Original Article

HEART score improves efficiency of coronary computed tomography angiography in patients suspected of acute coronary syndrome in the emergency department

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Abstract

Aims: Coronary computed tomography angiography is increasingly employed in the emergency department for suspected acute coronary syndrome patients. The HEART score has been proposed for initial risk stratification in these patients. The aim of this study was to investigate the diagnostic value and efficiency of the HEART score before coronary computed tomography angiography.

Methods and results: We included patients suspected of acute coronary syndrome who underwent coronary computed tomography angiography in the emergency department. Based on the HEART score, patients were stratified as low-risk (HEART≤3), intermediate-risk (HEART4–6) and high-risk (HEART≥7). We assessed coronary computed tomography angiography for the presence of significant coronary artery disease (>50% stenosis). The primary outcome, the level of major adverse cardiac events, was a composite endpoint of all-cause mortality, acute coronary syndrome or coronary revascularisation within 30 days. The study population consisted of 340 patients (mean age: 55.6±10.1 years, 44.7% women), major adverse cardiac events occurred in 45 (13.2%) patients. The incidence of major adverse cardiac events in patients stratified as low-risk (35.0%), intermediate-risk (56.8%) and high-risk (8.2%) was 3.4%, 12.4% and 60.7%, respectively. All four low-risk patients with major adverse cardiac events had a HEART score of three. An algorithm where coronary computed tomography angiography is reserved for patients with HEART 3–6 resulted in a sensitivity of 97.8%, specificity of 84.1%, negative predictive value of 99.6% and positive predictive value of 48.4%, while reducing the need for coronary computed tomography angiography by 22% (*n*=75).

Conclusion: The predictive value of coronary computed tomography angiography for 30-day major adverse cardiac events in suspected acute coronary syndrome patients is good, and reserving coronary computed tomography angiography for HEART score 3–6 patients reduces the number of needed coronary computed tomography angiograms without affecting diagnostic accuracy.

Keywords

Coronary computed tomography angiography, HEART score, acute coronary syndrome, emergency department, coronary artery disease

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Introduction

Patients with symptoms of a possible acute coronary syndrome (ACS) are frequently seen at the emergency department (ED).[1–3] Physicians strive to achieve an effective but safe diagnostic work-up, as misdiagnoses can have serious consequences.[2–4] The HEART score, a clinical tool for rapid risk stratification, has been proposed to improve decision making in patients suspected of ACS.[5–8] Based on history, electrocardiogram (ECG), age, risk factors and initial troponin levels, the HEART score provides the physician with recommendations for further management. Recent studies suggest that the HEART score permits safe discharge of a considerable number of patients, effectively reducing downstream testing.[7] At the same time, several randomised trials have shown that coronary computed tomography angiography (CCTA) allows safe and early discharge from the ED providing valuable prognostic information as well.[5,9,10] However, CCTA is a costly test and requires radiation exposure to the patient. Combining the HEART score with CCTA may provide a more efficient diagnostic work-up, where CCTA can be reserved for a subset of patients. The aim of this study was to investigate the diagnostic value and efficiency of the HEART score before CCTA in patients suspected of ACS in the ED.

Methods

Patient population

We conducted a secondary analysis of two prospective studies of patients presenting to the ED with symptoms suggestive of ACS. The methods, including study designs, inclusion and exclusion criteria have previously been published.[9,11] In the current analysis, we included patients who underwent CCTA of diagnostic image quality. Both studies were performed according to the principles of the Declaration of Helsinki, approved by the local institutional review boards and all patients provided written informed consent.

CCTA

Image acquisition was performed on 64-slice or newer computed tomography systems, using ECG-synchronised axial or spiral scan protocols combined with radiation minimising measures, depending on local practices, available technology, and patient characteristics. Results of CCTA were reported by certified radiologists with a minimum of two years of experience reading CCTA. The presence of coronary plaque and the degree of stenosis was assessed for each evaluable coronary segment. The degree of stenosis was quantified as: no stenosis, ≤50% stenosis (non-obstructive plaque) or >50% stenosis (obstructive plaque).

