A 0-Hour/1-Hour Protocol for Safe, Early Discharge of Chest Pain Patients

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ABSTRACT

Objectives: Guidelines recommend a 0-hour/1-hour high-sensitivity cardiac troponin T (hs-cTnT) diagnostic strategy in acute chest pain patients. There are, however, little data on the performance of this strategy when combined with clinical risk stratification. We aimed to evaluate the diagnostic accuracy of an accelerated diagnostic protocol (ADP) using the 0-hour/1-hour hs-cTnT strategy together with an adapted Thrombolysis In Myocardial Infarction (TIMI) score and electrocardiogram (ECG) for ruling out major adverse cardiac events (MACE) within 30 days.

Methods: This prospective observational study enrolled consecutive emergency department (ED) chest pain patients. TIMI score variables, ED physicians' assessments of the ECG, and 0- and 1-hour hs-cTnT were collected. Thirty-day MACE was defined as acute myocardial infarction (AMI), unstable angina (UA), cardiogenic shock, ventricular arrhythmia, atrioventricular block, cardiac arrest, or death of cardiac or unknown cause.

Results: A total of 1,020 patients were included in the final analysis. The combination of an adapted TIMI score ≤1, a nonischemic ECG, and either a 0-hour hs-cTnT < 5 ng/L or a 0-hour hs-cTnT < 12 ng/L combined with a 1-hour increase < 3 ng/L identified 432 (42.4%) patients as very low risk with a negative predictive value of 99.5% (95% confidence interval [CI] = 98.3%–99.9%) and a negative likelihood ratio of 0.04 (95% CI = 0.01–0.14) for 30-day MACE. The ADP missed only two patients with UA and no patients with AMI or other forms of MACE.

Conclusion: An ADP using the guideline recommended 0-hour/1-hour hs-cTnT strategy rapidly identified patients with a very low risk of 30-day MACE including UA where no further cardiac testing would be needed. This could potentially allow safe early discharge of about 40% of ED chest pain patients.

Chest pain is a common chief complaint in the emergency department (ED).[1] Due to the fear of missing cases of acute coronary syndrome (ACS), i.e., acute myocardial infarction (AMI) or unstable angina (UA), many patients undergo lengthy ED assessments or are admitted for further investigations such as stress testing.[2] Since only a minority of these patients prove to have ACS,[2,3] this contributes to ED and hospital crowding and to significant healthcare costs.[2] There is a need for better methods to rapidly identify patients with a very low risk of ACS who can safely be discharged from the ED and where no further cardiac evaluation is needed.

High-sensitivity cardiac troponins (hs-cTn) have been shown to have an improved sensitivity and to

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enable faster rule-out of AMI.[4–7] The European Society of Cardiology (ESC) guidelines recommend the use of a 0-hour/1-hour strategy (class 1 recommendation) where AMI is considered ruled out either if a high-sensitivity cardiac troponin T (hs-cTnT) is < 5 ng/L at presentation (below referred to as the "0-hour component" of the strategy) or if 0-hour hs-cTnT is < 12 ng/L together with a 0- to 1-hour increase < 3 ng/L (below called the "1-hour component").[8]

Studies have evaluated the 0-hour and 1-hour components separately and indicated high negative predictive values (NPV) for ruling out AMI.[4,5,7,9–13] Several of these studies have, however, shown a <99% sensitivity,[10–13] which has caused some controversy as to whether this is adequate for a diagnostic strategy aiming to rule out AMI.[11,14] In accordance with the ESC guidelines,[8] it has therefore been recommended that these hs-cTnT protocols should be combined with electrocardiogram (ECG) and clinical risk stratification, with the National Institute for Health and Care Excellence (NICE) guidelines as well as others proposing the use of the Thrombolysis In Myocardial Infarction (TIMI) score.[9,11,15] There are, however, few studies that have evaluated the performance of the 0-hour or 1-hour components when combined with clinical risk stratification,[4,5] and none have evaluated the combination with the TIMI score or when using the complete 0-hour/1-hour hs-cTnT rule-out strategy.

