

Computerized Self-Reported Medical History-Taking Improves Early Rule-Out of Major Adverse Cardiac Events in Acute Chest Pain Patients: The CLEOS-CPDS Prospective Cohort Study

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Abstract

Background: Self-reported, computerized history-taking (CHT) may provide efficient and automated collection of medical histories for calculating risk scores recommended in acute chest pain management.

Objective: We aimed to determine if risk scores, populated by CHT data, can rule-out a 30-day major adverse cardiac events (MACE), evaluate their diagnostic accuracy, and assess their impact on acute chest pain management.

Methods: In this prospective cohort study (2017–2019) at a tertiary hospital ED, clinically stable patients aged ≥18 years with chest pain and an ECG not indicating an acute coronary syndrome provided medical histories through a tablet-based CHT program (Clinical Expert Operating System, CLEOS), owned by a public university. The Danderyd History, ECG, Age, Risk factors, and Troponin (D-HEART), HEART, Emergency Department Assessment of Chest Pain Score Accelerated Diagnostic Protocol (EDACS-ADP), and Troponin-only Manchester Acute Coronary Syndrome (T-MACS) scores, were calculated from relevant CHT data and electronic health record (EHR) data, extracted by research staff. EHRs were reviewed for International Classification of Diseases (ICD) codes indicating any 30-day 3-point MACE.

Results: In the 1,000 participants included (mean age 55±17 years; 46% women), the risk scores could be calculated in 73–83% using only CHT data, depending on the risk score applied. A 30-day MACE occurred in 7.2% of the total population. The negative predictive value for a 30-day MACE was 0.98–0.99 (95% CI: 0.97–1.00) and a substantial fraction (up to 17%) of patients admitted with acute chest pain could be reclassified from “not low risk” to “low risk” using this method.

Conclusions: Automated medical history-taking using CHT can offer reliable risk scores in a majority of acute chest pain patients, with high diagnostic accuracy to rule-out a 30-day three-point MACE. This tool could facilitate the management and safe discharge of low-risk patients with acute chest pain in the ED. Clinical Trial: ClinicalTrials.gov NCT03439449. Registration date: 2018-02-13.

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Original Manuscript

Original Paper

Computerized Self-Reported Medical History-Taking Improves Early Rule-Out of Major Adverse Cardiac Events in Acute Chest Pain Patients: The CLEOS-CPDS Prospective Cohort Study

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Results: In the 1,000 participants included (mean age 55 ± 17 years; 46% women), the risk scores could be calculated in 73–83% using only CHT data, depending on the risk score applied. A 30-day MACE occurred in 7.2% of the total population. The negative predictive value for a 30-day MACE

was 0.98–0.99 (95% CI: 0.97–1.00) and a substantial fraction (up to 17%) of patients admitted with acute chest pain could be reclassified from “not low risk” to “low risk” using this method.

Conclusions: Automated medical history-taking using CHT can offer reliable risk scores in a majority of acute chest pain patients, with high diagnostic accuracy to rule-out a 30-day three-point MACE. This tool could facilitate the management and safe discharge of low-risk patients with acute chest pain in the ED.

Trial Registration: ClinicalTrials.gov NCT03439449. Registration date: 2018-02-13.

Keywords: Chest pain; Risk assessment; Coronary artery disease; Emergency service, hospital; Medical informatics; Artificial intelligence; Medical history taking

Introduction

Chest pain, a common chief complaint in emergency departments (EDs) world-wide [1,2], contributes to overcrowding in these settings [3]. Prompt and accurate management is crucial, not only for identifying life-threatening conditions, such as an acute coronary syndrome (ACS), but also for the safe discharge of the majority of patients with benign conditions. An integrated assessment, combining medical history, signs and symptoms, electrocardiogram (ECG), and high sensitivity cardiac troponins (hs-cTn), is recommended for initial short-term risk stratification [4]. To consolidate these observations, risk scores are recommended for structured and individual patient assessment [5,6]. The History, ECG, Age, Risk factors and Troponin (HEART) score [7], ED Assessment of Chest Pain Score –Accelerated Diagnostic Protocol (EDACS-ADP) [8] and Troponin-only, Manchester Acute Coronary Syndrome (T-MACS) [9] have scientific support [10-12] and have recently demonstrated a reduction by half in the risk of major adverse cardiac events (MACE) among chest pain patients discharged from the ED [13]. However, chest pain risk scores are underutilized in EDs [14], and when used, issues such as miscalculation [15] or discordance among physicians [16] are common.

Digital tools are increasingly integrated into healthcare, offering potential enhancements in efficiency and decision-making [17,18]. In acute chest pain management, international societies are advocating improved symptom classification methods through machine learning [19]. In addition to biometric data such as vital signs or ECG, a prompt and reliable acquisition of medical history data is essential for use of these techniques. Computerized history-taking (CHT) is a possible solution, offering an automated, structured, and standardized approach to self-reported medical history. Previous studies indicate that CHT can assist physicians by providing a more detailed and complete medical history in both emergent and non-emergent settings [20-23]. Studies have also shown that CHT is well-received by acute chest pain patients, with a majority being able to interact effectively,

providing sufficient data for risk stratification using the HEART score [24-26]. However, there is a knowledge gap regarding the impact of CHT on clinical management and outcomes in an acute care setting [27]. This study proposes a standardized, automated approach to collect medical history data, enabling real-time use of clinical decision support tools. This method has the potential to significantly impact the management of the large population of patients presenting to EDs with chest pain.

We hypothesized that risk scores populated with CHT data would reliably identify acute chest pain patients at low risk for MACE, enabling early and safe rule-out, thereby reducing unnecessary admissions and diagnostic testing without compromising patient safety. Our aims were, therefore, to (1) establish whether three well-established risk scores populated by data collected by a digital tool for medical history taking can be used for early rule-out of a MACE, defined as an ACS diagnosis, revascularization, or cardiovascular death within 30 days; (2) determine the overall diagnostic accuracy of the three risk scores populated with CHT data for a MACE rule-out; and (3) assess the potential impact of this method on the disposition for patients presenting with acute chest pain.

Methods

Study design and setting

The Clinical Expert Operating System Chest Pain Danderyd Study (CLEOS-CPDS; ClinicalTrials.gov identifier: NCT03439449) was a prospective cohort study designed to determine the value of self-reported CHT in acute chest pain management [28].