HEART score

The HEART score, a clinical risk tool for rapid risk stratification of patients with acute chest pain, was calculated for each patient. The score consists of five components: History, ECG, Age, Risk factors and Troponin. Each of these components may be scored with 0, 1 or 2 points with a maximum score of 10 points.[8] Detailed information on the composition of the HEART score and how each component is scored can be found in Supplemental Material Table S1. Information regarding all components were retrieved from hospital records from the day of index presentation. As suggested by the original authors, patients were also categorised as: low risk (HEART ≤3), intermediate risk (HEART 4–6) and high risk (HEART ≥7).[8]

Clinical endpoints

The primary outcome was occurrence of major adverse cardiac events (MACEs) within 30 days by analogy with prior publications on the HEART score;[12,13] a composite of all-cause mortality, ACS or coronary revascularisation (emergent or elective within 30 days). ACS was defined as acute myocardial infarction or unstable angina according to the universal definition of acute myocardial infarction.[14,15] All clinical endpoints were adjudicated by two cardiologists who independently reviewed medical records of patients. The result of the CCTA was blinded to the cardiologists performing the event adjudication.

Statistical analysis

Continuous data are presented as mean±standard deviation (SD) or median (interquartile ranges), and categorical data are presented as proportions (percentages). Differences between independent groups were compared using analysis of variance or the Kruskal-Wallis test for continuous variables, and the Fisher's exact test or the Pearson's chi-square test for categorical variables. Parameters of diagnostic accuracy, i.e. sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) for the prediction of 30-day MACEs were calculated with their corresponding 95% confidence intervals using exact binomial confidence intervals. When evaluating the CCTA, >50% stenosis was considered a positive test. Areas under the curve (AUCs) were calculated and compared using the test of DeLong et al.[16] All statistical analyses were performed using MedCalc Statistical Software version 18.10 (MedCalc Software bvba, Ostend, Belgium) and SPSS version 24.0 (IBM, Armonk, New York, USA). All tests were two-tailed and a *p*-value <0.05 was considered statistically significant.
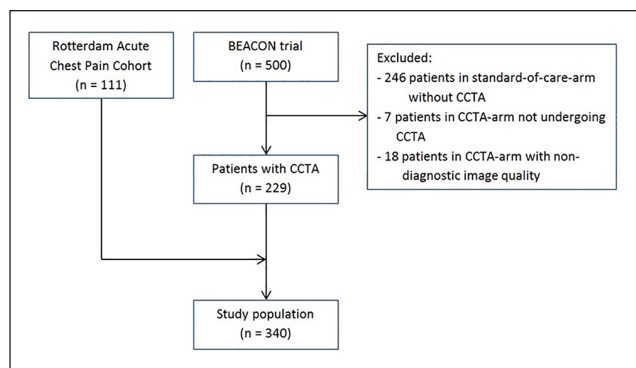
Figure 1. Flow diagram shows the enrolment process for the study population.
CCTA: coronary computed tomography angiography.

Results

Baseline characteristics and clinical endpoints

Of 500 patients included in the Better Evaluation of Acute Chest Pain with Computed Tomography Angiography (BEACON) trial, 229 patients underwent CCTA and had diagnostic image quality.[9] Additionally, 111 patients in the Rotterdam Acute Chest Pain cohort underwent CCTA of diagnostic image quality.[11] In total, 340 patients met eligibility and were included for the current study (Figure 1). The mean age was 56±10 years and the proportion of women was 44.7%. MACEs occurred in 45 (13.2%) patients within 30 days (Table 1). The adjudicated diagnosis of ACS was established in 42 (12.4%) patients: 27 (7.9%) had myocardial infarction and 15 (4.4%) had unstable angina pectoris. Coronary revascularisation was performed in 38 (11.2%) patients. Seven patients with an adjudicated diagnosis of ACS did not undergo revascularisation within 30 days; Of these, two were managed medically and underwent revascularisation after 30 days and five were found to have no significant stenosis on invasive coronary angiography (ICA). Additionally, three patients underwent elective percutaneous coronary intervention (PCI) for stable angina pectoris. Cardiac troponins were available in all patients. Troponins were measured with high-sensitive troponin assays in 180 (53%) patients, of whom 177 patients with the high-sensitive Troponin T assay (Roche diagnostics). In the remaining 160 (47%) patients cardiac troponins were measured with conventional troponin assays. Supplemental

Table 1. Baseline patient characteristics.

