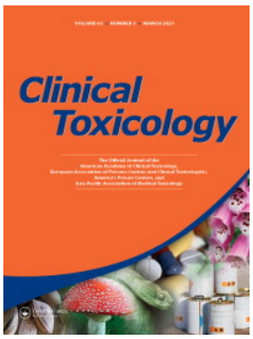

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Comparative evaluation of the ability to detect major cardiac events with the modified cocaine history, electrocardiogram, age, risk factors and troponin (HEART) score, HEART pathway and original HEART score in patients with cocaine-associated chest pain presenting at the emergency department

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Comparative evaluation of the ability to detect major cardiac events with the modified cocaine history, electrocardiogram, age, risk factors and troponin (HEART) score, HEART pathway and original HEART score in patients with cocaine-associated chest pain presenting at the emergency department

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ABSTRACT

Introduction: This study primarily aimed to assess the ability to detect major cardiac events using the history, electrocardiogram, age, risk factors and troponin (HEART) pathway, modified cocaine HEART score, and HEART score among patients with cocaine-associated chest pain.

Methods: This single-centre retrospective study included consecutive patients with cocaine-associated chest pain admitted between January 2016 and December 2022 who were age and sex-matched in a 1:2 ratio to patients with chest pain not associated with cocaine use. The primary outcome was the percentage of major adverse cardiovascular events within 30 days.

Results: In total, 1,412 patients were included, with 1,653 presentations, of whom 551 presented with cocaine-associated chest pain and were ≥18 years old. Most presentations involved male patients (84%). Major adverse cardiovascular events occurred in 139 presentations: 50 (9.1%) among patients with cocaine-associated chest pain and 89 (8.1%) among patients with non-cocaine-associated chest pain. The number of low-risk presentations of cocaine-associated chest pain patients was 409 (74.2%), 345 (62.6%) and 394 (71.5%) according to the HEART score, modified cocaine HEART score and HEART pathway, respectively. The HEART pathway had the lowest percentage of observed major adverse cardiac events in low-risk patients (0%; 95% CI: 0–0.9%), followed by the modified cocaine HEART score (0.3%; 95% CI: 0.007–1.6%) and the HEART score (0.7%; 95% CI: 0.2–2.1%). Sensitivity, negative predictive value, and area under the curves were very similar between the three scores.

Discussion: The occurrence of missed major adverse cardiovascular events in low-risk patients was below 0.7% (95% CI: 0.2%–2.1%) in all three risk stratification scores. The HEART pathway was the safest risk stratification tool with a sensitivity and negative predictive value of 100%. Nevertheless the differences with the other risk stratification scores were non-significant.

Conclusions: All three risk stratification scores performed well in a low-risk population with cocaine-associated chest pain, with a percentage of 0.7% of patients with a missed major adverse cardiovascular event.

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Cocaine; cocaine-associated chest pain; HEART pathway; HEART score; major adverse cardiovascular event

Introduction

In 2021, cocaine was ranked in the top five recreational drugs involved in drug-related emergency department visits (4.7%) [1]. Most cocaine-related symptoms are of a cardiovascular nature, with chest pain most frequently reported (40%) [2]. Also, cocaine is a risk factor for developing acute myocardial infarction, with a 24-fold increased risk the first hour after cocaine use. Among patients admitted to the emergency department and chest pain units, 4.7% of them will be because of cocaine-associated chest pain [3,4]. Although two-thirds of patients with cocaine-induced myocardial infarction develop symptoms within 3 h of exposure, onset can be delayed for up to four days [5]. Therefore, it is essential to triage patients at high risk for developing acute myocardial infarction and other major adverse cardiovascular events from those who are at low risk and can be safely discharged.

The history, electrocardiogram, age, risk factors and troponin (HEART) score predicts the risk of acute myocardial infarction in the emergency department by categorizing patients as low, intermediate or high-risk [6–10]. However, this score was not validated for cocaine-associated chest pain and, in a

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previous study Faramand and colleagues [11], performed poorly. Therefore, Faramand and colleagues [12] developed a modified cocaine HEART score by adding cocaine as a risk factor. According to the European Society of Cardiology guidelines, acute myocardial infarction can be rapidly and safely excluded in patients with low-risk chest pain with the use of high-sensitivity cardiac troponin T concentration, resulting in a faster discharge time and lower costs [13–16]. Using this information, the HEART pathway integrated high-sensitivity cardiac troponin T concentrations (either at presentation and 3 h or at presentation and repeated at 1 h) into the troponin component of the original HEART score [17–19]. Nevertheless, none of these scores have been validated in patients with cocaine-associated chest pain.