The current study reports on diagnostic accuracy and adheres to the Standards for Reporting Diagnostic Accuracy (STARD 2015) guideline [29], complies with the Declaration of Helsinki, and was approved by the Stockholm Regional Ethical Committee (now Swedish Ethical Review

Authority) (reference number 2015/1955-1). Informed consent was obtained from all participants prior to inclusion in the study.

Participants

Patients presenting at Danderyd University Hospital, a tertiary hospital in Stockholm, Sweden, were consecutively enrolled between October 1, 2017, and May 16, 2019. Eligible participants were women and men, aged ≥ 18 years, fluent in Swedish, with a presenting complaint of chest pain recorded by an ED triage nurse or registrar, a non-diagnostic first ECG and/or serum markers for an acute disease requiring immediate care, and with clinical stability, as defined by the Rapid Emergency Triage and Treatment System (RETTS) levels: orange, yellow, green, and blue [30]. Exclusion criteria included the inability to carry out a CHT interview (e.g., agitation, severely impaired vision, or confusion). The most common causes for exclusion were language barriers (e.g., inability to read Swedish), tiredness, and difficulties in using a tablet [25]. Patients were managed according to standard care protocols recommended by regional guidelines [31]. The data from the CHT and the calculated risk scores were not accessible to the treating physicians or other healthcare professionals and were used solely for clinical research purposes.

Interventions

Computerized history-taking (CHT)

Medical history was collected using the CHT software CLEOS on tablets (iPad, Apple Inc, Cupertino, CA, USA), as described in detail previously [28,32]. Briefly, CLEOS is an expert system, a form of artificial intelligence software that employs a rule-based approach for guiding the history-taking process. It incorporates a comprehensive medical knowledge base, algorithmically represented

by decision trees comprising >17,000 decision nodes. By directly interacting with the patient, CLEOS automates history-taking through a series of structured questions, mainly in text format (i.e. yes/no or multiple-choice questions), but also image-based questions. A limited number of free-text entries are available for instances where patients are unable to select a suitable option, such as describing the quality of their pain. Based on prior responses and their clinical relevance, CLEOS adapts the interview and dynamically determines the next most appropriate questions, emulating clinical reasoning continuously as data are collected [32]. In a study evaluating inter-rater reliability between data collected using CHT and physician-acquired data, we observed high agreement for traditional risk factors (e.g., diabetes mellitus or hypercholesterolemia), but low to moderate agreement for chest pain characteristics (e.g., pain radiating to the arm or relief by rest) [33]. As previously reported, the median time to collect sufficient information to calculate the HEART score was 23 (IQR 18-31) min [25].

Chest pain risk scores

The HEART score, EDACS-ADP, and T-MACS were calculated as described in their respective derivation study [7-9]. The Danderyd HEART score (D-HEART) was calculated according to guidelines in Region Stockholm [31], combining a modified HEART score hs-cTn assays with the European Society of Cardiology (ESC) 0/1-hour rule-out and rule-in algorithm [34,35]. When assessing the History component in the modified HEART score, the traditional clinical classification of suspected anginal symptoms was used, i.e., (1) central chest pain, (2) triggered by physical or emotional exertion, and (3) relieved by rest or nitrates. Based on the number of criteria met, patient history was categorized as highly (three criteria met), moderately (two criteria met), or slightly suspicious (none or one criterion met). This approach differs from the derivation study, where the clinician's clinical judgment, rather than a predefined set of criteria, is used to evaluate the likelihood

of chest pain being related to a MACE [7]. We also defined a clinically decisive risk score as “not low risk” status, indicating the need for hospitalization, if D-HEART ≥ 4 , HEART ≥ 4 , EDACS ≥ 16 , T-MACS ≥ 0.02 , or a rule-in troponin using the European Society of Cardiology (ESC) 0/1-hour algorithm [4]. Detailed descriptions of chest pain characteristics and risk factors components for D-HEART, HEART, EDACS, and T-MACS are provided in Table 1.

Table 1. Components and interpretation of assessed risk scores.

Component	Risk score			
	D-HEART	HEART	EDACS-ADP	T-MACS
Age	X	X	X	
Sex			X	
Chest pain characteristics				
History suspicious for ischemia		X		
Central chest pain	X			
Provoked by physical exertion or emotional stress	X			
Relieved by rest or nitrates	X			
Diaphoresis			X	X
Radiation to arm or shoulder			X	
Radiation to right arm or shoulder				X
Pain occurred/worsened with inspiration			X	
Pain is reproduced by palpation			X	
Worsening or crescendo angina				X
Pain associated with vomiting				X
Risk factors				
Atherosclerotic disease	X	X		
Known CAD (not stroke)			X	
Diabetes mellitus	X	X	X	
Current smoker	X	X	X	
Family history of premature CAD	X	X	X	
Hypertension	X	X	X	
Hypercholesterolaemia	X	X	X	
Reported obesity	X	X		
ECG, vital signs, and biomarkers				
Signs of ischemia on ECG	X	X	X	X
Hypotension, SBP <100 mmHg				X
Elevated biomarker (troponin)	X	X	X	X
Possible range of score	0–8	0–10	-10–34	0–1
Threshold for “not low risk”	≥4 ^a	≥4	≥16 ^b	≥0.02

^a and/or new ischemia on ECG and/or a rule-in 0 or 2 h troponin. ^b and/or a rule-in troponin using the European Society of Cardiology 0/1-hour algorithm (4). CAD: coronary artery disease. ECG: electrocardiogram.

Data collection

At presentation to the ED, all acute chest pain patients were triaged by a cardiology consultant or senior cardiology resident (from 8:00 to 17:00) or by a triage nurse using the RETTS protocol (from 17:00 to 08:00) to determine the degree of urgency [30]. After obtaining ECG and biomarkers during triage, patients underwent a more thorough examination and standard history-taking by the attending physician in the ED cardiology unit or the inpatient day-care unit. Details on the disposition of patients are available in previous publications [25,28].

The process of participant enrollment has been previously described in detail [25,28]. In short, patients were offered to participate in the study by a research staff member in the ED cardiology unit or in the inpatient day-care unit. Patients were provided with standardized information and offered the opportunity to ask questions before signing a consent form to give their informed consent, all according to procedures approved by the ethical committee.

