A modified HEART risk score in chest pain patients with suspected non-ST-segment elevation acute coronary syndrome

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Objective To validate a modified HEART [History, Electrocardiograph (ECG), Age, Risk factors and Troponin] risk score in chest pain patients with suspected non-ST-segment elevation acute coronary syndrome (NSTE-ACS) in the emergency department (ED).

Methods This retrospective cohort study used a prospectively acquired database and chest pain patients admitted to the emergency department with suspected NSTE-ACS were enrolled. Data recorded on arrival at the ED were used. The serum sample of high-sensitivity cardiac Troponin I other than conventional cardiac Troponin I used in the HEART risk score was tested. The modified HEART risk score was calculated. The end point was the occurrence of major adverse cardiac events (MACE) defined as a composite of acute myocardial infarction (AMI), percutaneous intervention (PCI), coronary artery bypass graft (CABG), or all-cause death, within three months after initial presentation.

Results A total of 1,300 patients were enrolled. A total of 606 patients (46.6%) had a MACE within three months: 205 patients (15.8%) were diagnosed with AMI, 465 patients (35.8%) underwent PCI, and 119 patients (9.2%) underwent CABG. There were 10 (0.8%) deaths. A progressive, significant pattern of increasing event rate was observed as the score increased (P < 0.001 by χ² for trend). The area under the receiver operating characteristic curve was 0.84. All patients were classified into three groups: low risk (score 0–2), intermediate risk (score 3–4), and high risk (score 5–10). Event rates were 1.1%, 18.5%, and 67.0%, respectively (P < 0.001).

Conclusions The modified HEART risk score was validated in chest pain patients with suspected NSTE-ACS and may complement MACE risk assessment and patients triage in the ED. A prospective study of the score is warranted.

Keywords: Acute coronary syndrome; Chest pain; Emergency; Risk assessment; Troponin I

1 Introduction

Chest pain is one of the most common reasons for patient admission to the emergency department (ED).1,2 It is a major clinical challenge to differentiate patients with acute coronary syndrome (ACS) from these chest pain patients. Guideline suggests using risk scores in the ED for early stratification of chest pain patients with suspected acute coronary syndrome, and then giving different treatment strategies for different prognostic patients.3 The HEART [History, Electrocardiograph (ECG), Age, Risk factors and Troponin] risk score based on clinical experience and medical literature was developed specifically to stratify chest pain patients with suspected non-ST-segment elevation ACS (NSTE-ACS) in the ED.4,5 HEART is an acronym of its five components: History, Electrocardiograph (ECG), Age, Risk factors and Troponin. Each of these components may be scored with 0, 1 or 2 points, based on the extent of the abnormality. The HEART risk score has been validated retrospectively and prospectively in many studies.5–9 To our knowledge, however, high-sensitivity cardiac troponin I (hs-cTnI) was unused in these studies.

This study aimed to validate a modified HEART risk score in chest pain patients with suspected NSTE-ACS in the ED. In the risk score, hs-cTnI was used as a component. The study hypothesis was that the modified HEART risk score may complement major adverse cardiac events (MACE) risk assessment and patients triage in the ED.

2 Methods

2.1 Study design

This was a retrospective study with analysis of the data.
base of consecutive ED patients from September 2014 to February 2015. Data recorded on arrival at the ED were used. The serum sample of hs-cTnI (Beckman-Coulter, Enhanced ACCU Troponin I) was tested. The study enrolled patients with chest pain presenting to the ED of an urban academic tertiary hospital in Beijing, China, with 1500 beds, an ED volume of approximately 100,000 per year, and a catchment area serving a population of over one million. The hospital ethics committee approved the study and all patients gave informed consent.

2.2 Study population

Included patients were those admitted to the ED due to chest pain (“pain” encompasses not only pain, but also symptoms such as discomfort, pressure, and squeezing) suspicious of NSTE-ACS, irrespective of pre-hospital assumptions and previous medical treatments. Additionally, selected patients were at least 18 years old, and with more than 2 h from onset of symptoms to arrival at the ED.

Patients were excluded if there was a clear cause for chest pain other than NSTE-ACS (e.g., trauma, ST-elevation ACS, aortic dissection, pulmonary embolism, or arrhythmia), suffered from terminal disease, pregnant, or unable or unwilling to provide informed consent. Patients were also excluded if their data were incomplete.

