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Original Article

Heart-type fatty acid binding protein (H-FABP) in patients in an emergency department setting, suspected of acute coronary syndrome: Optimal cut-off point, diagnostic value and future opportunities in primary care*

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KEY MESSAGE:

- In patients with chest pain, heart-type fatty acid binding protein (H-FABP) and high sensitivity troponin T (hs-cTnT) have a similar diagnostic potency.
- The optimal cut-off value for H-FABP is 4 ng/ml.
- The diagnostic value of combining H-FABP measurement with clinical findings should be studied in primary care.

ABSTRACT

Background: Most patients presenting chest complaints in primary care are referred to secondary care facilities, whereas only a few are diagnosed with acute coronary syndrome (ACS).

Objective: The aim is to determine the optimal cut-off value for a point-of-care heart-type fatty acid binding protein (H-FABP) test in patients presenting to the emergency department and to evaluate a possible future role of H-FABP in safely ruling out ACS in primary care.

Methods: Serial plasma H-FABP (index test) and high sensitivity troponin T (hs-cTnT) (reference test) were determined in patients with any new-onset chest complaint. In a receiver operating characteristic (ROC) curve, the optimal cut-off value of H-FABP for ACS was determined. Predictive values of H-FABP for ACS were calculated.

Results: For 202 consecutive patients (prevalence ACS 59%), the ROC curve based on the results of the first H-FABP was equal to the ROC curve of hs-cTnT (AUC 0.79 versus 0.80). Using a cut-off value of 4.0 ng/ml for H-FABP, sensitivity for ACS of the H-FABP (hs-cTnT) tests was 73.9% (70.6%). Negative predictive value (NPV) of H-FABP for ACS in a population representative for primary care (incidence of ACS 22%) thus could reach 90.8%.

Conclusion: In patients presenting chest pain, plasma H-FABP reaches the highest diagnostic value when a cut-off value of 4 ng/ml is used. Diagnostic values of an algorithm combining point-of-care H-FABP measurement and a score of signs and symptoms should be studied in primary care, to learn if such an algorithm could safely reduce referral rate by GPs.

Keywords: Acute coronary syndrome, point-of-care systems, heart-type fatty acid binding protein, early diagnosis, referral

INTRODUCTION

Background

Patients with symptoms possibly due to acute coronary syndrome (ACS) frequently contact their general

practitioner (GP) first. In case of suspected ACS, patients will be urgently referred to a secondary care facility since early treatment of ACS markedly increases survival and quality of life (1,2). In primary

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care, however, differential diagnosis of chest complaints is broad, and ACS is present only in a minority of patients (3). In addition, signs or symptoms decisively distinguishing ACS (with a low prevalence) from high prevalent diagnoses with an advantageous course have not been described earlier (4,5). Furthermore, an electrocardiogram (ECG) reveals no signs of ischaemia in a significant number of patients (6). Therefore, diagnostic means accessible for GPs lack potency to safely rule out ACS and a low threshold for referring patients with possible ACS is maintained. In literature, incidence of ACS among patients presenting symptoms suspected for ACS, is at most 22% and incidence of acute myocardial infarction (AMI) 17% (7,8). In a Dutch cohort of such patients, 27% of patients were not referred, in 8% of whom ACS was diagnosed at a later stage, leading to a false negativity rate of 2%. A total of 73% of patients were referred, 75% of whom were not diagnosed with ACS (false positivity rate or 'unnecessary referral rate' 54.8%) (7,9). For a safer and more cost-effective referral policy by GPs, new diagnostic means should become available.

