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ORIGINAL RESEARCH

Cardiology

Outcomes in ED patients with non-specific ECG findings and low high-sensitivity troponin

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Abstract

Background: Although some emergency department risk stratification tools consider non-specific ECG findings as an aid in disposition decisions, their clinical value in patients with an initially low high-sensitivity cardiac troponin I (hsTnI) is unclear.

Objective: Our purpose was to determine if non-specific ECG (ns-ECG) findings are associated with 30-day major adverse cardiac events (MACE) in ED patients presenting with suspected acute coronary syndromes (ACS) who have a low initial hsTnI.

Methods: Using the prospective Siemens Atellica hsTnI Food and Drug Administration submission observational database, we conducted a retrospective cohort study of the association between ns-ECG findings (defined as left bundle branch block [LBBB], ST depression [STD], or T-wave inversions [TWI]) and 30-day MACE (death, myocardial infarction, heart failure hospitalization, or coronary revascularization). Eligible patients presented with suspected ACS to one of 29 US EDs from April 2015 to April 2016, had stable vital signs, a blood sample for hsTnI (Siemen's Atellica, Siemens Healthineers, Inc, Malvern, PA) obtained at 1, 3, and 6 hours after ED presentation, and were followed for 30 days. The relationship between 30-day outcome, initial hsTnI, and ns-ECG was evaluated using chi-square testing.

Results: Of 2676 enrolled, 1313 patients met the inclusion criteria and are included in the analysis. Median (interquartile range) age was 62 years (54, 72), 54% were male, with 56% white, and 39% African American. Median (interquartile range) times from symptom onset to presentation and presentation to specimen collection were 92 (0, 216) and 146 (117, 177) minutes, respectively. The most common presenting symptoms were chest pain (84%), followed by dyspnea (9%). ECG findings were categorized as T-wave inversion or non-specific T wave changes (42%), ST depression ns-ECG ST changes (16%), or LBBB (2%). Thirty-day MACE occurred in 72 (5.5%) patients, with coronary revascularization (35 patients, 2.7%) and heart failure (25 patients, 1.9%) being the most frequent outcomes. In patients with an initial hsTnI below the limit of

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quantitation (LOQ) of 2.5 ng/L (n = 449), there was no association between ns-ECG changes and 30-day MACE ($P = 0.42$). If the hsTnI was ≥LOQ (2.5 ng/L), there were increased rates of 30-day MACE and ns-ECG findings ($P = 0.01$).

Conclusion: In ED suspected ACS patients without unstable vital signs, and an initial hsTnI less than the LOQ (2.5 ng/L), ns-ECG findings are not associated with 30-day major adverse cardiac events. The use of ns-ECG findings in ACS disposition should be considered in the context of hsTnI levels.

KEYWORDS
ACS, Emergency, High-sensitivity cardiac troponin, hsTnI, LBBB, MACE, non-specific ECG findings, ST depressions, T-wave inversions

1 | INTRODUCTION

1.1 | Background

Non-specific ECG (ns-ECG) findings are commonly defined as ST-segment depression, T-wave inversion, and left bundle branch block (LBBB).[1] These changes are frequently included in risk stratification tools that often result in further evaluation and potential hospitalization. ns-ECG findings are included as an important constituent of the HEART score (history, ECG, age, risk factors, and initial troponin), a tool that is commonly used as an aid in disposition decision making for ED patients presenting with symptoms suggestive of acute coronary syndromes (ACS). For example, when using the HEART score in an ED patient older than 65 years, ns-ECG findings would place the patient in the "not low risk" category, as they are reported to be associated with a major adverse cardiac event (MACE) rate of 12%–16.6%.[2,3] (Supporting Information)

