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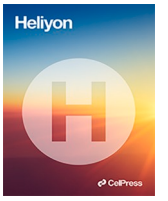

Research article

A patient-centric chest pain management approach utilizing a high sensitivity Troponin-I assay

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ABSTRACT

Objective: The purpose of this study was to assess the impact of adoption of a new cardiac chest pain pathway that included hs-cTnI in the emergency department (ED) when evaluating chest pain patients.
Methods: A new pathway incorporating both hs-cTnI testing (Seimens Healthineers Atellica) and risk stratification tools was developed. The impact of the new algorithm was assessed through a retrospective observational review of patients admitted to the ED with chest pain before implementation and after implementation. Before implementation, the conventional Seimens troponin Vista assay was utilized without a defined algorithmic approach. Bivariate analyses were performed comparing the time periods to determine differences in patient discharge dispositions, length of stay, outcomes, and rate of diagnostic cardiac catheterization.
Results: The proportion of patients discharged from the ED increased while the proportion of patients placed in observation or admitted as in-patient decreased. Variation amongst providers regarding patient disposition decreased. The stress testing rate of patients placed in observation decreased over baseline. There was no change in 30-day MACE rate, but there was a decrease in 30-day MI rate.
Conclusions: The new standardized hs-cTnI algorithm approach is safe as demonstrated by no change in 30-day MACE and is also more appropriate and efficient for patients presenting to the ED with chest pain compared to the non-standardized approach with cTnI used previously.

1. Introduction

Chest pain represents a common chief complaint among adult patients who present at emergency departments (EDs) [1].

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Additionally, it serves as a frequent basis for litigation in Emergency Medicine, causing healthcare providers to exercise caution, potentially leading to excessive or unnecessary testing [2]. Diagnostic pathways that incorporate clinical assessments, risk stratification tools, and electrocardiogram findings have demonstrated their utility in the triage and management of patients who present to the ED with chest pain [3,4]. Furthermore, the integration of troponin testing into these care algorithms enhances the diagnosis of acute myocardial infarction (AMI) and provides valuable prognostic insights when combined with risk stratification.

Troponin is a protein found in heart muscle cells that is released into the bloodstream following heart muscle damage. Because of this, cardiac troponins are highly specific and sensitive biomarkers that are used to aid in the diagnosis of AMI along with other clinical findings [5]. Measurements of troponin can be performed with assays described as either conventional (older assays) or high sensitivity (newer assays). These tests differ in their analytical sensitivity and ability to detect small concentrations of troponin [5]. While high-sensitivity troponin assays have been rigorously validated in both Europe and the United States (U.S.) [6,7], there remains limited practical experience with these assays in community-based healthcare settings.

In our single-center hospital, the transition from conventional troponin I (cTnI) testing to high-sensitivity troponin I (hs-cTnI) testing warranted review of current provider practice patterns which showed significant variability in the treatment approach to chest pain management A standard order set existed in the ED using the conventional troponin assay with $<$0.06g mcg/L as the low likelihood/rule-out cutoff, 0.060–0.17, indeterminate and $>$0.17 as high likelihood/rule-in thresholds with serial sampling of 0 h, 3 h and 6 h draws. In accordance with current guidelines that recommend the use of high-sensitivity troponin assays to triage patients with suspected acute coronary syndrome (ACS) [5,8,9], we implemented a new algorithmic approach. A preliminary literature search at the time revealed no clinically validated or widely accepted specific protocols in the U.S. that utilized the hs-cTnI assay performed on Siemens Healthineers Atellica or Centaur analyzers. The transition was facilitated by the development and implementation of an evidence-based, mutually agreed-upon care standard for managing chest pain patients who arrive at the ED.

Amid the ongoing healthcare transformation aimed at relocating patients with lower acuity to medically appropriate outpatient environments, the objective of this study was to assess the impact on both patient outcomes and system resource utilization following implementation of an evidence-based care standard that included hs-cTnI for the management of chest pain patients presenting to the ED.

