A Rule-Out Strategy Based on High-Sensitivity Troponin and HEART Score Reduces Hospital Admissions

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Study objective: We evaluate whether a combination of a 1-hour high-sensitivity cardiac troponin algorithm and History, ECG, Age, Risk Factors, and Troponin (HEART) score reduces admission rate (primary outcome) and affects time to discharge, health care–related costs, and 30-day outcome (secondary outcomes) in patients with symptoms suggestive of an acute coronary syndrome.

Methods: This prospective observational multicenter study was conducted before (2013 to 2014) and after (2015 to 2016) implementation of a strategy including level of high-sensitivity cardiac troponin T or I at 0 and 1 hour, combined with the HEART score. Patients with a nonelevated baseline high-sensitivity cardiac troponin level, a 1-hour change in high-sensitivity cardiac troponin T level less than 3 ng/L, or high-sensitivity cardiac troponin I level less than 6 ng/L and a HEART score less than or equal to 3 were considered to be ruled out of having acute coronary syndrome. A logistic regression analysis was performed to adjust for differences in baseline characteristics.

Results: A total of 1,233 patients were included at 6 centers. There were no differences in regard to median age (64 versus 63 years) and proportion of men (57% versus 54%) between the periods. After introduction of the new strategy, the admission rate decreased from 59% to 33% (risk ratio 0.55 [95% confidence interval {CI} 0.48 to 0.63]; odds ratio 0.33 [95% CI 0.26 to 0.42]; adjusted odds ratio 0.33 [95% CI 0.25 to 0.42]). The median hospital stay was reduced from 23.2 to 4.7 hours (95% CI of difference −20.4 to −11.4); median health care–related costs, from $1,748 to $1,079 (95% CI of difference −$953 to −$391). The number of clinical events was very low.

Conclusion: In this before-after study, clinical implementation of a 1-hour high-sensitivity cardiac troponin algorithm combined with the HEART score was associated with a reduction in admission rate and health care burden, with very low rates of adverse clinical events. [Ann Emerg Med. 2019;73:491-499.]

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INTRODUCTION

Early assessment of chest pain is challenging. Depending on definitions, 5% to 20% of patients presenting to the emergency department (ED) with chest pain will receive a diagnosis of acute coronary syndrome.[1-3] In a few patients, acute coronary syndrome is falsely ruled out, with a high risk of patients' experiencing a cardiac event shortly after leaving the hospital.[4,5] A safe early rule-in and rule-out algorithm of acute coronary syndrome would enhance decisionmaking in the ED, but so far there are few large prospective multicenter studies examining the consequences for health care burden (ie, admission rate, time in the ED and hospital ward, and health care–related costs) and outcome measures of actually implementing such an algorithm in routine clinical care.[6-8]

Compared with conventional cardiac troponin assays, the high-sensitivity cardiac troponin (hs-cTn) assays have enabled earlier testing and provide more reliable results in the lower measurement range.[9-11] In 2012, a 1-hour hs-cTn decision algorithm was presented,[12] and it has thereafter been validated in several cohorts.[13-16] Since 2015, the European Society of Cardiology has recommended 1-hour hs-cTn decision algorithms in combination with clinical assessment,[17] and a structured way of clinically assessing chest pain patients is the History, ECG, Age, Risk Factors,

Editor's Capsule Summary

What is already known on this topic

The History, ECG, Age, Risk Factors, and Troponin (HEART) score has been tested worldwide in multiple observational studies of various size. Impact studies are the final stage in the development of clinical decision tools, but few are performed.

What question this study addressed

This before-after study of the Swedish Fast Assessment of Thoracic Pain in the Emergency Department Using High-Sensitive Troponins and a Simple Risk Score study assessed the actual influence of using the HEART score along with baseline and 1-hour high-sensitivity troponins on admission rates of 1,233 patients.

What this study adds to our knowledge

Adherence to the protocol was high, and admission rates decreased from 59% to 33%. Adjusted odds of admission were 0.33 (95% confidence interval 0.25 to 0.42).

