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Systematic Review/Meta-analysis

Risk Scores for Clinical Risk Stratification of Emergency Department Patients With Chest Pain but No Acute Myocardial Infarction: A Systematic Review

Q7 Q1

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ABSTRACT

Background: Chest pain is a common cause for emergency department (ED) presentations. After myocardial infarction (MI) has been ruled out by means of electrocardiography and troponin testing, decisions around anatomic or functional testing may be informed by clinical risk scores. We conducted a systematic review to synthesize evidence of the prognostic performance of chest pain risk scores among ED patients who have had MI ruled out by means of a high-sensitivity troponin assay.

Methods: We queried multiple databases from inception to May 17, 2022. We included studies that quantified risk of 30-day major adverse cardiac events (MACE), at different cutoffs of clinical risk scores, among adult patients who had MI ruled out by means of a high-sensitivity troponin assay. Prognostic performance of each score was synthesized and described, but meta-analysis was not possible.

Results: Six studies met inclusion criteria. Short-term MACE risk

RÉSUMÉ

Contexte : La douleur thoracique est une cause courante des visites à l'urgence. Une fois que l'infarctus du myocarde (IM) est écarté grâce à l'électrocardiogramme et au dosage de la troponine, les décisions concernant les examens anatomiques ou fonctionnels à effectuer peuvent être guidées par le score de risque clinique. Nous avons effectué une revue systématique pour résumer les données probantes sur la performance pronostique des scores de risque de la douleur thoracique parmi les patients admis à l'urgence chez qui l'IM a été écarté après le dosage de la troponine à haute sensibilité.

Méthodologie : Nous avons interrogé de nombreuses bases de données, à partir de leur création jusqu'au 17 mai 2022. Nous avons inclus les études qui quantifient le risque d'événement cardiaque indésirable majeur (ECIM) à 30 jours, à différents seuils de score de risque clinique, chez les patients adultes dont l'IM a été écarté après un dosage de la troponine à haute sensibilité. La performance

Chest pain and symptoms of acute coronary syndrome (ACS) are a leading cause of emergency department (ED) visits worldwide.^{1,2} During these visits, ED physicians must rapidly identify which presentations represent an ACS (including ST-segment elevation myocardial infarction [STEMI], non-ST-segment elevation myocardial infarction [NSTEMI], and unstable angina [UA]) in order to initiate

appropriate management and minimize associated morbidity and mortality.³ In accordance with recently updated clinical practice guidelines,⁴ ED physicians should rule out acute ACS through a combination of clinical judgement, electrocardiographic (ECG) findings and high-sensitivity cardiac troponin (hs-cTn) testing. The evidence supports a sequential approach whereby the history, physical examination, and ECG interpretation help to first ensure swift identification of STEMI, followed by algorithmic application of hs-cTn testing to rule in or rule out NSTEMI.^{5,6} While hs-cTn algorithms reliably identify patients at high risk likely to benefit from inpatient treatment, most patients are ultimately classified as low or indeterminate risk. They can do so with remarkable accuracy such that a hs-cTn concentration

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among patients who had MI ruled out by means of high-sensitivity cardiac troponin assays was very low. The HEART score, with a cutoff of 3 or less, predicted a very low risk of MACE among the greatest proportion of patients. Other scores had lower sensitivity or classified fewer patients as low risk.

Conclusions: The HEART score with a cutoff value of 3 or less accurately identified the greatest number of patients at low risk of 30-day MACE. However, MACE risk among patients who have MI ruled out by means of high-sensitivity troponin testing is sufficiently low that clinical risk stratification or noninvasive testing may be of little additional value in identifying patients with coronary disease.

below the assay's limit of detection, taken 3 hours after symptom onset, carries a 30-day risk of major adverse cardiac events (MACE) of less than 2%.⁷ Even so, some patients with low-risk hs-cTn concentrations may benefit from additional testing to diagnose symptomatic coronary disease.⁸ Decision pathways based on clinical risk scores have been advocated to accurately estimate pre-test probability and to guide rational and efficient use of anatomic or functional testing in appropriate patients.^{9,10}

