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HEART score performance in Asian and Caucasian patients presenting to the emergency department with suspected acute coronary syndrome

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Abstract

Background: The HEART score is a simple and effective tool to predict short-term major adverse cardiovascular events in patients suspected of acute coronary syndrome. Patients are assigned to three risk categories using History, ECG, Age, Risk factors and Troponin (HEART). The purpose is early rule out and discharge is considered safe for patients in the low risk category. Its performance in patients of Asian ethnicity is unknown. We evaluated the performance of the HEART score in patients of Caucasian, Chinese, Indian and Malay ethnicity.

Methods: The HEART score was assessed retrospectively in 3456 patients presenting to the emergency department with suspected acute coronary syndrome (1791 Caucasians, 1059 Chinese, 344 Indians, 262 Malays), assigning them into three risk categories.

Results: The incidence of major adverse cardiovascular events within six weeks after presentation was similar between the ethnic groups. A smaller proportion of Caucasians was in the low risk category compared with Asians (Caucasians 35.8%, Chinese 43.5%, Indians 45.3%, Malays 44.7%, $p<0.001$). The negative predictive value of a low HEART score was comparable across the ethnic groups, but lower than previously reported (Caucasians 95.3%, Chinese 95.0%, Indians 96.2%, Malays 96.6%). Also the c-statistic for the HEART score was not significantly different between the groups.

Conclusions: These results show that the overall performance of the HEART score is equal among Caucasian and Asian ethnic groups. The event rate in the low risk group, however, was higher than reported in previous studies, which queries the safety of early discharge of patients in the low risk category.

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Acute coronary syndrome, risk stratification, HEART score, ethnicity, major adverse cardiovascular outcome

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Introduction

Acute myocardial infarction (MI) remains a major cause of morbidity and mortality worldwide despite major improvements in prevention strategies and therapy in recent decades.[1,2] Annually millions of people present to the emergency department (ED) with symptoms suggestive of an acute coronary syndrome (ACS), constituting approximately 6–10% of all ED consultations.[3,4]

Accurately distinguishing non-cardiac chest pain from ACS is often challenging, especially in patients presenting early after the onset of symptoms.[5,6] Since early treatment greatly influences prognosis after MI, early diagnosis is crucial.[6,7] Up to 85% of chest pain patients presenting to the ED do not have an ACS but have non-cardiac chest pain.[8,9] Many of these patients are admitted to the hospital for serial troponin measurements and additional investigations. Early identification of patients at very low short-term risk for major adverse cardiovascular events (MACEs) will avoid unnecessary hospital admissions and reduce patient burden.

The HEART score is a risk score for early risk stratification in chest pain patients in the ED and is specifically designed to identify patients at low risk of short-term MACE.[10,11] The HEART score is easy and intuitive and includes well-established factors associated with the probability of having an ACS: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels (HEART).[10] Several validation studies showed that approximately one-third of chest pain patients in the ED have a low HEART score, with a short-term MACE rate of 0.4–2.5%.[10–13] These studies suggest that patients with a low HEART score (0–3) might be safely dismissed from the ED, patients with an intermediate HEART score (4–6) require careful monitoring and serial troponin measurements, and patients with a high HEART score (7–10) should be considered for direct treatment and/or early invasive strategies. A large prospective, multi-centre cluster randomized trial to assess the impact of implementation of the HEART score on patient outcomes and costs is currently ongoing (ClinicalTrials.gov 80-82310-97-12154).[14]

The HEART score was developed and validated in predominantly Caucasian populations and has not been tested in other ethnic groups. Ethnic validation of risk scores is important, since inter-ethnic differences in cardiovascular risk factors and course of disease potentially influence risk score performance and extrapolation of risk stratification models to different ethnicities cannot be assumed.[15–23] Here, we present a retrospective analysis of the performance of the HEART score in four major ethnic groups – Caucasian, Chinese, Indian and Malay – in the Netherlands and Singapore.

Methods

Study design

This is a multi-ethnic cohort study involving consecutive patients who presented to the ED with symptoms arousing suspicion of an ACS. Patients were enrolled in three centres: Meander Medical Centre Amersfoort, the Netherlands (January 2012–June 2014), National University Hospital Singapore (December 2010–April 2013) and Singapore General Hospital (January 2010–September 2011). The study has been evaluated and approved by the Ethics Committees of all participating centres and written informed consent was obtained from all participants. The study conforms to the Declaration of Helsinki.

Study population

Consecutive patients presenting to the ED with possible cardiac symptoms for a duration of at least five minutes and in whom the physician intended to perform serial cardiac troponin measurements were eligible for inclusion.[24] Possible cardiac symptoms were defined as acute chest, epigastric, neck, jaw, or arm pain, or discomfort or pressure without an apparent non-cardiac source, according to the American Heart Association case definitions.[25] Patients younger than 21 years, patients who were unable or unwilling to give their informed consent and patients with an ethnicity other than Caucasian, Chinese, Indian or Malay were excluded. Furthermore, patients with an ST-segment elevation MI were directly referred for percutaneous coronary intervention (PCI) and were not included in this study. Patients were also excluded if the available data was insufficient to calculate the HEART score or when follow-up was missing or incomplete.