How this is relevant to clinical practice

In this health care system, use of the proposed algorithm to identify low-risk patients for discharge was associated with a substantial reduction in admission rates. Other health care systems would likely vary in the reduction achieved, but this study demonstrates it can be done.

and Troponin (HEART) score.[18-20] This score has shown precision at least as good as that of the Thrombolysis in Myocardial Infarction score and better than that of the Global Registry of Acute Coronary Events score to identify low-risk patients.[3,7,21,22]

The primary objective of this study was to evaluate whether the clinical implementation of a 1-hour hs-cTn decision algorithm combined with the HEART score would reduce admission rates. We also wanted to examine whether this new assessment strategy would affect the time to discharge, health care–related costs, and outcome.

MATERIALS AND METHODS

Study Design

The Fast Assessment of Thoracic Pain in the Emergency Department Using High-Sensitive Troponins and a Simple Risk Score study was a prospective observational multicenter study in 2 phases conducted at 6 centers in Stockholm and Uppsala, Sweden. The centers, located in urban areas, serve approximately 2.7 million people and are university or teaching hospitals with constant access to catheterization laboratories on site or nearby. Patients presenting with symptoms interpreted as suggestive of acute coronary syndrome by the emergency physician were eligible for inclusion in the ED. Inclusion criteria were patients aged 18 years or older, chest pain suggestive of acute coronary syndrome with a duration of greater than or equal to 10 minutes and an onset of last episode less than or equal to 12 hours, willingness to have blood samples taken according to the study protocol, and a signed written informed consent in Swedish. Exclusion criteria were ST-segment elevation or new left bundle branch block on ECG at presentation or previous participation in the study. Inclusion was made only on weekdays during office hours and required the presence of a research assistant. The study was approved by the Regional Ethical Review Board, Stockholm, Sweden.

Setting

The study was divided into 2 phases, before and after the implementation of a new diagnostic strategy for patients presenting to the ED with symptoms suggestive of acute coronary syndrome. During phase 1 (June 4, 2013, to September 2, 2014), patients were assessed according to local guidelines based on recommendations from the European Society of Cardiology and American College of Cardiology/American Heart Association (ACC/AHA).[23,24] This included clinical assessment, ECG recordings, and measurement of conventional or hs-cTn at presentation and after 3 to 9 hours if myocardial infarction was still suspected. The new diagnostic strategy was implemented in routine clinical care during December 2014. The regional and local written guidelines were updated. Attending physicians in the EDs were educated about the algorithm and provided written information. During phase 2 (January 27, 2015, to May 20, 2016), patients were assessed according to the new strategy (Figure), which applied a modified 1-hour hs-cTn algorithm in combination with calculation of the HEART score (Figure E1, available online at http://www.annemergmed.com). The standard, nonmodified version of the HEART score was used. A HEART score of less than or equal to 3 implies a very low risk of a major adverse cardiac event, whereas a score of greater than or equal to 4 implies an elevated risk.[1,18,19,25] For all patients with a baseline level of hs-cTn within the normal reference range (defined as high-sensitivity cardiac troponin T [hs-cTnT] level $\leq$14 ng/L, high-sensitivity cardiac troponin I [hs-cTnI]

