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Validation of the HEART Score in Patients with Undifferentiated Chest Pain: A Prospective Cohort Study

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ABSTRACT

Background: Chest pain represents one of the most common and challenging presentations in emergency medicine, requiring rapid differentiation between life-threatening cardiac conditions and benign etiologies. The HEART score was developed to risk stratify patients with chest pain for major adverse cardiac events (MACE), yet validation across diverse populations and healthcare settings remains essential for confident clinical implementation.
Methods: A prospective observational cohort study was conducted at our tertiary care hospital over 20 months, enrolling 892 adult patients presenting with chest pain suggestive of possible acute coronary syndrome. HEART scores were calculated at presentation, and patients were followed for 6 weeks. The primary outcome was occurrence of MACE, defined as acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, or all-cause mortality.
Results: The mean age was 54.8 ± 14.2 years, with 58.4% male patients. The mean HEART score was 4.2 ± 1.8. MACE occurred in 142 patients (15.9%). The area under the ROC curve for MACE prediction was 0.867 (95% CI: 0.838–0.896). Low-risk patients (HEART score 0-3) experienced MACE in 2.1% of cases (8/386), intermediate-risk (score 4-6) in 18.4% (68/370), and high-risk (score 7-10) in 48.5% (66/136). A HEART score ≤3 demonstrated 94.4% sensitivity and 65.7% specificity with negative predictive value of 97.9%.
Conclusion: The HEART score demonstrates excellent discriminatory ability for predicting MACE in patients with undifferentiated chest pain, effectively identifying low-risk patients suitable for early discharge and outpatient management.

Introduction

Chest pain constitutes one of the most frequent chief complaints in emergency departments worldwide, accounting for approximately 5-8% of all ED visits and representing a significant diagnostic challenge [1]. The spectrum of underlying etiologies ranges from immediately life-threatening conditions such as acute coronary syndrome, pulmonary embolism, and aortic dissection to benign causes including musculoskeletal pain and gastroesophageal reflux [2]. This heterogeneity necessitates systematic approaches to identify patients requiring urgent

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intervention while avoiding unnecessary hospitalization and invasive testing in low-risk individuals [3].

Acute coronary syndrome (ACS) remains the primary concern in chest pain evaluation due to its potential for significant morbidity and mortality if unrecognized [4]. However, only 15-25% of patients presenting with chest pain are ultimately diagnosed with ACS, meaning the majority undergo extensive evaluation for conditions that prove to be non-cardiac [5]. This diagnostic uncertainty drives resource utilization, with estimated annual costs exceeding $10 billion in the United States alone for chest pain evaluation [6].

Traditional risk stratification tools such as the Thrombolysis in Myocardial Infarction (TIMI) score and Global Registry of Acute Coronary Events (GRACE) score were developed primarily for patients with confirmed ACS to guide treatment intensity and predict prognosis [7]. Their application to undifferentiated chest pain populations has shown suboptimal performance, particularly in identifying low-risk patients suitable for early discharge [8].

The HEART score was developed by Six and colleagues in 2008 specifically for risk stratification in ED chest pain patients [9]. This clinical decision tool (HEART SCORE) incorporates five elements: History, ECG findings, Age, Risk factors, and Troponin levels, generating a score from 0 to 10 that correlates with short-term MACE risk [10]. The mnemonic structure and reliance on readily available clinical information facilitate bedside application and have contributed to widespread adoption [11].

Subsequent validation studies have demonstrated promising performance characteristics, with the HEART score consistently showing superior discrimination compared to TIMI and GRACE scores in ED chest pain populations [12]. The HEART Pathway, incorporating serial troponin testing with the HEART score, has been shown to safely reduce admissions and cardiac testing in randomized controlled trials [13]. Recent meta-analyses confirm low MACE rates in HEART score 0-3 patients, supporting early discharge protocols [14].

Despite accumulating evidence, several knowledge gaps persist. Geographic and demographic variation in patient populations, prevalence of coronary disease, and healthcare system characteristics may influence score performance [15]. Additionally, the transition to high-sensitivity troponin assays has raised questions regarding optimal integration with the HEART score framework [16]. External validation in diverse settings remains essential for confident implementation and guideline development.

The aim of this study was to prospectively validate the HEART score for predicting major adverse cardiac events within 6 weeks in patients presenting with undifferentiated chest pain to a tertiary care emergency department.