Data acquisition

After patients gave informed consent, clinical data (including clinical presentation, duration of symptoms, medical history, cardiovascular risk factors, electrocardiogram (ECG) evaluation, blood biochemical parameters and the

Table 1. HEART score algorithm.[10]

HEART score for chest pain patients at the emergency department		
Variable	Description	Score
History	Highly suspicious	2
	Moderately suspicious	1
	Slightly- or non-suspicious	0
ECG	Significant ST-depression	2
	Nonspecific repolarization disturbances	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
	One or two risk factors	1
	No risk factors known	0
Troponin	⩾3× normal limit	2
	1–2× normal limit	1
	⩽ normal limit	0

Total score: 0–10 points. 0–3 points, low risk; 4–6 points, intermediate risk; 7–10 points, high risk.
HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels; ECG: electrocardiogram.

results of additional investigations) were gathered from medical records and recorded in a digital case record form.

Ethnicity was self-reported in the Netherlands and was determined at hospital registration in Singapore, based on information from state-issued identification cards. Smoking was defined as current smoking or smoking within the last three months. Diabetes was defined as any type of diabetes diagnosed previously by a physician or during the index visit.[26] Dyslipidaemia was scored when diagnosed previously by a physician or diagnosed during the index visit, according to the European Society of Cardiology/European Atherosclerosis Society guidelines.[27] Hypertension was scored when reported in the medical history, when diagnosed during the index visit or when the patient was treated for hypertension.[28] Renal impairment was defined as a glomerular filtration rate (GFR) of <60 ml/min (moderate renal impairment GFR 30–60 ml/min, severe renal impairment GFR <30 ml/min, calculated using the Cockroft–Gault equation).

HEART score protocol

Patient data collected at time of presentation to the ED were used to calculate the HEART score. Patients were given no, one or two points for each variable. Based on the total score, patients were categorized as low risk (0–3 points), intermediate risk (4–6 points) or high risk (7–10 points). The HEART score algorithm[10] is depicted in Table 1. A detailed description of the HEART score protocol used can be found in the Supplementary Material online.

Clinical outcome

The primary outcome was MACEs, defined as MI, coronary revascularization or all cause death, within six weeks after presentation to the ED (as defined by previous studies).[13] This included the diagnosis adjudicated during the index visit. The diagnosis of MI was made according to European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation guidelines (2012).[29] Diagnoses were adjudicated in retrospect by two cardiologists, taking into consideration all patient information available, including investigations and treatment after the index presentation. In the case of dispute, a third cardiologist decided the final diagnosis. Coronary revascularization was defined as PCI or coronary artery bypass grafting.

Statistical analysis

All statistical analyses were performed using the R software package (version 3.1.2 GUI 1.65). A p-value of <0.05 was considered statistically significant.

Continuous variables were presented as mean ± SD and categorical variables as percentages, unless stated otherwise. Comparisons of continuous variables between two groups were performed with two-sided Student's t-test and between multiple groups with one-way analysis of variance with Bonferroni post-hoc testing, to correct for multiple testing. Categorical variables were compared with Pearson's chi-squared tests. Since the comparisons between four groups require six statistical tests, a p-value below 0.05/6 = 0.008 was considered significant, according to the Bonferroni principle.

HEART score test characteristics (sensitivity, specificity, negative predictive value (NPV) and positive predictive value) per ethnic group were derived from 2 × 2 tables and were calculated for all patients as well as separately for patients who presented within 4 h after the initiation of symptoms. The c-statistics of the HEART score were derived from receiver operating curves (ROCs) for each ethnic group and compared with DeLong tests. Crude adverse event rates (MACE within six weeks after inclusion, defined as MI, coronary revascularization and all cause death) were presented per ethnic group using Kaplan–Meier curves and were compared with the log-rank test.

Results

Patient population

Between 2010 and 2014, 3857 eligible patients were enrolled at the three participating centres. Sufficient data to calculate the HEART score as well as complete six week follow-up data were available in 3456 patients: 1791 from

Table 2. Clinical characteristics.

