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Predictive risk stratification using HEART (history, electrocardiogram, age, risk factors, and initial troponin) and TIMI (thrombolysis in myocardial infarction) scores in non-high risk chest pain patients

An African American urban community based hospital study

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Abstract

Validated risk scoring systems in African American (AA) population are under studied. We utilized history, electrocardiogram, age, risk factors, and initial troponin (HEART) and thrombolysis in myocardial infarction (TIMI) scores to predict major adverse cardiovascular events (MACE) in non-high cardiovascular (CV) risk predominantly AA patient population.

A retrospective emergency department (ED) charts review of 1266 chest pain patients where HEART and TIMI scores were calculated for each patient. Logistic regression model was computed to predict 6-week and 1-year MACE and 90-day cardiac readmission. Decision curve analysis (DCA) was constructed to differentiate between clinical strategies in non-high CV risk patients.

Of the 817 patients included, 500 patients had low HEART score vs. 317 patients who had moderate HEART score. Six hundred sixty-three patients had low TIMI score vs. 154 patients had high TIMI score. The univariate logistic regression model shows odds ratio of predicting 6-week MACE using HEART score was 3.11 (95% confidence interval [CI] 1.43–6.76, $P = .004$) with increase in risk category from low to moderate vs. 2.07 (95% CI 1.18–3.63, $P = .011$) using TIMI score with increase in risk category from low to high and c-statistic of 0.86 vs. 0.79, respectively. DCA showed net benefit of using HEART score is equally predictive of 6-week MACE when compared to TIMI.

In non-high CV risk AA patients, HEART score is better predictive tool for 6-week MACE when compared to TIMI score. Furthermore, patients presenting to ED with chest pain, the optimal strategy for a 2% to 4% miss rate threshold probability should be to discharge these patients from the ED.

Abbreviations: AA = African American, ACS = acute coronary syndrome, AMI = acute myocardial infarction, CAD = coronary artery disease, CV = cardiovascular, DCA = decision curve analysis, ED = emergency department, HEART = history, electrocardiogram, age, risk factors, and initial troponin, MACE = major adverse cardiovascular events, NPV = negative predictive value, PPV = positive predictive value, Sn = sensitivity, Sp = specificity, SD = standard deviation, TIMI = thrombolysis in myocardial infarction.

Keywords: cardiac risk, chest pain, decision analysis, history, electrocardiogram, age, risk factors, and initial troponin score, thrombolysis in myocardial infarction score

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1. Introduction

Chest pain is the second most common reason for emergency department (ED) visits, accounting for 5% of all annual encounters.[1] Half of these patients are admitted to an observation unit, of which only 10% have an acute coronary syndrome (ACS).[2] Some patients that are considered "low risk" still have major adverse cardiovascular event (MACE) that prompted development of a number of risk scoring systems in this group. Although the presence of a clear-cut noncardiac diagnosis reduces the likelihood of a composite outcome of death and cardiovascular (CV) event rate to 4% at 30 days, it still is not acceptable to allow ED discharge of these patients.[3] There is no single absolute risk scoring system that can be used safely to discharge a patient from the ED with a high degree of certainty in all age groups. Kline et al[4] calculated that a 2% miss rate for 30-days follow-up period after initial ED evaluation should be acceptable based on the testing threshold at which the risk of harm from further testing equals or exceeds the chance of benefit from confirming an acute CV event.

The thrombolysis in myocardial infarction (TIMI) score, developed in 2000, is used to predict outcomes of death and myocardial ischemia within 14 days of unstable angina/non-ST segment elevation myocardial infarction.[5] Alley and Mahler's[6] review article reported MACE among patients with TIMI score 0 to 1 as 4.7%; TIMI score of 6 to 7 as 40.9%. With a 4.7% MACE rate for lower TIMI score, it did not serve as an adequate tool to discharge patients safely from ED.

The history, electrocardiogram, age, risk factors, and initial troponin (HEART) score originally developed in the Netherlands in 2007, is a short-term risk-stratification tool that could be used to safely risk stratify patients who are at low risk for having a MACE over the next 6 weeks.[7] A HEART score of 0 to 3 points holds a risk of 2.5% for a 6-week MACE and supports an immediate discharge. With a risk of 20.3% for a 6-week MACE, a HEART score of 4 to 6 points implies admission for clinical observation.[7]

In low risk chest pain patients, the incidence of MACE was 2.0% with HEART score 0 to 3 as studied by Poldervaart et al.[8] Six et al[9] reported that HEART score provides for an excellent determination of risk for 30-day MACE, and can help identify low-risk patients, in whom early discharge without additional testing goes with a MACE risk of only 1.7%. So in low-risk chest pain patients, the HEART score may be a better predictor than TIMI score in excluding ACS and cardiac related causes of chest pain.[10]

African Americans (AA) are understudied with respect to risk scoring of CV events when compared to whites and differential use of coronary revascularization may contribute to the poorer functional outcomes observed among AA patients with documented coronary disease.[11–14] All-cause 30-day readmission rates from the nationwide Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of American College of Cardiology/American Heart Association Guidelines (CRUSADE) registry data on acute myocardial infarction (AMI) patients were noted to be higher in AA patients as compared to Caucasians (23.6% vs. 20%; $P < .001$) accounting for increased health care costs.[15] Connecticut hospital discharge data for patients admitted for chest pain also showed increased odds ratio (OR) of all cause 30-day readmissions in AA when compared to whites (OR = 1.19, confidence interval [CI] = 1.04, 1.37).[13]

Table 1

Components of history, electrocardiogram, age, risk factors, and initial troponin score.

