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Abstract

The objective of our study was to determine the utility of a baseline high sensitivity cardiac troponin (hs-cTnI) value below the limit of quantitation to rule out acute myocardial infarction (AMI) in patients presenting to the emergency department with any suspicious symptoms of a cardiac etiology. We enrolled subjects presenting to the Emergency Department with symptoms suspicious for AMI. Blood specimens were collected within one hour after a triage electrocardiogram. Cardiac troponin I was measured using the Beckman Coulter Access hs-cTnI assay. The diagnosis of AMI was adjudicated by two cardiologists using the Third Universal Definition of AMI and Roche Diagnostics Troponin T Generation 5 assay with all available clinical data at 30 days after presentation. A total of 567 subjects had all data required for data analyses. AMI was diagnosed in 46 (8.1%) patients. 232 (40.9%) individuals had presentation hs-cTnI results < 4.0 ng/L. None of the patients with baseline hs-cTnI < 4.0 ng/L had an AMI, yielding a negative predictive value of 100.0% and a sensitivity of 100%, and a good prognosis (no AMIs or cardiac-related deaths at 30 days). In this single center emergency department study, a baseline presenting novel hs-cTnI value of < 4.0 ng/L effectively ruled out AMI in 40.9% of all patients presenting to the emergency department and having any symptoms suspicious for AMI. Importantly all patients, not only those with chest pain, and those having symptoms for any duration or those with end-stage renal disease requiring dialysis were included.

Keywords:
High sensitivity troponin, myocardial infarction, emergency rule-out
Introduction

In the United States (US), the incidence of acute myocardial infarction (AMI) has been estimated at 1,055,000 individuals per year.\(^1\) Chest pain and other related symptoms are very common presentations to the emergency department (ED) with approximately 7 million patients in the United States evaluated annually.\(^2\) Due to delays in AMI exclusion, most patients presenting to the ED with symptoms suspicious for AMI are admitted or have an extended stay in an observation unit (up to 88% in some centers).\(^3\) However, only a minority of these patients are diagnosed with AMI. In the US, the annual estimated cost of evaluating patients with possible AMI in the ED is approximately $5 billion.\(^4\) In addition, the delay in exclusion of AMI can lead to ED overcrowding and contribute to increased associated health care costs.\(^5\) Hence, there is a need for a rapid and accurate tool for AMI diagnosis.

Clinical history and electrocardiography (ECG) alone are not enough to achieve early and efficient AMI diagnosis without additional testing with cardiac troponin (cTn) assays.\(^6\) High sensitivity cardiac troponin (hs-cTn) assays can quantify low cTn concentrations with great precision and can help in early detection of AMI.\(^7\) A meta-analysis of studies using the hs-cTnT assay (Roche Diagnostics, Indianapolis, IN) demonstrated that cut-offs of 3-5 ng/L (6 studies) had a sensitivity of 97.4% and specificity was 42.4%.\(^8\) The overall negative predictive value (NPV) of the hs-cTnT assay (< 5 ng/L cut-off), used alone or accompanied with no-ischemic-ECG changes, was > 99%.\(^9,10\) cTn results below these very low levels could help discharge patients safely and early from the ED and allow resources to be focused on intermediate and high risk cases.
The American Heart Association/American College of Cardiology guidelines from 2014 for management of patients with non-ST-elevation AMI still recommend the measurement of cTn over 3 to 6 hours with levels above the 99th percentile upper reference limit for determination of AMI. However, these recommendations were made prior to the introduction of hs-cTn assays that are now widely available in the United States. On the other hand, the European Society of Cardiology guidelines recommend a rule-out strategy that can be applied by using a focus on the value at presentation and at 1 hour, or very low levels below level of detection at presentation. There is evidence suggesting that triage decisions using hs-cTn results at presentation could potentially decrease cost and time compared to serial testing in certain patients.