2. Methods

A multidisciplinary team with clinical and technical expertise assembled to develop, implement, and monitor adherence to an evidence-based clinical pathway for managing chest pain patients that included hs-cTnI. Many of the commonly described strategies for troponin testing were considered [10,11]. The 0/2-h protocol was chosen due to the practicality of adhering to the draw strategy while still enabling rapid disposition ability. The team felt that a majority of patients would have symptoms for an hour by the time the first troponin draw was obtained and therefore only two total draws were required. Consensus amongst the team was that timing for the blood draw for hs-cTnI testing be no more than 15 min before or 30 min after the 2-h time frame for patients presenting to the ED with complaints of chest pain. The protocol specifics were determined by internally assessing previously published literature along with assessment of concordance between the two assays relative to their respective 99th percentile cutoffs. The History, EKG, Age, Risk factors, Troponin (HEART) score was chosen based on familiarity with this score at the institution, the prevalence of use in the literature and the practicality of its use by ED providers in rapidly assessing patients when considering the Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI) scores.

The new cardiac chest pain pathway algorithm was designed to align with ED provider workflow and incorporated both hs-cTnI testing and the HEART score for risk stratification. Although published available algorithms typically guide chest pain decision making to flow from HEART score to troponin values, an alternative approach was pursued utilizing troponin values to prompt the simultaneous consideration of the HEART score and patient disposition. The HEART score is then applied to patients with an indeterminate hs-cTnI values to guide diagnostics and further care. Because the HEART score was not a decision anchor for patients who were determined to be MI likely/high risk or MI unlikely/low risk, confidence was gained in use of hs-cTnI as the initial diagnostic tool for chest pain; the HEART score is reserved for patients where doubt exists as to the possibility of ACS. The multidisciplinary team identified the need for institutional education and agreement regarding recommendations for stress testing as patient expectations, combined with a culture of apprehension might encourage excessive, unnecessary testing. Consequently, educational sessions and recommendations led by cardiology experts were organized for hospital medicine providers, aligning with the prevailing chest pain guidelines [12].

Prior to development of the new algorithm, patients were often referred for a 72-h outpatient stress test (e.g., fast-track stress test). This was converted to a fast-track appointment to evaluate low and moderate risk patients in the outpatient cardiology environment with a more comprehensive cardiology approach instead of an automatic stress test referral. Patients were prioritized based on ordinal variables (HEART score, hs-cTnI values) documented by ED providers and referred to the “fast-track” program through an electronic medical record (EMR) referral order. This shifted decision making and risk stratification to cardiologists who sought to provide a more thoughtful approach given the modern armamentarium of available imaging modalities to evaluate coronary ischemia and enabled patients to establish a relationship with cardiology for longitudinal risk mitigation. Observation evaluations were expected to require less than 24 h of evaluation and care to include an additional troponin at hour four from baseline, telemetry and consideration of a stress test if the patient had a convincing clinical story, elevated but no significant change in hs-cTnI or if the patient was unlikely to follow up as an outpatient.

To establish a baseline, consecutive patient data from 3695 unique patients presenting to a single center 800 bed hospital with chest pain identified by ICD-10 codes endorsed by the American College of Cardiology Chest Pain Center accreditation criteria were

retrospectively gathered from November 1, 2019, to October 31, 2020. During this time, troponin testing was performed using the conventional Atellica IM Troponin I Ultra assay (Siemens Healthcare Diagnostics Inc., Tarrytown, New York, U.S.). The project was reviewed by the institution's IRB and determined it did not constitute human subjects research as defined under federal regulations [45 CFR 46.102 (e or l) and 21 CFR 56.102(c)(e)(l)] and did not require IRB approval nor was it deemed to require consent other than what was already obtained in clinical practice.

