Troponin assay use in the emergency department for management of patients with potential acute coronary syndrome: current use and future directions

William R. Fox, Deborah B. Diercks

Department of Emergency Medicine, University of Texas Southwestern, Dallas, TX , USA

Troponins are proteins commonly found in cardiac tissue that are released during myocardial ischemia or necrosis. These troponins can be detected by assays that can then be used to guide clinical decision-making and disposition, especially if the suspected insult is related to acute coronary syndrome. Timing of troponin measurement can be important as elevations may not be detectible immediately after an insult. New assays have been designed to detect troponin concentrations previously too low to be detected by conventional assays. These tests are known as high-sensitivity cardiac troponin assays. Current research is aimed at evaluating the clinical significance of troponin elevations detected by these new assays especially in management of patients with suspected acute coronary syndrome. A number of risk-stratification scores exist to assist physicians with evaluating chest pain in the emergency department in the context of detection (or absence) of troponins in systemic circulation. Additionally, investigators are working to integrate data generated by hs-cTn measurements into existing and new risk-stratification scores.

Keywords Myocardial infarction; Troponin; Risk stratification; Diagnostic test; Prognosis

Capsule Summary

What is already known
Conventional troponin assays are a valuable tool in the emergency department in patients with chest pain to determine if they are suffering from acute chest syndrome. Newer assays are designed to detect troponins in peripheral blood at lower concentrations then previously allowed by conventional assays. Serial troponin measurements are utilized in patients with chest pain onset in close chronological proximity to their arrival in the emergency department.

What is new in the current study
This review discusses primary literature relating to the implementation of high-sensitivity troponin assays in the emergency department and discusses them in the relative context of conventional troponins. In settings where conventional and high sensitivity assays are available, there is no increase in negative predictive value of serial high-sensitivity troponin values when compared to serial conventional troponin values.

INTRODUCTION

The thorough evaluation and accurate diagnosis of the myriad of disorders that cause chest pain is of utmost importance for the emergency department (ED) physician. Time-sensitive management and dispositions are essential to the health of the almost 6 million Americans who come to the ED with chest pain every year.[1] The diagnosis of non-ST segment myocardial infarctions depends on the detection of proteins specific to cardiac tissue in the bloodstream.[2] The presence of troponins, creatine kinase, and other proteins in the bloodstream merits close attention, as patients may require aggressive interventions (i.e., catheterization) to prevent further damage to cardiac tissue. Thus, early detection of cardiac troponins (cTns) specifically can alter patient dispositions from the ED. Questions have been raised, however, about the diagnostic accuracy of troponin detection in the ED. Specifically, concerns still exist as to the appropriate timing and the actual detection of clinically significant troponin elevations. This has led to significant research and development of novel troponin assays. These new detection methods are known as "high-sensitivity cardiac troponins" (hs-cTn) and have been a promising avenue for potentially detecting previously-missed clinically significant myocardial damage. The goal of this review is to discuss basic aspects of troponins; their use in the ED management of patients with suspected acute coronary syndrome (ACS), while also exploring the ongoing research relating to high-sensitivity troponins, and how they compare to the standard of care. In this review will also answer the questions relating to what changes practitioners can expect with the further development and increased availability of hs-cTn detection in the United States. Finally, the review will discuss risk stratification strategies to assist providers in determining disposition for patients with suspected ACS from the ED when utilizing these new assays.

BACKGROUND

cTns are proteins distributed within the cytoplasm and sarcomere of a cardiac myocyte. A small amount of the protein is located in the cytoplasm, with the vast majority remaining in the sarcoplasmic reticulum. Specifically, there are three subunits that make up the troponin complex. There is an inhibitory component (troponin I), a tropomyosin binding component (troponin T), and a calcium binding component (troponin C).[3] The T and I subunits (cTnT and cTnI, respectively) are specific for cardiac muscle, and thus can serve as suitable markers for cardiac injury. Detection of these specific troponins can be modulated based on a number of factors, including duration of hypoxia and perfusion, however limit-