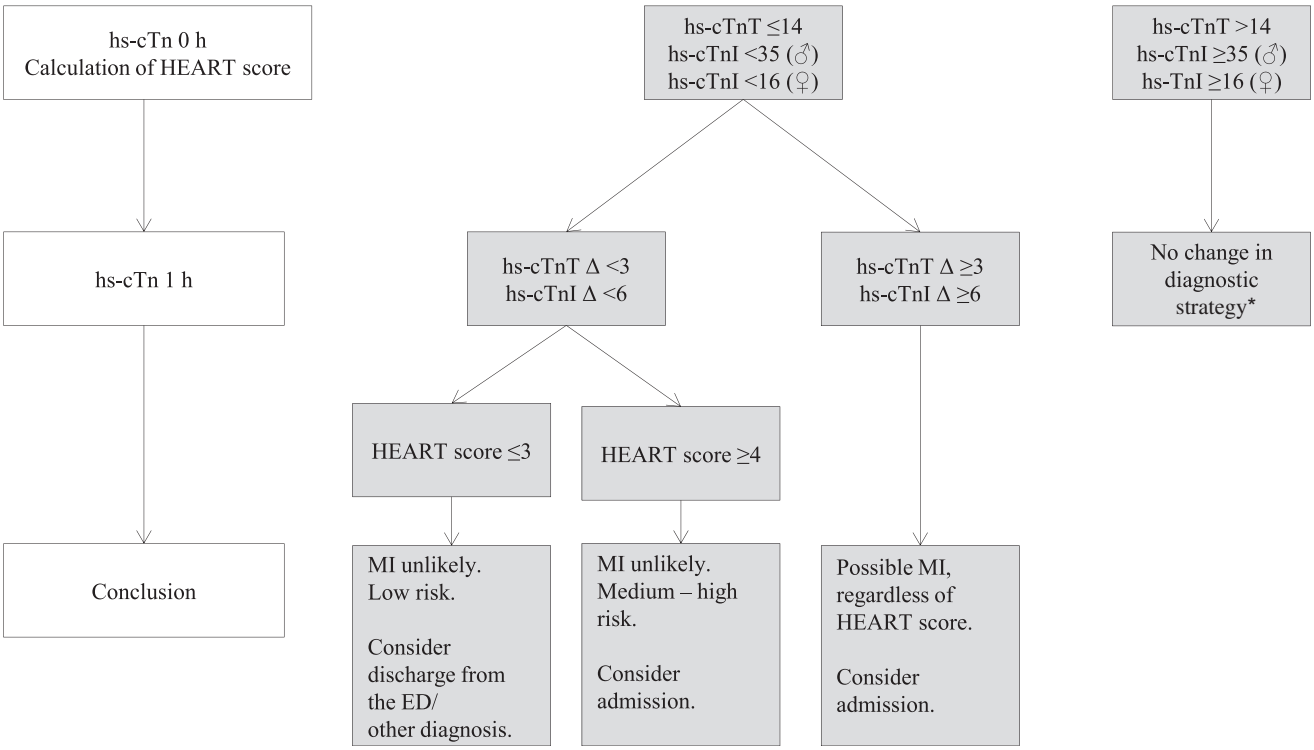

Figure. The new diagnostic strategy. This strategy included measurement of hs-cTn at presentation and after 1 hour, combined with the HEART score. For a patient to be considered low risk, hs-cTn needed to be within the normal reference range at baseline (ie, the HEART score for troponin=0). ♂, Men; ♀, women; *MI*, myocardial infarction. *For patients with an elevated baseline hs-cTn level, no change in assessment strategy was made, and they were assessed in regard to a possible acute coronary syndrome according to the recommendations from the European Society of Cardiology and ACC/AHA. If the patient was judged to have a chronically elevated hs-cTn level, it was not a reason for admission.

level <35 ng/L in men, or hs-cTnI level <16 ng/L in women), a 1-hour hs-cTn sample was obtained, and the Δ value (ie, the absolute 1-hour change in hs-cTn) was calculated. In patients with a Δ value less than 3 ng/L for hs-cTnT or less than 6 ng/L for hs-cTnI, and a HEART score less than or equal to 3, acute coronary syndrome was considered unlikely (Figure). In patients with a Δ value below these cutoffs and a HEART score greater than or equal to 4, myocardial infarction was considered unlikely, but the risk of an acute coronary syndrome was considered elevated. In patients with a Δ value greater than or equal to 3 ng/L for hs-cTnT or greater than or equal to 6 ng/L for hs-cTnI, an ongoing myocardial infarction was recommended to be considered regardless of the HEART score. The emergency physicians could overrule the recommendation provided by the algorithm if it was considered to be clinically indicated. For patients with an elevated baseline hs-cTn level, no change in assessment strategy was made and they were assessed in regard to a possible acute coronary syndrome according to the recommendations from the European Society of Cardiology and ACC/AHA. If the patient was judged to have a chronically elevated hs-cTn level, this was not a reason for admission.

Five centers used the Elecsys hs-cTnT assay (Roche Diagnostics, Basel, Switzerland) during both phase 1 and 2, whereas one center used the Architect Stat hs-cTnI assay (Abbott Laboratories, Chicago, IL) or the Stratus CS instrument (Siemens Healthcare Diagnostics, Deerfield, IL) during phase 1 and only the hs-cTnI assay during phase 2. The Elecsys assay has a limit of detection of 5 ng/L and a 99th percentile of healthy controls of 14 ng/L.[9] The Architect $i2000_{SR}$ assay has a limit of detection of 1.2 to 1.9 ng/L[26,27] and a sex-specific 99th percentile of healthy controls of 34.2 ng/L (men) and 15.6 ng/L (women) according to the manufacturer. The limit of detection of the Stratus CS assay is 0.03 μg/L and the 99th percentile of healthy controls is 0.07 μg/L.[28]