This study primarily aimed to assess the safety of three diagnostic risk stratification scores among patients with cocaine-associated chest pain (the HEART score, the modified cocaine HEART score, and the HEART pathway) by comparing the observed percentage of major adverse cardiac events within 30 days in patients triaged as low-risk by these three scores. Secondary aims were to assess the usefulness of these scores by calculating the sensitivity, specificity, and positive and negative predictive values. Furthermore, the discriminative ability of the three scores in patients with cocaine-associated chest pain and non-cocaine-associated chest pain were compared.

Methods

Study design and setting

A single-centre retrospective study was conducted, which included all patients presenting to the emergency department and chest pain unit of the OLVG Hospital, Amsterdam, the Netherlands, with cocaine-associated chest pain between January 2016 and December 2022. Patients were identified via CTcue® (CTcue B.V., Amsterdam, The Netherlands), an electronic health record text-mining tool [20,21]. Patients with cocaine-associated chest pain were age/sex-matched with those with non-cocaine-associated chest pain.

Selection of participants

Inclusion criteria for the cocaine-associated chest pain group were patients ≥18 years old, presenting with chest pain or symptoms suggestive of acute myocardial infarction, with a cardiological evaluation (including at least one high-sensitivity cardiac troponin T concentration and electrocardiogram), and a positive self-reported recreational cocaine use history within 72 h prior of presentation to the hospital, or laboratory-confirmed cocaine use. Laboratory confirmation was performed by urine toxicology screening using the Triage TOX Drug Screen® and/or by the Toxtyper®, an ultra-high-performance liquid chromatography coupled to an MSN ion trap system [22]. If a patient presented with cocaine-associated chest pain multiple times, each presentation was included separately. Because follow-up information regarding potential major adverse cardiac events within 30 days was required and is most reliable with local OLVG patients, only Amsterdam residents (postal address within the catchment area of the hospital or the OLVG Hospital is their primary healthcare-providing hospital), were included. Exclusion criteria were chest pain caused by trauma, missing criteria for calculating the HEART score (e.g., history, electrocardiogram, age, high-sensitivity cardiac troponin T concentration), patients taken immediately to the coronary intervention room via ambulance and patients with out-of-hospital cardiac arrest. Identification of eligible cocaine-associated chest pain patients was conducted via CTcue®, and the patient's electronic record was screened for eligibility by one author (JE) (Supplementary Figure 1) [20,21].

Patients eligible for the age/sex-matched non-cocaine-associated chest pain cohort group met the same inclusion/exclusion criteria as the cocaine-associated chest pain group, except they were excluded if they had a self-reported history of recreational drug use, a positive toxicology screen for recreational drugs or if information on both of these was missing in the patient's electronic record. Patients with non-cocaine-associated chest pain were identified similarly and age/sex-matched to patients with cocaine-associated chest pain in a ratio of 2:1.

Data collection

Data regarding the demographics, presentation date, age, sex, recent use of cocaine, presenting symptoms, past medical history, cardiovascular risk factors, prescription medication, electrocardiogram, laboratory results, the occurrence of major adverse cardiac events within 30 days after presentation, cardiac catheterization results and discharge diagnosis were retrospectively collected. Data were manually collected and registered in Castor EDC® (v2023.1.0.3) (JE). When information regarding cardiovascular risk factors was absent in the patient's electronic records, it was considered negative. Additional information regarding definitions, collected data, and missing data are provided in Supplementary Table 1. To prevent selection bias, all non-Amsterdam residents with unreliable OLVG follow-ups were excluded in case of missing potential major adverse cardiac events.

Calculation of the HEART scores

After collecting all data, Castor EDC® (v2023.1.0.3.) automatically calculated the HEART scores. A participant received 0-2 points for each different component of the HEART score (history, electrocardiogram, age, risk factors and high-sensitivity cardiac troponin T concentration [normal value of ≤14 ng/L]) according to the original derivation method [7,9]. The history component of the HEART score was reviewed, blinded from the discharge diagnosis (JE), and when in doubt ($n = 19$), a second author scored the history as well (FG). The electrocardiogram was reviewed, and the written interpretation in the electronic patient record given by the treating physician was analyzed (JE). When in doubt, a second author interpreted the electrocardiogram as well (RR). To calculate the modified cocaine HEART score, the history component was considered moderately suspicious for all slightly/non-suspicious cocaine-associated chest pain, and the use of cocaine was added as

a risk factor [12]. For the HEART pathway, patients where acute myocardial infarction was excluded with high-sensitivity cardiac troponin T concentrations according to the European Society of Cardiology guidelines (either at presentation and 3 h or at presentation and repeated at 1 h) and a HEART score ≤3 were identified as low-risk [13,15]. In all other cases, the patient was rated non-low-risk.

