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Heart-Type Fatty Acid-Binding Protein in the Early Diagnosis of Acute Myocardial Infarction

The potential for influencing patient management

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دور البروتين الرابط للحمض الدهني – النوع القلبي في التشخيص المبكر للجلطة القلبية الحادة

امكانية التأثير في علاج المريض

حافظ الهادي وكيث فوكس

الملخص: الهدف: دراسة قدرة البروتين الرابط للحمض الدهني – النوع القلبي على التشخيص المبكر للجلطة القلبية عند المرضى الذين يعانون من آلام حادة في الصدر ومقارنتها مع الواصمات القلبية القياسية. **الطريقة:** أجريت دراسة استباقية لمئة حالة متعاقبة أُدخلوا عن طريق الطوارئ بآلام صدرية حادة كمؤشر لوجود جلطة قلبية. تم قياس تركيز تروبونين القلب (آ). تروبونين القلب (ت). كتلة كاينيز الكرياتين (م ب). مايوجلوبين. والبروتين الرابط للحمض الدهني – النوع القلبي مباشرة عند الوصول للطوارئ. وبعد ساعتين و 4 ساعات. وبين 8-10 ساعة. و 16-24 ساعة من وصول المريض. مقياس النتيجة الرئيسية هو قياس أفضل نتيجة للتحسس خلال 6 ساعات من وقوع الآلام. **النتائج:** أظهرت النتائج أن ذروة تركيز البروتين الرابط للحمض الدهني – النوع القلبي حصل بعد 8 ساعات من بداية الإحساس بآلام الصدر. وكان أفضل واصم مبكر على وجود جلطة قلبية مقارنة بالآخرين. حيث حصل على معدل تحسس بنسبة (79.9% و 98%) عند المرضى المصابين بجلطة قلبية حين وصولهم للطوارئ وبعد ساعتين على التوالي. كانت حساسية الواصمات الأخرى (تروبونين القلب - آ. تروبونين القلب – ت. كتلة كاينيز الكرياتين (م ب). والمايوجلوبين) أقل من (62%) عند الوصول للطوارئ. القدرة التنبؤية السلبية للبروتين الرابط للحمض الدهني – النوع القلبي (94%) وكانت أيضا أفضل من الواصمات الأخرى خلال أول ساعتين من وصول المريض للطوارئ. حصل المايوجلوبين على الترتيب الثاني كأعلى معدل تحسس. قمة التحسس لتروبونين القلب –آ. كتلة كاينيز الكرياتين (م ب). تروبونين القلب - ت حصلت بين الساعة 4.8 - 10. و 8-10 على التوالي بعد وصول المريض للطوارئ. **الخلاصة:** القياس المشترك للبروتين الرابط للحمض الدهني – النوع القلبي و تروبونين القلب – آ. مرتين خلال الساعات الثمان الاولى بعد ظهور الأعراض ذو حساسية ونوعية كافية للتشخيص المبكر لمعظم المرضى الذين يعانون من جلطة قلبية حادة. وهذا الفحص المشترك يوفر امتيازات أفضل من الفحوص المشتركة لبقية الواصمات الأخرى.

مفتاح الكلمات: جلطة قلبية حادة، متلازمة تاجية حادة، البروتين الرابط للحمض الدهني – النوع القلبي ، الواصمات القلبية.

ABSTRACT: ***Objectives:*** The objective of this study was to evaluate the diagnostic value of heart-type fatty acid-binding protein (H-FABP) in patients with acute chest pain and compare it with standard cardiac markers. ***Methods:*** We undertook a prospective evaluation of 100 consecutive patients admitted with acute chest pain suggestive of acute coronary syndromes (ACS). Serum cardiac troponin I (cTnI), cardiac troponin T (cTnT), creatine kinase-MB (CK-MB) mass, myoglobin, and H-FABP were determined at presentation and 2, 4, 8–10, and 16–24 hours after presentation. The main outcome measure was the best sensitivity value within 6 hours after symptom onset. ***Results:*** H-FABP peak concentration occurred at 8 hours after symptoms onset and was the most sensitive early marker with 79.9% and 98% of patients with AMI identified at presentation and 2 hours after presentation respectively. The sensitivity of all other cardiac markers (CK-MB mass, cTnI, cTnT, and myoglobin) at presentation was < 62%. The negative predictive value of H-FABP (94%) was also superior to other markers within the first 2 hours of presentation. Myoglobin was the second most sensitive early marker at presentation. Peak sensitivity of cTnI, CK-MB mass, and cTnT were present at 4, 8–10, and 8–10 hours respectively after presentation. ***Conclusion:*** Combined measurement of H-FABP and cTnI on two occasions during the first 8 hours after symptom onset was sufficiently sensitive and specific for the early diagnosis of most patients with acute MI and may provide advantages over other cardiac marker combinations.