Outcome Measures

The primary endpoint of the study was admission rate, defined as the rate of patients admitted to an inpatient ward. No ED observational units were available at any of

the centers. Secondary endpoints were time to discharge from the hospital, health care–related costs, and clinical outcomes, defined as new presentation to the ED, readmission to the hospital, unplanned revascularization, myocardial infarction, or death. Time to discharge was defined as the time from registration in the ED to the time when the patient left the hospital. The estimations of the hospitals' health care–related costs for hospitalization and procedures were based on price lists obtained from the Stockholm and Uppsala County Councils (Table E1, available online at http://www.annemergmed.com). All data collection in the hospital was performed by a research assistant, who entered the data onto a Web-based case report form. After discharge, patients were followed up by a telephone call 30 days from inclusion in regard to procedures and clinical outcomes. Patients were also asked to estimate their perception of their own health status and their confidence in the management, using a nonvalidated scale between 0 and 100. Cases for all study patients with an elevated troponin level during the index visit or readmission to the hospital within 30 days were adjudicated by 2 independent cardiologists in regard to whether the myocardial infarction criteria were fulfilled. Myocardial infarction was defined according to its universal definition.[29] In cases of disagreement, a third cardiologist adjudicated the study case.

Primary Data Analysis

We expected the admission rate to be 45% during phase 1 and 35% during phase 2. To detect a reduction in admission rate of 10% with a power of 0.90 and an α of .05, the required sample size was 524 patients in each phase. Categoric variables are presented as numbers and percentages and continuous data as medians with interquartile ranges (IQRs). The 2 study groups in phases 1 and 2 were compared according to the intention-to-treat principle. The χ^2 test and Fisher's exact test were used to compare differences in proportions between the 2 groups. We also calculated risk ratio (RR) and 95% confidence interval (CI). The Mann-Whitney *U* test or nonparametric bootstrapping was used to compare continuous variables, and the CIs of the median differences were computed with the percentile method with 10,000 bootstrap replicates. A logistic regression analysis was performed to compare admission rates in phases 1 and 2 (Table E2, available online at http://www.annemergmed.com). In this analysis, we adjusted for age, sex, risk factors, previous cardiovascular diseases, medications at presentation listed in Table 1, and the following presentation characteristics: pulse rate, systolic blood pressure, pulmonary rales, and atrial fibrillation or flutter on the ECG. In a sensitivity analysis, adjustment was also made for an index diagnosis of myocardial infarction versus nonmyocardial infarction because the absolute number of myocardial infarctions was lower during phase 2. All statistical analyses were performed with IBM SPSS Statistics (version 23; Armonk, North Castle, NY) or R (version 3.5.0; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Characteristics of Study Subjects

A total of 1,233 patients met the inclusion criteria and completed the study. The 612 patients in phase 1 had a median age of 64 years and 57% were men (Table 1). The 621 patients in phase 2 had a median age of 63 years and 54% were men. The 2 groups were similar in regard to most risk factors and comorbidities. Patients during phase 1, however, more often had a history of angina pectoris, revascularization, and use of aspirin, P2Y12-receptor blockers, and β-blockers, but no significant difference was observed in regard to previous myocardial infarction, stroke, or heart failure. The median time from symptom onset to presentation was 2.8 hours (IQR 1.2 to 5.6) and 3.0 hours (IQR 1.6 to 5.3) during phases 1 and 2, respectively. A majority of the patients in both phases had a normal ECG result at presentation, as well as a baseline troponin level within the normal reference range. The median HEART score calculated during phase 2 was 3 (IQR 2 to 5) (Table E3, available online at http://www.annemergmed.com). The incidence of myocardial infarction in the study population was 10%. The absolute number of myocardial infarctions was higher during phase 1 (n=83, ie, 14%) compared with phase 2 (n=44, ie, 7%), but the proportion of myocardial infarctions among admitted patients was comparable between the 2 phases (23% and 22% for phases 1 and 2, respectively).