History	Highly suspicious	2
	Moderately suspicious	1
	Slightly suspicious	0
EKG	Significant ST-depression	2
	Nonspecific repolarization disturbance	1
	Normal	0
Age	≥65 years	2
	45–65 years	1
	≤45 years	0
Risk factors	≥3 risk factors or history of atherosclerotic disease	2
	1 or 2 risk factors	1
	No risk factors known	0
Troponin	≥3× normal limit	2
	1–3× normal limit	1
	≤ normal limit	0

EKG = electrocardiogram.

Therefore, we proposed to study a non-high CV risk predominantly AA patient population to assess their event rates in terms of 6-week and 1-year MACE as a primary end point and compare the HEART and TIMI scores in them. In addition, although conventionally, HEART and TIMI score were used to study MACE, we also wanted to assess their ability to predict cardiac readmissions that contribute to increased cost of care.

2. Methods

2.1. Study design and population

We retrospectively studied consecutive patients who presented with a primary concern of chest pain to the ED of Mercy Philadelphia Hospital, Philadelphia from January 2012 to December 2014. Patients were placed into low, moderate, or high HEART score categories depending on their history of presenting symptom, age, number of cardiac risk factors (hypertension, diabetes, dyslipidemia, obesity, cigarette smoking, and family history of coronary artery disease [CAD]), initial troponin, and electrocardiogram (EKG) changes. The "history" component of the HEART criteria was scored as "moderately suspicious" for all patients that did not have any clear documentation. To compare HEART score in our hospital, with an older established ACS scoring tool, we also categorized patients into low or high TIMI score.

All patients who had an EKG, at least 2 sets of cardiac enzymes, and ER stay or observation unit admission were included. Of the total 1266 medical records, 449 patients with documented ACS

Table 2

Components of thrombolysis in myocardial infarction score.

Age ≥65	+1
≥3 CAD risk factors	+1
Known CAD (stenosis ≥50%)	+1
ASA use in past 7 days	+1
Severe angina (≥2 episodes in 24 h)	+1
EKG ST changes ≥0.5 mm	+1
Positive cardiac marker	+1

ACS = acute coronary syndrome, CAD = coronary artery disease, EKG = electrocardiogram.

Table 3

Risk score categories for history, electrocardiogram, age, risk factors, and initial troponin and thrombolysis in myocardial infarction.

HEART score	
Low HEART score	1–3
Moderate HEART score	4–6
High HEART score	≥7
TIMI score	
Low TIMI score	0–1
High TIMI score	≥2

HEART = history, electrocardiogram, age, risk factors, and initial troponin, TIMI = thrombolysis in myocardial infarction.

or high-risk chest pain (particularly HEART score of more than 7) were excluded (Supplementary Figure 1, http://links.lww.com/MD/D96). The components and categories of HEART and TIMI score are listed in Tables 1–3.[6,7]

2.2. Outcome measures

The primary endpoint was 6-week MACE defined as all-cause mortality, myocardial infarction, or coronary revascularization. Secondary endpoints were 1-year MACE and 90-day cardiac readmission. Cardiac readmissions were defined as patients getting readmitted within 90-days of index admission with complaints of chest pain.

Human subject consideration: the Institutional Review Board deemed the study exempt from review, and informed consent was waived since it was a de-identified dataset. The institutional review board of Mercy Health System, Philadelphia, PA, approved the study.

2.3. Statistical analyses

The cohort was divided into low and moderate HEART score and low and high TIMI score as described above. All variables were analyzed as categorical variables and were reported as percentages, continuous data with a normal distribution with mean and standard deviation. Univariate logistic regression analysis model was constructed. The primary outcome of interest was 6-week MACE. Secondary outcomes of interest were 1-year MACE and 90-day cardiac readmission. A priori cut offs for the HEART and TIMI risk tool comparison based on the validated scoring criterion were used. The HEART and TIMI risk tools were compared with regards to test characteristics of sensitivity (Sn) and specificity (Sp) for primary outcome of 6-week MACE using McNemar chi-squared or McNemar exact test as appropriate. Measures for binary outcomes to indicate overall model performance and discriminative ability were constructed to calculate the concordance (or c) statistic.

