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ORIGINAL ARTICLE

A novel diagnostic protocol to identify patients suitable for discharge after a single high-sensitivity troponin

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ABSTRACT

Objective To establish whether a novel accelerated diagnostic protocol (ADP) for suspected acute coronary syndrome (ACS) could successfully identify low-risk patients suitable for discharge after a single high-sensitivity troponin T (hs-cTnT) taken at presentation to the emergency department. We also compared the diagnostic accuracy of this ADP with strategies using initial undetectable hs-cTnT.

Methods This prospective observational study evaluated the ability of the Triage Rule-out Using high-Sensitivity Troponin (TRUST) ADP to identify low-risk patients with suspected ACS. The ADP incorporated a single presentation hs-cTnT of <14 ng/L, a non-ischaemic ECG and a modified Goldman risk score. Diagnostic performance of the ADP was compared with the detection limit cut-offs of hs-cTnT (<5 ng/L and <3 ng/L). The primary end point was fatal/non-fatal acute myocardial infarction (AMI) within 30 days.

Results 960 participants were recruited, mean age 58.0 years, 80 (8.3%) had an AMI. The TRUST ADP classified 382 (39.8%) as low-risk with a sensitivity for identifying AMI of 98.8% (95% CI 92.5% to 99.9%). hs-cTnT detection limits (<5 ng/L and <3 ng/L) had a sensitivity of 100% (94.3 to 100) and 100% (94.4 to 100), respectively. The TRUST ADP identified more patients suitable for early discharge at 39.8% vs 29.3% (<5 ng/L) and 7.9% (<3 ng/L) ($p<0.001$) with a lower false-positive rate for AMI detection; specificity 43.3% (95% CI 42.7% to 43.4%) vs 32.0% (95% CI 31.5% to 32.0%) and 8.6% (95% CI 8.1% to 8.6%), respectively.

Conclusions The TRUST ADP, which incorporates structured risk-assessment and a single presentation hs-cTnT blood draw, has potential to allow early discharge in 40% of patients with suspected ACS and has greater clinical utility than undetectable hs-cTnT strategies.

Trial registration number ISRCTN No. 21109279.

INTRODUCTION

Patients with suspected acute coronary syndrome (ACS) make up to 10% of all emergency department (ED) attendances and 25% of acute hospital admissions.¹ Current guidelines recommend two serial measurements of non-high-sensitivity troponin between 6 h and 12 h after patient presentation to the ED.² As a result, the majority of patients require prolonged assessment prior to safe discharge despite the fact that only 15–25% of these patients have a final diagnosis of ACS.¹

Consensus reports suggest that high-sensitivity troponin (hs-cTn) assays may be used to reduce door-to-discharge times by using serial testing over 3–6 h.³ Investigators have reduced blood draw times further by incorporating structured clinical risk assessment protocols with hs-cTn,⁴ or analysing δ change over time.⁵ Despite successfully identifying between 40% and 60% of low-risk patients, these algorithms still require serial testing of hs-cTn which will delay discharge from the ED. This delay may be associated with significant healthcare costs,⁶ and contribute to ED overcrowding.

To address these issues, several studies have investigated the effectiveness of a single undetectable hs-cTn value taken at presentation to the ED in identifying those at very low risk of acute myocardial infarction (AMI).^{7–9} Despite demonstrating promising results as a rule-out strategy for AMI, this protocol has not been recommended by expert guidelines due to concerns over assay analytical interference and poor test specificity.³ Therefore, a clinically applicable protocol that allows the discharge of a significant proportion of patients after just a single hs-cTn blood draw at presentation remains an attractive yet elusive goal.

Using binary hs-cTn results alone to guide discharge decisions fails to use a wealth of clinical information available to treating physicians. The Goldman risk score¹⁰ uses simple variables that are immediately available to the ED physician and are derived from the history, examination and ECG findings. Since its inception, the score has been modified to improve physician decision making in the identification of low-risk patients. This has led to improved use of hospital resources.¹¹ Despite achieving the highest level of evidentiary support for use in ED patients with chest pain the modified Goldman (m-Goldman) risk score remains untested as a discharge tool in combination with a single presentation hs-cTn.

