

# Chest Pain in the Emergency Room

## A Multicenter Validation of the HEART Score

Barbra E. Backus, MD,\* A. Jacob Six, MD, PhD,† Johannes C. Kelder, MD,‡ Thomas P. Mast,§  
Frederieke van den Akker,§ E. Gijis Mast, MD,¶ Stefan H. J. Monnink, MD, PhD,|| Rob M. van Tooren, MD,\*\*  
and Pieter A. F. M. Doevendans, MD, PhD\*

**Objective:** Decision-making in chest pain patients is hampered by poor diagnostic power of patient's history, electrocardiogram, age, risk factors, and troponin. Each of these findings may be qualified with 0, 1, or 2 points. Together they compose the HEART score. We tested the hypothesis that the HEART score predicts major adverse cardiac events.

**Design:** Retrospective multicenter analysis in patients presenting at the cardiology emergency room.

**Setting:** Patient inclusion between January 1 and March 31, 2006.

**Patients:** A total of 2161 patients were admitted, of which 910 patients (42%) presented with chest pain. Analysis was performed in 880 cases (96.7%).

**Main Outcome Measures:** The primary endpoint was a composite of acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery and death, within 6 weeks after presentation, together called major adverse cardiac events.

**Results:** A total of 158 patients (17.95%) reached the primary endpoint. Ninety-two patients had an acute myocardial infarction (10.45%), 82 a percutaneous coronary intervention (9.32%), 36 a coronary artery bypass graft (4.09%), and 13 died (1.48%). Of 303 patients with HEART score 0 to 3, three (0.99%) had an endpoint. In 413 patients with HEART score 4 to 6, 48 cases (11.6%) reached an endpoint. In case of a HEART score of 7 to 10, an endpoint was reached in 107/164 cases (65.2%).

**Conclusions:** The HEART score helps in making accurate diagnostic and therapeutic decisions without the use of radiation or invasive procedures. The HEART score is an easy, quick, and reliable predictor of outcome in chest pain patients and can be used for triage.

**Key Words:** acute coronary syndromes, risk score, chest pain, emergency room

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Chest pain is one of the most common reasons for which patients are admitted to the emergency room. A differential diagnosis must be made between an acute coronary syndrome (ACS) and other diagnoses. The diagnosis of non-ST-elevation-ACS (nSTE-ACS), often called unstable angina or pending infarction, typically causes uncertainty as this is not a strictly defined, exclusive diagnosis.<sup>1–3</sup>

From the \*Department of Cardiology, Universitair Medisch Centrum, Utrecht, Nieuwegein, The Netherlands; †Department of Cardiology, Hofpoort Ziekenhuis, Woerden, The Netherlands; ‡Department of R&D Cardiology, St Antonius Ziekenhuis, Nieuwegein, The Netherlands; §Utrecht University, Utrecht, The Netherlands; ¶Department of Cardiology, St Antonius Ziekenhuis, Nieuwegein, The Netherlands; ||Department of Cardiology, Reinier de Graaf Groep, Delft, The Netherlands; and \*\*Department of Cardiology, MESOS-Antonius Ziekenhuis, Utrecht, The Netherlands.

Reprints: A. J. Six, MD, PhD, Hofpoort Ziekenhuis Woerden, Polanerbaan 2, 3447 GN Woerden, The Netherlands. E-mail: jacobsix@zonnet.nl

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Individual considerations are made in each patient. Various relative arguments play a role. A suspicious patient history may be reason enough to consider the diagnosis, but typically it is supported by other diagnostic elements such as electrocardiogram (ECG) abnormalities, advanced age, risk profile, and/or increased troponin levels. Each of these findings may be a separate, convincing argument for the diagnosis of ACS.

With this in mind, various parameters were combined into the HEART score. The acronym is an abbreviation of the words: History, ECG, Age, Risk factors, and Troponin. Each of these may be qualified with 0, 1, or 2 points. The composition of the HEART score is shown in Table 1.