To evaluate the ability to engage with the CHT program, a research assistant monitored whether the patient could independently answer the initial questions of the program (regarding demography). If not, the patient was not included in the study. After this initial step, the CHT interview was conducted by the patient without any research assistant present, though they were available if needed, e.g., if any technical issues should occur. CHT was conducted during waiting times in the ED, both before and after physician consultations. The CHT interview could be paused during standard clinical procedures, e.g., blood sampling or radiographic examinations, and resumed afterwards. The environment in which the CHT took place, ranging from the general ED waiting area to curtained or walled spaces, varied in privacy and noise levels. Discontinuation of CHT occurred either upon completion, by the patient's own decision, or upon discharge to home or admission to a ward. Reasons for discontinuation were documented by the research assistant. The CHT interview did not interfere with standard management, and the ED staff had no access to any data collected with CHT.

Data relevant to this study were extracted from the EHR (TakeCare, CompuGroup Medical Sweden AB, Solna, Sweden) by research staff and from the CHT database. To align with the variables used in the risk scores, we predefined the variables to be collected and established an interpretation scheme to allow all variables to be converted into a binary format (yes/no responses; see example of interpretation scheme for crescendo angina pectoris in [33]). Demographic information (age and sex) of the general ED population at Danderyd University Hospital during the study period was extracted from the EHR system using QlikView version 12.10 (QlikTech International AB, Lund, Sweden).

ECG findings, interpreted by both physicians and computer, were collected by the research assistant from the EHR. In assessing the impact of CHT on chest pain management, the physician-reported ECG interpretations were used for populating the risk scores. In cases where a physician's report was missing, the automated ECG interpretation (EC Sense ECG, Cardiolex Medical AB, Stockholm, Sweden) was imputed. A detailed description of ECG findings and their categorization is available in Supplementary material, Table 1. Blood samples were collected in lithium heparin-containing test tubes (BD Vacutainer, BD Sweden AB, Stockholm, Sweden) to assess plasma high-sensitivity cardiac troponin T (hs-cTnT) levels using the Elecsys electrochemiluminescence immunoassay (Roche Diagnostics, Basel, Switzerland, according to standard procedures at the Karolinska University Laboratory, Stockholm. The detection limit of this assay is 5 ng/L with a 99th percentile upper reference limit, used to identify elevated levels indicative of myocardial injury, of 14 ng/L [36].

Outcome measures

The primary outcome was defined as a diagnosis of ACS [28]. To facilitate comparison with other diagnostic accuracy studies on acute chest pain, we also report on a 30-day MACE, comprising (1)

an ACS diagnosis, (2) revascularization, or (3) cardiovascular death within 30 days. As outlined in the study protocol, the diagnosis of an ACS was verified by a cardiologist following the prevailing European guidelines at the time of the study [37,38]. The cardiologist then assigned the corresponding International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes I20.0 (unstable angina), I21.0–9 (acute myocardial infarction) or I24.0–9 (other acute ischemic heart diseases) [39,40]. Previous studies have concluded that the overall positive predictive value of Swedish discharge ICD codes was 85-95% for most diagnoses, including acute myocardial infarction [41,42].

Using EHR data, only a minority of patients had sufficient data for risk score calculation [43]. Thus, the patient's disposition was used as a proxy of the attending physician's assessment of risk level. Participants discharged from the ED to home were classified as "low risk", while those admitted to a ward, or a day-care-unit were categorized as "not low risk".

Statistical analysis

In evaluating the diagnostic accuracy, a risk score populated with data from CHT was considered as the index test, and an outcome of a MACE or ACS was considered as the reference test. Descriptive statistics were given as mean values $\pm$ SD or 95% confidence intervals, or proportions, as appropriate. To test for differences between groups with and without MACE and ACS, Student's t-test was used for continuous variables, and Pearson's chi-square test for binomial and categorical variables. Diagnostic accuracy was assessed using cross tabulation of the index test against the reference test. For each index test, the performance was evaluated by calculating the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the reference test. Pearson's chi-square test was used to compare the NPV between the index tests. Receiver operating characteristic (ROC) curves were plotted for respective risk score, and the Hanley and

McNeil method [44] was used to test for difference between the area under the receiver operating curve (AUC). Analyses were performed with STATA software, version 14.2 (StataCorp, College Station, TX, USA).

The sample size was determined according to targeted precision of sensitivity and specificity, as previously described [28]. Briefly, as the prevalence of MACE and ACS in the study population was unknown, we based the calculation on the assumption that the prevalence was 0.5 (50%), maximizing the estimated sample size. To achieve a ± 0.03 (3%) precision of sensitivity and specificity, as calculated using nQuery, version 7.0 (Statistical Solutions Ltd, Boston, MA, USA), 1,000 participants were required.

Results

Study population characteristics

During the study period, a total of 13,044 patients presented with a chief complaint of chest pain at the ED. During time periods with on duty research staff, (office hours, evenings, and weekends) 1,000 patients were consecutively included (Figure 1). Age and sex distribution of the study population (mean age 55.3 ± 17.4 years; 46% female) align closely with the demographics of the general chest pain population at Danderyd University Hospital (mean age 57.6 ± 19.1 years; 49% female). Further baseline characteristics collected by CHT and selected ED, and the disposition of patients are summarized in Table 2 and 3.