	Total (n=340)	HEART Low risk (0–3) (n=119)	HEART intermediate (4–6) (n=193)	HEART high risk (7–10) (n=28)	p-Value
Mean age, years	55.6±10.1	51.3±9.4	57.2±9.5	63.3±9.9	<0.001
Women	152 (44.7)	52 (43.7)	90 (46.6)	10 (35.7)	0.53
Cardiovascular risk factors					
Hypertension	170 (50.0)	39 (32.8)	110 (57.0)	21 (75.0)	<0.001
Dyslipidaemia	116 (34.1)	14 (11.8)	80 (41.5)	22 (78.6)	<0.001
Diabetes mellitus	44 (12.9)	5 (4.1)	32 (16.6)	7 (25.0)	<0.001
Smoking	131 (38.5)	40 (33.6)	78 (40.4)	13 (46.4)	0.33
Family history positive for CAD	139 (40.9)	43 (36.1)	82 (42.5)	14 (50.0)	0.32
Prior atherosclerotic disease	40 (11.8)	4 (3.4)	28 (14.5)	8 (28.6)	<0.001
Blood pressure					
Systolic	141.7±21.1	137.1±18.6	143.9±21.2	145.4±27.0	0.01
Diastolic	81.9±13.6	81.5±12.7	82.7±14.3	78.7±12.1	0.32
CCTA assessment for CAD					
No stenosis	151 (44.4)	74 (62.2)	76 (39.4)	1 (3.6)	<0.001
1–50% stenosis	103 (30.3)	32 (26.9)	67 (34.7)	4 (14.3)	0.05
>50% stenosis	86 (25.3)	13 (10.9)	50 (25.9)	23 (82.1)	<0.001
Radiation dose, mSv	4.9 (3.1–8.8)	4.5 (2.7–8.1)	5.3 (3.3–9.4)	4.7 (3.3–6.5)	0.05
Occurrence of MACEs within 30 days of index visit					
MACEs 30 days	45 (13.2)	4 (3.4)	24 (12.4)	17 (60.7)	<0.001
All-cause mortality	1 (0.3)	0 (0)	0 (0)	1 (3.6)	0.08
ACS	42 (12.4)	3 (2.5)	23 (11.9)	16 (57.1)	<0.001
Unstable angina	15 (4.4)	2 (1.7)	6 (3.1)	7 (25.0)	<0.001
Myocardial infarction	27 (7.9)	1 (0.8)	17 (8.8)	9 (32.1)	<0.001
Coronary revascularisation	38 (11.2)	4 (3.4)	21 (10.9)	13 (46.4)	<0.001

ACS: acute coronary syndrome; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; MACE: major adverse cardiac event; mSv: millisievert; SD: standard deviation.
MACEs defined as all-cause mortality, ACS or coronary revascularisation. Values are mean±SD, median (interquartile ranges) or n (%).
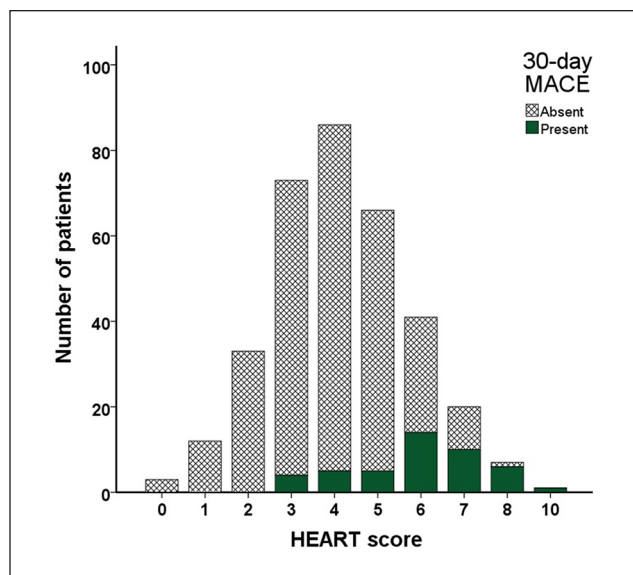
Figure 2. Frequency of 30-day major adverse cardiac events (MACEs) according to HEART score.
MACEs defined as all-cause mortality, acute coronary syndrome or coronary revascularisation.