Keywords: Acute myocardial infarction; Acute coronary syndromes; Heart-type fatty acid-binding protein; Cardiac markers.

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Advances in knowledge

1. *This article broadens our knowledge of the novel marker, heart-type fatty acid binding protein, and its place in the hierarchy system of currently available cardiac markers for the very early diagnosis of acute myocardial infarction in patients who present with acute chest pain.*

Application to patient care

1. *The information in this article will help health care professionals, who deal directly with patients with acute coronary syndromes, to understand better the advantages and limitations of the cardiac marker, heart-type fatty acid-binding protein.*
2. *This article offers some recommendations to clinicians on the best combination of cardiac markers for the early diagnosis of ACS and when to use them.*

Chest pain is a non-specific complaint and is the most frequent reason for patients to seek urgent medical attention.[1] A proportion of these patients will be in the process of evolving acute myocardial infarction (AMI) and, of these, about 25% lack the diagnostic features of infarction at presentation despite subsequently evolving Q wave infarcts. Current diagnostic and triage systems based on clinical history and electrocardiogram (ECG) results lack both sensitivity and specificity. Between 2 and 10% of patients with AMI may be inadvertently discharged from accident and emergency (A&E) departments leading to serious health and legal consequences. Conversely, inappropriate admissions of a large number of patients without acute coronary syndromes (ACS) will have substantial cost implications.[2] Cardiac markers are critical in making the diagnosis of AMI but, thus far, their role has mainly been for retrospective confirmation of AMI, 12-24 hours after admission. Creatine kinase (CK), CK muscle and brain (CK-MB) and troponins lack sufficient precision within the first 6 hours of presentation. Myoglobin is an early marker of myocardial injury, but has poor specificity.[3]

Heart-type fatty acid-binding protein (H-FABP) is a novel marker with the potential for the early diagnosis of AMI within 6 hours of symptoms onset.[4] Its sensitivity for the diagnosis of AMI is comparable with myoglobin; however, the specificity of H-FABP for myocardial tissue is significantly better than that of myoglobin.[5] This early release of H-FABP coupled with relative cardiac tissue specificity are potential advantages that may be valuable for the early diagnosis, triage, and management of patients with AMI.[6-7] To date, there have been few studies comparing the value of these markers for the early diagnosis of AMI.[8] The aim of the current study is to compare the value of H-FABP for the early diagnosis of AMI with other cardiac markers such as myoglobin, creatine CK-MB mass, serum cardiac troponin I (cTnI), and cardiac troponin T (cTnT) in a standardised setting.