n	Caucasian 1791	Chinese 1059	Indian 344	Malay 262	*p*-value
Demographics					
Age (years ± SD)	62.7 ± 13.5	59.1 ± 11.9[a]	53.5 ± 11.2[b,c]	52.7 ± 12.1[d,e]	<0.001
Male gender (%)	56.4	67.2[a]	69.2[b]	64.1	<0.001
Risk factors					
BMI (kg/m^2 ± SD)	27.1 ± 4.4	25.2 ± 4.3[a]	27.3 ± 4.7[c]	28.3 ± 5.3[d,e]	<0.001
Smoking (%)	27.3	26.7	32.6	39.3[d,e]	<0.001
Hypertension (%)	47.7	56.2[a]	53.2	49.2	<0.001
Dyslipidaemia (%)	30.9	56.0[a]	51.7[b]	56.5[d]	<0.001
Diabetes (%)	14.9	22.8[a]	42.2[b,c]	30.9[d,e,f]	<0.001
Medical history					
Previous MI (%)	21.3	8.9[a]	15.1[c]	13.7[d]	<0.001
Previous PCI (%)	23.0	12.4[a]	20.6[c]	14.5[d]	<0.001
Previous CABG (%)	7.4	6.1	9.0	6.5	0.288
Stroke/TIA (%)	2.7	3.7	2.0	2.7	0.333
Renal impairment (%)	17.3	24.0[a]	15.2[d]	14.3[e]	<0.001
Moderate (%)	15.6	19.2	11.1[c]	10.0[e]	<0.001
Severe (%)	1.8	4.8[a]	4.0	4.3	<0.001

Baseline characteristics of all patients (*N* = 3456). Differences between ethnic groups were tested with chi-squared tests for categorical variables and with one-way ANOVA for continuous variables. The last column represents overall *p*-values. The level of significance has been set at 0.05/6 = 0.008 to correct for multiple testing by the Bonferroni method.
[a]Caucasian *vs*. Chinese.
[b]Caucasian *vs*. Indian.
[c]Chinese *vs*. Indian.
[d]Caucasian *vs*. Malay.
[e]Chinese *vs*. Malay.
[f]Indian *vs*. Malay ($p<0.008$).
BMI: body mass index; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; CVA: cerebrovascular attack; TIA: transient ischemic attack; ANOVA: analysis of variance.

Meander Medical Centre Amersfoort, 1513 from Singapore General Hospital and 152 from National University Hospital Singapore. Of these patients 1791 were Caucasian (51.8%), 1059 Chinese (30.6%), 344 Indian (10.0%) and 262 Malay (7.6%).

Clinical characteristics are reported in Table 2. Patients of Asian ethnicity were significantly younger than Caucasians, although the difference was less pronounced in Chinese patients. Dyslipidaemia and diabetes were more prevalent in all Asian groups compared with Caucasians. Chinese more frequently had hypertension and had a lower body mass index (BMI) compared with Caucasians. Malays had the highest BMI and smoking rate. Caucasians most often had a history of cardiovascular disease: significantly more than Malays (previous PCI) and Chinese (history of MI and PCI). Renal impairment was more prevalent in Chinese than in Caucasians.

Clinical outcome

The percentage of MACE within six weeks after presentation, including index diagnosis, did not differ significantly between ethnic groups (Caucasians 16.4%, Chinese 14.3%, Indians 13.1%, Malays 14.5%, $p = 0.275$) (Table 3). Accordingly, Kaplan–Meier curve analysis of MACEs up to six weeks post-presentation revealed no differences between ethnic groups ($p = 0.271$) (Figure 1). The incidence of MI, however, was higher in Caucasians than in Chinese.

Patient distribution across the HEART score categories

Of the 3456 patients, 1376 (39.9%) were assigned to the low risk category, 1897 (54.9%) to the intermediate risk category and 183 (5.3%) to the high risk category. In Asian patients, 43.5–45.3% were classified as having low risk (HEART score 0–3), whereas only 35.8% of the Caucasians were assigned to this category ($p<0.001$, Figure 2). More Caucasian patients were assigned to the intermediate and high risk categories (Figure 2).

Incidence of MACE per HEART score category among different ethnic groups

The incidence of MACE per HEART score category per ethnic group is reported in Table 4. The relationship between HEART score and six week MACE per ethnic

Table 3. Clinical outcome: MACE within six weeks after initial presentation.

n	Caucasian 1791	Chinese 1059	Indian 344	Malay 262	*p*-value
MACE (%)	16.4	14.3	13.1	14.5	0.275
Death (%)	0.6	0.3	0.3	0	0.511
MI (%)	12.7	7.6[a]	7.6	12.2	<0.001
Coronary revascularization (%)	12.3	11.8	10.2	8.8	0.300

Differences between ethnic groups were tested with chi-squared tests. The last column represents overall *p*-values. The level of significance has been set at 0.05/6 = 0.008 to correct for multiple testing by the Bonferroni method.
[a]Caucasian *vs*. Chinese.
MACE: major adverse cardiovascular event (combination of MI, coronary revascularization and death); MI: myocardial infarction.

