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Diagnostic Performance of a Combination Biomarker Algorithm for Rule-Out of Acute Myocardial Infarction at Time of Presentation to the Emergency Department, Using Heart-Type Fatty Acid-Binding Protein and High-Sensitivity Troponin T tests

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Abstract

Background: Chest pain of suspected cardiac origin is a common complaint for presentation at the emergency department; however only 10% to 13% of patients will have acute myocardial infarction (AMI). This study examined a decision support 'rule-out' algorithm to stratify risk of AMI in these patients.

Methods: Five hundred and forty-eight patients with chest-pain of suspected cardiac origin were recruited. Blood samples were collected at presentation (t=0) and after 1, 2, 3, 6, 12 and 24 h. Serum troponin I, heart-type fatty acid-binding protein (H-FABP), myoglobin, carbonic anhydrase III (CAIII), creatine phosphokinase MB isoenzyme (CK-MB) and glycogen phosphorylase isoenzyme BB (GPBB) were measured using the Randox Cardiac Plus Array; Troponin T (cTnT), high sensitivity troponin T (hs-cTnT), high sensitivity CRP (hs-CRP), NT-pro-BNP, total cholesterol, and HDL were measured using a Modular P Analyser. Clinical and demographic information was recorded for each patient.

Results: For biomarker analysis, STEMIs were excluded, leaving 360 patients at presentation (72 NSTEMI and 288 non-AMI) and 320 patients at 1 h (66 NSTEMI and 254 non-AMI). A rule-out algorithm was developed based on H-FABP and hs-cTnT. When the H-FABP hs-cTnT combination algorithm was applied to the data, 106 additional patients at presentation were identified as non-AMI compared to the standard ESC algorithm, 189/288 (65.6%) *vs.* 83/288 (28.8%) ($p<0.0005$), respectively. Furthermore, the H-FABP hs-cTnT combination algorithm, identified 71% of non-AMI patients at 1 hour with no false negatives.

Conclusion: Deployment of the H-FABP hs-cTnT combination algorithm at the emergency department could assist in the identification of non-AMI patients at presentation with the potential to reduce the number of hospital admissions by 106/288 (36.8%). Using the H-FABP hs-cTnT combination algorithm would have a significant impact on patient health ensuring that the appropriate care and efficient use of resources are directed to patients identified as high risk.

Keywords: H-FABP; Hs-cTnT; AMI; Rule-out; Algorithm; Emergency department

Introduction

Chest-pain is a common complaint for presentation at the emergency department; however only 10% to 13% will have acute myocardial infarction (AMI). The diagnosis of AMI is by clinical history, examination, ECG and measurement of cardiac biomarkers, e.g. hs-cTnT [1]. High sensitivity-cTnT is less specific than conventional troponins [1,2] and is not effective at ruling out AMI at presentation [3].

Patients presenting to the emergency department with chest pain of suspected cardiac origin that have ST elevations (STEMIs) are optimally managed by primary percutaneous coronary intervention (primary PCI) and biomarker results are not required for triage. However, most patients present with chest pain and nonspecific or normal ECG findings and the diagnosis of AMI is aided by measurement of cardiac biomarker changes over at least two time points. Current diagnostic algorithms employed in emergency departments do not exhibit sufficient specificity to rule-out AMI at presentation [4]. An earlier exclusion of AMI in the emergency department would avoid prolonged patient observation and in some cases, hospital admission for measurement of sequential cardiac biomarkers.

Heart-type Fatty Acid-Binding Protein (H-FABP) is present in high concentrations unbound in the cytoplasm of myocardiocytes. The stability and solubility of H-FABP together with its low molecular weight (15 kDa compared with 18, 37, and 80 kDa for myoglobin, cTnT and creatine phosphokinase MB isoenzyme (CK-MB), respectively [5]), its rapid release into plasma after myocardial injury (30 min after an ischemic episode [6]) and its high tissue specificity [7] make H-

FABP a suitable candidate biomarker to investigate for the early diagnosis of AMI. We hypothesized that H-FABP could aid in the diagnosis of, and ruling out of, early AMI.

The study aimed to identify an algorithm to rule-in and/or rule-out AMI in patients who present at the emergency department with chest pain of suspected cardiac origin. Too many patients have prolonged waits for diagnosis. Deployment of the proposed algorithm at the emergency department would provide evidence-based decision-making to clinicians enabling them to stratify and manage risk in these patients. The algorithm used biomarker measurements at presentation and at 1 hour to assist with the diagnosis and ruling out AMI. The algorithm was developed using retrospective data.