The Triage Rule-out Using high-Sensitivity Troponin (TRUST) study's primary aim was to establish whether a novel accelerated diagnostic protocol (ADP) for patients with suspected ACS consisting of hs-cTn, a non-ischaemic ECG and the m-Goldman score, could successfully identify low-risk patients suitable for discharge after a single blood draw at presentation to the ED. Secondary aims were to compare the diagnostic accuracy of the ADP with strategies using initial undetectable hs-cTnT levels.

METHODS

This prospective observational clinical trial was designed to assess the predefined TRUST ADP. The protocol was designed to be truly pragmatic in order to enhance the widespread applicability of the study results¹²; with attending clinicians performing m-Goldman risk scores, rostered clinical (not research) staff undertaking blood sampling, real-time sample processing and 24/7 recruitment. The study was designed using the Standards for Reporting Diagnostic Accuracy¹³ and approved by the UK National Research Ethics Service. All participants provided written informed consent. The TRUST study was registered with the Controlled Trials Database (ISRCTN No. 21109279) and complies with the *Declaration of Helsinki*.

Study setting, recruitment and data collection

Poole NHS Foundation Trust is a UK District General Hospital, its ED has approximately 62 000 new patient attendances per year. Patients with suspected ACS are managed according to the local hospital protocol, which involves risk assessment by ED physician staff using the m-Goldman risk score and blood drawn for hs-cTnT at 6 h after presentation. As part of the study protocol, blood was also taken at presentation for hs-cTnT analysis. While historical clinical protocols, at the time of this study, did not include troponin measurement at presentation, this had the benefit of ensuring that treating physicians were blinded to the initial hs-cTnT result to avoid selection bias.¹⁴

The fifth generation Roche ELECSYS hs-cTnT assay (Roche, Switzerland), which has a limit of detection (lowest analyte concentration likely to be reliably distinguished from the limit of blank at which detection is feasible) of 5 ng/L, limit of blank (highest apparent analyte concentration expected to be found when replicates of a blank sample containing no analyte are tested) of 3 ng/L, 99th centile of 14 ng/L and 10% coefficient of variation of <10% at 9 ng/L, was used for research (presentation) and reference (6-h) samples. During initial assessment clinical staff drew blood for routine admission samples and an additional 3.5 mL of whole blood in a prelabelled study-specific serum settling tube for hs-cTnT analysis. All serum samples were tested in real time.

Consecutive patients attending the ED with suspected ACS were prospectively screened from July 2012 to August 2013. Patients were included if they were at least 18 years of age and had at least 5 min of chest pain suggestive of ACS, and for whom the attending physician determined inpatient evaluation was required. Possible cardiac symptoms included acute chest, epigastric, neck, jaw or arm pain, or discomfort or pressure without an apparent non-cardiac source, in accordance with the American Heart Association case definitions.¹⁵ Patients were excluded if any of the following were present: ST-segment elevation myocardial infarction or left bundle branch block not known to be old, ECG changes diagnostic of ischaemia (ST segment depression ≥1 mm or T-wave inversion consistent with the presence of ischaemia),² arrhythmias (new-onset atrial fibrillation, atrial flutter, sustained supraventricular tachycardia, second-degree or complete heart block, or sustained or recurrent ventricular arrhythmias), hs-cTnT not suitable for analysis (eg, haemolysis), age ≥80 years, atypical symptoms in the absence of chest discomfort, a clear non-ACS cause for chest pain was found at presentation (eg, pulmonary embolism, pneumonia, aortic dissection), another medical condition requiring hospital admission, refusal or inability to give informed consent, non-English speaking, pregnancy, renal failure requiring dialysis or inability to be contacted after discharge.

Data were collected prospectively using a published data dictionary.¹⁶ Attending ED clinicians completed the m-Goldman

risk score on a predesigned clinical report form. Follow-up was undertaken by independent review of hospital electronic patient records, summary of health records from the patient’s general practitioner (GP) obtained at least 6 months after attendance and a national clinical records search (which identifies death). The ethics committee did not grant permission for direct patient contact as they felt that comprehensive follow-up data relating to adverse events could be obtained accurately through GP records. This is because in the UK, GPs hold comprehensive records for individuals relating to primary, secondary and tertiary care. GP records have been demonstrated to be more accurate at reporting hospital admissions, including those for cardiac related events, than patients.¹⁷ GPs were therefore requested to provide all information regarding presentation to other institutions with chest pain, cardiology outpatient review and cardiac testing, including angiography with or without intervention. Where a participant had not attended hospital follow-up and/or a GP had failed to provide a health record/not GP-registered, the patient was regarded as lost to follow-up.