In a pilot study of 122 patients, conducted at a single site, we tested the hypothesis that the HEART score predicts the short-term occurrence of myocardial infarction, revascularization, and death.<sup>4</sup> These outcomes are all adverse events typically related to an ACS, and therefore considered indirect proof of the diagnosis. The results were favorable. A HEART score  $\leq 3$  implied a chance of only 2.5% for reaching the end point, whereas in patients with a HEART score  $\geq 7$  this chance was 72.7%. As a result of these findings, we believed that this score was of potential use when making treatment decisions in chest pain patients in the emergency room. To confirm the findings of the pilot study and to validate the HEART score in various subgroups, we conducted a new retrospective study at 4 sites. In summary, we investigated the predictive value of early clinical findings for the final outcome.

## METHODS

This study was performed at 4 separate hospitals in the Netherlands. Three sites were community-based hospitals with 262 beds (Zuwe Hofpoort Ziekenhuis, Woerden, The Netherlands), 529 beds (MESOS, Utrecht, The Netherlands), and 881 beds (Reinier de Graaf Groep, Delft, The Netherlands) and 1 was an academic hospital (University Medical Center, Utrecht, The Netherlands) with 1042 beds.

## Inclusion Criteria

Inclusion criteria for this study included any patient admitted to the (cardiology) emergency room because of chest pain irrespective of age; prehospital assumptions; and previous medical treatment. In most cases, patients with chest pain and significant ST-segment elevations on the ECG during transportation in the ambulance were immediately taken to a coronary intervention room elsewhere. Consequently, most patients with ST-elevation myocardial infarction were not enrolled in the study.

## Data Acquisition

All admission data were retrieved from the hospital charts of the study patients. The same applies to follow-up data. In case there was no follow-up, either the patients or their General Practitioners were called to inform about their condition and check for possible hospital admissions, myocardial infarction, and revascularization at other medical centers.

**TABLE 1.** Composition of the HEART Score for Chest Pain Patients in the Emergency Room

HEART score for chest pain patients		
<b>H</b> istory	Highly suspicious	2
	Moderately suspicious	1
	Slightly suspicious	0
<b>E</b> CG	Significant ST-depression	2
	Non specific repolarization disturbance	1
	Normal	0
<b>A</b> ge	≥ 65 year	2
	45 – 65 year	1
	≤ 45 year	0
<b>R</b> isk factors	≥ 3 risk factors or history of atherosclerotic disease	2
	1 or 2 risk factors	1
	No risk factors known	0
<b>T</b> roponin	≥ 3x normal limit	2
	1-3x normal limit	1
	≤ normal limit	0
<b>Total</b>		

ECG indicates electrocardiogram.

## Scoring of Predictors

### History

For the purpose of this study, patient history was classified by at least 2 investigators on the basis of narration in the hospital charts in the emergency room, without regard for risk factors, ECGs, laboratory results, and later developments. In absence of specific elements in the patient history for coronary ischemia, the history was classified as nonspecific and granted 0 points. In case the patient history contained both nonspecific and suspicious elements, the history was classified moderately suspicious and assigned 1 point. In case the history contained mainly suspicious elements, such as middle- or left-sided, heavy chest pain, radiation, and/or relief of symptoms by sublingual nitrates, the history was classified highly suspicious and granted 2 points.

### Electrocardiogram

The ECG taken at the emergency room was reviewed and scored by 2 cardiologists. In case of a normal ECG according to Minnesota criteria,<sup>5</sup> 0 points were given. In case of repolarization abnormalities without significant ST-segment depression or elevation, 1 point was given. Also in case of the presence of a bundle branch block or pacemaker rhythm, typical abnormalities indicative of left ventricular hypertrophy, repolarization abnormalities probably caused by digoxin use, or in case of unchanged known repolarization disturbances, 1 point was given. In case of significant ST-segment depressions or elevations in absence of a bundle branch block, left ventricular hypertrophy, or the use of digoxin, 2 points were given.