ed, of affected area.[4] Though cTns are specific for cardiac myocytes, they can be released by a number of other pathologic causes in the body including sepsis, chronic kidney disease, hypertensive emergency, gastrointestinal bleeds, stroke, and rhabdomyolysis. In these situations detection of troponin may be a result of release of the 5% to 8% of the cytosolic component of troponin in response to myocyte cell turnover, cellular release of degradation products, and increased cellular wall permeability.[5,6] This reinforces the need for appropriate clinical consideration of troponin elevations in patients where ACS may not be the only pathology.[7] In one paper, researchers noted that the diagnosis of acute myocardial infarction (MI) is not definite with solely an elevated troponin. Authors showed 804/4,928 had elevated hs-cTnI (measured on TnI-Ultra; Siemens Healthcare Diagnostics, Tarrytown, NY, USA) but that 277 patients with elevated cTnI had final cardiovascular diagnoses other than type I MI, including patients with congestive heart failure, dysrhythmias, and hypertension. Additionally, 438 of those patients had noncardiovascular diagnoses including infection, intracranial hemorrhage, and blood loss. The study does comment that higher troponin elevations (>1 μg/L) had a much higher likelihood of being an MI as opposed to smaller elevations. The study is limited, however, as there was no set guideline or protocol for when physicians would send a troponin, thus potentially increasing the rate of alternate diagnoses. Despite this limitation, it serves as a solid example of the lack of specificity of troponin elevations, and by extension the hazard of directly attributing troponin elevation to acute coronary syndrome.[8]

CONVENTIONAL TROPONIN TIMING

The timing of troponin elevation after an ischemic event is another topic of research, as serial troponin measurements have been found to be an effective tool to detect developing myocardial injury. Initial research on troponins has shown cTnT and cTnI are most commonly elevated 4 to 9 hours after myocardial injury, with a peak at 12 to 24 hours. These enzymes may remain elevated in the blood for 7 to 14 days.[3] Thus, the time from onset of chest pain is crucially important for ED practitioners to discern, as troponin elevations may not be detected with commonly used assays if the insult occurred immediately prior (i.e., less than two hours) to presentation. To account for this discrepancy, practitioners will frequently "observe" patients who lack the electrocardiographic (ECG) changes indicative of ST-segment myocardial infarctions in addition to having a negative initial troponin. The observation period usually involves repeat physical examinations and telemetry monitoring along with repeat cTn measurements over a period of hours. Many researchers have attempted to char-

acterize the minimum time necessary for this observation period in order to improve ED throughput while encouraging safe disposition. Early work cited cTn reevaluation 6 to 8 hours after presentation.[3] However, these time points are not as feasible in the ED where patient flow is crucial, frequently leaving admission to the inpatient wards or observation units as the only appropriate dispositions. Based on further research regarding troponin release and measurements, other researchers have determined that a 2 to 3 hours time point for re-measurement may be appropriate in certain patients.[9] Studies have shown improved sensitivities with serial troponin measurements in patients with chest pain that developed 6 to 24 hours prior to ED presentation.[10] In conjunction with risk stratification scores (reviewed later in this paper) researchers noted that in appropriately risk-stratified patients, chest pain evaluation with standard troponin I at 0 and 2 hours lead to decreased disposition times without any significant increase in major adverse cardiac events when compared to a "standard" serial troponin measurement at 0h, followed by a second troponin at 6 to 12 hours after an observation period. Patients found to be low risk on the "accelerated diagnostic protocol" were scheduled to have a stress test within 72 hours, which may not be feasible in certain centers with high ED volumes and limited ability for close follow-up with specialists.[11]

HIGH-SENSITIVITY TROPONINS

As the detection of cardiac injury via troponin elevation became the standard of care, further development of more sensitive assays occurred. This has led to decreased diagnostic cut-offs for the identification of a MI from 0.5 μg/L in first generation assays, to 0.01 μg/L in current contemporary assays, to 0.001 μg/L in high sensitivity troponins. Assays referred to as "high-sensitivity troponins" (hs-cTn) and can detect either troponin I or T.[9] The development of these more sensitive assays will theoretically reduce the number of patients with undetected myocardial injuries. While hs-cTn assays are not currently available in the United States, the body of literature is growing examining the clinical applications of hs-cTn. One meta-analysis compared high sensitivity troponins T and I to conventional troponins to evaluate for differences in sensitivity and specificity, in addition to negative predictive value (NPV) and positive predictive value (PPV) in a meta-analysis of 17 studies.[12] The authors found that hs-cTn had significantly increased sensitivity and NPV at the expense of specificity and PPV when compared to cTn measurements. Studies examining serial troponin measurements taken 2.6 ± 1.5 (cTn) and 2.5 ± 1.4 hours after admission show continued increases in sensitivity for hs-cTn and specificity for cTn. Additionally, the meta-analysis showed eleva-

tions in baseline hs-cTn but negative cTn had greater risk of death, nonfatal MI, or a combination of both versus those with both tests resulting negative. Interestingly, when comparing the NPVs of second cTn and hs-cTn measurements, the confidence intervals (CIs) significantly overlap (0.982 [95% CI, 0.977 to 0.986] for cTn, 0.985 [95% CI, 0.980 to 0.990]).[12] In the management of patients with suspected ACS in the ED increased sensitivity of hs-Tn has its drawbacks, as it may lead to increased unnecessary diagnostic testing and procedures.