Outcomes

The primary outcome was the percentage of patients with major adverse cardiac events within 30 days. Major adverse cardiac events were classified as acute myocardial infarction (ST-elevation myocardial infarction/non-ST-elevation myocardial infarction, defined according to the 2018 Fourth Universal Definition of Myocardial Infarction), unstable angina pectoris, percutaneous intervention, coronary artery bypass graft, coronary angiography revealing significant stenosis (>50%) treated conservatively and death by any cause [6,7,23,24]. To determine if a major adverse cardiac event had occurred, the electronic patient record was reviewed until 30 days after presentation and the final diagnosis by the treating physician was extracted. The HEART pathway, as currently defined by the European Society of Cardiology, was considered the gold standard, and a missed major adverse cardiac events percentage <1% was considered acceptable.

Statistical analysis

For age, a Kolmogorov-Smirnov test was used as a normality test; since the Kolmogorov-Smirnov test was significant (Kolmogorov-Smirnov statistic: 0.103; *P*-value Kolmogorov-Smirnov test <0.001), the median and the 25th to 75th percentiles were calculated because of a non-normal distribution. Thereafter, the continuous variable "age" was converted into a categorical variable "age group", in which the age groups were defined as <45 years old, 45-64 years old, 45-64 years old, and ≥65 years old. Results about categorical variables, such as gender, are presented as numbers and proportions. The Pearson chi-square test or the exact Fisher test was used to compare the characteristics of the two different groups (cocaine-associated chest pain/non-cocaine-associated chest pain). The primary outcome (major adverse cardiac events) was treated as a dichotomous variable (yes/no).

To assess the usefulness of each risk stratification score, the observed percentage of major adverse cardiac events in patients was compared to the theoretically accepted percentage of 1% in patients with cocaine-associated chest pain triaged as low risk. Usefulness measures (sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio and diagnostic odds ratio) were calculated separately for cocaine-associated chest pain and non-cocaine-associated chest pain patients, based on 2-by-2 tables, using MedCalc® software [25]. Exact 95% confidence intervals were calculated using the Clopper-Pearson method.

Receiver operating characteristic analysis was used to compare the discriminative ability of the three scores in cocaine-associated chest pain and non-cocaine-associated chest pain patients. Multivariate logistic regression models including major adverse cardiac events as the outcome (binary variable: "yes" or "no"), the score of interest (considered as a continuous variable), and patient type (binary variable: "patient with cocaine-associated chest pain" or "patient with non-cocaine-associated chest pain") as explanative variables were fitted on all patients and the predicted probability stored and subsequently used as an input variable in the receiver operating characteristic analysis to determine the area under the receiver operating characteristic curves for each score. Three multivariate logistic models including the same outcome and explanative variables were also fitted in the low-risk presentation groups to test whether the occurrence of major adverse cardiac events differed between cocaine-associated chest pain and non-cocaine-associated chest pain patients after adjustment for the score of interest. Statistical analysis was performed using PS IMAGO PRO Data analysis - SPSS Statistics 29.0 and R studio version 2023.06.2 for Windows (R version 4.2.2.; Boston, MA). The local ethical committee of OLVG Hospital approved the research protocol.

Results

Of the 1,440 patients with potential cocaine-associated chest pain screened for eligibility via CTcue®, 456 patients met the inclusion criteria (Figure 1). They had a total of 551 presentations with cocaine-associated chest pain (range 1–9 presentations per patient) and were age/sex-matched with 956 patients with non-cocaine-associated chest pain, with a total of 1,102 presentations (Supplementary Table 2). Most presentations involved male patients (84%) (Table 1). Major adverse cardiac events occurred in 139 of 551 presentations: 50 (9.1%) in the cocaine-associated chest pain group and 89 (8.1%) in the non-cocaine-associated chest pain group (Figure 1). Patient characteristics are shown in Table 1. Median age was 38 years (IQR: 30-50 years). Patients with cocaine-associated chest pain were significantly ($P<0.001$) more likely to smoke tobacco (64.2%) compared to patients with non-cocaine-associated chest pain (39.6%) but had fewer other risk factors.

Table 2 shows the specifications of major adverse cardiac events. In the cocaine-associated chest pain group, 1.8% had an ST-elevation myocardial infarction, whereas in the non-cocaine-associated chest pain group, 2.1% had an ST-elevation myocardial infarction ($P=0.709$). In the cocaine-associated chest pain group, 5.6% had a non-ST-elevation myocardial infarction, whereas in the non-cocaine-associated chest pain group, 4.4% had a non-ST-elevation myocardial infarction ($P=0.292$). Mortality was comparable (0.2%) in both groups.