Materials and Methods

Patient population

Patients with chest pain of presumed cardiac origin presenting to the emergency department in Craigavon Area Hospital or Daisy Hill Hospital, UK between October 2009 and October 2011, were recruited to the Rapid Diagnosis and Risk Stratification of Acute Coronary Syndromes (RADAR ACS) study (ISRCTN60873148).

Patients over 18 years of age with ischaemic-type chest pain were included. Patients were excluded if symptom onset was greater than 12h prior to recruitment, they had a terminal malignancy, received thrombolysis prior to recruitment, were receiving chronic anticoagulant therapy, or had previously been recruited into the study. Time of symptom onset was determined following patient interview.

A 12-lead ECG was obtained for all patients on presentation. Blood samples were collected at presentation and at subsequent time points. Diagnosis of AMI was established according to the universal definition of AMI at the time of the study [8]. Final diagnosis was adjudicated by two independent clinicians who had access to the clinical, laboratory and imaging data.

The study complied with the Declaration of Helsinki, was approved by the Office for Research Ethics Committee Northern Ireland and the Southern Health and Social Care Trust Research and Development Department and written informed consent was obtained from all participating patients. The study complied with Standards for Reporting Diagnostic Accuracy (STARD) guidelines [9].

Blood sampling and laboratory methods

Blood samples were collected at presentation (t=0) and after 1, 2, 3, 6, 12 and 24 h. Samples were immediately centrifuged and serum aliquots stored at -80°C. Troponin I (cTnI), H-FABP, myoglobin, carbonic anhydrase III (CAIII), glycogen phosphorylase isoenzyme BB (GPBB) and CK-MB were measured simultaneously for all the time points using the Cardiac Plus Array, Evidence Investigator platform (Randox Laboratories Ltd, Crumlin, County Antrim, UK). Remaining biomarkers, cTnT, high sensitivity troponin T (hs-cTnT), high sensitivity C-reactive protein (hs-CRP), NT-pro-BNP, total cholesterol, and HDL/LDL were measured using Roche assays and the Roche Modular P Analyser (Roche Diagnostics, Basel, Switzerland).

N.B. after the biomarker results had been analysed, the hospital laboratory was informed by Roche that the batches of hs-cTnT used in the study had been compromised by a calibration shift [10]. As such, fresh aliquots of patient sample were re-measured using new hs-cTnT assays and the results reanalysed. As a result, this contributed to the missing values noted in the study.

Statistical analyses and feature selection

Areas under the receiver operator curve (AUROC) were initially evaluated to compare different biomarkers for segregating cases of AMI from non-AMI. The biomarkers were measured at different time points and statistical comparisons of their AUROC were carried out using R version 3.1.0 package "pROC" [11]. The biomarkers exhibiting the highest AUROC where chosen as candidate biomarkers for further exploration. Patients with missing values were excluded from the analyses. The statistical analysis used for comparing algorithms was Net Reclassification Improvement (NRI) [12]. For comparison between groups, the Fisher's exact and Mann-Whitney U test were applied. A $p<0.05$ was considered statistically significant.

Results

Baseline characteristics

Five hundred and forty-eight patients with suspected ischemic chest pain were included in the study. Patient demographics and biomarkers measurements at presentation are shown in Table 1. One hundred and sixty-seven patients were diagnosed AMI (167/548 (30.5%)); 97/167 (58.1%) patients were diagnosed NSTEMI.

Patient Characteristics	Patients who had AMI[a] (n=167)	Patients who did not have AMI[a] (n=381)	p value
Age, years mean range	66.4 40.0-89.0	62.5 28.0-90.0	0.001
Male sex, n (%)	128 (76.6)	253 (66.4)	0.020
Cardiovascular Risk Factors			
Hypertension, n (%)	98 (57.7)	221 (58.0)	0.925
Hyperlipidemia, n (%)	115 (68.9)	287 (75.3)	0.117
Diabetes, n (%)	34 (20.4)	69 (18.1)	0.720
Current smoker, n (%)	52 (31.1)	69 (18.1)	0.001