Material Table S2 lists all troponin assays used, their characteristics and the algorithm in which they were implemented.

CCTA

When assessed for coronary artery disease (CAD), 151 (44.4%) patients had no stenosis, 103 (30.3%) patients had 1–50% stenosis and 86 (25.3%) patients had >50% stenosis on CCTA (Table 1). The incidence of 30-day MACEs in patients with no stenosis, 1–50% stenosis and >50% stenosis was 0% (*n*=0), 1.9% (*n*=2) and 50% (*n*=43), respectively. Sensitivity, specificity, NPV and PPV of >50% stenosis on CCTA for the prediction of 30-day MACEs was 95.6% (84.9–99.5), 85.4% (80.9–89.2), 99.2% (97.0–99.8) and 50.0% (43.0–57.0), respectively. The AUC of >50% stenosis on CCTA for prediction of 30-day MACEs was 0.91 (0.87–0.93).

HEART score

The HEART score classified 119 (35.0%) patients as low-risk, 193 (56.8%) as intermediate-risk and 28 (8.2%) as high-risk. The incidence of 30-day MACEs in patients stratified as low-risk, intermediate-risk and high-risk was 3.4% (*n*=4), 12.4% (*n*=24), and 60.7% (*n*=17), respectively (Table 1). All patients (*n*=4) in the low-risk category with 30-day MACEs had a HEART score of three (Figure 2). Table 2 shows detailed characteristics of patients with a low HEART score (≤3) and MACEs within 30 days. All low-risk patients with 30-day MACEs had >50% stenosis on CCTA. Sensitivity, specificity, NPV and PPV of the HEART score for the prediction of 30-day MACEs at different cut-offs are shown in Table 3. The AUC of the HEART score for prediction of 30-day MACEs was 0.83 (0.78–0.87).

HEART score and CCTA

The association between HEART risk categories and CCTA findings are shown in Table 1. In intermediate-risk patients,

Table 2. Detailed characteristics of patients with a low HEART score (≤3) or coronary computed tomography angiography (CCTA)≤50% stenosis and major adverse cardiac events (MACEs) within 30 days.

Patient	Age, years	Sex	HEART						Type of troponin assay	Initial troponin	Highest troponin	MACE	>50% stenosis on CCTA	Additional information
			History	ECG	Age	Risk factors	Initial troponin	Total						
I	46	Male	2	0	I	0	0	3	TnT	Negative	Negative	UA; PCI	Yes	Patient admitted for ICA after positive ExECG
2	63	Female	I	0	I	I	0	3	Hs-TnT	4 ng/l	4 ng/l	UA; PCI	Yes	Patient admitted for ICA after obstructive plaque on CCTA
3	63	Female	I	0	I	I	0	3	Hs-TnT	5 ng/l	5 ng/l	PCI	Yes	PCI after elective ICA
4	45	Male	2	0	I	0	0	3	TnT	Negative	0.69 µg/l	NSTEMI; PCI	Yes	Patient admitted for ICA after significant rise of troponin
5	69	Male	I	0	2	2	I	6	Hs-TnT	24 ng/l	30 ng/l	MINOCA	No	Patient admitted for ICA. No significant stenosis detected during ICA

ECG: electrocardiogram; ExECG: exercise stress electrocardiography; Hs-TnT: high-sensitivity troponin T; ICA: invasive coronary angiography; MACE: major adverse cardiac events; MINOCA: myocardial infarction with nonobstructive coronary artery disease; NSTEMI: non-ST segment elevation myocardial infarction; PCI: percutaneous coronary intervention; TnT: troponin T; UA: unstable angina.
MACEs defined as all-cause mortality, acute coronary syndrome or coronary revascularisation.