Table 3 shows the observed percentage of presentations with patients who developed major adverse cardiac events in cocaine-associated chest pain patients classified as low risk according to the three risk stratification scores. The number of low-risk presentations of cocaine-associated chest pain patients was 409 (74.2%), 345 (62.6%) and 394 (71.5%) according to the HEART score, modified cocaine HEART score

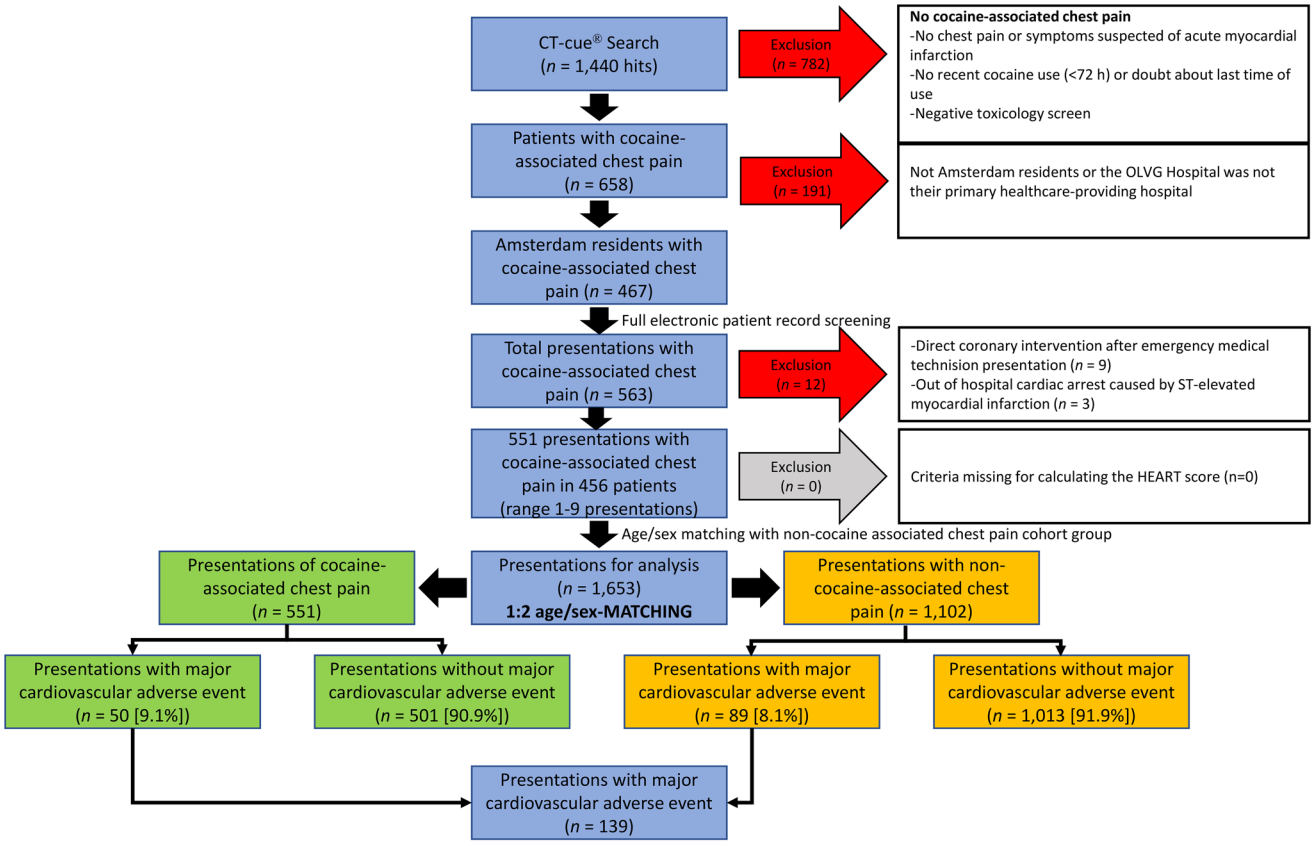

Figure 1. Patient flow diagram.

Table 1. Patient characteristics/demographics.