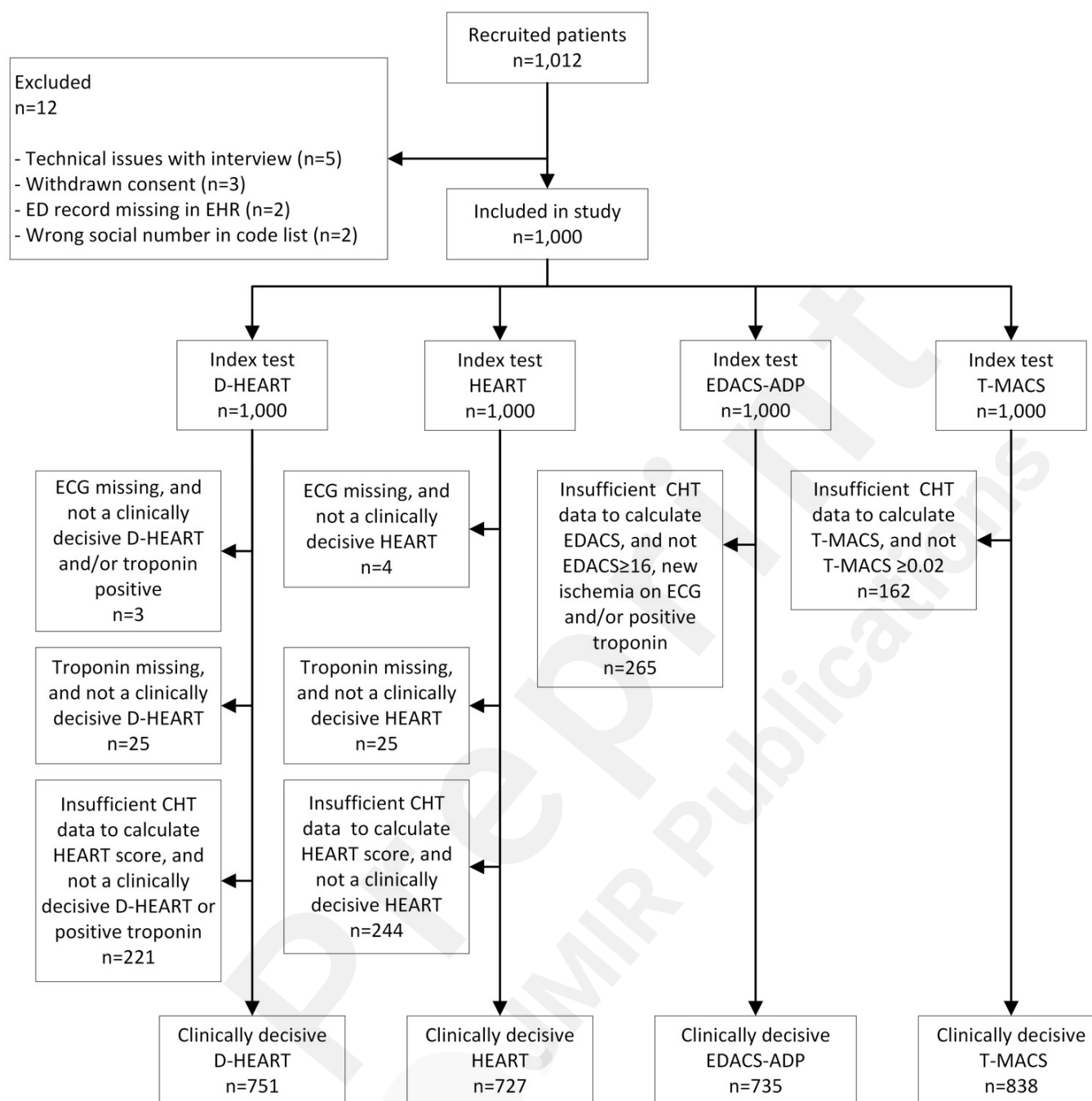


Figure 1. Study flow diagram. ED: emergency department; ECG: electrocardiogram; CHT: computerized history-taking. During the study period, a total of 13,044 patients presented with a chief complaint of chest pain at the ED. Of these, 1,012 individuals provided informed consent and met the inclusion criteria during periods when research staff were on duty.

2025-04-15

Table 2. Demography and background of all included patients divided into groups depending on outcome (30-day MACE and ACS).

Characteristic	All		MACE		Non-MACE		P-value	ACS		Non-ACS		P-value
	Value	n	Value	n	Value	n		Value	n	Value	n	
Age, years	54.7 ± 17.2	1000	67.6 ± 11.0	72	53.7 ± 17.1	928	<.001	68.0 ± 10.9	64	53.9 ± 17.1	930	<.001
Sex (females)	456 (46)	1000	19 (26)	72	437 (47)	928	.001	18 (28)	64	438 (47)	930	.004
Body mass index, kg/m2	26.4 ± 4.7	1000	26.6 ± 4.3	72	26.3 ± 4.7	928	.627	26.2 ± 3.9	64	26.4 ± 4.7	928	.813
Diabetes mellitus type 1 or 2	62 (8)	788	8 (16)	51	54 (7)	737	.032	5 (11)	44	57 (8)	740	.382
Ongoing lipid lowering medication	128 (20)	640	21 (48)	44	107 (18)	596	<.001	18 (46)	39	110 (18)	597	<.001
Hypertension	316 (41)	765	34 (64)	53	282 (40)	712	<.001	31 (67)	46	285 (40)	715	<.001
Family history of coronary artery disease	200 (26)	774	18 (38)	48	182 (25)	726	.057	17 (41)	41	183 (25)	729	.020
Known coronary artery disease	137 (16)	851	31 (55)	56	106 (13)	795	<.001	27 (55)	49	110 (14)	798	<.001
History of angina pectoris	88 (10)	850	23 (41)	56	65 (8)	794	<.001	20 (41)	49	68 (9)	797	<.001
History of myocardial infarction	82 (10)	850	21 (38)	56	61 (8)	794	<.001	18 (37)	49	64 (8)	797	<.001
History of percutaneous coronary intervention	76 (9)	833	16 (29)	55	60 (8)	778	<.001	13 (27)	48	63 (8)	781	<.001
History of coronary artery bypass graft	18 (2)	833	10 (18)	55	8 (1)	778	<.001	9 (19)	48	9 (1)	781	<.001
Current smoker	90 (11)	790	5 (9)	53	85 (12)	737	.642	5 (11)	46	84 (11)	740	.920
Region of birth												
Nordic countries	829 (83)	1000	63 (8)	72	766 (83)	928	.282	55 (86)	64	769 (83)	930	.504
Europe (outside the Nordic countries)	46 (5)	1000	1 (1)	72	45 (5)	928	.177	1 (2)	64	45 (5)	930	.228
Outside Europe	125 (13)	1000	8 (11)	72	117 (13)	928	.711	8 (13)	64	116 (12)	930	.995
Occupational status												
Active worker (employed, student)	616 (62)	1000	26 (36)	72	590 (64)	928	<.001	23 (36)	64	589 (63)	930	<.001
Not at work (unemployed, on sick leave)	69 (7)	1000	1 (1)	72	68 (7)	928	.055	1 (2)	64	67 (7)	930	.084
Retired	315 (32)	1000	45 (63)	72	270 (29)	928	<.001	40 (63)	64	274 (29)	930	<.001
Arrived at ED by ambulance	189 (21)	917	14 (24)	58	175 (20)	859	.493	13 (25)	51	176 (20)	862	.385
Ongoing chest pain during CHT	544 (61)	892	19 (35)	55	525 (63)	837	<.001	16 (33)	48	524 (62)	840	<.001

Data are presented as mean values ± SD or n (%), as appropriate. Self-reported medical history data derived from CHT. MACE: 30-day major adverse cardiac event. ACS: 30-day acute coronary syndrome. CHT: computerized history-taking. ED: emergency department.