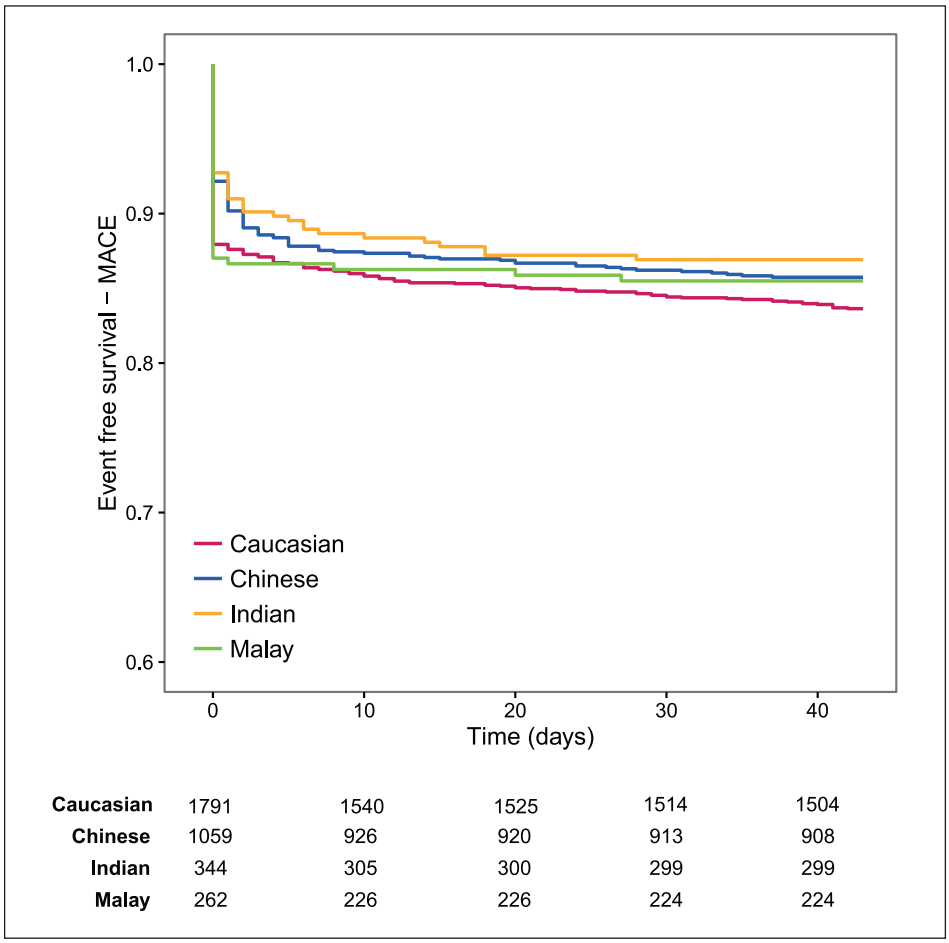

Figure 1. Kaplan–Meier curves for major adverse cardiovascular event free (combination of myocardial infarction, coronary revascularization and all-cause mortality) survival within six weeks of follow-up, including the diagnosis adjudicated during index visit, per ethnic group. Log-rank test for difference between the ethnic groups: $p = 0.271$.
MACE: major adverse cardiovascular event.

group is depicted in Figure 3. The risk of MACE increased gradually with total HEART score in all ethnic groups. In the low risk category, the risk of MACE within six weeks was 3.4% (Malay) to 5.0% (Chinese) and was statistically comparable between the different ethnic groups. None of the patients in the low risk category died during follow-up. The majority of MACEs occurring during follow-up of patients designated as low-risk were coronary revascularizations (2.6–4.2%) whereas MI occurred in 0.9–2.6%.

Inter-ethnic differences per HEART score variable

The mean total HEART score and HEART score per variable per ethnic group are reported in Table 5. The total