Before implementation of the high-sensitivity assay, a conventional Siemens troponin assay was utilized performed on the Siemens Vista analyzer with cutoffs as follows: <0.06 mcg/L, (low-likelihood of ACS/MI), 0.06–0.17mcg/L (indeterminate), >0.17 mcg/L (high likelihood, >99th percentile). There was no standard protocol, although there were order sets that included serial troponin measurements at 0, 3 and 6 h. However, these order sets were inconsistently followed and there was a high level of variability in evaluation and management between providers. After implementation we used the high-sensitivity Siemens assay performed on the Atellica instrument with cutoffs as described in the algorithm (Fig. 1), with 99th percentile cutoffs of <53 pg/mL for men and <34 for women. The algorithm was developed using 99th percentile cutoffs as a key component and 0/2-h change (delta) as previously published [6]. Comparison of results from the previous standard sensitivity assays were also used to confirm validity of the algorithmic approach. Per the Siemens whitepaper supplement for the package insert for the assay, clinical sensitivity and specificity for acute myocardial infarction at the 99th percentile cutoff, with combined genders, ranged from 84.3 % to 94.4 % and 86.9 %–91.1 %, respectively. The absolute value for rule in/high likelihood of MI was ≥120 pg/mL and the delta was considered greater than or equal to 20 pg/mL based on previous studies [6]. Patient data were also collected after implementation of the Atellica IM High-Sensitivity Troponin I (TnIH) assay from 6156 unique individuals from November 1, 2020, to April 30, 2022, using the same criteria noted above. Patients who were classified as MI likely/high risk or diagnosed with AMI were excluded from the data set analysis concerning low-risk chest pain but were examined separately to assess algorithm adherence for MI likely/high risk cases.

The discharge dispositions of patients in the study cohort were (1) discharged from the ED, (2) admitted to observation, or (3) admitted to inpatient care.

We identified a set of metrics (Table 1) aimed at assessing the effectiveness of the algorithm which were categorized into three broad groups: safety, adherence, and patient care and system efficiency.

Safety was evaluated with the following metrics: the 30-day incidence of major adverse cardiac events (MACE) [13,14], 30-day incidence of myocardial infarction (MI), the 30-day rate of patients returning to the ED with abnormal troponin levels, and the 7-day rate of patients returning for catheterization.

Adherence to the algorithm was assessed by monitoring the following factors: physician compliance with the algorithm, the timing of blood draws in relation to the 2-h timeframe from patient presentation to the ED, the percentage of patients who underwent triage as per the algorithm's recommendations, and the percentage of documentation related to the HEART score.

Patient care was tracked by examining the percentage of patients who were admitted to cardiology, referred for nuclear stress tests, admitted for observation, referred for the "fast-track" program, and discharged home. Additionally, compliance of the outpatient "fast-track" process was assessed by evaluating volumes, the appropriateness of referrals, the timeliness of patient contact and visits, and the outcomes of these patient visits. The impact on system efficiency was evaluated by monitoring several key indicators, including the average length of stay, the number of bed-days saved, the instances where stress tests were avoided. All LOS tests were done using non-parametric tests and reported as Median [IQR].