The analytical performance of the new Beckman Coulter Access hs-cTnI (Brea, CA) has been examined with excellent results reported. Most of the clinical reports found in the literature have utilized hs-cTnT (Roche Diagnostics) and hsTnI (Abbott Diagnostics, Abbott Park, IL) assays and validated the utility of these assays in ruling out AMI. However, less evidence is published on the clinical performance of the new Beckman Coulter Access hs-cTnI and these are primarily from outside the United States. The objective of our study was to determine the optimal cutoff(s) for ruling out AMI at presentation using the Beckman Coulter Access hs-cTnI assay in the United States population, and to confirm baseline low hs-cTnI threshold using a validated hs-cTnT criteria.

Methods

A prospective, observational trial enrolled subjects presenting to the ED at Henry Ford Hospital (Detroit, Michigan) who were evaluated for possible AMI. Inclusion criteria were subjects 21 years or older presenting with clinical symptoms suspicious for AMI that led the responsible
clinician to order an ECG and cTn, and were able to consent and comply with the protocol. Exclusion criteria were patients needing immediate life-saving interventions, cardioversion/defibrillation or thrombolytic therapy in the previous 24 hours, ST-segment myocardial infarction requiring immediate reperfusion therapy, traumatic injuries, transfers from other facilities, and pregnant or breast-feeding females. The study was approved by the Henry Ford Hospital Institutional Review Board and subjects provided written informed consent before being enrolled. The study was conducted according to the Declaration of Helsinki and International Conference of Harmonization good clinical practice guidelines. Study subjects were assessed by an emergency physician, which included patient history, physical examination, a review of ECG, customary blood testing that included cTnI, and chest X-ray. The treating emergency physician determined the timing and implementation of these tests, treatments, and dispositions. After obtaining informed consent, research study coordinators obtained a detailed symptoms history, which was recorded on the study case report form. Subjects were directly asked about their medical history and this was verified by review of their electronic medical record.

**Blood Testing**

Blood specimens were collected in plain (no additive) serum tubes and dipotassium ethylenediaminetetraacetate evacuated plasma tubes within 1 hour after the triage ECG was completed (usually within 10 minutes of presenting). An additional blood specimen was obtained at 3 hours after presentation (SD 15 minutes or +/- 15 minutes). Specimens were centrifuged to obtain serum or plasma and stored at -80°C within 1 hour of collection. Frozen plasma specimens (-80°C) were thawed once and hs-cTnI was measured using the Access 2
immunoassay system (Beckman Coulter, Inc.) in the clinical laboratory at Henry Ford Hospital. Samples from the presentation and 3 hours collections were measured. The Beckman Coulter published limit of detection (equivalent to the limit of quantitation [LoQ] at a 20% coefficient of variation) and LoQ at 10% coefficient of variation are 2.0 and 4.0 ng/L, respectively. The hs-cTnI assay is reported by Beckman Coulter to have an overall 99th percentile upper reference limit of healthy subjects of 18.2 ng/L, with sex-specific upper reference limits of 11.8 ng/L (females) and 19.7 ng/L (males).

Clinical Outcomes

The final diagnosis of type 1 AMI or type 2 AMI was adjudicated by a cardiologist and an emergency physician with additional review by a second cardiologist in cases of disagreement. The diagnosis of AMI was based on the Third Universal Definition of Myocardial Infarction and Elecsys Troponin T Generation 5 assay using a Roche Cobas e601 analyzer (Roche Diagnostics) with all available clinical data 30 days after presentation and required at least 1 hs-cTnT result > 19 ng/L. The adjudicators were not aware of the research study biomarker data. A telephone call and a subsequent medical record review was used to obtain follow-up information. When subjects or family members were not able to be contacted, a death registry search was completed. The Social Security Death Index was searched if the subject’s social security number was known, and unknown cases were searched using Ancestry.com, Michigan obituaries, and a Google search. An Access hs-cTnI assay LoQ cut-off of 4.0 ng/L was used to categorize to either a rule-in or rule-out group. Additionally, for subjects not assigned to the ruled-out group, we calculated the positive predictive value and specificity for diagnosing AMI. As appropriate, 95% confidence limits were calculated around all statistics. The patients with a baseline hs-cTnI result less than
4.0 versus 4.0 or greater were compared using 2-sample t-tests for the continuous data, chi-square tests for the non-sparse categorical data, and Fisher exact tests for sparse categorical data. P-values less than 0.05 were considered statistically significant. All analysis was performed using SAS versions 9.4 (SAS Institute, Inc., Cary, NC).