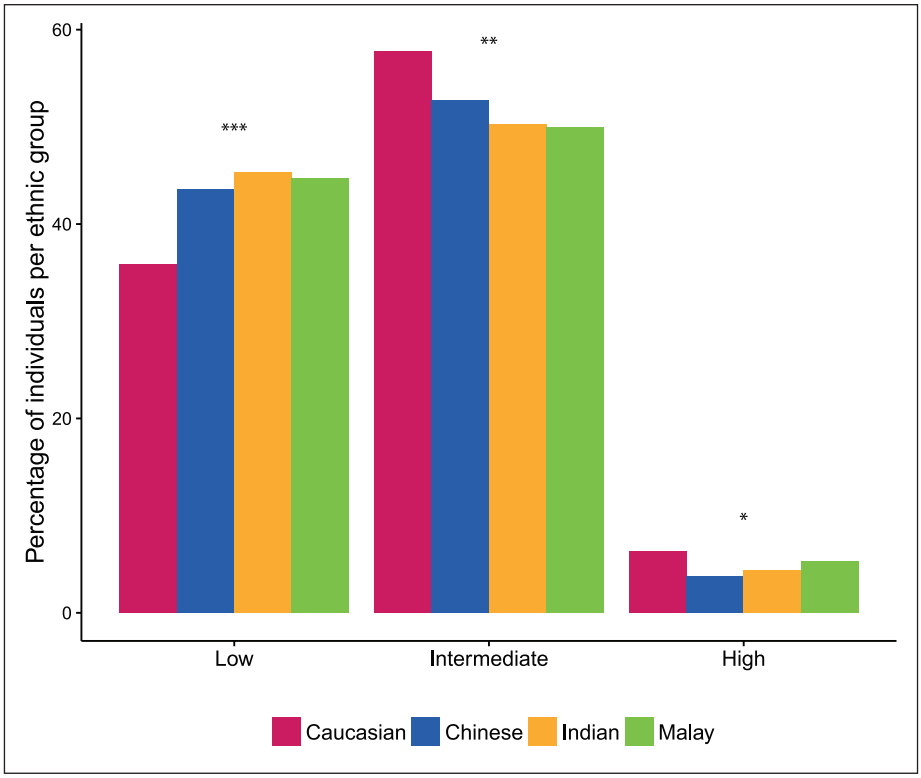

Figure 2. Distribution of patients across HEART score categories (% of patients per ethnicity, per category). Low risk category: 0–3 points; intermediate risk category: 4–6 points; high risk category: 7–10 points. Comparisons between ethnic groups within the HEART score categories were performed with chi-squared tests.
*$p<0.05$.
**$p<0.01$.
***$p<0.001$.
HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels.

Table 4. Incidence of MACE within six weeks after presentation, per HEART score category per ethnicity.

n	Caucasian 1791	Chinese 1059	Indian 344	Malay 262
MACE – *n/n* (%)				
Low, 0–3	30/642 (4.7)	23/461 (5.0)	6/156 (3.8)	4/117 (3.4)
Intermediate, 4–6	181/1035 (17.5)	102/558 (18.2)	28/173 (16.1)	23/131 (17.6)
High, 7–10	82/114 (71.9)	26/40 (65.0)	11/15 (73.3)	11/14 (78.6)
Death – *n/n* (%)				
Low, 0–3	0/642 (0)	0/461 (0)	0/156 (0)	0/117 (0)
Intermediate, 4–6	6/1035 (0.6)	3/558 (0.5)	0/173 (0)	0/131 (0)
High, 7–10	5/114 (4.4)	0/40 (0)	1/15 (7.1)	0/14 (0)
MI – *n/n* (%)				
Low, 0–3	15/642 (2.3)	4/461 (0.9)	2/156 (1.3)	3/117 (2.6)
Intermediate, 4–6	132/1035 (12.8)	54/558 (9.7)	14/173 (8.1)	18/131 (13.7)
High, 7–10	80/114 (70.2)	23/40 (57.5)	10/15 (66.7)	11/14 (78.6)
Coronary revascularization – *n/n* (%)				
Low, 0–3	27/642 (4.2)	20/461 (4.3)	5/156 (3.2)	3/117 (2.6)
Intermediate, 4–6	138/1035 (12.6)	82/558 (14.7)	22/173 (12.7)	14/131 (10.7)
High, 7–10	56/114 (49.1)	23/40 (57.5)	8/15 (53.3)	6/14 (42.9)

Low risk category: 0–3 points; intermediate risk category: 4–6 points; high risk category: 7–10 points. There are no significant differences in any of the clinical endpoints among the different ethnicities.
HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels; MACE: major adverse cardiovascular events (combination of MI, coronary revascularization and death); MI: myocardial infarction.