Materials and Methods

Study Design and Setting

This prospective observational cohort study was conducted at the Emergency Department of a 1000-bed tertiary care teaching hospital between NOVEMBER 2023 and October 2025. The ED serves approximately 7200 patients annually, with dedicated chest pain evaluation pathways and 24-hour access to cardiac catheterization facilities.

Study Population

Consecutive adult patients aged 18 years and older presenting to the ED with a chief complaint of chest pain or chest discomfort suggestive of possible acute coronary syndrome were screened for eligibility. Inclusion criteria comprised: (1) chest pain or equivalent symptoms (jaw pain, arm pain, dyspnea, or epigastric discomfort) as the primary presenting complaint; (2) symptom onset within 24 hours of presentation; and (3) clinical suspicion for possible ACS warranting ECG and troponin evaluation as determined by the treating physician.

Exclusion criteria included: ST-elevation myocardial infarction (STEMI) identified on initial ECG; clear non-cardiac etiology established at presentation (e.g., chest wall tenderness with trauma history, herpes zoster); hemodynamic instability requiring immediate intervention; pregnancy; patients with terminal illness and life expectancy less than 6 weeks; prisoners or individuals unable to provide informed consent; patients who left against medical advice before evaluation completion; and those with prior enrollment in the study.

Sample Size Calculation

Based on published literature suggesting MACE rates of approximately 15-20% in ED chest pain populations and anticipated AUC of 0.85 for the HEART score, a minimum sample size of 820 patients was calculated to achieve 80% power with α=0.05, precision of ±0.03 for AUC estimation, and adequate events in each risk category. Accounting for potential 8% loss to follow-up, we targeted enrollment of 900 patients.

HEART Score Calculation

HEART scores were calculated by trained research coordinators using information available at initial presentation, with components assessed as follows:

History (0-2 points): Assessed based on characteristics of chest pain. Highly suspicious history (typical angina with exertional component, radiation, diaphoresis, and response to nitrates) received 2 points; moderately suspicious (mixed features) received 1 point; slightly suspicious (atypical

features predominating) received 0 points.

ECG (0-2 points): Normal ECG received 0 points; non-specific repolarization abnormalities without significant ST deviation received 1 point; significant ST depression, T-wave inversions in anatomically contiguous leads, or bundle branch block with ischemic features received 2 points.

Age (0-2 points): Age <45 years received 0 points; 45-64 years received 1 point; ≥65 years received 2 points.

Risk Factors (0-2 points): Cardiovascular risk factors included hypertension, hypercholesterolemia, diabetes mellitus, current smoking, obesity (BMI ≥30), and family history of premature coronary artery disease. No risk factors received 0 points; 1-2 risk factors received 1 point; ≥3 risk factors or history of atherosclerotic disease received 2 points.

Troponin (0-2 points): Initial high-sensitivity troponin I levels were interpreted using the local 99th percentile upper reference limit (URL). Values ≤URL received 0 points; 1-3 times URL received 1 point; >3 times URL received 2 points.

Risk categories were defined as: low risk (0-3 points), intermediate risk (4-6 points), and high risk (7-10 points).

Clinical Care

Patient management was conducted according to institutional protocols and attending physician discretion, independent of research team calculations. Treating physicians had access to individual HEART score components but were not provided calculated scores to avoid incorporation bias. Decisions regarding admission, observation unit placement, stress testing, and coronary angiography followed standard clinical pathways.

Outcome Measures

The primary outcome was occurrence of major adverse cardiac events (MACE) within 6 weeks of index presentation. MACE was defined as the composite of: acute myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and all-cause mortality. MI was defined according to the Fourth Universal Definition, requiring troponin elevation with clinical evidence of ischemia.

Secondary outcomes included: individual components of the composite endpoint, ED length of stay, admission rate, stress testing utilization, coronary angiography rate, 30-day ED revisit, and 30-day hospitalization.

Follow-up

All enrolled patients underwent structured follow-up. Index visit outcomes were captured through electronic medical records. Patients discharged from the ED or observation unit were contacted by telephone at 2 weeks and 6 weeks to ascertain interim symptoms, healthcare encounters, and vital status. Medical records from affiliated institutions were reviewed to capture events occurring at other facilities. For patients unreachable by telephone, vital status was verified through state death registry databases and primary care provider contact.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median with interquartile range (IQR) as appropriate. Categorical variables were presented as frequencies and percentages. Comparisons between groups (MACE vs. no MACE) utilized Student's t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables.