**Results**

During the period of May 2013 through April 2015, there were 575 subjects enrolled, of which 567 had acceptable data for inclusion in the analysis (Figure 1). The adjudicated final diagnosis demonstrated AMI present in 46 AMI patients (8.1%). Twenty-eight of the AMIs were type 1 and 18 were type 2.

Patients were divided into those with hs-cTnI values < 4.0 ng/L (rule-out) and ≥ 4.0 ng/L (not rule-out) along with clinical features, comorbidities, vital signs, ECG findings, and medications (Table 1). Those subjects with intermittent symptoms had time of symptom onset and the longest duration of these symptoms documented.

Two hundred thirty-two (40.9%) patients had values < 4.0 ng/L (Table 2). Further, a presentation hs-cTnI value of < 4.0 ng/L yielded an NPV of 100.0% (95% CI 98.4%-100.0%), and a sensitivity of 100.0% (95% CI 92.3%-100.0%). Among the patients who had a baseline value < 4.0 ng/L, only 1 patient died of non-cardiac etiology within 30-days and no AMI occurred.

Within the set of 232 subjects who had a baseline hs-cTnI result of < 4.0 ng/L, the emergency discharge disposition consisted of 91 (39%) to home, 94 (41%) to observation, 38 (16%) were admitted, 8 (3%) left against medical advice, and 1 (0.4%) transferred to another facility. Electronic medical records of all study subjects were reviewed. One hundred nine of the subjects could not be contacted for the 30-day telephone interview. Of the subjects who could not be contacted by phone, no AMIs or cardiac-related deaths occurred. On further analysis of the 30-
to 45-day follow-up period, there were 8 AMIs and 7 deaths (4 with a cardiac-caused death). Two of the patients had an AMI resulting in death, resulting in a total of 13 AMI/death outcomes after 30-45 days of follow-up. During the 12- to 18-month follow-up period, there were 19 AMIs and 21 deaths (9 from cardiac causes). Five of the patients had an AMI resulting in death, resulting in a total of 35 AMI/death outcomes after 12 to 18 months of follow-up.

Discussion

In this single center prospective ED study, a baseline Beckman Coulter hs-cTnI assay value of < 4.0 ng/L at presentation could have effectively ruled out AMI in 40.9% of all patients presenting to the ED with AMI symptoms. The 100% diagnostic sensitivity result demonstrates the safety of these baseline thresholds to rule out AMI at presentation and 30 days. Noteworthy, all patients with symptoms suspicious for AMI regardless of symptoms duration, recent AMI diagnosis in the last 3 weeks, or renal function status (chronic kidney disease or dialysis) were included in the study. Our cohort could represent a practical assessment of performance of the hs-cTnI assay for patients presenting to ED with symptoms suspicious for AMI.

To our knowledge, this is the first report of the utility of a baseline hs-cTnI assay by using the Beckman Coulter hs-cTnI assay to rule in or rule out AMI in a US ED. Other groups have reported effective triaging of chest pain patients using hs-cTn assays (both cTnT and cTnI).

Recently, Boeddinghaus et al reported excellent diagnostic accuracy of the Beckman Coulter hs-cTnI assay in a large European multi-center validation. Because the Beckman Coulter hs-cTnI assay is now available in the US as an aid in the diagnosis of myocardial infarction, it is vital to determine how best to capitalize on the added sensitivity of this assay in a US population. Our results obtained using the Beckman Coulter hs-cTnI assay at a cut-off of the LoQ (10% coefficient of variation) ruled out AMI with high confidence. Similar to our study, Boeddinghaus
et al demonstrated essentially equivalent performance with a NPV of 99.8% and a sensitivity of 98.9% in their validation cohort. We were able to rule out AMI in 40.9% of subjects, which compares favorably with the 43% rule out that Boeddinghaus reported.

