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SPECIAL CONTRIBUTION

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Use of high-sensitivity cardiac troponin in the emergency department: A policy resource and education paper (PREP) from the American College of Emergency Physicians

Susan B Promes MD, MBA[1] | **Seth Gemme MD**[2] | **Lauren Westafer DO**[2] | **Stephen J. Wolf MD**[3] | **Deborah B. Diercks MD, MSc**[4]

[1]Department of Emergency Medicine, Penn State College of Medicine, Hershey, Pennsylvania, USA

[2]Department of Emergency Medicine, UMass Chan Medical School-Baystate, Springfield, Massachusetts, USA

[3]Department of Emergency Medicine, Denver Health Medical Center, Denver, Colorado, USA

[4]Department of Emergency Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA

Correspondence
Seth Gemme, MD, Department of Emergency Medicine, UMass Chan Medical School-Baystate, Springfield, Massachusetts, USA.
Email: seth.gemme@baystatehealth.org

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Abstract

This Policy Resource and Education Paper (PREP) from the American College of Emergency Physicians (ACEP) discusses the use of high-sensitivity cardiac troponin (hs-cTn) in the emergency department setting. This brief review discusses types of hs-cTn assays as well as the interpretation of hs-cTn in the setting of various clinical factors such as renal dysfunction, sex, and the important distinction between myocardial injury versus myocardial infarction. In addition, the PREP provides one possible example of an algorithm for the use of a hs-cTn assay in patients in whom the treating clinician is concerned about potential acute coronary syndrome.

1 | INTRODUCTION

Chest pain is a common emergency department (ED) complaint with heart disease being a leading cause of death in the United States.[1] Myocardial infarction (MI) is a diagnosis with significant morbidity and mortality that has many atypical presentations such that it may be misdiagnosed. Criteria for diagnosing an acute MI include detection of a rise and/or fall of cardiac biomarkers with at least 1 value above the 99th percentile of the upper reference limit (URL) and at least 1 of the following: symptoms of myocardial ischemia, electrocardiogram (ECG) changes indicative of new ischemia, development of pathological Q waves, imaging evidence of new loss of viable myocardium (eg, new regional wall motion abnormality) or coronary thrombus.[2] Over the years, various biomarkers, each with their own unique profiles (eg, creatine kinase, myoglobin, troponin), have been used to establish the diagnosis of acute MI. Cardiac troponin is currently considered the industry standard biomarker.

The latest generation of troponin is a high-sensitivity troponin (hs-cTnT or hs-cTnI), which can detect very small levels of troponin in the bloodstream. Given an increase in the detectability of hs-cTn, it is important for emergency physicians to understand that a detectable level does not mean a patient is necessarily having an acute MI. There are multiple other conditions that can result in an elevated hs-cTn result other than acute coronary syndrome (ACS) such as renal failure, chronic heart failure, sepsis, pulmonary embolism, myocarditis, or aortic dissection (Table 1).[3] Therefore, emergency physicians must interpret the hs-cTn results in the context of the patient's history and clinical presentation. A diagnostic

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TABLE 1 Etiologies of elevation of coronary troponin unrelated to acute coronary syndrome.

	Acute	Chronic
Supply and demand mismatch	Arrhythmias	
	Coronary spasm	
	Endothelial dysfunction	
	Aortic dissection	Severe aortic valve disease
	Shock (cardiogenic, hypovolemic, septic)	Hypertrophic cardiomyopathy
	Respiratory failure	Left ventricular hypertrophy
	Cocaine use	Hypertension
	Coronary embolism or vasculitis	Anemia
Non-ischemic myocardial damage	Myopericarditis	
	Pacing or defibrillation shocks	
	Cardiotoxic agents	
	Cardiac contusion	
	Cardiac surgery	
	Radiofrequency or cryoablation	
	Carbon monoxide poisoning	
Multifactorial causes of myocardial damage	Heart failure	
	Renal failure	
	Sepsis	Sarcoidosis
	Pulmonary embolism	Amyloidosis
	Takotsubo cardiomyopathy	
	Extreme exertion	
	Gastrointestinal bleeding	
	Rhabdomyolysis	
	Stroke	
	Skeletal myopathy	

algorithm is useful to inform the clinical decision-making for patients who present to the ED with suspected ACS. As with any diagnostic workup, engaging patients in shared decision-making, taking into account their values and preferences is prudent. The objective of this paper is to discuss interpretation of high-sensitivity troponin and present a sample algorithm for patients undergoing evaluation for potential ACS.