Table 3. Predictive value of the HEART score for 30-day major adverse cardiac events (MACEs) at various cut-offs.

HEART score	Number of patients ruled-out (%)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
≥0	0 (0)	100.0 (92.1–100.0)	0.0 (0.0–1.2)	13.2 (13.2–13.2)	NA
<1	3 (0.9)	100.0 (92.1–100.0)	1.0 (0.2–2.9)	13.4 (13.2–13.5)	100.0
<2	15 (4.4)	100.0 (92.1–100.0)	5.1 (2.9–8.3)	13.9 (13.5–14.2)	100.0
<3	47 (13.8)	100.0 (92.1–100.0)	15.9 (11.9–20.6)	15.4 (14.7–16.0)	100.0
<4	119 (35.0)	91.1 (78.8–97.5)	39.0 (33.4–44.8)	18.6 (16.7–20.6)	96.6 (91.8–98.7)
<5	205 (60.3)	80.0 (65.4–90.4)	66.4 (60.7–71.8)	26.7 (22.6–31.1)	95.6 (92.4–97.5)
<6	271 (79.7)	68.9 (53.4–81.8)	87.1 (82.8–90.7)	44.9 (36.4–53.8)	94.8 (92.2–96.6)
<7	312 (91.8)	37.8 (23.8–53.5)	96.3 (93.4–98.1)	60.7 (43.7–75.5)	91.0 (89.0–92.7)
<8	332 (97.6)	15.6 (6.5–29.5)	99.7 (98.1–100.0)	87.5 (46.9–98.2)	88.6 (87.2–89.8)
<9	339 (99.7)	2.2 (0.1–11.8)	100.0 (98.8–100.0)	100.0	87.0 (86.5–87.5)
>10	340 (100)	0.0 (0.0–7.9)	100.0 (98.8–100.0)	NA	86.8 (86.8–86.8)

CI: confidence interval; NA: not applicable; NPV: negative predictive value; PPV: positive predictive value.
MACEs defined as all-cause mortality, acute coronary syndrome or coronary revascularisation.
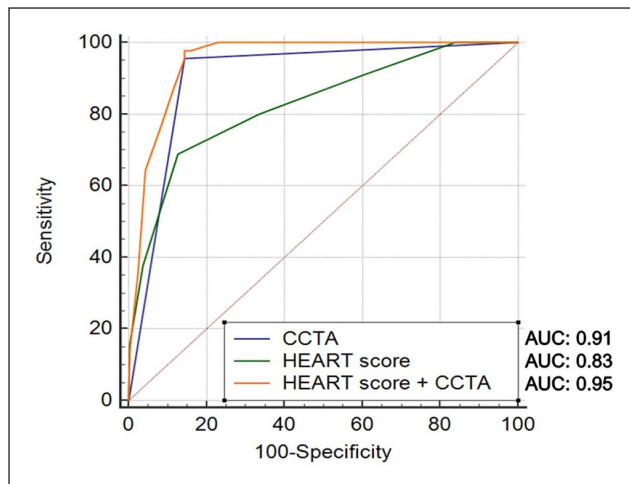

Figure 3. Predictive value of coronary computed tomography angiography (CCTA), HEART score and HEART score combined with CCTA for 30-day major adverse cardiac events (MACEs). Receiver-operating-characteristic curves show the predictive value of CCTA, the HEART score and the HEART score combined with CCTA for 30-day MACEs. MACEs defined as all-cause mortality, acute coronary syndrome or coronary revascularisation. AUC: area under the curve.