Decision curve analysis (DCA)[16,17] was performed to assess the clinical value of using HEART or TIMI risk prediction scores and to distinguish between strategies, namely, admit all vs. use prediction scores vs. discharge all. The decision curves were constructed by plotting net benefit against a range of clinically acceptable threshold probabilities for a particular binary outcome. A net benefit model was plotted against wide range of threshold probabilities to construct a decision curve.[17] The unit of net benefit is true positives.[18] Decision curve helps with distinguishing clinical value between different strategies in the statistical model, namely,

(1) admit all: admit the non-high CV risk patients presenting to the ED with chest pain, or
(2) use TIMI/HEART score: prediction scores to determine eligibility for further evaluation strategies for the patient presenting to the ED with chest pain, or
(3) admit none: discharge the non-high CV risk patients presenting with chest pain.

The basic interpretation of a decision curve is that the strategy with the highest net benefit at a particular threshold probability has the highest clinical value.[18] An acceptable clinical threshold miss rate with an upper limit of 4%, for decision-making for 6-week and 1-year MACE outcomes was selected for the DCA model. Similarly, an acceptable clinical threshold upper limit of 15% for 90-day cardiac readmission outcome was selected for the DCA model.

All analyses were performed in Stata 14.2 (StataCorp, 2017, College Station, TX).

3. Results

Of the 817 patients included, 500 patients (mean age 38 [±13], 60.6% females [n = 303], 95.4% AA [n = 477]) had low HEART score vs. 317 patients (mean age 58 [±12], 61.2% females [n = 194], 93.9% AA [n = 297]) had moderate HEART score. Six hundred sixty-six patients (mean age 42 [±14], 61.5% females [n = 408], 94.8% AA [n = 629]) had low TIMI score vs. 154 patients (mean age 61 [±13], 57.8% females [n = 89], 94.2% AA [n = 145]) had high TIMI score (Supplementary Figures 2A and B, http://links.lww.com/MD/D96 and Tables 4–6). Four hundred eighty-four patients were found to fall under both low TIMI and low HEART score category and 138 patients were classified under both high TIMI and moderate HEART score category. Of the 817 patients, 6 patients had MACE and 100 patients had cardiac readmission.

The univariate logistic regression model (Table 7) shows OR of predicting 6-week MACE using HEART score is 3.11 (95% CI 1.43–6.76, $P = .004$) with increase in risk category from low to moderate vs. 2.07 (95% CI 1.18–3.63, $P = .011$) using TIMI score with increase in risk category from low to high and c-statistic of 0.86 (95% CI 0.74–0.95) vs. 0.79 (95% CI 0.59–0.97), respectively. The OR of predicting 1-year MACE using HEART score is 2.25 (95% CI 1.48–3.39, $P < .001$) with increase in risk category from low to moderate vs. 2.39 (95% CI 1.69–3.39, $P < .001$) using TIMI score increase in risk category from low to high and c-statistic of 0.79 (95% CI 0.71–0.87) vs. 0.79 (95% CI 0.69–0.92), respectively. The OR of predicting 90-day cardiac readmission using HEART score is 1.53 (95% CI 1.29–1.81, $P < .001$) with increase in risk category from low to

Table 4

Demographics of study population.

	Age (mean, SD)	Female gender
HEART score		
Low (n = 500)	38.00 ± 13.00	60.6% (n = 300)
Moderate (n = 317)	58.00 ± 12.00	61.2%(n = 194)
TIMI score		
Low (n = 663)	42.00 ± 14.00	61.5% (n = 408)
High (n = 154)	61.00 ± 13.00	57.8% (n = 89)

HEART = history, electrocardiogram, age, risk factors, and initial troponin, SD = standard deviation, TIMI = thrombolysis in myocardial infarction.

Table 5

Patient characteristics according to history, electrocardiogram, age, risk factors, and initial troponin score parameters.

Parameter (points as per HEART score criteria)	Low HEART score, total N = 500 (n) %	Moderate HEART score, total N = 317 (n) %
EKG changes		
Normal (0)	(436) 87	(160) 50
Nonspecific repolarization (1)	(64) 13	(154) 49
Significant ST depression (2)	0	(3) 1
Sex, females	(303) 61	(194) 61
Age		
<45 years (0)	(345) 69	(20) 6
45–64 years (1)	(154) 30	(209) 66
>65 years (2)	(1) 0.2	(88) 28
Risk factors		
None (0)	(136) 27	(2) 0.6
1–2 risk factors (1)	(321) 64	(86) 27
>3 risk factors/+CAD (2)	(43) 9	(229) 72
Troponin levels		
Normal (0)	(497) 99	(308) 97
1–3 times normal (1)	(3) 0.6	(6) 2
>3 times normal (2)		(3) 1
6-week MACE	0	(6) 1.9
1-year MACE		
ACS (0)	0	(2) 0.6
PCI (1)	(2) 0.4	(10) 3
Death (2)	(1) 0.2	(2) 0.6
90-day readmission	(36) 7.2	(64) 20

ACS = acute coronary syndrome, CAD = coronary artery disease, EKG = electrocardiogram, HEART = history, electrocardiogram, age, risk factors, and initial troponin, MACE = major adverse cardiovascular events, PCI = percutaneous coronary intervention.

moderate vs. 1.27 (95% CI 1.06–1.53, $P = .010$) using TIMI score, with increase in risk category from low to high and c-statistic of 0.69 (95% CI 0.59–0.71) vs. 0.71 (95% CI 0.52–0.83), respectively (Fig. 1).

