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Original Article

Effect of a High-Sensitivity Troponin I and Associated Diagnostic Protocol on Emergency Department Length of Stay: A Retrospective Cohort Study

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ABSTRACT

Background: The objective of this study was to assess the introduction of a high-sensitivity troponin I (hs-TnI) assay and its associated accelerated protocol on emergency department (ED) length of stay (LOS) for patients presenting with chest pain, compared to an accelerated diagnostic protocol using conventional troponin (TnI) testing.

Methods: We conducted a retrospective cohort study of all adults with a primary presenting complaint of chest pain of cardiac origin and a Canadian Triage and Acuity Scale score of 2 or 3, between November 8, 2019 and November 9, 2021, to a tertiary-care urban Canadian ED. The primary outcome was ED LOS. Secondary outcomes included consultation proportions and major adverse cardiac events within 30 days of the index ED visit.

Results: A total of 2640 patients presenting with chest pain were included, with 1333 in the TnI group and 1307 in the hs-TnI group. Median ED LOS decreased significantly, from 392 minutes for the TnI

RÉSUMÉ

Contexte : Cette étude visait à évaluer l'introduction du dosage de la troponine I de haute sensibilité (hs-TnI) et le protocole accéléré qui lui est associé sur la durée des séjours aux urgences dans le cas des patients qui consultent pour une douleur thoracique, comparativement à un protocole diagnostique accéléré faisant appel à un test de troponine classique (TnI).

Méthodologie : Nous avons mené une étude de cohorte rétrospective portant sur tous les adultes qui se sont présentés aux urgences d'un établissement urbain de soins tertiaires canadien entre le 8 novembre 2019 et le 9 novembre 2021 principalement pour une douleur thoracique d'origine cardiaque et dont le score était de 2 ou 3 à l'Échelle canadienne de triage et de gravité (ETG). Le principal critère d'évaluation était la durée du séjour au service des urgences. Les critères d'évaluation secondaires comprenaient la fréquence des consultations et les événements cardiaques indésirables majeurs dans les 30 jours ayant suivi la visite de référence aux urgences.

Evaluation of patients presenting with chest pain is a cornerstone of emergency department (ED) care. Chest pain is the second most common ED presenting complaint in Canada.[1] Many serious underlying medical conditions may be heralded by chest pain, so most of these patients undergo thorough ED assessment and testing. Standard investigations include an electrocardiogram (ECG), chest radiograph, complete blood count, and electrolytes evaluation, plus or minus special investigations (eg, D-dimer, advanced imaging). One of the mainstays of assessment is serial measurement of cardiac biomarkers. For example, troponin (Tn) accumulates in blood after cardiac muscle necrosis, and rising levels act as a surrogate marker of acute coronary syndromes.

Conventional Tn detection thresholds vary in analytical sensitivity and precision at lower concentrations, with approximate ranges of 40-100 ng/L.[2] High-sensitivity Tn (hs-Tn) assays have improved detection further. For example, the Beckman hs-TnI assay has a detection threshold of 3 ng/L,

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group, and 371 minutes for the hs-TnI group (median difference = 21 minutes; 95% confidence interval: 5.3, 36.7). The numbers of consultations and admissions were not statistically different between study periods. The major adverse cardiac events outcomes did not change following the implementation of the hs-TnI test (13.6% vs 13.1%; $P = 0.71$).

Conclusions: The implementation of an accelerated chest pain protocol using an hs-TnI assay in a tertiary-care Canadian ED was associated with a modest reduction of LOS for all patients, and a substantial reduction of LOS for patients undergoing serial troponin testing. This strategy was safe, with no increase in adverse outcomes.

Résultats : Au total, 2640 patients qui s'étaient présentés aux urgences pour une douleur thoracique ont été inclus, 1333 se trouvant dans le groupe TnI et 1307 dans le groupe hs-TnI. La durée médiane du séjour aux urgences a diminué considérablement, passant de 392 minutes dans le groupe TnI à 371 minutes dans le groupe hs-TnI (différence médiane de 21 minutes; intervalle de confiance [IC] à 95 % : 5,3-36,7). Les consultations et les admissions n'ont pas affiché de différence statistique entre les périodes de l'étude. Les événements cardiaques indésirables majeurs n'ont pas varié après l'introduction du dosage de la hs-TnI (13,6 % vs 13,1 %; $p = 0,71$).

Conclusions : L'adoption d'un protocole accéléré pour la douleur thoracique à l'aide du dosage de la hs-TnI au service des urgences d'un établissement de soins tertiaires canadien a été associée à une légère réduction de la durée du séjour pour l'ensemble des patients et à une réduction substantielle de cette durée pour les patients soumis à des analyses de la troponine en série. De plus, cette stratégie était sûre sans hausse des événements indésirables.

which has led to decreased time between repeat measures of troponin levels from the recommended 6 hours to as little as 1 hour with some hs-Tn assays.[3] Clearly, this decrease represents an opportunity to improve ED throughput for patients presenting with chest pain. More efficient and timely care of these patients has the potential to decrease ED length of stay (LOS), cost, and overcrowding. Initial studies on hs-Tn assay usage were characterized by confirmation of adequate sensitivity and appropriate safety profiles.[4-6] The encouraging results of these early studies have led to widespread adoption of hs-Tn test use in EDs across the world.[4-8]

Increased Tn sensitivity has several potential unintended consequences. For example, minor Tn elevations caused by non–acute coronary syndrome issues may now be detected with increasing frequency.[5] In addition, such elevations may result in more consultations with cardiologists as well as admissions personnel. Subtle elevations warrant further testing in patients who previously would have been deemed to have a negative test result using less-sensitive Tn assays. This increased test sensitivity could be partly responsible for the relatively modest or negligible reductions, or even increases in some cases, in ED LOS reported after transitions have been made from Tn to hs-Tn assays.[7-13] For example, in a recent systematic review of chest pain protocols, the median ED LOS ***increased*** in 4 studies after implementation of a hs-Tn assay.[8-10,13] Conversely, within a Canadian context, observational data demonstrated a reduction as small as 30 minutes in total ED LOS after the transition from a 6-hour to a 2-hour protocol using a hs-TnT troponin assay.[7] Thus, the current literature shows differing effects on ED LOS of implementing hs-Tn testing, and more studies are needed.