Former smoker, n (%)	53 (31.7)	152 (39.9)	0.084
History of CAD			
Family History of CAD, n (%)	75 (44.9)	209 (54.9)	0.033
Past Angina, n (%)	64 (38.3)	204 (53.5)	0.001
Past EST, n (%)	42 (25.1)	160 (42.0)	0.000
Past non-IR, n (%)	62 (37.1)	207 (54.3)	0.000
Past Angiogram, n (%)	4 (38.3)	188 (49.3)	0.020
Past PCI, n (%)	36 (21.6)	101 (26.5)	0.239
Past CABG, n (%)	16 (9.6)	31 (8.1)	0.620
LBBB, n (%)	11 (6.6)	13 (3.4)	0.112
Vital Parameters			
Systolic BP, mmHg, mean (range)	140.4 (72-219)	137.5 (85-234)	0.176
Diastolic BP, mmHg, mean (range)	78.9 (49-128)	77.2 (34-130)	0.455
Heart rate, bpm, mean (range)	76.2 (40-140)	75.4 (40-180)	0.545
ECG Rhythm			
ST-segment shift, n (%)	85 (50.9)	21 (5.5)	0.000
T-wave inversion, n (%)	21 (12.6)	25 (6.6)	0.028
Laboratory Results			
Creatinine, µmol/min (range)	98.1 (52.6-266.8)	92.1 (39.8-223.9)	0.079
Biomarker Results			
cTnT, ng/l, mean (range)	0.2 (0.00-2.9)	0.01 (0.0-1.2)	0.000
hs-cTnT, ng/l, mean (range)	202.9 (0.0-3399)	16.3 (0.0-1140)	0.000
H-FABP, µg/l, mean (range)	19.7 (0.7-100.0)	2.6 (0.0-72.3)	0.000
CK-MB, µg/l, mean (range)	10.2 (0.6-100.0)	2.3 (0.0-51.0)	0.000
Myoglobin, µg/l, mean (range)	149.9 (5.4-700.0)	45.3 (3.7-301.7)	0.000
cTnI, µg/l, mean (range)	0.7 (0.0-35.5)	0.1 (0.0-7.2)	0.000
GPBB, µg/l, mean (range)	18.4 (0.0-213.0)	11.7 (0.0-61.6)	0.000
hs-CRP, mg/l, mean (range)	6.6 (0.01-103.3)	6.7(0.01-215.1)	0.933
CAIII, µg/l, mean (range)	56.4 (8.5-199.0)	50.8 (7.7-199.0)	0.154
NT-proBNP, pg/l, mean (range)	1209.2 (10.2-38355)	440.4 (5.0-8150.0)	0.000
ED: emergency department; CAD: coronary artery disease; EST: exercise stress test; non-IR: non-insulin requiring; LBBB: left bundle-branch block; BP: blood pressure; ECG: electrocardiogram. [a]The definition of AMI includes patients with ST and non-ST-elevation myocardial infarction.			

Table 1: Baseline patient characteristics at presentation to emergency department.

STEMI patients (70/167 (41.9%)) were not included in the analyses (Table 2). Of the n=97 NSTEMI patients, complete data sets were available for n=72 at presentation and n=66 at 1 hour (t=1). Of the n=381 non-AMI patients, data was available for n=288 at presentation and n=254 at 1 h (Figure 1).

Biomarker	AUROC	SE (95% CI)	p value[a]	p value[b]
hs-cTnT	0.908	0.021 (0.867-0.950)	0.008	NA
H-FABP	0.848	0.024 (0.802-0.895)	0.414	0.059
cTnT	0.820	0.026 (0.768-0.871)	NA	0.008
CK-MB	0.797	0.027 (0.744-0.850)	0.556	0.001
Myoglobin	0.730	0.031 (0.668-0.791)	0.028	0.000
cTnI	0.658	0.027 (0.605-0.710)	0.000	0.000
NT-proBNP	0.650	0.033 (0.585-0.715)	0.000	0.000
GPBB	0.577	0.034 (0.510-0.644)	0.000	0.000
hs-CRP	0.536	0.034(0.469-0.602)	0.000	0.000
CAIII	0.526	0.033 (0.459-0.587)	0.000	0.000
SE: Standard Error; CI: 95% confidence interval; [a]compared to cTnT; [b]compared to hs-cTnT; NA: not applicable.				

Table 2: Areas under the receiver operating characteristic curve (AUROC) for high-sensitive troponin T (hs-cTnT), heart-type fatty acid-binding protein (H-FABP), troponin T (cTnT), creatinine phosphokinase MB isoenzyme (CK-MB), myoglobin, troponin I (cTnI), N-terminal pro b-type natriuretic peptide (NT-proBNP), glycogen phosphorylase isoenzyme BB (GPBB), high sensitivity C-reactive protein (hs-CRP) and carbonic anhydrase III (CAIII) after exclusion of patients with ST-elevation myocardial infarction.