The risk score test characteristics for 6-week MACE, 1-year MACE, and 90-day cardiac readmission are enumerated in Table 8. For outcome of 6-week MACE, HEART score vs. TIMI score had a positive predictive value (PPV) of 1.9% vs. 3.25%,

Table 6

Patient characteristics according to thrombolysis in myocardial infarction score parameters.

Parameter	Low TIMI score, total N = 663 (n) %	High TIMI score, total N = 154 (n) %
Age ≥65 years	(26) 4	(68) 45
≥3 CAD risk factors	(44) 7	(100) 66
Known CAD	(7) 1	(75) 49
Aspirin use in 7 days	(53) 8	(125) 82
Severe angina (≥2 episodes in 24 h)	(4) 0.6	(9) 6
EKG ST changes ≥0.5 mm	(5) 0.8	(8) 5
Positive cardiac marker	(1) 0.2	(3) 2
6-week MACE	(1) 0.15	(5) 3.25
1-year MACE		
ACS (0)	(1) 0.15	(1) 0.65
PCI (1)	(2) 0.30	(10) 6.5
Death (2)	(2) 0.30	(1) 0.65
90-day readmission	(52) 8	(48) 31

ACS = acute coronary syndrome, CAD = coronary artery disease, EKG = electrocardiogram, MACE = major adverse cardiovascular events, PCI = percutaneous coronary intervention, TIMI = thrombolysis in myocardial infarction.

Table 7

Univariate logistic regression analysis model.

	OR (95% CI)	*P*	c-statistic
6-week MACE (number of events, n = 6 events)			
HEART score	3.11 (1.43–6.76)	.004	0.86
TIMI score	2.07 (1.18–3.63)	.011	0.79
1-year MACE (number of events, n = 17 events)			
HEART score	2.25 (1.48–3.39)	<.0001	0.79
TIMI score	2.39 (1.69–3.39)	<.001	0.79
90-day cardiac readmission (number of events, n = 100 events)			
HEART score	1.53 (1.29–1.81)	<.001	0.69
TIMI score	1.27 (1.06–1.53)	.010	0.71

CI = confidence interval, HEART = history, electrocardiogram, age, risk factors, and initial troponin, MACE = major adverse cardiovascular events, OR = odds ratio, TIMI = thrombolysis in myocardial infarction.

negative predictive value (NPV) of 100% vs. 99%, Sn of 100% vs. 83%, and Sp of 62% vs. 82%, respectively. McNemar exact test for Sn comparison between the 2 diagnostic tests $P = .45$ and McNemar test for Sp comparison was $P < .001$.

For 1-year MACE, HEART score vs. TIMI score had a PPV 4.42% vs. 7.79%, NPV of 99.4% vs. 99.3%, Sn of 82 vs. 71, and Sp of 62% vs. 82%, respectively. McNemar exact test for Sn comparison between the 2 diagnostic tests $P = .25$ and McNemar test for Sp comparison was $P < .001$.

For 90-day cardiac readmission, HEART score vs. TIMI score had a PPV 20.19% vs. 31.17%, NPV of 92.8% vs. 92%, Sn of 64 vs. 48, and Sp 65% vs. 85%, respectively. McNemar test for Sn and Sp comparison between the 2 diagnostic tests yielded $P < .001$.

DCA as shown in Figure 2 helps to distinguish between the 3 strategies based on the net benefit of the model over a range of acceptable miss rate thresholds.

Figure 2A shows net benefit of using either the HEART score or the alternative strategies of admit all or admit none, irrespective of the score, to predict outcome of 6-week MACE. The X-axis shows range of threshold probabilities with an upper limit of 4% for predicting 6-week MACE.

At threshold probability of 1%, the net benefit of using the HEART score is higher than net benefit of either strategies of admit all or admit none. Decision curve demonstrates that at 2% threshold probability, where the curves cross, the net benefit of using the HEART score slowly starts to get lower than net benefit of admit none. The net benefit of admit all remains lower than either strategy at all threshold probabilities. Similarly, at threshold probability of 3% and 4%, the decision curve suggests, net benefit of admit none is a better strategy than using HEART score.

Figure 2B shows net benefit of using either the TIMI score or the alternative strategies of admit all or admit none, irrespective of the score, to predict outcome of 6-week MACE. The X-axis shows range of threshold probabilities with an upper limit of 4% for predicting 6-week MACE.