Index tests

The primary index test was the TRUST ADP (table 1), this defined a patient as ‘low-risk’ if all of the following conditions were satisfied at presentation: a m-Goldman Score of 0 or 1, a non-ischaemic ECG and a single central laboratory hs-cTnT of <14 ng/L at presentation.

Secondary index tests were the detection limits for hs-cTnT (5 ng/L and 3 ng/L) and non-ischaemic ECG at presentation.

Outcome measures

The primary end point was the presence of fatal or non-fatal AMI occurring within 30 days of hospital attendance (including the index visit).

The presence of AMI was defined according to the Third Universal Definition of MI which states that a rise and/or fall in

Table 1 The Modified Goldman Score and the TRUST accelerated diagnostic protocol (ADP)

Modified Goldman risk score	1 point for each variable present
Typical new-onset chest pain at rest	
Pain the same as previous myocardial infarction	
Pain not relieved by glyceryl trinitrate (GTN) spray within 15 min	
Pain lasting more than 60 min	
Pain occurring with increasing frequency	
Hypotension (systolic blood pressure <100 mm Hg)	
Acute shortness of breath	
Pain within 6 weeks of a myocardial infarction or revascularisation	
Modified Goldman total	
Trust ADP	
Low risk* (Suitable for discharge)	1. Modified Goldman score ≤1 2. Non-ischaemic ECG 3. Presentation high-sensitivity troponin T <14 ng/L
Not low risk	1. Modified Goldman score >1 2. Ischaemic ECG 3. Presentation high-sensitivity troponin T ≥14 ng/L

*Safety point: protocol not validated in age ≥80 years. TRUST, Triage Rule-out Using high-Sensitivity Troponin.

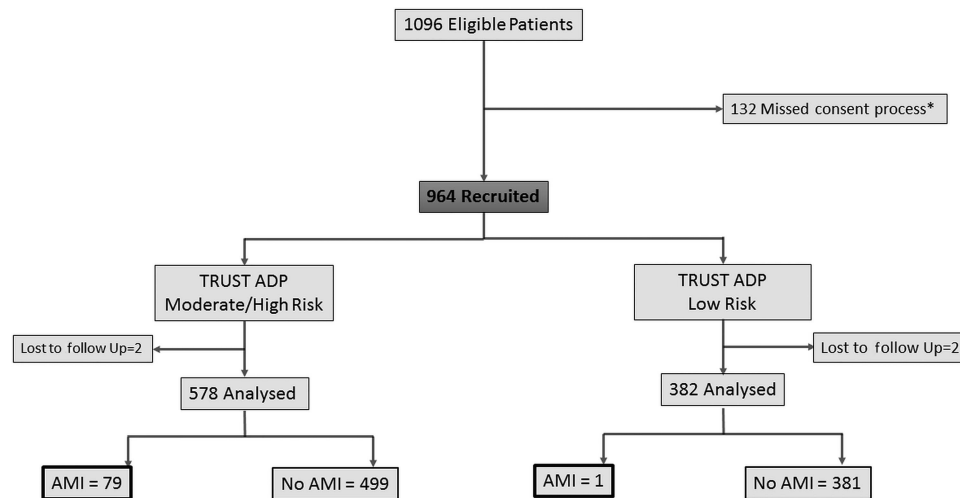


Figure 1 Participant recruitment flow chart. The 132 patients who missed the consent process were similar in age, gender, risk factors and m-Goldman scores ($p>0.05$ for all). ADP, accelerated diagnostic protocol; AMI, acute myocardial infarction; TRUST, Triage Rule-out Using high-Sensitivity Troponin.

troponin, with at least one value above the 99th centile value in the context of a patient with ischaemic symptoms or signs (ECG changes or imaging evidence) would satisfy the diagnosis.¹⁸ Based on current consensus guidance for hs-cTn assays, a rise or fall of 20% (δ) was considered statistically significant and consistent with a diagnosis of AMI.³ Adjudication of the primary end point was carried out by two local cardiologists blinded to the m-Goldman score but who had access to the clinical record, ECG and serial hs-cTnT results. If a troponin result was above the 99th centile value and a non-ischaemic cause of troponin

elevation was identified this was considered by the adjudicating cardiologist in accordance with expert consensus.¹⁹