Given the increased possibility of adverse outcomes with elevated hs-cTn, the need for close monitoring and evaluation of a patient with positive hs-cTn is important.[12] A study compared hs-cTnT (Roche Elecsys) with third-generation cTnI (Abbott Diagnostics, Abbott Park, IL, USA) and cTnT (Roche Diagnostics, Rotkreuz, Switzerland) at both initial presentation and follow up. Researchers found that in a population of 332 ED patients, 33.1% (n = 110) had evidence of myocardial infarction, generating equivalent ROC-area under the curve's at baseline for hs-cTnT and third-generation cTnI which were both superior to the cTnT assay. Additionally, using a delta troponin ≥ 20% greater than the initial troponin on repeat measurement (median time, 9.4 hours; range, 6 to 24 hours) increased specificity (80.6% to 93.7%) of the hs-cTnT assay at the expense of sensitivity (90.9% to 71.8%).[13] One publication discussed the introduction of hs-cTnT to an ED previously using cTnT. They retrospectively examined 137 patients with chest pain that had samples drawn suitable for cTn and hs-cTn (Roche Elecsys 2010) analysis. Researchers found an increase in diagnoses of myocardial ischemia and a decrease in the diagnosis of unstable angina when the hs-cTnT was used versus cTnT. There also was a significantly lower likelihood of myocardial damage if the hs-cTnT was negative (< 0.014 μg/L per this study). It is important to note that in patients with elevated cTn, there was no significant change in the diagnostic rate of noncardiac chest pain, chest pain of unknown origin, and troponin elevation secondary to renal disease. Additionally, the study found a significant number of adverse events (death or acute myocardial infarction) in patients with elevated hs-cTnT but cTnT below the standard cut-off (< 0.04 μg/L) when compared to those with negative hs-cTnT and cTnT assays.[14]

Combining hs-cTnT measurements with ECG findings may be use to identify a group of patients with an extremely low risk for MI and death at 30 days.[15] Researchers collected hs-cTnT (Roche Elecsys 2010) and ECG data from 14,636 patients who presented to the ED with chest pain. Of those patients, 8,907 patients had a negative (< 5 ng/L) hs-cTnT and an ECG without evidence of ischemic ST-segment changes (elevation or depression). At 30 days, researchers found that in patients without ischemic changes on

ECG and a negative initial hs-cTnT, the NPVs of MI and death were calculated at 99.8% (n = 15) and 100% (n = 2), respectively. They also found that of the 15 patients with MI and negative hs-cTnT/ECGs, 11 had chest pain for < 2 hours prior to arrival in the ED.[15] This study highlights the need for consideration of timing of symptoms in relationship to troponin testing. Another study evaluated 718 consecutive patients with symptoms suggestive of MI with onset/peak of symptoms within 12 hours before presentation with four hs-cTn assays in addition to the standard of care, which included myoglobin and Creatine kinase-MB. They found that sample collection at two hours after chest pain initiation led to a significant improvement in the accuracy of the testing (measured by area under the curve) versus measurement of CK-MB/myoglobin.[16]

Current research has attempted to characterize the appropriate timing of troponin measurements with new high sensitive assays. A recent publication has validated a 1 hour algorithm that utilized a hs-cTn at presentation and 1 hour coupled with a history, physical, and EKG in a blinded diagnostic study. A cohort of 1,320 patients who presented to multiple centers with chest pain were divided into groups based on hs-cTn values (Roche Elecsys 2010) at presentation with "rule out" being defined as < 12 ng/L and a change of the value at one hour < 3 ng/L and a "rule in" defined as > 52 ng/L measurement at baseline, or an absolute change of ≥ 5 ng/L. Of these entire cohort, 786 patients were stratified in the rule-out MI group based solely on the troponin values, which gave a sensitivity and NPV of 99.6% and 99.9%. Additionally, those in the "rule-out" group had a 30-day mortality rate of 0%. For patients in the "rule-in" category (n = 216), the actual number of patients with an acute MI was 169, leading to the calculation of a PPV of 78.2%. Based on just diagnostic thresholds of the hs-cTnT values, researchers were able to classify 75.9% of patients in rule out and rule in groups. The patients not fitting the criteria for "rule in/out" were classified to an observation group. This algorithm allows for a more rapid and effective disposition of patients, but authors noted similar 30 day and 2 years mortality data in the "rule in" and "observational" groups, thus meriting a higher index of suspicion and need for closer monitoring for those who do not have a negative hs-cTn value or the value increase over 2 hours.[17] Two hour algorithms has been validated, as researchers have found that hs-cTnT (Roche Elecsys 2010) at 0 and 2 hours after presentation in appropriate patients could identify patients for stress testing, but with sensitivities/NPVs less than 100% and with large (> 10%) 95% CIs.[18] Additionally, with highly sensitive assays, there is a noticeable drop in specificity likely due to the multiple systemic pathologies that could result in nonspecific elevations.

