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Case Report

60-day major adverse cardiac events in emergency department patients with non-low modified HEART scores

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ABSTRACT

Background: A low (0–3) History, Electrocardiogram, Age, Risk factors and Troponin (HEART) score reliably identifies ED chest pain patients who are low risk for near-term major adverse cardiac events (MACE). To optimize sensitivity, many clinicians employ a modified HEART score by repeating troponin measurements and excluding patients with abnormal troponin values or ischemic electrocardiograms (ECGs). The residual MACE risk among patients with otherwise non-low (≥4) modified HEART scores is thus likely much lower than with non-low original HEART scores.
Objective: To explore residual 60-day MACE risks among patients with non-low modified HEART scores.
Methods: Secondary analysis of a retrospective cohort of ED patients presenting with chest pain to an integrated healthcare system between 2013 and 2015. Patients with serial troponin measurements within 6 h of ED arrival were considered for inclusion. Exclusions included an ischemic ECG, troponin values above the 99th percentile or a lack of continuous health plan coverage through the 60-day follow-up period. MACE was defined as a composite of myocardial infarction, cardiac arrest, cardiogenic shock or death.
Results: There were 22,976 study eligible patients encounters, 13,521 (59%) of which had non-low (≥4) modified HEART scores. The observed 60-day MACE risk among non-low HEART score patients was 2.0% (95% CI 1.8–2.3). When including all coronary revascularizations (MACE-R), the risk was 4.4% (95% CI 4.1–4.4).
Conclusion: Risk of near-term MACE among patients with non-low modified HEART scores (excluding those with abnormal troponin or ischemic ECGs) appears to be much lower than in the original HEART score validation studies.

1. Introduction

The History, Electrocardiogram, Age, Risk factors and Troponin (HEART) score reliably identifies emergency department (ED) patients with possible acute coronary syndromes (ACS) who are low-risk for near-term major adverse cardiac events (MACE). However, when applied in its original form, patients with objective signs of myocardial ischemia and/or injury, specifically abnormal serum troponin levels or ischemic electrocardiograms (ECGs), can still register low-risk HEART scores (e.g. 3 or less) despite the strongly positive likelihood ratios for ACS of these individual findings [1,2]. Accordingly, many centers currently employ modified criteria (modified HEART scores or the HEART pathway) by classifying patients with ischemic-appearing ECGs (e.g. new T-wave inversions or ST-depressions in contiguous leads) and/or abnormal troponin values as high-risk [3,4]. Absent this high-risk subset of differentiated patients, the residual near-term MACE risk using modified HEART score criteria may be considerably lower than the six-week MACE risks of up to 16.6% and 65% for moderate (i.e. 4 to 6 points) and high (i.e. 7 or more points) scores in the original HEART validation studies [5]. However, MACE risk estimates for this remainder of non-low risk patients within modified HEART score classification schemes has not been well documented since these patients are typically aggregated alongside those with abnormal troponin results and ischemic ECGs in

Abbreviations: ACS, Acute coronary syndrome; ECG, electrocardiogram; EHR, electronic health record; HEART, History, Electrocardiogram, Age, Risk factors and Troponin; KPNC, Kaiser Permanente Northern California; MACE, major adverse cardiac event.

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outcome reports. This report thus aims to provide 60-day MACE risk estimates for this remainder of patients with non-low modified HEART risk scores.

2. Methods

2.1. Study setting and population

We performed a secondary analysis of a retrospective cohort of ED patients presenting with chest pain [6]. This study was approved by the Kaiser Permanente Northern California (KPNC) Institutional Review Board. The cohort was drawn from the electronic health record (EHR) of KPNC, an integrated healthcare system inclusive of 21 medical centers. Cohort patients were health plan members evaluated for chest pain between 2013 and 2015 at a KPNC ED with a serum troponin I measurement. For the purpose of this report, only patients with serial serum troponin I measurements obtained within 6 h of ED arrival were included to improve the likelihood of clinical concern for ACS.