The presence of major adverse cardiac events (MACEs) occurring within 30 days of hospital attendance (including the index visit) was a secondary outcome measure. MACE included: death due to ischaemic heart disease, cardiac arrest, urgent revascularisation, cardiogenic shock, ventricular arrhythmia, high-degree atrioventricular block needing intervention and AMI. MACE was defined according to previous large scale studies assessing the safety of rapid discharge protocols.^{4 20 21}

Table 2 Patient characteristics

	Total (N=960)	Fatal/non-fatal AMI positive at 30 days (N=80)	TRUST ADP intermediate/high risk (N=578)	TRUST ADP low risk (N=382)
Age, years (Mean \pm SD)	58.0 \pm 13.3	63.3 \pm 10.6	60.4 \pm 12.8	55.6 \pm 19.4
Sex (% male)	565 (58.9)	53 (66.3)	360 (62.3)	205 (53.7)
Ethnicity (% British Caucasian)	914 (95.2)	72 (90.0)	549 (95.0)	365 (95.5)
Risk factors N (%)				
Hypertension	452 (47.1)	59 (73.8)	319 (55.2)	123 (34.8)
Diabetes	164 (17.1)	20 (25.0)	124 (21.4)	40 (10.5)
Dyslipidaemia	635 (66.1)	63 (78.6)	429 (74.2)	206 (53.9)
Smoking current	231 (24.1)	19 (23.8)	129 (22.3)	102 (26.7)
Smoker ex	343 (35.1)	30 (37.5)	229 (39.6)	114 (29.8)
Family history of coronary artery disease	354 (36.9)	29 (36.3)	215 (37.2)	139 (36.4)
Medical history				
Angina	251 (26.1)	29 (36.3)	207 (35.8)	44 (11.5)
Myocardial infarction	204 (21.3)	26 (32.5)	174 (30.1)	30 (7.9)
Percutaneous coronary intervention	183 (19.1)	22 (27.5)	146 (25.3)	37 (9.7)
Congestive cardiac failure	30 (3.1)	4 (5.0)	25 (4.3)	5 (1.3)
Atrial arrhythmia	119 (12.4)	8 (10.0)	86 (14.9)	33 (8.6)
Stroke	63 (6.6)	5 (6.3)	45 (7.7)	18 (4.7)
Coronary artery bypass graft	50 (5.2)	7 (8.8)	41 (7.1)	9 (2.4)
Baseline medications				
Aspirin	361 (37.6)	40 (50.0)	276 (47.8)	85 (22.3)
Clopidogrel	112 (11.7)	8 (10.0)	84 (14.5)	28 (7.3)
β blocker	281 (29.3)	25 (31.3)	210 (36.3)	71 (18.6)
ACE inhibitor	272 (28.3)	29 (36.3)	195 (33.7)	77 (20.2)
Statin	369 (38.4)	37 (46.3)	276 (47.8)	93 (24.3)
Median length of hospital stay (h) \pm IQR	18.8 \pm 32.4	107.5 \pm 110.3	22.4 \pm 62.0	14.0 \pm 11.9

ADP, accelerated diagnostic protocol; AMI, acute myocardial infarction; TRUST, Triage Rule-out Using high-Sensitivity Troponin.

Statistical analysis

Baseline characteristics of the study population were analysed with conventional group descriptive statistics. Diagnostic protocol results and outcome status were cross-tabulated to permit calculation of sensitivity, specificity, negative predictive value (NPV), positive predictive value, positive likelihood ratio and negative likelihood ratio. Statistical significance was evaluated using McNemar's test. All statistical analysis was carried out using SPSS V20.

RESULTS

Nine hundred and sixty-four consenting patients were recruited (figure 1). Four patients were lost to follow-up (health records pertaining to presence of outcome measures unobtainable) meaning that 99.6% were successfully monitored for 30 days. However, no patient lost to follow-up died within 30 days of attendance. Participants were predominantly white, older men who commonly had risk factors for coronary artery disease (table 2). Of the patients 80/960 (8.3%) had a primary outcome event (fatal or non-fatal AMI) and 97/960 (10.1%) had a MACE within 30 days, and 30/960 (3.1%) patients had a non-ischaemic cause of hs-cTnT elevation above the 99th centile identified (diagnoses summarised in the online supplementary appendix). Patients presented to the ED at a median of 2 h 20 min (IQR±228 min) after chest pain onset. Blood was taken for hs-cTnT at a median of 35 min (IQR±14 min) after patient arrival.

