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A prospective validation of the HEART score for chest pain patients at the emergency department ☆

B.E. Backus [a,b,*], A.J. Six [c], J.C. Kelder [d], M.A.R. Bosschaert [d], E.G. Mast [e], A. Mosterd [f], R.F. Veldkamp [g], A.J. Wardeh [h], R. Tio [i], R. Braam [j], S.H.J. Monnink [k], R. van Tooren [e], T.P. Mast [l], F. van den Akker [l], M.J.M. Cramer [a], J.M. Poldervaart [m], A.W. Hoes [m], P.A. Doevendans [a]

[a] Department of Cardiology, University Medical Center, Utrecht, The Netherlands
[b] Department of Emergency Medicine, Albert Schweitzer Hospital, Dordrecht, The Netherlands
[c] Department of Cardiology, Zuwe Hofpoort Hospital, Woerden, The Netherlands
[d] Department of R&D Cardiology, St Antonius Hospital Nieuwegein, The Netherlands
[e] Department of Cardiology, St Antonius Hospital Nieuwegein, The Netherlands
[f] Department of Cardiology, Meander Medisch Centrum, Amersfoort, The Netherlands
[g] Department of Cardiology, Medisch Centrum Haaglanden, Leidschendam, The Netherlands
[h] Department of Cardiology, Medisch Centrum Haaglanden, Den Haag, The Netherlands
[i] Department of Cardiology, Universitair Medisch Centrum, Groningen, The Netherlands
[j] Department of Cardiology, Gelre Hospital, Apeldoorn, The Netherlands
[k] Department of Cardiology, Reinier de Graaf Gasthuis, Delft, The Netherlands
[l] Utrecht University, Utrecht, The Netherlands
[m] Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, The Netherlands

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ABSTRACT

Background: The focus of the diagnostic process in chest pain patients at the emergency department is to identify both low and high risk patients for an acute coronary syndrome (ACS). The HEART score was designed to facilitate this process. This study is a prospective validation of the HEART score.
Methods: A total of 2440 unselected patients presented with chest pain at the cardiac emergency department of ten participating hospitals in The Netherlands. The HEART score was assessed as soon as the first lab results and ECG were obtained. Primary endpoint was the occurrence of major adverse cardiac events (MACE) within 6 weeks.
Secondary endpoints were (i) the occurrence of AMI and death, (ii) ACS and (iii) the performance of a coronary angiogram. The performance of the HEART score was compared with the TIMI and GRACE scores.
Results: Low HEART scores (values 0–3) were calculated in 36.4% of the patients. MACE occurred in 1.7%. In patients with HEART scores 4–6, MACE was diagnosed in 16.6%. In patients with high HEART scores (values 7–10), MACE occurred in 50.1%. The c-statistic of the HEART score (0.83) is significantly higher than the c-statistic of TIMI (0.75)and GRACE (0.70) respectively ($p<0.0001$).
Conclusion: The HEART score provides the clinician with a quick and reliable predictor of outcome, without computer-required calculating. Low HEART scores (0–3), exclude short-term MACE with >98% certainty. In these patients one might consider reserved policies. In patients with high HEART scores (7–10) the high risk of MACE may indicate more aggressive policies.

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1. Introduction

Chest pain is the most common reason for admitting patients to the cardiac emergency department [1,2]. The first challenge in these patients is to identify those with acute coronary syndrome (ACS). This diagnostic process should be quick and efficient, since the prognosis improves dramatically when ACS patients receive targeted treatment as early as possible [3]. In today's practice, approximately 80% of chest pain patients have no clear ACS at presentation [4]. Clinicians tend to postpone the decision making process and to admit these patients for clinical observation, meanwhile treating the patients as an ACS. Consequently, over diagnosis and unnecessary treatment are common, resulting in redundant patient burden and high cost. In order to improve risk stratification of all cause chest patients at the emergency department and to place relative arguments for ACS into perspective, we designed the HEART score (Table 1).

☆ All authors mentioned above take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.
E-mail addresses: backus@heartscore.nl (B.E. Backus), six@heartscore.nl (A.J. Six).