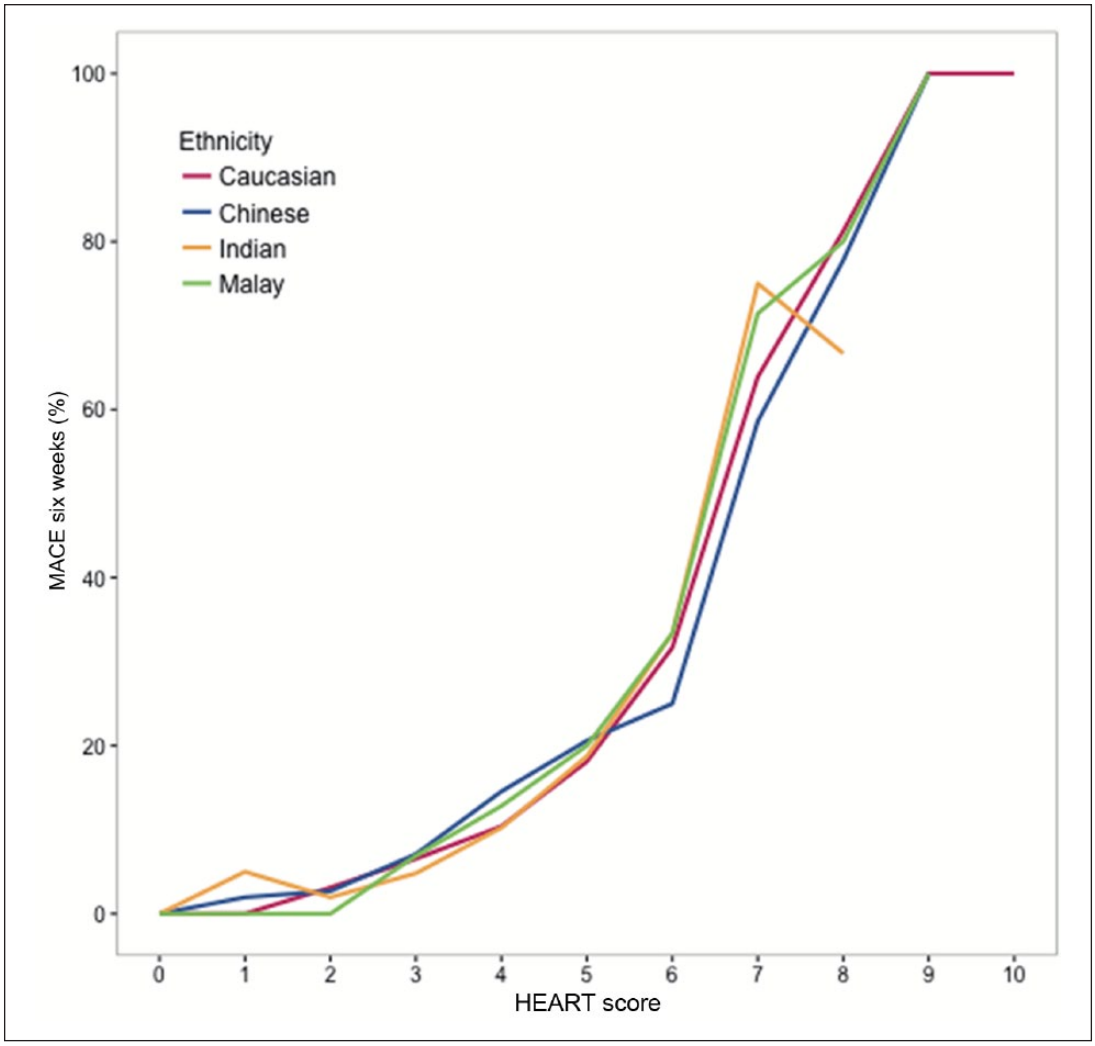

Figure 3. Relationship between total HEART score and the percentage of patients who experienced MACE within six weeks after inclusion, per ethnic group. Note that not all ethnic groups fall into the full range of total HEART score values.
MACE: major adverse cardiovascular event; HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels.

Table 5. Mean HEART score per ethnicity per HEART score variable.

n	Caucasian 1791	Chinese 1059	Indian 344	Malay 262	*p*-value
History	0.88 ± 0.57	0.85 ± 0.44	0.86 ± 0.44	0.86 ± 0.47	0.470
ECG	0.37 ± 0.54	0.35 ± 0.53	0.35 ± 0.54	0.36 ± 0.55	0.904
Age	1.38 ± 0.66	1.19 ± 0.65[a]	0.94 ± 0.64[b,c]	0.89 ± 0.62[d,e]	<0.001
Risk factors	1.32 ± 0.72	1.26 ± 0.71	1.41 ± 0.69[c]	1.42 ± 0.67[e]	<0.001
Troponin	0.16 ± 0.50	0.13 ± 0.44	0.15 ± 0.48	0.19 ± 0.53	0.215
Total	4.10 ± 1.60	3.78 ± 1.50[a]	3.71 ± 1.50[b]	3.71 ± 1.61[d]	<0.001

Differences between ethnic groups were tested with one-way ANOVA. The last column represents overall *p*-values. The level of significance has been set at 0.05/6 = 0.008 to correct for multiple testing by the Bonferroni method.
[a]Caucasian *vs*. Chinese.
[b]Caucasian *vs*. Indian.
[c]Chinese *vs*. Indian.
[d]Caucasian *vs*. Malay.
[e]Chinese *vs*. Malay.
HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels; ECG: electrocardiogram; ANOVA: analysis of variance.

Table 6. Test characteristics of the HEART score per ethnicity (low risk category versus others).

	Caucasian	Chinese	Indian	Malay
A. All patients, *n*	1791	1059	344	262
NPV	95.3 (93.4–96.8)	95.0 (92.6–96.8)	96.2 (91.8–98.6)	96.6 (91.5–99.1)
PPV	22.9 (20.5–25.4)	21.4 (18.2–24.9)	20.7 (15.2–27.2)	23.4 (16.8–31.2)
Sensitivity	89.8 (85.7–93.0)	84.8 (78.0–90.1)	86.7 (73.2–94.9)	89.5 (75.2–97.1)
Specificity	40.9 (38.4–43.4)	48.2 (44.9–51.5)	50.2 (44.4–56.0)	50.4 (43.7–57.2)
B. <4 h, *n*	764	374	126	99
NPV	94.7 (91.3–97.1)	92.7 (87.6–96.2)	94.6 (85.1–98.9)	98.0 (89.4–99.9)
PPV	24.3 (20.6–28.3)	24.4 (18.7–30.8)	32.9 (22.1–45.1)	30.6 (18.3–45.4)
Sensitivity	89.6 (83.2–94.2)	81.0 (69.1–89.8)	88.5 (69.8–97.6)	93.8 (69.8–99.8)
Specificity	40.1 (36.2–44.0)	49.2 (43.5–54.9)	53.0 (42.8–63.1)	59.0 (47.7–69.7)

A: all patients (N = 3456); B: patients who presented to the emergency department within 4 h after the onset of symptoms (n = 1363).
HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels; NPV: negative predictive value; PPV: positive predictive value.