To examine the diagnostic capabilities of hs-cTn, Aldous and colleagues enrolled patients with chest pain and no ST-elevation on their electrocardiogram and collected both cTnI and hs-cTnT measurements at 0 and 2 hours.[19] Their primary outcome was non-ST-segment elevation MI diagnosis with a secondary outcome of all-cause mortality, nonfatal myocardial infarction, and heart failure requiring admission. Researchers found that standard cutoffs for positivity at > 14 ng/L did not capture all patients with non-ST segment elevations, but that hs-cTn samples collected 4 to 6 hours after symptom onset gave a sensitivity of 100%. Additionally, the hs-cTnI assay more accurately predicted death and heart failure (hazard ratio [HR], 5.4; 95% CI 2.7 to 10.7; HR, 27.8; 95% CI, 6.6 to 116.4), while cTnI more accurately predicted nonfatal myocardial infarctions (HR, 4.0; 95% CI, 2.4 to 6.7).[20] In patients with unknown coronary anatomy hs-cTnT elevations have been found to predict all-cause mortality and nonfatal MI when elevated, with gradually increasing hazard ratios of death or MI with increasing measured concentrations.[19]

RISK STRATIFICATION

A key aspect of management patients with suspected ACS is a clear determination of the factors that modulate the likelihood that a patient is having a coronary event. As newer generation troponins have decreased the need for a prolonged period of evaluation for serial biomarker assessment, ED physicians have the opportunity to identify those patients that can potentially managed in numerous locations such as early outpatient follow-up, an observation unit, or a traditional hospital admission. A number of clinical tools have been developed that incorporate contemporary troponin testing to aid practitioners in the ED determine the risk of an individual patient based on prior data from similar cohorts. The thrombolysis in myocardial infarction (TIMI), global registry of acute coronary events (GRACE), North American Chest Pain Rule, HEART, and the Emergency Department Assessment of Chest pain Score (EDACS) are some risk scores that may aid providers by providing quick and efficient access to synthesized data that can help risk stratify chest pain patients in the ED utilizing troponin results and clinical characteristics. Utilization of clinical tools can further aid disposition decision process.

TIMI

The TIMI score incorporated age ≥ 65, > 3 risk factors for coronary artery disease (including a family history of CAD, hyperlipidemia, diabetes, active smoking, or hypertension), evidence of significant coronary stenosis (≥ 50% per researchers), ST-segment deviation, use of aspirin within past week, severe anginal symptoms, and elevated CK-MB or cTn. Event risk was calculated at

4.7% for 0/1, 8.3% for 2, 13.2% for 3, 19.9% for 4, 26.2% for 5, and 40.9% for 6/7 factors being present. Providers can then utilize the patient's risk of adverse outcomes to help determine treatment options and disposition.[21]

GRACE

Researchers utilized the GRACE cohort to determine risk of death or nonfatal MI within six months from initial presentation in patients who came to hospitals with ACS. They found that 9 characteristics such as age, history of CHF, Killip class, peripheral vascular disease, pulse, systolic blood pressure, ST segment deviation, physical exam findings such as presence or absence of CHF findings, in addition to presentation creatinine level and abnormal cardiac enzymes helped determine this risk based on end-point analysis from 43,810 patients (21,688 in derivation, 22,122 in validation). The GRACE score picks up where prior scores have left off by accounting for comorbidities such as CHF that could confound risk analysis in other models.[22]