Serial measurement of plasma high sensitivity cardiac specific troponin (hs-cTn), the cornerstone in diagnosing as well as ruling out AMI, is impossible to perform in primary care (10,11). Furthermore, current point-of-care troponin tests are less accurate due to detection limits higher than the widely used cut-off values for a positive test, usually set at the 99th percentile of a healthy population (12). Heart-type fatty acid binding protein (H-FABP) is a small sized protein (molecular mass 15 kD) (13). Therefore, in case of AMI, elevation of plasma H-FABP can be detected within the first one–two hours after onset of complaints (14–16). Several studies have described an added value of H-FABP when measured besides troponin in an emergency room setting in an early phase (17,18). As a solitary rule-out test at admission, high sensitivity cardiac specific troponin T (hs-cTnT) outperforms H-FABP slightly but H-FABP tested in addition to hs-TnT leads to an increase in sensitivity compared to hs-TnT alone (19). The value of H-FABP as a solitary marker in a primary care setting with a typical low prevalence of ACS has been studied once using a point-of-care H-FABP test. Prevalence of ACS was 22% in this study (7). Safe implementation of this test in daily care was opposed by excessive false negative results. This was possibly caused by the relatively high cut-off value for H-FABP (7 ng/ml) of the point-of-care test and a high number of early presenters (presenting within three hours after onset of symptoms) included in this study. In daily general practice, however, a point-of-care test facilitating early rule-out of ACS and reducing unnecessary referral to secondary care facilities would improve the interface between primary and secondary care. It would add to an evidence-based approach of unselected and early presented problems that GPs are faced with

and it would increase efficient use of diagnostic facilities in primary care. Thus, several main goals, as formulated by the European General Practice Research Network in the research agenda for general practice/family medicine and primary health care in Europe (<http://www.egprn.org>) are met.

Objectives

The main objectives of this study are twofold. First, the intention to determine the optimal cut-off value for a point-of-care H-FABP test. Second, to evaluate H-FABP as a potential marker for early triage of patients presenting complaints possibly due to ACS in primary care. Therefore, in an emergency department setting, plasma H-FABP and high sensitivity troponin T (hs-cTnT) levels were compared in an early phase after onset of chest complaints. This study is part of a larger project focusing on point-of-care H-FABP testing in suspected ACS in primary care.

METHODS

Study design

A delayed type cross-sectional diagnostic study was performed in the emergency department of Ziekenhuis Oost-Limburg (ZOL), a large academic hospital in Genk, Belgium.

Patient selection

Patients consecutively presenting with cardiac symptoms (presence of acute pain, discomfort or pressure in either chest, epigastric, neck, jaw or arm) or atypical symptoms suspected of cardiac origin (fatigue, nausea, vomiting, diaphoresis, faintness and back pain, without apparent non-cardiac source like a trauma) after triage by an emergency department physician were included. Excluded were patients from whom no informed consent could be obtained and patients with symptoms lasting more than 24 h (H-FABP levels return to baseline 24–36 h after onset of myocardial ischaemia) (13). Patients visited the emergency department on their initiative or they were brought in by an emergency service after referral by a GP or after contacting the emergency service themselves. All patients received routine care considering rule in and rule out of ACS and subsequent treatment. Treating physicians were blind to H-FABP results. A flowchart summarizing patient numbers and the process of inclusion is presented in Figure 1.

Informed consent

Obtaining patients' written informed consent in an acute life-threatening situation was considered inconvenient.

Figure 1. Study flow chart as executed in the emergency service of the hospital of Genk, Belgium. AMI, acute myocardial infarction; H-FABP, heart-type fatty acid binding protein.

Furthermore, all medical acts were part of usual care, including blood sampling, except for the additional determination of H-FABP. Patients were, therefore, asked for written informed consent at a later stage. They could decide to withdraw their consent then or at any time after. Only H-FABP results and clinical data of patients who returned a written informed consent were included in the study. The study protocol was in agreement with the WMA Declaration of Helsinki for Ethical Principles for Medical Research Involving Human Subjects and was approved by the Ethical Review Board of ZOL that specifically agreed on the solution for the consent procedure as described above.

Measurements

Presence of the inclusion criteria, symptoms, ECG-findings, time of onset of symptoms, time of drawing the initial blood sample and all laboratory test results were documented. The initial blood samples to measure H-FABP and hs-cTnT were collected by the ambulance staff immediately upon arrival at the patient's site or arrival in our hospital. Routinely, in all venous blood samples—at presentation and any time later during the evaluation at the emergency department—plasma creatinine and hs-cTnT (using Elecsys Cobas fifth-generation hs-cTnT assay by Roche Diagnostics) were measured. Estimated glomerular filtration rate (eGFR) was measured in order to determine the influence of renal clearance on H-FABP and hs-cTn test results. Additionally, a quantitative H-FABP measurement was performed using

an H-FABP assay developed by FABPulous BV (limit of detection: 0.5 ng/ml; 99th percentile in a healthy reference population: 5.3 ng/ml) (20).