Methods

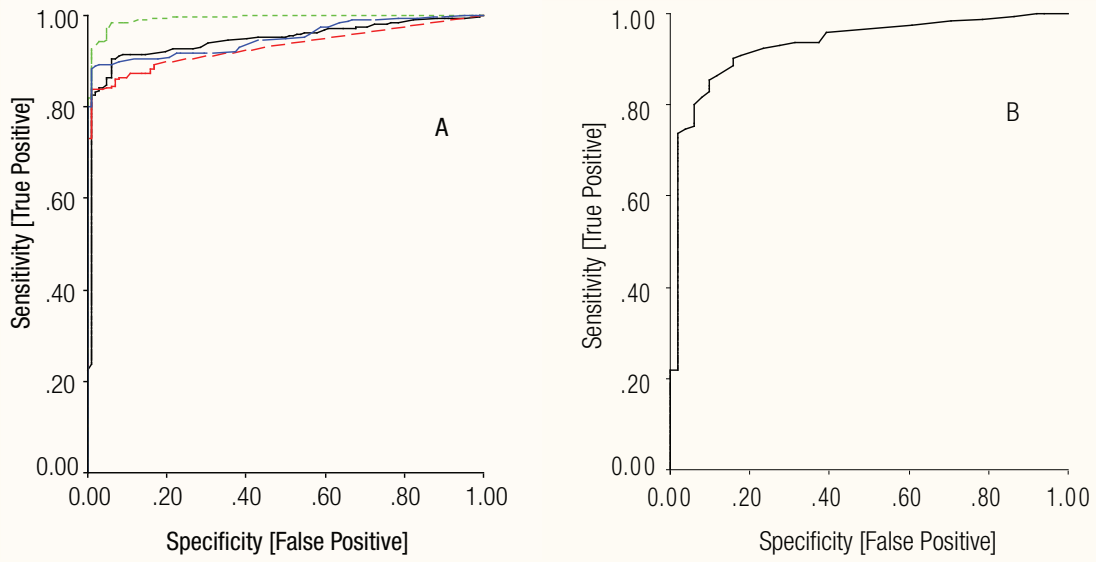
Included in the study, over a seven months period in 2002, were 100 consecutive patients with acute chest pain admitted within 6 hours of symptoms onset through the A&E Department at the Royal Infirmary of Edinburgh. Ethical approval was obtained from the local ethical committee, the Lothian Health Board, Edinburgh, UK. Informed consent was obtained from each patient before beginning the study. All enrolled patients were evaluated by the A&E Department physician. The evaluation included a brief history and physical examination and a recording of a 12-lead ECG. The time of onset of symptoms was carefully recorded for each patient at presentation. Five serial blood samples beginning at 0 hour (at presentation), 2 hours, 4 hours, 8–10 hours, and 16–24 hours after presentation and cTnI, cTnT, CK-MB mass, myoglobin, and H-FABP were measured at each time interval. All sequential patients were included in this study if they presented within 6 hours after the onset of symptoms, and had prolonged ischaemic chest pain (≥ 10 minutes in duration) suggestive of ACS, with or without ECG changes suggestive of ischaemia. Patients were excluded from the study if they had: 1) repeated intramuscular injection; 2) cardiac arrest at presentation; 3) recent surgery, coronary artery bypass graft (CABG) or AMI (< 1month); 4) any evidence of renal impairment or hypothyroidism.

The diagnosis of ST elevation myocardial infarction (MI) was based on the revised definition of MI and had to include at least two of the following three findings:[9] 1) clinical history of prolonged ischaemic chest pain ≥ 30 minutes in

Table 1: Demographic and clinical data of patients in the various study groups. Continuous variables are presented as mean ± SD and categorical variables are presented as percentages (in brackets).

Demographic & clinical data	STEMI Group 1	Non-STEMI Group 2	UA Group 3	Angina/atypical Group 4	*P* value
No. Patients	45	14	20	21	
Age (years)	66.58 ± 11.74	67.36 ± 11.34	67.45 ± 12.31	64.55 ± 9.54	NS
Male	29 (64)	9 (64)	16 (80)	12 (57)	NS
Female	16 (36)	5 (36)	4 (20)	9 (43)	NS
Time to presentation (hrs)	3.57 ± 2.33	5.3 ± 1.28	5.63 ± 1.17	5.0 ± 1.95	NS
Previous history					
Angina	6 (13)	9 (64)	10 (50)	15 (71)	< 0.05
UA	6 (13)	3 (21)	3 (15)	4 (19)	NS
AMI	1 (2)	6 (43)	10 (50)	8 (38)	NS
CABG	6 (13)	5 (36)	2 (10)	5 (23)	NS
PCI	10 (22)	4 (29)	2 (10)	3 (14)	NS
Risk factors					
DM	8 (18)	2 (14)	3 (15)	2 (10)	NS
HTN	11 (24)	5 (36)	4 (20)	3 (14)	NS
Smoker	15 (33.3)	5 (36)	3 (15)	9 (43)	NS
Ex-smoker	4 (8.7)	1 (7)	8 (40)	2 (10)	NS
High cholesterol	31 (69)	10 (71)	9 (45)	13 (62)	NS
FHx of IHD	10 (22.2)	3 (21)	1 (5)	6 (29)	NS
Admission					
HR	72.97 ± 17.14	75.56 ± 17.99	66.92 ± 11.18	77.0 ± 16.35	NS
Systolic BP	136.4 ± 25.93	133.22 ± 34.26	151.92 ± 17.93	134.67 ± 10.49	0.024
Diastolic BP	71.83 ± 16.86	71.44 ± 18.44	74.92 ± 11.7	79.0 ± 13.99	NS
Typical chest pain	34 (76)	13 (93)	17 (85)	13 (62)	0.027
Atypical chest pain	11 (24)	1 (7)	3 (15)	8 (38)	NS
ECG changes at admission					
Persistent ST elevation	39 (87)	-	-	-	-
Transient ST elevation	-	3 (21)	2 (10)	1 (5)*	-
ST depression ±	6 (13)	9 (64)	14 (74)	3 (14)	-
T wave changes	-	-	-	-	-
Other ECG changes	-	1 (7)	1 (5)	2 (10)	-
No acute changes	-	1 (7)	2 (10)	15 (71)	-
Old Q waves present	-	1 (7)	5 (25)	6 (29)	-
ECG changes at admission:					
Persistent ST elevation	39 (87)	-	-	-	-
Transient ST elevation	-	3 (21)	2 (10)	1 (5)*	-
ST depression ±	6 (13)	9 (64)	14 (74)	3 (14)	-
T wave changes	-	-	-	-	-
Other ECG changes	-	1 (7)	1 (5)	2 (10)	-
No acute changes	-	1 (7)	2 (10)	15 (71)	-
Old Q waves present		1 (7)	5 (25)	6 (29)	-