HEART

The HEART score aims to characterize the physician reasoning to admit patients to a coronary care unit from the ED in addition to determining predictors of negative outcomes including MI, coronary artery bypass graph/percutaneous coronary intervention (CABG/PCI), and death. Unlike the TIMI and GRACE score it was derived from an ED population presenting with chest pain and not patients already identified as having ACS. The study assigned scores of 0–2 to a patient's history, EKG (with ST-segment elevation myocardial infarction patients excluded), age, risk factors (diabetes mellitus, active smoking, hypertension, hyperlipidemia, and family history of obesity and coronary artery disease), and elevated cTnI, with each category serving as the first letter of the acronym of the risk score. Researchers determined that HEART scores of 0–3 had a risk of incurring an MI/needing PCI or CABG/death of 2.5%, versus 20.3% at 4 to 6 points and 72.7% at ≥ 7 points.[23]

North American Chest Pain Rules

The North American Chest Pain Rules were developed to identify patients who merit invasive testing/close follow up. The absence of 5 particular characteristics (new ischemia on EKG, history of CAD, typical ACS pain, positive initial troponin, and age ≤ 40 or age 41 to 50 with second negative troponin within six hours) led to a high sensitivity (100% as calculated by researchers) in detecting ACS events in 30 days. The study is limited due to the need for close follow up within 30 days, which may be limited in certain settings. However, in settings where a "chest pain observation unit" is a prolonged stay in an ED bed, these rules allow for more prompt dispositions without unnecessary testing or observation.[24]

EDACS

Researchers developed the EDACS to identify patients with elevated short-term risk of major adverse cardiac events (MACE). Researchers found that male gender, age (per 5 years), history of CAD or known risk factors (defined as premature CAD, dyslipidemia, diabetes, hypertension, active smoker), the presence of diaphoresis or pain radiating to arm or shoulder, or the worsening/reproducibility of pain with palpation or inspiration. Based on the assigned point values for the above characteristics, an EKG with no ischemic changes, and two negative troponin measurements, patients are classified as "low risk" of MACE at 30 days and may be eligible for discharge at two hours.[25]

COMBINATION OF RISK SCORE AND hs–cTn

A number of recent publications have discussed the development and implementation of protocols requiring using cTn or hs–cTn in chest pain patients. The 2-hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker (2-Hour Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker, ADAPT) trial examined the utility of two troponin measurements at 0 and 2 hours in addition to history and EKG findings to define a group of low-risk patients that would be suitable for discharge with close outpatient follow up. Patients with a low pre-test probability of ACS determined by a TIMI score of 0, no ischemic EKG changes, and cTnI levels below institutional cutoff levels were deemed "low risk" of MACE at 30 days. Of the 1,975 patients examined in the study, 20% (n = 392) were low risk, with 0.25% of the low risk patients (n = 1) having a MACE at 30 days. This gave a sensitivity of 99.7% (95% CI, 98.1% to 99.9%) and an NPV of 99.7% (95% CI, 98.6% to 100%).[26]

Cullen and researchers later validated an accelerated diagnostic protocol similar to that in the ADAPT trial but instead utilized hs–cTnI measurements at 0 and 2 hours. Researchers evaluated 1,635 patients and grouped them based on TIMI score of 0 or ≤ 1 and negative hs–cTnI (defined as < 26.2 ng/L) and an EKG without ischemic changes. For patients with all of these "low risk" criteria (TIMI = 0, n = 230; TIMI ≤ 1, n = 351), they found a 30 day MACE rate of 0% and 0.8%, respectively. This allowed for a sensitivity and NPV calculation of 100% (95% CI, 98.5% to 100%) and 100% (95% CI, 98.8% to 100%) for TIMI = 0. For TIMI ≤ 1, the sensitivity was 99.2% (95% CI, 97.1% to 99.8%) and 99.7 (95% CI, 98.9% to 99.9%). This supported the use of hs–cTnI as-

says in accelerated diagnostic protocols. Of note, a comparison of the sensitivities for patients with a TIMI score of 0 and no EKG changes between the ADAPT trial and this paper showed a significant overlap of the 95% CIs when measuring serial cTn (for AD-APT) and hs-cTnI. This is particularly important for physicians who may utilize both hs-cTn and cTn measurements in their practice, as any advantage of utilizing a hs-cTn measurement may be limited if the clinical appearance or presentation of the patient necessitates a two-troponin measurement.[27]