2025-04-15

Table 3. Vital signs, electrocardiogram, circulating biomarkers and disposition of all included patients divided into groups depending on outcome (30-day MACE and ACS) or not.

	All		MACE		Non-MACE		P-value	ACS		Non-ACS		P-value
Characteristic	Value	n	Value	n	Value	n		Value	n	Value	n	
Vital parameters at triage												
Systolic blood pressure, mmHg	143 ± 22	995	148 ± 22	72	143 ± 22	923	.056	148 ± 22	64	143 ± 22	926	.081
Diastolic blood pressure, mmHg	83 ± 13	993	81 ± 14	72	84 ± 13	921	.178	81 ± 15	63	83 ± 13	910	.178
Heart rate	77 ± 16	984	74 ± 15	72	77 ± 16	912	.151	74 ± 16	64	77 ± 16	913	.193
Respiration rate	16 ± 3	984	16 ± 2	72	16 ± 3	912	.849	16 ± 2	64	16 ± 3	915	.861
Body temperature (°C)	36.8 ± 0.4	947	36.6 ± 0.4	70	36.8 ± 0.4	877	<.001	36.6 ± 0.4	63	36.8 ± 0.4	879	.001
Electrocardiogram												
New signs diagnostic for ischemia	68 (7)	994	14 (20)	71	54 (6)	923	<.001	14 (22)	63	53 (6)	926	<.001
New nonspecific ST-T changes	131 (13)	994	20 (28)	71	111 (12)	923	<.001	16 (25)	63	115 (12)	926	.003
Normal or known ST-T alterations	795 (80)	994	37 (52)	71	758 (82)	923	<.001	33 (52)	63	758 (82)	926	<.001
High sensitive troponin T values												
>3 x normal limit (> 42 ng/L)	47 (5)	970	29 (41)	71	18 (2)	899	<.001	28 (44)	63	19 (2)	901	<.001
1-3 x normal limit (15-42 ng/L)	112 (12)	970	19 (27)	71	93 (10)	899	<.001	16 (25)	63	96 (11)	901	<.001
Normal limit* (≤14 ng/L)	811 (84)	970	23 (32)	71	788 (88)	899	<.001	19 (30)	63	786 (86)	910	<.001
5-14 ng/L	397 (41)	970	15 (21)	71	367 (41)	899	.001	11 (17)	63	368 (41)	901	<.001
1 h troponin T elevated (>2 ng/L)	21 (2)	970	2 (3)	71	19 (2)	899	.695	2 (3)	63	19 (2)	901	.575
<5 ng/L	414 (43)	970	4 (6)	71	410 (46)	899	<.001	4 (6)	63	407 (45)	901	<.001
Admitted to the ward or day-care unit	528 (53)	990	69 (96)	72	459 (50)	918	<.001	62 (97)	64	466 (50)	926	<.001
Ward (not via day-care unit)	203 (21)	990	61 (85)	72	141 (15)	918	<.001	57 (89)	64	146 (16)	926	<.001
Day-care-unit	325 (33)	990	7 (10)	72	318 (35)	918	<.001	5 (8)	64	320 (35)	926	<.001
Day-care unit then to ward	33 (3)	990	7 (10)	72	26 (3)	918	.002	5 (8)	64	28 (3)	926	.039
Day-care unit then sent home	292 (29)	990	0 (0)	72	292 (32)	918	<.001	0 (0)	64	292 (32)	926	<.001

Data are presented as mean values ± SD or n (%), as appropriate. Data derived from EHR. MACE: 30-day major adverse cardiac event. ACS: acute coronary syndrome. *99th percentile. For definitions of interpretation of electrocardiograms see supplementary material (Supplementary material, Table 1).

Endpoints reached within 30 days.

Among the 1,000 included patients, 72 experienced a MACE, including 65 with an ACS, 7 underwent coronary revascularizations without an ACS diagnosis, and no cases of cardiovascular death occurred. Types of MACE and ACS are presented in Table 4. MACE and ACS were associated with increasing age, male sex, diabetes mellitus, lipid lowering therapy, hypertension or a history of coronary artery disease (Table 2). Primary diagnoses for participants discharged from either the ED or the day-care-unit, as well as those hospitalized, are reported in Table 5 and 6, respectively.

Diagnostic accuracy for a MACE or ACS

A clinically decisive D-HEART, HEART, EDACS-ADP, or T-MACS could be calculated in 75%, 73%, 74%, and 84%, respectively using only CHT acquired data (Figure 1). Results from cross tabulation and the diagnostic performance for each risk score populated with CHT data for a MACE or ACS are summarized in Table 7 and Supplementary material, Table 2. The diagnostic accuracy of T-MACS at a threshold of <0.05 (low risk), compared to the very low threshold of <0.02 for rule-out, is provided in the Supplementary material, Table 3. No differences were found for AUC between any of the risk scores, see Figure 2 and Supplementary material, Table 4. No adverse events occurred during the CHT interviews.

D-HEART versus HEART

In comparing the NPV (95% CI) for ruling out a MACE and ACS, no difference ($P<.001$) was found between D-HEART and HEART scores: 0.99 (0.98–1.00) versus 0.99 (0.97–1.00), and 0.99 (0.98–1.00) versus 0.99 (0.97–1.00), for a MACE and ACS, respectively. Similarly,

no difference was found in the diagnostic accuracy when comparing the AUCs (supplementary material, Table 4).

Table 4. Major adverse cardiac events within 30-days among the 1,000 participants.

Outcome	7-day	30-day	Total
MACE	70	2	72
Acute coronary syndrome	64	1	65
Unstable angina (I20.0)	22	0	22
Revascularization	19	0	19
PCI	16	0	16
CABG	3	0	3
No revascularization	3	0	3
Acute subendocardial myocardial infarction (I21.4)	33	1	34
Revascularization	24	1	25
PCI	23	1	24
CABG	1	0	1
No revascularization	9	0	9
Acute myocardial infarction, unspecified, type 1 (I21.9 + I98.1)	6	0	6
Revascularization	4	0	4
PCI	4	0	4
CABG	0	0	0
No revascularization	2	0	2
Acute myocardial infarction, unspecified, type 2 (I21.9 + I98.2)	3	0	3
Revascularization	0	0	0
PCI	0	0	0
CABG	0	0	0
No revascularization	0	0	0
Revascularization without ACS diagnosis	6	1	7
PCI	6	1	7
CABG	0	0	0
Cardiovascular death	0	0	0

MACE: major adverse cardiac event. PCI: percutaneous coronary intervention. CABG: coronary artery bypass graft. ACS: acute coronary syndrome. 7-day: Outcome at discharge or ≤7 days from the emergency department visit. 30-day: Outcome after discharge or >7 days,

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and ≤ 30 days from the emergency department visit. Data derived from the electronic health record.