At threshold probabilities of 1% and 2%, the net benefit of using the TIMI score is higher than net benefit of either strategies of admit all or admit none. The net benefit of admit none slightly increases with increase in threshold probability at 2.5% (where the curves cross), 3%, and 4%. The decision curve also suggests, net benefit of admit all remains lower than net benefit of either strategies at all possible threshold probabilities.

Figure 2C shows net benefit of using either HEART score or the alternative strategies to admit all or admit none, irrespective of

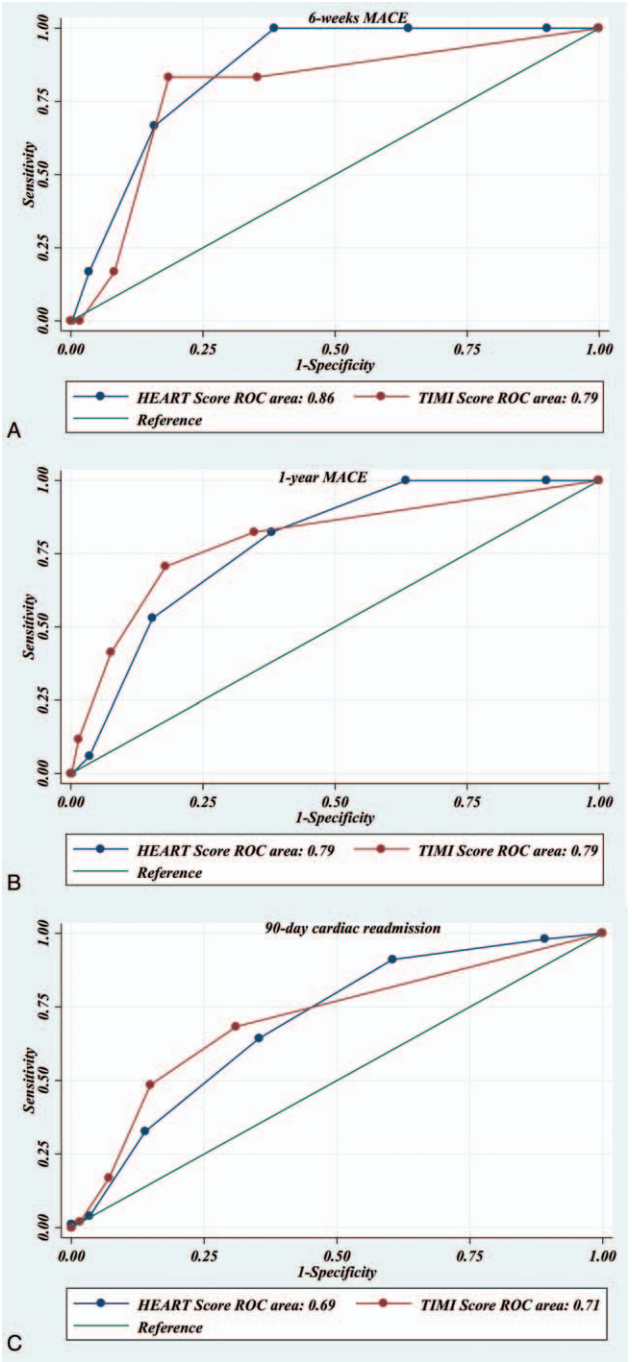

Figure 1. (A) ROC of HEART vs. TIMI for 6-weeks MACE; (B) ROC of HEART vs. TIMI for 1-year MACE; (C) ROC of HEART vs. TIMI for 90-day readmission. HEART = history, electrocardiogram, age, risk factors, and initial troponin, MACE = major adverse cardiovascular events, ROC = receiver operator curve, TIMI = thrombolysis in myocardial infarction.

the score, to predict outcome of 1-year MACE. The X-axis shows range of threshold probabilities with an upper limit of 4% for predicting 1-year MACE.

At threshold probabilities of 1% and 2%, the net benefit of using the HEART score is higher than net benefit of admit all or admit none. Similarly, is the case for threshold probabilities of 3% and 4%. The alternative strategies here are either admit all or admit none. The alternative strategy decision curves cross at a threshold probability between 2% and 4%. Beyond threshold probability of 2%, the net benefit of admit none is higher than admit all. Overall the decision curve graph suggests that at all threshold probabilities, using HEART score has a higher net benefit than the other strategies.

Figure 2D shows net benefit of using either the TIMI score or the alternative strategies to admit all or admit none, irrespective of the score, to predict outcome of 1-year MACE. The X-axis shows range of threshold probabilities with an upper limit of 4% for predicting 1-year MACE.

At all threshold probabilities between 1% and 4%, the net benefit of using the TIMI score is higher than net benefits of admit all or admit none.

Figure 2E shows a decision curve with net benefit of using either the HEART score or the alternative strategies to admit all or admit none, irrespective of the score, to predict outcome of 90-day cardiac readmission. The X-axis shows range of threshold probabilities with an upper limit of 15% for predicting readmissions at 90 days.