1.2 | Importance

The association between ns-ECG findings and 30-day adverse events is poorly documented in the era of highly sensitive cardiac troponin (hsTnI). Highly sensitive troponin assays have the advantage of detecting lower concentrations than conventional troponin testing.[4] This improved sensitivity may provide superior risk assessment, compared to ns-ECG findings, for predicting 30-day outcomes in patients presenting to the emergency department with suspected ACS given that hsTnI is independently associated with adverse cardiac outcomes in asymptomatic outpatient populations.[5–7]

1.3 | Goals of this investigation

We hypothesize that ns-ECG findings have a limited association with short-term MACE outcomes in the setting of a symptomatic ED patient with a low hsTnI concentration that is below the limit of quantification (LOQ). Our purpose was to determine if ns-ECG changes are associated with adverse 30-day outcomes in suspected ACS patients with initial low troponin levels compared with those with higher levels, as measured by a hsTnI assay in ED patients presenting with suspected ACS.

2 | METHODS

2.1 | Study design and setting

Using data from High-Sensitivity Cardiac Troponin I Assays in the United States (HIGH-US) Food and Drug Administration (FDA) submission database,[8] the FDA clearance trial of the Siemens Healthineers Atellica hsTnI assay, we performed a retrospective observational cohort study to evaluate the association between ns-ECG changes and 30-day MACE in patients with low presenting hsTnI concentrations. MACE was defined as death, myocardial infarction, heart failure hospitalization, or undergoing coronary artery catheterization with a subsequent finding of a coronary artery obstruction exceeding 70% and requiring coronary revascularization.

The HIGH-US study was a prospective observational study, enrolling 2676 patients over 22 years of age, from 29 US centers, who presented to the ED with angina or angina-equivalent symptoms, with blood drawn for troponin testing within 1, 3, and 6 hours after ED presentation, from April 2015 to April 2016. Patients were required to provide informed consent before enrollment and the protocol was approved by each contributing institution's review board.

Inclusion criteria for this analysis were availability of documentation of troponin results, ECG findings, and 30-day outcomes after ED encounter. Ns-ECG findings were defined as ST-segment depression (STD or non-specific ST-segment changes, T-wave inversion [TWI] or non-specific T-wave changes, or left bundle branch block [LBBB]) that was not classified as acute myocardial infarction (AMI) by the treating clinical team. All ECGs were interpreted by board certified cardiologists, blinded to the assay results and clinical course.

Patients were excluded for absent data, the presence of ECG changes specific for cardiac pathology as the reason for presentation, or hemodynamic instability. ECGs changes specific for cardiac

The Bottom Line

In this paper, we evaluate whether non-specific ECG findings in patients presenting with chest pain or its equivalent who have low high-sensitivity troponin have any association with short-term mortality. Our findings revealed that non-specific ECG findings in the setting of a high-sensitivity troponin below the limit of quantification are not associated with 30-day major adverse cardiac events. This is significant because it may help reduce the burden on both the health care system, and more important, the patients themselves as they can be further evaluated for these findings in an outpatient setting rather than needing to be admitted to the hospital for further workup of such findings.

pathology were defined as ST segment elevation MI, atrial fibrillation, atrial flutter, ventricular fibrillation, ventricular tachycardia, ventricular-paced rhythm, supraventricular tachycardia, and complete heart block. Hemodynamic instability was defined as heart rate > 120 bpm or systolic blood pressure <90 mmHg at ED presentation. The primary outcome of interest of this analysis is the development of any MACE within 30 days of ED presentation.