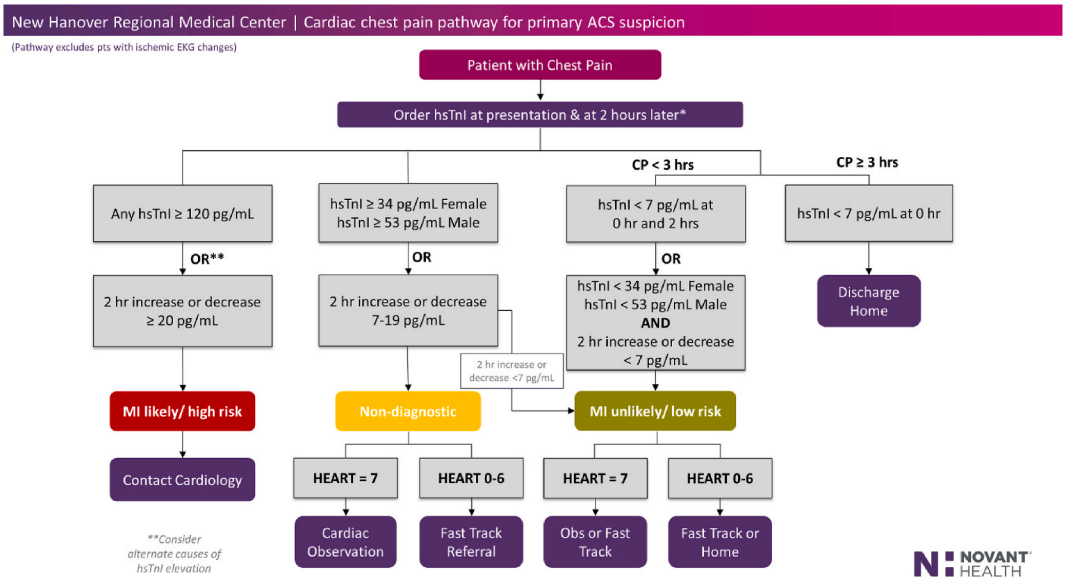

Fig. 1. Cardiac Chest Pain Pathway Algorithm for primary ACS suspicion.

Table 1
Metrics to evaluate efficacy of algorithm.

	Process Metrics	Outcome Metrics
Safety		
	Chart reviews of 30-day returns to ED with abnormal troponin	30-day rate of MACE
		7-day rate of return for catheterization
	# Cardiology Fast-Track Referrals	24-h contact rate
		<72 h completed appointment rate
		>72 h to 14-day completed appointment rate
Adherence		
	Physician compliance with algorithm	Care variation by ED physician
	Timeliness of phlebotomy	
	HEART Score Documentation	
Patient Care and System Efficiency		
	Patient algorithm placement	Number stress tests avoided
	Number stress tests performed	Interventional catheterization rates
	Diagnostic catheterization rates	Average length of stay for observation patients (hours)
	% Patients admitted for observation stay	Average length of stay for inpatients (days)
	% Patients admitted for inpatient stay	Average length of stay for ED patients (hours)
	% Patients discharged from ED	Bed-Days saved

ED, Emergency Department; HEART, History Electrocardiogram Age Risk Factors, Troponin; MACE, major adverse cardiac events.

2.1. Data analysis

Demographic, clinical, and outcome characteristics of the patients by pre- and post-implementation status are presented as means (SD) or frequencies. Differences in these characteristics between the pre- and post-implementation cohorts were assessed using *t*-test for continuous measures or chi-squared test for categorical measures. Normality assumption for continuous measures was assessed by Kolmogrov-Smirnov test and the Shapiro-Wilk test.

P values were estimated. R Statistical software (v4.2.1; R Core Team 2021) was used for all statistical analyses.

3. Results

A total of 9851 unique patients were included in the study, of them 3695 before and 6156 after implementation. The populations defined as pre-implementation and post-implementation of the cardiac chest pain pathway algorithm were similar. Pre-implementation median age was 52 years, 52.5 % of patients were female and patient breakdown by race consisted of 69.6 % White. 24.8 % Black, 0.5 % American Indian or Alaska native, 0.4 % Asian and 10.8 % other. Post implementation median age was 52 years, 52.8 % were female, and patient breakdown by race consisted of 69.8 % White, 23.6 % Black, 0.4 % American Indian or Alaska Native, 0.2 % Asian and 13.5 % other (Table 2).

An overview of ED provider practice with respect to patient disposition prior to implementation of the cardiac chest pain pathway algorithm (Fig. 1) is shown in Fig. 2A. Following adoption of the new algorithm, a reduction in variability among ED providers' practices was observed (Fig. 2B). Over the 18-month post implementation period, 67 % of blood draws were within the ideal window with 6 % being early and 27 % beyond the ideal window.