Different hs-cTn assays offer very high NPV and very good identification of low risk patients who present with symptoms suspicious for AMI. The concentration threshold has been fairly similar in variable assays in different studies. Abbott hs-cTnI assay, Roche Diagnostics hs-cTnT, Abbott Atellica IM hs-cTnI assay and Siemens ADVIA Centaur hs-cTnI (Malvern, PA) have used a threshold of < 5 ng/L, which could help simplify the diagnostic approach in different institutions.10,23-26 Our study demonstrated that a cut off of < 4.0 ng/L can effectively rule-out AMI in symptomatic patients presenting to the ED, which is very close to thresholds reported in other studies, and produced excellent results with 5 ng/L although slightly poorer but 1 AMI was missed. In fact, all 46 AMI patients had a baseline hs-cTnI reading of 4.0 ng/L or greater while 45 had a baseline hs-cTnI reading of 5.0 ng/L or greater. It is recognized that troponin assays are not standardized between manufacturers and comparison of cut-offs has certain limitations. For the potential clinical application of this cut-off, a practical consideration would be to use whole numbers for reporting patient values to physicians.

Recently published data from the HIGH-US multi-center study demonstrated the applicability of U.S. Food and Drug Administration-cleared hs-cTnI assays in the US for risk stratification and ruling out AMI using the Siemens assay.23 The hs-cTnI threshold of < 5 ng/L was used and allowed identification of 46%-47% of subjects at lower risk with an NPV of 99.6% for AMI or death at 30 days. Our study demonstrated comparable outcomes, with 41% being ruled out of AMI and a similarly excellent NPV using the Beckman Coulter hs-cTnI assay.
Although it has not been implemented in the American Heart Association/American College of Cardiology guidelines yet, the use hs-cTnI has been acknowledged in the European guidelines for many years and it is a Class I recommendation.\textsuperscript{11} The use of single baseline hs-cTnI could help with early discharge of patients and provide economic value by decreasing length of stay and overall healthcare costs. Our study provides evidence that using a single cardiac marker measurement with very high sensitivity and NPV can support decisions in accurate disposition of patients presenting with symptoms suspicious for AMI to the ED. This has been demonstrated to be true using a different hs-cTnI assay in the US population in a prior study.\textsuperscript{23}

A single baseline hs-cTnI result below the 10\% CV LoQ portends a good prognosis, as only 1 patient died from non-cardiac causes and no AMIs were documented at 30 days. The modest number of events beyond 30 days in the current report, and inability of very low hs-cTnI values to recognize those patients at very low risk in future months and years, is not entirely consistent with published work from others and deserves further study.\textsuperscript{27-29}

Further tools for risk stratification, including ECG, HEART score, or further coronary artery disease testing may not provide an incremental value at these very low hs-cTnI concentrations. Nestelberger et al found that factoring in the likelihood of acute coronary syndrome or ischemic ECG changes did not improve prediction of AMI or major adverse cardiac events and actually lessened the number of subjects who were ruled out as low risk or those discharged home.\textsuperscript{30}

Additionally, it has been shown that there is an incremental but still extremely low risk of AMI and major adverse cardiac events at hs-cTn threshold values of < 2 ng/L and < 5 ng/L, compared to hs-cTn of > 5 ng/L but less than the 99\textsuperscript{th} percentile upper reference limit, allowing more patients to be discharged with a slightly higher threshold value.\textsuperscript{27} Additional studies are needed to validate our single baseline value < LoQ for AMI rule out and to determine the appropriate 1-
or 3-hour delta values that might provide further guidance for managing ED patients with possible AMI.