In case there was disagreement in the scoring of History and/or ECG, a third opinion was taken to reach a conclusion.

### Age

Zero points were given if the patient was younger than 45 years at the time of admission, 1 point if the patient was 45 to 65 years, and 2 points if the patient was 65 years or older.

### Risk Factors

The number of risk factors for coronary artery disease present in the individual was counted. The following risk factors were taken into account: currently treated diabetes mellitus, current or recent (<90 days) smoker, diagnosed and/or treated hypertension, diagnosed hypercholesterolemia, family history of coronary artery disease, obesity (body mass index [BMI] >30), or a history of significant atherosclerosis (coronary revascularization, myocardial infarction, stroke, or peripheral arterial disease, irrespective of the risk factors for coronary artery disease). If the patient had no risk factors at all, 0 points were given. If the patient had 1 or 2 risk factors, 1 point was given. Two points were given if the patient had 3 or more risk factors, and also if the patient had a history of significant atherosclerosis.

### Troponin

Troponin T or I levels were measured according to local laboratory standards. If the Troponin T or I level on admission was below the threshold for positivity, 0 points were given. If the level was between 1 and 3 times the threshold for positivity, 1 point was given. If the level was higher than 3 times the threshold for positivity, 2 points were given.

### Other Definitions

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

An acute myocardial infarction (AMI) was defined as a syndrome consisting of typical chest pain, ECG changes, and rise of creatine phosphokinase and troponin serum levels. In case 1 of the 4 elements was absent or nonevaluable (eg, patients without chest pain or with a bundle branch block), the case was discussed in the adjudication committee.

### Primary Endpoints

The primary end point in this study was a composite of: AMI, PCI, CABG surgery, and death, all occurring within 6 weeks, together called major adverse cardiac events (MACE). These outcomes are typically related to an ACS, and therefore considered indirect proof of the diagnosis.

In the pilot study with 122 patients, all end points occurred within 3 months. Most occurred within 6 weeks.<sup>4</sup> MACE occurring within 6 weeks after an ACS were likely to be the result of the index ACS. In case of a MACE after 6 weeks, the causal connection becomes less evident. Therefore, a window of 6 weeks was chosen for the primary end point.

### Secondary Endpoints

Secondary endpoints were MACE after 6 weeks and coronary angiography.

### Statistics

Statistical analysis was performed with R (Version 2.9; The R foundation for Statistical Computing, Vienna, Austria).<sup>6</sup> Descriptive statistics are given as average ± Standard deviation (SD), percentage, or Kaplan-Meier cumulative event-free curve. Differences between groups were assessed by means of the Student *t* test when normally distributed; for scalar data we used the Fisher exact test or in case of ordinal data the Cochran-Armitage Trend Test. The probability of reaching an end point was calculated as the percentage of cases with an end point within a category. The area under the receiver-operator characteristic curve (c-statistic) was computed to give a measure of diagnostic discriminative strength, combining sensitivity and specificity, especially for nonbinomial variables. Statistical significance was defined as *P* < 0.05, 2-sided.

## RESULTS

During the study period, which lasted from January 1 to March 31 2006, a total of 2161 patients were admitted to the (cardiac) emergency rooms of the participating sites. Race was not routinely noted in the patient charts; in the geographic area of the hospitals the population is predominantly Caucasian. Data retrieved from hospital charts were almost complete, except from notes on the absence or presence of obesity, which were missing in a majority of cases. In case obesity was not mentioned, it was assumed the patient was unlikely to be morbidly obese.