Legend: SD = standard deviation; STEMI = ST elevation myocardial infarction; UA = unstable angina; AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; DM = diabetes mellitus; HTN = hypertension; FHX of IHD = family history of ischaemic heart disease; HR = heart rate; BP = blood pressure; ST, T, Q, = ST segment, T wave segment, Q wave segment of electrocardiogram (ECG); NS = not significant.



Figures 1A and B: Receiver operator characteristic (ROC) curves that were used to derive the cut-off concentrations for **A**) the various cardiac markers (blue = CK-MB mass concentrations; green = cTnI concentrations; red = cTnT concentrations; black = myoglobin concentrations); and **B**) H-FABP. See text for sensitivity and specificity values.

duration; 2) evolution of typical changes in at least two adjacent leads of the ECG, appearance of ST segment elevation > 2 mm 0.08 seconds after J point persisting for at least 24 hours with or without Q waves, defined as ST elevation MI; 3) a time-dependent rise in concentration of CK-MB or troponins and a subsequent fall. Unstable angina was diagnosed when patients had two or more of the following criteria without clear-cut ECG changes of infarction or cardiac markers (troponins or CK-MB) elevations diagnostic of AMI: 1) ischaemic chest pain ≥ 10 minutes in duration; 2) transient ST segment elevation ≥ 1 mm 0.08 seconds after J point less than 30 minutes in duration; 3) transient or persistent ST segment depression ≥ 1 mm 0.08 seconds after J point in two adjacent leads; 4) symmetrical or asymmetrical T wave inversion ≥ 1 mm excluding T wave inversion in leads III, AVR, and V1 only. Patients were diagnosed as having non ST elevation MI if they had one or more of the criteria listed above and in addition, they had evidence of myocardial necrosis as reflected by CK-MB or troponin elevation and a subsequent fall. Patients were diagnosed as having atypical or anginal chest pain if they had all the following criteria: 1) typical or atypical presentation of chest pain; 2) none of the above listed ECG changes and 3) no rise in CK-MB or cTnI.

Patients were divided into four main groups for comparison: Group 1 included patients with ST elevation MI, the 'STEMI group'; Group 2 included patients with non ST elevation MI, the 'Non-STEMI' group; Group 3 included patients with unstable angina (UA), the 'UA group'; Group 4 included a heterogeneous population of patients with mixed medical diagnoses other than the above. Patients in Group 4 were referred to as 'atypical/anginal chest pain group'. The selected diagnostic cut-off concentrations were based on receiver operator characteristic (ROC) curve analysis [Figures 1A and 1B] between patients with MI (STEMI and non-STEMI groups, n = 59) and controls (atypical/anginal chest pain group, n = 21 and healthy blood donor controls, n = 20). These cut-off concentrations were CK-MB mass ≥ 5 µg/L (sensitivity = 86.3%, specificity = 99%); cTnI ≥ 0.18 µg/L (sensitivity = 90.8%, specificity = 99%); cTnT ≥ 0.1 µg/L (sensitivity = 76.4%, specificity = 99%); H-FABP ≥ 12.5 µg/L (sensitivity = 91.4%, specificity = 86%), and myoglobin ≥ 95 µg/L (sensitivity = 81.2%, specificity = 99%).

The laboratory analysis of CTnI, CK-MB mass, and myoglobin was done on a Stratus CS analyser machine (Dade Behring, Germany), using commercially available test materials. The coefficients of variations for cTnI were 6.8%, and 6.7% at concentration range 0.24–0.36 µg/L, and 4.6–6.9 µg/L respectively. H-FABP was analysed by an enzyme linked immunosorbent assay method using commercially available assays (Hycult, Cambridge,

Table 2: Sensitivity, specificity, positive predictive value, and negative predictive value of cardiac markers for the early diagnosis of AMI within 6 hours after symptoms onset.