CCTA reclassified 143 (74.1%) patients to low-risk (<50% stenosis with a 30-day MACE rate 0.7%) and 50 (25.9%) patients to high-risk (>50% stenosis with a 30-day MACE rate 46%). One intermediate-risk patient (HEART score six) with non-obstructive plaque on CCTA had an adjudicated diagnosis of myocardial infarction, however this was considered a myocardial infarction with nonobstructive coronary arteries (MINOCA) with a minimal rise pattern in cardiac troponin and no significant stenosis on subsequent ICA (Table 2). The addition of CCTA to the HEART score was associated with a significant improvement of the diagnostic accuracy for 30-day MACEs (AUC 0.95 (0.92–0.97) vs 0.83 (0.78–0.87); $p<0.001$) (Figure 3). Sensitivity, specificity, NPV and PPV
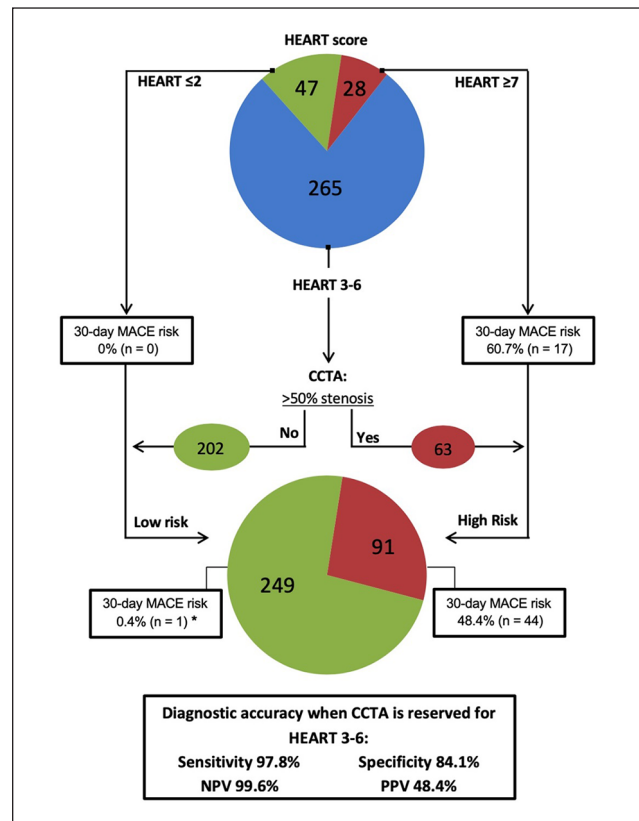

Figure 4. Predictive value of the HEART score combined with coronary computed tomography angiography (CCTA) assessment in HEART scores 3–6 for 30-day major adverse cardiac events (MACEs).
MACEs defined as all-cause mortality, acute coronary syndrome or coronary revascularisation.
*One patient with a HEART score of six and ≤50% stenosis on CCTA had an adjudicated diagnosis of myocardial infarction, however this was considered a myocardial infarction with nonobstructive coronary arteries (MINOCA) with a minimal rise pattern in cardiac troponin and no significant stenosis on subsequent invasive coronary angiography.
NPV: negative predictive value; PPV: positive predictive value.

for the prediction of 30-day MACEs of an algorithm where CCTA is reserved for intermediate HEART scores (4–6) was 88.9% (76.0–96.3), 87.1% (82.8–90.7), 98.1% (95.7–99.2) and 51.3% (43.5–59.0), respectively. This algorithm reduces the need for CCTA by 43% (n=147). An algorithm where CCTA is reserved for HEART score 3–6 patients had a sensitivity, specificity, NPV and PPV for the prediction of 30-day MACEs of 97.8% (88.2–99.9), 84.1% (79.4–88.1), 99.6% (97.3–99.9) and 48.4% (41.8–55.0), respectively (Figure 4). This algorithm reduces the need for CCTA by 22% (n=75).