Diagnostic accuracy of the TRUST ADP

The TRUST ADP classified 382/960 (39.8%) of patients as at low risk of fatal or non-fatal AMI (table 3), with a sensitivity for identifying AMI of 98.8% (95% CI 92.4% to 99.9%) and NPV of 99.7% (95% CI 98.4% to 100%) and had a similar diagnostic performance for the secondary outcome measure (MACE) (table 4).

A single patient (0.3%) classified as low-risk by the TRUST ADP had an AMI during the initial hospital attendance and follow-up. This patient was a 78-year-old woman classified as low-risk on the m-Goldman score and had a hs-cTnT of 13 ng/L at presentation. However, a minor hs-cTnT elevation to 20 ng/L (δ change 27%) occurred on the second hs-cTnT test at 6 h and was therefore diagnosed with an AMI. The patient was medically managed and had no further complications.

Undetectable troponin strategies

The diagnostic performance of hs-cTnT limit of detection cut-off values in patients with a non-ischaemic ECG are shown in table 4. By using the limit of detection cut-off value of 5 ng/L for the primary outcome measure (AMI) the sensitivity was 100% (95% CI 94.3% to 100%) and 270/922 (29.3%) of patients were eligible for early discharge (table 3). However, using the secondary outcome measure (MACE), three patients (1.1%) identified as suitable for discharge using this strategy required urgent revascularisation (all three were aged in their 40s, two had severe left anterior descending artery disease and one severe right coronary artery disease). Using the limit of blank (<3 ng/L) the sensitivity for fatal/non-fatal AMI was 100% (95% CI 94.4% to 100%) and only 7.9% would have been eligible for early discharge. One patient (1.4%) with a hs-cTnT <3 ng/L required urgent revascularisation.

Table 3 Occurrence of fatal/non-fatal AMI and MACE during the index hospital visit or at 30 days according to index test

	AMI	No AMI	Total
TRUST ADP			
Not low risk	79	499	578
Low risk	1	381	382
Hs-cTnT<5 ng/L *			
≥5 ng/L	78	574	652
<5 ng/L	0	270	270
Hs-cTnT<3 ng/L *			
≥3 ng/L	78	771	849
<3 ng/L	0	73	73
	MACE	No MACE	Total
TRUST ADP			
Not low risk	96	482	578
Low risk	1	381	382
Hs-cTnT<5 ng/L *			
≥5 ng/L	92	560	652
<5 ng/L	3	267	270
Hs-cTnT<3 ng/L *			
≥3 ng/L	94	755	841
<3 ng/L	1	72	73

*922/960 (96%) results are reported for the hs-cTnT detection limits. This was due to computer error whereby 38 results were only reported as <14 ng/L.

ADP, accelerated diagnostic protocol; AMI, acute myocardial infarction; hs-cTnT, high-sensitivity troponin T; MACE, major adverse cardiac event; TRUST, Triage Rule-out Using high-Sensitivity Troponin.

Comparison of strategies

The TRUST ADP identified significantly more patients suitable for immediate discharge at 39.8% vs 29.3% (<5 ng/L) and 7.9% (<3 ng/L) ($p<0.001$) with a lower false-positive rate for AMI detection; specificity 43.3% (95% CI 42.7% to 43.4%) vs 32.0% (95% CI 31.5% to 32.0%) and 8.6% (95% CI 8.1% to 8.6%) respectively, while maintaining a high diagnostic accuracy for the rule-out of AMI.

DISCUSSION

This study demonstrates that the TRUST ADP for suspected ACS can successfully identify 40% of patients as low-risk after just a single hs-cTnT taken at presentation to the ED, with a NPV of >99.5%. When compared with strategies using undetectable hs-cTnT, more patients are eligible for early discharge with lower false-positive rates, suggesting this approach has greater clinical utility. Furthermore, by incorporating clinical risk stratification, the TRUST ADP has improved accuracy in identifying those who require urgent revascularisation.