2.3 Modified HEART risk score

In the modified HEART risk score, the “Troponin” component was hs-cTnI other than conventional troponin (T or I) or high-sensitivity cardiac Troponin T (hs-cTnT). After the serum sample of hs-cTnI was collected, it was immediately sent to laboratory and measured by chemiluminescence assay. The result of test was delivered to ED physicians within 60 min after patients arrived at the ED. Laboratory technicians were blinded to patient information. The specific explanation of each component was shown in previous publication.[5] The modified HEART risk score is shown in Table 1.

2.4 End point

The end point was the occurrence of MACE defined as a composite of acute myocardial infarction (AMI), percutaneous intervention (PCI), coronary artery bypass graft (CABG), or all-cause death, within 3 months after initial presentation. AMI was defined according to the third universal definition of myocardial infarction.[10] PCI was defined as any therapeutic catheter intervention in the coronary arteries. CABG was defined as any cardiac surgery in which coronary arteries were operated.

| Components | Ranks | Points |
|------------|-------|--------|
| History    | Slightly or non-suspicious | 0 |
|            | Moderately suspicious      | 1 |
|            | Highly suspicious           | 2 |
| ECG        | Normal                      | 0 |
|            | Nonspecific repolarization disturbance | 1 |
|            | Significant ST-depression   | 2 |
| Age        | ≤ 45 years                  | 0 |
|            | 45–65 years                 | 1 |
|            | ≥ 65 years                  | 2 |
| Risk factors | No risk factors known        | 0 |
|            | 1 or 2 risk factors         | 1 |
|            | ≥ 3 risk factors*, or history of atherosclerotic disease# | 2 |
| hs-cTnI    | ≤ 1 × normal limit          | 0 |
|            | 1–3 × normal limit          | 1 |
|            | ≥ 3 × normal limit          | 2 |

Range 0–10

ECG: electrocardiogram; HEART: History, ECG, Age, Risk factors and Troponin; hs-cTnI: high-sensitivity cardiac troponin I. *Risk factors: diagnosed hypertension, diagnosed hypercholesterolemia, diagnosed diabetes mellitus, family history of premature coronary artery disease, current smoking (< 1 month), and obesity (body mass index ≥ 30 kg/m²); #History of atherosclerotic disease: myocardial infarction, percutaneous intervention, coronary artery bypass graft, ischemic stroke, peripheral arterial disease, or carotid artery disease.

2.5 Follow-up

A 3-month follow up was performed by telephone interview and, if appropriate, by evaluation of the patient hospital record.

2.6 Statistical analysis

Statistical analysis was performed using SPSS statistical package (version 20.0, SPSS Inc., Chicago, Illinois, USA). The continuous variable was presented as mean ± SD. Categorical variables were given as frequencies and percentages. The discriminative power of the score was evaluated using the C statistic, which is the area under a receiver operating characteristic (ROC) curve for dichotomous outcomes. Differences among groups were assessed by means of the Student’s t-test when normally distributed, or by means of nonparametric test when non-normally distributed. χ² test was used to evaluate differences in the event rates for increasing risk score. Fisher’s exact test was used when expected frequencies were less than 5. P values were two-sided, and a P value of less than 0.05 was considered statistically significant.
3 Results

The study population was derived from 1,735 consecutive patients with chest pain presenting to the ED for evaluation. A total of 408 patients were excluded according to exclusion criteria, leaving a total of 1,327 patients meeting the inclusion criteria. Twenty-seven patients were lost to follow-up, as they could not be contacted telephonically. Finally, 1,300 eligible patients were enrolled (Figure 1). A total of 606 patients (46.6%) had a MACE within three months: 205 patients (15.8%) were diagnosed with AMI, 465 patients (35.8%) underwent PCI, and 119 patients (9.2%) underwent CABG. Two patients underwent both PCI and CABG. There were 10 (0.8%) deaths. Altogether, 799 events occurred in 606 patients, an average of 1.32 events per MACE patient. The baseline characteristics of the study cohort are shown in Table 2.