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Table 5. Primary ICD-10 code and diagnosis for the 754 patients discharged to home.

ICD-10 code	Diagnosis	n (%)
R07	Pain in throat and chest	574 (76)
R00-09 (excl. R07)	Symptoms and signs involving the circulatory and respiratory systems	57 (8)
R10-49	Symptoms and signs involving other organ systems	23 (3)
I48	Atrial fibrillation and flutter	16 (2)
R50-69	General symptoms and signs	14 (2)
M79	Other soft tissue disorders, not elsewhere classified	11 (2)
K29.7, K21.9	K30.9, Gastritis, unspecified; Functional dyspepsia; Gastro-oesophageal reflux disease without oesophagitis	10 (1)
I20.1–9	Angina pectoris	4 (<1)
I26.9	Pulmonary embolism without mention of acute cor pulmonale	3 (<1)
J18.9	Pneumonia, unspecified	2 (<1)
J45.9	Asthma, unspecified	2 (<1)
I30.9	Acute pericarditis, unspecified	1 (<1)
I63.9	Cerebral infarction, unspecified	1 (<1)
J44.1	Chronic obstructive pulmonary disease with acute exacerbation, unspecified	1 (<1)
	Other non-severe diagnosis	35 (5)

Diagnosis reported by the physician in the electronic health record for patients with a chief complaint of chest pain that were discharged to home (n=754), either directly from the ED (n=462), or passing the day-care-unit (n=292).

Table 6. Primary discharge ICD-10 code and diagnosis for hospitalized patients.

ICD code	Diagnosis	n (%)
I20.0, I21	Acute coronary syndrome ^a	62 (26)
I20.1–9	Angina pectoris	14 (6)
I25.9	Chronic ischaemic heart disease, unspecified	8 (3)
I05.0	Mitral stenosis	1 (<1)
I10.9	Essential (primary) hypertension	1 (<1))
I26-I28	Pulmonary heart disease and diseases of pulmonary circulation	6 (3)
I30-I52	Other forms of heart disease	35 (15)
	I30 Acute pericarditis	2
	I35 Nonrheumatic aortic valve disorders	3
	I40 Acute myocarditis	5
	I42 Cardiomyopathy	1
	I44 Atrioventricular and left bundle-branch block	1
	I47 Paroxysmal tachycardia	2
	I48 Atrial fibrillation and flutter	10
	I49 Other cardiac arrhythmias	3
	I50 Heart failure	8
I95-I99	Other and unspecified disorders of the circulatory system	1 (<1)
J09-J18	Influenza and pneumonia	4 (2)
J20	Acute bronchitis	1 (<1)
J44.1	Chronic obstructive pulmonary disease with acute exacerbation, unspecified	1 (<1)
K00-93	Diseases of the digestive system	7 (3)
R07.4	Chest pain, unspecified	64 (27)

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R00-09 (not R07.4)	Symptoms and signs involving the circulatory and respiratory systems	11 (5)
R10-49	Symptoms and signs involving other organ systems	1 (<1)
R50-69	General symptoms and signs	2 (1)
Other non-severe diagnosis singularly reported		17 (7)

^aPrimary diagnosis of I20.0 (unstable angina) or I21 (acute myocardial infarction).

Data reported by the physician in the electronic health record for patients with a chief complaint of chest pain that was admitted from the emergency department (n=236). Of these 15 patients was admitted to a non-cardiac ward.

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Table 7. Performance of risk scores populated with data derived from computerized history taking for a major adverse cardiac event within 30 days.

	True pos	False pos	False neg	True neg	Sensitivity	Specificity	PPV	NPV
D-HEART	65	270	4	412	0.94 (0.86–0.98)	0.60 (0.57–0.64)	0.19 (0.15–0.24)	0.99 (0.98–1.00)
HEART	60	261	6	400	0.91 (0.81–0.97)	0.61 (0.57–0.64)	0.19 (0.15–0.23)	0.99 (0.97–1.00)
EDACS-ADP	66	323	4	342	0.94 (0.86–0.98)	0.51 (0.48–0.55)	0.17 (0.13–0.21)	0.99 (0.97–1.00)
T-MACS	67	485	2	284	0.97 (0.90–1.00)	0.37 (0.34–0.39)	0.12 (0.10–0.15)	0.99 (0.98–1.00)

pos: positive. neg: negative. PPV: positive predictive value. NPV: negative predictive value. Data are presented as n or probability with 95% confidence interval. If T-MACS with a threshold of <0.05 for low risk was used, the true positive, false positive, false negative, true negative, sensitivity, specificity, PPV and NPV was 55, 294, 7, 418, 0.89 (0.78–0.95), 0.59 (0.55–0.62), 0.16 (0.12–0.20) and 0.98 (0.97–0.99), respectively.