However, most existing clinical risk scores were not developed to estimate risk of major adverse cardiac events (MACE) among patients who have already undergone clinical, ECG, and troponin testing in the ED. Rather, they were developed to estimate the risk of an acute coronary syndrome, including myocardial infarction on the index visit, among undifferentiated patients with chest pain presenting to the ED. Or they have been developed in non-emergency patients and adapted for use in the ED. Therefore, existing risk scores may not accurately estimate risk of adverse cardiac events in patients who remain a diagnostic dilemma after myocardial injury has been ruled out by means of sequential ECG and hs-cTn testing as recommended in recent guidelines.¹¹

We conducted a systematic review to identify and synthesize studies evaluating the performance of chest pain risk scores in the population of patients who have had MI ruled out, to identify patients with low risk of cardiac events after discharge who do not require risk stratification with noninvasive testing. This evidence synthesis will guide decision making for patients who are eligible for discharge after an ED evaluation for chest pain, facilitating more rational use of outpatient noninvasive testing.

Methods

The design and reporting of this systematic review was guided by the Cochrane Collaboration Prognosis Methods Group methodologic recommendations¹² and reported according to the Preferred Reporting Items in Systematic Reviews and Meta-analyses (PRISMA) guidelines¹³ standards as outlined in the Transparent Reporting for Individual Prognosis or Diagnosis checklist.^{12,14}

pronostique de chaque score est résumée et décrite, mais il n'a pas été possible d'effectuer de méta-analyse.

Résultats : Six études répondaient aux critères d'inclusion. Le risque d'ECIM à court terme chez les patients chez qui l'IM a été écarté après dosage de la troponine cardiaque à haute sensibilité est très faible. Le score HEART (History, ECG, Age, Risk Factors, Troponin / antécédents, ECG, âge, facteurs de risque, troponine), avec un seuil de 3 ou moins, a prédit un risque très faible d'ECIM parmi la plus grande proportion de patients. Les autres scores ont une sensibilité moindre ou classaient moins de patients comme étant à faible risque.

Conclusions : Le score HEART à un seuil de 3 ou moins a permis de cibler correctement le plus grand nombre de patients présentant un risque faible d'ECIM à 30 jours. Cependant, le risque d'ECIM chez les patients chez qui l'IM a été écarté après dosage de la troponine à haute sensibilité est si faible qu'une stratification du risque clinique ou un examen non effractiv serait peu utile pour repérer les patients ayant une maladie coronarienne.

Study design

This systematic review sought to answer the following question: What is the prognostic performance of different chest pain risk prediction scores when used in patients who have had MI ruled out in the ED by means of an hs-cTn assay? A study protocol describing the review methods, search methodology and analytical goals of the review was developed and registered to PROSPERO (CRD42019131264) before the commencement of our literature search.

Search strategy

An electronic search strategy was developed by the investigators (C.M.O'R., A.D.M.) and further refined by information specialists with expertise in systematic reviews (H.L.R. and D.L.).

Six electronic databases (Ovid Medline, Embase, Cochrane Central, Scopus, Web of Science, and CINAHL) were searched to identify articles published from database inception to May 16, 2019. Update searches were run on February 12, 2021, and May 17, 2022, for all databases except for Cochrane Central to identify additional studies. Central was excluded from the update searches because it was not observed to identify additional studies in the initial search. The search strategy included terms describing the population, study designs, risk prediction scores and cardiac troponin assays of interest. Headings and keywords were adapted for use in each database. No publication language constraints were applied to the search. Reference lists of the included studies were also examined to identify any relevant articles not captured in the electronic literature search.

Study selection

The study selection procedure described below was implemented in accordance with the PRISMA guidelines¹³ and summarised in the corresponding flow diagram (Figure 1).

Following the removal of duplicate records, a minimum of two authors (C.M.O., T.G.H., or A.D.M.) independently screened titles and abstracts in duplicate against established criteria. The full-text articles of abstracts selected for inclusion were subsequently also screened in duplicate for eligibility.

During both stages of the selection process, a third reviewer was available to resolve any disagreements.