Outcomes

To allow for a final (gold standard) diagnosis, an ECG was recorded and serial venous blood samples to determine hs-cTnT—used as the reference standard—were analysed. Final diagnoses were established by propounding all data available after an in hospital follow-up of at least 12 h to an expert panel of one independent GP and one independent cardiologist. The expert panel had access to all clinical data including, if performed, the results of coronary angiography. In cases of disagreement, two extra cardiologists and GPs were consulted to determine the final diagnosis unanimously. The expert panel based all decisions on definitions of final diagnoses that were unambiguous and determined beforehand according to current guidelines (10,11,21–24). The expert panel thus utilized the following possible diagnoses: acute myocardial infarction (AMI) with or without ST elevations on ECG (STEMI or NSTEMI), unstable angina (UA), stable angina, no coronary disorders. See Table 1 for complete definitions.

(Statistical) analysis

Receiver operating characteristic (ROC) curves have been used to find the mathematical optimal cut-off point of the venous H-FABP-test for ACS as well as to compare

Table 1. Outcome definitions as used by the expert panel.

Diagnosis	Definition as used by expert panel
AMI	Clinical presence of ACS with ECG-changes, hs-cTn results or results of imaging techniques supporting myocardial infarction. Exact cut-off values of hs-cTn were defined using the 99th percentile of the upper reference limit in a normal reference population, as is widely accepted (10,11). In all cases of AMI, distinction was made between STEMI and non-STEMI.
nSTEMI	A situation of complaints indicative for ACS combined with at least one measurement of hs-cTn above the 99th percentile and thereby a change between two measurements of at least 20%, without ST elevations on ECG recordings (21).
STEMI	Complaints indicative for ACS combined with ST elevations on ECG recordings (23).
Unstable angina	Clinical presence of ACS based on typical and recently developed or altered symptoms of myocardial ischemia without changes in ECG or hs-cTn indicative for AMI (21).
Stable angina	Angina pectoris occurring in a patient in predictable situations for months, without a recent change in severity or amount of exertion that is needed for angina pectoris to occur (22).
No coronary disorder	No coronary disorder was diagnosed when AMI, stable angina and unstable angina were excluded.

AMI, acute myocardial infarction; ACS, acute coronary syndrome; ECG, electrocardiogram; hs-cTn, high sensitivity cardiac specific troponin; STEMI, ST elevated myocardial infarction; nSTEMI, non-ST elevated myocardial infarction.

H-FABP to the reference test, hs-cTnT. We used exact tests for comparisons between two areas under the curve (AUC) (25). Sensitivity, specificity, positive and negative likelihood ratios (PLR and NLR) for AMI and ACS of H-FABP (cut-off value between positive and negative: greater or equal to 4 ng/ml) and hs-cTnT (cut-off value between positive and negative: above 14 pg/ml) were determined, using outcomes of the expert panel as undisputed diagnoses. Potential negative and positive predictive value (NPV and PPV) in a primary care setting were calculated using Bayes' theorem. SPSS statistics version 21 and MedCalc were used for the statistical analyses. Before the start of the study, a power calculation revealed that 100 AMI patients were required to compare properly the performance of the plasma biomarkers.

RESULTS

Agreement to the study consent was given by 221 consecutive patients. Four patients appeared to have complaints for more than 24 h. For 15 patients, data collection was insufficient. Therefore, data of 202 patients meeting the inclusion criteria was analysed. Patient characteristics are displayed in Table 2. Duration of the complaints ranged between 15 min and 23.3 h. Median duration of complaints was 3 h and 54 min. Of the 202 admitted patients, 119 (59%) were diagnosed with ACS among whom 111 (55% of the total population) had an AMI. A total of 157 patients were males, 93 (59%) of whom had an AMI. Of 45 female patients, 18 (40%) had an AMI. Median age was 62 years (range 26–93 years) and ages of AMI and non-AMI patients overlapped. The duration of the complaints at first contact was 0–3, 3–6, 6–12, and 12–24 h in 82, 40, 56, and 24 patients, respectively. There was no relation between duration of the complaints and AMI risk ($P = 0.11$; Mann–Whitney). In 193 (96%) patients, the eGFR was > 30 .