In the modified ADAPT-ADP (2-hour Accelerated Diagnostic protocol to Assess Patients with chest pain symptoms using contemporary Troponins as the only biomarker study—accelerated diagnostic protocol), a low adapted TIMI score is combined with negative ECG and hs-cTn at 0 and 2 hour and has been shown to accurately identify low-risk patients.[16,17] This ADP has not been evaluated together with the 0-hour/1-hour hs-cTnT strategy, which could allow faster rule-out.

We aimed to evaluate the diagnostic accuracy of the guideline recommended 0-hour/1-hour hs-cTnT strategy when used as part of the modified ADAPT-ADP for ruling out 30-day major adverse cardiac events (MACE).

METHODS

Study Design and Participants

This was a secondary analysis of data collected in a prospective observational study, and the methods have been described in detail previously.[4] We enrolled consecutive patients during weekdays between 9 AM and 9 PM from February 2013 to April 2014 at the Lund ED of Skåne University Hospital, a tertiary care center. We included patients ≥ 18 years with a primary complaint of chest pain of nontraumatic origin and for whom hs-cTnT was ordered. We did not enroll patients with severe communication barriers, and other patients who were unable to provide written informed consent. Patients with STEMI were also not included as this diagnosis is not based on biomarkers. We excluded patients with hemolysis with an H-index ≥ 100 (the level recommended by the manufacturer) in either the 0- or the 1-hour sample and those with missing data required to calculate the ADP. This study was approved by the regional ethical review board and all patients provided written informed consent.

Data Collection

Clinical data were collected by research assistants using a custom-made data form. TIMI score variables were prospectively collected, and the presence of cardiac risk factors or previous coronary stenosis were also obtained from the electronic medical records if documented. The research assistants also collected the 1-hour hs-cTnT samples, using timers to achieve accurate timing, with sample times rounded to the nearest 10-minute mark in accordance with practice at our central laboratory. The ED physician's assessment of whether the ECG showed signs of acute ischemia was also prospectively collected. We did not provide a definition of signs of acute ischemia as to obtain the physician's unbiased assessment as in real-life practice. The data form did, however, include the definitions of significant ST-elevation, ST-depression, T-wave inversion, and Q-waves as recommended by the universal AMI guidelines.[18]

Samples for hs-cTnT, which was the assay in clinical use during the study period, were collected in lithium heparin tubes and analyzed with the Roche Cobas e602 (Roche Diagnostics). The assay has a limit of blank of 3 ng/L and a limit of detection of 5 ng/L, and the coefficient of variation is <10% at the 99th percentile cutoff point of 14 ng/L.[19]

Further diagnostic testing and treatment were performed, as in routine care, at the discretion of the responsible physician. Testing included serial troponins at 2–6 hours after presentation, radiography, noninvasive testing, and coronary angiography as deemed appropriate.

Index Test

The evaluated index test was the 0-hour/1-hour hs-cTnT strategy used as part of the modified ADAPT-ADP (Figure 1) where patients were identified as very low risk if they had an adapted TIMI score ≤1, no signs of acute ischemia on the ECG, and either 0-hour hs-cTnT < 5 ng/L *or* 0-hour hs-cTnT < 12 ng/L with a 1-hour increase < 3 ng/L.

Outcomes and Reference Standard

The primary outcome was MACE within 30 days, including the index visit. MACE was defined as an adjudicated diagnosis of AMI, UA, cardiac arrest, cardiogenic shock, ventricular arrhythmia requiring intervention, high degree AV-block requiring intervention, or death from a cardiac or unknown cause.

The reference standard was a final adjudicated diagnosis of 30-day MACE, as decided by independent reviews by two cardiologists, and in case of disagreement, by a third cardiologist. The cardiologists were blinded to the 1-hour hs-cTnT and the data form with the collected TIMI score data. A detailed account of the adjudication process has been provided previously.[4] For this we had access to medical records from all hospitals and all diagnostic examinations in the region, including those ordered by primary care physicians. To not miss hospital visits outside our region, data for all admissions for in-hospital care in Sweden were also obtained from the National Patient Register. Deaths and causes of death were obtained from medical records, the national population registry, and the national cause-of-death registry. The adjudicators were then provided with all available clinical information from all hospitals in Sweden within 60 days from the index visit, including complete medical records, results of blood samples and radiologic investigations, ECGs, echocardiograms, stress tests, and coronary angiographies.