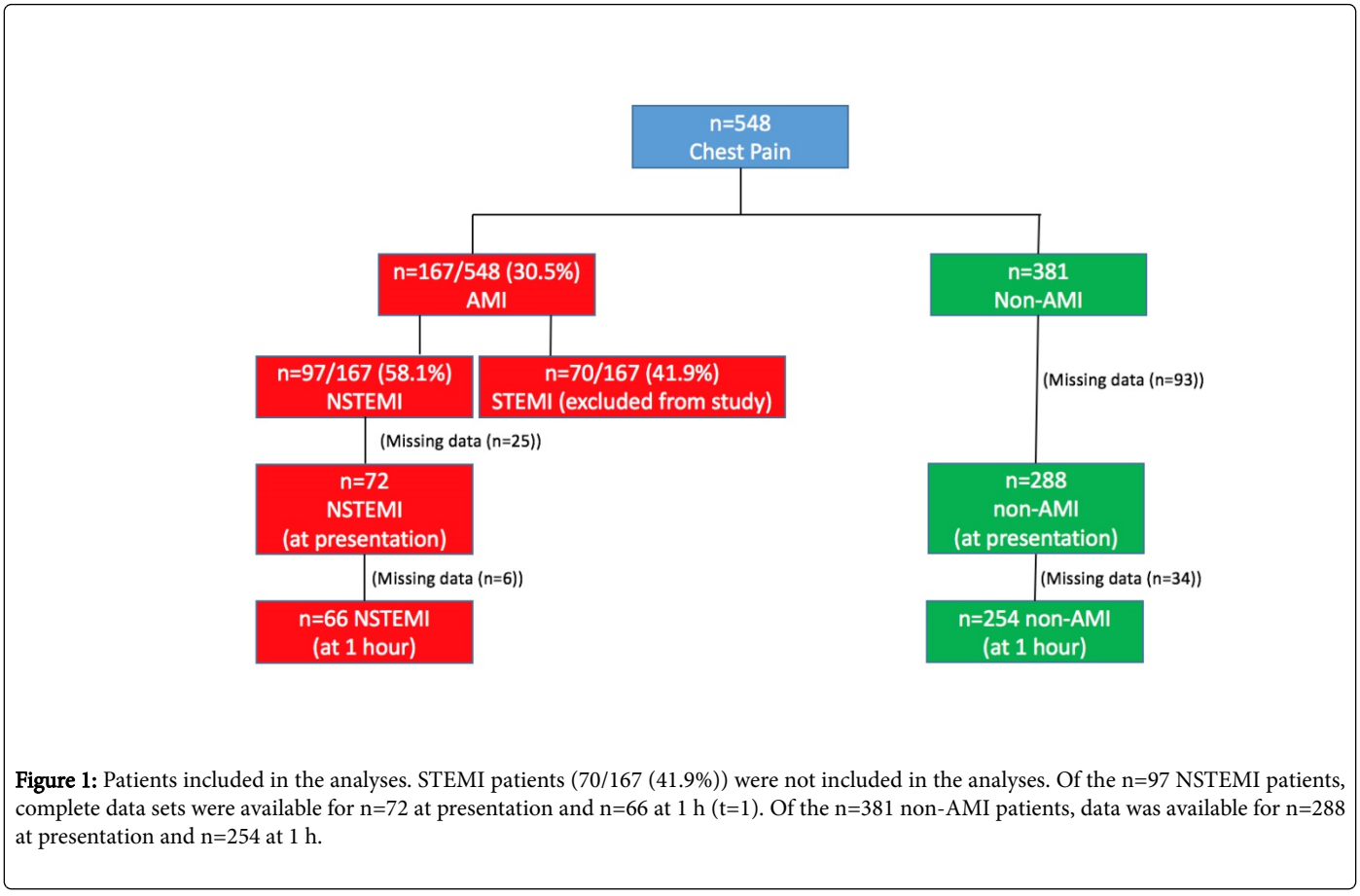


Figure 1: Patients included in the analyses. STEMI patients (70/167 (41.9%)) were not included in the analyses. Of the n=97 NSTEMI patients, complete data sets were available for n=72 at presentation and n=66 at 1 h (t=1). Of the n=381 non-AMI patients, data was available for n=288 at presentation and n=254 at 1 h.

Biomarker diagnostic accuracy

At presentation (t=0), hs-cTnT had the highest AUROC for diagnosis of NSTEMI (AUC 0.908 CI 95% (0.867-0.950)) followed by H-FABP (AUC 0.848 CI 95% (0.802-0.895)) (Table 2). Hs-cTnT *vs.* H-FABP for identification of NSTEMI patients was not statistically significant (p=0.06).

Proposed 'rule-out' algorithms

Rule-out algorithms were established by focusing on early time points t=0 and t=1, and a combination of the most promising biomarkers (hs-cTnT and H-FABP). The algorithms for presentation (t=0; n=360 patients) and 1 h (t=1; n=320 patients) are described in Figures 2A and 2B. Thresholds for hs-cTnT were taken from ESC guidelines [13]. H-FABP cut-offs and delta changes for hs-cTnT were selected to ensure the algorithm demonstrated high specificity and sensitivity (close to 1.0) when applied to the study dataset.