2.2 | Data collection

Blood samples were collected in lithium heparin and serum blood tubes and analyzed at core labs for research purposes (Siemens Healthcare Diagnostics, Tarrytown, NY; Research & Development Institute, Calabasas, CA; Baylor Scott & White Healthcare Texas A&M Health Science Center, Temple, TX; University of Maryland, Baltimore, MD; or Minneapolis Medical Research Foundation, Minneapolis, MN) on the Atellica Immunoassay Analyzer and ADVIA Centaur XP systems. The Atellica Immunoassay hs-cTn assay is a 3-site sandwich immunoassay that uses direct chemiluminescent technology and has a measuring range of 2.5–25,000 ng/L, a limit of detection of 1.6 ng/L, and limit of quantitation of 2.5 ng/L. The 10% coefficient of variation is found at 6 ng/L, and the 99th percentile upper reference limit (URL) is 45 ng/L, with sex-specific 99th percentile URLs of 34 and 53 ng/L, for women and men, respectively.[9–11]

2.3 | Analysis

Unadjusted comparison between groups was accomplished using the Mann–Whitney U test for continuous variables and the Pearson χ^2 statistic for categorical variables. The association between ns-ECG findings on the initial ECG stratified by the initial hsTnI with 30-day MACE, was evaluated using χ^2 test. Alpha was defined as $P < 0.05$. All statistical analyses were performed using the SAS 9.4 software (SAS Institute Inc, Cary, NC, 2014). Graphs were generated using Microsoft Excel 2020 (Redmond, WA) version 16.41.

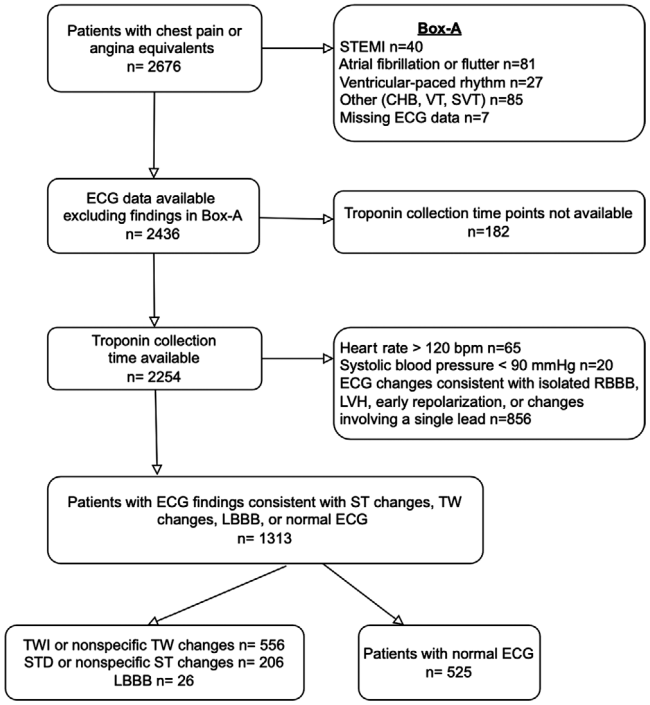

FIGURE 1 Study flow chart. Abbreviations: CHB, complete heart block; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; RBBB, right bundle branch block; STD, ST-segment depression; STEMI, ST-segment elevation myocardial infarction; SVT, supraventricular tachycardia; TWI, T-wave inversion; VT, ventricular tachycardia

3 | RESULTS

A total of 1313 patients met all inclusion, and no exclusion, criteria for this analysis (Figure 1). Median (interquartile range [IQR]) time from symptoms onset to ED presentation was 92 minutes (0, 216), and the median (IQR) duration between presentation to sample collection was 146 minutes (117,177). Descriptive statistics of this cohort are summarized in Table 1. Median (IQR) age was 62 years (54, 72), 54% were male, 56% and 39% were white and African American, respectively. The most common chief complaint was chest pain (n = 1101, 84%) followed by dyspnea (9%). ECGs were interpreted as normal in 525 (40%), with non-specific findings in the majority (Table 1). Coronary artery disease (CAD) risk factors were most commonly hypertension (n = 916, 69.8%) and hyperlipidemia (n = 552, 42%) (Table 1). Overall, more than one third (n = 472, 36%) of patients had established CAD; 272 (21.7%) had a prior MI, 330 (25.1%) had a previous percutaneous coronary intervention, and 105 (8%) had a history of coronary artery bypass grafting.