Part of the challenge of implementing a new hs-Tn assay is in designing a protocol that is appropriate for achieving an acceptable level of sensitivity while being sensitive to clinician needs. The objective of this study was to assess the impact of the introduction of an hs-TnI assay and its associated accelerated protocol on ED LOS for patients presenting with chest pain, while holding serial troponin measurement intervals constant. Reporting on ***all*** patients undergoing troponin testing means the possibility exists of underestimating the impact of the hs-Tn test for a specific subgroup of patients with chest pain. Consequently, we sought to analyze patients in subgroups that were predicted to benefit variably from the lower detection threshold of an hs-Tn test.

Methods

Ethics

The study was approved by the University of Alberta Health Research Ethics Board (reference ID: Pro00096932) at the University of Alberta, in Edmonton, Alberta, Canada. The project was assessed as having minimal risk, and approval was given to access electronic medical records from an administrative database. Written informed consent was not obtained from any patient or physician participants. Operational and administrative approvals were provided by Alberta Health Services (AHS), and a data-sharing agreement was signed. The clinicians practicing during the study periods were unaware of the study at the time of data collection.

Setting

The Royal Alexandra Hospital (RAH) is an academic tertiary-care hospital in Edmonton, Alberta, Canada. The RAH is a referral centre for cardiology and assesses approximately 73,000 adult patients per year, with an admission proportion of 18%.[14] This hospital is considered an inner-city hospital, and many of their patients struggle with homelessness, addiction, and poverty. The ED is staffed with full-time emergency physicians, and it functions as a teaching site for emergency and other resident services.

Assays and pathways

The RAH operated with different chest pain protocols based on troponin laboratory reporting between 2019 and 2021. From November 9, 2019 to November 8, 2020, the RAH used the Beckman AccuTnI+3 assay (Beckman Coulter Canada, Mississauga, Ontario, Canada) (conventional TnI), with a limit of detection of 0.04 ug/L. ED physicians at the RAH site were provided with education on the safety of accelerated chest pain protocols and encouraged to use a 3-hour serial measurement, in conjunction with the HEART

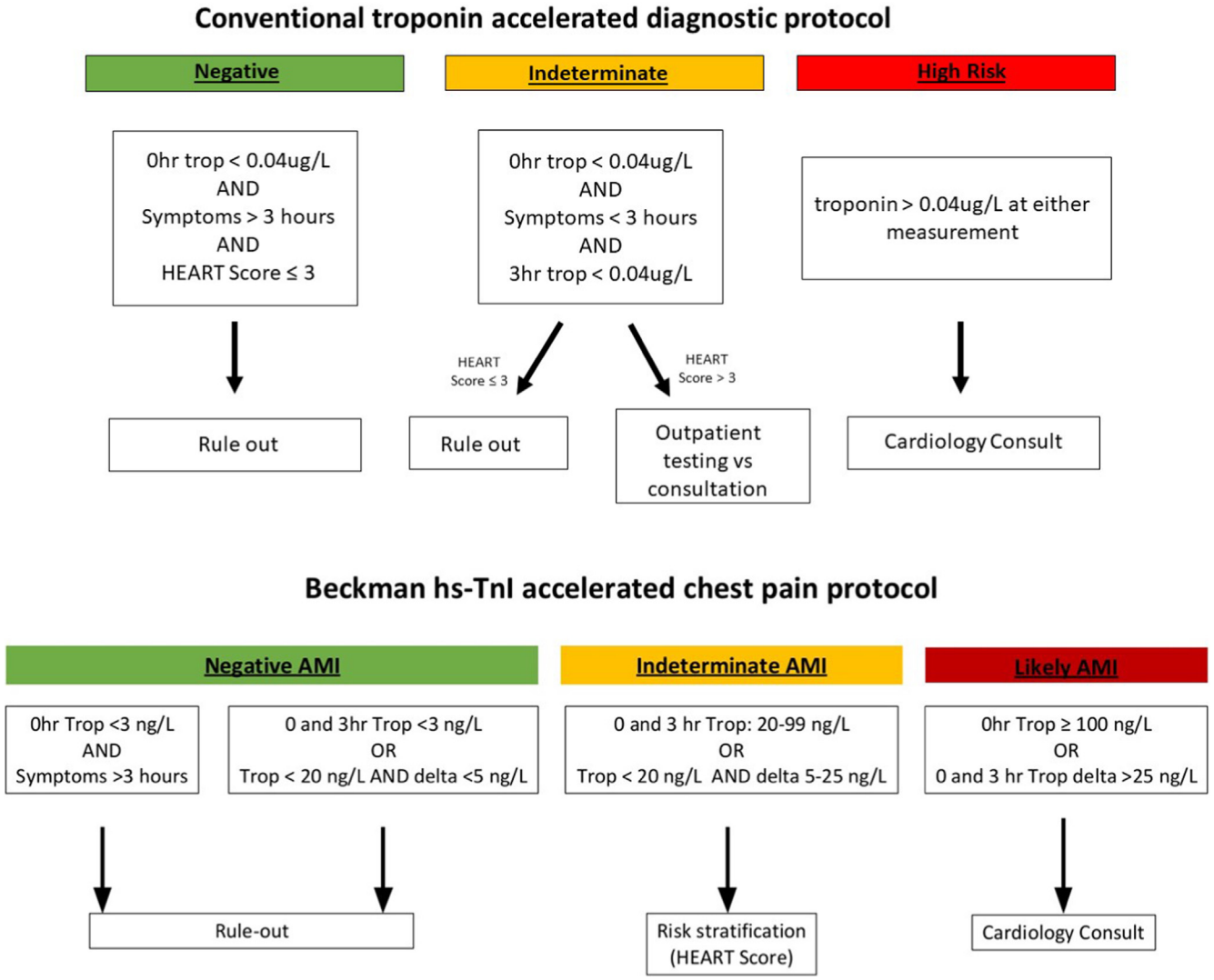

Figure 1. Accelerated chest pain protocols before and after introduction of a high-sensitivity troponin assay (hs-TnI). AMI, acute myocardial infarction; HEART, **H**istory, **E**lectrocardiogram, **A**ge, **R**isk Factors, and **T**roponin; trop, troponin.