Presentation time point

ESC guidelines [13] for suspected NSTEMI suggest rule-out for (i) hs-cTnT <5 ng/l at presentation (t=0 h); (ii) or hs-cTnT<12 ng/l at presentation with a delta change <3 ng/l at t=1 h. For suspected NSTEMI rule-in (i) hs-cTnT >52 ng/l at t=0 h, (ii) or hs-cTnT delta change t=1 h >5 ng/l (Figure 3).

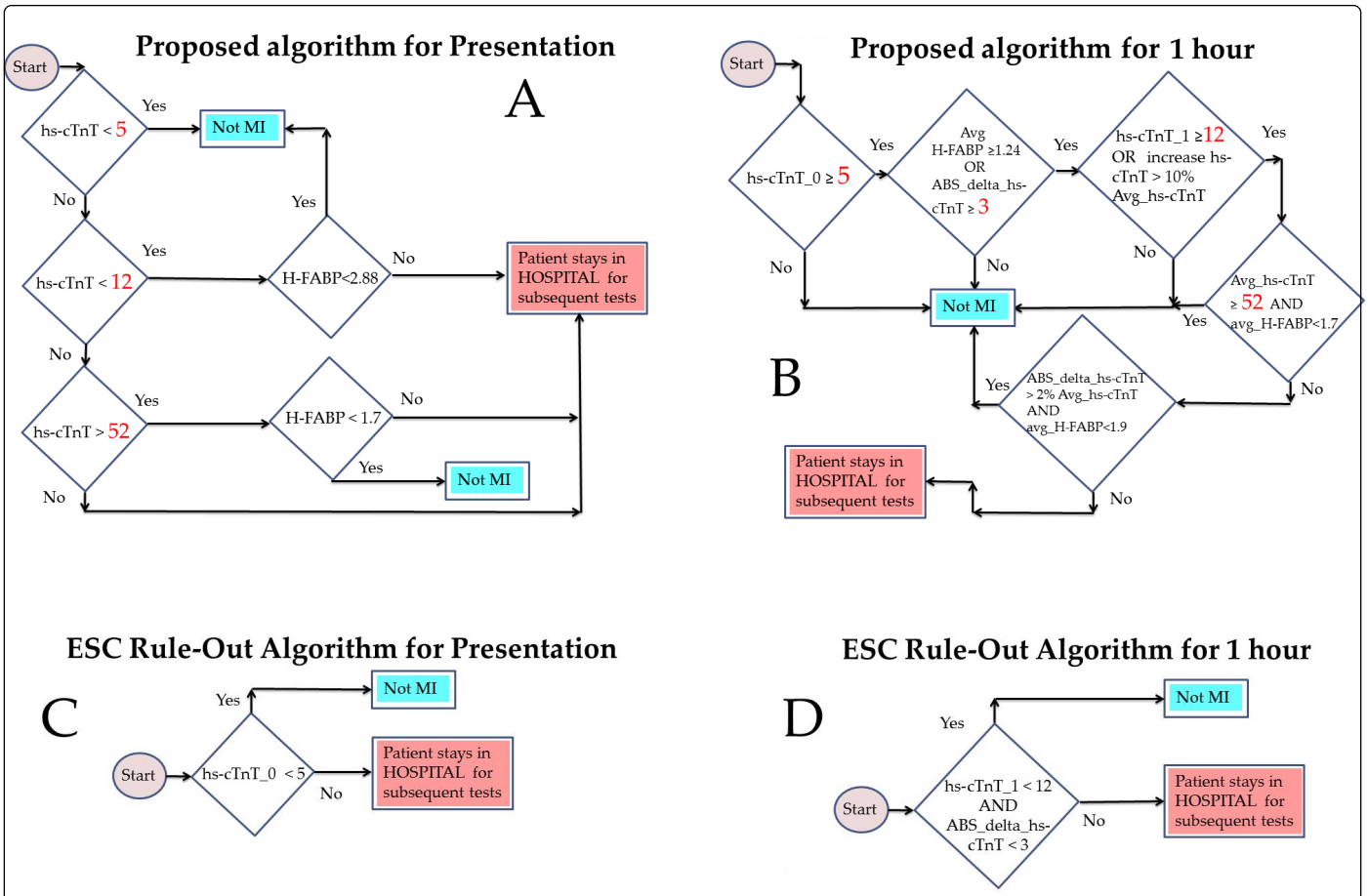


Figure 2: Proposed decision tree algorithms based on biomarkers of high-sensitive troponin T (hs-cTnT) and heart-type fatty acid-binding protein (H-FABP) for ruling out NSTEMI patients at presentation (A) and 1 h (B). ESC rule-out algorithms for presentation (C) and 1 h (D). Units for hs-cTnT and H-FABP are ng/l and µg/l, respectively.