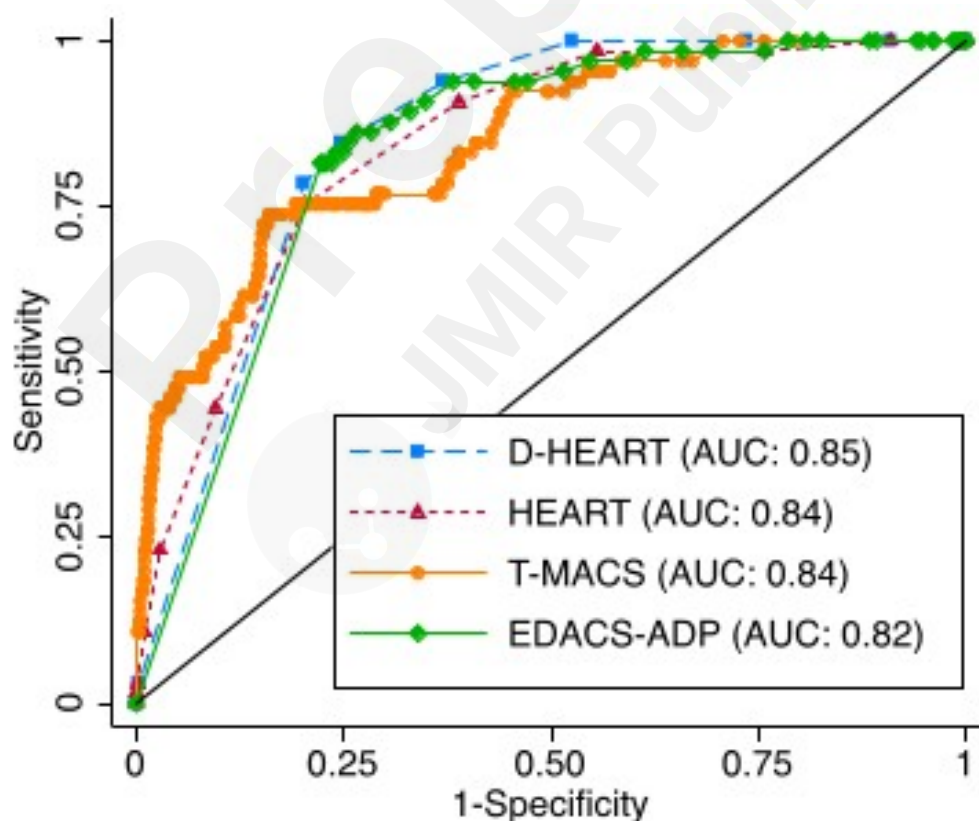


Figure 2. Receiver operating curves for HEART, D-HEART, EDACS-ADP and T-MACS for a 30-day major adverse cardiac event. AUC: area under the receiver operating curve

Risk reclassification for MACE or ACS

Of the 1,000 participants, 528 were admitted, with 203 to the ward and 325 to the day-care unit. Of the day-care unit admissions, 33 were subsequently admitted to the ward, and 292 were discharged to home (Table 3). If CHT data had been used instead of standard management, to calculate D-HEART, HEART, and EDACS-ADP, there would have been a net reclassification from “not low risk” to “low risk” in 89 (17%), 89 (17%), and 31 (6%) cases, respectively. However, due to the lower specificity, using the T-MACS, 91 (17%) of patients would instead have been net reclassified from “low risk” to “not low risk”. See details in Table 8.

Table 8. Reclassification if risk scores populated with computerized history taking data had been used for disposition of patients instead of physician management.

Reclassification	D-HEART	HEART	EDACS-ADP	T-MACS
Low to not low risk	93	97	128	220
Not low risk to low risk	182	186	159	129
Difference	89	89	31	-91
Proportion of admissions	-17%	-17%	-6%	+17%

Admission to ward or day-care-unit (n=528) was considered as proxy for not low risk and if sent home (n=462) a proxy for low risk. Data for one (1) participant is missing and nine left the emergency department without seeing a physician. Difference indicates *n* and % change of admissions that could have been safely sent home.

Discussion

This study shows that CHT can be used to calculate three established risk scores in 73–84% (depending on the risk score applied) of acute chest pain patients with high diagnostic accuracy, including a 30-day three-point MACE rule-out with an NPV of 0.98–0.99 (95% CI: 0.97–1.00). We also show that using this method, a substantial fraction (up to 17%) of patients admitted with acute chest pain could be reclassified from a “not low risk” to a “low

risk” group using D-HEART, HEART, or EDACS-ADP, potentially facilitating safe discharge instead of hospital admission.

Our findings on diagnostic accuracy align with multiple validation studies [8,10-13,45], where traditional physician-acquired medical histories were used, demonstrating the efficacy of risk scores in safely ruling out MACE in the ED. However, this appears to be the first study to report on the performance of an automated way to calculate these risk scores. Considering the significant volume of patients presenting to the ED with chest pain, automating the risk stratification process through CHT could more effectively identify patients eligible for safe discharge, with less resource utilization, and reduce physician workload.

The risk scores assessed had similar performance for ruling out a 30-day MACE or ACS. While there was a trend in favor of the HEART score, this could not be statistically confirmed. Our findings align with previous studies reporting on the performance of the risk scores. The diagnostic performance of HEART score was evaluated in a meta-analysis of 25 studies (n=25,266) from 2010 to 2017, showing a pooled sensitivity of 96% (95% CI: 0.93–0.98) and NPV of 99% (95% CI: 0.98–0.99) [10]. A meta-analysis of EDACS score (8 studies, n=11,578) reported pooled sensitivity of 95% (95% CI: 90-99) but did not specifically report NPV [46]. In a North American external validation study (n=763), EDACS-ADP demonstrated a sensitivity and NPV of 100% (95% CI: 0.94–1.00) and 100% (95% CI: 0.99–1.00), respectively [11]. For T-MACS, secondary analyses of four UK cohort studies (n=1,459) reported a sensitivity and NPV of 98% (95% CI: 0.95–1.00) and 99% (95% CI: 0.98–1.00), respectively, in the validation dataset [9]. However, the HEART score, which has undergone more extensive validation, consistently demonstrates good performance and is endorsed by international societies [5,47]. Therefore, if CHT in its current form is to be integrated into risk score assessment, the HEART score should preferably be used.

In our study, a modified HEART score combined with the ESC 0/1-hour algorithm (D-HEART) demonstrated equivalent performance for MACE rule-out, as compared to the original HEART score using only the initial troponin sample. This suggests employing the simpler HEART score without repeated troponin measurements. However, this contrasts with Nilsson et al.'s findings, where the original HEART score had a slightly lower diagnostic accuracy, than a combination of the HEART score and a 0/1-hour troponin algorithm [48]. As the HEART score is mainly created and validated for safe rule-out of MACE, it is reasonable to assume that integrating a 0/1-hour algorithm enhances the ability for a rule-in, as suggested previously [49].

During our study, two patients receiving standard care experienced a MACE after ED discharge to home within 30 days; one patient lacked sufficient data for risk score calculation and another had a low-risk HEART score of three points. Our findings show an AUC of 0.82–0.85 and a NPV of 0.98–0.99, varying by the risk score used. While there is no universal benchmark for AUC or NPV in risk stratification, an AUC of 0.8–0.9 is generally considered excellent, and >0.9 outstanding [50]. Interpretation of NPV varies by clinical context; for MACE a high NPV is desirable for safe rule-out [51]. Overall, our findings suggest that risk calculation using CHT data performs at least equally well, as compared to traditional history-taking. It is reassuring to notice that all scores reproduce similar results. However, a further refinement CHT data collection could potentially further enhance MACE rule-out capability.