Between threshold probabilities of 1% and 7%, the net benefit of admit all, is higher than net benefit of using the HEART score. Beyond threshold probability of 7% (where the curves cross), the net benefit of using the HEART score becomes higher than net benefit of admit all. The net benefit of admit none remains lower than net benefit of both the alternative strategies at all threshold probabilities between 1% and 12%.

Figure 2F shows net benefit of using either the TIMI score or the alternative strategies to admit all or admit none, irrespective of the risk score, to predict outcome of 90-day cardiac readmission. The X-axis shows range of threshold probabilities with an upper limit of 15% for predicting 90-day cardiac readmission.

At all threshold probabilities between 1% and 12%, the net benefit of admit all is higher than the net benefit of both the alternative strategies. The decision curves for admit all and using the TIMI risk score cross at about 12%. Between threshold probability of 12% and 15%, the net benefit of using TIMI score becomes higher than net benefit of admit all. The net benefit of admit none remains lower than the net benefit of both the alternative strategies at all threshold probabilities between 1% and 12%.

4. Discussion

AA are twice as likely than whites to select the ED as their usual place of healthcare (OR 2.24, 95% CI 1.22–4.08)[19] and with higher prevalence of hypertension among AA, hypertensive heart disease may present with ischemic symptoms despite not having significant CAD.[20] Thomas et al[21] reported that in patients with CAD, AA have lower long-term survival compared to whites (hazard ratio 2.54, 95% CI 1.60–4.04, $P < .001$). Cardiac risks scoring performance for CV event outcomes are understudied in AA population.

Our study aimed at studying AA population with non-high HEART scores and compares that to TIMI score. Our study suggests, HEART score has better overall discrimination than the TIMI score to predict 6-week MACE in non-high CV risk AA population, consistent with prior reports.[9,22,23] Our c-statistic of 0.86 for HEART indicates an excellent ability to discriminate patients presenting with chest pain for their risk of 6-week MACE.

Table 8

Risk score test characteristics for 6-week MACE, 1-year MACE, and 90-day cardiac readmission.

	HEART score (95% CI)	TIMI score (95% CI)	
6-week MACE (number of events, n = 6 events)			
Sensitivity	100% (54–100%)	83.3% (35.88–99.58%)	$P = .45$
Specificity	62% (58–65%)	81.6% (79–84%)	$P \leq .001$
PPV	1.9% (1.74–2.06%)	3.25% (2.23–4.7%)	
NPV	100%	99.8% (99.1–99.7%)	
Prevalence	0.7% (0.27–1.6%)		
1-year MACE (number of events, n = 17 events)			
Sensitivity	82.35% (56.57–96.2%)	70.59% (44.04–89.69%)	$P = .25$
Specificity	62% (59–66%)	82% (79–85%)	$P \leq .001$
PPV	4.42% (3.52–5.53%)	7.79% (5.67–10.62%)	
NPV	99.4% (98.34–99.78%)	99.3% (98.44–99.64%)	
Prevalence	2.1% (1.2–3.3%)		
90-day cardiac readmission (number of events, n = 100 events)			
Sensitivity	64% (53.79–73.36%)	48% (37.90–58.22%)	$P \leq .001$
Specificity	65% (61–68%)	85% (82–88%)	$P \leq .001$
PPV	20.19% (17.48–23.20%)	31.17% (25.70–37.22%)	
NPV	92.8% (90.80–94.39%)	92.16% (90.66–93.43%)	
Prevalence	12.2% (10.1–14.7%)		

McNemar test for comparison of sensitivity and specificity between 2 diagnostic tests, each measured on the same patient, when the same end-point is used.

CI = confidence interval, HEART = history, electrocardiogram, age, risk factors, and initial troponin, MACE = major adverse cardiovascular events, NPV = negative predictive value, PPV = positive predictive value, TIMI = thrombolysis in myocardial infarction.

We also demonstrate that both TIMI and HEART score could moderately discriminate patients for 1-year MACE and 90-day cardiac readmission outcomes. There was no difference in the discrimination ability of both scores since c-statistic for both the scores were in moderate range (c-statistic of 0.69 vs. 0.71) and cannot accurately distinguish patients at risk for 90-day cardiac readmission and 1-year MACE. A significant amount of patients with low HEART score had recurrent admission within 90-days (7.2%) and only 3 patients (0.6%) with low HEART score had MACE during 1 year follow-up.

Kline et al[4] calculated that a 2% miss rate for 30-days follow-up period after initial evaluation should be acceptable based on the testing threshold at which the risk of harm from further testing equals or exceeds the chance of benefit from confirming ACS. However, the most frequently sited acceptable miss rate is less than 1%,[24] which suggests that clinicians may expect diagnostic strategies for the assessment of suspected ACS to achieve a Sn of 99% or higher for AMI or other MACE and a NPV >99%. Based on this, we decided to take miss rate range with an upper limit of 4% as acceptable clinical thresholds for decision-making for 6-week and 1-year MACE outcomes. According to the Centers for Medicare & Medicaid Services, the national readmission rate (i.e., instances when patients return to the same or different hospital within 30 days of discharge) was 17.5% in 2013; hence we decided to take 15% as the upper limit as acceptable clinical threshold for 90-day cardiac readmission outcome.