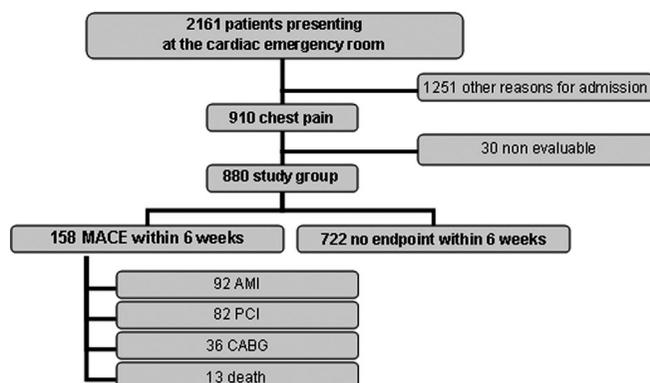
The main reasons for admission to the cardiac emergency room included chest pain (42.1%), palpitations or rhythm disturbances (16.8%), dyspnea or heart failure (13.4%), syncope (9.3%), or other/noncardiac complaints (18.2%). Chest pain was the main reason for admission in 910 patients (42.1%) (Fig. 1). Thirty cases (3.3%) were nonevaluable as the follow-up data were too limited. The group of excluded patients consisted mainly of young men (mean age, 44 ± 20) and had a mean HEART score of 2.1 ± 1.6. The study group consisted of the remaining 880 patients. Mean age was 61.9 ± 15.7 years. The male/female distribution was 500/380. Patient characteristics are presented in Table 2.

### Follow-up

In 880 patients (96.7%), long term follow-up data are available, with total duration of 1681 patient years and a mean duration of 697 ± 265 days. As mentioned earlier, follow-up in 30 cases is absent. Their data are not part of the group comparisons of the study.

### Primary Endpoints

A total of 158 patients (17.95%) had a MACE within 6 weeks: an AMI was diagnosed in 92 patients (10.45%), 82 patients (9.32%) underwent PCI, and 36 patients (4.09%) had CABG. One patient underwent both PCI and CABG. The mortality was 13



**FIGURE 1.** MACE indicates major adverse cardiac events; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

**TABLE 2.** Patient Characteristics

	N	%
Age (mean [SD])	61.3	(15.7)
Male gender	521	57.3
Diabetes mellitus	175	19.9
Smoking	257	29.2
Hypercholesterolemia	229	26.0
Hypertension	321	36.5
Family history	281	31.9
Systolic blood pressure (mean [SD])	148.1	(26.5)
Diastolic blood pressure (mean [SD])	83.8	(14.9)
History of AMI	180	20.5
History of CABG	73	8.3
History of PCI	118	13.4
History of stroke	85	9.7
History of peripheral arterial disease	47	5.2
Salicylates	319	36.2
HEART score (mean [SD])	4.51	(2.24)

SD indicates standard deviation; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

(1.48%). Altogether, 223 major events occurred in 158 patients, an average of 1.4 events/MACE patient.

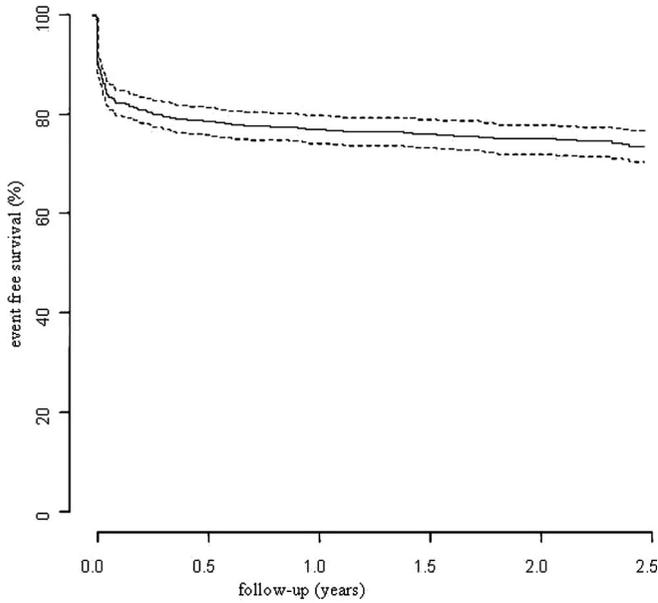
### Time Frame of Endpoints

The graph for survival without AMI and revascularization is displayed in Figure 2.