Patients are ADP negative if they fulfill the following:

Adapted TIMI score* ≤1:

- Age ≥65 years
- ≥3 risk factors for coronary artery disease†
- Use of aspirin in the last 7 days
- Previous coronary stenosis ≥50%
- ≥2 anginal events in last 24 h or persistent discomfort

AND

No signs of acute ischemia on the ECG

AND

Either 0h hs-cTnT <5 ng/L OR 0h hs-cTnT <12 ng/L with a 1h increase <3 ng/L

Figure 1. Modified ADAPT-ADP using a 0-hour/1-hour hs-cTnT strategy. *The original TIMI score includes ECG and troponin as variables, but as both are required to be negative in the ADP they are not included in the score. The original score also does not include "persistent discomfort." All variables are assigned a value of 1. †Risk factors defined as family history of coronary artery disease, hypertension, hypercholesterolemia, diabetes, or being a current smoker. ADP = accelerated diagnostic protocol; ECG = electrocardiogram; hs-cTnT = high-sensitivity cardiac troponin T; MACE = major adverse cardiac event; TIMI = Thrombolysis In Myocardial Infarction.

AMI was defined according to the universal definition requiring a significant rise and/or fall of hs-cTnT levels with at least one value above the 99th percentile, combined with symptoms or signs of cardiac ischemia.[18] Significant hs-cTnT change was defined as an absolute change of >7 ng/L within 2–3 hours or ≥9 ng/L within 6 hour[20–23] and/or a change of >20% if the 0-hour hs-cTnT was >14 ng/L.[23] To avoid misclassification of patients presenting in a troponin plateau phase, an AMI diagnosis could still be adjudicated in patients with elevated hs-cTnT levels in the absence of a significant rise or fall, if considered to be the most likely diagnosis based on all available information.[18]

The diagnosis of UA required normal or slightly elevated hs-cTnT levels without a significant rise or fall *and* a history consistent with UA defined as rest angina, new-onset angina of Canadian Cardiovascular Society class ≥ 3, or increasing angina *and* at least one of the following: stenosis ≥ 70% in a vessel on coronary angiography, positive stress test if no angiography was performed, or new ischemic ECG changes in patients managed without stress test or angiography. An UA diagnosis could also be adjudicated in patients who were discharged after AMI was ruled out and were subsequently diagnosed with AMI or suffered death of cardiac or unknown cause within 30 days from the index visit. The other components of the 30-day MACE outcome were defined according to published standardized data definitions.[24]

Data Analysis

For descriptive data, continuous variables are described with mean and standard deviation (SD) and categorical variables are described with proportions. Sensitivity, specificity, NPV, and negative likelihood ratios (LR–) and corresponding 95% confidence intervals (CIs) were calculated for the different diagnostic strategies for the outcome of 30-day MACE. This was a secondary analysis and sample size was based on the primary analysis of this study, but as the number of included patients was similar to previous well-powered studies, it was estimated to be adequate.[17] When

calculating the 0- to 1-hour hs-cTnT change, hs-cTnT results < 5 ng/L (i.e. below the limit of detection) were assigned a value of 2.5 ng/L. IBM SPSS v21 (IBM Corp.) and MedCalc statistical software version 14.8.1 (MedCalc Software bvba) were used for all statistical analyses.

RESULTS

Patient Characteristics

As shown in Figure 2, a total of 1,167 patients were enrolled in the study. Of these, 147 patients were excluded, leaving 1,020 for the final analysis. There were no important differences with regard to age, sex, baseline characteristics, or 30-day MACE prevalence between included patients and those excluded due to missing data (Data Supplement S1, available as supporting information in the online version of this paper, which is available at https://doi.org/onlinelibrary.wiley.com/doi/10.1111/acem.13224/full).