2 | INTERPRETATIONS

2.1 | Types of high-sensitivity troponin

Both hs-cTnI and hs-cTnT assays are approved for use. In the United States, available hs-cTnI assays include Abbott Architect Stat and the Siemens HsVista; and only 1 hs-cTnT assay, the Roche Elecsys Troponin T STAT. Each assay has different analytic characteristics including different sensitivities (limit of detection) and 99th percentile cutoffs) and, as a result, their values cannot be compared interchangeably.[4,5] Although few studies directly compare these assays, most evidence evaluating hs-cTn assays show similar clinical performance.[6] One meta-analysis evaluating the performance of a 0- and-1-hour rule-in/rule-out algorithm in detecting acute MI, found all 3 assays had similar diagnostic characteristics, with negative predictive values >99% and sensitivities of ≈98%.[7] Some hs-cTn manufacturers provide conversion factors to aid in comparing a patient's baseline conventional troponin with hs-cTn measurements, which may be useful in trending troponin levels during transitions to hs-cTn assays at individual institutions.

2.2 | Myocardial injury versus infarction

One concern with high-sensitivity troponin assays is an increase in the number of patients with abnormal troponin levels and the assumption that the abnormal troponin levels indicate acute MI rather than myocardial injury. Several clinical entities aside from ACS can cause elevations in troponin, which are more detectable with hs-cTn assays. According to the fourth universal definition of MI, myocardial injury can be associated with either stable troponin levels or rise and fall

in troponin. However, myocardial injury is not always associated with signs and/or symptoms of MI.[2] Examples of myocardial injury include acute heart failure, chronic kidney disease, sepsis, and myocarditis. In 1 trial of 48,282 patients with suspected ACS in Scotland, 21% had hs-cTnI concentrations above the 99th percentile, which would be considered abnormal. Of those cases that were adjudicated with a final diagnosis, 67% were classified as having MIs and 33% as having myocardial injury. A higher proportion of patients were reclassified as having myocardial injury by the hs-cTnI compared with conventional troponin. Although 7% more of these patients underwent angiography, MI and cardiovascular death remained unchanged, introducing some concern for overdiagnosis leading to increased unnecessary testing and potential for iatrogenic complications.[8] Similarly, a prospective observational study in the United States found that when hs-cTnT assay was used, 16% of patients were classified as myocardial injury.[9] These studies demonstrate that, compared with conventional troponin assays, a significantly higher proportion of patients undergoing testing with hs-cTn assays will have elevated baseline troponin values, but this should not necessarily be mistaken for ACS. Although abnormal hs-cTn levels do not necessarily indicate the presence of ACS, abnormal troponin levels are associated with increased morbidity and mortality.[10,11]

2.3 | Sex-specific cutoffs

Sex-specific differences in pathophysiology and clinical presentation of cardiovascular diseases have been well described. Additionally, the 99th percentile URL of hs-cTnI assays in healthy adults is consistently higher for men than women.[12] There is considerable debate regarding the clinical utility of these cutoffs.[2] A study of over 1600 patients presenting to US EDs with suspected ACS found that the use of sex-specific cutoffs did not significantly change test characteristics.[13] Another observational study in the United States found that the use of sex-specific cutoffs with hs-cTnT increased the number of patients diagnosed with myocardial injury but not with MI.[9] Both of these studies used serial troponin testing and the value of sex-specific cutoffs may depend on the use of serial testing.