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Table 1
The HEART score for chest pain patients at the emergency department.

History	Highly suspicious	2
(=anamnesis)	Moderately suspicious	1
	Slightly or non-suspicious	0
ECG	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
Total		

The HEART score is composed of 5 components: history, electrocardiogram (ECG), age, risk factors and troponin. For each component 0, 1 or 2 points is given (see methods for further details).

HEART was not developed from a database as modern scores often are. The HEART score was based on clinical experience and medical literature and designed to be as easy to use as the Apgar score for newborns [5]. HEART is an acronym of its components: History, ECG, Age, Risk factors and Troponin. Each of these may be scored with 0, 1 or 2 points. We retrospectively evaluated the HEART score in two smaller studies and obtained promising results [6,7]. This resulted in the prospective study in 2440 patients at 10 sites described in this paper. We compared the performance of the HEART score with other scoring systems, such as TIMI [8] and GRACE [9–11], although both have been designed for risk stratification of patients with proven ACS and not for the chest pain population at the emergency department.

2. Methods

2.1. Participants

This study was performed at ten hospitals in the Netherlands. Participating hospitals and numbers of included patients are listed in Appendix A. Any patient admitted to the (cardiac) emergency department due to chest pain irrespective of age, pre-hospital suspicions and previous medical treatment was eligible. Patients presenting with only dyspnea or palpitations were not included. Only patients presenting to the emergency department were eligible for the study. Typically, patients with chest pain and significant ST segment elevations on the ECG during transportation in the ambulance were immediately taken to the nearest available coronary intervention room in the area and, consequently, not presented at the emergency department. Therefore, patients with ST-elevation acute myocardial infarction (STEMI) were only exceptionally included in this study. The ethics committees of all participating hospitals approved the study. As this was an observational non-intervention study, informed consent procedures were waived. However, patients were informed of the registration of data and the follow up policy.

2.2. Data acquisition and management

Emergency department residents of participating hospitals were instructed carefully about the admission Case Report Form (CRF) and interpretation of the elements of patient history. The resident entered the initial patient data in writing on the admission CRF, upon arrival of the patient. The CRF consisted of separate entries for classical elements of patient history, cardiovascular risk factors, medication, physical examination and past medical history.

Laboratory values, including troponin I or T levels, were collected throughout the study period, starting with the moment of admission and typically repeated with 6 h intervals. According to the original study design the measured troponin values were interpreted according to local lab standards and reference values (see Appendix A). Only the troponin value of the first blood sample was used for the HEART score calculation. High sensitive troponin was not used at any participating hospital at the time of the study conduct.

A copy of the admission ECG was added to the study files. The ECG was blindly reviewed and classified afterwards by independent, experienced cardiologists, according to the Minnesota criteria [12]. In case of disagreement, a third cardiologist was consulted. A secured web based database was built for this study. An algorithm was devised to calculate the TIMI [8], GRACE [9–11] and HEART [6,7] scores automatically from the admission data, without interpretations by the investigators.

2.3. HEART score criteria

The HEART score was calculated on admission data only. Data acquired more than 1 h after presentation were ignored for score calculations.

For specific explanation of each HEART element, please see previous publications [6,7].

2.4. Follow-up

Follow up data were retrieved from digital and written patient records, including discharge letters, revascularization reports and any other relevant documentation.

In a few cases where follow-up data were not available from hospital records, the patient or their general practitioner was called to obtain information on their condition, hospital admissions, myocardial infarction and revascularization.

2.5. Outcomes

The diagnosis of acute myocardial infarction (AMI) was made according the applicable guidelines when the protocol was written, the joint ESC-ACCF-AHA-WHF task force for the redefinition of myocardial infarction [13], and consisted of a rise and fall of troponin values with at least one value above the 99th percentile of the upper reference limit together with evidence of myocardial ischemia. Within the diagnosis of AMI, distinction was made between either: ST-elevation myocardial infarction (STEMI), defined as a syndrome consisting of a rise and fall of troponin values as described above, typical patient history and transient ST segment elevations on the consecutive 12 lead ECGs, or non ST-elevation myocardial infarction (NSTEMI), defined as a syndrome consisting of a rise and fall of troponin values as described above, typical patient history and persistent or transient ST-segment depression or T-wave inversion, flat T-waves, pseudo-normalization of T-waves, or no changes at presentation.