Table 1 describes the baseline characteristics of the included patients. Mean (±SD) age was 60.7 (±17.4) years, 45.9% were female, and 19.5% had a history of AMI. The median time from ED presentation to 0-hour hs-cTnT sampling was 32 minutes (interquartile range [IQR] = 19–54 minutes), and the median time between the 0-hour and the 1-hour sample was 60 minutes (range = 30–90 minutes, IQR = 60–60 minutes).

MACE within 30 days occurred in 119 (11.7%) patients. Most cases of MACE were index visit AMI (*n* = 77; 7.5%) and UA (*n* = 38; 3.7%; Data Supplement S2, available as supporting information in the online version of this paper, which is available at https://doi.org/onlinelibrary.wiley.com/doi/10.1111/acem.13224/full). All UA patients had a significant stenosis on angiography (*n* = 35) and/or pathologic provocative testing (*n* = 11) and/or ECG signs of acute ischemia (*n* = 11). A TIMI score of ≤1 was present in 521 (51.1%) patients of whom 6.7% had a 30-day MACE, and with the addition of a non-ischemic ECG, the 30-day MACE rate decreased to 3.9%.

Main Results

Table 2 and Figure 3 describes the performance of the ADP using the guideline-recommended 0-hour/1-hour hs-cTnT strategy, and the corresponding 2 × 2 tables are presented in Data Supplement S3 (available as supporting information in the online version of this paper, which is available at https://doi.org/onlinelibrary.wiley.com/doi/10.1111/acem.13224/full). The combination of an adapted TIMI score of ≤1, a nonischemic ECG, and either a 0-hour hs-cTnT < 5 ng/L or a 0-hour hs-cTnT < 12 ng/L combined with a 0- to 1-hour increase < 3 ng/L identified 432 (42.4%) patients as very low risk with an excellent NPV and LR–. Among ADP-negative patients 0.5% had a 30-day MACE, with the ADP missing only two patients with UA (described in Data Supplement S4, available as supporting information in the online version of this paper, which is available at https://doi.org/onlinelibrary.wiley.com/doi/10.1111/acem.13224/full). Further,

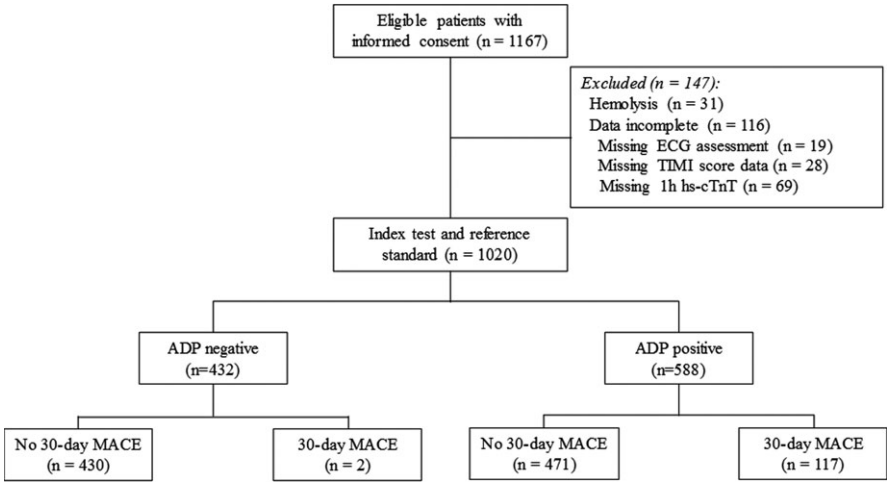

Figure 2. Patient flow chart. Flow diagram of patient inclusion and exclusion. ADP negative = adapted TIMI score ≤ 1 *and* nonischemic ECG *and* either 0-hour hs-cTnT < 5 ng/L *or* 0-hour hs-cTnT < 12 ng/L with a 1-hour increase < 3 ng/L. ADP = accelerated diagnostic protocol; ECG = electrocardiogram; hs-cTnT = high-sensitivity cardiac troponin T; MACE = major adverse cardiac event; TIMI = Thrombolysis In Myocardial Infarction.