**Study Limitations**

This study has several limitations that may affect application or generalization of our findings. This is a single center urban ED study, which may require further validation of our cut-off of 4.0 ng/L with different demographics for widespread adoption of this assay threshold. Additionally, as this was an opportunistic study, patients presenting were screened for enrollment only when research staff were present. Typically, there were 3 shifts a day dedicated to the study on Monday through Thursday and 1 or 2 shifts on Fridays. No subject recruitment occurred Saturdays or Sundays. The adjudicated diagnosis of AMI in our cohort used the Roche Elecsys TnT Generation 5 assay. It is not entirely understood the relationship between the cTnT assay used to adjudicate and our hs-cTnI assay given these two assays measure different forms of cTn and potentially different aspects of pathophysiologic processes occurring in cardiac ischemia. Last, we were unable to conduct the 30-day telephone interview with almost half of the study cohort; however, chart reviews were conducted to complete the necessary follow-up.

In conclusion, in this single center ED study, a baseline presenting novel hs-cTnI value < 4.0 ng/L effectively ruled out AMI in 40.9% of all patients presenting to the ED and having any symptoms suspicious for AMI. Importantly, all patients presenting with acute coronary syndrome symptoms having symptoms for any duration were enrolled, including patients on dialysis and with end-stage renal disease.
References


Figure Legends

Figure 1. Patients’ enrollment process and the included final qualified patient cohort.

Abbreviations: ECG, electrocardiogram; TnI, troponin I.
Table 1. Baseline clinical characteristics for all patients and for patients with baseline Beckman Coulter’s hs-cTnI assay of < 4.0 ng/L (rule-out) vs ≥ 4.0 ng/L (rule-in) groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Qualified Patients (N=567)</th>
<th>Beckman Baseline hs-cTnI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, median (IQR), years</td>
<td>55.8 ± 11.1, 55 (49-63)</td>
<td>52.7 ± 10.3, 52 (46-59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>296 (52.2)</td>
<td>84 (36.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>462 (81.5)</td>
<td>159 (68.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>164 (28.9)</td>
<td>58 (25.0)</td>
<td>0.086</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>285 (50.3)</td>
<td>91 (39.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>211 (37.2)</td>
<td>92 (39.7)</td>
<td>0.317</td>
</tr>
<tr>
<td>Personal history of CAD</td>
<td>204 (36.0)</td>
<td>60 (25.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>220 (38.8)</td>
<td>73 (31.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Revascularization</td>
<td>140 (24.7)</td>
<td>38 (16.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCI</td>
<td>129 (22.8)</td>
<td>37 (15.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>CABG</td>
<td>31 (5.5)</td>
<td>6 (2.6)</td>
<td>0.012</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>168 (29.6)</td>
<td>46 (19.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>137 (24.2)</td>
<td>27 (11.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis</td>
<td>30 (5.3)</td>
<td>0 (0.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD</td>
<td>98 (17.3)</td>
<td>39 (16.8)</td>
<td>0.804</td>
</tr>
</tbody>
</table>

Presenting vital signs, mean ± SD, median (IQR)
Systolic BP, mm Hg 144.8 ± 25.9, 143 (127-140.5 ± 22.2, 138.5 147.7 ± 27.9, 145 (128-<0.001 159) (125-153) 164)

Diastolic BP, mm Hg 85.5 ± 17.5, 83 (74-97) 84.4 ± 15.4, 82 (74.5-86.3 ± 18.8, 83 (73-98) 0.175 95)

Heart rate, beats/min 83.9 ± 18.9, 82 (70-95) 82.9 ± 17.7, 81 (70.5-84.5 ± 19.7, 82 (70 0.337-96)

ECG findings (%) Atrial fibrillation 20 (3.5) 2 (0.9) 18 (5.4) 0.004 0.065 Sinus tachycardia Other tachycardia 10 (1.8) 4 (1.7) 6 (1.8) 1.000 Left ventricular hypertrophy 94 (16.6) 21 (9.1) 73 (21.8) <0.001 Left bundle branch block 10 (1.8) 0 (0.0) 10 (3.0) 0.007 Right bundle branch block 27 (4.8) 3 (1.3) 24 (7.2) 0.001 V-paced 13 (2.3) 1 (0.4) 12 (3.6) 0.014 ST-segment elevation ≥ 1 9 (3.9) 11 (3.3) 0.705 ST-segment depression ≥ 1 25 (4.4) 3 (1.3) 22 (6.6) 0.003 Rightward T-wave inversion 34 (14.7) 135 (40.3) <0.001 ECG tracing within normal limits 51 (15.2) <0.001