A significant fraction (up to 17%) of the participants were reclassified from “not low risk” to “low risk”, when using D-HEART, HEART, and EDACS-ADP populated with CHT data as compared to standard management. These findings align with those reported by Hyams et al.'s in an external validation study, which observed a reduction in hospital admissions of acute chest pain patients by approximately 15% following the implementation of the HEART score [52]. The improvements in classification can reduce anxiety,

unnecessary examinations, and save healthcare resources [53]. Yet, a large Dutch multicenter randomized controlled trial observed a limited impact of risk score calculations on resource usage, attributing nonadherence to management recommendations as a potential cause [54]. Notably, if using T-MACS, more patients would be reclassified from “low risk” to “not low risk”, which could lead to increased admissions (+17%) as compared to standard care due to its lower specificity. Using a higher threshold for T-MACS (<0.05 for “low risk”) increases specificity but with a lower NPV, supporting that this is not the preferred score for disposition of patients. Further studies on optimal CHT implementation, and its impact on resource utilization and quality of care in chest pain management, are warranted.

The current study extends our previous reports on substantial agreement between data collected with CHT and standard history-taking in risk score assessment [33]. Our prior works also established that risk score calculation was possible to a much greater extent when using CHT collected data instead of physician-reported in the EHR (74%–83% vs 10–31%, depending on the risk score used), and that a HEART score excluding the troponin variable (HEAR score) can effectively predict clinical outcomes [54]. The present analysis underscores the broader utility of CHT in facilitating the calculation of established risk scores commonly used in clinical practice. Moreover, this study introduces a *clinically decisive* risk score to align with how these types of risk stratification tools are used in practice. Additionally, we present unique outcomes for the first 1,000 acute chest pain patients enrolled in the CLEOS-CPDS study. Further main strengths of this study include the prospective cohort design, a large and representative population from an ED chest pain population, evaluation under real-world conditions in the typical clinical environment where the tool would be used, and reliable outcomes defined by strict, well-established criteria. The findings’ consistency across multiple validated risk scores underscores the robustness of the results. Further, the generic layout of the CHT software, which is not limited to cardiology or

the ED setting, suggests that our results could be applicable to other clinical settings.

Additionally, the study is initiated and driven in an academic setting, without any commercial interests.

However, several limitations warrant consideration. The single-center design, introduces a risk of selection bias, potentially limiting population diversity. Additionally, the exclusion of patients unable to carry through CHT further exacerbates this bias. Further, risk score determination using CHT data was not feasible for about a quarter of the participants. Premature termination, previously shown to be associated with ED discharge and fatigue, was most common among older adults, individuals born outside Europe, and retirees, thereby limiting conclusions for these groups [25]. This highlights the need for a more user-friendly tool that supports interviews in patients' native languages. Another potential confounder is the influence of patient data, such as ECG or blood samples, collected in the triage prior to history-taking. These data, and prior EHR reports, were accessible to the physician before obtaining the medical history and quite likely impacted the decision-making process. Even though ECG data and blood sample results could have been incorporated into the CHT system and its logic, it was decided not to do so in the present study. For example, CLEOS asks the patient about prior ED visits for chest pain, any previous hospitalization due to chest pain, prior diagnoses of angina, and myocardial infarction, as well as the specifics for any past revascularizations. The primary focus of this study is the safe rule-out of MACE using a clinically decisive risk score. This approach implies that once patients surpass the threshold for “not low risk” (e.g., HEART ≥ 4), the patient is considered as rule-in. However, it should be noted that some patients within this clinically decisive risk group who did not complete the CHT interview might potentially have achieved even higher total risk scores. This suggests that while our results provide a higher level of certainty for ruling out MACE or ACS, they are less definitive for rule-in scenarios. Further, this study carries the risk of

verification bias. However, we believe this risk is minimal, as patients were managed according to standard care protocols, independent from CHT-derived risk scores, which were not available to the treating physician during clinical decision-making. Finally, the variability in physician performance, and the unique ED setup, with a dedicated cardiology unit and day-care-unit staffed by cardiologists may underestimate the CHT performance compared to a setting with less specialist competence in the ED, but also limit the generalizability of our findings to diverse clinical settings.

Future development of this method includes customizing CHT for the ED setting to reduce interview times and broadening its scope to diagnose a wider array of acute conditions e.g., pulmonary embolism and aortic dissection, as well as other non-cardiac causes of chest pain. Additionally, incorporation of multiple languages into the CHT software will enable history-taking in patients' native languages.

Conclusions

Automated medical history-taking using CHT can offer reliable risk scores in a majority of acute chest pain patients, with high diagnostic accuracy to rule-out a 30-day three-point MACE and ACS. This tool could facilitate the management and safe discharge of low-risk patients with acute chest pain in the ED.

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Conflicts of Interest

All patent rights and copyrights to technology, language, images, and knowledge content are assigned without royalty rights to Karolinska Institutet, Stockholm, Sweden, which is a public university. HB: Speaker honoraria for AstraZeneca. TK: Research grants to Karolinska Institutet from Amgen, Medtronic, and ReCor Medical; all outside the submitted work. JS: Speaker honoraria for AstraZeneca, Bayer, NovoNordisk, Medtronic, and shareholder in Beats Vascular Health.

Abbreviations

ACS	Acute coronary syndrome
AUC	Area under the receiver operating curve
CABG	Coronary artery bypass graft
CHT	Computerized history taking
CI	Confidence interval
CLEOS	Clinical expert operating system
CLEOS-CPDS	CLEOS-chest pain Danderyd study
D-HEART	Danderyd HEART
ECG	Electrocardiogram
ED	Emergency department
EDACS	Emergency department assessment of chest pain score
EDACS-ADP	EDACS-accelerated diagnostic pathway

EHR	Electronic health record
ESC	European society of cardiology
HEART	History, ECG, age, risk factors, and troponin
hs-cTn	High sensitivity cardiac troponin
ICD-10	International statistical classification of diseases and related health problems, 10th revision
MACE	Major adverse cardiac event
NPV	Negative predictive value
PCI	Percutaneous coronary intervention
PPV	Positive predictive value
RETTS	Rapid emergency triage system
ROC	Receiver operating characteristic
SD	Standard deviation
STARD	Standards for Reporting Diagnostic Accuracy
T-MACS	Troponin-only Manchester acute coronary syndrome

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Supplementary Files

Multimedia Appendixes

Supplementary tables.

URL: <http://asset.jmir.pub/assets/17bed985ca90f8c9c6c468e684512b53.doc>

TOC/Feature image for homepages

Patient filling out computerized history taking.