Receiver operating characteristic (ROC) curve analysis evaluated discriminatory ability of the HEART score for MACE prediction. Area under the curve (AUC) with 95% confidence intervals was calculated. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios were determined for each score threshold and risk category boundary. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test and calibration plots.

Subgroup analyses examined score performance across age groups, sex, diabetes status, and prior coronary artery disease history. Multivariable logistic regression evaluated independent associations between HEART score components and MACE. Statistical significance was defined as $p<0.05$. Analyses were performed using SPSS version 28.0, MedCalc version 20.0, and R version 4.2.

Results

Patient Characteristics

During the study period, 1,048 patients were screened for eligibility. After excluding 156 patients (68 with STEMI, 42 with clear non-cardiac etiology, 28 who left before evaluation, 18 others), 892 patients were enrolled and completed 6-week follow-up. The mean age was 54.8 ± 14.2 years (range 19-94), and 521 patients (58.4%) were male. Common cardiovascular risk factors included hypertension (52.6%), diabetes mellitus (28.4%), hypercholesterolemia (44.8%), and current smoking (26.2%). Prior coronary artery disease was documented in 18.6% of patients.

HEART Score Distribution and Outcomes

The mean HEART score was 4.2 ± 1.8 (range 0-10). Distribution across risk categories: 386 patients (43.3%) were classified as low risk (score 0-3), 370 (41.5%) as intermediate risk (score 4-6), and 136 (15.2%) as high risk (score 7-10).

MACE within 6 weeks occurred in 142 patients (15.9%),

comprising: acute myocardial infarction in 118 (13.2%), PCI in 94 (10.5%), CABG in 26 (2.9%), and all-cause mortality in 12 (1.3%). Multiple MACE components occurred in 78 patients.

Table 1: Baseline Characteristics Stratified by MACE Occurrence

Variable	Total (n=892)	No MACE (n=750)	MACE (n=142)	p-value
Age (years), mean ± SD	54.8 ± 14.2	53.2 ± 14.0	63.4 ± 12.4	<0.001
Male sex, n (%)	521 (58.4)	424 (56.5)	97 (68.3)	0.008
Risk Factors, n (%)				
Hypertension	469 (52.6)	372 (49.6)	97 (68.3)	<0.001
Diabetes mellitus	253 (28.4)	192 (25.6)	61 (43.0)	<0.001
Hypercholesterolemia	400 (44.8)	318 (42.4)	82 (57.7)	0.001
Current smoking	234 (26.2)	188 (25.1)	46 (32.4)	0.067
Obesity (BMI ≥30)	312 (35.0)	264 (35.2)	48 (33.8)	0.746
Family history CAD	198 (22.2)	158 (21.1)	40 (28.2)	0.060
Prior CAD	166 (18.6)	118 (15.7)	48 (33.8)	<0.001
Prior MI	124 (13.9)	86 (11.5)	38 (26.8)	<0.001
Prior PCI/CABG	142 (15.9)	98 (13.1)	44 (31.0)	<0.001
Presenting Characteristics				
Symptom duration (hours), median (IQR)	4.2 (1.8-10.4)	4.0 (1.6-9.8)	5.6 (2.4-12.2)	0.024
Typical angina features, n (%)	342 (38.3)	248 (33.1)	94 (66.2)	<0.001
Dyspnea, n (%)	286 (32.1)	224 (29.9)	62 (43.7)	0.001
Diaphoresis, n (%)	198 (22.2)	142 (18.9)	56 (39.4)	<0.001
HEART Score, mean ± SD	4.2 ± 1.8	3.8 ± 1.6	6.2 ± 1.4	<0.001

Discriminatory Performance

The HEART score demonstrated excellent discrimination for MACE prediction, with an AUC of 0.867 (95% CI: 0.838–0.896). The Hosmer-Lemeshow test indicated adequate calibration (χ^2=8.42, p=0.394).