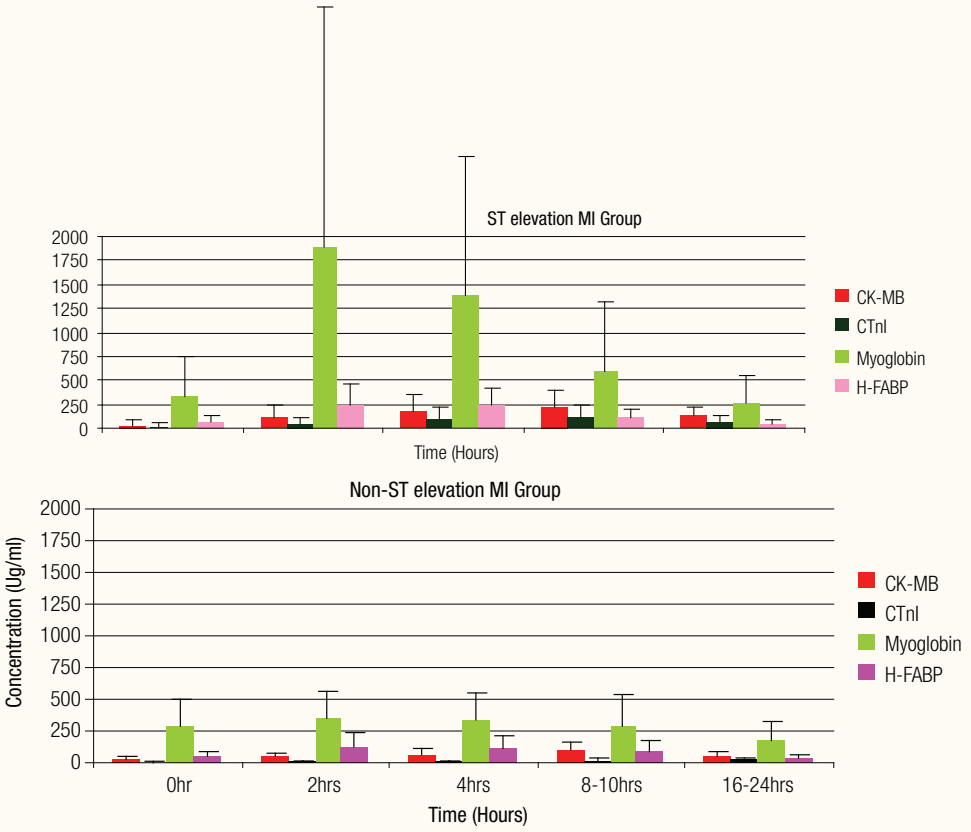
Marker(s)	Validity Indicator	0 hr	2 hrs	4 hrs	8-10 hrs	16-24 hrs
CK-MB	Sensitivity	42	92.2	95.3	95.3	90.6
	Specificity	93.75	93.75	93.75	93.75	86.7
	PPV	96	98.3	98.4	98.4	96.7
	NPV	29	75	83.3	83.3	81.25
CTnI	Sensitivity	56	95.3	100	100	100
	Specificity	81.25	87.5	93.75	96.88	100
	PPV	92.3	96.8	98.46	99.2	100
	NPV	31.7	82.35	100	100	100
CTnT	Sensitivity	32.8	67.2	85.9	96.9	95.3
	Specificity	93.75	93.75	93.75	93.75	93.75
	PPV	95.5	97.7	98.2	98.4	98.4
	NPV	25.4	41.7	62.5	88.23	83.3
H-FABP	Sensitivity	79.7	98	95.3	93.75	75
	Specificity	92.3	.93.3	93.75	87.5	93.3
	PPV	98	98.4	98.4	98	98
	NPV	52	94	83	78	47
Myoglobin	Sensitivity	59.4	87.5	89.1	84.38	68.75
	Specificity	94	93.75	93.75	93.75	93.75
	PPV	97.4	98.24	98.3	98.18	97.8
	NPV	38.1	65.22	68.2	60	42.8

Legend: CK-MB = creatine kinase-muscle & brain; PPV = positive predictive value; NPV = negative predictive value; cTnI = serum cardiac troponin I; cTnT = serum cardiac troponin T; HFABP = heart-type fatty acid-binding protein