Before implementation of the new cardiac chest pain pathway algorithm, there were a total of 4060 encounters (3695 unique patients), whereas after the implementation, there were 7021 (6156 unique patients) encounters. In the pre-implementation phase 79.7 % (3237/4060) of the encounters were discharged from the ED, compared to 95.8 % (6724/7021) of encounters in the post-implementation phase ($p < 0.0001$). For the pre-implementation period, 17.8 % (722/4060) of the encounters were placed in observation, whereas in the post-implementation period, 3 % (214/7021) of the encounters were placed in observation ($p < 0.0001$). In the pre-implementation phase, 2.5 % (101/4060) of the encounters were admitted, while in the post-implementation phase, 1.2 % (83/7021) of the encounters were admitted ($p < 0.0001$) (Fig. 3a).

Table 2
Characteristics of patients used in study.

	Pre-Implementation (N = 3695)	Post-Implementation (N = 6156)
Age, yrs (median [IQR])	53 [38.00, 66.00]	52 [38.00, 66.00]
Female	53.5 % (1978)	52.8 % (3249)
Race		
White	69.6 % (2558)	69.8 % (4252)
Black	24.8 % (911)	23.6 % (1435)
American Indian or Alaska Native	0.5 % (20)	0.4 % (22)
Asian	0.4 % (15)	0.2 % (12)
Other	10.8 % (397)	13.5 % (834)

IQR, interquartile range; yrs, years.

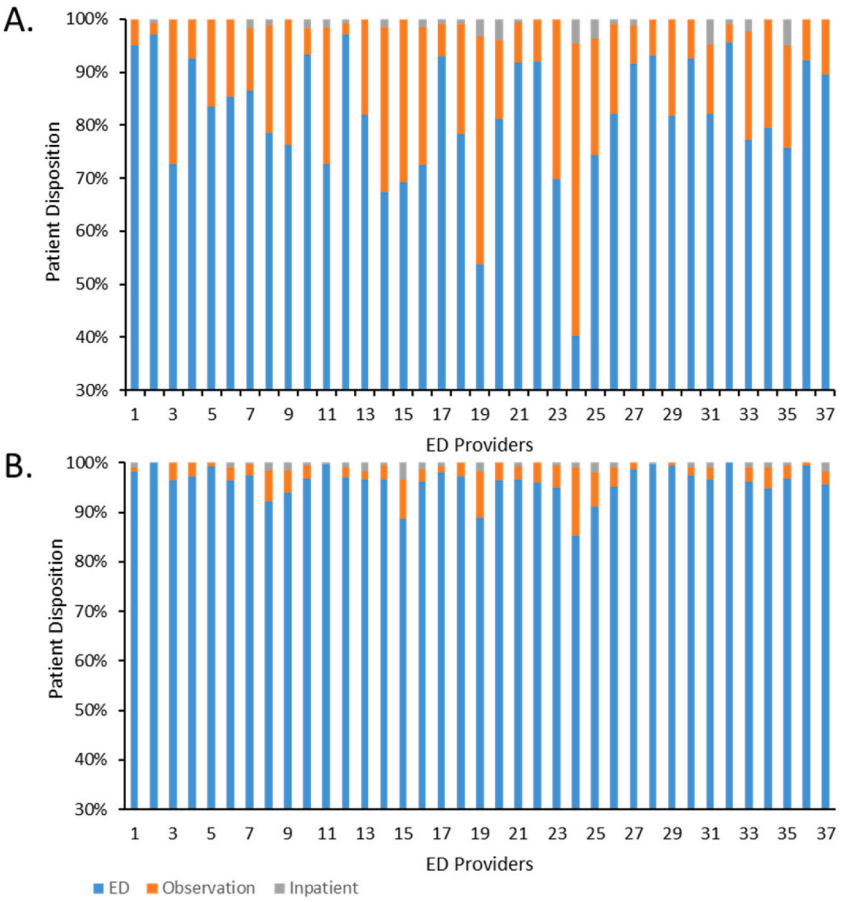

Fig. 2. Disposition of low-risk chest pain patients by ED provider (A) before and (B) after implementation of the cardiac chest pain pathway algorithm.