The admission rate was reduced from 59% (95% CI 55% to 63%) during phase 1 to 33% (95% CI 29% to 36%) during phase 2 (RR 0.55 [95% CI 0.48 to 0.63]; unadjusted odds ratio [OR] 0.33 [95% CI 0.26 to 0.42]) (Table 2 and Figure E1, available online at http://www.annemergmed.com). After adjustment for differences in baseline and presentation characteristics, the odds of being admitted were still lower (OR 0.33; 95% CI 0.25 to 0.42) during phase 2. In a sensitivity analysis, the association between the 2 phases and admission rate was similar after adjustment for index myocardial infarctions (OR 0.33; 95% CI 0.25 to 0.44). Adherence to the new decision algorithm during phase 2 was 87%; of 308 patients determined as being at low risk (ie, those with hs-cTn level

Table 1. Baseline characteristics (n=1,233).

Demographics	Phase 1 (n=612)	Phase 2 (n=621)
Age, y	64 (54–74)	63 (53–71)
Men	346 (57)	331 (54)
Risk factors		
Family history of coronary artery disease	233 (38)	180 (29)
Previous or current smoking	300 (49)	324 (52)
BMI ≥30 kg/m^2	112 (18)	118 (19)
Hypertension	280 (46)	265 (43)
Diabetes mellitus	89 (15)	73 (12)
Chronic kidney disease	19 (3.1)	18 (2.9)
Previous cardiovascular disease		
Angina pectoris	148 (24)	107 (17)
Myocardial infarction	137 (22)	120 (19)
PCI or CABG	141 (23)	115 (19)
Known heart failure or LVEF <0.45	33 (5)	22 (4)
Stroke/TIA	54 (9)	51 (8)
Peripheral artery disease	36 (6)	12 (2)
Medication at presentation		
Aspirin/P2Y12-receptor blockers	211 (35)	176 (28)
β-Blockers	244 (40)	198 (32)
ACEI/ARB	216 (35)	199 (32)
Lipid-lowering therapy	202 (33)	176 (28)
Presentation characteristics		
Pulse rate, beats/min	72 (63–83)	69 (61–80)
Systolic blood pressure, mm Hg	146 (132–164)	144 (130–162)
Diastolic blood pressure, mm Hg	83 (75–90)	80 (74–90)
Pulmonary rales	37 (6)	13 (2)
ECG		
Sinus rhythm	534 (90)	564 (92)
Atrial fibrillation/flutter	41 (7)	41 (7)
QRS-ST interval normal	548 (93)	558 (91)
BBB	2 (0.3)	1 (0.2)
Q waves	5 (0.8)	4 (0.7)
ST-segment depressions	16 (2.7)	17 (2.8)
T-wave inversions	21 (3.5)	35 (5.7)
Time delay		
Onset of symptoms to presentation, h	2.8 (1.2–5.6)	3.0 (1.6–5.3)
Onset of symptoms to first troponin, h	3.8 (2.0–6.7)	4.0 (2.4–6.1)
Troponin results		
Troponin T (Roche) at 0 h, ng/L	8 (<5–16)	6 (<5–13)
Troponin T (Roche) at 0 h >ULN	126 (27)	124 (23)
Troponin I (Abbott) at 0 h, ng/L	4.3 (<2–9.1)	3.9 (<2–8.5)
Troponin I (Abbott) at 0 h >ULN	9 (15)	6 (10)
Troponin I (Siemens) at 0 h, ng/L*	<0.03 (<0.03–<0.03)	–†
Troponin I (Siemens) at 0 h >ULN*	5 (8)	–†
Troponin at 0 h (×ULN)	0.43 (<0.36–1.00)	0.43 (<0.36–0.86)
Troponin at 0 h >ULN	140 (23)	130 (21)

BMI, Body mass index; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *LVEF*, left ventricular ejection fraction; *TIA*, transient ischemic attack; *ACEI*, angiotensin converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *BBB*, bundle branch block; *ULN*, upper limit of normal.
Data are presented as median (IQR) or No. (%).
*In phase 1, 65 of the troponin measurements (10.6%) were performed with a conventional assay (Stratus CS instrument).
†Dashes indicate not applicable.

≤99th percentile, a 1-hour change in hs-cTnT level <3 ng/L, or hs-cTnI level <6 ng/L and a HEART score ≤3), 269 were discharged from the ED (Table E4, available online at http://www.annemergmed.com).