Pathway[15] to help perform risk stratification. The HEART score (for **H**istory, **E**lectrocardiogram, **A**ge, **R**isk factors, and **T**roponin) is a risk-stratification tool designed for use in the ED and has been shown to outperform other popular risk-scoring tools for discriminating patients with major adverse cardiac events (MACE).[16] From November 9, 2020 to November 9, 2021, the RAH switched to the Beckman hs-TnI assay. A new protocol was developed to utilize the hs-TnI assay. The rapid rule-out arm was based on a previous study[17] and internal analytical evaluation[18] of this assay. The rapid rule-in arm was based on a troponin level > 5 times the upper reference limit of the assay.[3] The limit of detection was set at 3 ng/L, and the 99th percentile upper limit was 20 ng/L. Clinicians reached a consensus to adjust the rule-in threshold upward to 100 ng/L, for better specificity and ease of implementation. A coefficient of variation of < 10% was achieved at the 99th percentile.[18] No sex-specific cutoffs were used for hsTnI. The protocol for each respective period is illustrated in Figure 1.

Implementation strategy

Prior to the implementation of the hs-TnI protocol, extensive efforts were made to educate emergency, internal medicine, and cardiology clinicians across the zone. A 10-minute video was produced that detailed the new protocol, and a "Survival Guide" was developed by a multidisciplinary team of laboratory medicine leaders and emergency medicine, internal medicine, and cardiology clinician–scientists. A paper-based version of the protocol was distributed to the EDs, and the clinical group received an in-service from the 2 lead ED clinicians (B.H.R.; S.D.). Immediately prior to the implementation, a Laboratory Bulletin was sent through the Medical Affairs Department secure e-mail channels to remind staff of the pending changes. No run-in period was used for the introduction of the new assay.

Design

We conducted a retrospective cohort study, more specifically a before-and-after design, of all adults (aged ≥ 18 years)

with a primary presenting complaint of chest pain of cardiac origin from the Canadian Emergency Department Information System (CEDIS) presenting complaints list.[19] The majority of EDs in Canada employ the 5-level Canadian Triage and Acuity Scale (CTAS). In this study, patient enrollment was restricted to those with chest pain of cardiac origin and a CTAS score of 2 or 3 between November 8, 2019 and November 9, 2021. When patients had multiple ED visits, we included only their first index visit. Patients with a clear diagnosis of ST-segment elevation myocardial infarction (STEMI), those who died during ED transport or upon arrival, and non-Alberta residents and those who were not registered with the Alberta Health Care Insurance Plan were excluded. Although we did not exclude patients on the basis of known risk-modifying comorbidities, such as chronic kidney disease (CKD), we did investigate the balance in a post hoc sensitivity analysis.

Data sources

Population-based linked health administrative data from Alberta were obtained. Eight databases were used to identify the final study cohort. All datasets are maintained and updated in the Alberta Health Services (AHS) Enterprise Data Warehouse.

We used the following: the National Ambulatory Care Reporting System (NACRS; which captures all visits to any ED in Alberta and records up to 10 diagnostic fields using the International Classification of Diseases, 10th revision, Canadian Enhancement [ICD-10-CA] diagnoses per visit); the Emergency Department Information Tracking System (EDIS; which captures all ED visits in Edmonton and records presenting complaints and consultation services); the provincial laboratory databases (which captures all general laboratory tests performed across the province); the provincial diagnostic imaging database (which captures all imaging performed across the province within AHS facilities); the Discharge Abstract Database (DAD; which captures all acute care hospital admissions and includes interventions and discharge destinations and records up to 25 diagnoses coded with ICD-10); Vital Statistics (which captures date of death, including out of hospital); the Provincial Registry (which captures Alberta residents with Alberta Health Care Insurance Plan coverage); and the Practitioner Claims Database (which captures all physician billing claims and includes up to 3 recorded diagnoses per visit using ICD-9 and a Schedule of Medical Benefits [SOMB] billing code).

Outcomes

Descriptive statistics were calculated for both groups. In addition, baseline data are reported on physician initial assessment and on patients who left without being seen, to compare ED crowding metrics.

Our primary outcome was ED LOS. Secondary outcomes included consultation proportions, disposition status (ie, admission or discharge), and MACE, defined as a composite of all-cause death, hospitalization for heart failure, hospitalization and/or ED visit for myocardial infarction (MI) or stroke, or cardiac interventions (eg, coronary artery bypass graft surgery [CABG], percutaneous coronary intervention [PCI]) within 30 days of the index ED visit. We identified comorbidities for each patient using previously validated case definitions based on ICD-10 and ICD-9 codes for all hospitalizations and ED visits in the 2 years prior to the index ED visit (and including the index ED visit) and at least 2 hits in the Practitioner Claims Database.[19] Other nonclinical covariates included the arrival by emergency medical services, a modified Charlson Comorbidity Index (CCI) score,[20] and imaging received during their ED visit. Patients who had at least one troponin test were divided into groups categorized as negative, indeterminate, or positive, based on the reference ranges (Fig. 1). When more than 2 troponins were measured, we included the first 2 test results.