The C statistic for the score in the whole study group was 0.84 (95% CI: 0.82–0.87). The discriminative power of the score retained good in four relevant subgroups: in diabetes mellitus (DM), the MACE rate was 52.5% (190/362) with a C-statistic of 0.73 (95% CI: 0.68–0.78), in non-DM the MACE rate was 44.3% (416/938) with a C-statistic of 0.78 (95% CI: 0.76–0.81); in females the MACE rate was 32.7% (147/449) with a C-statistic of 0.80 (95% CI: 0.76–0.84), in males the MACE rate was 53.9% (459/851) with a C-statistic of 0.76 (95% CI: 0.73–0.79); in age 65 years or older the MACE rate was 50.1% (200/399) with a C-statistic of 0.71 (95% CI: 0.66–0.76), in age less than 65 years the MACE rate was 45.1% (406/901) with a C-statistic of 0.81 (95% CI: 0.78–0.83); in elevated hs-cTnI the MACE rate was 95.0% (226/238) with a C-statistic of 0.90 (95% CI: 0.82–0.97), in normal hs-cTnI the MACE rate was 35.8% (380/1062) with a C-statistic of 0.67 (95% CI: 0.63–0.70).

There was a progressive, significant pattern of increasing event rates as the score increased in the study cohort ($P < 0.001$ by $\chi^2$ for trend; Figure 2). The numerical distribution of the score’s five components in the groups with or without MACE is shown in Table 3. It differed significantly between the groups with and without MACE ($P < 0.05$ by $\chi^2$ for trend). The score was $6.2 \pm 1.57$ in the MACE group and $4.1 \pm 1.33$ in the non-MACE group ($P < 0.001$ by $\chi^2$ test).

Figure 1. Flow chart of study participants. ACS: acute coronary syndrome; AMI: acute myocardial infarction; CABG: coronary artery bypass graft; MACE: major adverse coronary events; PCI: percutaneous coronary intervention.
Table 2. Baseline characteristics of the study cohort.

|                       |       |
|-----------------------|-------|
| Age, yrs              | 59.1 ± 10.2 |
| Male                  | 851 (65.5%) |
| Hypertension          | 823 (63.3%) |
| Hypercholesterolemia  | 244 (18.8%) |
| DM                    | 361 (27.8%) |
| Family history of premature CAD | 170 (13.1%) |
| Current smoking       | 364 (28.0%) |
| Obesity               | 165 (12.7%) |
| History of atherosclerotic disease | 165 (12.7%) |
| MI                    | 144 (11.1%) |
| PCI                   | 262 (20.2%) |
| CABG                  | 28 (2.2%)   |
| Ischemic stroke       | 135 (10.4%) |
| Peripheral arterial disease | 8 (0.6%)   |
| Carotid artery disease | 21 (1.6%)   |
| Elevated hs-cTnI      | 238 (18.3%) |

Data are mean ± SD or n (%). CABG: coronary artery bypass graft; CAD: coronary artery disease; DM: diabetes mellitus; hs-cTnI: high-sensitivity cardiac troponin I; MI: myocardial infarction; PCI: percutaneous coronary intervention.

To stratify chest pain patients in the ED, patients were classified into three groups (Table 4).

### 4 Discussion

Several risk scores have been developed to help stratify patients with chest pain of different cardiac origins, including the PURSUIT,[11] TIMI,[12] GRACE,[13] Sanchis,[14] FRISC,[15] HEART,[4] and Florence[16] scores. However, only the HEART score was developed specifically for chest pain patients with suspected NSTE-ACS. All the five components of the score were trichotomous, due to the unsuitability of simple yes/no rating in clinical practice. Similar to the Apgar score,[17] each of the score’s components may be scored with 0, 1 or 2 points, based on the extent of the abnormality. The HEART score is a simple and reliable predictor of outcome in chest pain patients and has been validated widely.[5–9] In these studies, the “Troponin” component was conventional troponin (T or I)[5–7,9] or hs-cTnT.[8] To our knowledge, however, hs-cTnI was unused.