Table 2: MACE Rates and Diagnostic Performance Across HEART Score Categories

HEART Score	n (%)	MACE n (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	-LR
Individual Scores								
0	42 (4.7)	0 (0)	100	5.6	16.7	100	1.06	0
1	78 (8.7)	1 (1.3)	99.3	15.9	18.3	98.7	1.18	0.04
2	124 (13.9)	3 (2.4)	97.2	31.6	21.2	98.3	1.42	0.09
3	142 (15.9)	4 (2.8)	94.4	48.0	25.6	97.8	1.82	0.12
4	156 (17.5)	18 (11.5)	81.7	65.7	31.1	95.0	2.38	0.28
5	128 (14.3)	26 (20.3)	64.1	79.9	37.6	92.2	3.19	0.45
6	86 (9.6)	24 (27.9)	45.8	91.6	50.8	89.9	5.45	0.59

7	68 (7.6)	28 (41.2)	29.6conver-gence	96.7	62.7	87.9	8.97	0.73
8	42 (4.7)	22 (52.4)	14.8	98.9	72.4	86.0	13.45	0.86
9	18 (2.0)	10 (55.6)	7.0	99.5	71.4	85.2	14.00	0.93
10	8 (0.9)	6 (75.0)	4.2	99.7	75.0	84.9	14.00	0.96
Risk Categories								
Low (0-3)	386 (43.3)	8 (2.1)	-	-	-	-	-	-
Intermediate (4-6)	370 (41.5)	68 (18.4)	-	-	-	-	-	-
High (7-10)	136 (15.2)	66 (48.5)	-	-	-	-	-	-
Cutoff Thresholds								
Score ≤3 vs >3	-	-	94.4	65.7	34.2	97.9	2.75	0.09
Score ≤4 vs >4	-	-	81.7	79.9	43.5	95.8	4.06	0.23

HEART Score Component Analysis

Multivariable logistic regression demonstrated that all five HEART score components independently predicted MACE. Troponin elevation showed the strongest association (OR 4.82, 95% CI: 3.24–7.16, p<0.001), followed by ECG abnormalities (OR 3.14, 95% CI: 2.18–4.52, p<0.001).

Table 3: Multivariable Analysis of HEART Score Components

Component	Points	MACE Rate (%)	Adjusted OR (95% CI)	p-value
History				
Slightly suspicious	0	6.2	Reference	-
Moderately suspicious	1	14.8	1.86 (1.12-3.08)	0.016
Highly suspicious	2	28.4	2.94 (1.82-4.75)	<0.001
ECG				
Normal	0	7.4	Reference	-
Non-specific changes	1	16.2	1.92 (1.24-2.98)	0.003
Significant ST-T changes	2	34.6	3.14 (2.18-4.52)	<0.001
Age				
<45 years	0	5.8	Reference	-
45-64 years	1	14.2	1.68 (0.98-2.88)	0.059
≥65 years	2	24.8	2.24 (1.28-3.92)	0.005
Risk Factors				
None	0	4.2	Reference	-
1-2 factors	1	12.6	2.12 (0.94-4.78)	0.071
≥3 or known CAD	2	22.4	2.86 (1.32-6.19)	0.008
Troponin				
≤URL	0	5.4	Reference	-
1-3× URL	1	28.6	3.42 (2.18-5.36)	<0.001
>3× URL	2	52.8	4.82 (3.24-7.16)	<0.001

Secondary Outcomes and Resource Utilization

Among 386 low-risk patients, 148 (38.3%) were admitted or placed in observation; 8 experienced MACE (2.1%). Of 238 low-risk patients discharged from ED, 0 experienced MACE. The 30-day ED revisit rate was 12.4% overall, with no significant difference across risk categories (p=0.342). Stress testing was performed in 284 patients (31.8%), and coronary angiography in 198 patients (22.2%). Median ED length of stay was 6.4 hours (IQR: 4.2–9.8).

Subgroup Analyses

Score performance remained robust across subgroups. AUC values: males 0.854 (0.814–0.894), females 0.886 (0.842–0.930); age <65 years 0.872 (0.832–0.912), age ≥65 years 0.848 (0.798–0.898); diabetics 0.856 (0.802–0.910), non-diabetics 0.874 (0.838–0.910); prior CAD 0.824 (0.756–0.892), no prior CAD 0.878 (0.844–0.912). All subgroup AUCs exceeded 0.82.