Table 1
Patient Characteristics

Characteristics	All Patients (*n* = 1,020)	30-Day MACE (*n* = 119)	No MACE (*n* = 901)
Age (y)	60.7 (±17.4)	70.1 (±11.5)	59.5 (±17.7)
Female sex	468 (45.9)	35 (29.4)	433 (48.1)
Arrival by ambulance	424 (41.6)	64 (53.8)	360 (40.0)
Medical history			
Diabetes	141 (13.8)	38 (31.9)	103 (11.4)
Hypertension	451 (44.2)	82 (68.9)	369 (41.0)
Hypercholesterolemia	238 (23.3)	44 (37.0)	194 (21.5)
AMI	199 (19.5)	36 (30.3)	163 (18.1)
PCI	175 (17.2)	34 (28.6)	141 (15.6)
CABG	88 (8.6)	18 (15.1)	70 (7.8)
Stable angina	214 (21.0)	45 (37.8)	169 (18.8)
Stroke/TIA	95 (9.3)	19 (16.0)	76 (8.4)
COPD	75 (7.4)	9 (7.6)	66 (7.3)
Other risk factors			
Family history of CAD	241 (23.6)	30 (25.2)	211 (23.4)
Current smoker	135 (13.2)	15 (12.6)	120 (13.3)
Previous smoker	441 (43.2)	65 (54.6)	376 (41.7)
Medication			
Aspirin	286 (28.0)	59 (49.6)	227 (25.2)
Statin	299 (29.3)	53 (44.5)	246 (27.3)
Acute ischemia on ECG	66 (6.5)	36 (30.3)	30 (3.3)
Symptom onset to 0-h hs-cTnT*			
≤3 h	321 (31.8)	46 (39.0)	275 (30.8)
>3 h	689 (68.2)	72 (61.0)	617 (69.2)
TIMI score ≤ 1	521 (51.1)	35 (29.4)	486 (53.9)

Values are mean (±SD) or *n* (%).
n = 1,010.
AMI = acute myocardial infarction; CABG = coronary artery bypass graft; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; hs-cTnT = high-sensitivity cardiac troponin T; MACE = major adverse cardiac event; PCI = percutaneous coronary intervention; TIA = transient ischemic attack; TIMI = Thrombolysis In Myocardial Infarction.

among the ADP-negative patients three (0.7%) had a final diagnosis of pulmonary embolism (PE), and none had an aortic dissection (AD).

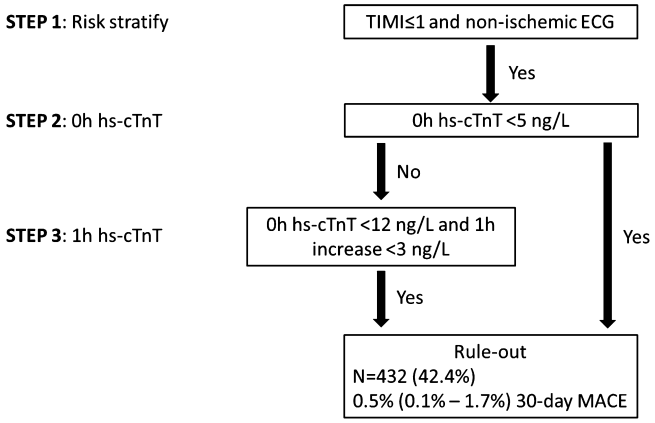

Figure 3. Stepwise approach to identifying very-low-risk patients. ADP = accelerated diagnostic protocol; ECG = electrocardiogram; hs-cTnT = high-sensitivity cardiac troponin T; MACE = major adverse cardiac event; TIMI = Thrombolysis In Myocardial Infarction.