	Total	Cocaine-associated chest pain group	Non-cocaine-associated chest pain group	*P* values
Total visits	1,653 (1,412 patients)	551 (456 patients)	1,102 (956 patients)	Not applicable
Age				
<45 years, *n* (%)	1,068 (64.6)	356 (64.6)	712 (64.6)	Not applicable
45–64 years, *n* (%)	525 (31.8)	175 (31.8)	350 (31.8)	Not applicable
≥65 years, *n* (%)	60 (3.6)	20 (3.6)	40 (3.6)	Not applicable
Male, *n* (%)	1,395 (84.4)	465 (84.4)	930 (84.4)	Not applicable
Risk factors				
History of atherosclerotic disease, *n* (%)	230 (13.9)	56 (10.2)	174 (15.8)	*P*=0.002
Hypertension, *n* (%)	265 (16.0)	78 (14.2)	187 (17.0)	*P*=0.142
Diabetes mellitus, *n* (%)	106 (6.4)	30 (5.4)	76 (6.9)	*P*=0.256
Hypercholesterolaemia, *n* (%)	245 (14.8)	66 (12.0)	179 (16.2)	*P*=0.021
Obesity, *n* (%)	124 (7.5)	18 (3.3)	106 (9.6)	*P*<0.001
Smoking, *n* (%)	790 (47.8)	354 (64.2)	436 (39.6)	*P*<0.001
Positive family history, *n* (%)	288 (17.4)	68 (12.3)	220 (20.0)	*P*<0.001
No risk factors, *n* (%)	520 (31.5)	153 (27.8)	367 (33.3)	*P*=0.022
History				
Slightly/non-suspicious, *n* (%)	826 (50.0)	318 (57.7)	508 (46.1)	*P*<0.001
Moderately suspicious, *n* (%)	619 (37.4)	180 (32.7)	439 (39.8)	*P*=0.005
Highly suspicious, *n* (%)	208 (12.6)	53 (9.6)	155 (14.1)	*P*=0.010
Electrocardiogram				
Normal, *n* (%)	944 (57.1)	323 (58.6)	621 (56.4)	*P*=0.380
Non-specific repolarisation disturbances, *n* (%)	548 (33.2)	180 (32.7)	368 (33.4)	*P*=0.768
Significant ST-deviation, *n* (%)	101 (6.1)	48 (8.7)	113 (10.3)	*P*=0.319
Risk factors				
No risk factors, *n* (%)	520 (31.5)	153 (27.8)	367 (33.3)	*P*=0.022
1–2 risk factors, *n* (%)	805 (48.7)	312 (56.6)	493 (44.7)	*P*<0.001
>2 risk factors or history of atherosclerotic disease, *n* (%)	328 (19.8)	86 (15.6)	242 (22.0)	*P*=0.002
High-sensitivity troponin T concentration				
≤1 normal limit (≤14 ng/L), *n* (%)	944 (57.1)	461 (83.7)	621 (56.4)	*P*=0.012
1–3x normal limit (15–41 ng/L), *n* (%)	548 (33.2)	54 (9.8)	368 (33.4)	*P*=0.005
≥3x normal limit (≥42 ng/L), *n* (%)	101 (6.1)	36 (6.5)	113 (10.3)	*P*=0.611
Major adverse cardiovascular event (<30 days), *n* (%)	139 (8.4)	50 (9.1)	89 (8.1)	*P*=0.491

Table 2. Specifications of major adverse cardiac events.

Major adverse cardiac events	Cocaine-associated chest pain	Non-cocaine-associated chest pain	*P*-values
Major adverse cardiac events <30 days, *n*/total (%)	50/551 (9.1%)	89/1,102 (8.1%)	NS
ST-elevation myocardial infarction, *n* (%)	10 (1.8%)	23 (2.1%)	NS
Non-ST-elevation myocardial infarction, *n* (%)	31 (5.6%)	49 (4.4%)	NS
Unstable angina pectoris, *n* (%)	4 (0.7%)	11 (1.0%)	NS
Percutaneous coronary intervention, *n* (%)	19 (3.4%)	55 (5.0%)	NS
Coronary artery bypass graft, *n* (%)	5 (0.9%)	11 (1.1%)	NS
Significant stenosis (>50%) treated conservatively, *n* (%)	6 (1.1%)	5 (0.5%)	NS
All cause death, *n* (%)	1 (0.2%)	2 (0.2%)	NS

Table 3. Observed percentage of presentations with patients who developed major adverse cardiac events in cocaine-associated chest pain patients classified as "low risk" according to the different risk stratification scores. The theoretical accepted percentage of a missed major adverse cardiac event of <1% when a patient was triaged as "low-risk" was considered acceptable.

