VOL. 2, NO. 7, 2023
ISSN 2772-963X

Letters

RESEARCH LETTER

Diagnostic Performance of High-Sensitivity Cardiac Troponin I in a Multicenter U.S. Emergency Department Cohort

The clinical question being addressed is how well does an accelerated diagnostic algorithm using high-sensitivity cardiac troponin I (hsTnI) perform in a U.S. population?

The hsTnI-based algorithm identified 70% of patients for expedited emergency department (ED) discharge with a 99.8% negative predictive value for 30-day myocardial infarction (MI).

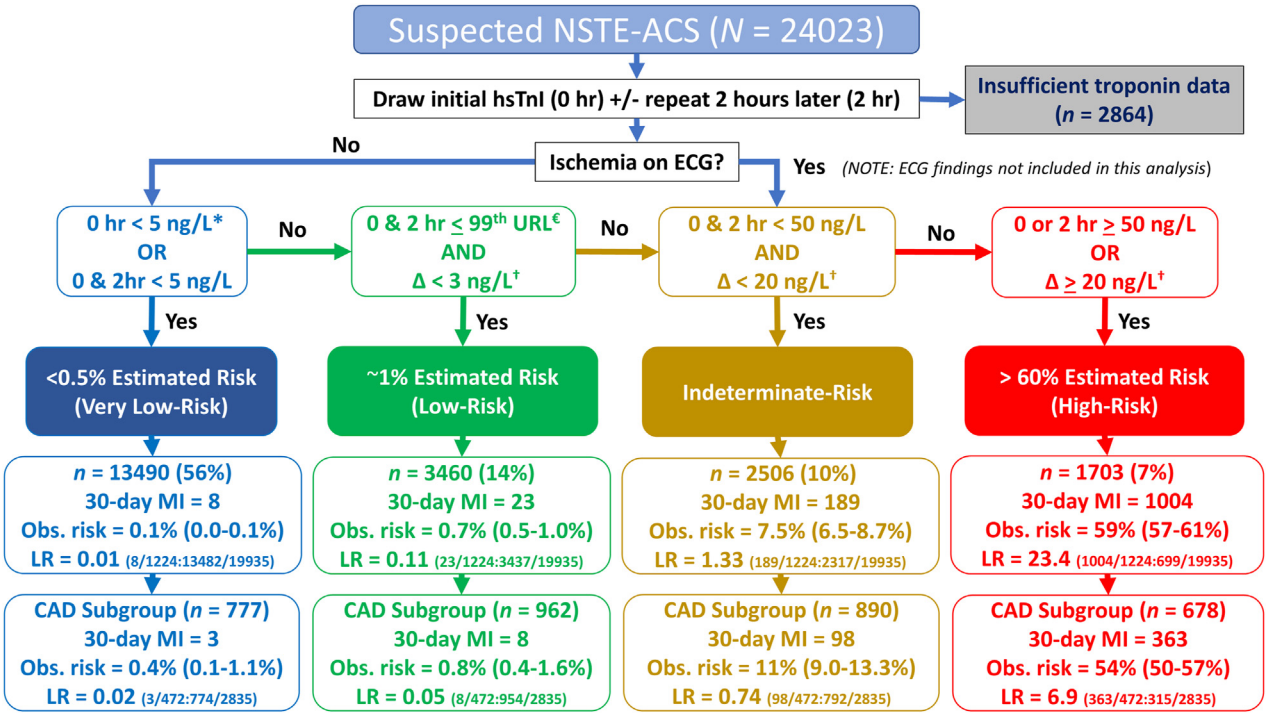
Implementation of hsTn assays in the United States has been associated with lower hospital length of stay and less invasive coronary angiography among low-risk patients.[1] While hsTn-only risk stratification strategies, such as the European Society of Cardiology (ESC) 0/1-h algorithm, have been extensively validated outside of the United States, initial reports from U.S. populations using the ESC 0/1-h algorithm and an hsTnT assay have raised concern about the diagnostic accuracy of low-risk designations.[2,3] Still, there have been limited data examining the performance of alternative algorithms and/or hsTnI assays among U.S. populations. Thus, we examined the performance of a hybrid hsTnI-based risk stratification algorithm during the first 100 days following implementation across a large integrated U.S. healthcare delivery system, with a principal aim of ensuring the safety of low-risk designations.