In this study, the three ESC thresholds for hs-cTnT (5, 12 and 52 ng/l) were used in conjunction with two cut-offs for H-FABP (1.7 and 2.88 µg/l) to separate three potential situations when AMI was suspected at presentation (Figure 2A). From the analyses, we identified the following criteria to rule-out AMI at presentation:

(a) hs-cTnT <5 ng/l then rule-out AMI (ESC guidelines for presentation)

(b) hs-cTnT <12 ng/l and H-FABP <2.88 µg/l then rule-out AMI

(c) hs-cTnT >52 ng/l and H-FABP <1.7 µg/l then rule-out AMI

Results for this algorithm at presentation are presented in Table 3 (algorithm A).

Time point 1 hour

For the proposed algorithm at t=1 (Figure 2, algorithm B) there were two measurements for each biomarker (t=0 and t=1). The two biomarker measurements were used to calculate an increase (if any), in absolute values for differences (deltas) and averages. To identify a

possible AMI (not rule-out AMI) each of the following criteria had to occur:

(a) hs-cTnT at t=0h ≥5ng/l and,

(b) delta t=0-1h hs-cTnT≥3ng/l or average of H-FABP (t=0-1h) ≥1.24µg/l and,

(c) hs-cTnT t=1h ≥12ng/l or its increase >10% of the average [(t=0 + t=1)]/2

There were two patients with elevated hs-cTnT and low H-FABP who required further investigation. To rule-out the suspicion of an AMI (and confirm the 'rule out') we applied the following rules:

(d) average (t=0-1h) hs-cTnT≥52 ng/l and average (t=0-1h) H-FABP<1.7 µg/l

or

(e) delta hs-cTnT <2% of average (t=0-1h) when average (t=0-1h) of H-FABP <1.9 µg/l.

Results for this algorithm are presented in Table 3 (algorithm B).

Algorithms for comparisons

The ESC 'rule-out' algorithms [13] for presentation and for 1 h (Figure 2, algorithms C (t=0) and D (t=1)) were compared to the proposed algorithms (Figure 2A (t=0) and B (t=1)). The statistical analysis used for comparing algorithms was Pencina's NRI, data are shown in Tables 3 and 4. The results demonstrated that the ESC 'rule-out' algorithm at presentation (algorithm C, Table 4) had similar sensitivity (1.000 *vs.* 0.958 respectively, net gain 0.046, Table 4) to the proposed combination algorithm (algorithm A, Table 3) (0 *vs.* 3 false negatives, respectively). However, the ESC 'rule-out' algorithm was less specific (0.288), had 205 false positives when compared to the proposed combination algorithm (algorithm A Table 3) which had a specificity of 0.656 and only 99 false positives (net gain for non-AMI of -0.330, Table 4).

Id.	Algorithm[a]	AMI	TP	TN	FP	FN	Sen	Spec	PPV	NPV
0 h (presentation)										
A	H-FABP and hs-cTnT	72	69	189	99	3	0.958	0.656	0.411	0.984
C	ESC rule-out	72	72	83	205	0	1.00	0.288	0.260	1.000
0 h-1 h										
B	H-FABP and hs-cTnT	66	66	181	73	0	1.000	0.713	0.475	1.000
D	ESC rule-out	66	63	175	79	3	0.955	0.689	0.444	0.983

Id.: Identifier of algorithm; [a] Algorithm relates to the decision tree in Figure 2; n: number of patients; AMI: number of NSTEMI patients; TP: number of true positives; TN: number of true negatives; FN: number of false negatives; FP: number of false positives; Sen: sensitivity; Spec: specificity; PPV: positive predictive value; NPV: negative predictive value; h: hour.