Our population had low event counts for 6-week MACE (n = 6), so we compared the risk scoring characteristics for HEART and TIMI, specifically looking at NPV and Sn. The predictive capability of HEART score was higher as compared to TIMI score for primary outcome of 6-week MACE (NPV 100, Sn 100 vs. NPV 99, Sn 82). Similarly, for 1-year MACE (n = 17), predictive capability of HEART score was comparable to TIMI score (NPV 99, Sn 82 vs. NPV 99, Sn 71) and 90-day cardiac readmission (NPV 93, Sn 64 vs. NPV 92, Sn 48). Thus, HEART score has higher NPV and Sn when compared to TIMI score for 6-week MACE, 1-year MACE, and 90-day cardiac readmission but TIMI score has higher PPV and Sp values than HEART score for 6-week and 1-year MACE and 90-day cardiac readmission in low risk AA patients in our cohort and this is similar to previous reports[9,22](Table 4).

DCA using HEART score for chest pain patients to predict 6-week MACE (Fig. 2A) shows that using the HEART score tool for threshold probabilities of 1% to 2% miss rate is optimal strategy over other alternatives, while if threshold probability is between 2% and 4%, the optimal strategy should be discharging these patients. Similarly, DCA using TIMI score for 6-week MACE (Fig. 2B) shows that using TIMI score for threshold probability of 1% to 2.5% miss rate is optimal strategy over other alternative strategies, while is threshold probability of 2.5% to 4% miss rate, the optimal strategy should be to discharge these patients.

DCA using HEART and TIMI score for 1-year MACE (Fig. 2C and D) shows that using the risk stratification tool is best strategy with maximal net benefit when compared to alternative strategies at all clinical acceptable threshold probabilities.

DCA using HEART score for 90-day cardiac readmission (Fig. 2E) shows that using the risk stratification tool is the optimal strategy between threshold probabilities of 7% and 15%, but if the threshold probability is between 1% and 7%, admitting these patients is optimal strategy. DCA using TIMI score for 90-day cardiac readmission (Fig. 2F)[25] shows that using risk stratification tool is optimal between threshold probabilities of 12% and 15%. Between threshold probabilities of 1% and 12%, the optimal strategy is admitting these patients.

There are multiple benefits of HEART over the TIMI risk score. Firstly, the TIMI risk score was established to risk stratify patients presenting with ACS but since its validation, clinicians have extended its use to risk stratify all cause chest pain patients presenting to the ED. In contrast, HEART was specifically established to stratify all patients presenting to emergency room with chest pain and have been validated prospectively. Secondly, the TIMI score does not include patient history component, which defines the characteristics of chest pain, even though clinicians rely heavily on this and guidelines advise to involve history as part of decision-making process.[26,27]