Our results suggest that the introduction of this ADP has the potential to reduce the length of stay for low-risk patients (currently 14 h in our institution) after a single laboratory-based troponin and avoid the necessity for two separate blood draws. Uptake of this protocol may have significant benefits for health-care services worldwide by reducing hospital admission rates, ED overcrowding, duplication of staff time and resource use. Furthermore, by using ED physicians to carry out risk-stratification and real-time troponin sampling with 24-h recruitment we have demonstrated that this ADP is truly applicable.

This analysis confirms the results of recent large-scale exploratory research that showed undetectable hs-cTnT held promise as a tool for rule-out of AMI or death.⁹ However, we demonstrate that by using MACE (which also includes urgent revascularisation) missed-event rates of the undetectable troponin strategies

Table 4 Diagnostic accuracy of TRUST ADP and detection limit cut-offs of hs-cTnT for the prediction of fatal/non-fatal AMI and MACE in patients with a non-ischaemic ECG

	Number of events (%)	Sensitivity (95% CI)	NPV (95% CI)	Specificity (95% CI)	PPV (95% CI)	+LR (95% CI)	–LR (95% CI)	Percentage of eligible for early discharge
Primary outcome fatal/non-fatal AMI								
TRUST ADP Low risk	1/382 (0.3)	98.8 (92.4 to 99.9)	99.7 (98.4 to 100)	43.3 (42.7 to 43.4)	13.7 (12.8 to 13.8)	1.741 (1.613 to 1.766)	0.029 (0.002 to 0.178)	39.8
hs-cTnT <5 ng/L	0/270 (0.0)	100 (94.3 to 100)	100 (98.3 to 100)	32.0 (31.5 to 32.0)	12.0 (11.3 to 12.0)	1.470 (1.375 to 1.470)	0.000 (0.000 to 0.183)	29.3
hs-cTnT <3 ng/L	0/73 (0.0)	100 (94.4 to 100)	100 (94.0 to 100)	8.6 (8.1 to 8.6)	9.2 (8.7 to 9.2)	1.095 (1.028 to 1.095)	0.000 (0.000 to 0.685)	7.9
Secondary outcome MACE								
TRUST ADP Low risk	1/382 (0.3)	99.0 (93.7 to 99.9)	99.7 (98.4 to 100)	44.1 (43.6 to 44.3)	16.6 (15.7 to 16.8)	1.772 (1.659 to 1.793)	0.023 (0.001 to 0.145)	39.8
hs-cTnT <5 ng/L	3/270 (1.1)	96.8 (90.6 to 99.2)	98.9 (96.7 to 99.7)	32.3 (31.6 to 32.6)	14.1 (13.2 to 14.5)	1.430 (1.323 to 1.470)	0.098 (0.025 to 0.299)	29.3
hs-cTnT <3 ng/L	1/73 (1.4)	98.9 (93.8 to 99.9)	98.6 (91.9 to 99.9)	8.7 (8.1 to 8.8)	11.1 (10.5 to 11.2)	1.084 (1.020 to 1.096)	0.121 (0.006 to 0.769)	7.9

ADP, accelerated diagnostic protocol; AMI, acute myocardial infarction; hs-cTnT, high-sensitivity troponin T; +LR, positive likelihood ratio; –LR, negative likelihood ratio; MACE, major adverse cardiac event; NPV, negative predictive value; PPV, positive predictive value; TRUST, Triage Rule-out Using high-Sensitivity Troponin.

rise above 1%, this may be unacceptable to the majority of ED clinicians.²² Therefore, consistent with consensus guidelines,³ we cannot recommend uptake of undetectable hs-cTnT rule-out strategies in this setting.

Our data suggest that focus move away from strategies that use a stand-alone single initial undetectable hs-cTn result to guide discharge decisions, and towards protocols that also incorporate structured clinical risk assessment. A number of reports combining these two strategies have been reported recently and show early promise. For example, the History, ECG, Age, Risk Factors and Troponin (HEART) score,²³ may enable safe early discharge after a single troponin at presentation but requires validation with hs-cTn, and the Manchester Acute Coronary Syndromes (MACS) decision rule,²⁴ has demonstrated excellent discriminatory power but requires the use of heart-type fatty acid binding protein in addition to hs-cTn. Prospective comparison of these strategies is required.

There are some limitations to this study. The inclusion of predominantly British Caucasian patients may limit the applicability to international settings. The upper age cut-off of ≥80 years was chosen for pragmatic reasons. In our institution, patients above this age are admitted to a separate and dedicated assessment area. Therefore we recognise that this may affect the applicability of TRUST ADP in those >80 years of age.