A total of 449 had an initial concentration <2.5 ng/L and 864 patients had an initial troponin ≥2.5 ng/L. Overall, 72 patients had MACE within 30 days of presentation; 17 (3.8%) and 55 (6.4%) and in the <2.5 and ≥2.5 ng/L hsTnI groups, respectively (Table 2A,B). There were differences in baseline characteristics between those with higher initial hsTnI, defined as ≥2.5 ng/L, versus those below. Patients with a higher troponin were older, had a median (IQR) age of 64 (56, 74)

TABLE 1 Baseline characteristics of study population

Demographics	No. (%) n = 1313	HsTnI ≥LOQ (2.5 ng/L) n = 864 (%)	HsTnI <LOQ (2.5 ng/L) n = 449 (%)	*P* value
Age, median (IQR), y				**<0.001**
Age, y	62 (54, 72)	64 (56, 74)	58 (50, 66)	
18–34	16 (1)			
35–49	185 (15)			
50–59	388 (32)			
60–69	374 (30)			
70–79	175 (14)			
80 and above	92 (7)			
Sex				**<0.001**
Female	608 (46)	336 (39)	271 (61)	
Race				0.318
White	734 (56)	468 (54)	266 (59)	
Black	518 (39)	359 (42)	159 (35)	
American Indian	16 (1)	9 (1)	7 (2)	
Asian	17 (1)	11 (1)	6 (1)	
Hawaiian	1	1	0	
All other	27 (2)	16 (2)	11 (2)	
Chief complaint				**0.013**
Chest pain	1101 (84)	704 (81)	397 (88)	
Dyspnea	119 (9)	94 (11)	25 (6)	
Dizziness	19 (1)	14 (2)	5 (1)	
Palpitations	8 (1)	4	4 (1)	
Fatigue	3	3	0	
Other, non-specific	63 (5)	45 (5)	18 (4)	
ECG findings				**<0.001**
Normal	525 (40)	277 (32)	248 (55)	
Left bundle branch block	26 (2)	21 (2)	5 (1)	
ST-segment depression or non-specific ST changes	206 (16)	162 (19)	44 (10)	
T-wave inversion or non-specific T-wave changes	556 (42)	404 (47)	152 (34)	
Risk factors and comorbidities				**<0.001**
Hypertension	916 (69.8)	659 (8)	257 (57)	
Hyperlipidemia	552 (42)	406 (47)	146 (33)	
Heart failure	232 (17.7)	197 (23)	35 (8)	
Diabetes mellitus	400 (30.5)	298 (34)	102 (23)	
Coronary artery disease	472 (36)	364 (42)	108 (24)	
Prior MI	272 (21.7)	212 (25)	60 (13)	
Prior PCI	330 (25.1)	262 (30)	68 (15)	
Prior CABG	105 (8)	88 (10)	17 (4)	
Chronic kidney disease	139 (10.6)	122 (14)	17 (4)	
Peripheral vascular disease	49 (3.7)	42 (5)	7 (2)	
Stroke	118 (9)	81 (9)	37 (8)	
Tobacco use	391 (29.8)	254 (29)	137 (31)	
Current	383 (29.2)	264 (31)	119 (27)	
Former				

Abbreviations: CABG, coronary artery bypass graft; HsTnI, high-sensitivity cardiac troponin I; IQR, interquartile range; LOQ, limit of quantitation; MI, myocardial infarction; PCI, percutaneous coronary intervention

$P < 0.05$ is considered statistically significant.