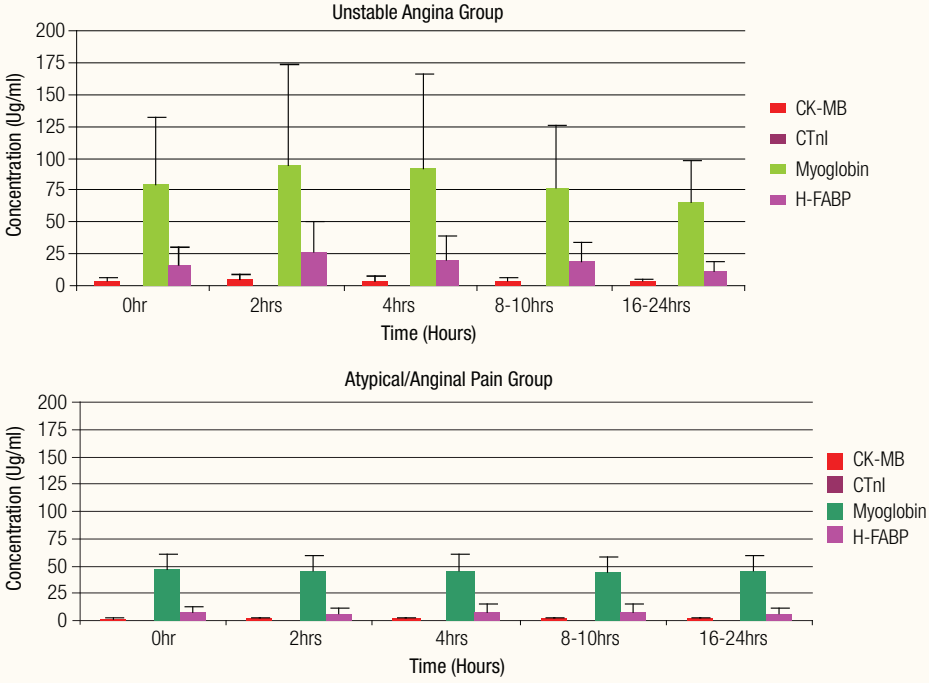
UK). The analytical sensitivity of H-FABP (mean ± 2SD) was 0.206 ± 0.047 μg/L. The coefficient of variation for H-FABP measurements was always < 10%. Cardiac-TnT was analysed on Elecsys 2010 using commercial assays (Roche, Germany). The reference ranges quoted by the manufacturer for CK-MB mass, cTnI, myoglobin, cTnT, and H-FABP assays were validated by assaying the normal ranges of 20 healthy blood donor samples (10 males and 10 females). The mean ± SD concentrations of these markers were CK-MB mass = 1.52 ± 0.8 μg/L; cTnI = 0.015 ± 0.006 μg/L; myoglobin = 41.5 ± 13.3 μg/L; cTnT = 0.011 ± 0.002 μg/L, and H-FABP = 6.86 ± 2.21 μg/L.

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS™, Pittsburgh, statistical software, Version 12). Variables were expressed as mean ± SD. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were measured for each marker at each time interval after presentation and compared. Chi-square tests were used to explore the group differences with respect to categorical variables. The Kruskal–Wallis H-test was conducted to compare continuous variables and mean cardiac markers concentrations differences in the four groups. Significant results are indicated by probability values less than or equal to 0.05.

Panel A: Patients with ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (Non-STEMI)

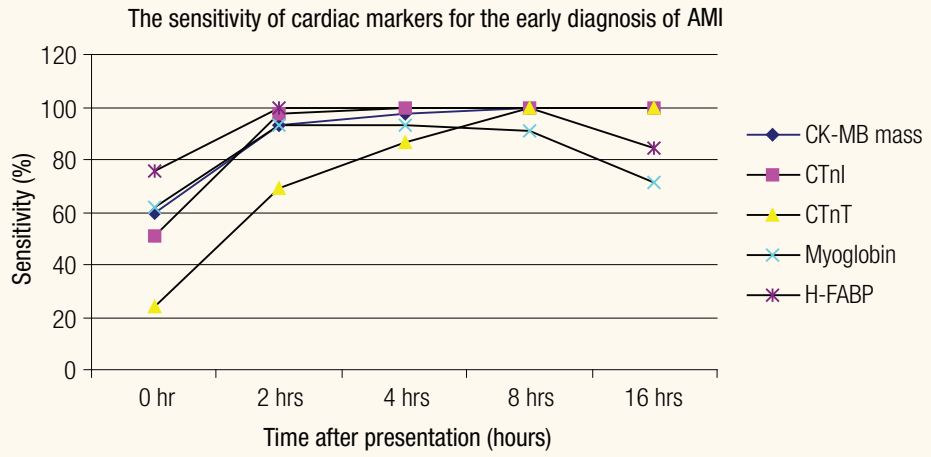


Panel B: Patients with unstable angina and atypical/anginal pain



Legend: CK-MB = creatine kinase-muscle & brain; cTnI = serum cardiac troponin I; H-FABP = heart-type fatty acid-binding protein