The median hospital stay was shorter during phase 2 (4.7 hours; IQR 3.5 to 24.7 hours) compared with phase 1 (23.2 hours; IQR 4.3 to 48.2 hours; 95% CI of the median difference –20.4 to –11.4) (Table 2), which was mainly explained by the difference in admission rates between the 2 groups. Compared with phase 1, the median time to discharge for patients admitted (46.7 hours [IQR 24.4 to 73.6 hours] versus 32.2 hours [IQR 25.2 to 72.9 hours]; 95% CI of the median difference –15.5 to 19.8) and for those discharged from the ED (3.8 hours [IQR 3.1 to 4.9 hours] versus 4.0 hours [IQR 2.4 to 4.8 hours]; 95% CI of the median difference –0.5 to 0.2) was similar in phase 2 (Table E5, available online at http://www.annemergmed.com). The overall estimated median health care–related costs were lower during phase 2 compared with phase 1 ($1,079 [IQR $1,079 to $2,448] versus $1,748 [IQR $1,079 to $5,648]; 95% CI of the median difference –$953 to –$391), with $1,079 being the estimated cost of an ED visit including laboratory costs (Table E1, available online at http://www.annemergmed.com). This was mainly driven by fewer admissions and fewer procedures, such as

Table 2. Inhospital and 30-day outcomes (n=1,233).

Inhospital and 30-Day Outcomes	Phase 1 (n=612)	Phase 2 (n=621)	RR	95% CI	Median Difference	95% CI
Admission to hospital	362 (59)	202 (33)	0.55	(0.48 to 0.63)	—*	—
Time to discharge, h	23.2 (4.3 to 48.2)	4.7 (3.5 to 24.7)	—	—	-18.5	-20.4 to -11.4
Health care–related costs, $	1,748 (1,079 to 5,648)	1,079 (1,079 to 2,448)	—	—	-669	-953 to -391
New presentation to the ED	78 (13)	81 (13)	1.02	(0.77 to 1.37)	—	—
Readmission to hospital	44 (8.0)	36 (6.0)	0.75	(0.49 to 1.14)	—	—
Unplanned revascularization†	3 (0.5)	6 (1.0)	1.97	(0.50 to 7.85)	—	—
Myocardial infarction after discharge	3 (0.5)	3 (0.5)	0.99	(0.20 to 4.86)	—	—
Death after discharge	2 (0.3)	0	—‡	—‡	—	—
Persistent chest complaints	212 (39)	214 (37)	—‡	—‡	—	—
Rating of own health (0–100)	75 (50 to 85)	75 (50 to 85)	—	—	0.0	-5.0 to 5.0
Confidence in management (0–100)	90 (80 to 100)	95 (80 to 100)	—	—	5.0	0.0 to 10.0

Data are presented as median (IQR) or No. (%).
*Dashes indicate not applicable unless otherwise indicated.
†Defined as a new presentation to the ED, followed by admission and revascularization.
‡Not calculated.

exercise ECG tests and coronary angiography (Table 3 and Tables E5 and E6 [available online at http://www.annemergmed.com]). In phases 1 and 2, respectively, a total of 3 (0.5%; 95% CI 0.1% to 1.4%) and 3 (0.5%; 95% CI 0.1% to 1.4%) patients had a myocardial infarction after discharge, and 2 (0.3%; 95% CI 0.04% to 1.2%) and 0 (0%; 95% CI 0.0% to 0.6%) patients died after discharge (Table 2). The proportion of patients with persistent chest complaints was similar. The patients' perception of their own health status and their confidence in the management was rated clinically similar during the 2 phases (Table 2).