The ADP with only the 0-hour component (<5 ng/L) of the hs-cTnT strategy identified 268 (26.3%) patients with a 0.4% 30-day MACE event rate, missing only a single patient with UA (Data Supplement S4). Using instead only the 1-hour hs-cTnT component in the ADP identified 428 (42.0%) patients as very low risk, with 0.5% having a 30-day MACE, missing the same two patients with UA as with the complete 0-hour/1-hour strategy above.

Data Supplement S5 (available as supporting information in the online version of this paper, which is available at https://doi.org/onlinelibrary.wiley.com/doi/10.1111/acem.13224/full) shows the performance of the complete 0-hour/1-hour strategy ± ECG, without the TIMI score. Leaving out the TIMI score resulted in a larger proportion of patients being identified for rule out: 679 (66.6%) with hs-cTnT alone and 658 (64.5%) with the addition of the ECG. The 30-day MACE risks in ruled-out patients were higher, however, with a 2.4% risk with hs-cTnT alone (two missed AMIs, 14 missed UAs) and a 2.0% risk with hs-cTnT + ECG (one missed AMI, 12 missed UAs).

Table 2
Diagnostic Accuracy of the ADP Using 0-Hour/1-Hour hs-cTnT for 30-Day MACE

	Sensitivity % (95% CI)	Specificity % (95% CI)	NPV % (95% CI)	LR– (95% CI)
TIMI ≤1 *and* negative ECG* *and*				
0-h hs-cTnT < 5 ng/L *or* 0-h hs-cTnT < 12 ng/L with 1-h increase < 3 ng/L (*n* = 432)	98.3 (94.1–99.8)	47.7 (44.4 - 51.0)	99.5 (98.3–99.9)	0.04 (0.01–0.14)
0-h hs-cTnT < 5 ng/L (*n* = 268)	99.2 (95.4–100)	29.6 (26.7–32.7)	99.6 (97.9–100)	0.03 (0.00–0.20)
0-h hs-cTnT < 12 ng/L with 1-h increase < 3 ng/L (*n* = 428)	98.3 (94.1–99.8)	47.3 (44.0–50.6)	99.5 (98.3–99.9)	0.04 (0.01–0.14)

ADP = accelerated diagnostic protocol; hs-cTnT = high-sensitivity cardiac troponin T; LR– = negative likelihood ratio; MACE = major adverse cardiac event; NPV = negative predictive value; TIMI = Thrombolysis In Myocardial Infarction.
*Defined as ECG showing no signs of acute ischemia.

Among the 247 patients who met the 0-hour/1-hour hs-cTnT rule-out criteria but had a higher pretest probability (adapted TIMI score > 1 and/or ischemic ECG) 5.7% had a 30-day MACE.

In a sensitivity analysis, the 0-hour/1-hour hs-cTnT strategy alone had a sensitivity of 97.4% (95% CI = 90.9%–99.7%) and a NPV of 99.7% (95% CI = 98.9%–100%) for an outcome of index visit AMI, while the ADP had a sensitivity of 100% (95% CI = 95.3%–100%) and a NPV of 100% (95% CI = 99.2%–100%). If the ADP utilized the original TIMI score, thereby not including the variable "persistent discomfort," 491 (48.1%) patients were identified for rule-out with a NPV of 99.4% (95% CI = 98.2%–99.9%) for 30-day MACE, missing three patients with UA.

DISCUSSION

In this study, we combined the 0-hour/1-hour hs-cTnT rule-out strategy with ECG and the adapted TIMI score and could identify acute chest pain patients with only a 0.5% risk of 30-day MACE, missing just two patients with UA and no patients with AMI or other forms of MACE. This protocol could thereby allow safe early discharge of up to 40% of ED chest pain patients.