2.2. Measurements and exclusions

HEART scores were calculated using a combination of demographics, problem list diagnoses and text string searches of clinical notes and ECG interpretations [6]. Details regarding electronic calculation of the modified HEART score are provided in the supplemental data (Appendix A). Patients were excluded from this secondary analysis if they had evidence of ischemia by ECG (as per the finalized interpretation by a cardiologist in the EHR) or a serum troponin I value above the reference 99th percentile upper limit of normal (0.04 ng/ml, Access AccuTnI+3, Beckman-Coulter, Brea, CA). We restricted these exclusion criteria to the first 6 h following ED arrival so that patients with delayed objective evidence of ACS during the initial evaluation would be counted in the outcomes.

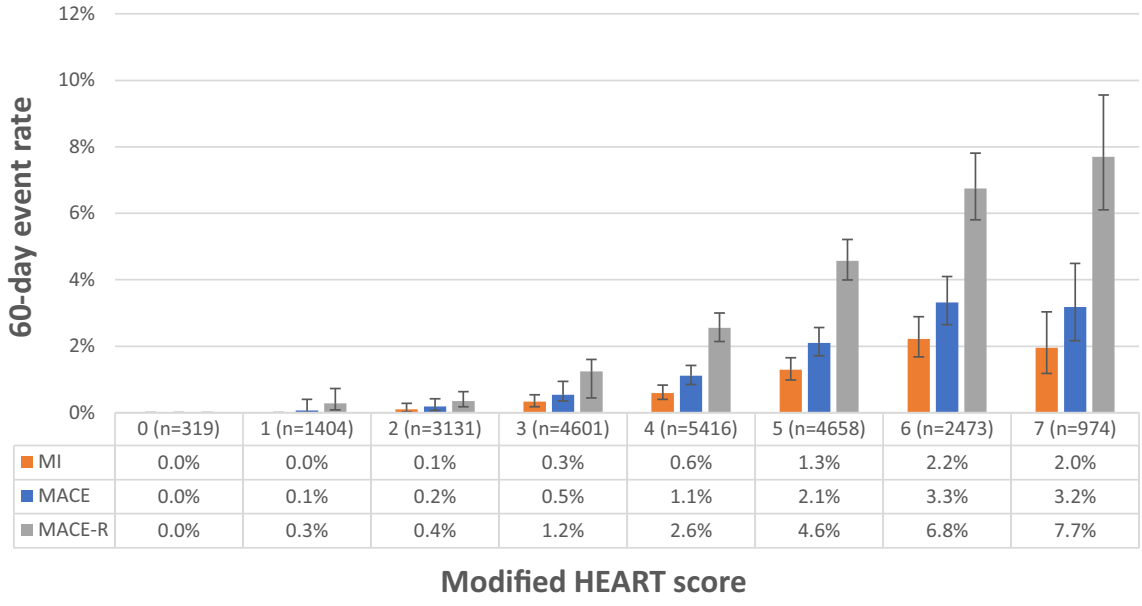
2.3. Outcomes

Clinical outcomes were determined from International Statistical Classification of Diseases (ICD) codes in the first or second position, and mortality from a composite death database of internal health system mortality statistics cross-referenced with state (California death index) and federal (social security death index) data as previously reported [6]. MACE was defined as a composite of myocardial infarction, cardiac arrest, cardiogenic shock or all-cause mortality. Coronary revascularizations (percutaneous or surgical) are reported as a composite measure of MACE or revascularization (MACE-R). This distinction was made due to a lack of differentiation between urgent and elective (or non-target) coronary revascularizations in our dataset, with only the former being typically considered a MACE. We also used a 60-day outcome period as opposed to conventional 30-day or 6-week windows in order to generate more conservative risk estimates. All study patients had continuous health plan membership during the 60-day follow-up period allowing capture of diagnoses made both within and outside (via reimbursement claims) the integrated healthcare system.

3. Results

149,441 patients with continuous health plan membership presented with chest pain and had a serum troponin measurement in a KPNC ED during the study period, of which 8.0% had a 60-day MACE. 35,664 were excluded for having no troponin measured within 6 h of ED arrival. Of the remaining 113,777 patients, 26,648 (23%) had serial troponin I measurements within 6 h of ED arrival, of which 3672 (13.8%) had an abnormal serum troponin I level (>0.04 ng/ml) and 1617 (5.7%) had ischemic ECGs (not mutually exclusive), leaving 22,976 eligible study patients. The median age was 60.8 years, 55% were female and 9455 (41%) had low (3 or less) modified HEART scores. The median time between the first and last troponin I measurements was 3.1 h (interquartile range 2.3 to 3.9 h).