Statistical analysis

Descriptive data are reported using proportions, means with standard deviations (SDs), or medians with interquartile ranges (IQRs), as appropriate. Baseline characteristics were compared between groups using the following: Pearson's χ^2 test for categorical variables; the Student t test for normally distributed variables; and the Mann-Whitney test for non-normally distributed variables for continuous variables. Multivariable stepwise Cox proportional hazard regression was used to quantify the relationship between the hs-TnI period (cTn period as reference category) and MACE, adjusting for age, sex, and covariates that were statistically significant after using stepwise selection (entry criterion $P < 0.2$, retention criterion $P < 0.05$). Adjusted hazard ratios with 95% confidence intervals (CIs) are reported. This analysis was focused specifically on the subgroup of patients who had at least one troponin test. Finally, we used an interrupted time series analysis to determine if the level (immediate) and slope (trend) changed after the implementation of the hs-TnI test. Median differences with 95% CIs are reported for continuous variables. Statistical significance for our primary outcome was set at $P < 0.05$. For all other tests (except the multivariable Cox regression analysis), significance was set at $P < 0.001$ because of the multiple tests performed. All analyses were conducted using SAS, version 9.4 (SAS Institute, Cary, NC).

Results

Demographics

The characteristics of the patient presentations are reported in Table 1. A total of 2640 patients who presented with chest pain were included in the study period, with 1333 (50.5%) in the TnI group, and 1307 (49.5%) in the hs-TnI group. The median age of all included patients was 57 years (IQR: 44, 69), with 54.8% being male. No differences between the groups were present in patient demographics, timing, or severity of presentation. Time to initial physician assessment was stable between study periods, with median times of 59 and 60 minutes—before and after the hs-TnI test introduction, respectively (median differences = -1.0 minutes; 95% CI: -6.4, 4.4).

Investigative details

Among all patients presenting with chest pain of cardiac origin, 91.4% underwent troponin testing (Table 2). No increase occurred in the proportion of patients receiving 2 troponins after the introduction of the hs-TnI assay (44.3% vs 38.3%), using adjusted significance levels ($P < 0.001$). In the hs-TnI group, 60.1% of patients were classified as negative,

Table 1. Characteristics of patients presenting to the emergency department with chest pain before and after the introduction of an accelerated pathway using a high-sensitivity cardiac troponin assay and a 3-hour serial troponin interval

Characteristic	Total N = 2640	TnI n = 1333	hs-TnI n = 1307
Age, y	57 (44, 69)	58 (44, 70)	56 (43, 68)
Male sex	1448 (54.8)	700 (52.5)	748 (57.2)
Mode of arrival			
No ambulance	1463 (55.4)	731 (54.8)	732 (56.0)
Ground ambulance	1174 (44.5)	600 (45.0)	574 (43.9)
Air ambulance	3 (0.1)	2 (0.2)	1 (0.1)
CTAS score			
2	2612 (98.9)	1316 (98.7)	1296 (99.2)
3	28 (1.1)	17 (1.3)	11 (0.8)
Time of day			
Daytime (8:01 AM −4:00 PM)	1198 (45.4)	592 (44.4)	606 (46.4)
Evening (4:01 PM −12:00 AM)	934 (35.4)	489 (36.7)	445 (34.0)
Early morning (12:01 AM−8:00 AM)	508 (19.2)	252 (18.9)	256 (19.6)
Pre-existing conditions			
Hypertension	1257 (47.6)	658 (49.4)	599 (45.8)
CAD	982 (37.2)	519 (38.9)	463 (35.4)
Diabetes mellitus	656 (24.8)	356 (26.7)	300 (23.0)
Atrial fibrillation	594 (22.5)	299 (22.4)	295 (22.6)
Stroke	477 (18.1)	232 (17.4)	245 (18.7)
Asthma	322 (12.2)	172 (12.9)	150 (11.5)
Heart failure	312 (11.8)	158 (11.9)	154 (11.8)
COPD	353 (13.4)	189 (14.2)	164 (12.5)
CHF	266 (10.1)	130 (9.8)	136 (10.4)
Myocardial infarction	247 (9.4)	131 (9.8)	116 (8.9)
Renal disease	135 (5.1)	72 (5.4)	63 (4.8)
Dementia	101 (3.8)	49 (3.7)	52 (4.0)
Charlson Comorbidity Index Score	1 (0, 2)	1 (0, 2)	0 (0, 2)

Values are n (%) or median (interquartile range).

CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CTAS, Canadian Triage and Acuity Scale; hs-TnI, high sensitivity troponin I assay; TnI, conventional troponin I assay.

and 29.2% of patients as indeterminate; these changes represent significant increases and decreases ($P < 0.0001$) from the year prior using the TnI assay, respectively. The proportion of patients classified as high-risk remained unchanged between groups. Consultation occurred in 37.4% of patient presentations in the Tn group, and in 33.8% in the hs-TnI group ($P = 0.06$); among patients who had specialist consultation, the majority involved the cardiology department (67.3%; Table 2).

Primary LOS outcomes

Overall, the median ED LOS decreased significantly after the introduction of the hs-TnI assay; median times were 392 minutes for the TnI group, and 371 minutes for the hs-TnI group (median difference = 21 minutes; 95% CI: 5.3, 36.7). Among patients who were discharged, a significant decrease occurred in LOS, by 34 minutes (95% CI: 18.1, 49.9) following the implementation of the hs-TnI assay. Those stratified as being indeterminate saw the largest decrease in LOS following the implementation of the hs-TnI assay (median difference = 100 minutes; 95% CI: 69.6, 130.1; Table 3). Patients in the group classified as negative experienced an increase in LOS (median difference = −38 minutes; −56.1, −19.9).

Secondary outcomes

As displayed in Table 3, the final patient dispositions were similar between groups. Overall, most patients (71.5%) were discharged home. No differences in discharges were present for the TnI vs hs-TnI groups (71.1% vs 71.9%; $P = 0.65$). Similar proportions of patients left without being seen by physicians for the 2 study periods (2% vs 2.5%; $P = 0.32$); however, these patients would not have had any biomarker testing.