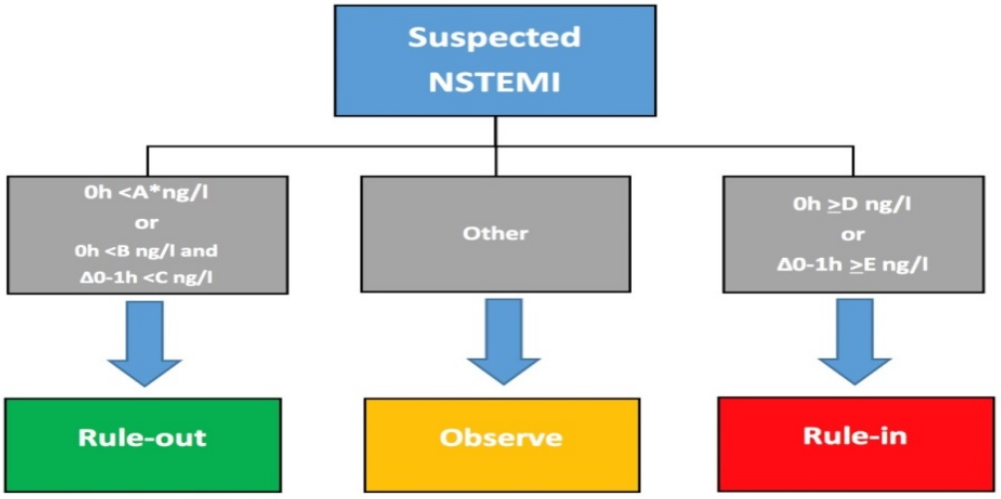
Table 3: Diagnostic accuracy of decision tree algorithms related to Figure 2, based on biomarkers of high-sensitive troponin T (hs-cTnT) and heart-type fatty acid-binding protein (H-FABP) for ruling out NSTEMI patients at presentation (n=360) and 1 h (n=320). The ESC rule out algorithms at 0 hour and 1 hour are included for comparison.

The probability of a resulting NRI to be >0.330 or <-0.330 was low (p<0.0005), if the hypothesis of NRI zero is assumed. The ESC 'rule-out' for 1 h (Figure 2D) (3 false negatives) was compared to the proposed combination algorithm (0 false negatives) for the same time point (Figure 2B) and the results are shown in Tables 3 and 4 for algorithm D. The proposed combination algorithm had a higher specificity at both time points (t=0, 0.656 *vs.* 0.288: t=1, 0.713 *vs.* 0.689, respectively).

Id.	Algorithm[a]	Net Gain AMI	Net Gain non-AMI	NRI	p value
0 h (presentation)					
A	H-FABP & hs-cTnT	NA	NA	NA	NA
C	ESC rule-out	0.046	-0.376	-0.330	0.000
0 h-1 h					
B	H-FABP & hs-cTnT	NA	NA	NA	NA
D	ESC rule-out	-0.045	-0.026	-0.069	0.031

Id.: Identifier of algorithm; [a]Algorithm relates to the decision tree in Figure 2; AMI refers to NSTEMI patients; NRI: net reclassification index; p value for algorithm C being compared to algorithm A and for algorithm D being compared to algorithm B; NA: not applicable; h: hour

Table 4: Statistical comparison using the Pencina's Net Reclassification Improvement of the decision tree algorithms related to Figure 2, based on biomarkers of high-sensitive troponin T (hs-cTnT) and heart-type fatty acid-binding protein (H-FABP) for ruling out AMI on NSTEMI data at presentation (n=360) and 1 h (n=320). The ESC rule-out algorithms at 0 h and 1 h are included for comparison.



	A	B	C	D	E
hs-cTnT (Elecsys)	5	12	3	52	5
hs-cTnI (Architect)	2	5	2	52	6
hs-cTnI (Dimension Vista)+	0.5	5	2	107	19

Figure 3: ESC guidelines 0 h/1 h rule-in and rule-out algorithms using high-sensitivity cardiac troponin (hs-cTn) assays in patients presenting with suspected non-ST-elevation myocardial infarction (NSTEMI) to the emergency department. 0 h and 1 h refer to the time from the first blood test. NSTEMI can be ruled-out already at presentation, if the hs-cTn concentration is very low. NSTEMI can also be ruled-out by the combination of low baseline levels and the lack of a relevant increase within 1 h. Patients have a high likelihood for NSTEMI if the hs-cTn concentration at presentation is at least moderately elevated or hs-cTn concentrations show a clear rise within the first hour. Cut-off levels are assay specific. Cut-off levels for other hs-cTn assays are in development. *Only applicable if chest pain onset >3 h. +At the time of the publication of the guideline not yet commercially available (redrawn from [13]).