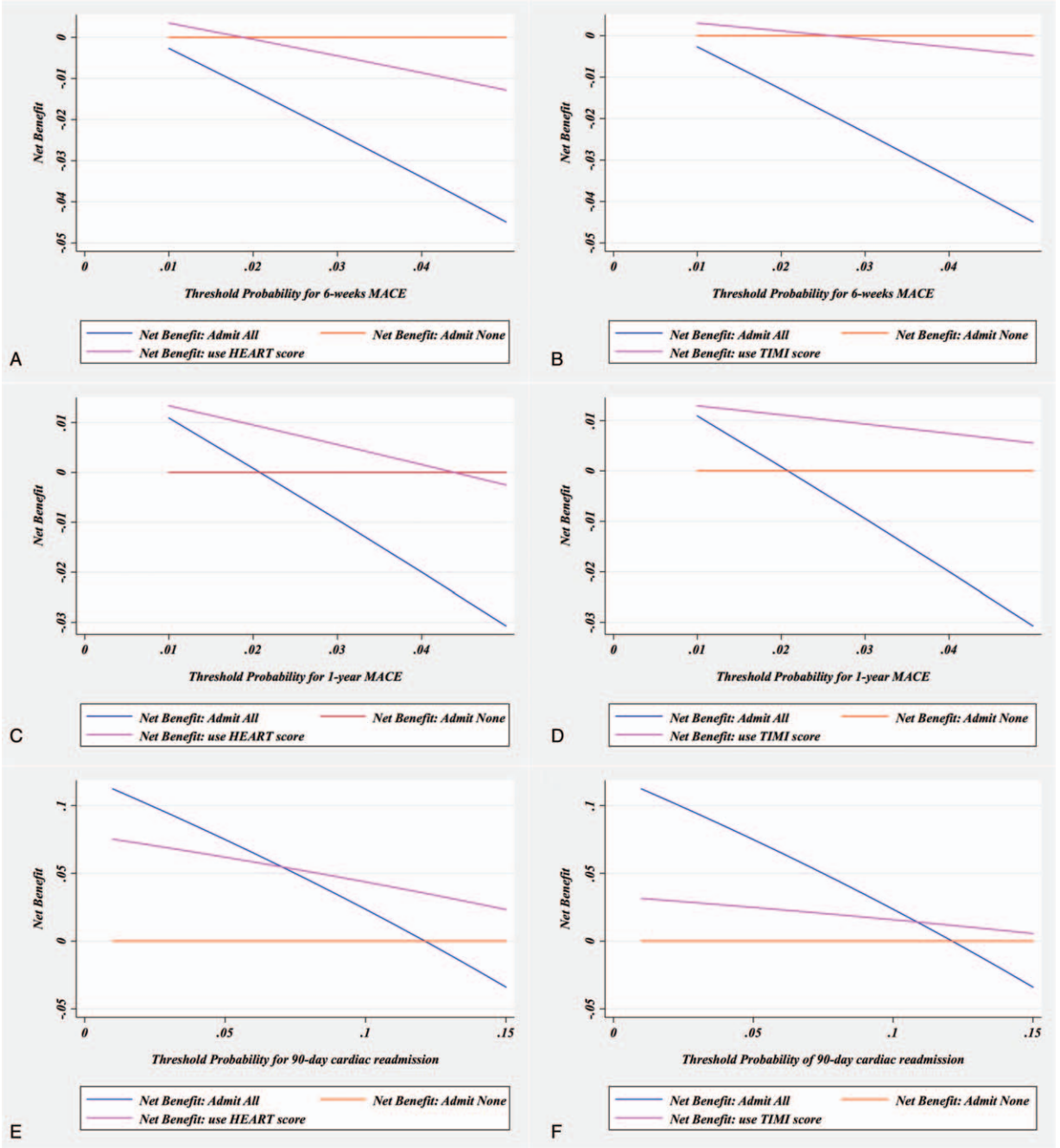

Figure 2. Decision curves. (A) Decision curve at threshold probability of 4% for 6-week MACE, using HEART score. (B) Decision curve at threshold probability of 4% for 6-week MACE, using TIMI score. (C) Decision curve at threshold probability of 4% for 1-year MACE, using HEART score. (D) Decision curve at threshold probability of 4% for 1-year MACE, using TIMI score. (E) Decision curve at threshold probability of 15% for 90-day readmission, using HEART score, (F) Decision curve at threshold probability of 15% for 90-day readmission, using TIMI score. HEART = history, electrocardiogram, age, risk factors, and initial troponin, MACE = major adverse cardiovascular events, TIMI = thrombolysis in myocardial infarction

Our study compares 2 of the best-known risk scores in ED settings in non-high CV risk AA population, and our results suggests HEART score is superior to TIMI for 6-week MACE.

There is evolving demand for easy and rapid evaluation protocols, such as the use of coronary computerized tomography (CT) angiography[27] and identification of patients who might safely defer stress testing.[28] Cardiac risk scores are generally used to identify such patients who may be eligible for these protocols.[26,27] With further evidence from DCA, we can triage eligible patients who will benefit from requiring the scoring tool and further evaluation strategies (e.g., stress test vs. no stress test in low-risk patients).

The findings of our study have important clinical implications even though the number of events is low. The HEART score allows clinicians to immediately decide about the treatment plan in the ED. Almost two thirds of the patients in our cohort were "low" risk with HEART score 0 to 3, and none of them had MACE during 6-week follow-up. These findings will allow

clinicians to avoid redundant diagnostic testing. It will allow clinicians to triage patients who will benefit from early discharge, as evidenced by DCA in our study, and others who will require additional testing with either stress testing or CT coronary angiography.

4.1. Limitations

HEART weights were retrieved from retrospective chart review of medical records and the "history" component of the HEART criteria was scored as "moderately suspicious" for all patients that did not have any clear documentation (n=9 ~1%). A potential for differential misclassification bias that is affecting the HEART score may have been introduced, with bias toward the null, since none of the patients had a documented history component scored as "highly suspicious."

Lastly, since this is a single center medical chart review of data on majority low risk AA subjects, generalizability of the results may be limited in other racial groups across other practices, but the superiority of c-statistic of HEART risk scores in addition to high Sn and NPV of HEART score for 6-week MACE outcome to TIMI score from our study is consistent with prior published reports.[10,28]

5. Conclusions

In non-high CV risk AA patients, HEART score is better predictive tool for 6-week MACE with Sn and NPV of 100%, c-statistic of 0.86, and OR of 3.11 when compared to TIMI score in patients presenting to ED with chest pain. DCA shows that net benefit of using HEART score is equally predictive of 6-week MACE when compared to TIMI and that the optimal strategy for a 2% to 4% miss rate threshold probability should be to discharge these patients from the ED.

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