The proportion of patients who were admitted to the hospital remained similar (25.1% vs 23.9%; $P = 0.48$) following the pathway changes. The overall 30-day clinical outcomes were similar between groups. MACE outcomes did not change following the implementation of the hs-TnI test (13.6% vs 13.1%; $P = 0.71$). Table 4 illustrates the Cox regression analysis for MACE. Many conventional cardiac risk factors (eg, age, history of coronary artery disease, diabetes) demonstrated statistically significant unadjusted hazard ratios. Although patients with CKD had more comorbidities, they were balanced between the time periods, and in the sensitivity analysis excluding patients with CKD, ED LOS (377 minutes; 95% CI: 274, 504) was similar to that for all patients (379 minutes; 95% CI: 277, 512). After adjustment in Cox regression modelling, no overall difference in MACE was noted between the hs-TnI group compared with the TnI group (adjusted hazard ratio = 1.12; 95% CI: 0.90, 1.41). Our interrupted time series failed to demonstrate a significant change in troponin level or trends of MACE after the introduction of the hs-TnI assay ($P = 0.60$; Fig. 2).

Discussion

This study was designed to evaluate the effectiveness and safety of an accelerated protocol associated with a change to a high-sensitivity troponin in an urban, high-volume teaching ED for patients presenting with chest pain assessed to be cardiac in nature. Between the study periods, the patient populations appear unchanged, and no important changes in the characteristics of patients were detected, even though the chaos of a global COVID-19 pandemic continued. No corresponding increase occurred in the amount of specialist consultation. Given the oft-cited concern that clinically irrelevant troponin results will increase cardiology department consultations to unsustainable levels, this finding was reassuring. Additionally, the proportion of patients being discharged home from the ED remained stable. Finally, the hs-TnI assay and the associated protocol resulted in a significant reduction in overall ED LOS for all patients presenting with chest pain. The magnitude of the reduction for unstratified all-comers (21 minutes) is consistent with other reported Canadian experience.[7]

Important differences can be noted between the chest pain protocols. The HEART pathway,[15] which was the basis of the accelerated diagnostic pathway in the TnI period, required calculating a HEART score for all patients. Technically, only those with scores of 3 or less can be in the early rule-out group. Additionally, the pathway is effectively binary:

Table 2. Testing and outcomes of patients presenting to a high-volume urban Canadian emergency department (ED) with cardiac chest pain before and after the introduction of an accelerated pathway using a high-sensitivity cardiac troponin assay and a 3-hour serial troponin interval

Test	Total N = 2640	TnI n = 1333	hs-TnI n = 1307	*P*
Troponin tests				**0.0034**
0	228 (8.6)	120 (9.0)	108 (8.3)	0.5
1	1275 (48.3)	669 (50.2)	606 (46.4)	0.05
2	1090 (41.3)	511 (38.3)	579 (44.3)	**0.002**
≥ 3	47 (1.8)	33 (2.5)	14 (1.1)	**0.006**
Troponin results				
Negative	1302/2412 (54.0)	581/1213 (47.9)	721/1199 (60.1)	**< 0.0001**
Indeterminate	826/2412 (34.3)	476/1213 (39.2)	350/1199 (29.2)	**< 0.0001**
Positive	284/2412 (11.8)	156/1213 (12.9)	128/1199 (10.7)	0.0960
Chest imaging				
CXR	2080 (78.8)	1041 (78.1)	1039 (79.5)	0.3788
CTPE	263 (10.0)	129 (9.7)	134 (10.3)	0.6218
V/Q scan	39 (1.5)	20 (1.5)	19 (1.5)	0.9208
ED consultation				
Yes	940 (35.6)	498 (37.4)	442 (33.8)	0.0574
Number of ED consultations	1 (1, 1)	1 (1, 1)	1 (1, 1)	0.0969
Consult service				
Cardiology	633 (67.3)	332 (66.7)	301 (68.1)	0.6401
General medicine	229 (24.4)	121 (24.3)	108 (24.4)	0.9610
Gastroenterology	48 (5.1)	20 (4.0)	28 (6.3)	0.1070
General practitioner	46 (4.9)	24 (4.8)	22 (5.0)	0.9107
General surgery	29 (3.1)	14 (2.8)	15 (3.4)	0.6063

Values are n (%) or median (interquartile range). Boldface on values indicates a statistically significant result.

CTPE, computed tomography for pulmonary embolism; CXR, chest radiograph. hs-TnI, high-sensitivity troponin I assay; TnI, conventional troponin I assay; V/Q, pulmonary ventilation and perfusion.

patients either had no detectable troponin, or else they had an elevated result and cardiology consultation was recommended. By comparison, the hs-TnI accelerated chest pain protocol was more nuanced. Specific guidance was provided to physicians on acceptable troponin thresholds and changes in troponin levels between serial measurements (delta). Risk stratification was recommended for only patients in the indeterminate category. The advice on stratification was similar to that of the HEART pathway, whereby a score of 3 or less would warrant outpatient stress testing, and higher scores may call for

Table 3. Patient outcomes before and after the implementation of an accelerated pathway using a high-sensitivity troponin assay and a 3-hour serial troponin interval