A total of 461 patients (75%) during phase 1 and 476 (77%) during phase 2 had a baseline troponin level within the normal reference range. The admission rate was significantly lower during phase 2 compared with phase 1 (24% [n=113] versus 50% [n=229], respectively; RR 0.48; 95% CI 0.40 to 0.58). The median time to discharge was 4.3 hours (IQR 3.3 to 6.8 hours) during phase 2 compared with 7.5 hours (IQR 3.8 to 27.9 hours) during phase 1 ($P<.001$). The overall estimated median health care–related costs were $1,079 (IQR $1,079 to $1,972) during phase 2 compared with $1,470 (IQR $1,079 to $2,813) during phase 1 ($P<.001$). One patient (0.4%) died before discharge during phase 1, whereas none of the patients in phase 2 died during the 30-day follow-up. The number of myocardial infarctions among patients presenting with a baseline troponin level within the normal reference range was 14 (3.0%) during phase 1 compared with 10 (2.1%) during phase 2 (RR 0.69; 95% CI 0.31 to 1.54). Additionally, one patient (0.4%) admitted during phase 1 had a myocardial infarction after discharge. Of the 232 patients discharged from the ED during phase 1, 2 (0.9%) had a myocardial infarction within 30 days. Of the 363 patients who were discharged from the ED during phase 2, 2 (0.6%) had a subsequent myocardial infarction and both had an elevated Δ troponin level and a HEART score greater than 3.

LIMITATIONS

The present study has some important limitations. The patients were not randomized to the 2 assessment strategies. Instead, we had to use a controlled before-after design, which is the weakest form of quasi-experimental design and has a notable risk of bias because there may be unidentified differences in regard to case mix, selection, and clinical practice between the control and intervention groups that may affect changes in outcome. Because of a varying availability of research assistance, the recruitment rate was low, especially during phase 2, which increased the risk of selection bias. Indeed, there was an imbalance in regard to recruitment. Patients in phase 2 had a history of angina pectoris somewhat less often and were at a lower overall risk. As a consequence, the proportion of patients with an index diagnosis of myocardial infarction in phase 2 was smaller, with a lower rate of revascularization compared with patients in phase 1. The reduction in admission rate was still significant after adjustment for differences in baseline characteristics, including an index diagnosis of myocardial infarction. But the difference in admission rate could still be an overestimation caused by residual unmeasured confounders.

A randomized controlled trial would eliminate residual confounders from unmeasured covariates. However, such

Table 3. Inhospital and out-of-hospital procedures (number of patients with at least one procedure).

Inhospital and Out-of-Hospital Procedures	Phase 1 (n=612)	Phase 2 (n=621)	RR	95% CI
Chest radiography	61 (10)	33 (5)	0.53	(0.35–0.80)
CT chest	35 (5.7)	34 (5.5)	0.96	(0.61–1.51)
Echocardiography	128 (21)	111 (18)	0.85	(0.68–1.07)
Exercise ECG test	111 (18)	51 (8)	0.45	(0.33–0.62)
Myocardial scintigraphy	12 (2.0)	20 (3.2)	1.64	(0.81–3.33)
Stress echocardiography	11 (1.8)	4 (0.6)	0.35	(0.11–1.12)
Any stress test*	121 (20.6)	68 (11.0)	0.53	(0.40–0.70)
CT heart	0	1 (0.2)	–†	–
Coronary angiography	118 (19)	77 (12)	0.64	(0.49–0.84)
PCI and coronary angiography	63 (10)	40 (6.5)	0.63	(0.43–0.92)
CABG	2 (0.3)	4 (0.6)	1.97	(0.36–10.7)
Any test for ischemia‡	230 (37.6)	137 (22.1)	0.59	(0.49–0.70)
MRI heart	5 (0.8)	12 (1.9)	2.37	(0.84–6.67)

CT, Computed tomography; *MRI*, magnetic resonance imaging.
Data are presented as No. (%).
*Includes exercise ECG test, myocardial scintigraphy, and stress echocardiography.
†Dashes indicate not calculated.
‡Includes exercise ECG test, myocardial scintigraphy, stress echocardiography, CT of the heart, coronary angiography, PCI, and CABG.

trials are resource demanding and are seldom used to evaluate diagnostic strategies. There is also a risk that the assessment strategy in one group influenced the assessment in the other one. Another, preferable, option would have been a stepped-wedge cluster randomized trial.