Patients were only recruited if they had a non-ischaemic ECG at presentation—thereby reducing the prevalence of MACE in the study population. Expansion of the inclusion criteria to include those patients with ECG changes consistent with ACS would have added little practical value because this group is not suitable for early discharge anyway. We therefore intentionally excluded patients with a clear diagnosis of ACS to focus on a particular group that remains a major diagnostic challenge.

Key messages

What is already known on this subject?

The use of undetectable high-sensitivity troponin levels and risk scores in combination with early biomarker testing have recently been put forward as diagnostic tools aiming to reduce door-to-discharge times in patients with suspected acute coronary syndromes. However, a clinically applicable protocol that allows the discharge of a significant proportion of patients after just a single high sensitivity troponin blood draw at presentation to the emergency department remains an attractive yet elusive goal.

What might this study add?

Using a simple clinical risk score, together with the results of a single high-sensitivity troponin result, the Triage Rule-out Using high-Sensitivity Troponin accelerated diagnostic protocol, may enable immediate discharge in up to 40% of patients. This strategy identifies more patients suitable for early discharge, with lower false-positive rates than undetectable troponin strategies.

How might this impact on clinical practice?

Chest pain makes up a quarter of medical admissions in the UK. A diagnostic strategy that prevents unnecessary hospital admission in a large proportion of this patient group would have significant benefits for healthcare services by reducing hospital admission rates, emergency department overcrowding, duplication of staff time and resource use.

We recognise that the TRUST ADP now requires validation as part of a multicentre randomised controlled trial. However, without first analysing the safety of this diagnostic strategy through an observational cohort design, the principle of clinical equipoise may not have justified a randomised study design.²⁵

CONCLUSION

The TRUST ADP, which incorporates a structured risk-assessment and single presentation hs-cTnT blood draw, has the potential to allow early discharge in 40% of patients with suspected ACS. This ADP has superior clinical utility when compared with undetectable hs-cTnT strategies. Future research should focus on methodologies that incorporate clinical assessment with hs-cTn testing rather than troponin testing alone.

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Contributors Each author has contributed to the analysis and interpretation of the data, and drafting and approval of the final manuscript. All authors have also contributed to the conception/design of the study reported in this manuscript.

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Patient consent Obtained.

Ethics approval Frenchay Research Ethics Committee (reference 12/SW/0133).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement All requests for further data from this study should be addressed to the corresponding author.