2.4 | Delta troponin

When hs-cTn is undetectable, ACS is extremely unlikely, although most patients in these studies had an initial troponin drawn at least 2–3 hours after chest pain onset.[14–16] However, few patients presenting with suspicion of ACS will have undetectable hs-cTn. Most patients will have low hs-cTn levels that are below the abnormal threshold. In cases of low but detectable hs-cTn levels, serial troponin testing can help exclude ACS.[2] One widely used and well-studied algorithm uses the change (delta) in troponin in either a positive or negative direction between 0 and 1 hour.[17,18] For patients with a low but detectable level of hs-cTn, the algorithm recommends that MI can be safely excluded if the delta hs-cTn value is <3 ng/L. However, if the patient has a delta troponin of ≥5 ng/L, then the patient meets the diagnostic criteria for an acute MI.[17,18] In a recent meta-analysis, an algorithm using delta troponins with any hs-cTn had a pooled sensitivity of 98.7% (95% confidence interval 97.3%–99.3%) across diverse cohorts.[7]

2.5 | Renal dysfunction

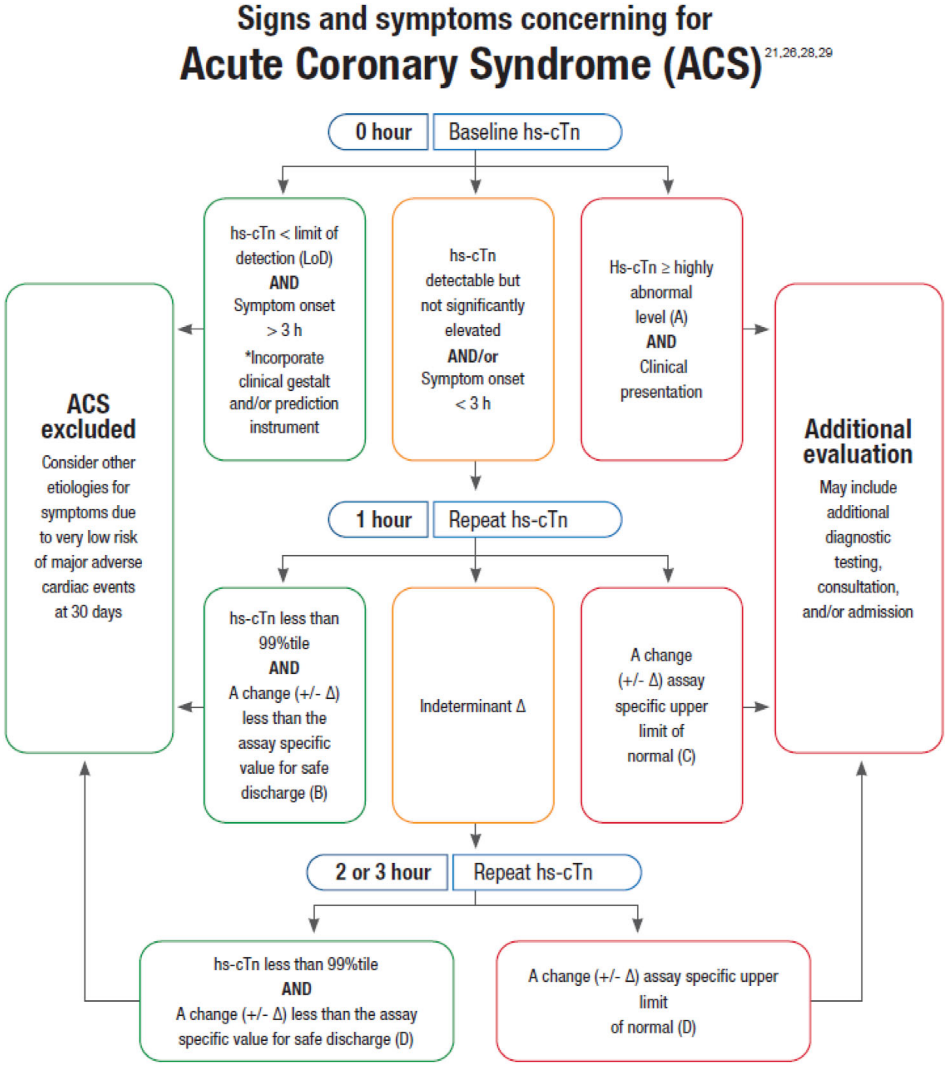
The diagnosis of MI in patients with renal insufficiency can be difficult as many patients with chronic kidney disease have elevated troponin values and the majority of patients with end-stage renal disease (ESRD) have elevated hs-cTn values. As might be expected, the specificity of troponin for MI is reduced at lower levels of renal function.[19–22] One meta-analysis found that hs-cTnT may be less specific compared to hs-cTnI assays; however, the studies included in this analysis were heterogeneous making definitive conclusions difficult.[23] Some authors have proposed alternative cutoff values in patients with ESRD, but none have been externally validated.[24] Therefore, clinicians should continue to integrate a patient's pretest probability, based on clinical history and exam, with the hs-cTn lab results and use serial troponin measurements as appropriate.