HEART score was significantly lower in all Asian groups compared with Caucasians (Caucasians 4.10 ± 1.60, Chinese 3.78 ± 1.50, Indians 3.71 ± 1.50, Malays 3.71 ± 1.61, p<0.001). All Asian ethnic groups were younger than Caucasians, and Chinese patients had a lower risk factor score than Indians.

Performance of the HEART score among different ethnic groups

Test characteristics of the HEART score per ethnic group are depicted in Table 6. The NPV for patients in the low risk category was highest in Malay (96.6%) and lowest in Chinese (95.0%; ns). Also in the subgroup of patients presenting within 4 h after the onset of symptoms there were no significant inter-ethnic differences (Table 6).

Although there seems to be a trend to a lower performance of the HEART score in Chinese versus Caucasian patients, the c-statistic of the HEART score for 6 week MACE, derived from the HEART score ROC per ethnic group, did not differ between groups (p = 0.075) (Figure 4).

Discussion

The HEART score has been validated in several studies as an effective risk stratification tool to safely identify patients with suspected ACS who are at low risk of short-term cardiovascular events.[10–13] This study investigated the overall performance and the ability of the HEART score to identify patients at low risk of short-term MACE between four major ethnic groups: Caucasians, Chinese, Indians and Malays. There were no significant differences in the negative predictive value of a low HEART score (0–3 points) and the c-statistic did not differ between ethnic groups (p = 0.075).

As previously shown in several studies, the HEART score identifies 30–40% of patients as at low short-term risk of MACE.[10–13] The proportion of patients adjudicated to the low risk HEART score category was larger in Chinese, Malay and Indian patients compared with Caucasians (43.5–45.3% *vs*. 35.8% in Caucasians).

Clinical characteristics (age, risk factors and medical history) differed between the ethnic groups, as reflected in the HEART scores. Indians and Malays, and to a lesser extent Chinese, were younger than Caucasians, with differences up to 10 years. Since the age categories used in the HEART score calculation are based on Caucasian chest pain populations, this difference might influence performance of the HEART score in Asian ethnic groups. Likewise, the differences in risk factor burden led to dissimilar contributions of this variable to the total HEART score in the different ethnic groups. Overall, the mean total HEART score was significantly lower in all Asian ethnic groups compared with Caucasians. This difference was driven by age in Indian, Malay and Chinese patients. Six week MACE per risk category, however, was not significantly different between the ethnic groups. The observed differences in clinical characteristics are also largely responsible for the higher proportion of patients with a low HEART score in the Asian ethnic groups compared with Caucasians.

The negative predictive value of a low HEART score (0–3 points) was 95.0–96.6%, which is lower than reported in previous studies (97.5–99.6%).[10–13] This value is also lower than the negative predictive value using the 0h–3h hs-cTn rule-out protocol as proposed by the 2015 ESC guideline of >98%, according to several validation studies.[5] Since wrongful discharge can seriously harm patients, the negative predictive value should be as high as possible. In a recent survey among physicians, the majority of physicians considered a negative predictive value of >99% acceptable.[30] No patients in the low risk category died during six weeks of follow-up. The majority of events were revascularizations (2.6–4.3%), whereas 0.9–2.6% of patients experienced an MI. It is important to note that discharge does not mean loss from medical follow-up. Patients might be subjected to short-term follow-up at the outpatient