In case of rises of troponin levels without evidence of myocardial ischemia or in case of non-availability of data the case was discussed in the adjudication committee where a final diagnosis was made according to the guidelines [3,13,14].

Percutaneous coronary intervention (PCI) was defined as any therapeutic catheter intervention in the coronary arteries. Coronary artery bypass graft (CABG) surgery was defined as any cardiac surgery in which coronary arteries were operated on.

The primary endpoint in this study was the occurrence of a major adverse cardiac event (MACE), within six weeks of initial presentation. MACE consists of: AMI, PCI, CABG, coronary angiography revealing procedurally correctable stenosis managed conservatively, and death due to any cause.

Coronary angiography revealing procedurally correctable stenosis managed conservatively was defined as significant coronary stenosis thought to be the cause of the chest pain, but revascularization was withheld for reasons of co-morbidity or risk of complications.

2.6. Secondary endpoints

Secondary endpoints were: (i) the six-week occurrence of AMI and death, (ii) the diagnosis of ACS within three months after presentation. The spectrum of ACS was described according to the definitions in the guideline for non-ST-segment elevation acute coronary syndrome [3,14] and consisted of: definite ACS, defined as: STEMI or NSTEMI (as defined above), or suspected ACS, defined as: likely to be an ACS based on typical patient history consistent with unstable angina and/or ST segment depression or T wave inversion or significant stenosis at coronary angiography, but without a rise of troponin levels, (iii) the performance of coronary angiography within three months after presentation.

2.7. Statistical analysis

Statistical analysis was performed with R (Version 2.9; The R foundation for Statistical Computing, Vienna, Austria) [15]. Descriptive statistics are given as average +/− SD, percentage or Kaplan–Meier cumulative event-free curve. Differences between groups were assessed by means of the Student's t-test when normally distributed. For scalar data we used the Fisher's exact test, or for ordinal data the Cochran–Armitage Trend Test.

The probability of reaching an endpoint was calculated as the percentage of cases with an endpoint within a given category. The area under the receiver operator characteristic curve (c-statistic) was computed in order to give a measure of diagnostic discriminative strength, combining sensitivity and specificity, especially for non-binomial variables. The DeLong's test was used for testing two correlated ROC curves. Statistical significance was defined as $p<0.05$ two-sided.

3. Results

3.1. Study population

The patient inclusion period lasted from October 2008 to November 2009. The patient flow in the HEART study is given in Fig. 1. A total of 2440 patients were included. Seven patients (0.3%) were non-evaluable due to invalid data on admission. In another 45 cases (1.8%)