### Risk Factors Leading to MACE

A comparison was made of the risk profile in patient groups with and without a MACE. Independent predictors of MACE included age (*P* = 0.0035), male gender (*P* < 0.0001), diabetes mellitus (*P* = 0.0181), hypertension (*P* = 0.0474), history of myocardial infarction (*P* = 0.0149), use of aspirin (*P* = 0.0369), and the HEART score (*P* << 0.0001).

The 5 predefined elements of the HEART score for chest pain patients and the occurrence of end points were evaluated. History, ECG, and troponin were independent predictors of the combined end point (*P* < 0.0001). The average HEART score in the no end point group was 3.8 ± 1.9 and in the patients with at least one end point was 7.2 ± 1.7 (*P* < 0.0001). The c-statistic



**FIGURE 2.** Patients free from death, acute myocardial infarction, PCI, and CABG. Kaplan-Meier curve with 95% confidence interval.

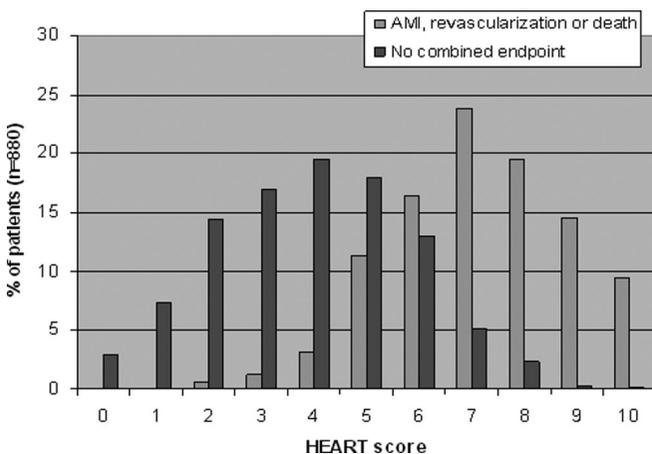
for the HEART score was 0.897, which indicates a good to excellent ability to discriminate.

**Distribution**

The distribution of HEART scores in patients with or without the combined end point of AMI, revascularization, or death is shown in Figure 3. The HEART score follows Gaussian distribution in both groups.

**HEART Score at the ER**

The HEART score helps to stratify chest pain patients in the emergency room into low, intermediate, and high likelihood groups for clinically important irreversible adverse cardiac events. Three of the 303 patients (0.99%) with HEART score between 0 and 3 points had a MACE. Of the 413 patients with HEART score between 4 and



**FIGURE 3.** Percentage of patients in each HEART score in groups without (darker bar) and with (lighter bar) the combined endpoint of AMI, revascularization or death.

6 points (48 [11.6%]) had a MACE. In case of a HEART score of 7 to 10 points, 107 of 164 patients (65.2%) had a MACE.

Figure 4 illustrates an almost perfect S-shape relation between the HEART score and the probability of reaching an end point (*P* for trend <0.001). The relation was close to linear between HEART scores 3 to 9.

**Secondary Endpoints**

MACE after 6 weeks and within the first year occurred in 54 patients: 5 had an AMI, 19 had a PCI, 11 had a CABG, and 24 patients died. The HEART score was  $4.5 \pm 2.2$  in the group with no MACE after 6 weeks and within the first year, and  $6.3 \pm 1.8$  in the group with MACE after 6 weeks and within the first year.

Kaplan-Meier estimates of the coronary angiography rate within the first 6 weeks was 17.8% and within the first year 23.0%. The HEART score was  $3.8 \pm 1.9$  in the group with no catheterization in the first 6 weeks and  $6.9 \pm 1.8$  in the group with a catheterization in the first 6 weeks (*P* < 0.001).