TABLE 2 30-day outcomes, stratified by ECG and hsTnI. Relation of ECG and 30-day MACE if hsTnI < 2.5 ng/L (A); Relation of ECG and 30-day MACE if hsTnI ≥2.5 ng/L (B); Relation of 30-day MACE and hsTnI if abnormal ECG (C)

A			
In cohort with hsTnI <2.5 ng/L			
	30-day MACE		
ECG findings	**Yes (%)**	**No (%)**	**Total**
Non-specific	6 (3)	195 (97)	201
Normal	11 (4.4)	237 (95.6)	248
Total	17	432	449
B			
In cohort with hsTnI ≥2.5 ng/L			
	30-day MACE		
ECG findings	**Yes (%)**	**No (%)**	**Total**
Non-specific	46 (7.8)	541 (92.2)	587
Normal	9 (3.2)	268 (96.8)	277
Total	55	809	864
C			
In cohort with abnormal ECG			
	30-day MACE		
hsTnI	**Yes (%)**	**No (%)**	**Total**
hsTnI >= 2.5 ng/L	46 (7.8)	541 (92.2)	587
hsTnI < 2.5 ng/L	6 (2.9)	195 (97.1)	201
Total	52	736	788

Abbreviations: HsTnI, high-sensitivity cardiac troponin I; MACE, major adverse cardiac events

TABLE 3 30-day MACE rate by hsTnI level

30-day events, N (%)[a]	**HsTnI < LOQ (< 2.5 ng/L) n = 17 (%)**	**HsTnI ≥LOQ (2.5 ng/L) n = 60 (%)**
Death	0 (0)	3 (0.35)
Acute myocardial infarction	1 (0.2)	8 (0.9)
Coronary revascularization	10 (2.2)	25 (2.9)
Heart failure hospitalization	6 (1.3)	19 (2.2)

[a]Numbers do not sum as patients could have multiple events

Abbreviations: HsTnI, high-sensitivity cardiac troponin I; LOQ, limit of quantitation; MACE, major adverse cardiac events

versus 58 (50, 66) years, and were more likely male, 61% versus 39%, respectively, compared to the low hsTnI group. The patients in the high hsTnI group were also less likely to have normal ECG findings; 32% vs 55% when compared to the low hsTnI population. Finally, patients with hsTnI <2.5 ng/L had a MACE rate of almost half of those in the higher troponin cohort, with each of the subcategories being consistently lower (Table 3).

Non-specific ECG changes were common, with T-wave inversions or non-specific T-wave changes comprising the majority of abnormal ECG findings (42%). This compared to ST-segment depression or non-specific ST changes, which constituted only 16%. Last, only 2% of the participants had ECG findings of LBBB.

Overall, there was an association between initial hsTnI concentration and 30-day MACE ($P < 0.001$). There was also an association between abnormal ECG findings, specifically LBBB, STD, and TWI, and 30-day MACE with 6.6% of patients with ns-ECG findings having a MACE within 30 days of follow up, versus 3.8% of those with a normal ECG ($P = 0.03$).

Additionally, patients with non-specific ECG findings had an association between hsTnI and 30-day MACE ($P = 0.0168$) [Table 2C]. However, stratifying by the initial hsTnI found the association between the initial ns-ECG findings and 30-day MACE was significant only if the hsTnI was ≥2.5 ng/L (30-day MACE = 7.8% vs 3.2%, in those with non-specific vs normal ECGs, respectively, $P = 0.010$) and insignificant below this level (3% vs 4.4%, respectively, $P = 0.42$). Of patients with a hs-cTnI ≥2.5 ng/L, the odds of having non-specific ECG changes were 2.53 times higher among those whho had 30-day MACE than those who did not have any significant short-term MACE. In those with the hs-cTnI below 2.5 ng/L (odds ratio [OR] = 2.53, 95% confidence interval [CI]:1.22, 5.25), the odds of having non-specific ECG changes were 0.34 times lower among those who had 30-day MACE than those who had not (OR = 0.66, 96% CI: 0.24, 1.82).

There was no significant difference in proportion of males (62%) with non-specific ECG compared to females (57%, $P = 0.06$). However, there were significant differences between sexes when evaluating the association between non-specific ECG findings and adverse outcomes when the initial hsTnI ≥2.5 ng/L. Whereas males with higher hsTnI and ns-ECG findings were more likely to have 30-day MACE ($P = 0.01$) women were not ($P = 0.77$).