Overall 60-day MACE and MACE-R rates among eligible study patients were 1.3% and 2.9%, respectively. Risks of myocardial infarction, MACE and MACE-R by absolute modified HEART score are shown in Fig. 1. When stratified into low, moderate and high risk scores, 60-day risks of MACE and MACE-R were 0.3% (95% CI 0.2–0.5%) and 0.8% (95% CI 0.6–1.0%) for low risk patients (score of 3 or less), 1.9% (95% CI 1.7–2.2%) and 4.1% (95% CI 3.8–4.5%) for moderate risk patents (score of 4 to 6) and 3.2% (95% CI 2.2–4.5%) and 7.7% (95% CI 6.1–9.6%) for



	0 (n=319)	1 (n=1404)	2 (n=3131)	3 (n=4601)	4 (n=5416)	5 (n=4658)	6 (n=2473)	7 (n=974)
MI	0.0%	0.0%	0.1%	0.3%	0.6%	1.3%	2.2%	2.0%
MACE	0.0%	0.1%	0.2%	0.5%	1.1%	2.1%	3.3%	3.2%
MACE-R	0.0%	0.3%	0.4%	1.2%	2.6%	4.6%	6.8%	7.7%

Fig. 1. Observed risks of 60-day outcomes among emergency department patients with possible acute coronary syndromes by modified HEART scores. Error bars depict 95% confidence intervals for the point estimates listed in the table. Abbreviations: HEART = History, Electrocardiogram, Age, Risk factors and Troponin; MACE = Major Adverse Cardiac Event (defined as myocardial infarction, cardiac arrest, cardiogenic shock or death); MACE-R = MACE including percutaneous or surgical coronary revascularization; MI = myocardial infarction.

high risk patients (score of 7). Grouping of outcomes by low (0–3) versus non-low (≥ 4) modified HEART score is shown in Table 1. Of note, the median time to coronary revascularization absent MACE was 2 days (interquartile range 1 to 13 days), with 59% of these events occurring within 3 days.

When comparing electronically calculated modified HEART scores to manual chart abstraction of 450 charts performed by six clinicians, percent agreement and unweighted kappa values were 93.1% and 0.92 for the total modified HEART score and ranged between 94.4% and 99.1%, and 0.77 to 0.96 for individual variables, respectively (Appendix A).

4. Discussion

We conclude that when applying a modified HEART score, the observed risks of MACE among patients with moderate to high scores are much lower than in the original HEART validation studies. This observation remained true when including patients who underwent coronary revascularization for any reason, yielding a MACE-R risk of 4.4% among patients with non-low risk scores. Our findings are consistent with a contemporaneous U.S. cohort study from an associated but separate integrated health care system [7]. After excluding patients with an ED diagnosis of acute myocardial infarction, Sharp et al. found a similar range of 6-week MACE-R risks (2.4% for moderate and 8.7% for high HEART scores). Likewise in the prospective multicenter implementation study of the HEART pathway by Mahler et al., after excluding events occurring during the index hospitalization, the post-implementation 30-day MACE-R risk was 2.6% among patients with non-low risk scores [3]. Our findings are novel in that we placed a finite time for risk adjudication at 6 h from ED arrival and excluded patients with abnormal serum troponins or ischemic ECGs from the non-low risk subgroup, thus arguably better representing the common clinical conundrum: ED chest pain patients without objective evidence of ACS but in need of a disposition decision.

It is furthermore arguable that we are overestimating the risk of emergent and/or related adverse outcomes, particularly among non-low risk patients, for two reasons. First, a considerable proportion (roughly 40%) of observed MACE in both this and the study by Mahler et al. were due to all-cause mortality absent myocardial infarction, which lessens the likelihood that ACS was causal. Second, while coronary revascularizations occurred in over twice as many patients absent MACE as compared to patients with MACE, over 40% of these occurred beyond 3 days from the index visit, raising the possibility that these revascularizations were performed electively for stable angina as opposed to unstable angina/ACS. If we theoretically assume that half of these event subsets (i.e. 20% of MACE and 20% additional revascularizations) were not associated with ACS, then considering a patient with a modified HEART score of 4, in whom the estimated MACE and MACE-R risks are 1.1% and 2.6% in this study, a better approximation of the traditional MACE risk definition (which only includes cardiovascular deaths and urgent coronary revascularizations) may be 2%. Thus, if applying a 1 to 2% acceptable "miss" rate following chest pain evaluations, as recently proposed by the American College of Emergency Physicians, only patients with modified HEART scores of 5 or greater might routinely warrant further diagnostic investigation [8].

