴ The delta value (ie, the change in cardiac troponin level in a defined time period) has been studied for this purpose; although the absolute change is more reflective of the different types of myocardial infarction than the percent change, neither can reliably distinguish between them.^{4,5}

Other causes of troponin elevation

Cardiac troponin levels can be elevated in other conditions that commonly arise in medically complex patients, eg, sepsis, acute stroke, respiratory failure, hypertensive crisis, or with some chemotherapy regimens.⁶ In some diseases, such as heart failure and chronic kidney disease, levels may be persistently elevated. Hence, trying to find a peak value in a patient with persistently elevated levels may be futile and is an inappropriate use of this biomarker.

DOES TROPONIN PREDICT ADVERSE EVENTS?

The degree of cardiac troponin elevation in myocardial infarction can indicate the extent of myocardial damage and help predict ad-

Once troponin is over the 99th percentile, finding the peak value does not aid diagnosis

verse events.^{7,8} Treatment decisions, however, should not be based on degree of elevation alone. Rather, patients should be managed with guideline-directed medical therapies, procedures, and education,¹ regardless of the degree of troponin elevation.

All patients who are diagnosed with acute coronary syndrome with elevated cardiac troponin should undergo echocardiography, which provides prognostic information similar to that of the peak troponin value, obviating the need to follow troponin levels until they peak.⁹

After acute coronary syndrome is diagnosed, and especially if confirmed with angiography, further troponin testing may confuse the clinical picture. Studies have found that although cardiac troponin levels rise after angiography or percutaneous coronary intervention, the increase is not associated with adverse events.¹⁰

■ IF SYMPTOMS RECUR

Cardiac troponin levels are often elevated in hospitalized patients experiencing recurrent symptoms after a myocardial infarction.¹¹ In this situation, the patient should be managed on the basis of ischemic symptoms, echocardiographic changes, and hemodynamic status rather than on the elevated troponin alone. Troponin rises with reinfarction, but for the initial evaluation, monitoring levels to a peak will not lead to differences in management, rendering it unnecessary in this context.

■ TESTING INCREASES COSTS

Chest pain is one of the most common presentations in the emergency department, and

costs run high for its evaluation.¹² After the first set of cardiac troponin levels has been obtained, additional measurements (including prolonged monitoring until a peak occurs) do not add useful or reliable information to the workup or change the treatment plan. Excessive troponin testing also leads to unnecessary cost, increased length of stay, and further blood draws.¹³

Addressing the issue of inappropriate troponin monitoring will help reduce unnecessary resource utilization at both the individual provider and systems levels. Love et al,¹⁴ in a study analyzing electronic medical record requests over 2 months, found that providers overrode a best practice alert (that recommended not conducting unwarranted cardiac troponin testing) 97% of the time. Further education and collaboration between emergency medicine and laboratory medicine physicians and clinical chemists is recommended to help limit overuse and misinterpretation of cardiac troponin testing.¹⁵

■ NEW TESTS DO NOT CHANGE THE MESSAGE

New troponin assays are becoming more sensitive; in practice this means that elevated values will likely be detected much sooner. Although these assays are sometimes called “high-sensitivity,” their characteristics vary, and what high sensitivity means is not clearly defined in current guidelines.

The potential for overtesting remains if providers continue to follow cardiac troponin levels after the rising or falling pattern has become apparent, particularly when a diagnosis has already been made.

After acute coronary syndrome is diagnosed, further testing may confuse the clinical picture

■ REFERENCES

- O’Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013; 61(4):485–510. doi:10.1016/j.jacc.2012.11.018
- Thygesen K, Alpert JS, Jaffe AS, et al; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol* 2018; 72(18):2231–2264. doi:10.1016/j.jacc.2018.08.1038
- Saaby L, Poulsen TS, Hosbond S, et al. Classification of myocardial infarction: frequency and features of type 2 myocardial infarction. *Am J Med* 2013; 126(9):789–797. doi:10.1016/j.amjmed.2013.02.029
- Reichlin T, Irfan A, Twerenbold R, et al. Utility of absolute and relative changes in cardiac troponin concentrations in the early diagnosis of acute myocardial infarction. *Circulation* 2011; 124(2):136–145. doi:10.1161/CIRCULATIONAHA.111.023937
- Irfan A, Reichlin T, Twerenbold R, et al. Early diagnosis of myocardial infarction using absolute and relative changes in cardiac troponin concentrations. *Am J Med* 2013; 126(9):781–788.e2. doi:10.1016/j.amjmed.2013.02.031
- Sebastian K, Wester A, Kottam A, Soubani AO. Are serum troponin levels elevated in conditions other than acute coronary syndrome? *Cleve Clin J Med* 2018; 85(4):274–277. doi:10.3949/ccjm.85a.17011
- Ohman EM, Armstrong PW, Christenson RH, et al. Cardiac troponin T levels for risk stratification in acute myocardial ischemia. GUSTO IIA Investigators. *N Engl J Med* 1996; 335(18):1333–1341. doi:10.1056/NEJM199610313351801
- Antman EM, Tanasijevic MJ, Thompson B, et al. Cardiac-specific

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- troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. *N Engl J Med* 1996; 335(18):1342–1349. doi:10.1056/NEJM199610313351802
9. **Cheitlin MD, Armstrong WF, Aurigemma GP, et al; American College of Cardiology; American Heart Association; American Society of Echocardiography.** ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *Circulation* 2003; 108(9):1146–1162. doi:10.1161/01.CIR.0000073597.57414.A9
 10. **Okmen E, Cam N, Sanli A, Unal S, Tartan Z, Vural M.** Cardiac troponin I increase after successful percutaneous coronary angioplasty: predictors and long-term prognostic value. *Angiology* 2006; 57(2):161–169. doi:10.1177/000331970605700205
 11. **Apple FS, Murakami MM.** Cardiac troponin and creatine kinase MB monitoring during in-hospital myocardial reinfarction. *Clin Chem* 2005; 51(2):460–463. doi:10.1373/clinchem.2004.042887
 12. **Forberg JL, Henriksen LS, Edenbrandt L, Ekelund U.** Direct hospital costs of chest pain patients attending the emergency department: a retrospective study. *BMC Emerg Med* 2006; 6:6. doi:10.1186/1471-227X-6-6
 13. **Fraga OR, Sandoval Y, Love SA, et al.** Cardiac troponin testing is overused after the rule-in or rule-out of myocardial infarction. *Clin Chem* 2015; 61(2):436–438. doi:10.1373/clinchem.2014.232694
 14. **Love SA, McKinney ZJ, Sandoval Y, et al.** Electronic medical record-based performance improvement project to document and reduce excessive cardiac troponin testing. *Clin Chem* 2015; 61(3):498–504. doi:10.1373/clinchem.2014.234310
 15. **Apple FS, Jaffe AS, Sharkey S, et al.** Best practices for monitoring cardiac troponin in detecting myocardial injury. *Clin Chem* 2017; 63(1):37–44. doi:10.1373/clinchem.2016.257428
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Address: Samuel T. Ives, MD, Department of Medicine, University of Minnesota, 516 Delaware Street SE, Minneapolis, MN 55414; samuel.ives@hcmed.org