Outcome	Total N = 2640	TnI n = 1333	hs-TnI n = 1307	*P*	Median differences with 95% CI
Disposition					
Admitted	646 (24.5)	334 (25.1)	312 (23.9)	0.479	N/A
Discharged	1888 (71.5)	948 (71.1)	940 (71.9)	0.648	N/A
LWBS	59 (2.2)	26 (2.0)	33 (2.5)	0.318	N/A
LAMA	46 (1.7)	25 (1.9)	21 (1.6)	0.598	N/A
Died	1 (0.0)	0 (0.0)	1 (0.1)	N/A	N/A
ED physician initial assessment	60 (31, 103)	59 (31, 100)	60 (32, 108)	0.340	−1.0 (−6.4 to 4.4)
ED length of stay					
Overall	379 (277, 512)	392 (277, 525)	371 (276, 490)	0.0198	21.0 (5.3 to 36.7)
Negative	359.5 (277, 463)	336 (249, 444)	374 (305, 475)	**< 0.0001**	−38.0 (−56.1 to −19.9)
Indeterminate	448.5 (350, 567)	484 (391.5, 600.5)	384 (267, 537)	**< 0.0001**	100 (69.9 to 130.1)
Positive	411.5 (273.5, 561.5)	407 (246.5, 563.5)	415 (317.5, 553.5)	0.5285	−7.0 (−62.1 to 48.1)
Discharged	378 (284, 491)	397.5 (291.5, 518.5)	363.0 (281.5, 462.5)	**< 0.0001**	34.0 (18.1 to 49.9)
Discharged (repeat tests)	439 (365, 549)	476.5 (390, 574.5)	410 (352, 504)	**< 0.0001**	66.0 (43.5 to 88.5)
Readmissions within 30 d (all-cause)	772 (29.2)	407 (30.5)	365 (27.9)	0.1411	N/A
Readmissions within 30 d (heart failure)	75 (2.8)	40 (3.0)	35 (2.7)	0.6176	N/A
Clinical outcomes within 30 d					
Stroke	8 (0.3)	5 (0.4)	3 (0.2)	0.4963	N/A
MI	202 (7.7)	106 (8.0)	96 (7.3)	0.5575	N/A
Cardiac interventions*	188 (7.1)	92 (6.9)	96 (7.3)	0.6579	N/A
Death	39 (1.5)	17 (1.3)	22 (1.7)	0.3851	N/A
MACE†	352 (13.3)	181 (13.6)	171 (13.1)	0.7083	N/A

Values are n (%) or median (interquartile range), unless otherwise indicated. Boldface on values indicates statistically significant result.

CI, confidence interval; ED, emergency department; hs-TnI, high-sensitivity troponin; LAMA, leaving against medical advice; LWBS, leaving without being seen; MACE, major adverse cardiac events; MI, myocardial infarction; N/A, not applicable; TnI, conventional troponin I assay.

*Cardiac interventions include coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI).

†MACE is defined as a composite of all-cause death, hospitalization for heart failure, hospitalization or/and ED visit for stroke or MI, or cardiac interventions.

Table 4. Major adverse cardiac events (MACE) outcomes of Canadian emergency department with chest pain before and after the introduction of an accelerated pathway using a high-sensitivity cardiac troponin assay and a 3-hour serial troponin interval (N = 2412)

Variable	Unadjusted HR (95% CI)	*P*	aHR (95% CI)*	*P*
Age, y				
≤ 45	Ref		Ref	
46–64	4.24 (2.55–7.07)	< 0.0001	1.99 (1.18–3.36)	**0.0094**
≥ 65	8.22 (5.00–13.5)	< 0.0001	2.31 (1.38–3.87)	**0.0015**
Male sex	1.52 (1.20–1.92)	0.0005	1.10 (0.86–1.40)	0.4464
EMS	2.51 (1.98–3.18)	< 0.0001	—	—
Hypertension	2.75 (2.15–3.53)	< 0.0001	—	—
CAD	8.88 (6.57–12.0)	< 0.0001	2.64 (1.90–3.68)	**< 0.0001**
Diabetes	2.33 (1.86–2.91)	< 0.0001	1.34 (1.06–1.70)	**0.0132**
AFIB	1.72 (1.36–2.18)	< 0.0001	0.75 (0.58–0.95)	**0.0199**
Stroke	1.60 (1.24–2.06)	0.0003	—	—
Asthma	0.91 (0.64–1.30)	0.6125	—	—
HF	4.10 (3.24–5.18)	< 0.0001	1.69 (1.31–2.18)	**< 0.0001**
COPD	1.37 (1.03–1.84)	0.0336	—	—
Dementia	1.36 (0.82–2.24)	0.2341	—	—
Charlson score	1.21 (1.17–1.26)	< 0.0001	—	—
Troponin test results				
Negative	Ref		Ref	
Indeterminate	1.83 (1.30–2.59)	0.0006	1.04 (0.73–1.48)	0.8348
Positive	16.5 (12.2–22.1)	< 0.0001	5.28 (3.83–7.29)	**< 0.0001**
CT scan	0.71 (0.47–1.08)	0.1109	0.55 (0.36–0.84)	**0.0052**
Consultation	15.6 (10.9–22.4)	< 0.0001	6.09 (4.12–9.00)	**< 0.0001**
Post-implementation of hs-TnI period	1.00 (0.80–1.25)	0.984	1.12 (0.90–1.41)	0.3076

aHR, adjusted hazard ratio for the Cox regression model; AFIB, atrial fibrillation; CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CT, computed tomography; EMS, emergency medical service; HF, heart failure; hs-TnI, high-sensitivity troponin test; HR, hazard ratio; Ref, referent.

*Adjusted for age, sex, and postimplementation of hsTn and statistically significant variables from stepwise variable selection: CAD, diabetes, AFIB, HF, Troponin test results, CT scan, and consultation. Boldface indicates a statistically significant result.

cardiology involvement. Patients with undetectable (< 3 ng/L) or grossly elevated (> 100 ng/L) troponin results, with symptoms at more than 3 hours since onset, were managed in a way very similarly to the TnI protocol.

The low-risk or rule-out group experienced an increased LOS after transition to the hs-TnI protocol. This change is likely driven by differences in the retrospective classification rather than by true clinical differences. In both the pre- and post- groups, patients with initially undetectable troponin, and symptoms for more than 3 hours, could be ruled as being negative or low-risk; however, in the hs-TnI group, patients undergoing serial troponin testing also could be classified as low-risk if their troponin level was < 20 ng/L and they had a delta change of < 5 ng/L. We suggest that this difference also accounts for the increased proportion of patients in the group of the hs-TnI protocol classified as negative.