Studies were included if they 1) included adult patients (≥ 18 years old) presenting to the ED with a primary complaint of chest pain or symptoms suggestive of ACS, 2) quantified risk score performance in a population of patients who had MI ruled out at the index visit by means of hs-cTn assays, and 3) assessed the prognostic performance of at least 1 risk prediction score applied in the ED for 30-day MACE (not including events on the index ED visit). Both quantitative risk prediction models and categorical clinical decision rules were eligible for inclusion in the review, provided that all the variables included in the prediction tool would have been available to the treating physician at the time of the ED assessment. In accordance with the Checklist for Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies, eligible study designs included prediction model development studies without external validation, prediction score model development studies with external validation, and external score validation studies (with or without model updating).¹⁵ Studies were excluded if they 1) used only contemporary (fourth generation or earlier

cardiac troponin assays or 2) assessed troponin-only prognostication tools (ie, accelerated diagnostic and prognostic algorithms). The second exclusion criterion was implemented as we screened articles because risk scores including several clinical variables are meaningfully different in application and interpretation than diagnostic biomarker algorithms.

Outcomes of interest

The primary outcome for this review was the proportion of patients identified as low risk for 30-day MACE by the prognostic prediction tools of interest. Secondary outcomes included classification measures such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), as well as measures of model or score discrimination (eg, area under the receiver operating characteristic curve, C-statistic, etc) and calibration (eg, Hosmer-Lemeshow test result, etc).

Study quality (risk of bias) assessment

Study quality was appraised by means of the Prognostic Model Risk of Bias Assessment Tool (PROBAST),¹⁶ a domain-based tool that enables the targeted and transparent

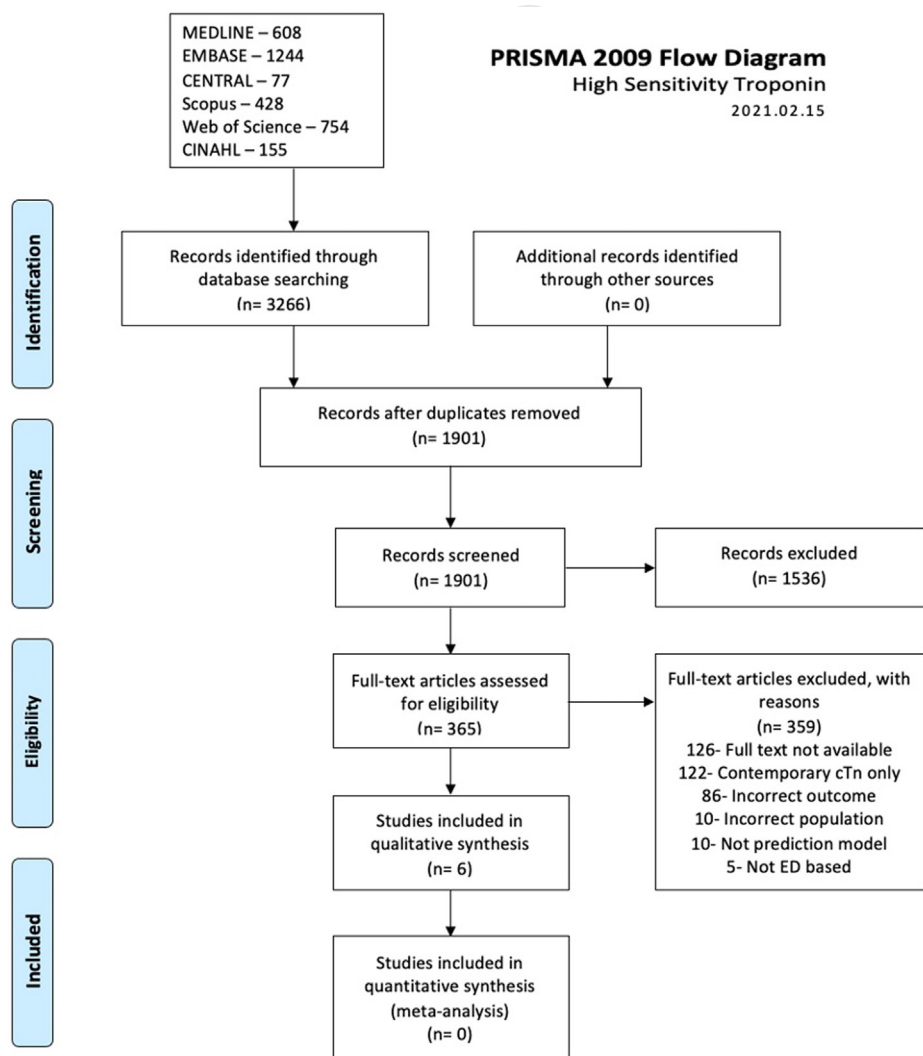


Figure 1. Preferred Reporting Items in Systematic Reviews and Meta-analyses (PRISMA) flow diagram.