Risk stratification scores	Patients with cocaine-associated chest pain *n* = 551	Patients with cocaine-associated chest pain and major adverse cardiac events *n* = 50
HEART score, median (IQR)	2.0 (IQR 1.0–4.0)	
Low-risk (0–3), *n* (%)	409 (74.2)	3 (0.7)
Intermediate-risk (4–6), *n* (%)	109 (19.8)	22 (20.2)
High-risk (7–10), *n* (%)	33 (6)	25 (75.8)
Modified cocaine HEART score, median (IQR)	3.0 (IQR 2.0–4.0)	
Low-risk (0–3), *n* (%)	345 (62.6)	1 (0.3)
Intermediate-risk (4–6), *n* (%)	166 (30.1)	19 (11.4)
High-risk (7–10), *n* (%)	40 (7.3)	30 (75.0)
HEART pathway, median (IQR)	2.0 (IQR: 1.0–4)	
Low-risk (HEART score ≤3 AND negative high-sensitivity cardiac troponin T concentration*), *n* (%)	394 (71.5)	0
Non-low-risk (HEART score >3 OR positive high-sensitivity cardiac troponin T*), *n* (%)	157 (28.5)	50 (31.8)

*According to the European Society of Cardiology guidelines (either 0/3h or 0/1h protocols). [13,15].

and HEART pathway, respectively. The HEART pathway had the lowest percentage of observed major adverse cardiac events in low-risk patients (0%; 95% CI: 0–0.9%), followed by the modified cocaine HEART score (0.3%; 95% CI: 0.007–1.6%) and the HEART score (0.7%; 95% CI: 0.2–2.1%) (Table 3).

Table 4 shows the usefulness measures of the three scores in the cocaine-associated chest pain group. Between the three scores, there was no significant difference regarding the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio or diagnostic odds ratio.

The observed percentage of presentations who developed major adverse cardiac events in the non-cocaine-associated chest pain groups is shown in Supplementary Table 3. In patients triaged as low-risk, those with non-cocaine-associated chest pain had a major adverse cardiac event percentage of 0.5% (95% CI: 0.14–1.3%) with the HEART score and modified cocaine HEART score and 0.3% (95% CI: 0.03–0.95%) with the HEART pathway. No significant difference was found compared to patients with cocaine-associated chest pain.

The discriminative ability of all risk stratification scores was excellent, with the area under the receiver operating characteristic curve values of 0.94 and 0.95 and had no significant difference between the three scores (Figure 2).

Discussion

This study aimed to determine the percentage of major adverse cardiac events among patients triaged as low-risk in the cocaine-associated chest pain group using the HEART score, modified cocaine HEART score and HEART pathway score. The occurrence of missed major adverse cardiac events in low-risk patients was below 0.7% (95% CI: 0.2–2.1%) in all three risk stratification scores. Additionally, the occurrence of missed major adverse cardiac events in cocaine-associated chest pain patients was comparable to non-cocaine-associated chest pain patients for all three risk stratification scores. The HEART pathway was the safest risk stratification tool for discharging patients who were triaged as low-risk with a sensitivity and negative predictive value of 100%. Although the HEART pathway performed slightly better, the differences with the other risk stratification scores were non-significant.

Cocaine is a risk factor for acute myocardial infarction because it increases myocardial oxygen demand due to its sympathomimetic effects while simultaneously decreasing the oxygen supply due to coronary vasoconstriction induced by alpha-adrenergic stimulation [26]. These cardiovascular effects increase in combination with tobacco use [27]. Furthermore, cocaine is prothrombotic and is associated with premature atherosclerosis when taken chronically [26]. Patients with cocaine-induced myocardial infarction are typically young, tobacco-smoking males with relatively few other risk factors [4,28], as also shown in this study. In addition, the history of presenting symptoms and electrocardiogram findings have a poorer predictive value in this population of patients [29]. This altered clinical presentation and pathophysiology can be misleading for the correct prediction of the risk of major adverse cardiac events.

Accurately ruling out acute myocardial infarction and predicting a low risk of major adverse cardiac events is vital in the emergency department and chest pain unit. Therefore, a risk stratification tool should have a high negative predictive value and sensitivity when patients are triaged as low-risk. One survey [30] among emergency medicine physicians in Australia, the United States of America and Canada concluded that a missed percentage of major adverse cardiac events <1.0% might be acceptable; all three studied risk stratification scores met this requirement.

Previously, Faramand and colleagues [11] found a low reliability of the HEART score in cocaine-associated chest pain patients. They reported a higher percentage of major adverse cardiac events in the cocaine-associated chest pain group compared to this study (17.9% versus 9.1%, respectively) and

Table 4. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio of the different scores in patients presenting with cocaine-associated chest pain ($n = 551$).