The group classified as indeterminate is perhaps the most directly comparable pre- vs post- implementation. These patients did not meet the criteria for rule-out or rule-in cardiac damage and thus required serial measurements. An impressive 100-minute median reduction in ED LOS (95% CI: 69.9, 130.1 minutes; $P < 0.0001$) was demonstrated with the adoption of the hs-TnI assay and protocol for this group. Given the consistent 3-hour serial interval, this reduction is more difficult to explain. A possible explanation is increasing physician comfort with trending troponin measurements. Troponin pathways were relatively novel in the ED setting in 2015,[15] compared to more recent years in which they have become much more common. As part of this change, nurses have become comfortable drawing repeat measurements at the appropriate intervals, and electronic medical systems have enabled ordering from anywhere in the department. Certainly, a component of lack of protocol adherence persists, such as physicians not ordering a repeat troponin test despite the initial value being > 3 ng/L. This approach would cause a patient to be analyzed in the indeterminate group despite potentially being discharged after a single troponin test. Lack of protocol compliance has been documented in similar studies.[7] To account for this, we also analyzed the subgroup of discharged patients who received 2 troponin tests. A decrease still occurred in median LOS, from 476.5 to 410 minutes ($P < 0.0001$), although by definition, this subgroup can include patients in any of the 3 groups from the hs-TnI protocol.

The stable proportions of clinical outcomes across the groups are consistent with other reported literature, including both observational[7,8] and randomized[21] clinical trials. The 30-day all-cause mortality was 1.5%, which was comparable to the rate in other Canadian studies.[7] Furthermore, the interrupted time series (Fig. 2) illustrates a stable trend in MACE across both protocols, which is reassuring and suggests that the strategy is safe.

Limitations

Some limitations to this research warrant discussion. The study design was observational, rather than randomized; however, these protocol changes were mandated by the health authority at a regional and hospital level, meaning that randomization at the individual patient level was not feasible. All data were taken from a Canadian healthcare system, in which services are available without charge to all citizens who are registered, which may limit its external validity to other healthcare regions. Enrollment was restricted to patients triaged with symptoms of chest pain of cardiac origin; those presenting who described their chest pain without certain

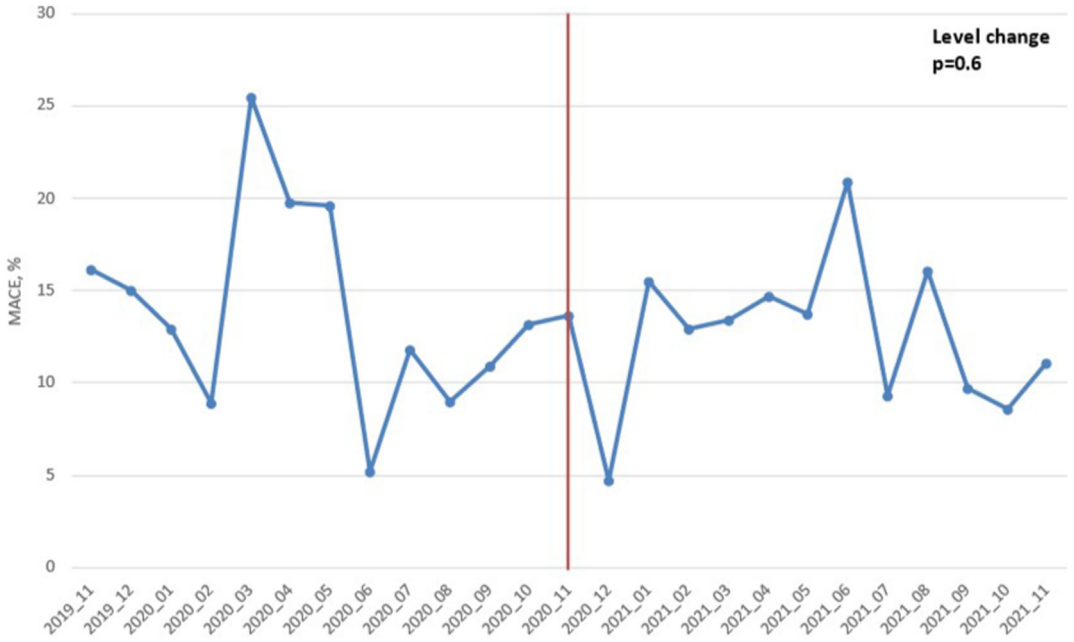

Figure 2. Trends in major adverse cardiac events (MACE) within 30 days of index emergency department visit for patients with chest pain before and after the introduction of an accelerated pathway using a high-sensitivity cardiac troponin assay and a 3-hour serial troponin interval. 01, January; 02, February; 03, March; 04, April; 05, May; 06, June; 07, July; 08, August; 09, September; 10, October; 11, November; 12, December.

classic features or with atypical chest pain/cardiac presentations may have been excluded. Some laboratory samples do undergo hemolysis prior to lab analysis and thus need to be redrawn; this granularity is not captured in our administrative data. This protocol was implemented during the severe respiratory distress syndrome coronavirus-2 (SARS-CoV-2 or COVID-19) pandemic, and it was difficult to control for the impact of the pandemic on patient presentations (eg, delays, volumes, co-infection, etc.) and operational issues. COVID was first detected within Alberta during March 2020, and significant changes occurred in patient volumes and ED functioning, with actual case volumes remaining low until November 2020.[22] Anecdotally, during the period from November 2020 to January 2021, the healthcare system was under significant strain, and wait times were generally longer for all presentations. Available data from this period are reflective of this change, demonstrating a decrease in overall daily patient volumes beginning in January of 2020, followed by a relative increase in the proportion of both higher-acuity patients and patients requiring admission (Supplemental Fig. S1).[14] Additionally, no washout period occurred between the 2 protocols, and physicians may have taken some time to become comfortable with the new protocols. Finally, administrative data do not contain detailed behavioural (eg, smoking, vaping, cannabis use, alcohol intake, exercise, diet), management (eg, medication, adherence), and/or sociodemographic (eg, race, employment, income) factors that may impact acute and longer-term health outcomes. Sex- and race-based analyses were not included in this study; however, the databases did contain information on patient sex, and future analyses of sex-based differences are planned.