Discussion

In the current study, we investigated the predictive value and efficiency of the HEART score before CCTA for 30-day MACEs in suspected ACS patients in the ED and report several important findings. First, CCTA is a good predictor of 30-day MACEs in suspected ACS patients in the ED (AUC 0.91). Second, rule-out of 30-day MACEs based on the originally proposed low-risk HEART category (HEART score ≤3) is suboptimal (sensitivity 91.1% and NPV 96.6%). Third, addition of CCTA to the HEART score significantly improves the diagnostic accuracy for 30-day MACEs (AUC: 0.83 to 0.95; p<0.001). Finally, an algorithm where CCTA is reserved for patients with HEART score 3–6 reduces the need for CCTA by 22% (n=75) without compromising diagnostic accuracy or safety.

HEART score

In our study, the HEART score identified a large proportion (35%) of low-risk patients proposed for early discharge. However, the incidence of MACEs in low-risk patients was higher (3.4%) compared to previous reports, where the incidence ranged from 0.4–2.5%.[8,12,13,17–19] Using the originally proposed score of ≤3 resulted in a generally unacceptable sensitivity and NPV in this population.[20] Notably, all four low-risk patients with 30-day MACEs had a score of three, of whom only one was diagnosed with non-ST segment elevation myocardial infarction (NSTEMI). Lowering the cut-off value for discharge to HEART scores ≤2 increased the diagnostic accuracy to acceptable levels in our study, something that has been proposed previously.[21] Further improvement of the diagnostic accuracy can probably be achieved by modifying the HEART score to incorporate serial troponin measurements.[22–24]

CCTA following HEART score

The addition of CCTA to the HEART score resulted in a substantial improvement in diagnostic accuracy, mainly by reclassifying intermediate-risk patients to their appropriate risk group. At the same time, using the HEART score to select patients that will benefit most from CCTA can result in a more efficient approach. Very low-risk HEART patients

(score ≤2) did not experience 30-day MACEs in the current study and can be discharged safely from the ED, with further screening in an outpatient setting. High-risk HEART score patients, of whom 60.7% experienced 30-day MACEs in the current study, probably benefit most from an approach with early ICA. The algorithm HEART 3–6+CCTA reduced the number of needed coronary computed tomography angiograms while maintaining a high diagnostic accuracy and identifying a large proportion (73%) of patients who are eligible for safe and early discharge from the ED. In a similar fashion to the PRospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) minimal risk tool in suspected stable angina patients, which identifies individuals with low risk of CAD, the HEART score is able to reduce the need for non-invasive testing without comprising safety.[25]

Limitations

The current study is a secondary analysis of patients suspected of ACS that underwent CCTA in the ED and should therefore be regarded as hypothesis generating. Our study population, which consisted mostly of low- to intermediate-risk patients, may not be representative of other populations of patients presenting with suspected ACS. The study population also consisted of patients in whom results of CCTA were used as part of their clinical work-up which in turn might have introduced a work-up bias. Furthermore, due to the heterogeneity of troponin assays implemented in current study, the results may be less applicable to individual troponin assays in clinical practice. In the current analysis, we were unable to investigate the diagnostic accuracy of the HEART pathway, an algorithm which incorporates serial troponin measurements into the HEART score, as serial troponin measurements were available in a minority of the patients. A disadvantage of CCTA is the exposure to radiation, however recent developments in scanner technology and dose-reducing protocols have led to a reduction in radiation exposure.[9] Furthermore, in the current analysis the HEART score helps reduce the number of coronary computed tomography angiograms performed, which also minimises the number of patients that are exposed to radiation.

Conclusion

The predictive value of CCTA for 30-day MACEs in suspected ACS patients is good and reserving CCTA for HEART score 3–6 patients reduces the number of needed coronary computed tomography angiograms without affecting diagnostic accuracy.