Table 1. Characteristics of included studies and populations, by study design

Study	Country	Sample size	Mean age, y	Male (%)	30-day MACE	Troponin assay(s)	Risk score(s) and cutoff(s)
Willems ¹⁷ (2014)	Netherlands	89	61.0	52 (58.4)	9 (10.1)	hs-cTnT	HEART \leq 3
McCord ¹⁸ (2017)	USA	661	58.3 \pm 13.0	385 (58.2)	6 (0.91)	hs-cTnT	HEART \leq 3 TIMI = 0 TIMI \leq 1
Carlton ¹⁹ (2018)	UK	7691	58.1 \pm 13.2	4830 (62.8)	821 (10.7)	hs-cTnT hs-cTnI	TIMI = 0 TIMI \leq 1 TIMI \leq 2
Marcusohn ²⁰ (2020)	Israel	9236	46.3 \pm 16.0	4653 (60.4)	179 (2.30)*	hs-cTnI	GRACE $<$ 73
Ratmann ²¹ (2020)	Switzerland	2374	NR	NR	332 (14.0)	hs-cTnI	NOTR
Khan ²² (2021)	Australia	1638	58.7 (48.6-69.4)	871 (53.2)	89 (5.4) [†]	hs-cTnT	TIMI \leq 1 HEART \leq 3 EDACS $<$ 16

Values are mean \pm SD, median (interquartile range), or n (%).

GRACE, Global Registry of Acute Coronary Events; HEART, History, ECG, Age, Risk Factors, Troponin; hs-cTnI, high-sensitivity cardiac troponin I; hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiac events; NOTR, No Objective Testing rule; NR, not reported; TIMI, Thrombolysis in Myocardial Infarction.

* 60-day MACE.

[†] All-cause mortality and MI only.

assessment of risk of bias for derivation, validation, or score updating studies. A single form is completed for each study with risk of bias ratings being made for all applicable designs (ie, derivation, internal validation, and external validation), resulting in 2 domain-based ratings and an overall rating per study. One author (C.M.O.) completed a PROBAST form in full for each included study, with every form reviewed for completion and risk of bias rating appropriateness by a second author (T.G.H., A.D.M.).

Data extraction and synthesis

Relevant study and outcomes data were collected with the use of a standardised data collection form. The data abstracted from each study included date of publication, country of origin, sample size and characteristics, study type (derivation and internal validation, external validation), hs-cTn assay type (manufacturer, hs-cTnI or hs-cTnT), risk score assessed and cutoff values, and patient outcome data.

Our *a priori* registered protocol for this study delineated our intentions to perform a meta-analysis on the classification characteristics reported in the included studies. However, a prognostic meta-analysis requires the availability of the 2 \times 2 contingency tables that correspond to each result reported in a study. We attempted to recreate these tables with data available in the included studies, but often that was not possible, and as such, the meta-analysis was not feasible.

Results

A total of 1901 unique records were identified through database and other searching. Following abstract and full-text review, 6 studies were included in this review.¹⁷⁻²² The most common reasons for exclusion at the full-text phase was the lack of an available full text (ie, conference abstract only, etc) and use of previous-generation troponin assays (Figure 1).