There was a total of 3 deaths reported, and all were associated with a hsTnI > 45 ng/L. One was attributed to end-stage lung cancer, a second to an unknown cause, and the third was cardiac related. The cardiac death patient had concomitant ns-ECG ST-segment changes and inverted T-waves on the ECG, and the other 2 deceased patients had normal ECG findings.

When examining patients with 30-day MACE based on specific ECG changes (n = 72), it was found that 37 (51.4%) had T-wave inversions or non-specific T-wave changes. This comprised 6.7% of the group with T-wave changes who suffered 30-day MACE (1 death, 6 AMI, 14 heart failure hospitalization, and 16 with CAD requiring revascularization). Similarly, 6.3% of the cohort with ST-segment depression or non-specific ST changes had 30-day MACE (5 heart failure hospitalizations and 8 CAD requiring revascularization), whereas only 2 with LBBB experienced 30-day MACE. However, given the small LBBB cohort (n = 26), this comprised 7.7% of this group (1 AMI, 1 heart failure hospitalization). Conversely, only 3.8% of those with normal ECG findings had 30-day MACE (2 deaths, 2 AMI, 5 heart failure hospitalization, 11 CAD requiring revascularization) [Figure 2].

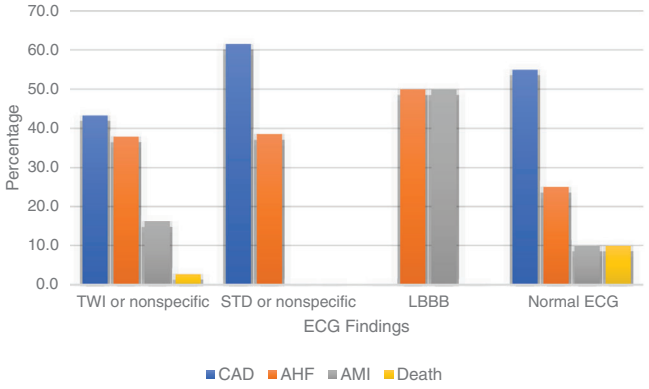

FIGURE 2 30-day MACE by ECG findings. Abbreviations: AHF, acute heart failure; AMI, acute myocardial infarction; CAD; coronary artery disease; LBBB, left bundle branch block; STD, ST-segment depression; TWI, T-wave inversion

3.1 | Limitations

This was a retrospective study that included 29 different sites, and although large, a prospective validation will be needed before patient management should be universally altered based on these results. Usual care workups were dictated by contemporary generation troponin assays, and thus there is the potential to identify more or less MACE using hsTnI assays, which could affect our findings. Additionally, the individual parameter definition of non-specific ECG changes is not standardized, and institutional variation may have occurred. How the differential interpretation (the way one physician defines non-specific T-wave changes vs another) could affect our results is unclear. Furthermore, although it is unclear if ST-elevation MI (STEMI) equivalents such as deWinter's T-waves or Wellen's morphology were accounted for, because of the very low MACE rate in the < 2.5 ng/L troponin group, the clinical impact of a potential misclassification is minimal. Finally, another limitation to generalizing our data is that troponin assay cut-points are not universal and cannot be considered for assays other than the Siemens Healthineers Atellica hsTnI.

Further studies are needed, particularly in the United States, which has been slow to adopt highly sensitive troponins on a widespread scale, to evaluate the validity of these findings and to determine the most accurate cutoffs to incorporate into risk stratification scores among the US population.