Notwithstanding the above concerns, we believe the large sample size and the pragmatic nature and comprehensive reporting of outcomes provide a valid assessment of the efficiency and safety of the implementation of this approach. Moreover, the results compare favourably with those of a recently completed systematic review.[23]

Conclusion

The implementation of an accelerated chest pain protocol using an hs-TnI assay in a tertiary-care Canadian ED was associated with a modest reduction of ED LOS for all patients; however, this reduction was more substantial for patients undergoing serial testing. Review of admissions numbers, and the incidences of MACE outcomes and deaths, which remained the same following the protocol implementation, demonstrated the safety of this approach. Further research on protocol adherence and avoidance of Tn testing in patients with very-low-risk chest pain of suspected cardiac origin remains necessary. EDs with prolonged assessments for chest pain should consider implementing similar approaches.

Ethics Statement

The study was approved by the University of Alberta Health Research Ethics Board (Reference ID: Pro00096932) at the University of Alberta, in Edmonton, Alberta, Canada.

Patient Consent

As this is a retrospective study using de-identified data, the authors confirm that patient consent is not applicable to this article.

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Disclosures

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References

1. Canadian Institute for Health Information (CIHI). NACRS Emergency Department Visits and Length of Stay by Province/Territory, 2018—2019. Ottawa: CIHI, 2019.
2. Bhoi S, Verma P, Vankar S, Galwankar S. High sensitivity troponins and conventional troponins at the bedside. Int J Crit Illn Inj Sci 2014;4:253-6.
3. Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in patients presenting without persistent ST-segment elevation of the European Society of cardiology (ESC). Eur Heart J 2016;37:267-315.
4. Cullen L, Mueller C, Parsonage WA, et al. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. J Am Coll Cardiol 2013;62:1242-9.
5. Christ M, Bertsch T, Popp S, et al. High-sensitivity troponin assays in the evaluation of patients with acute chest pain in the emergency department. Clin Chem Lab Med 2011;49:1955-63.
6. Freund Y, Chenevier-Gobeaux C, Bonnet P, et al. High-sensitivity versus conventional troponin in the emergency department assessment of acute myocardial infarction. Crit Care 2011;15:R147.
7. Crowder KR, Jones TD, Lang ES, et al. The impact of high-sensitivity troponin implementation on hospital operations and patient outcomes in 3 tertiary care centers. Am J Emerg Med 2015;33:1790-4.
8. Ford JS, Chaco E, Tancredi DJ, Mumma BE. Impact of high-sensitivity cardiac troponin implementation on emergency department length of stay, testing, admissions, and diagnoses. Am J Emerg Med 2021;45:54-60.
9. Furmaga J, McDonald SA, Hall HM, et al. Impact of high-sensitivity troponin testing on operational characteristics of an urban emergency department. Acad Emerg Med 2021;28:114-6.
10. Ljung L, Frick M, Linder R, et al. A rule-out strategy based on high-sensitivity troponin and HEART score reduces hospital admissions. Ann Emerg Med 2019;73:491-9.
11. Mungai E, Hamilton BK, Burns D. Comparison of high-sensitivity troponin T assay to conventional troponin T assay for rule out of acute coronary syndrome in the emergency department. Adv Emerg Nurs J 2020;42:304-14.
12. Twerenbold R, Jaeger C, Gimenez MR, et al. Impact of high-sensitivity cardiac troponin on use of coronary angiography, cardiac stress testing, and time to discharge in suspected acute myocardial infarction. Eur Heart J 2016;37:3324-3332a.
13. Vigen R, Pandey A, Joglar JA, et al. Association of a novel protocol for rapid exclusion of myocardial infarction with resource use in a US safety net hospital. JAMA Netw Open 2020;3:e203359.
14. Health Quality Council of Alberta. Healthcare areas: emergency department. Available at: https://focus.hqca.ca/charts/emergency-department-volumes/. Accessed October 6, 2022.
15. Mahler SA, Hiestand BC, Hoekstra JW, et al. The HEART Pathway Randomized Trial: identifying emergency department patients with acute chest pain for early discharge. Circ Cardiovasc Qual Outcomes 2015;8:195-203.
16. Poldervaart JM, Langedijk M, Backus BE, et al. Comparison of the GRACE, HEART, and TIMI score to predict major adverse cardiac events in chest pain patients at the emergency department. Int J Cardiol 2017;227:656-61.
17. Greenslade J, Cho E, Van Hise C, et al. Evaluating rapid rule-out of acute myocardial infarction using a high-sensitivity cardiac troponin I assay at presentation. Clin Chem 2018;64:820-9.
18. Raizman JE, Tsui AKY, Goudreau BL, et al. Multi-platform analytical evaluation of the Beckman Coulter Access high-sensitivity troponin I assay across different laboratory sites using Barricor plasma. Clin Biochem 2020;78:25-31.
19. Grafstein E, Bullard MJ, Warren D, Unger B; the CTAS National Working Group. Revision of the Canadian Emergency Department Information System (CEDIS) presenting complaint list version 1.1. CJEM 2008;10:151-61.
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
21. Anand A, Lee KK, Chapman AR, et al. High-sensitivity cardiac troponin on presentation to rule out myocardial infarction: a stepped-wedge cluster randomized controlled trial. Circulation 2021;143:2214-24.
22. Government of Alberta. Respiratory virus dashboard. Available at: https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#total-cases. Accessed September 12, 2022.
23. Hill J, Essel NO, Yang EH, Dennett L, Rowe BH. Effectiveness of accelerated diagnostic protocols for reducing emergency department length of stay in patients presenting with chest pain: a systematic review. *journal*, in press.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.09.007.