We retrospectively studied adult (aged 18 years and older) ED patients undergoing hsTnI testing for the evaluation of chest discomfort within Kaiser Permanente Northern California (KPNC) between November 16, 2022 and February 23, 2023. The KPNC Institutional Review Board approved the study. KPNC operates 21 medical center-based EDs serving a diverse population with over 1.5 million annual ED visits. KPNC introduced an hsTnI assay (Access hsTnI, Beckman-Coulter) on November 16, 2022. At the same time, an hsTnI-based algorithm was introduced for the risk stratification of patients with concern for non-ST-segment elevation acute coronary syndrome (the KPNC NSTE-ACS HsTnI algorithm). The KPNC NSTE-ACS HsTnI algorithm was designed as a hybrid of the High-STEACS[4] (lower-risk criteria) and ESC 0/2-h algorithms[5] (high-risk criteria), and places patients into one of 4 risk designations (**Figure 1**). Sex-specific 99th centile upper reference limits (12 ng/L for females, 20 ng/L for males) are per manufacturer recommendations, and the very low-risk cutoff (<5 ng/L) was extrapolated from the hsTnI assay studied in High-STEACS. Very low and low-risk patients were recommended for ED discharge, indeterminate-risk for further testing, and high-risk for admission/consultation. Electrocardiogram findings, while part of the algorithm, were not considered in this analysis due to the retrospective study design, though patients with an ED diagnosis of ST-elevation MI were excluded.

Comorbidities and outcomes were based on diagnostic codes (International Classification of Diseases [ICD]-10th Revision). The primary outcome was all-cause 30-day MI, inclusive of index diagnoses. A subgroup analysis was performed among patients with coronary artery disease (CAD), given prior reports of inadequate low-risk discrimination in these patients when using the ESC 0/1-h algorithm and an hsTnI assay.[2] The observed incidence of 30-day MI was calculated with Wilson 95% confidence intervals, along with likelihood ratios. Differences in proportions were assessed using the "N-1" chi-squared test (MedCal Version 22.007). P values <0.05 were considered statistically significant.

Of 24,023 eligible patients, the median age was 57 years, 23% had diabetes, 17% had CAD, and 8% had prior coronary revascularization. The 30-day MI incidence was 5.9%, of which 4.9% were diagnosed during the index hospitalization. Overall, 16,950 (70%) patients were eligible for expedited ED discharge (56% very low-risk and 14% low-risk), 2,506 (10%) were indeterminate-risk, and 1,703 (7%) were

FIGURE 1 The KPNC Non-ST-Segment Elevation Acute Coronary Syndrome hsTnI Algorithm



Ranges represent 95% confidence intervals. *0 hour rule out applicable only if chest pain onset >3 hours; €Female = 12 ng/L; Male = 20 ng/L; †Δ = change in value over 2 hours. ECG = electrocardiogram; hsTnI = high-sensitivity cardiac troponin I; KPNC = Kaiser Permanente Northern California; LR = likelihood ratio; MI = myocardial infarction; URL = upper reference limit.

high-risk. There were insufficient troponin data to determine risk for the remaining 2,864 (12%) due to having only a single hsTnI result between the very low-risk (<5 ng/L) and high-risk (≥50 ng/L) thresholds. The observed incidence of 30-day MI was as follows: very low-risk 0.1% (95% CI: 0.0%-0.1%), low-risk 0.7% (95% CI: 0.5%-1.0%), indeterminate-risk 7.5% (95% CI: 6.5%-8.7%), and high-risk 59% (95% CI: 57%-61%). There was a small difference in 30-day MI between those with and without CAD at very low-risk (0.39% vs 0.04%, $P < 0.001$) but not among those at low-risk (0.8% vs 0.6%, $P = 0.45$).

Strengths of this study include the use of an hsTnI assay with little published data as well as a large inclusive patient sample with a liberal outcome (all-cause MI vs type 1 MI) to better ensure the safety of low-risk designations. At the same time, ICD codes likely overestimate acute coronary syndrome risk among all risk groups. Additional limitations include the retrospective design and unmeasured cardiovascular deaths, though relatively infrequent absent MI in similar studies. In summary, we found that 70% of patients were eligible for expedited ED discharge with a sensitivity of 97.5% (95% CI: 96.4%-98.2%) and a negative predictive value of 99.8% (95% CI: 99.7%-99.9%) for 30-day MI, while a high-risk designation had a specificity of 96.5% (95% CI: 96.2%-96.7%) and a positive predictive value of 59.0% (95% CI: 56.6%-61.3%), thus demonstrating the safety and efficiency of an hsTnI-based algorithm in a U.S. ED population presenting with chest discomfort. Within the very low-risk group, patients with CAD had a statistically significant higher incidence of 30-day MI, albeit still within low-risk parameters. Notably, this analysis did not reclassify patients with ischemic electrocardiograms as higher risk, which can further improve sensitivity for 30-day MI.

ACKNOWLEDGMENTS The authors would like to thank the KPNC Delivery Science and Applied Research Program for supporting this work.

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https://doi.org/10.1016/j.jacadv.2023.100558

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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