Conflict of interest

Funding

References

1. Goodacre S, Cross E, Arnold J, et al. The health care burden of acute chest pain. *Heart* 2005; 91: 229-230.
2. Reichlin T, Hochholzer W, Bassetti S, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. *N Engl J Med* 2009; 361: 858-867.
3. Than M, Cullen L, Reid CM, et al. A 2-h diagnostic protocol to assess patients with chest pain symptoms in the Asia-Pacific region (ASPECT): A prospective observational validation study. *Lancet* 2011; 377: 1077-1084.
4. Mokhtari A, Borna C, Gilje P, et al. A 1-h combination algorithm allows fast rule-out and rule-in of major adverse cardiac events. *J Am Coll Cardiol* 2016; 67: 1531-1540.
5. Hoffmann U, Truong QA, Schoenfeld DA, et al. Coronary CT angiography versus standard evaluation in acute chest pain. *N Engl J Med* 2012; 367: 299-308.
6. Litt HI, Gatsonis C, Snyder B, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. *N Engl J Med* 2012; 366: 1393-1403.
7. Poldervaart JM, Reitsma JB, Backus BE, et al. Effect of using the HEART score in patients with chest pain in the emergency department: A stepped-wedge, cluster randomized trial. *Ann Intern Med* 2017; 166: 689-697.
8. Six AJ, Backus BE and Kelder JC. Chest pain in the emergency room: Value of the HEART score. *Neth Heart J* 2008; 16: 191-196.
9. Dedic A, Lubbers MM, Schaap J, et al. Coronary CT angiography for suspected ACS in the era of high-sensitivity troponins: Randomized multicenter study. *J Am Coll Cardiol* 2016; 67: 16-26.
10. Schlett CL, Banerji D, Siegel E, et al. Prognostic value of CT angiography for major adverse cardiac events in patients with acute chest pain from the emergency department: 2-Year outcomes of the ROMICAT trial. *JACC Cardiovasc Imaging* 2011; 4: 481-491.
11. Dedic A, Ten Kate GJ, Neefjes LA, et al. Coronary CT angiography outperforms calcium imaging in the triage of acute coronary syndrome. *Int J Cardiol* 2013; 167: 1597-1602.
12. Mahler SA, Hiestand BC, Goff DC, et al. Can the HEART score safely reduce stress testing and cardiac imaging in patients at low risk for major adverse cardiac events? *Crit Pathw Cardiol* 2011; 10: 128-133.
13. 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.
14. Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the Management of Acute Coronary Syndromes (ACS) in Patients Presenting Without Persistent ST-segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011; 32: 2999-3054.
15. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012; 60: 1581-1598.
16. DeLong ER, DeLong DM and Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. *Biometrics* 1988; 44: 837-845.
17. 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.
18. 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.
19. Melki D and Jernberg T. HEART score: A simple and useful tool that may lower the proportion of chest pain patients who are admitted. *Crit Pathw Cardiol* 2013; 12: 127-131.
20. Than M, Herbert M, Flaws D, et al. What is an acceptable risk of major adverse cardiac event in chest pain patients soon after discharge from the emergency department? A clinical survey. *Int J Cardiol* 2013; 166: 752-754.
21. Carlton EW, Khattab A and Greaves K. Identifying patients suitable for discharge after a single-presentation high-sensitivity troponin result: A comparison of five established risk scores and two high-sensitivity assays. *Ann Emerg Med* 2015; 66: 635-45.e1.
22. Mahler SA, Riley RF, Hiestand BC, et al. The HEART pathway randomized trial: Identifying emergency department patients with acute chest pain for early discharge. *Circ Cardiovasc Qual Outcomes* 2015; 8: 195-203.
23. Mahler SA, Stopyra JP, Apple FS, et al. Use of the HEART pathway with high sensitivity cardiac troponins: A secondary analysis. *Clin Biochem* 2017; 50: 401-407.
24. McCord J, Cabrera R, Lindahl B, et al. Prognostic utility of a modified HEART score in chest pain patients in the emergency department. *Circ Cardiovasc Qual Outcomes* 2017; 10.
25. Fordyce CB, Douglas PS, Roberts RS, et al. Identification of patients with stable chest pain deriving minimal value from noninvasive testing: The PROMISE minimal-risk tool, a secondary analysis of a randomized clinical trial. *JAMA Cardiol* 2017; 2: 400-408.