Included studies were conducted in the United States,¹⁸ United Kingdom,¹⁹ Switzerland,²¹ Israel,²⁰ The Netherlands,¹⁷ and Australia²² and were all external validation studies. In all, these studies evaluated risk score prognostic performance in 20,959 patients with study sample sizes

ranging from 89 to 9236. The hs-cTn criteria used for ruling out MI in each study population are presented in Supplemental Table S1. Risk scores assessed included the History, ECG, Age, Risk Factors, Troponin (HEART) Score (n = 3),^{17,18,22} the Thrombolysis in Myocardial Infarction (TIMI) score (n = 3),^{18,19,22} the Global Registry of Acute Coronary Events (GRACE) score (n = 1),²⁰ the NOT (No Objective Testing) rule (n = 1),²¹ and the Emergency Department Assessment of Chest Pain Score (EDACS) (n = 1)²² at a variety of cutoff values. Details including sample characteristics, outcomes, and risk scores assessed are presented in Table 1. Evidence quality was variable, with 2 studies having low risk of bias, 1 having high risk of bias, and 1 having features making its risk of bias ratings unclear. Concerns with bias were due to lack of information regarding patient sample or the failure to use a standard diagnostic definition for their outcome measures. Domain-specific and overall risk of bias ratings for all included studies are shown in Figure 2.

Based on the reported demographics, the mean ages of study samples ranged from 46.3 to 61.0 years. All studies included predominantly male participants, ranging from 58.2% to 62.8% of the study samples. The incidence of the primary outcome, 30-day MACE, varied widely across the included studies, ranging from 0.9% to 13.9%. When a breakdown of the composite outcome components was reported, MACE rates were often driven by revascularisation as rather than acute MI or death.

Included studies typically compared a single score across a number of cutoff values, and only 1 study directly compared 2 distinct scores. Below, we discuss the performance of specific risk score cutoffs in combination with different hs-cTn assays.

HEART score

Compared with other risk scores, the HEART score used in combination with an hs-cTnT assay maximised the proportion of patients identified as low risk with as many as 62.5% of patients having a HEART score \leq 3 (Table 2). The sensitivity of a HEART score \leq 3 for ruling out 30-day MACE among patients classified as having an MI ruled out

Study	Risk of bias				Overall
	D1	D2	D3	D4	
Willems 2014	+	+	+	✗	✗
McCord 2017	+	+	+	-	-
Carlton 2018	+	+	+	+	+
Marcusohn 2020	+	+	-	+	-
Ratmann 2020	-	+	+	-	-
Khan 2021	+	+	+	+	+

D1: Participants
D2: Predictors
D3: Outcomes
D4: Analysis

Judgement
 ✗ High
 - Unclear
 + Low

Figure 2. Risk of bias summary.

ranged from 93.8% to 100%. However, the 2 largest studies^{18,22} demonstrated the lowest sensitivity for 30-day MACE. In the Khan et al. study,²² which had a low risk of bias, the primary outcome included only death and MI as MACE components and reported a sensitivity of 96.6%. If revascularisation had been included in their definition of MACE, sensitivity likely would have been lower.

TIMI score

Several studies evaluated different cutoff values of the TIMI score in combination with different hs-cTn assays (Table 2). A TIMI score ≤ 1 , with troponin concentrations measured by means of an hs-cTnT assay, classified similar proportions of patients as low risk compared with the HEART score. The McCord et al.¹⁸ and Khan et al.²² studies directly compared TIMI ≤ 1 with HEART ≤ 3 . McCord et al. found similar proportions of patients ruled out for the HEART score ≤ 3 compared with TIMI ≤ 1 . The Khan et al. study, which had a low risk of bias, observed excellent sensitivity for both HEART ≤ 3 and TIMI ≤ 1 , although the sensitivity for TIMI ≤ 1 was slightly higher and HEART ≤ 3 classified a slightly greater proportion of patients as low risk. The Carlton et al. study,¹⁹ which also had a low risk of bias, similarly

observed excellent sensitivity for TIMI ≤ 1 , albeit with a relatively small proportion of patients classified as MI ruled out. As noted above, MACE events may have been underestimated in the Khan et al. study, which quantified only mortality and MI as components of their composite outcome.

When used in combination with an hs-cTnI assay, a TIMI score ≤ 1 also had excellent sensitivity for 30-day MACE events but classified a small proportion of patients as low risk.

Other risk scores

One study evaluated the prognostic performance of the EDACS.²² When used with an hs-cTnT assay, EDACS had a sensitivity of 96.6% (95% CI 90.5%-99.3%) for 30-day MI or mortality and classified 46% of patients as low risk. The NOT rule in combination with an hs-cTnI assay exhibited sensitivity of 97.7% across a range of cutoff values but classified only a maximum of 23% of patients as low risk. The GRACE score, with a cutoff value of 73 points or lower in combination with a hs-cTnI assay exhibited a sensitivity of 75.4% (Table 3).