The monthly average of observation hours for low-risk chest pain patients decreased by 78.5 % from 1522 h–326 h, while inpatient hours per month decreased by 44 % from 333 to 186 h. When annualized, these reductions translate to a total savings of 598 observation bed days and 73.5 inpatient bed days.

The length of stay for all admitted encounters increased by 7.5 % (0.22/2.93) from 2.93 days before the implementation to 3.15 days after ($p = 0.14$). When focusing on the subset discharged directly from the ED, their length of stay increased by 26.34 % (0.64/2.43) from 2.43 h before implementation to 3.07 h after implementation ($p < 0.0001$). For the encounters placed in observation, the length of stay increased by 8.30 % (2.1/25.3) from 25.3 h before to 27.4 h after implementation ($p = 0.0002$). In the case of the subset of admitted encounters, their length of stay increased by 1.74 % (0.69/39.58) from 39.58 h before implementation to 40.27 h after implementation ($p = 0.8$).

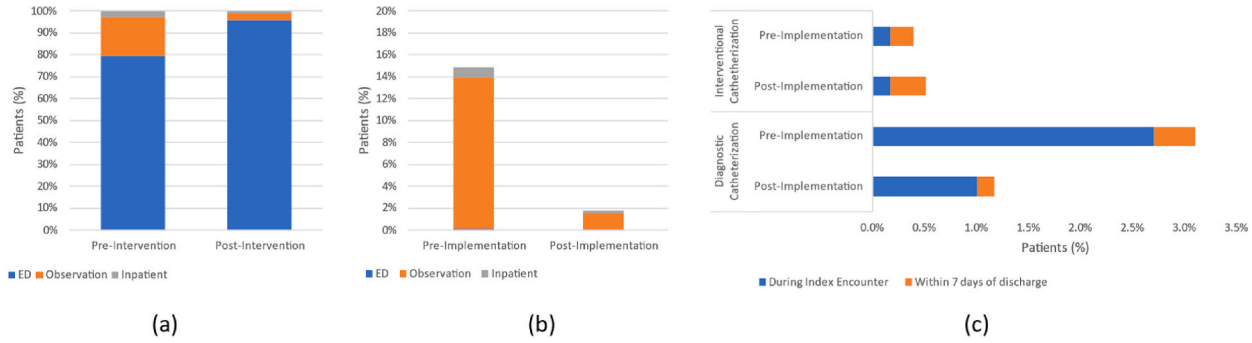

Fig. 3. (a). Disposition summary of all low-risk chest pain patients pre- and post-implementation of the new care pathway algorithm. (b). Stress test rates in low-risk chest pain patients. (c). Diagnostic and interventional catheterization rates in low-risk chest pain patients.

Before the implementation, cardiac stress testing was conducted for 14.8 % (602/4060) encounters. Among these, 0.15 % (6/4060) were discharged directly from the ED, 13.8 % (560/4060) transferred to observation status, and 0.89 % (36/4060) transferred to inpatient status. In contrast, after the implementation, only 1.8 % (127/7021) underwent stress testing during their initial encounter. Of these, 0.03 % (2/7021) of encounters were discharged from the ED, 1.5 % (106/7021) transferred to observation status, and 0.27 % (19/7021) transferred to inpatient status (Fig. 3b).

In the baseline period, diagnostic cardiac catheterization was carried out during the initial encounter for 2.6 % (106/4060) encounters and within 7 days for 0.44 % (18/4060). Interventions were conducted during the index encounter for 0.17 % (7/4060), and within 7 days of discharge for 0.22 % (9/4060) of encounters. After the implementation, diagnostic cardiac catheterization was performed on 1 % (70/7021) of patients during their initial encounter, and within 7 days for 0.63 % (44/7021). Interventions took place during the index encounter for 0.17 % (12/7021), and within 7 days of discharge for 0.34 % (24/7021) (Fig. 3c).