4 | DISCUSSION

Our data are the first to demonstrate that highly sensitive troponins have greater prognostic value than isolated ns-ECG changes. Thus, when faced with ns-ECG changes and a very low hsTnI, the clinician may consider the hsTnI concentration as more indicative of 30-day prognosis. Although others have evaluated ns-ECG changes, when combined in a risk stratification score (eg, the HEART score), they have not evaluated this as an individual outcome predictor stratified by highly sensitive troponin testing results. In fact, Mahler et al. reported no difference in the performance of the HEART score when using either conventional cardiac TnI or hsTnI. They showed that incorporating either assay achieved 100% sensitivity and negative predictive value.[12] However, as sensitivity is a function of false negatives, it can be maximized simply by excessive admission rates (eg, a 100% ED admission rate results in no false negative discharges).

Other analyses have demonstrated that, although the HEART score can identify a cohort of patients who are safe discharge candidates, scoring systems that do not weigh ns-ECG parameters (eg, ED ACS score) are more effective at maximizing the safe discharge rate.[13,14] These findings are consistent with our data that demonstrate hospitalization based on isolated ns-ECG changes, although expensive, would be associated with minimal outcome changes.[15]

Our study shows that non-specific ECG changes are not associated with short-term adverse cardiac outcomes in the setting of a hsTnI < LOQ (2.5 ng/L). Hemodynamically stable patients who present within 3 hours of symptom onset have non-specific findings on initial ECG, and have an initial hsTnI level of <LOQ (2.5 ng/L) obtained within 2–3 hours after presentation are safe to discharge home from the ED and can be provided with outpatient follow-up for further workup.

LBBB has historically been regarded as a STEMI equivalent and can be concerning for a serious underlying myocardial injury. This is especially true if it is new, or presumably new, and associated with concerning clinical symptoms. However, the prognostic value of the presence of a LBBB is unclear. Jain et al reported that one third of patients diagnosed with new, or presumably new, LBBB had non-cardiac final diagnoses, which was particularly seen in younger patients with low cardiac risk scores, low troponin, and ECG Sgarbossa score of zero.[16] Studies have been inconsistent with regard to its predictive value for mortality and morbidity, as some regarded the LBBB as an independent predictor, whereas others have found it to be attributed to other confounders.[17–20] We hypothesize that LBBB in the setting of a low hsTnI is low risk, with limited association with short-term MACE, as highly sensitive biomarkers such as hsTnI are able to detect minimal myocardial injury. However, because of the smaller proportion of our patients having LBBB (only 2%) our results may not be generalizable to patients with this specific finding. Furthermore, ECGs with LBBB should be interpreted based on modified Sgarbossa criteria to indicate the presence of AMI that, if present, would require the activation of the cardiac lab.[21] It is unclear whether Sgarbossa criteria were considered when recording these findings by each of our respective facilities.[22] Thus, we suggest caution when considering our findings to this particular group.

Sex differences were also noted in our analysis. Males were more likely to have 30-day MACE, despite having no difference in the frequency of non-specific ECG changes. Mosca et al. reported that, although a higher proportion of females have cardiovascular disease, strokes, and subsequent mortality, the case is reversed with regard to CAD, where males constitute a higher proportion of those affected by adverse outcomes.[23] Further studies are needed to explain this disparity.

The United States has not universally implemented the use of highly sensitive troponin assays, potentially owing to concerns of greater capture of type 2 MI and overdiagnosis. However, the greatest utility of hsTnI is in the ED setting, where it can rapidly rule out ACS. Its greatest value is its incorporation into protocols that do not necessitate as much as 6 hours to determine whether a low-risk chest pain patient is safe for discharge. The ability of hsTnI to expedite the process to a 1 hour rule-out protocol reduces unnecessary resource use, shortens ED length of stay, and may reduce ED overcrowding.[24] Furthermore, even greater ED impact is expected, given the potential for highly sensitive troponins to enter the point-of-care market in the very near future.