Discussion

This prospective validation study demonstrates excellent discriminatory ability of the HEART score for predicting major adverse cardiac events in patients presenting with undifferentiated chest pain. Our findings, with an AUC of 0.867 and MACE rate of only 2.1% in low-risk patients, support the utility of this clinical decision tool for risk stratification and disposition decision-making in the emergency department setting [17].

The observed performance characteristics align closely with the original derivation cohort reported by Six and colleagues and subsequent validation studies [18]. The low MACE rate of 2.1% in patients with HEART scores 0-3 falls within the range of 0.6-2.5% reported in meta-analyses, supporting the identification of a truly low-risk population suitable for early discharge consideration [19]. Importantly, among the 238 low-risk patients discharged directly from the ED, no MACE events occurred during follow-up, providing reassurance regarding the safety of HEART-guided early discharge protocols.

The negative predictive value of 97.9% at the low-risk threshold demonstrates the score's primary clinical utility—its ability to reliably exclude significant short-term cardiac risk [20]. This characteristic addresses a fundamental challenge in chest pain evaluation, where the goal is not only identifying patients requiring intervention but also confidently reassuring and discharging those at minimal risk [21]. The corresponding positive likelihood ratio of 2.75 and negative likelihood ratio of 0.09 indicate meaningful post-test probability shifts with score application.

Our component analysis confirms the independent predictive value of all five HEART score elements, with troponin elevation demonstrating the strongest association with MACE. This finding supports the integration of high-sensitivity troponin assays within the HEART framework while maintaining the clinically derived elements of history, ECG interpretation, and risk factor assessment [22]. The synergistic combination of objective biomarker data with clinical judgment distinguishes the HEART score from purely biomarker-based approaches [23].

Comparison with other risk stratification tools provides important context. The HEART score has consistently demonstrated superior performance to TIMI and GRACE scores in ED chest pain populations, with our AUC of 0.867 exceeding published values for these alternative instruments [24]. This superiority likely reflects the HEART score's specific development for the undifferentiated chest pain population rather than adaptation from confirmed ACS cohorts [25].

The relatively high intermediate-risk category proportion (41.5%) highlights an ongoing challenge in chest pain risk stratification. While the HEART score effectively identifies low and high-risk extremes, the intermediate group requires additional evaluation strategies [26]. The HEART Pathway, incorporating serial troponin testing, addresses this gap by enabling further risk refinement within the intermediate category [27]. Our observed MACE rate of 18.4% in intermediate-risk patients underscores the need for individualized assessment approaches in this substantial patient subset.

Implementation considerations merit discussion. The HEART score requires only information routinely obtained in chest pain evaluation, facilitating seamless integration into clinical workflows [28]. The subjective nature of the history component has raised concerns regarding inter-rater reliability, though studies have demonstrated acceptable agreement when standardized criteria are applied [29]. Educational efforts emphasizing consistent history characterization may optimize score reproducibility.

Several limitations warrant acknowledgment. Single-center design may limit generalizability, although our patient demographics reflect typical ED chest pain populations. The 6-week follow-up period, while standard for HEART validation studies, may not capture later cardiac events. Additionally, clinical decisions were made independently of calculated scores, and implementation studies may demonstrate different real-world performance.

Future directions include integration with emerging biomarkers, machine learning optimization of component weighting, and development of electronic clinical decision support tools to facilitate consistent score application [30]. Investigation of score performance in special populations, including elderly patients and those with atypical

presentations, remains an important research priority.

Conclusion

This prospective validation study confirms the excellent discriminatory ability of the HEART score for predicting major adverse cardiac events in patients presenting with undifferentiated chest pain. With an AUC of 0.867 and MACE rate of only 2.1% in low-risk patients (score 0-3), the HEART score effectively identifies a substantial proportion of chest pain patients who can be safely considered for early discharge and outpatient management. The negative predictive value of 97.9% at the low-risk threshold provides clinicians with confidence in excluding significant short-term cardiac risk. All five score components independently contribute to risk prediction, with troponin elevation demonstrating the strongest association with adverse outcomes. These findings support widespread implementation of the HEART score as a standardized approach to chest pain risk stratification, with potential to improve patient outcomes through appropriate triage while reducing unnecessary resource utilization. Clinical integration should be accompanied by education regarding consistent score application and appropriate management pathways for each risk category.

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