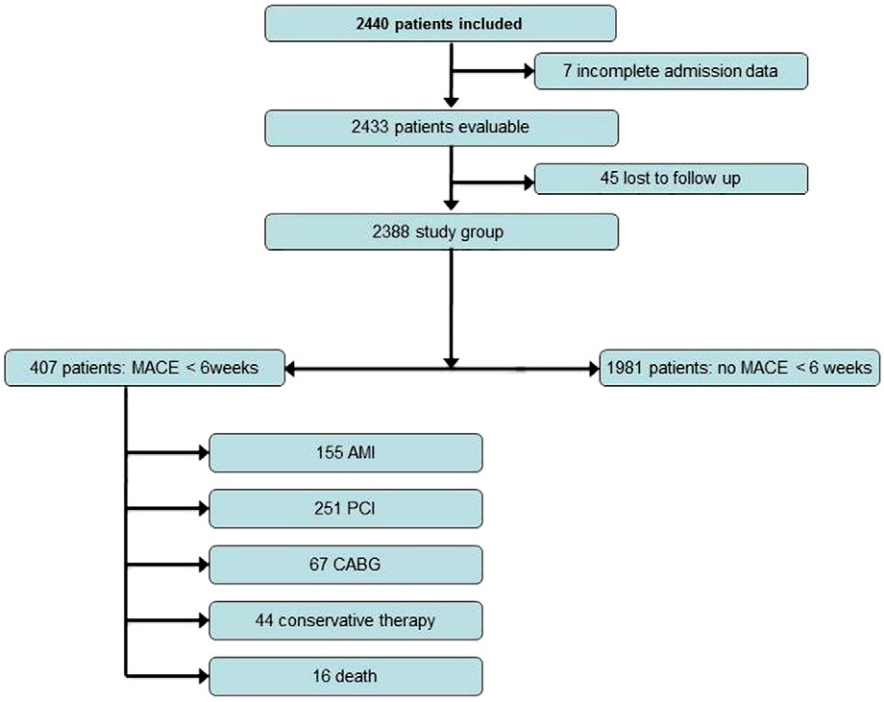

Fig. 1. Patient flow in the HEART score validation study. AMI = acute myocardial infarction. CABG = coronary artery bypass graft. PCI = percutaneous coronary intervention. MACE = major adverse coronary events.

the 6-week follow up was incomplete. The study population consisted of the remainder of 2388 patients with a follow up duration of 222 +/− 127 days (mean +/− SD). The total follow up duration of the entire study group was 1449 patient years. Patient characteristics of the study group are presented in Table 2.

3.2. Primary end points

Of a total of 2388 patients 407 (17.0%) were diagnosed with MACE within 6 weeks: AMI was diagnosed in 155 patients (6.4%), 251 patients (10.5%) underwent PCI, 67 patients (2.8%) had a CABG and 44 patients (1.8%) had coronary angiography revealing procedurally correctable stenosis managed conservatively. Sixteen patients (0.7%) died within 6 weeks after presentation. Thirteen patients died of a cardiac cause: 1 patient in the low-risk HEART group, 5 in the intermediate-risk HEART group and 7 in the high-risk HEART group. Three of these 16 patients died due to non-cardiovascular causes. Altogether, 533 MACE occurred in 407 patients: an average of 1.30 events/MACE patient.

Table 2
Patient characteristics.

	N	SD	%
Study group	2388		100
Mean age	60.6	15.4	
Male gender	1372		57.5
Diabetes mellitus	444		18.6
Smoker	779		32.7
Hypercholesterolemia	856		35.8
Hypertension	1034		43.3
Family history	866		36.3
Obesity	582		24.4
Mean systolic blood pressure	141.4	24.3	
Mean diastolic blood pressure	78.1	21.9	
History of AMI	379		15.9
History of CABG	243		10.2
History of PCI	510		21.4
History of stroke	112		4.7
History of peripheral arterial disease	110		4.6

AMI = acute myocardial infarction. CABG = coronary artery bypass graft. PCI = percutaneous coronary intervention.

3.3. Diagnosis at admission

On admission, the 2388 patients that were analyzed were diagnosed as follows:

419 (17.5%) acute coronary syndrome, 144 (6.0%) AMI of which 2 died at the ED, 230 (9.6%) stable angina, 68 (2.8%) rhythm, 90 (3.8%) other cardiac diseases, 106 (4.4%) gastro-esophagitis, 347 (14.5%) other non-cardiac diagnoses, 984 (41.2%) with atypical/undifferentiated chest pain.

Eventually 142/155 AMIs (91.6%) were diagnosed at presentation: 110 NSTEMI, 18 STEMI and 14 recent AMI (onset 12–48 h before presentation). Mean duration of time to AMI was 0.3 days (range 0–17). 165/407 (40.8%) of MACE were reached upon presentation. Mean duration of time to MACE was 5.6 days (range 0–41). Mean time to PCI 6.9 days (0–41), mean time to CABG 12.1 (1–39) days and mean time to death 13.6 days (1–33). The time elapsed between arrival of the patient and the occurrence of MACE is given in Fig. 2.