ROC curves based on the results of the first H-FABP and hs-cTnT tests, using ACS as outcome measure, were similar with an area under the curve (AUC) of 0.80 (95% CI: 0.735–0.856) for hs-cTnT and 0.79 (95% CI: 0.728–0.851) for H-FABP (Figure 2). The optimal cut-point for H-FABP, based on inspection of the curve, was at 4.0 ng/ml, resulting in a sensitivity for ACS of 74.8% and a specificity of 71.1%. Additionally, in Table 3, sensitivity and specificity of H-FABP for ACS at adjacent cut-off values are shown.

Sensitivity of H-FABP is strongly related to time between sample taking and the first complaints. Sensitivity for AMI was 63, 88, 96, 83% for patients presenting 0–3, 3–6, 6–12, 12–24 h after onset of symptoms (Table 4). During the first six hours after onset of complaints, sensitivity of H-FABP tended to be higher than that of hs-cTnT, without reaching statistical significance. However, within the first three hours after onset of complaints, sensitivity of H-FABP is lower than sensitivity of

Table 2. Patient characteristics.

	All	AMI (%)	No AMI (%)
Number	202	111 (55)	91 (45)
Gender			
Male	157	93 (59)	64 (41)
Female	45	18 (40)	27 (60)
Age group			
> 65 years	84	43 (51)	41 (49)
≤ 65 years	118	68 (58)	50 (43)
Duration complaints at presentation			
0–3 h	82	46 (56)	36 (44)
3–6 h	40	23 (58)	17 (43)
6–12 h	56	29 (52)	27 (48)
12–24 h	24	13 (54)	11 (46)
eGFR			
≥ 30	193	108 (56)	85 (44)
< 30	9	3 (33)	6 (67)

AMI, acute myocardial infarction; eGFR, estimated glomerular filtration rate (using modification of diet in renal disease (MDRD)—formula.

Figure 2. Receiver operating characteristic (ROC) curve of high sensitivity troponin and H-FABP, optimal cut-off point for H-FABP using ACS as outcome. ACS, acute coronary syndrome; H-FABP, heart-type fatty acid binding protein; hs-cTnT high sensitivity cardiac specific troponin T; ROC curve, receiver operating characteristic curve.

H-FABP at a time interval of 3–24 h after onset of complaints. Sensitivity for ACS (UA and AMI) is lower than sensitivity for AMI only (Table 5).

The overall sensitivity and specificity of H-FABP for AMI at presentation using a cut-off value of 4 ng/ml were 77.5% and 71.4% respectively. In a population of patients presenting chest complaints representative for primary care, with an incidence of AMI of 17%, NPV of H-FABP using a cut-off between positive and negative of 4 ng/ml would reach 93.9% for all patients and 97.1% for patients presenting complaints with a duration of at least three hours. For ACS, an overall sensitivity of 73.9% and a specificity of 71% was found. With an incidence of ACS in primary care among patients presenting chest complaints of 22%, NPV would reach 90.8% (Table 6). If only data of patients presenting complaints with a duration of more than three hours are regarded, NPV would amount 94.8%. Referral is made to Table 3 for NPVs of H-FABP at other cut-off values. Furthermore, negative and positive

Table 3. Sensitivity and specificity of H-FABP for ACS at different cut-off values between positive and negative. Sensitivity and specificity of H-FABP for ACS at different cut-off values are given for all patients presenting complaints with a duration of 0–24 h and for all patients presenting complaints with a duration of 3–24 h at presentation. NPV is estimated for a population representative for primary care (incidence of ACS = 22%). Sensitivity, specificity and NPV for hs-cTnT with a cut-off of 14 pg/ml are given for comparison.

Cut-off value	Interval onset complaints—presentation 0–24 h			Interval onset complaints—presentation (h) 3–24 (ng/ml)		
	Specificity	Sensitivity	NPV	Specificity	Sensitivity	NPV
3.0	43.5	85.7	91.5	45.7	94.2	96.5
3.5	60.9	79.0	91.1	65.2	88.4	95.2
4.0	71.7	73.9	90.7	73.9	85.5	95.8
4.5	78.3	66.4	89.2	82.6	84.1	94.9
5.0	78.3	58.8	87.1	82.6	79.7	93.5
hs-cTnT	73.9	70.6	89.9	67.4	88.4	95.4

ACS, acute coronary syndrome; H-FABP, heart-type fatty acid binding protein; hs-cTnT, high sensitivity cardiac specific troponin T; NPV, negative predictive value.

likelihood ratios as well as odds ratios—all independent of the incidence of ACS—are given in Table 6.