We assessed the 30-day MACE rate, which included occurrences of stroke, myocardial infarction, or cardiac death, at the baseline to examine the safety outcomes of low-risk chest pain patients and to verify that there was no adverse impact following the implementation of the new algorithm. At baseline, 0.27 % (11/4060) of encounters resulted in a MACE event within 30 days. Of those MACE events 54.5 % (6/11) of encounters readmitted with an acute myocardial infarction (AMI) diagnosis. After the implementation, 0.27 % (19/7021) encounters experienced a MACE event within 30 days. Of those MACE events 42.1 % (8/19) of encounters readmitted with AMI diagnosis.

4. Discussion

High-sensitivity troponin assays are quickly becoming the standard for assessing patients who arrive at the ED with chest pain. In this study, we report our experience with the implementation of a new cardiac chest pain pathway algorithm utilizing the Siemens Atellica hs-cTnI assay in a large, multi-site health system. We report four major findings.

First, consistent with recent studies [15–18], we found a reduction of the admission rate of patients evaluated before and after implementation of the high-sensitivity troponin assay.

Second, standardization of patient evaluation with hs-cTnI helped minimize variability and contributed to a decrease in admission rates. This is consistent with the prior findings [17] reporting shorter time to diagnosis with hs-cTnI compared to cTnI.

Third, similarly to previous reports demonstrating a decrease in the rate of stress testing [19], we found a reduction of stress testing utilization.

The main benefit of the pathway we adopted in our institution was the reduction in unnecessary hospital admissions. The most substantial impact was a notable 79 % decrease in admissions for observation status. This reduction translated to a saving of 50 observation-days each month and a total of 600 observation-days annually. Considering the ED's significant congestion due to the first COVID-19 surge, these bed-day savings came at an opportune time for the organization. Moreover, the decrease in the utilization of stress tests had a decongesting effect on the system, such as tasks and time for patient transporters, nuclear medicine technologists, radiology department personnel, and cardiology advanced practice providers. The length of stay in the ED for patients who were discharged from the ED increased by 26.34 % ($P < 0.001$). This is likely due to many patients already being discharged following a single normal conventional troponin result before the algorithm's implementation.

Variation in patient disposition among ED providers was diminished, as depicted in Fig. 2. This reduction in variability was observed in physicians across different patient volumes and even among those who had previously admitted a higher proportion of patients to observation or inpatient status. Feedback from ED physicians indicated that two crucial factors driving this change were the sensitivity of the protocol for defining low and high-risk patients and the confidence instilled by the fast-track referral process. Providers did not face punitive measures, nor were they given financial incentives to adhere to the algorithm. Minor deviations from the pathway were expected due to clinical judgment and unique patient circumstances. In fact, a major point of emphasis during implementation was the use of clinical judgement. Providers were encouraged to always consider the entire clinical picture and to not blindly adhere to the algorithm if clinical suspicion remained high in patients who were classified as low risk by the algorithm. Many providers appreciated having a structured framework for discussing the care pathway with patients. Implementing the algorithm streamlined the workflow in the ED, offering providers a more standardized approach to chest pain cases and providing patients with a more consistent and reproducible care plan.

Before implementing the protocol, ED provider practice variation for chest pain patients lead to inconsistent expectations among patients, providers, and staff. However, after the protocol's implementation, confidence in this standardized approach allowed for clear expectations to be set and consistently met, greatly enhancing the satisfaction of both providers and patients. Importantly, implementation of the pathway, along with subsequent improvements, did not result in an increase in the 30-day incidence of MACE, and the 30-day MI incidence decreased.

An integral component of the project involved the establishment of an expedited referral process, allowing patients with troponin levels in an uncertain range to be promptly examined by a cardiologist in an outpatient setting within 48 h. This new process replaced the previous approach of referring patients directly for a stress test. Instead, it offered a superior care pathway by facilitating a provider visit where risk factor modification, medical management, and the option for additional testing could be appropriately addressed. Beyond the immediate triage of chest discomfort within 48 h, recognizing that many patients with an intermediate-high HEART score either have or may develop cardiovascular disease, the fast-track appointment system allowed for the initiation of a long-term relationship with a cardiologist.