3.4. The HEART score

The numerical distribution of the HEART score's five elements in the groups with or without endpoints is shown in Table 3.

The five elements of the HEART score differed significantly between the groups with and without MACE. The average HEART score was 3.96 +/− 2.0 in the non-MACE group and 6.54 +/− 1.7 in the MACE group.

The c-statistic of the HEART score in the entire study group was 0.83. The HEART score retained its discriminative ability in three relevant subgroups: in diabetics the event rate was 81/440 with a c-statistic of 0.78 (non-diabetic 0.84), in females (event rate 116/1016) the c-statistic was 0.83 (males 0.82) and in elderly over the age of 75 (event rate 101/490) the c-statistic was 0.73 (age ≤ 75 0.86).

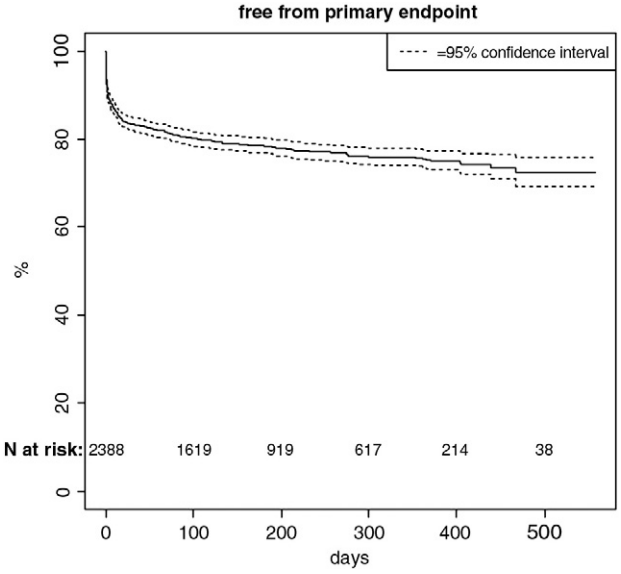

Fig. 2. Kaplan–Meier curves for the occurrence of major adverse cardiac events.

The c-statistic of troponin only was 0.70. With addition of the ECG the c-statistic improved significantly to a value 0.78, with a likelihood ration test p-value of <0.001. This combination of troponin plus ECG only had a significantly poorer performance as compared with the complete HEART score (p<0.001).

3.5. HEART, TIMI and GRACE scores

Average values of the HEART, TIMI and GRACE scores in groups with and without MACE are given in Table 4. All scores differed considerably between the group free from MACE and the group with MACE. Fig. 3 illustrates the relation between the scores (on the x-axis) and the risk of MACE within 6 weeks after initial presentation (on the y-axis).

Comparison of the c-statistics as represented in Table 4 shows a value of 0.83 for the HEART score, 0.75 for TIMI and 0.70 for GRACE. The HEART score performed significantly better (p<0.001) as compared with TIMI and GRACE.

3.6. Predictive values of low scores

The low risk boundaries for all scores were set at a risk of MACE<5%. In the group with TIMI scores of 0–1, which accounted for 34.0% of the study population, 23/811 (2.8%) had a MACE. The 14.0% of the patients who had GRACE scores 0–60 had MACE in 10/335 (2.9%) of the cases. The group with a low HEART score (values 0–3) represents 36.4% of the study population. Six-week MACE occurred in 15/870 (1.7%) of these patients. This included nine AMIs, nine PCI, three CABG and one death. This 20 year old male committed suicide, seven days after the index chest pain event.

Table 4
Average values of the three scores in patients with chest pain presenting at the emergency department in groups with and without MACE.

	Total study population	No MACE<6w n=1981	MACE<6w n=407	C-statistic	p value
HEART	4.4 (2.2)	3.96 (2.0)	6.54 (1.7)	0.83	<0.0001
TIMI	2.5 (1.7)	2.21 (1.6)	3.68 (1.4)	0.75	<0.0001
GRACE	99.9 (36.1)	95.5 (35.0)	121.2 (34.0)	0.70	<0.0001

Averages are given as mean (SD).