Discussion

In this systematic review, we synthesized evidence on the prognostic performance of different chest pain risk scores when used in patients who have had myocardial infarction ruled out with the use of hs-cTn assays. The quality of evidence was variable. Among the risk scores evaluated in the included studies, the HEART score, with a cutoff value of 3 points or lower, classified the greatest proportion of patients as low risk. However, the sensitivity of this cutoff value for ruling out 30-day MACE among low-risk patients was as low as 93.8%. A TIMI score of 1 or less ruled out a reasonable proportion of patients as low risk, but the sensitivity of this score value was highly variable across studies, ranging from 66.7% to 98.9%. These results and focus on HEART and TIMI scores were informed by the quality of the evidence, in that these risk scores were evaluated in the highest-quality studies.

This systematic review only included studies performed in populations of patients who have had MI ruled out by means of hs-cTn assays, and evaluated the prognostic performance

Table 2. Classification characteristics for 30-day major adverse cardiac events in external validation studies using high-sensitivity cardiac troponin assays

Study	Ruled out, n (%)	Sensitivity	Specificity	NPV	PPV
EDACS < 16					
Khan ²²	754 (46.0)	96.6 (90.5-99.3)	48.9 (46.4-51.4)	99.6 (98.8-99.9)	9.9 (8.0-12.1)
TIMI = 0					
Carlton ¹⁹	566 (17.9)	99.5 (98.1-99.9)	20.3 (18.8-21.8)	99.6 (98.7-100)	14.4 (13.1-15.8)
McCord ¹⁸	200 (30.8)	83.3 (35.9-99.6)	30.9 (27.4-34.6)	99.5 (97.1-99.9)	1.11 (0.78-1.59)
TIMI ≤ 1					
Carlton ¹⁹	887 (28.1)	98.9 (97.3-99.7)	31.7 (30.0-33.5)	99.5 (98.8-99.9)	16.4 (14.9-18.0)
Khan ²²	879 (53.6)	98.9 (93.9-100)	57.2 (54.6-59.7)	99.9 (99.4-100)	11.8 (9.6-14.3)
McCord ¹⁸	366 (56.3)	66.7 (22.3-95.7)	56.5 (52.6-60.4)	99.5 (98.3-99.8)	1.41 (0.80-2.47)
TIMI ≤ 2					
Carlton ¹⁹	1054 (33.4)	98.1 (96.2-99.1)	37.6 (35.8-39.5)	99.3 (98.6-99.7)	17.5 (15.9-19.2)
HEART ≤ 3					
McCord ¹⁸	413 (62.5)	93.8 (89.6-96.7)	—	99.8 (98.7-100)	—
Khan ²²	933 (56.9)	96.6 (90.5-99.3)	60.5 (58.1-63.0)	99.7 (99.1-99.9)	12.4 (10.1-15.1)
Willems ¹⁷	31 (46.0)	100 (29.2-100)	47.7 (35.2-60.5)	100 (—)	8.11 (6.54-10.0)

Ranges in parentheses are 95% confidence intervals.

EDACS, Emergency Department Assessment of Chest Pain Score; GRACE, Global Registry of Acute Coronary Events; HEART, History, ECG, Age, Risk Factors, Troponin; NPV, negative predictive value; PPV, positive predictive value; TIMI, Thrombolysis in Myocardial Infarction.

Table 3. Classification characteristics for 30-day major adverse cardiac events in external validation studies using high-sensitivity cardiac troponin assays

Study	Ruled-out (%)	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)
GRACE < 73					
Marcusohn ²⁰	—	75.4 (—)	59.5 (—)	—	—
NOTR (continuous)					
Ratmann ²¹	454 (19.0)	99.7 (—)	—	99.8 (—)	—
NOTR (categorical)					
Ratmann ²¹	545 (23.0)	99.7 (—)	—	99.8 (—)	—
NOTR (simplified)					
Ratmann ²¹	546 (23.0)	99.7 (—)	—	99.8 (—)	—
TIMI = 0					
Carlton ¹⁹	952 (21.0)	98.9 (97.4-99.6)	23.2 (21.9-24.5)	99.5 (98.8-99.8)	12.3 (11.2-13.4)
TIMI ≤ 1					
Carlton ¹⁹	1617 (35.7)	98.4 (96.8-99.4)	39.4 (37.9-40.9)	99.6 (99.1-99.8)	15.0 (13.7-16.4)
TIMI ≤ 2					
Carlton ¹⁹	1059 (40.5)	97.3 (95.3-98.6)	45.8 (44.2-47.3)	99.4 (98.9-99.7)	16.3 (15.0-17.8)

Ranges in parentheses are 95% CIs.