**SUBGROUPS**

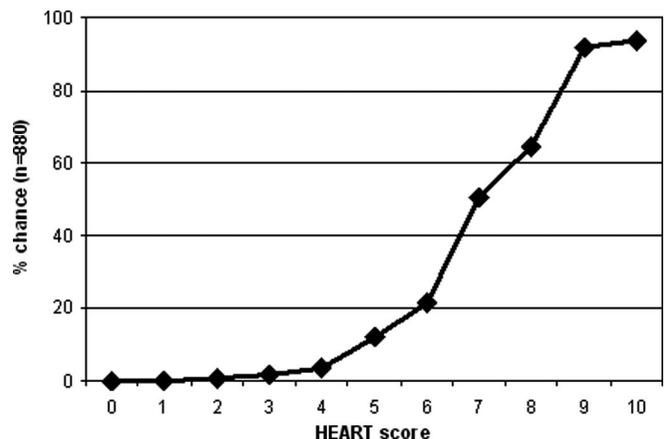
We have computed the c-statistic of the HEART score in 3 relevant subgroups with regard to the diagnosis of acute coronary syndromes. In patients with diabetes, the event rate was 38/175 and the HEART score retained its discriminative ability, with the c-statistic being 0.909. In women (event rate 41/380) the c-statistic was also 0.909. In the elderly over the age of 80 years (event rate 19/110), the c-statistic was 0.872.

**DISCUSSION**

**Definition of Acute Coronary Syndrome**

Chest pain patients at the emergency ward create uncertainty for treating physicians. The decision to discharge a patient without a diagnosis causes insecurity. A missed diagnosis may soon result in a seriously life-threatening outcome, whereas unnecessary hospital admissions may result in overtreatment, with all possible side-effect and higher medical cost.

The diagnosis of nSTE-ACS, often called unstable angina, may be easy to confirm but is often hard to rule out. This thesis is illustrated by the inclusion criteria for the major treatment trials in unstable angina or ACS, where patients were randomized only after a confirmed diagnosis by means of typical ECG changes and/or elevated troponin levels. Unconfirmed cases of ACS were excluded in such trials despite the real possibility that in fact such chest pain



**FIGURE 4.** Probability of reaching a MACE in each HEART category.

patients, without additional abnormalities, did suffer from ACS. Surprisingly, one of the most common diagnoses in hospital medicine has neither absolute nor widely accepted criteria. This is also reflected in the current American and European guidelines.<sup>7,8</sup>

### HEART Score

Challenged by a lack of exact definitions or criteria for nSTE-ACS, we attempted to define an easy-to-use, common sense-based policy for both junior and senior clinicians. The starting question was as follows: What, in practice, are the important decision-making factors? These are History, ECG, Age, Risk factors, and Troponin. Similar to the Apgar score,<sup>9</sup> which is used world-wide to stratify newborns in low- and high-risk categories, these 5 factors can be combined into the HEART score for chest pain patients. Our experience is that the HEART score for individual patients can be calculated without a calculator, or even pen and paper, by everyone from a young resident to an experienced cardiologist.

Unfortunately, a gold standard for nSTE-ACS is lacking. Therefore, we calculated the relation between HEART scores and the occurrence of adverse outcomes, which is by nature a heavy underestimation of the occurrence of nSTE-ACS. In absence of strict definitions of ACS, we used MACE as the primary end point. As shown in Figure 4, the relation between the HEART score and the occurrence of MACE within 6 weeks is reflected by a nearly perfect S-shaped curve. This enables the assessment of an individual patient's chances.