3.7. Predictive values of intermediate scores

The intermediate risk boundaries for all scores were set at a risk of MACE between 5 and 40%.In the group with TIMI scores of 2–5, which accounted for 62.7% of the study population, 350/1497 (23.4%) had a MACE. The 85.7% of the patients who had GRACE scores >60 had MACE in 389/2012 (19.3%) of the cases. The group with an intermediate HEART score (values 4–6) represents 46.1% of the study population. Six-week MACE occurred in 183/1101 (16.6%) of these patients.

3.8. Predictive values of high scores

Only the TIMI and HEART scores reached a high risk level, defined as a risk of MACE>40%. MACE occurred in 34/80 patients (42.5%) where TIMI scores were 6–7. The group with a high HEART score (7–10) represents 17.5% of the study population; six-week MACE occurred in 209/417 (50.1%) of those patients.

3.9. Secondary endpoints

A total of 164/2388 (6.9%) patients had an AMI (n=155) or died (n=16) within six weeks. The c-statistics for the occurrence of AMI or death of HEART, TIMI and GRACE are 0.82, 0.70 and 0.71 respectively (p<0.0001).

An ACS within three months after presentation was diagnosed in 536 patients (22.4%); 501 of these 536 ACS (93.4%) were already diagnosed during primary admission.

The c-statistics for the occurrence of ACS shows a value of 0.86 for the HEART score, 0.78 for TIMI and 0.72 for GRACE (p<0.0001).

Coronary angiography within three months was performed in 578 patients (24.2%). In 93 (16.2%) of these cases this diagnostic procedure was performed during primary admission. The results were: 58 (10.0%) normal coronaries, 104 (17.9%) non-significant stenosis, 44 (7.6%) significant stenosis with conservative treatment, 361 (62.4%) significant stenosis requiring revascularization and 11 (1.9%) were unclassified.

The HEART score was 3.9 +/− 2.0 in the group with no catheterization in the first three months and 6.0 +/− 1.8 in the group with a catheterization in the first three months (p<0.001).

4. Discussion

The use of the HEART score for chest pain patients at the emergency department provides the clinician with a reliable predictor of outcome,

Table 3
Number of patients in each element of the HEART score.

	No MACE<6w n=1981						MACE<6w n=407						p value for trend
Points	0		1		2		0		1		2		
History	902	(45.5%)	616	(31.1%)	462	(23.3%)	35	(8.6%)	110	(27.0%)	262	(64.4%)	p=0.000
ECG	1323	(66.8%)	380	(19.2%)	278	(14.0%)	147	(36.1%)	86	(21.1%)	174	(42.8%)	p=0.000
Age	376	(19.0%)	862	(43.5%)	743	(37.5%)	15	(3.7%)	171	(42.0%)	221	(54.3%)	p=0.000
Risk Factors	221	(11.2%)	729	(36.8%)	1031	(52.0%)	20	(4.9%)	116	(28.5%)	271	(66.6%)	p=0.000
Troponin	1825	(92.1%)	89	(4.5%)	67	(3.4%)	218	(53.6%)	55	(13.5%)	134	(32.9%)	p=0.000

MACE = Major Adverse Cardiac Events. ECG = electrocardiogram.

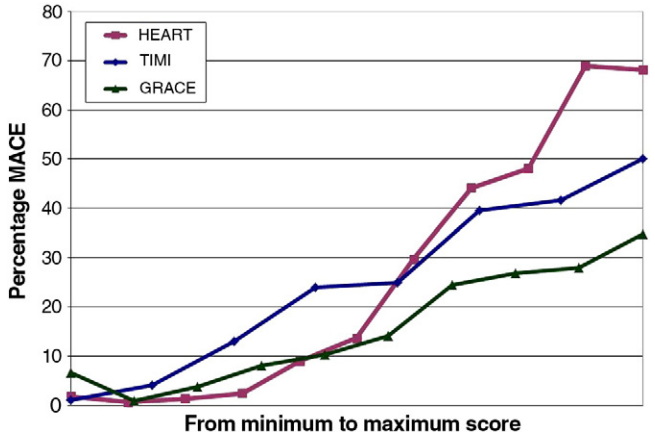

Fig. 3. Probability of reaching a MACE related to the three risk scores. Only for the purpose of comparing graphs we divided the TIMI and GRACE scores in deciles in order to achieve the same distribution as the HEART score on the x-axis. All other computations were made with the original values.

very soon after the arrival of the patient, based on already available clinical data and without computer-required calculating.