Figure 2: Illustrates the release pattern (time-concentration profile) of the different cardiac markers at each time after presentation in patients in the various study groups. The data for cTnT were omitted from the graph because they were on a different scale, but were similar to those of cardiac troponin I.



Legend: CK-MB = creatine kinase-muscle & brain; cTnI = serum cardiac troponin I; cTnT = serum cardiac troponin T; H-FABP = heart-type fatty acid-binding protein

Figure 3: Line chart representation of the sensitivity values. Each mark represents the percentage sensitivity of the cardiac marker at that time interval

Results

Out of 100 consecutive patients presenting with acute chest pain, 45 patients (45%) had ST elevation MI (Group 1), 14 patients (14 %) had non-STEMI (Group 2), 20 patients (20%) had UA (Group 3). The last 21 patients (21%) constituted Group 4. The demographic and clinical data of the patients in these four groups is shown in Table 1. The study group consisted of 66% males. The mean age, percentage of males/females, the prevalence of risk factors, and the prevalence of previous cardiac disease (CABG, PCI) were not significantly different between the groups. The prevalence of previous angina ($P < 0.05$), systolic blood pressure ($P < 0.024$) and type of chest pain at presentation ($P < 0.027$) were statistically different. Figure 2 illustrates the release characteristics of cardiac markers in the four groups. For the STEMI group, myoglobin and H-FABP were the earliest makers of myocardial injury. The peak concentrations of myoglobin and H-FABP were reached in samples taken 2 hours after presentation (8 hours after symptoms onset). The peak concentrations of CK-MB mass and cTnI occurred at 8–10 hours after presentation (14–16 hours after the onset of chest pain). The peak concentrations of cTnT occurred at 16–24 hours after presentation (24–30 hours after onset of symptoms). H-FABP and myoglobin concentrations decreased significantly at 16–24 hours, whereas CK-MB mass, cTnI, and cTnT were still present in high concentrations. For the non-STEMI group, H-FABP and myoglobin peak concentrations were achieved at 2 hours and the concentrations of these markers had decreased to normal levels at 16– 24 hours after presentation. For CK-MB mass, the peak concentration occurred at 8–10 hours. The maximum increase in cTnI and cTnT occurred late at 16–24 hours. The concentrations of CK-MB mass, cTnI, and cTnT were still present in significant levels at 16–24 hours.

Figure 3 is a line chart representation of the sensitivity values of cardiac markers for the diagnosis of MI in the STEMI only group, n = 45 patients. H-FABP was the most sensitive marker at presentation (75.5%), and it remained elevated with a sensitivity of 100% for the next 2–8 hours after presentation. H-FABP sensitivity was also superior to other markers within the first two hours of presentation. Myoglobin and CK-MB mass sensitivity were similar in the first 2 hours (93%). However, the peak sensitivity of myoglobin (93%) and CK-MB mass (100%) were reached at 2 hours, and 8–10 hours respectively. Cardiac-TnI reached higher sensitivity (97.7%) earlier (2 hours) than myoglobin, CK-MB mass, and cTnT. The sensitivity of cTnT gradually increased from a low level at presentation (24%) to the highest level (100%) at 8–10 hours after presentation [Figure 3].