If H-FABP was used as a stand-alone test at presentation, in this population of 202 patients among whom 119 patients were diagnosed with ACS, 31 patients (25 AMI, 6 UA) would test false negative (i.e., H-FABP < 4 ng/ml at presentation in an eventual case of ACS). Using only hs-cTnT at presentation, 35 patients would be missed (30 AMI, 5 UA). Among 24 false positive cases (i.e., H-FABP at or above 4 ng/ml in eventually ACS negative patients as based on serial hs-cTnT measurements and clinical judgment), 15 patients were diagnosed with either a non-cardiac mild disease or with stable angina, whereas 9 cases related to moderate to severe alternative cardiac diagnoses needing acute treatment.

H-FABP and hs-cTnT values were compared in patients with an eGFR at or above 30 ml/min versus below 30 ml/min according to their ROC curves and AUC. There was no significant difference between both markers in both subgroups and for each marker the 95% confidence intervals overlapped with both renal function groups. However, only 9 patients with an eGFR below 30 ml/min were included.

Table 4. Sensitivity and specificity of hs-cTnT and H-FABP. Sensitivity and specificity of hs-cTnT (cut-off 14 pg/mL) and H-FABP (cut-off 4 ng/mL) for AMI at different time intervals after onset of complaints.

Interval onset complaints—presentation (h)	0–3		3–6		6–12		12–24		0–24	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
hs-cTnT	54.9	75.7	83.3	56.3	91.7	77.8	91.7	63.3	73.0	71.4
H-FABP	62.7	70.3	87.5	56.3	95.8	81.5	83.3	72.7	77.5	71.4
n	51	37	24	16	24	27	12	11	111	91

H-FABP, heart-type fatty acid binding protein; hs-cTnT, high sensitivity cardiac specific troponin T.

Table 5. Sensitivity of hs-cTnT and H-FABP. Sensitivity and median plasma concentrations (25th, 75th percentile) of hs-cTnT (cut-off 14 pg/ml) and H-FABP (cut-off 4 ng/ml) for STEMI, nSTEMI, all AMI (STEMI and nSTEMI), unstable angina and all ACS (AMI and unstable angina) at presentation, for all patients presenting complaints with a duration of 0–24 h and 3–24 h respectively.

Final diagnosis	STEMI		nSTEMI		AMI		Unstable angina		ACS	
	0–24	3–24	0–24	3–24	0–24	3–24	0–24	3–24	0–24	3–24
Interval onset complaints—presentation (h)										
<i>n</i>	55	39	56	26	111	65	8	4	119	69
Sensitivity hs-cTnT	78.2	94.9	67.9	84.6	73.0	90.8	37.5	50.0	70.6	88.4
Sensitivity H-FABP	80.0	92.3	75.0	84.6	77.5	89.2	25.0	25.0	73.9	85.5
Median plasma concentration hs-cTnT (25th; 75th percentile)	129 (15;2140)	502 (49;3740)	24 (13;114)	88 (18;325)	45 (13;490)	194 (31;2140)	6 (3;15)	3 (3;15)	40 (13;325)	163 (31;1830)
Median plasma concentration H-FABP (25th; 75th percentile)	13.6 (4.3;24.9)	19.1 (10.0;25.6)	5.2 (3.9;11.3)	5.8 (4.2;11.7)	7.1 (4.1;18.4)	12.9 (5.4;21.6)	2.3 (2.2;3.5)	2.3 (2.3;3.1)	6.4 (3.9;18.1)	11.9 (4.9;21.2)

ACS, acute coronary syndrome; AMI, acute myocardial infarction; H-FABP, heart-type fatty acid binding protein; hs-cTnT, high sensitivity cardiac specific troponin T; nSTEMI, non-ST elevated myocardial infarction; STEMI, ST elevated myocardial infarction.

DISCUSSION

Main findings

The main objectives of this study were to determine the optimal cut-off point of H-FABP and to assess the possible diagnostic potency of plasma H-FABP in patients presenting with chest pain to the GP. The cut-off value for ACS of H-FABP, where sensitivity and specificity reached optimal values, is 4.0 ng/ml. Using this cut-off value for H-FABP, sensitivity for AMI of the H-FABP (hs-cTnT) tests was 77.5% (73.0%) for all patients at presentation and the sensitivity for ACS was 73.9% (70.6%). Based on the results of this study, H-FABP with a cut-off value of 4.0 ng/ml could reach an overall NPV for AMI of 93.9% and for ACS of 90.8% in an unselected primary care population (estimation based on a prevalence of ACS of 22%).