Hs-cTnI assay in our study has a 99th percentile concentration of 42 ng/L with a corresponding coefficient of variation of 8% and a limit of detection of 10 ng/L.[18]

Table 3. Number of patients in each component of the modified HEART score.

|                       | No MACE, n = 694 | MACE, n = 606 | P value for trend |
|-----------------------|------------------|---------------|------------------|
| History               | 75 (10.8%)       | 1 (0.1%)      | 515 (74.2%)      | 0 (1.0%)     | 256 (42.2%) | 349 (57.6%) | < 0.001 |
| ECG                   | 343 (49.4%)      | 61 (10.1%)    | 312 (45.0%)      | 39 (56.2%)   | 346 (57.1%) | 199 (32.8%) | < 0.001 |
| Age                   | 75 (10.8%)       | 42 (6.9%)     | 420 (60.5%)      | 199 (28.7%)  | 364 (60.1%) | 200 (33.0%) | 0.025   |
| Risk factors          | 98 (14.1%)       | 25 (4.1%)     | 308 (44.4%)      | 288 (41.5%)  | 246 (40.6%) | 335 (55.3%) | < 0.001 |
| hs-cTnI               | 682 (98.2%)      | 380 (62.7%)   | 12 (1.8%)        | 0 (0.0%)     | 45 (7.4%)   | 181 (29.9%) | < 0.001 |

*Data are n (%). HEART: History, ECG, Age, Risk factors and Troponin; hs-cTnI: high-sensitivity cardiac troponin I; MACE: major adverse cardiac events.

Table 4. Classifications of chest pain patients.

| Classification   | Score | Patients, n (%) | MACE (n) | Rate of MACE* |
|------------------|-------|-----------------|----------|--------------|
| Low risk         | 0–2   | 88 (6.8%)       | PCI (1)  | 1.1%         |
| Intermediate risk| 3–4   | 427 (32.8%)     | PCI (26), CABG (3) | 18.5%       |
| High risk        | 5–10  | 785 (60.4%)     | AMI (220), PCI (388), CABG (116), Death (10) | 67.0%       |

*The rate of MACE in the three groups was different (P < 0.001 by χ² test). AMI: acute myocardial infarction; CABG: coronary artery bypass graft; MACE: major adverse cardiac events; PCI: percutaneous coronary intervention.
The assay can be detected in AMI as early as 2 h after symptom onset\cite{19,20} and is recommended in evaluating the prognosis of suspected ACS, according to latest guidelines.\cite{3,10} It is reasonable that hs-cTnI was tested only once in our study, because all selected patients were with more than 2 h from onset of symptoms to arrival at the ED. In our study, the MACE rate was 35.8% (380/1062) if hs-cTnI score was 0 points; the MACE rate was 78.9% (45/57) if hs-cTnI score was one point; the MACE rate was 100% (181/181) if hs-cTnI score was two points. There was a progressive, significant pattern of increasing event rates as the hs-cTnI score increased ($P < 0.001$ by $\chi^2$ for trend). Hs-cTnI was a good predictor for MACE risk.

The discriminative power of the score in the whole study group was excellent (C statistic = 0.84). In the elevated hs-cTnI group, it was also excellent (C statistic = 0.90). But in the normal hs-cTnI group, it was poor (C statistic = 0.67). The possible reason is that the score of patients with normal hs-cTnI was lower than that of patients with elevated hs-cTnI ($4.5 \pm 1.44$ vs. $7.4 \pm 1.33$, $P < 0.001$), but some of them had MACE.

We classified patients into low, intermediate, and high risk groups according to the MACE rate to explore the potential usefulness of the score. However, boundaries for low, intermediate, and high risk in chest pain patients vary in different literature.\cite{41–1621–24} In our study, the boundaries of low, intermediate, and high risk were defined as $\leq 5\%$, $> 5\%$ but $\leq 20\%$, and $> 20\%$, respectively, which were consistent with other studies of HEART score.\cite{4–9} However, the score ranges in the three groups were 0–2 points, 3–4 points, and 5–10 points, respectively, which were different from other studies of HEART score.\cite{4–9} It may be attributed to hs-cTnI and/or different chest pain prevalence.

The MACE rate in our study was significantly different in three groups ($P < 0.001$ by $\chi^2$ test), and the score may complement patient triage in the ED. In the low risk group, the MACE rate was only 1.1%, and the only event was PCI. Patients in this group could be discharged early. In the intermediate risk group, the MACE rate was 18.5%, and no patients had AMI or death. Patients in this group should stay in the ED for further clinical evaluation, including repeat hs-cTnI and ECG testing. In the high risk group, the MACE rate rose up to 67.0%. Patients in this group should be immediately admitted to hospital and are probable candidates for invasive therapy.