3 | ALGORITHMS

There have been several proposed algorithms reported in the literature using hs-cTn in the evaluation of patients presenting to the ED with chest pain and suspected ACS. Most early algorithms developed and validated in Europe incorporated clinical gestalt, patient risk, and serial troponin measurement either at time 0 and 1 hour, 0 and 2 hour, and/or 0 and 3 hours from presentation to the ED.[25] These algorithms were found to perform similarly in the United States even in the absence of incorporating ECG changes and clinical risk stratification tools.[26]

The successful development and adoption of a hs-cTn clinical algorithm for suspected ACS require addressing inevitable challenges in adoption while involving appropriate stakeholders within individual health care organizations including cardiology, emergency medicine, internal medicine, and clinical laboratory technicians. All users of the algorithm must be educated on the nuances of hs-cTn and how it differs compared to prior conventional troponin use.[27] Furthermore, there is not 1 universally accepted clinical algorithm as each institution will have unique characteristics that need to be addressed such as patient population, practice environment, physician and non-physician healthcare practitioner risk tolerance, and the type of hs-cTn assay used. In addition, the role for point-of-care troponin testing as well as use of coronary computed tomography angiography for risk stratification are evolving.

Figure 1 is an example of one algorithm for the evaluation and management of patients presenting to the ED with chest pain using hs-cTn. The assay-specific values are included in the table to help with interpretation. It is important to note that this approach is exclusive to patients with signs and symptoms concerning for ACS. High-sensitivity troponin values require interpretation based on clinical context in conjunction



hs-cTn Assays (FDA approved in United States as of 2021)	LoD	99th percentile, female & male	A	B	C	D
Abbott, ARCHITECT i2000SR for hs-cTnI[30,31]	2 ng/L	26 ng/L; 16 & 34 ng/L	52	2	6	3
Siemens, HsVista for hs-cTnI[26]	3 ng/L	47 ng/L; 39 & 62 ng/L	120	3	12	7
Roche, Elecsys 2010 for hs-cTnT[30]	5 ng/L	19 ng/L; 14 & 22 ng/L	52	3	5	7

FIGURE 1 Example of one possible algorithm for patients undergoing evaluation for acute coronary syndrome using high-sensitivity cardiac troponin. Abbreviations: ACS, acute coronary syndrome; FDA, Food and Drug Administration; hs-CTn, high-sensitivity cardiac troponin; hs-CTnI, high-sensitivity cardiac troponin I.[28–31]

with a clinical algorithm. It is impossible to show one universal algorithm due to the different assays available and nuances at individual institutions. The algorithm depicted in Figure 1 has both the 0- and 1-hour, 0- and 2-hour, or 0- and 3-hour options overlaid in a single algorithm. In particular, an institution may choose not to implement the 1-hour component and use a 2- or 3-hour interval due to logistical challenges in getting the repeat hs-cTn drawn that quickly.