Strengths and limitations

The strength of this study is its performance in a population of consecutive patients presenting to an emergency setting covering the broad spectrum of referred and non-referred patients, complying with usual care for chest pain bridging primary and secondary care. The outcome measurement complied with recent evidence-based guidelines (11). Besides, with our emergency department based data in a high prevalence setting of ACS, estimations for an NPV in an unselected primary care setting with a lower prevalence could be made. These estimations are limited by the fact that data was not gathered in a true primary care population, where sensitivity and specificity could differ slightly, as it is known that these parameters are influenced by different characteristics of a given population (26). Thus, further research in primary care has to be carried out to evaluate the actual role of H-FABP in assessing patients who present complaints possibly due to ACS. All the more since in this study laboratory testing was used, whereas point-of-care testing in the field could be susceptible to more user error.

Compared to recent literature, a higher incidence of AMI was found in these patients of 55%. This is probably due to the presence of an emergency doctor that performs triage of patients before consultation by a cardiologist if necessary. Furthermore, using hs-cTnT combined with criteria meeting contemporary international guidelines, incidence of nSTEMI rises, while incidence of UA falls (only 4% in this population), as is described in current literature (27).

Interpretation, implications for future research

H-FABP as a stand-alone test seems unable to rule in and out ACS, especially in early presenters (<3 h) and in case of UA. However, the estimated NPV of 90.8% in a primary care population could be further improved

Table 6. Predictive values and likelihood ratios. PPV and NPV of hs-cTnT (cut-off 14 pg/ml) and H-FABP (cut-off 4 ng/ml) for AMI and ACS at time intervals of 0–24 h and 3–24 h after onset of complaints in a primary care setting with an incidence of AMI of 17% and ACS of 22%. PLR, NLR and OR of hs-cTnT (cut-off 14 pg/ml) and H-FABP (cut-off 4 ng/ml) for AMI and ACS at time intervals of 0–24 h and 3–24 h after onset of complaints.

	PPV		NPV		PLR		NLR		OR	
Interval onset complaints—presentation (h)	0–24	3–24	0–24	3–24	0–24	3–24	0–24	3–24	0–24	3–24
hs-cTnT										
AMI	34.3	39.5	92.8	97.3	2.55	2.94	0.38	0.13	6.75	22.0
ACS	42.9	47.6	89.9	94.8	2.66	3.22	0.40	0.16	6.65	20.2
H-FABP										
AMI	35.7	40.1	93.9	97.1	2.71	3.27	0.32	0.15	8.60	22.1
ACS	42.9	48.6	90.8	94.8	2.67	3.36	0.36	0.20	7.41	17.2

ACS, acute coronary syndrome; AMI, acute myocardial infarction; H-FABP, heart-type fatty acid binding protein; hs-cTnT, high sensitivity cardiac specific troponin T; NLR, negative likelihood ratio; NPV, negative predictive value; OR, odds ratio; PLR, positive likelihood ratio; PPV, positive predictive value.

when signs and symptoms are added to point-of-care H-FABP measurement in a clinical decision rule (CDR). False positivity of H-FABP alone would be 29% for ACS, whereas currently 54.8% of patients presenting chest complaints to their GP are referred without an underlying ACS. Actual effect on referral decisions of a CDR combining signs, symptoms and point-of-care H-FABP testing in primary care merits further study. We, therefore, intend to test the incremental diagnostic value of a recently launched point-of-care H-FABP test with a cut-off value of 4.0 ng/ml combined with signs and symptoms in primary care (28).

Conclusion

In patients presenting chest pain at an early stage, H-FABP and hs-cTnT have the similar diagnostic potency. The optimal cut-off value for H-FABP is 4 ng/ml. Possibly, H-FABP could be of value in reducing referrals by GPs of eventually ACS negative patients and in reducing missed cases of ACS in primary care. Thus, in future studies performed by GPs, the diagnostic value of a CDR, combining signs, symptoms and point-of-care H-FABP testing—using 4.0 ng/ml as a cut-off value—in a true primary care population should be studied.

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