Limitations of this report include the study setting of an integrated health care system, which attenuates generalizability. The retrospective derivation of HEART scores is also a potential limitation, though the observed trend and relative change in risks between absolute scores are consistent with prospective data. It is also worth noting that the largest prospective interrater reliability study of the history and ECG interpretation portions of HEART score components found only moderate agreement (weighted kappas of 0.52 and 0.46, respectively) [9]. This is particularly relevant to ECG interpretations in this study, which were derived from finalized overreads by cardiologists and may not represent real-time ED physician interpretations. However, prior studies have found negligible rates of missed ECG evidence of ischemia by ED physicians which were subsequently identified through this quality assurance process [10]. Finally, this study was limited to patients presenting with chest pain, preventing extrapolation to patients with atypical anginal equivalents such as isolated dyspnea. Accordingly, further study concerning observed MACE rates for patients with non-low modified HEART scores is warranted in a variety of settings and populations with possible ACS, including in the context of newer generation troponin assays. Such data will provide more accurate risk estimates to both clinicians and patients in the course of medical decision making, potentially raising the modified HEART risk score limit for which expedited discharge is a mutually acceptable disposition.

Table 1
Utilization and outcomes among emergency department patients with possible acute coronary syndromes using a modified HEART score criteria (e.g. normal range troponin levels within six hours of presentation and no evidence of ischemia on electrocardiography), stratified by low (0–3) and non-low (4–7) risk scores. Objective cardiac testing includes electrocardiographic stress testing, myocardial perfusion imaging, computed tomographic coronary angiography and coronary catheterization. 95% confidence intervals are reported in parenthesis

Modified HEART score	Low (0–3)	Non-low (4–7)
Number of patients	9455	13,521
Index visit hospital admission (%)	2.0	9.4
Objective cardiac testing within 30 days (%)	40.6	44.6
60-day outcomes (%)		
Myocardial infarction	0.2 (0.1–0.3)	1.2 (1.1–1.4)
Cardiac arrest	0.01 (0–0.06)	0.1 (0.1–0.2)
Cardiogenic shock	0.01 (0–0.06)	0.1 (0–0.1)
Death	0.2 (0.1–0.3)	0.8 (0.7–1.0)
Percutaneous coronary revascularization	0.4 (0.3–0.6)	2.7 (2.4–3.0)
Coronary artery bypass graft surgery	0.1 (0.1–0.2)	0.5 (0.4–0.6)
MACE	0.3 (0.2–0.5)	2.0 (1.8–2.3)
MACE-R	0.8 (0.6–1.0)	4.4 (4.1–4.4)

Abbreviations: HEART = History, Electrocardiogram, Age, Risk factors and Troponin; MACE = Major Adverse Cardiac Event (defined as myocardial infarction, cardiac arrest, cardiogenic shock or death); MACE-R = MACE including percutaneous coronary revascularization or coronary artery bypass graft surgery.

Presentations

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CRediT authorship contribution statement

Dustin G. Mark: Conceptualization, Methodology, Validation, Formal analysis, Writing - original draft, Writing - review & editing, Visualization, Supervision, Funding acquisition. **Jie Huang:** Methodology, Software, Formal analysis, Data curation, Writing - review & editing. **Chris J. Kennedy:** Software, Formal analysis, Data curation, Writing - review & editing. **David R. Vinson:** Conceptualization, Methodology, Validation, Writing - review & editing, Funding acquisition. **Dustin W. Ballard:** Conceptualization, Methodology, Validation, Writing - review & editing, Funding acquisition. **Mary E. Reed:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Funding acquisition.

Declaration of competing interest

DGM, JH, CJK, DRV, DWB and MER report no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2020.05.081.

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