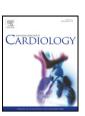
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ABSTRACT

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).

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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).

 $[\]dot{\vec{x}}$ All authors mentioned above take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1The 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	\geq 3 risk factors, <i>or</i> history of atherosclerotic disease	2
	1 or 2 risk factors	1
	No risk factors known	0
Troponin	≥3× normal limit	2
	$>1-<3\times$ 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%)

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