Test	Sensitivity, % [95% confidence interval]	Specificity, % [95% confidence interval]	Positive predictive value, % [95% confidence interval]	Negative predictive value, % [95% confidence interval]	Positive likelihood ratio [95% confidence interval]	Negative likelihood ratio [95% confidence interval]	Diagnostic odds ratio, % [95% confidence interval]
HEART score	94.0 [83.5–98.8]	81.0 [77.3–84.4]	33.2 [25.5–41.6]	99.3 [97.9–99.9]	4.96 [4.1–6.0]	0.07 [0.0–0.2]	58 [19–175]
Modified cocaine HEART score	98.0 [89.4–100.0]	68.7 [64.4–72.7]	23.8 [18.2–30.3]	99.7 [98.4–100.0]	3.13 [2.73–3.58]	0.03 [0.00–0.20]	72 [14–370]
HEART pathway	100.0 [92.9–100.0]	78.6 [74.8–82.2]	31.9 [24.7–39.8]	100.0 [99.1–100.0]	4.68 [3.96–5.54]	0	371 [23–6257]

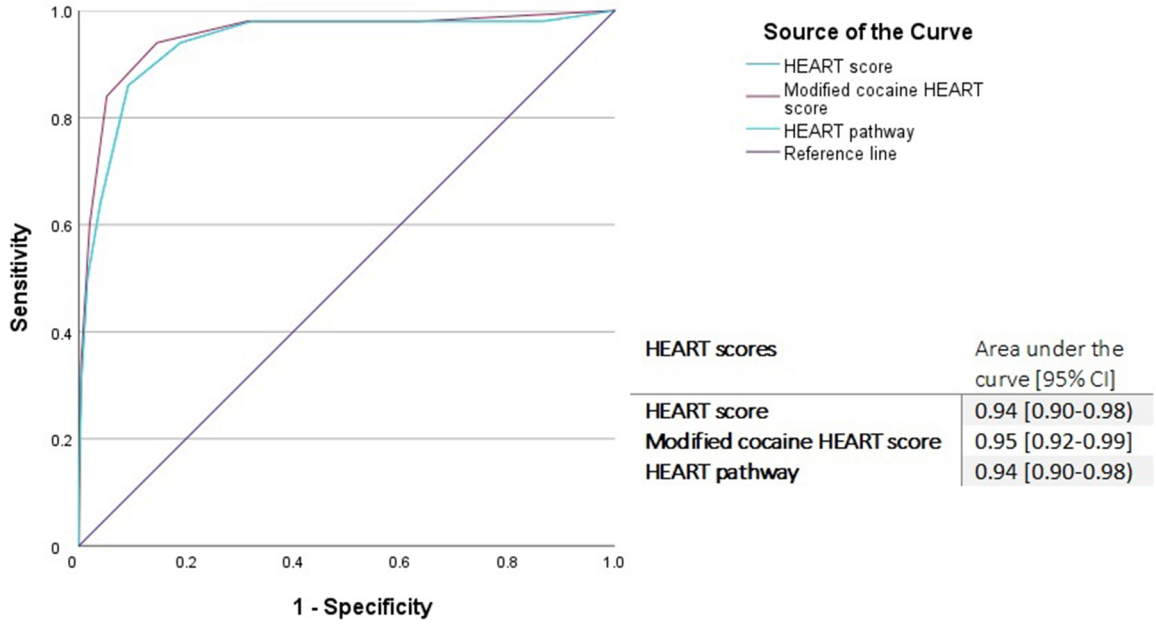

Figure 2. Area under the curve.

a considerably higher percentage of major adverse cardiac events in low-risk patients according to the original HEART score (14% versus 0.7%, respectively) [11]. This difference may be explained by the older population (mean age 51 years old versus 40 years old) and an increased number of other cardiovascular risk factors in the study by Faramand and colleagues [11]. In the original derivation studies for the original HEART score, the percentage of major adverse cardiac events was also higher (17.0% – 24.1%), but the patient population was also older (mean age 60 and 61 years old) with more cardiovascular risk factors, except for smoking [6,7,9]. Also, Faramand and colleagues [11] only included patients presented by ambulance to a tertiary care hospital, suggesting a preselected high-risk population [31]. In contrast, the current study also included self-referrals. In addition, Faramand and colleagues [11] used a different definition of major adverse cardiac events instead of the original major adverse cardiac events definition, also considering post-admission subsequent pulmonary embolus, cardiac arrest or fatal ventricular dysrhythmia, cardiogenic shock and acute heart failure as major adverse cardiac events [7,9,23]. Notably, also their percentage of missed major adverse cardiac events in patients with low-risk non-cocaine-associated chest pain was 4%, which is considerably higher than the 2.1% reported in a systematic review and meta-analysis conducted by Laureano-Phillips and colleagues [8,11]. When only studies using high-sensitivity cardiac troponin T concentration for the calculation of the HEART score were included, this percentage dropped to 0.8%, comparable to the results of this current study [8]. Nevertheless, Faramand and colleagues [11] did not report whether high-sensitivity cardiac troponin T concentration or conventional troponin concentrations were used [31].