Our study has several limitations. The development of HEART risk score was based on clinical experience and medical literature other than logistic regression analysis. Our study was a retrospective analysis in a single center, the modified HEART score needs to be prospectively validated in multiple centers. The study population of our ED has a relatively low prevalence of low-risk chest pain and high prevalence of high-risk chest pain; therefore this risk score will require further evaluation in other centers serving patient populations with different disease prevalence. Patients assessed less than 2 h from onset of symptoms to arrival at the ED were excluded, therefore, it is unknown whether the risk score is applicable to them. Finally, patients included were Chinese, limiting the generalizability of the results to other populations.

In conclusion, the modified HEART risk score was validated in chest pain patients with suspected NSTE-ACS and may complement MACE risk assessment and patients triage in the ED. A prospective study of the score is warranted.

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References

1. Niska R, Bhuiya F, Xu J. National Hospital Ambulatory Medical Care Survey: 2007 emergency department summary. Natl Health Stat Report 2010: 1–31.
2. Goodacre S, Cross E, Arnold J, et al. The health care burden of acute chest pain. Heart 2005; 91: 229–230.
3. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 64: e139–228.
4. Six AJ, Backus BE, Kelder JC. Chest pain in the emergency room: value of the HEART score. Neth Heart J 2008; 16: 191–196.
5. Backus BE, Six AJ, Kelder JC, et al. Chest pain in the emergency room: a multicenter validation of the HEART Score. Crit Pathw Cardiol 2010; 9: 164–169.
6. Six AJ, Cullen L, Backus BE, et al. The HEART score for the assessment of patients with chest pain in the emergency department: a multinational validation study. Crit Pathw Cardiol 2013; 12: 121–126.
7. Backus BE, Six AJ, Kelder JC, et al. A prospective validation of the HEART score for chest pain patients at the emergency department. Int J Cardiol 2013; 168: 2153–2158.
8. Willems MN, van de Wijngaart DJ, Bergman H, et al. Addition of heart score to high-sensitivity troponin T versus conventional troponin T in risk stratification of patients with chest pain at the coronary emergency rooms. Neth Heart J 2014; 22: 552–556.
9 Poldervaart JM, Reitsma JB, Koffijberg H, et al. The impact of the HEART risk score in the early assessment of patients with acute chest pain: design of a stepped wedge, cluster randomised trial. *BMC Cardiovasc Disord* 2013; 13: 77.

10 Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Circulation* 2012; 126: 2020–2035.

11 Boersma E, Pieper KS, Steyerberg EW, et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. The PURSUIT Investigators. *Circulation* 2000; 101: 2557–2567.

12 Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. *JAMA* 2000; 284: 835–842.

13 Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med* 2003; 163: 2345–2353.

14 Sanchis J, Bodi V, Nunez J, et al. New risk score for patients with acute chest pain, non-ST-segment deviation, and normal troponin concentrations: a comparison with the TIMI risk score. *J Am Coll Cardiol* 2005; 46: 443–449.

15 Lagerqvist B, Diderholm E, Lindahl B, et al. FRISC score for selection of patients for an early invasive treatment strategy in unstable coronary artery disease. *Heart* 2005; 91: 1047–1052.

16 Conti A, Vanni S, Taglia BD, et al. A new simple risk score in patients with acute chest pain without existing known coronary disease. *Am J Emerg Med* 2010; 28: 135–142.

17 Apgar V. A proposal for a new method of evaluation of the newborn infant. *Curr Res Anesth Analg* 1953; 28: 250–259.

18 Zaninotto M, Mion MM, Novello E, et al. Precision performance at low levels and 99th percentile concentration of the Access AccuTnl assay on two different platforms. *Clin Chem Lab Med* 2009; 47: 367–371.

19 Than M, Cullen L, Aldous S, et al. 2-Hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker: the ADAPT trial. *J Am Coll Cardiol* 2012; 59: 2091–2098.

20 Cullen L, Mueller C, Parsonage WA, et al. Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. *J Am Coll Cardiol* 2013; 62: 1242–1249.

21 Wilson PW, D’Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998; 97: 1837–1847.

22 Christenson J, Innes G, McKnight D, et al. A clinical prediction rule for early discharge of patients with chest pain. *Ann Emerg Med* 2006; 47: 1–10.

23 Amsterdam EA, Kirk JD, Bluemke DA, et al. Testing of low-risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. *Circulation* 2010; 122: 1756–1776.

24 Lee TH, Goldman L. Evaluation of the patient with acute chest pain. *N Engl J Med* 2000; 342: 1187–1195.