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REFERENCES

- Goodacre S, Cross E, Arnold J, *et al.* The health care burden of acute chest pain. *Heart* 2005;91:229–30.
- Amsterdam E, Kirk J, Bluemke D, *et al.* American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research. Testing of low risk patients presenting to the emergency department with chest pain: a scientific statement from the American Heart Association. *Circulation* 2010;122:1756–76.
- Thygesen K, Mair J, Giannitsis E, *et al.*; Study Group on Biomarkers in Cardiology of ESC Working Group on Acute Cardiac Care. How to use high-sensitivity cardiac troponins in acute cardiac care. *Eur Heart J* 2012;33:2252–7.
- Cullen L, Mueller C, Parsonage W, *et al.* Validation of high-sensitivity troponin I in a 2-hour diagnostic strategy to assess 30-day outcomes in emergency department patients with possible acute coronary syndrome. *J Am Coll Cardiol* 2013;62:1242–9.
- Reichlin T, Schindler C, Drexler B, *et al.* One-Hour Rule-out and Rule-in of Acute Myocardial Infarction Using High-Sensitivity Cardiac Troponin T. *Arch Intern Med* 2012;172:1211–8.
- Thokala P, Goodacre S, Collinson P, *et al.* Cost-effectiveness of presentation versus delayed troponin testing for acute myocardial infarction. *Heart* 2012;98:1498–503.
- Body R, Carley S, McDowell G, *et al.* Rapid exclusion of acute myocardial infarction in patients with undetectable troponin using a high-sensitivity assay. *J Am Coll Cardiol* 2011;58:1332–9.
- Rubini Gimenez M, Hoeller R, Reichlin T, *et al.* Rapid rule out of acute myocardial infarction using undetectable levels of high-sensitivity cardiac troponin. *Int J Cardiol* 2013;168:3896–901.
- Bandstein N, Ljung R, Johansson M, *et al.* Undetectable high sensitivity cardiac troponin T level in the Emergency Department and risk of Myocardial Infarction. *J Am Coll Cardiol* 2014;63:2569–78.
- Goldman L, Cook E, Johnson P, *et al.* Prediction of the need for intensive care in patients who come to the emergency departments with acute chest pain. *N Engl J Med* 1996;334:1498–504.
- Reilly B, Evans A, Schaidler J, *et al.* Impact of a clinical decision rule on hospital triage of patients with suspected acute cardiac ischemia in the emergency department. *JAMA* 2002;288:342–50.
- Tunis S, Stryer D, Clancy C. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 2003;290:1624–32.
- Bossuyt P, Reitsma JB, Bruns D, *et al.* Standards for Reporting of Diagnostic Accuracy. The STARD statement for reporting studies of diagnostic accuracy: explanation and elaboration. *Ann Intern Med* 2003;138:W1–12.
- Stiell I, Wells G. Methodologic standards for the development of clinical decision rules in emergency medicine. *Ann Emerg Med* 1999;33:437–47.
- Luepker R, Apple F, Christenson R, *et al.* Case definitions for acute coronary heart disease in epidemiology and clinical research studies: a statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. *Circulation* 2003;108:2543–9.
- Cullen L, Than M, Brown A, *et al.* Comprehensive standardized data definitions for acute coronary syndrome research in emergency departments in Australasia. *Emerg Med Australas* 2010;22:35–55.
- Taylor F, Reeves B, Ascione R, *et al.* Accuracy of reporting cardiac related events during long term follow up. *Heart* 2003;89:331–2.
- Thygesen K, Alpert J, Jaffe A, *et al.* Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012;60:1581–98.
- Newby L, Jesse R, Babb J, *et al.* ACCF 2012 expert consensus document on practical clinical considerations in the interpretation of troponin elevations: a report of the American College of Cardiology Foundation task force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2012;60:2427–63.
- Goodacre S, Bradburn M, Cross E, *et al.*; RATPAC Research Team. The Randomised Assessment of Treatment using Panel Assay of Cardiac Markers (RATPAC) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. *Heart* 2011;97:190–6.
- Than M, Cullen L, Reid CM, *et al.* A 2-h diagnostic protocol to assess patients with chest pain symptoms in the Asia-Pacific region (ASPECT): a prospective observational validation study. *Lancet* 2011;377:1077–84.
- Than M, Herbert M, Flaws D, *et al.* What is an acceptable risk of major adverse cardiac events in chest pain patients soon after discharge from the Emergency Department?: a clinical survey. *Int J Cardiol* 2012;166:752–4.
- Backus B, Six A, Kelder J, *et al.* A prospective validation of the HEART score for chest pain patients at the emergency department. *Int J Cardiol* 2013;168:2153–8.
- Body R, Carley S, McDowell G, *et al.* The Manchester Acute Coronary Syndromes (MACS) decision rule for suspected cardiac chest pain: derivation and external validation. *Heart* 2014;100:1462–8.
- Freedman B. Equipoise and the ethics of clinical research. *N Engl J Med* 1987;317:141–5.

Supplementary Appendix

Diagnoses of patients with at least one high-sensitivity troponin T result above the 99th percentile adjudicated to have a non-ischaemic cause of troponin elevation.

	Number (%)	Mean Presentation high-sensitivity troponin T (ng/L) (+/- Standard Deviation)
Injury related to supply/demand imbalance		
Tachy-arrhythmias	6 (0.6)	27.3 (10.2)
Hypovolaemia/Sepsis	7 (0.7)	26.8 (14.3)
Severe aortic valve disease	1 (0.1)	41.0 (n/a)
Respiratory failure/pneumonia	6 (0.6)	18.8 (4.4)
Injury not related to myocardial ischaemia		
Recent Pacing	1 (0.1)	246.2 (n/a)
Myocarditis	4 (0.4)	73.0 (84.8)
Troponin T antibodies	1 (0.1)	299.3 (n/a)
Multifactorial or indeterminate myocardial injury		
Pulmonary Embolism	2 (0.2)	114.9 (79.1)
Stroke	1 (0.1)	15.5 (n/a)
Strenuous Exercise	1 (0.1)	18.0 (n/a)
Total:	30 (3.1)	46.2 (63.7)