4 | CONCLUSION

The growing use of hs-cTn in clinical practice requires understanding the particular assay and the factors that influence the interpretation of a specific value in the context of the patient's clinical presentation. Future research is necessary to delineate meaningful cutoff values in patients with renal dysfunction and baseline elevated values and to understand the clinical impact of various diagnostic strategies.

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ORCID

Susan B Promes MD, MBA https://orcid.org/0000-0002-6279-6011
Seth Gemme MD https://orcid.org/0000-0003-3159-2160

REFERENCES

1. Centers for Disease Control and Prevention. Health, United States 2019: Table 6. Leading causes of death and numbers of deaths, by sex, race, and Hispanic origin: United States, 1980 and 2018. Published June 1, 2019. Accessed April 18, 2023. https://www.cdc.gov/nchs/data/hus/2019/006-508.pdf
2. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. *Circulation*. 2018;138(20):e618-e651.
3. Vasile V, Jaffe A. High-sensitivity cardiac troponin in the evaluation of possible AMI. American College of Cardiology. Published June 16, 2018. Accessed March 6, 2023. https://www.acc.org/latest-in-cardiology/articles/2018/07/16/09/17/high-sensitivity-cardiac-troponin-in-the-evaluation-of-possible-ami
4. Welsh P, Preiss D, Sattar N. Utility of high-sensitivity troponin T and I: Are they the same? American College of Cardiology. Published November 21, 2019. Accessed April 19, 2023. https://www.acc.org/latest-in-cardiology/articles/2019/11/21/07/26/utility-of-high-sensitivity-troponin-t-and-I
5. Karády J, Mayrhofer T, Ferencik M, et al. Discordance of high-sensitivity troponin assays in patients with suspected acute coronary syndromes. *J Am Coll Cardiol*. 2021;77(12):1487-1499.
6. Willeit P, Welsh P, Evans JDW, et al. High-sensitivity cardiac troponin concentration and risk of first-ever cardiovascular outcomes in 154,052 participants. *J Am Coll Cardiol*. 2017;70(5):558-568.
7. Chiang CH, Chiang CH, Lee GH, et al. Safety and efficacy of the European Society of Cardiology 0/1-hour algorithm for diagnosis of myocardial infarction: systematic review and meta-analysis. *Heart*. 2020;106(13):985-991.
8. Shah ASV, Anand A, Strachan FE, et al. High-sensitivity troponin in the evaluation of patients with suspected acute coronary syndrome: a stepped-wedge, cluster-randomised controlled trial. *Lancet*. 2018;392(10151):919-928.
9. Mumma BE, Casey SD, Dang RK, et al. Diagnostic reclassification by a high-sensitivity cardiac troponin assay. *Ann Emerg Med*. 2020;76(5):566-579.
10. Saunders JT, Nambi V, de Lemos JA, et al. Cardiac troponin T measured by a highly sensitive assay predicts coronary heart disease, heart failure, and mortality in the Atherosclerosis Risk in Communities Study. *Circulation*. 2011;123(13):1367-1376.
11. Neumann JT, Twerenbold R, Ojeda F, et al. Application of high-sensitivity troponin in suspected myocardial infarction. *N Engl J Med*. 2019;380(26):2529-2540.
12. Bhatia PM, Daniels LB. Highly sensitive cardiac troponins: the evidence behind sex-specific cutoffs. *J Am Heart Assoc*. 2020;9(10):e015272.
13. Peacock WF, Baumann BM, Bruton D, et al. Efficacy of high-sensitivity troponin T in identifying very-low-risk patients with possible acute coronary syndrome. *JAMA Cardiol*. 2018;3(2):104-112.
14. Nowak RM, Gandolfo CM, Jacobsen G, et al. Ultrarapid rule-out for acute myocardial infarction using the generation 5 cardiac troponin T assay: results from the REACTION-US Study. *Ann Emerg Med*. 2018;72(6):654-664.