The favorable results of this large prospective validation study confirm our previous retrospective evaluation studies [6,7]. A c-statistic of 0.83 for the HEART score indicates a good to excellent ability to discriminate all cause chest pain patients at the emergency department for their risk of MACE. Each element of the HEART score adds value significantly in statistical terms. The HEART score facilitates communication, and it can be used as a guidance to correctly place patients into low, intermediate and high risk groups. In addition, it closely follows clinical thinking. Less complex guidelines for clinical practice can be formulated when advised policies are based on a HEART score stratification.

Several risk scores for ACS have been published [16]. The most reputable of these are the TIMI [8] and GRACE [9–11] scores. Both were developed for risk stratification of patients admitted to the coronary care unit with an ACS, and may take observations at arbitrarily chosen points in time into account. Although not designed for this purpose, these scores are commonly applied and are recommended in European and American guidelines[3] at the emergency department for the whole range of chest pain patients, both in practice and in science [1,4,17,18]. Different from this, the HEART score was specifically designed for the much broader chest pain population at the emergency department. HEART is based on admission data only, typically complete within 1 h. This score is now validated in a prospective manner.

Neither the TIMI nor the GRACE score appreciates the specificity of patient history (anamnesis), even though clinicians rely heavily on this and guidelines advise to use patient history for making a diagnosis [3,14,19,20]. Some other scores, such as PURSUIT [21], FRISC [22] and SRI [23] are less specific and to some extent outdated, as troponin levels are not part of it; therefore, these are not reported in this paper.

The GRACE score is a well-validated prediction model of death in ACS patients. A practical disadvantage of the GRACE score is that it can only be calculated by means of a computer. Although it was not designed for making or excluding the ACS diagnosis in an unselected chest pain population, we applied the GRACE score in the chest pain setting at the emergency department. We found that the points given for 'age' accounted for 50.0 +/− 18.3% of the total number of GRACE points. Not surprisingly, higher age is related to higher mortality rates. The predominantly age based GRACE score assesses the risk of death of patients in the coronary care unit (CCU). Whether the GRACE score helps the clinician to choose the right treatment option in the ED is questionable.

The TIMI score, which was designed about 15 years ago for identifying high-risk ACS patients who benefit most from aggressive anti-clotting agents, is relatively easy to calculate. However, it is quite rough as it allows only binary choices, thus ignoring the fact that many variables have a 'grey area.' Than and co-investigators applied the TIMI score for the broad chest pain population at the cardiac emergency departments of 14 hospitals in 9 countries in the Asia-Pacific region [4]. In their prospective multi-center study 9.8% of the patients had a TIMI score = 0 assessed after 2 h and those patients had a 4-week risk of MACE of 0.9%. In our study at 10 sites in the Netherlands 36.4% of the patients had HEART scores 0–3 within 1 h, indicating a 6-week risk of MACE of 1.7%. Although the comparison is hampered to some extent by differences in end point definitions, we believe that the approach in the Pacific study may benefit significantly from the replacement of the TIMI score by the HEART score [24].

When comparing the GRACE, TIMI and HEART in terms of predictive values for low- and high-risk, and the c-statistics, we conclude that the HEART score is the best score for the group of all cause chest pain patients at the emergency department and that GRACE and TIMI should be reserved for ACS patients in the CCU.

As the purpose of the study was to validate the HEART score in daily practice, the study protocol stipulated to use all measurements, reference values and interpretations according to local standards. This held true for the cut off values of troponin measurements. In practice this resulted in differences in cut-off values for the same test in between participating sites in some cases. Consequently, some patients with slightly elevated troponins may have received somewhat different classifications depending on the hospital where they were enrolled. However, this influence is minimal and we considered it not appropriate to make retrospective changes in the study protocol.