Carlton et al.[28] attempted to merge troponin measurements with risk scoring when he and authors combined hs-cTnT and hs-cTnI (Roche Elecsys high sensitivity troponin T assay and Abbott Architect Stat high sensitivity Troponin-I assay, respectively) measurements with TIMI, HEART, Vancouver Chest Pain Risk Scores, modified Goldman, and GRACE scores. Their goal was to attain a 99.5% NPV while identifying 30% of patients for immediate discharge due to low-risk status. Their end point was acute MI in 30 days. They evaluated 959 patients with hs-cTnT (79 of which were determined to have an acute MI) and 867 patients with hs-cTnI (66 of which were determined to have an acute MI). They found that the combination of hs-cTn testing and risk stratification (specifically combinations of hs-cTnT and a TIMI score ≤1 and a modified Goldman score of ≤1 or the hs-cTnI and a TIMI score of 0 and a HEART score ≤3) has the potential to achieve their set goals at the expense of specificity/PPVs. Their study was limited, however, because the CIs of these combinations fell below the thresholds of 99.5% NPV and 30% suitable for discharge. Additionally, the study population was limited due to the restriction of patients with ischemic changes on EKG and those with other ischemic endpoints, such as unstable angina.[28]

In a separate study, Carlton et al.[29] built on prior research to develop the Triage Rule-out Using high-Sensitivity Troponin (TRUST) ADP study. The goal was to generate an ADP with only one troponin measurement. Researchers had utilized a non-ischemic EKG, a modified Goldman score of ≤1, and a negative hs-cTnT described as <14 ng/L measured at presentation. Primary and secondary end points were the presence of acute MI and MACE at 30 days from index visit, respectively. The study resulted in 382/960 patients being classified as "low risk", with primary/secondary sensitivities and NPVs of 98.8 (95% CI, 92.4% to 99.9%)/99.0 (95% CI, 93.7% to 99.9%) and 99.7 (95% CI, 98.4% to 100%)/99.7 (95% CI, 98.4% to 100%). Changing the cutoff value of hs-cTnT <5 ng/L allowed for a sensitivity and NPV of 100% for the primary outcome (with 95% CI, 94.3% to 100% and 98.3% to 100%, respectively). For the secondary outcome, the sensitivity and NPV were calculated at 96.8 (95% CI, 90.6% to 99.2%) and 98.9 (95% CI, 96.7% to 99.7%) at the lower hs-cTnT value.

As new cardiac markers are identified, investigators are still working toward the identification of the optimal marker combination in those patients identified as low risk by clinical tools that allow rapid disposition. In a study by Mockel et al.,[30] patients with GRACE <140 and no recurrent chest pain, investigators suggest that a single negative cTnT and negative copeptin level can identify patients who can be safely discharged. Studies are also been doing to look at hs-cTn levels less than the limit of detection and suggest that levels below this threshold may identify patients appropriate for early discharge.[31]

SUMMARY RECOMMENDATIONS

Careful consideration of the data and analyses presented in the previously-discussed papers has allowed for the generation of the following summary recommendations specifically relating to troponin measurements in the ED as part of the management of patients with suspected ACS. It is important for practitioners to remember that although cTn measurements detect varying concentrations of proteins normally sequestered within cardiac tissue, the release of those proteins are not always a result of ACS. Care must be taken to avoid treating every patient with chest pain as a potential ACS case especially with elevated troponins but a history concerning for alternate causes of chest pain (i.e., pulmonary embolism). The history and physical exam will not only help risk stratification to determine if the patient is eligible for early discharge, but can also aid providers in investigating whether the chest pain is related to ACS or another pathologic cause. Furthermore, the appropriate interpretation of the troponin is not simply binary (elevated versus normal) and may involve trending in patients who have risk factors for ACS. For patients that require trending, conventional troponin measurements may be sufficient, as there is no significant increase in NPV when comparing serial cTn and hs-cTn measurements. Ideally, sample collection will occur 4–6 hours after pain begins. Additionally, the degree of elevation can be significant, as increased hs-cTn elevations can correlate to increased hazard ratios for death and nonfatal myocardial infarction. With the anticipated dissemination of hs-cTn assays in the United States, it is important to remember the importance of the history and physical examination in determining the etiology of the elevation and how risk stratification scores may help physicians generate dispositions for patients with chest pain.

CONCLUSION

This review discussed a number of primary resources describing the use of troponin assays in the ED. A number of considerations

must be made when utilizing troponin assays in diagnosing ACS. Conventional troponin timing depends on the onset of chest pain relative to ED presentation. High sensitivity troponin assays are designed to detect troponin concentrations at levels that were previously undetectable. Troponin assay use (either high sensitivity or conventional) coupled with appropriate risk stratification will help identify patients at increased risk for ACS.

CONFLICT OF INTEREST

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