The modified cocaine HEART score resulted, as expected, in a lower missed major adverse cardiac events percentage compared to the original HEART score. However, this difference was not statistically significant. By using the modified cocaine HEART score, similar sensitivity and negative predictive value, close to 100%, were seen, comparable to the results of Faramand and colleagues [12]. However, they rightly noted that this could lead to over-triaging since only 6% of their cocaine-associated chest pain patients were triaged in the low-risk group [12]. On the contrary, when applying the modified cocaine HEART score in our cocaine-associated chest pain group, the majority of patients (62.6%) were still considered low-risk.

In previous studies, the percentage of missed major adverse cardiac events in non-cocaine-associated chest pain patients when applying the HEART pathway in conjunction with the European Society of Cardiology guidelines was between 0.2% and 1.6% [18,19,32–34]. Ruling out acute myocardial infarction with troponin concentrations in patients with cocaine-associated

chest pain was previously investigated [35–40]. However, these studies used conventional troponin concentrations, and no literature is available regarding the application of the most recent European Society of Cardiology guidelines combined with high-sensitivity cardiac troponin T concentrations in cocaine-associated chest pain patients [13,15]. Current data suggest that the HEART pathway has excellent discriminatory accuracy without the occurrence of major adverse cardiac events in all the 394 low-risk patients included in this study. Compared to the original HEART score, the HEART pathway identified 15 extra non-low-risk patients, three of whom experienced a major adverse cardiac events. Although a scientific statement by the American Heart Association in 2008 advises a 12-hour observation period for low-risk cocaine-associated chest pain patients, current data suggest that the appliance of the HEART pathway performs well in identifying low-risk cocaine-associated chest pain patients who can be safely discharged within the non-cocaine-associated chest pain timeframe, resulting in shorter admission time [2].

This study has several limitations, first and foremost being its retrospective nature. Second, the primary endpoint, major adverse cardiac events within 30 days, was based on the electronic patient record. Although only Amsterdam residents were included, potential major adverse cardiac events could be missed since no standard follow-up occurred, which can lead to underestimating the occurrence of major adverse cardiac events; nevertheless, this would be the same for both groups and all three risk stratification scores. Third, the reviewing author did not assess the patients in person, which may have led to misidentifying the history component and risk factors, potentially overestimating major adverse cardiac events in low-risk patients. Furthermore, although a second review of the history and electrocardiogram blinded to the occurrence of major adverse cardiac events was performed when indicated, one author performed most of the chart reviews and data collection, which could have led to bias, although the same limitation applies to both groups. In addition, no assessment of dose, route, frequency and duration of cocaine use was made. Chronic users have a higher risk of developing premature coronary atherosclerotic disease and, therefore, a higher risk of an acute myocardial infarction compared to sporadic recreational users. Finally, approximately half of the patients in the cocaine-associated chest pain group had a positive toxicology screening for cocaine, and the other half only had a positive self-reported cocaine use history without laboratory confirmation. To counter this problem, only patients where the time of usage before the onset of symptoms was reported in the electronic patient record were included.

Conclusions

In conclusion, the three risk stratification scores performed well in a low-risk population, with a percentage of 0.7% of patients with missed major adverse cardiac events and a high discriminative ability. All three scores can be used, therefore, to safely discharge low-risk patients with cocaine-associated chest pain patients when highly sensitive troponin assays are used. The HEART pathway performed best with a missed major adverse cardiac events percentage of 0%. The missed major adverse cardiac events percentages for all three scores were comparable between cocaine-associated chest pain and non-cocaine-associated chest pain patients.

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Authors contributions

FG and JE contributed equally. FG and JE conceived the study, designed the trial, and provided the draft of the research protocol for approval of the local ethical committee of the OLVG Hospital. All authors contributed substantially to the revision of the research protocol. JE was responsible for creating the database, collecting the data and managing the data, while being supervised by FG and CH. CH advised on the study design and analyzed the data. FG, JE and CH drafted the manuscript. All authors contributed substantially to its revision. FG and JE take full responsibility for the paper as a whole.

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Data availability statement

Data are available upon reasonable request to the corresponding author.

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