15. Pickering JW, Flaws D, Smith SW, et al. A risk assessment score and initial high-sensitivity troponin combine to identify low risk of acute myocardial infarction in the emergency department. *Acad Emerg Med*. 2018;25(4):434-443.
16. Bandstein N, Ljung R, Johansson M, Holzmann MJ. Undetectable high-sensitivity cardiac troponin T level in the emergency department and risk of myocardial infarction. *J Am Coll Cardiol*. 2014;63(23):2569-2578.
17. Reichlin T, Schindler C, Drexler B, et al. One-hour rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. *Arch Intern Med*. 2012;172(16):1211-1218.
18. Chew DP, Lambrakis K, Blyth A, et al. A randomized trial of a 1-hour troponin T protocol in suspected acute coronary syndromes: the rapid assessment of possible acute coronary syndrome in the emergency department with high-sensitivity troponin T study (RAPID-TnT). *Circulation*. 2019;140(19):1543-1556.
19. Jacobs LH, van de Kerkhof J, Mingels AM, et al. Haemodialysis patients longitudinally assessed by highly sensitive cardiac troponin T and commercial cardiac troponin T and cardiac troponin I assays. *Ann Clin Biochem*. 2009;46(Pt 4):283-290.
20. Vasudevan A, Singer AJ, Defilippi C, et al. Renal function and scaled troponin in patients presenting to the emergency department with symptoms of myocardial infarction. *Am J Nephrol*. 2017;45:304-309.
21. Twerenbold R, Wildi K, Jaeger C, et al. Optimal cutoff levels of more sensitive cardiac troponin assays for the early diagnosis of myocardial infarction in patients with renal dysfunction. *Circulation*. 2015;131(23):2041-2050.
22. Gunsolus I, Sandoval Y, Smith SW, et al. Renal dysfunction influences the diagnostic and prognostic performance of high-sensitivity cardiac troponin I. *J Am Soc Nephrol*. 2018;29(2):636-643.
23. Lee CC, Huang SS, Yeo YH, et al. High-sensitivity-cardiac troponin for accelerated diagnosis of acute myocardial infarction: a systematic review and meta-analysis. *Am J Emerg Med*. 2020;38(7):1402-1407.
24. Lim E, Lee MJ. Optimal cut-off value of high-sensitivity troponin I in diagnosing myocardial infarction in patients with end-stage renal disease. *Medicine (Baltimore)*. 2020;99(5):e18580.
25. Arslan M, Dedic A, Boersma E, Dubois EA. Serial high-sensitivity cardiac troponin T measurements to rule out acute myocardial infarction and a single high baseline measurement for swift rule-in: a systematic review and meta-analysis. *Eur Heart J: Acute Cardiovasc Care*. 2020;9(1):14-22.
26. Nowak RM, Christenson RH, Jacobsen G, et al. Performance of novel high-sensitivity cardiac troponin I assays for 0/1-hour and 0/2- to 3-hour evaluations for acute myocardial infarction: results from the HIGH-US Study. *Ann Emerg Med*. 2020;76(1):1-13.
27. Januzzi JL Jr, Mahler SA, Christenson RH, et al. Recommendations for institutions transitioning to high-sensitivity troponin testing: JACC scientific expert panel. *J Am Coll Cardiol*. 2019;73(9):1059-1077.
28. Kjeldsen K, Lancellotti P, Landmesser U, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the

management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016;37:267-315.
29. Vigen R, Kutscher P, Fernandez F, et al. Evaluation of a novel rule-out myocardial infarction protocol incorporating high-sensitivity troponin T in a US hospital. *Circulation*. 2018;138:2061-2063.
30. Twerenbold R, Costabel JP, Nestelberger T, et al. Outcome of applying the ESC 0/1-hour algorithm in patients with suspected myocardial infarction. *J Am Coll Cardiol*. 2019;74:483-494.
31. Chapman AR, Mills NL. High-sensitivity cardiac troponin and the early rule out of myocardial infarction: time for action. *Heart*. 2020;106:955-957.

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