The absence of a notable rise in outpatient stress test volumes indicates that most patients received medical management as their primary approach. Additionally, there were no significant changes observed in the overall volume of cardiac catheterizations, coronary

interventions, or the proportion of patients undergoing cardiac catheterization beyond the acute timeframe.

There are several limitations in this study. Firstly, the implementation occurred during the Coronavirus disease (COVID-19) pandemic, which may have influenced the results as some chest pain patients might have avoided the ED, particularly during the initial phases of the pandemic. Secondly, we lacked final independent diagnosis data as a reference standard for AMI. This prevented us from differentiating between true negatives and false negatives, determining the performance characteristics of each test against a commonly accepted reference standard. Having 30-day MACE data partially mitigated this limitation. Moreover, the data and outcomes could have been affected by significant nursing shortages and broader hospital challenges related to patient flow, resulting in prolonged stays in the ED. To address these concerns, we extended the post-implementation period to encompass months that were theoretically less influenced by the pandemic. Furthermore, we believed that this scenario was in line with the experiences of many healthcare systems over the past three years. Importantly, the overall incidence of chest pain patients evaluated both before the pandemic and before the algorithm's implementation remained consistent with the volumes assessed after the implementation. Our ability to access data for monitoring follow-up clinical visits was restricted to our health system.

Nevertheless, it's worth noting that we are the sole facility within a 90-mile radius equipped for cardiac catheterization. Consequently, we consider it improbable that a significant number of adverse events went unnoticed. It's important to acknowledge that we did not employ an independent panel of cardiologists to individually review each case for final disposition, which could potentially have led to inaccuracies in the final classification of patients. However, it's worth noting that this practice was not conducted prior to the implementation of the algorithm either, ensuring that the data comparison before and after the algorithm's implementation was carried out in a consistent manner.

5. Conclusions

The implementation of a novel chest pain algorithm incorporating hs-cTnI and the HEART score effectively reduced unnecessary hospital admissions, minimized variation in ED dispositions and decreased the need for stress testing. This led to reduced utilization of observation and inpatient beds and a reduction in diagnostic catheterization rates. These outcomes were achieved while preserving MACE rates. This illustrates that patients are now receiving improved, cost-effective care in the most appropriate setting and at the ideal time. Introduction of hs-cTnI utilizing a 0/2-h algorithm demonstrated safe, effective, and more streamlined care for individuals arriving at the ED with chest pain. We believe that these outcomes can be replicated in other healthcare institutions, provided there is a concerted effort involving a multidisciplinary team approach that engages all essential stakeholders and support staff.

Data availability statement

Data associated with the study has not been deposited into a publicly available repository. Preliminary data was presented in abstract form at the Institute for Healthcare Improvement annual national forum on quality improvement in health care, December 2021.

CRediT authorship contribution statement

Abby E. Roetger: Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Conceptualization. **Christopher D. McKinney:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **De B. Winter III:** Writing – review & editing, Visualization, Methodology, Conceptualization. **Charmaine Lewis:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Kristopher Swiger:** Writing – review & editing, Writing – original draft, Conceptualization. **Claire M. Corbett:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Conceptualization. **Gregory Hall:** Software, Resources, Methodology, Data curation. **Adam David:** Data curation. **Austin Gratton:** Formal analysis.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Adam David reports writing assistance was provided by Siemens Healthineers. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Austin Gratton reports writing assistance was provided by Siemens Healthineers. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Abby Roetger reports writing assistance was provided by Siemens Healthineers. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Charmaine Lewis reports writing assistance was provided by Siemens Healthineers. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Christopher D. McKinney reports a relationship with Siemens Healthineers that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. De B. Winter III reports writing assistance was provided by Siemens Healthineers. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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