To minimize the time-dependent differences, several steps were taken: the introduction of the new diagnostic strategy was initiated immediately after the completion of phase 1, and phase 2 started as soon as the new diagnostic strategy was considered implemented. A logistic regression analysis was performed, adjusting for differences in baseline characteristics. We also analyzed patients with a baseline troponin level within the normal reference range, with no difference in the proportion of patients with an index diagnosis of myocardial infarction, separately. The presence of a research assistant might have increased the adherence to the new diagnostic strategy (the Hawthorne effect), and it is possible that the adherence would be lower outside the study. The scales used for measuring perception of one's own health status and confidence in the management have not been validated. The structure and organization of the assessment of chest pain patients may differ between and within countries, and such differences may also influence the effect of different decision algorithms. The study was not powered to detect differences in clinical outcomes, but the excellent safety of 1-hour hs-cTn algorithms and the HEART score has been shown and validated in several previous studies.[7,8,14-16]

DISCUSSION

This prospective observational multicenter study is the first to our knowledge to evaluate the effects of implementing a diagnostic strategy based on a 1-hour hs-cTn algorithm combined with the HEART score in routine clinical care. In our study, the implementation of this diagnostic strategy was associated with a notably lower admission rate, shorter hospital stays, and lower health care–related costs, with very low rates of myocardial infarctions after discharge, unplanned revascularizations, deaths, new presentations to the ED, and readmissions to the hospital in both groups. The adherence rate to the new strategy was high (87%).

The admission rate decreased significantly after the implementation of the rapid rule-out strategy in routine clinical care (from 59% to 33%), with a lower proportion of admissions late during phase 2, which may indicate that physicians became more comfortable with the decision algorithm over time. The difference in admission rates between the 2 study phases remained significant after adjusting for the differences in baseline and presentation characteristics and the number of index myocardial infarctions (OR 0.33; 95% CI 0.25 to 0.44). Furthermore, in the separate analysis that included only patients with a baseline troponin level within the normal reference range (ie, those affected by the new strategy), the admission rate decreased from 50% to 24%. A similar positive effect on admission rate was recently shown in a small single-center study by Mahler et al,[30] who used a 3-hour measurement of conventional troponin level combined with the HEART score. In a recent, large, multicenter, randomized controlled trial comparing the HEART score alone with a traditional strategy, there was no effect on admission rate.[8] That finding might be due to a higher degree of nonadherence (18%) to the diagnostic strategy in low-risk patients compared with the one observed in our study (13%). However, this could also be explained by differences in study size and design and the fact that there still might be residual confounders in our study because of the observational design, which could have affected the difference in admission rate between the 2 phases.

The median time to discharge was markedly reduced in our study (23.2 to 4.7 hours), which is similar to the findings by Mahler et al.[30] However, the hs-cTn assays used in our study enable a 1-hour sample interval, which might explain the shorter median time to discharge observed in the

present study. Hs-cTn has also been used in previous studies evaluating a 2-hour measurement of hs-cTn combined with a modified Thrombolysis in Myocardial Infarction score or the Emergency Department Assessment of Chest Pain Score.[2,31,32] In these studies, a significant increase in the number of patients discharged within 6 hours without an increase in major adverse cardiac events was convincingly shown. A small pilot study combining hs-cTn measurement at baseline with the new Manchester Acute Coronary Syndromes decision rule has shown similar positive effects on the time to discharge.[33] Data on direct comparisons between the different strategies are still limited.

The reduction in admission rate did not result in longer stays in the ED or an increased number of tests and examinations in an outpatient setting. In contrast, the number of noninvasive tests inhospital decreased, suggesting that the identification of more low-risk patients also influenced the management of admitted patients. The overall estimated median health care–related costs during 30 days were reduced from $1,748 to $1,079. In the large multicenter study evaluating the HEART score, the costs were calculated during 3 months, which prevents comparison with our study, but no difference was observed in costs between patients assessed with the HEART score and those assessed in a traditional way.[8] We consider the reduction in costs in our study to be due to a combination of the decreased admission rate and the reduction of diagnostic procedures.

The study was not powered to detect a difference in major adverse cardiac events. No deaths occurred among any of the study patients who were discharged from the ED. Two patients in phase 1 (0.8%) and 2 in phase 2 (0.5%) had a myocardial infarction during follow-up after being discharged from the ED. However, both patients who were discharged from the ED and had a subsequent myocardial infarction during phase 2 had an elevated Δ troponin level and a HEART score greater than 3 (ie, were not deemed to be low-risk patients according to the rule-out protocol).

In conclusion, we demonstrated that a structured clinical implementation of a 1-hour hs-cTn decision algorithm combined with a simple risk score was associated with a reduction of admission rate, time to discharge, and health care–related costs for patients presenting to the ED with symptoms suggestive of an acute coronary syndrome. An adequately powered randomized study to confirm these findings is needed.

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