Home medications (%) Aspirin 300 (52.9) 98 (42.2) 202 (60.3) <0.001 Anti-coagulant 49 (8.6) 12 (5.2) 37 (11.0) 0.014
<table>
<thead>
<tr>
<th>Medication</th>
<th>Frequency</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>141 (24.9)</td>
<td>46 (19.8)</td>
<td>95 (28.4)</td>
<td>0.021</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>218 (38.4)</td>
<td>64 (27.6)</td>
<td>154 (46.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Angiotensin receptor</td>
<td>38 (6.7)</td>
<td>9 (3.9)</td>
<td>29 (8.7)</td>
<td>0.025</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>256 (45.1)</td>
<td>66 (28.4)</td>
<td>190 (56.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>144 (25.4)</td>
<td>41 (17.7)</td>
<td>103 (30.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nitrates</td>
<td>129 (22.8)</td>
<td>37 (15.9)</td>
<td>92 (27.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Anti-arrhythmic</td>
<td>14 (2.5)</td>
<td>2 (0.9)</td>
<td>12 (3.6)</td>
<td>0.040</td>
</tr>
</tbody>
</table>

ACE, angiotensin converting enzyme; BP, blood pressure; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; hs-cTnI, high sensitivity cardiac troponin I; PCI, percutaneous coronary intervention.

Categorical data is given as frequency (%) measurements. Numerical data is given as mean (standard deviation [SD]) and median (interquartile range [IQR]) values.
Table 2. The ability of various cut-points to predict hs-cTnI defined AMI final diagnosis

<table>
<thead>
<tr>
<th>hs-cTnI (ng/L)</th>
<th>4.0</th>
<th>5.0</th>
<th>18.0</th>
<th>20.0 (males)</th>
<th>15.0 (females)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>100.0</td>
<td>97.8</td>
<td>82.6</td>
<td>77.8</td>
<td>89.5</td>
</tr>
<tr>
<td></td>
<td>(92.3-100.0)</td>
<td>(88.5-99.9)</td>
<td>(68.6-92.2)</td>
<td>(57.7-91.4)</td>
<td>(66.9-98.7)</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>44.5</td>
<td>51.8</td>
<td>84.3</td>
<td>81.0</td>
<td>88.9</td>
</tr>
<tr>
<td></td>
<td>(40.2-48.9)</td>
<td>(47.4-56.2)</td>
<td>(80.8-87.3)</td>
<td>(75.8-85.6)</td>
<td>(84.3-92.5)</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>100.0</td>
<td>99.6</td>
<td>98.2</td>
<td>97.3</td>
<td>99.1</td>
</tr>
<tr>
<td></td>
<td>(98.4-100.0)</td>
<td>(98.0-100.0)</td>
<td>(96.5-99.2)</td>
<td>(94.3-99.0)</td>
<td>(96.8-99.9)</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>13.7</td>
<td>15.2</td>
<td>31.7</td>
<td>29.2</td>
<td>37.8</td>
</tr>
<tr>
<td></td>
<td>(10.2-17.9)</td>
<td>(11.3-19.8)</td>
<td>(23.5-40.8)</td>
<td>(19.0-41.1)</td>
<td>(23.8-53.5)</td>
</tr>
</tbody>
</table>

AMI, acute myocardial infarction; hs-cTnI, high sensitivity cardiac troponin I.
Figure 1

1699 Patients screened

ENROLLED

575 Enrolled in study

4 No clinically ordered TnI

2 Enrolled twice under different identities (first used)

2 Patients had missing TnI

567 Qualified for analysis

NOT ENROLLED

338 Baseline drawn could not be done <1 hour of triage ECG

327 Refused to participate

226 Impaired (substance abuse, active mental health issues)

86 Previously enrolled

147 Assorted other reasons