Patients with STEMI were excluded from this study. In this population, recent data showed a possible delay in the rise of hsTnI that is thought to be due to the complete vascular occlusion interfering with the release of myonecrosis markers into the blood stream. According to Wereski et al., a small percentage of confirmed STEMI cases had a hsTnI level of <5 ng/L (Abbott Architect Stat assay) upon presentation to the ED, which was more commonly seen in patients with posterior STEMI.[25]

Finally, our data incorporate a patient population with a mean age exceeding 60, and who commonly have multiple comorbidities such as hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, peripheral artery disease, cerebrovascular accident, and/or tobacco smoking. Applying the HEART score to this older cohort with low troponin and ns-ECG findings provides a non-low risk score of 4. This may systematically result in more hospitalizations in this subpopulation that are unlikely to reduce MACE based on our data. We suggest that future studies incorporate hsTnI in risk score analyses of outcomes and interventions.

In conclusion, in ED patients presenting with suspected acute coronary syndromes and stable vital signs, ns-ECG changes have no association with 30-day adverse cardiac events in patients with an initial hsTnI below the LOQ (2.5 ng/L). Further studies are needed to determine if the use of ns-ECG findings as a determinant of disposition decisions should be reconsidered in these patients.

CONFLICT OF INTEREST

Lamees Alshaikh: The author has no disclosures to report. Fred Apple: Board of Directors: HyTest Ltd; associate editor: Clinical Chemistry; Advisory Boards: Instrumentation Laboratory, Siemens Healthineers, Osler Diagnostics, Qorvo; Honorarium for Speaking at Industry Conferences: Siemens Healthineers, Abbott Diagnostics; principal investigator on Industry Funded Grants (non-salaried) on cardiac biomarkers through Hennepin Healthcare Research Institute: Abbott Diagnostics, Abbott POC, BD, Beckman Coulter, Ortho-Clinical Diagnostics, Roche Diagnostics, Siemens Healthcare, ET Healthcare, Qorvo. Frank Peacock: Research Grants: Abbott, Becton Dickenson, Brainbox, Calcimedica, CSL Behring, Cue, Ortho Clinical Diagnostics, Relypsa, Roche, Salix, Siemens. Consultant: Abbott, Astra-Zeneca, Beckman, Bosch, Fast Biomedical, Forrest Devices, Ischemia Care, Dx, Instrument Labs, Janssen, Nabriva, Ortho Clinical Diagnostics, Osler, Relypsa, Roche, Quidel, Salix, Siemens, Upstream. Stock/Ownership Interests: AseptiScope Inc, Brainbox Inc, Braincheck Inc, Coagulo Inc, Comprehensive Research Associates LLC, Comprehensive Research Management Inc, Emergencies in Medicine LLC, Fast Inc, Forrest Devices, Ischemia DX LLC, Lucia Inc, Prevencio Inc, ScPharma, Trivirum Inc, Upstream Inc. Christopher R. deFilippi: Research funding to Inova fromAbbott Diagnostics, Roche Diagnostics, Siemens Healthineers, and Ortho Diagnostics, and consults for FujiRebio, Roche Diagnostics, Siemens Healthineers, and Ortho Diagnostics. James McCord: Research Support: Beckman, Abbott, Siemens, Roche. Consulting: Beckman, Roche. Richard Nowak: The author has no disclosures to report. Robert H. Christenson: Consultant: Roche Diagnostics, Siemens Healthineers, Quidel Diagnostics, Sphingotech, Becton Dickinson, Beckman Coulter. Scientific Advisory Board: Roche Diagnostics, Siemens Healthineers, Quidel Diagnostics, Sphingotech, Becton Dickinson. Alexander T. Limkakeng: Research funding from the following entities: Roche Diagnostics, Inc., Abbott Laboratories 2020-now, Siemens Healthcare Diagnostics until 2020, Bristol Meyers Squibb 2019–2020, GE 2019—2020, Astrazeneca 2019—2020, Forest Devices, Inc: 2019—2020, Department of Defense/Henry Jackson Foundation, National Institutes of Health, Regeneron, Becton Dickinson.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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