The 0-hour/1-hour hs-cTnT strategy alone identified more patients for rule-out than when the ECG and adapted TIMI score were also incorporated, but missed more patients with 30-day MACE. Those missed were mostly patients with UA, while its NPV for AMI was high and on par with previous studies.[7,10,25] The sensitivity for AMI was, however, about 97%, which is similar to what was shown by Pickering et al.[11] Further, among patients who met the 0-hour/1-hour hs-cTnT rule-out criteria but who had a higher pretest probability (adapted TIMI score > 1 and/or ischemic ECG), the 30-day MACE rate was unacceptably high. Combining 0-hour/1-hour hs-cTnT with a low adapted TIMI score and a negative ECG, on the other hand, increased sensitivity and NPV for 30-day MACE and AMI, and this strategy did not miss a single AMI. Our results thus emphasize the importance of interpreting hs-cTnT together with ECG and clinical risk stratification for identification of patients suitable for early discharge.

No previous studies have evaluated the performance of the complete 0-hour/1-hour hs-cTnT rule-out strategy when combined with clinical risk stratification, and only one study has previously evaluated the diagnostic accuracy of the 1-hour hs-cTnT component when utilized in conjunction with clinical risk assessment.[4] In that study, 1-hour hs-cTnT was combined with the ED physician's assessment of patient history and ECG and performed well.[4] Some clinicians may, however, hesitate to use a protocol that includes their subjective assessment of the history. The modified ADAPT-ADP therefore provides an alternative, as it is a more objective tool that is well validated, relatively easy to use, and now part of routine care at some EDs.[16,17,26]

There has also been a lack of studies to evaluate the 0-hour hs-cTnT < 5 ng/L strategy in conjunction with clinical risk stratification, which more accurately reflects real-life practice where hs-cTnT is not used in isolation. Consequently, the recent NICE guidelines state that a 0-hour hs-cTnT < 5 ng/L should be combined with a low TIMI score for identifying low-risk patients.[15] This study is the first to evaluate this combination, and to incorporate the 0-hour hs-cTnT < 5 ng/L strategy into the modified ADAPT-ADP, and indicates that this approach is safe.

Previous studies on the modified ADAPT-ADP have used hs-cTn at 0 and 2 hours and, as in this study, have identified about 40% of patients as low risk.[16,17] Our results show that by using the 0-hour/1-hour strategy, a faster rule-out could potentially be achieved, especially since this protocol allows the ruling out of about 26% of patients using the 0-hour hs-cTnT alone. The previous studies have also not included UA in the MACE outcome,[16,17] and ADP-negative patients have been recommended further stress testing.[26] The present results indicate that this may not be necessary, at least in settings with a low ACS prevalence, as the risk in ADP-negative patients is very small. In this context, Kline et al.[27] have estimated that additional testing is more likely to be harmful than beneficial in patients with an ACS probability < 2%. In such low-risk patients, provocative testing gives few true positive results and does not improve outcome,[28–30] but may instead lead to unnecessary additional investigations and treatments, complications, radiation exposure, and increased cost.[29,30] Admitting such low-risk patients has also not been shown to confer any benefit.[31] Further evidence for a low ACS risk in ADP-negative patients has been provided by Aldous et al.,[32] who observed that a negative hs-cTnT at 0 and 2 hours, combined with a nonischemic ECG and a TIMI score of 0, had a sensitivity

of 99.2% for ACS within 30 days. Since the ACS prevalence was 36% in their cohort, a TIMI score of 0 was required to achieve a low pretest probability. Our study, however, indicates that the ≤1 TIMI score threshold is adequate in settings with a lower MACE/ACS prevalence.

Previous studies of the modified ADAPT-ADP have utilized an adapted TIMI score that incorporates the variable "persistent discomfort," which was not included in the original TIMI score.[33] In a sensitivity analysis, removal of this variable resulted in an additional 59 patients being identified for rule-out, but at the cost of missing an additional patient with UA. This suggests that the adapted TIMI score as used in the modified ADAPT-ADP is superior.

The event rate in ADP-negative patients will likely be somewhat higher in settings with a higher MACE prevalence than ours, and similarly even lower in settings with a lower prevalence, such as at many U.S. centers.[34] There are >7 million annual ED visits for chest pain in the United States alone, costing an estimated $10 to $13 billion.[28,31,35] By identifying up to 40% of patients for safe discharge with no need for further testing, and with more than half identified already by the hs-cTnT at presentation, this ADP has the potential to reduce ED crowding and healthcare costs.