Discussion

The aim of this study was to provide algorithms to support clinical management decisions to rule-in and/or rule-out AMI. These algorithms would aid in the decision-making pathway(s) to either admit or potentially discharge patients who present at the emergency department with chest pain of suspected cardiac origin. The algorithms used retrospective biomarker data measured at presentation and 1 h to assist with ruling out AMI in NSTEMI patients. The results demonstrated that measuring a combination of H-FABP and hs-cTnT in ECG negative patients (NSTEMI) at presentation was more effective at ruling out AMI than hs-cTnT on its own. Applying this combination algorithm (Figure 2A) to the data, identified 189 patients with chest pain who were non-AMI. This combination algorithm had a significantly higher specificity at presentation (0.656 *vs.* 0.288) compared to the ESC algorithm (Figure 2C) which only identified 83 patients as non-AMI. There were three false negative cases using this combination algorithm. For patient one, the hs-cTnT value at presentation was 5.66 ng/l and H-FABP was 0.98 µg/l. Patient two presented three hours after onset of chest-pain with a hs-cTnT of 5.84 ng/l and H-FABP 1.86 µg/l. For this patient, the biomarkers were still negative six hours after presentation. The third patient Presented 1 hour and 40 minutes after experiencing chest pain with a hs-cTnT 5.3 ng/l and H-FABP 1.35 µg/l. Interestingly there were two patients with hs-cTnT <12 ng/l who had elevated H-FABP (≥ 2.88 µg/l) who experienced an AMI and who were correctly identified by the proposed algorithm.

When the combination algorithm H-FABP and hs-cTnT (Figure 2B) was applied to the data at 0-1 h, all chest pain patients positive for AMI were correctly identified (Table 3). However, when the ESC rule-out 0-1 h (Figure 2D) was applied to the data, three patients who were AMI positive, were not identified (Table 3).

These new findings improve upon our previous work [14,15] demonstrating the importance or H-FABP and its value, when measured in combination with hs-cTnT to rule out AMI at presentation. In comparison with a rule-out algorithm that included ECG changes with H-FABP and hs-cTnT [16], we demonstrate that our combination algorithm of H-FABP and hs-cTnT, had comparable sensitivity (0.955 *vs.* 0.991, respectively) and NPV (0.984 *vs.* 0.997, respectively). Moreover, our combination algorithm had increased specificity (0.658 *vs.* 0.593, respectively) and a higher PPV (0.411 *vs.* 0.350, respectively). In addition, our combination algorithm identified more patients with chest pain to be non-AMI at presentation compared to a previous study using only hs-cTnT (65.6% *vs.* 27.7%, respectively) [17].

The H-FABP hs-cTnT combination algorithm employed in this current study identified 106 additional non-AMI patients *vs.* the ESC algorithm at presentation. Deployment of this combination algorithm to the current data, could have potentially reduced the total number of hospital admissions by 36.8%. The MACS rule, which comprises eight variables, including H-FABP and hs-cTnT, only reduced hospital admissions by 27%. Furthermore, the MACS rule requires complex calculations necessitating the use of computers [3].

The current study using the H-FABP hs-cTnT combination algorithm, identified 71% of non-AMI patients at 1 h with no false negatives. The TRAPID-AMI study, which also used a 0 and 1 h algorithm, ruled out 63.4% of patients with chest pain as non-AMI. However, seven false negatives were reported [18,19].

The proposed H-FABP hs-cTnT combination algorithm at presentation has clinical utility at the emergency department, where chest pain accounts for up to 20% of all admissions and was the primary reason for 5.5 million hospital visits in 2008 [20]. In the UK, patients who present with chest pain account for two-thirds of all admissions from the emergency department. However, only 25% of these patients are diagnosed with acute coronary syndrome. Furthermore, under current clinical guidelines, 6% of chest pain patients are discharged with missed myocardial damage, and similar figures are also observed in Europe [21-23].

The H-FABP hs-cTnT combination algorithm, described in this manuscript, would provide evidence-based decision-making enabling clinicians to correctly identify non-AMI patients from those presenting to the emergency department with chest pain at time of presentation. These non-AMI patients could be investigated for other causes of their chest pain, or indeed discharged. The H-FABP hs-cTnT combination algorithm would have an impact on patient health by allowing the stratification of risk of serious disease in patients presenting with chest pain. This would ensure that efficient uses of resources are provided to patients identified as high risk. Adoption of the H-FABP hs-cTnT combination algorithm could result in savings of over £300 (€374) per presenting patient with chest-pain [24].

Study limitations

This study looked at the efficacy of a new algorithm-based test for stratifying risk of AMI in patients presenting at the emergency department with chest pain of suspected cardiac origin. Although, the results are very encouraging, the relatively low number of patients recruited suggests, a larger study could be conducted to verify results.

Conclusions

We have derived a H-FABP hs-cTnT combination algorithm for ruling out AMI for use in patients presenting to the emergency department with chest pain of suspected cardiac origin. The algorithm described could stratify risk in 65.6% of these patients who could potentially be discharged at presentation. This would reduce the total number of chest pain patients admitted for further observation by 36.8% when compared to the ESC algorithm, and would represent a significant health care saving.

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