### Elements of the HEART Score

Each of the HEART score elements has a certain predictive value toward the occurrence of end points. Every clinician knows from experience that he or she can rely to some extent on a carefully taken history. Unfortunately, previously developed risk scores, such as the PURSUIT,<sup>10</sup> GRACE,<sup>11,12</sup> and TIMI<sup>13</sup> scores, did not classify the patient history. The HEART study classified a patient's history numerically. A nonsuspicious patient history ( $H = 0$ ) has a negative predictive value of 95.8% (296/309), whereas a suspicious patient history ( $H = 2$ ) goes with a positive predictive value of only 44.4% (107/241). The value of History is similar to the elements ECG, age, and risk factors in the sense of high-sensitivity counterbalances by low-specificity. In contrast, troponin has a high specificity. However, the single troponin measurement on admission lacks the necessary sensitivity to function as a sole basis for taking clinical decisions.

### HEART Versus Other Scoring Methods

Several other risk scores for ACS have been published. Most highly regarded are the PURSUIT,<sup>10</sup> GRACE,<sup>11,12</sup> and TIMI<sup>13</sup> scores, which were compared by De Araújo Gonçalves et al<sup>14</sup> and Yan et al.<sup>15</sup> Despite the firm scientific foundations and the guideline recommendations of these 3 scoring systems, none is widely applied in clinical practice. These scoring systems focus primarily on recognizing high-risk patients in a hospitalized population and show less of an interest in differentiation within most of low-risk patients. None of the 3 appreciates the value of patient history, despite the fact that clinicians rely so heavily on this aspect. The GRACE score is based on large population studies. A disadvantage is that in practice it can only be calculated with the use of a computer. Another objection is that the GRACE score is determined to a large extent by the age of the patient. Not surprisingly, higher ages accompany higher mortality rates. The TIMI score allows only binary scores, thereby ignoring the fact that many variables have a "gray area." Finally, the PURSUIT score is outdated; it was designed before the introduction of the troponin measurement for clinical use, and therefore not found its place in clinical practice.

### Clinical Consequences

A major advantage of the HEART score is that it facilitates communications between doctors. A single figure summarizes extensive descriptions and considerations about chest pain patients. A score of 0 to 3 points carries a risk of 0.99% for reaching a MACE, and therefore supports a policy of early discharge. With this very low-risk percentage in mind, it is doubtful whether additional diagnostic procedures at the outpatient clinic are useful.

In case of a HEART score of 4 to 6 points, immediate discharge is not an option, as this figure indicates a risk of 11.6% for a MACE within 6 weeks. Such patients should be admitted for clinical observation, treated as an ACS awaiting final diagnosis, and subjected to noninvasive investigations such as repeated Troponin, exercise testing, and possibly advanced ischemia detection.

A HEART score  $\geq 7$  points, with a risk of 65.2% for a MACE, calls for early aggressive treatments possibly including invasive strategies without preceding noninvasive testing.

### Limitations

The advantage of our retrospective approach is that this enabled us to analyze complete series of consecutive patients. Consequently, this study is not hampered by the selection bias that is often so harmful for prospective studies. The disadvantage of a retrospective study, namely possible interpretation bias, was kept minimal by the interpretation of separated data regarding patient history, ECG, and outcome by experienced cardiologists.

Our study was observational and retrospective for the simple reason that this was the most pragmatic and practical condition to answer the questions at hand. We believe that the study's unexpectedly high level of significance provides a firm basis for further research. Clearly, cut-off points may need to be validated in larger multicenter studies.

### CONCLUSIONS

The HEART score helps in making accurate decisions at the emergency room without the use of radiation or invasive procedures. Low HEART scores go with low likelihood of an ACS and high HEART scores predict high numbers of MACE. In these 2 patient groups, together 53% of patients, proper decisions may be taken based on the HEART score. In case of intermediate values, the HEART score is less helpful and additional diagnostics may be required. The HEART score is an easy, quick, and reliable predictor of outcome in chest pain patients, and can therefore be used for triage.

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### DISCLOSURES

Nothing to declare.

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