The ADP, as with any decision aid, should, however, be used together with clinical judgment and not as a substitute. This was also evident by the two patients missed by the ADP, who both had a history highly suggestive of UA.

Since the ADP provides an estimate of the patient's risk of 30-day MACE, it may also be used to inform patients. Patients tend to overestimate their risk,[36] and when informed of having a low risk of ACS often prefer outpatient follow-up.[37] Careful discharge information recommending patients to return if their symptoms do not resolve will likely also catch the few UA patients missed by the ADP and prevent harm.

The purpose of the present ADP is to identify patients who can be safely discharged from the ED. Among the remaining patients, only a minority will have a 30-day MACE, and their further assessment should be individualized. Before discharge, however, potentially dangerous diagnoses other than ACS need to be considered, although in our cohort, very few of the ruled-out patients had clinically important differential diagnoses such as PE or AD.

LIMITATIONS

This was a single-center study, which limits the generalizability of the results. The AMI/MACE prevalence was, however, similar to many previous ED chest pain studies,[2,34,38] and our MACE/ACS prevalence was similar to the reported average ED rate.[39] Nonetheless, these results should be validated in other settings before clinical implementation.

We did not include patients during all hours of the day or during weekends, but we have previously shown that those not enrolled did not differ from the included patients with regard to age, sex, and AMI prevalence.[4] Our AMI and UA prevalence was also similar to that in previous studies with 24-hour patient inclusion at our ED,[40,41] indicating that the present sample was representative of our ED chest pain population.

We excluded patients with missing data, which might introduce a risk of selection bias. However, as there seemed to be no important differences between included and excluded patients, any such bias is likely to be of limited importance.

ED physicians were not blinded to the 1-hour hs-cTnT, but they were unaware of the study hypotheses, and the TIMI score was not used in routine care. The adjudicating cardiologists were blinded to the 1-hour hs-cTnT, and the final diagnosis of AMI was therefore independent of these samples, which minimized the risk of incorporation bias.

Some have questioned the importance of UA in the hs-cTn era.[42] In this study, we included UA in the MACE outcome since it is a common condition[7] with a clear 30-day risk of AMI or death,[43] and since it leads to changes in both treatment and further testing.[8] We believe that omission of UA in the outcome may even introduce bias in an observational study, as UA patients commonly receive treatment, which may in turn prevent other MACE outcomes such as AMI and death.[44]

The 1-hour hs-cTnT samples were collected to achieve precise timing. In routine care, the 1-hour sample will likely in some cases be collected later than in this study. This is, however, unlikely to adversely affect the sensitivity and NPV of the protocol as there will be more time to detect a potential hs-cTnT rise.[11,45]

Few AMI patients in this study had hs-cTnT testing ≤ 2 hours from symptom onset, and the safety of this protocol in very early presenters is therefore unclear.

In cases where the 0-hour hs-cTnT is sampled ≤ 2 hours from symptom onset, we would recommend additional hs-cTnT testing at 3 hours.[46]

CONCLUSIONS

The use of the guideline-recommended 0-hour/1-hour high-sensitivity cardiac troponin T strategy as part of the modified ADAPT-ADP rapidly identified about 40% of ED chest pain patients with a very low risk of 30-day major adverse cardiac events including unstable angina. These patients may potentially be discharged from the ED with no further cardiac testing.

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Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/10.1111/acem.13224/full

Data Supplement S1. Comparison between included patients and patients excluded due to missing data.

Data Supplement S2. Description of 30-day major adverse cardiac events.

Data Supplement S3. 2x2 tables for the modified ADAPT-ADP using 0h/1h hs-cTnT for 30-day MACE.

Data Supplement S4. Description of the two patients missed by the ADP.

Data Supplement S5. Diagnostic accuracy of the 0h/1h hs-cTnT strategy ± ECG but without TIMI score for 30-day MACE.