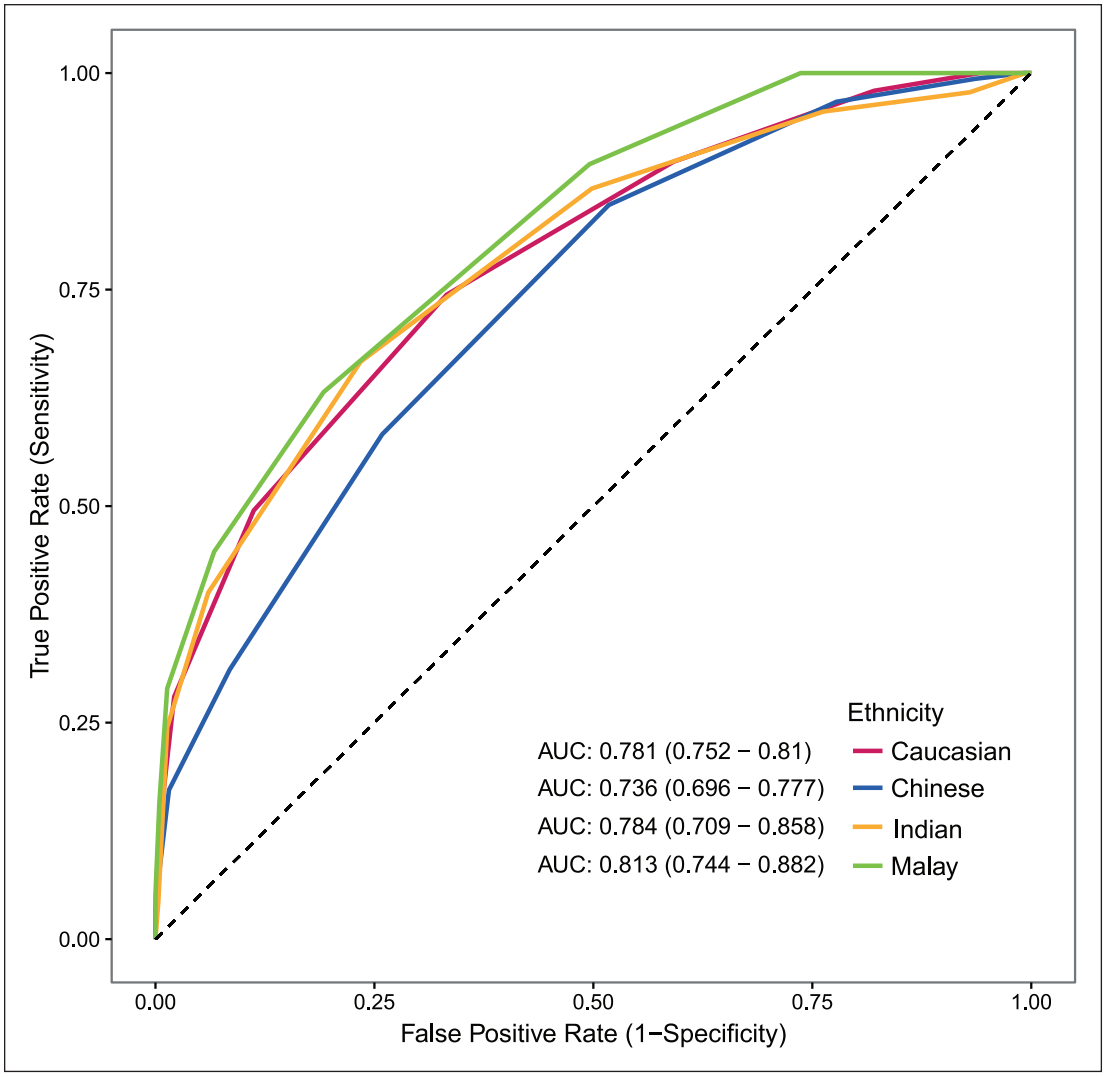

Figure 4. ROCs of the HEART score for the outcome six week MACE, per ethnic group. AUC Chinese *vs*. Caucasians, $p = 0.075$, Chinese *vs*. Malays, $p = 0.061$ (DeLong test).
ROC: receiver operating curve; MACE: major adverse cardiovascular event; HEART: History, ECG findings, Age, cardiovascular Risk factors and cardiac Troponin levels; AUC: area under the curve.

clinic for ischaemia detection and subsequent revascularization if necessary. Nonetheless, the relatively high event rate in the low risk categories might warrant adjustment of the HEART score. One option to improve the negative predictive value would be to lower the cut-off value for low-risk patients, for example, from three to two points. This would greatly improve the negative predictive value of a low HEART score to 97.3–100% but at the expense of the number of low risk patients identified (15.4–22.5% 0–2 points *vs*. 35.8–45.3% 0–3 points) (Supplementary Figures S1 and S2 and Supplementary Tables S1 and S2 online).

Limitations

Singapore and the Netherlands are both well-developed countries with good, accessible health care systems. Nevertheless, differences between the countries and between the ethnic groups such as cultural influences and differences in socio-economic status might have influenced the patient selection. Also differences in the local referral policy from the general practitioner to the ED might lead to selection bias of different patient populations. Nevertheless, it is important that the performance of a risk score is also maintained in varying populations.

There are large differences in sample size between the ethnic groups. The cohort contains fewer Indians and Malays compared with Chinese and Caucasians, which is largely explained by the demographic distribution of ethnicities in Singapore. Therefore the statistical power to assess differences in HEART score performance in these groups is lower and our results should be interpreted with care.

In this study the HEART score has been calculated and analysed retrospectively. Since the HEART score is designed for application in a clinical setting, our findings need to be confirmed in a prospective analysis and in other multi-ethnic cohorts. Especially symptom history is difficult to score retrospectively, since clinical judgment largely determines whether symptoms are considered typical for ACS. This might explain why a relatively large number of patients in our study was assigned to the low risk group and the event rate in this group was relatively high.

Conclusion

This study shows that there is no significant difference in overall performance and in negative predictive value of a low HEART score between Caucasian, Chinese, Indian and Malay patients presenting to the ED with symptoms suggestive of ACS. The occurrence of MACE within six weeks after presentation in the low risk category in our study was higher than reported in other studies of the HEART score's performance, possibly due to the retrospective design. Prospective studies are warranted to demonstrate the safety of early discharge of patients in the low risk category.

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Conflict of interest

The authors declare that there is no conflict of interest.

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