Other than in randomized trials, loss to follow up is an inevitable reality in an observational study at the emergency department: occasional visitors occur and they are sometimes hard to track afterwards. Our clinical review of the characteristics showed that the 45 patients lost to follow up (1.8% of the entire study population) were relatively young visitors with low likelihood of disease.

The HEART score gives immediate direction to the treatment policy. Over one third of our patients had HEART scores 0–3, with a risk of MACE of 1.7%. This observation may be a firm basis to omit redundant diagnostic and treatment steps and move into the direction of quick discharge. This issue was also addressed recently by Mahler and coworkers [25]. In a retrospective study in low-risk chest pain patients from North Carolina (USA) they found a 0.6% risk of MACE in 904 patients with HEART scores ≤ 3. The authors state "… the HEART score could substantially reduce cardiac testing in a population with low pretest probability of ACS". These conclusions were further supported by their other recent article in this journal, where HEART with 0 and 3 h serial troponin after presentation "identified 20% (95% CI 18–23%) for early discharge with 99% (95% CI 97–100%) sensitivity for ACS. The HEART score had a net reclassification improvement of 10% (95% CI 8–12%) versus unstructured assessment and 19% (95% CI 17–21%) versus the North American Chest Pain Rule" [26,27].

The group of high-risk patients (HEART scores 7–10) in our study concerns 17.5% of the entire study population. With a risk of MACE of 50.1% in these patients quick coronary intervention should be warranted according to studies by others [16,28–30]. Obviously, the early direction given by the HEART score should not prevent the treating physicians from further clinical thinking. In many patients the observation should continue for some more hours, with repeated troponins and ECGs, in order to confirm initial findings.

In conclusion, the HEART score for chest pain patients at the emergency department provides the clinician with a quick and reliable predictor of outcome shortly after arrival of the patient, without computer-required calculating. Low HEART scores (0–3), occurring in one third of the patients, exclude short-term MACE with > 98% certainty. In these patients one might consider reserved policies. In patients with high HEART scores (7–10) the high risk of MACE may indicate more aggressive policies.

Appendix A

Table A1
Participating hospitals, principal investigators and numbers of patients in the study

Hospital	Investigators	Patients
Universitair Medisch Centrum (Groningen)	René Tio, Iwan van der Horst, Marco Willemsen	464
St Antonius Ziekenhuis (Nieuwegein)	Gijs Mast, Thijs Plokker	455
Meander Medisch Centrum Amersfoort	Arend Mosterd, Jeff Senden	381
Gelre Ziekenhuis (Apeldoorn)	Richard Braam, Bjorn Groenemeijer, Luc Cozijnsen	257
Medisch Centrum Haaglanden (Den Haag)	Alexander Wardeh, Wouter Tietge	218
Reinier de Graaf Groep (Delft)	Stefan Monnink, Eelko Ronner	170
Medisch Centrum Haaglanden (Leidschendam)	Rolf Veldkamp	183
Antonius Ziekenhuis locatie Oudenrijn (Utrecht)	Rob van Tooren	118
Universitair Medisch Centrum (Utrecht)	Pieter Doevendans, Maarten Jan Cramer	106
Zuwe Hofpoort Ziekenhuis (Woerden)	Jacob Six, Bert Brinkman, Jan Slob and Bettina Massaar-Hagen	81
Total		2433

Table A2
Reference values troponin

Hospital	Troponin T or I	Reference value	Type of kit	99th percentile
1	T	0.015	Roche	0.014
2	T	0.015	Roche	0.014
3	I	0.040	Beckmann-Coulter	0.04
4	I	0.050	Abbott	0.028
5	I	0.100	Beckmann-Coulter	0.04
6	I	0.030	Beckmann-Coulter	0.04
7	I	0.030	Abbott	0.028
8	T	0.010	Roche	0.01
9	T	0.010	Roche	0.01
10	T	0.010	Roche	0.01

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