The overall sensitivity, specificity, PPV, and NPV were determined for the whole group (n = 100 patients). Table 2 shows the percentages of these values for the different cardiac markers at each time interval after presentation. H-FABP still had the

highest sensitivity at presentation (79.9%). Almost all patients (98%) with MI were diagnosed within 2 hours after admission (8 hours after onset of symptoms). The specificity of H-FABP at 2 hours was 93.3%. Compared to other markers, H-FABP had the highest NPV (94%) at 2 hours. The PPV of H-FABP was also high (98%). Myoglobin had the second highest sensitivity at 0 hour (59.4%) rising to 87.5% two hours after presentation. The corresponding specificity, PPV, and NPV were 93.75%, 98.24%, and 65.22% respectively. All other cardiac markers had low sensitivities at 0 hr (i.e. at presentation) 32.8%, 42%, 56% for cTnT, CKMB mass and cTnI respectively. The NPV of cardiac markers was also low at presentation 25%, 29%, 31.7%, 38.1%, 52% for cTnT, CKMB mass, cTnI, myoglobin, and H-FABP respectively. Most of the cardiac markers had high PPV (92–100%). The performance of cTnI was better than cTnT in terms of overall sensitivity, specificity, PPV, and NPV. Reliable sensitivity, specificity, PPV, and NPV by CK-MB mass and cTnI were observed at 4 hours after presentation. Reliable sensitivity (96.9%), specificity (93.75%), PPV (98.4%), and NPV (88.23%) of cTnT were evident at 8–10 hours after presentation.

Discussion

In patients presenting with AMI, H-FABP appeared to be a reliable cardiac marker indicator 6 hours after symptom onset, peaked at 8 hours and had decreased significantly towards normal concentrations by 16-24 hours after presentation. These two features of H-FABP, early concentration peak following myocardial injury and rapid return to normal base line concentration, differentiate this marker from the troponins and CK-MB. They suggest the potential of H-FABP for early detection of myocardial injury and early detection of re-infarction. The sensitivities of H-FABP (75.5% and 79.7%) for the detection of AMI, observed within the first 6 hours after symptoms onset in this study, was in agreement with some previously published data.[5,10] In our study, H-FABP was the most sensitive marker at presentation and within the first two hours after presentation (i.e. 8 hours after symptom onset) and demonstrated the highest NPV (94%). This was consistent with other previously published data.[11] A study by Alansari *et al*. showed that myoglobin and H-FABP provide little clinical value when measured on admission in patients presenting with chest pain.[8] Most of the standard cardiac markers in Alansari's study had limited diagnostic value at presentation. The overall NPV of all cardiac markers was low < 52% within the first 6 hours after symptom onset. The sensitivity of these markers for the early diagnosis of AMI was < 62%. Bakker *et al.* reported low sensitivity (< 64%) and low NPV of routine cardiac markers CK-MB mass, cTnT, myoglobin, CK-MB activity, and CK to allow early exclusion of AMI.[12]

This study highlights two important facts: 1) H-FABP was more sensitive than myoglobin and 2) H-FABP had higher NPV than myoglobin. High sensitivity is essential for the early 'rule in' of patients with AMI, and high NPV is important for the early 'rule out' of AMI, since more than 90% of patients who present with acute chest pain to an A&E department do not have AMI. This superiority of H-FABP over myoglobin may be attributable to the fact that 1) the myoglobin content of skeletal muscle is twice that of the heart (hence interference from skeletal muscle injury i.e. less specific) whereas the H-FABP content of skeletal muscles is only 10–50% of that of the heart and 2) the normal plasma concentration of H-FABP (< 5 μg/L) is 10–15 fold lower than that of myoglobin (20–80 μg/L).[5] Hence, the differing features of myoglobin and H-FABP allow the use of lower, but more discriminate, cut-off concentrations of H-FABP thus improving the sensitivity. The limitation of the enzyme-linked immunosorbent assay (ELISA) method, which produces results in around 90 minutes, could be overcome by using the new rapid bed-side H-FABP tests.[13] However, as it is solely excreted by the kidney, this cardiac marker has limitations in patients with renal impairment and skeletal muscle injury.[14]

Conclusion

The main conclusions of this study are, first, that H-FABP was superior to myoglobin (and other markers) for the early diagnosis of AMI within 6 hours after symptom onset. Second, the diagnostic window for H-FABP is relatively prolonged (up to 14 hours after symptom onset). This diagnostic window provides sufficient opportunity for the detection of AMI and initiation of appropriate therapy. Third, cTnI, as measured on the Stratus CS machine, was highly sensitive supporting its use for

the early detection of patients with AMI. Fourth, measurement of H-FABP and cTnI at two intervals during the first 8 hours after symptom onset was sufficiently sensitive and specific for the early diagnosis of most patients with AMI. We propose an alternative: that H-FABP should be combined with a specific marker like cTnI. The combination of H-FABP and cTnI improves specificity for a definitive diagnosis of AMI. We also propose that this combination should be tested in a larger-scale study and, if the current findings are confirmed, H-FABP and cTnI may constitute the standard combination for early diagnosis of MI.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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