CI, confidence intervals; GRACE, Global Registry of Acute Coronary Events; HEART, History, ECG, Age, Risk Factors, Troponin; NPV, negative predictive value; PPV, positive predictive value; NOTR, No Objective Testing rule; TIMI, Thrombolysis in Myocardial Infarction.

for events occurring after MI has been ruled out. In contrast, most of the body of related literature evaluates the performance of these scores in undifferentiated chest pain patients (ie, before ruling in or ruling out MI or alternative diagnoses), included MI on the index presentation among the measured outcomes, and used older-generation troponin assays. Therefore, our systematic review summarises the evidence for the performance of these scores in patients in whom structured risk scores to aid decision making around noninvasive testing after ED discharge are most relevant. Decisions around the need for functional or anatomic cardiac testing after ED discharge are relevant only to patients who have an MI ruled out after troponin testing, hence our focus on this patient population. Patients with clearly abnormal troponin concentrations require further investigation and do not require an ED chest pain score to guide clinical decision making. Similarly, patients with obvious noncardiac causes for their chest pain, such as pulmonary embolism or pneumonia, do not require emergency risk stratification for coronary disease.

Based on the findings of this systematic review, the HEART score (utilizing a cutoff of ≤ 3) appears to outperform other risk scores for identifying low-risk patients with chest pain who are unlikely to benefit from further objective cardiac testing after MI has been ruled out by means of hs-cTn. A TIMI score ≤ 1 in patients who have had MI ruled out by means of an hs-cTn assay also has excellent sensitivity but likely classifies fewer patients as low risk.

It is worth noting that the sensitivity of the risk score cutoffs observed in these studies is similar to the sensitivity of hs-cTn testing alone for predicting 30-day MACE. Patients who have MI ruled out by means of a validated hs-cTn testing algorithm are at exceptionally low risk of short-term MACE, with 30-day event rates of less than 1% reported in most studies.^{7,23,24} This means that quantitative risk scores may have limited additive value in risk stratification of patients who have MI ruled out by means of hs-cTn assays. Given that early outpatient stress testing has not been shown to reduce 30-day MACE,²⁵ and positive stress ECG results in low-risk patients are more likely to be false positives than true positives,²⁶ it could be argued that patients deemed to be at low risk by means of a validated hs-cTn algorithm can be safely discharged from the ED without

the need for any outpatient noninvasive testing, independently from their individual clinical characteristics. Instead, good discharge instructions and observation for symptom progression may represent a better balance of risk and benefit for this objectively low-risk population.

Limitations

We restricted our inclusion criteria to full-text published manuscripts, meaning that relevant conference abstracts and other scientific reports may have been excluded. The evidence synthesis is limited by the data reported in the included studies. Included studies did not generally report sufficiently granular data to enable meta-analysis. Several of the included studies had moderate to high risk of bias, limiting confidence in estimates of the prognostic accuracy for several of these risk scores. The studies with the lowest risk of bias support the use of the HEART score as the preferred risk prediction tool owing to its superior classification performance.

Conclusion

There is a paucity of robust evidence demonstrating additional prognostic utility of existing risk scores in predicting adverse cardiac events among ED patients who have MI ruled out by means of hs-cTn assays. A HEART score ≤ 3 or a TIMI score ≤ 1 carry a very low risk of 30-day MACE, but the HEART score classifies more patients as low risk. However, adverse cardiac events among patients who have had MI ruled out by means of a validated hs-cTn algorithm are rare, and existing risk prediction tools may have limited incremental value in identifying patients likely to benefit from noninvasive testing after a thorough ED evaluation.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <https://doi.org/10.1016/j.cjca.2022.12.028>.