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Original Research Article

Early Diagnosis of Acute Coronary Syndrome Using Heart-Type Fatty Acid–Binding Protein: A Comparative Diagnostic Accuracy Study with Troponin in Emergency Chest Pain

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Abstract: ***Background*** Early diagnosis of acute coronary syndrome (ACS) in patients presenting with acute chest pain is challenging, particularly within the first few hours after symptom onset, when cardiac troponin levels may remain below diagnostic thresholds. This diagnostic delay contributes to uncertainty in emergency triage and postponement of definitive therapy. Heart-type fatty acid–binding protein (H-FABP), a small cytosolic protein rapidly released following myocardial injury, may offer diagnostic advantage during this early phase. ***Objective*** To evaluate the diagnostic accuracy of H-FABP for early detection of ACS and to compare its temporal performance with cardiac troponin in emergency department presentations. ***Methods*** In this prospective diagnostic accuracy study, 245 patients presenting with acute chest pain within 12 hours of symptom onset were enrolled. Plasma H-FABP and cardiac troponin levels were measured at two predefined intervals: 0–4 hours and 6–10 hours after symptom onset. Acute coronary syndrome was defined using troponin-based criteria. Diagnostic performance indices, including sensitivity, specificity, predictive values, overall accuracy, and receiver operating characteristic (ROC) curve analysis, were calculated. Subgroup analyses and differentiation between cardiac and non-cardiac chest pain were performed. ***Results*** Within the early 0–4-hour window, H-FABP demonstrated high diagnostic accuracy, with a sensitivity of 89.5%, specificity of 91.4%, and an AUC of 0.874, outperforming troponin measured during the same period (AUC 0.689). Troponin sensitivity in the early window was low (25.7%) despite high specificity. H-FABP identified 98.1% of ACS cases that were troponin-negative at presentation. At 6–10 hours, troponin showed superior diagnostic performance (AUC 1.000), while H-FABP sensitivity declined. H-FABP maintained consistent performance across major cardiovascular risk subgroups and effectively differentiated cardiac from non-cardiac chest pain early. ***Conclusion*** H-FABP provides significant diagnostic advantage during the early phase of ACS presentation and complements troponin in emergency department triage, enabling earlier identification of ACS and reducing diagnostic delay.

Keywords: Acute coronary syndrome; Heart-type fatty acid–binding protein; Cardiac troponin; Early diagnosis; Emergency department; Chest pain; Point-of-care testing

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INTRODUCTION

Acute coronary syndrome (ACS)—encompassing unstable angina, non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI)—remains a leading cause of morbidity and mortality worldwide, with a disproportionately high burden in low- and middle-income countries.[1] Early recognition of ACS among patients presenting with acute chest pain is critical, as timely diagnosis enables prompt reperfusion therapy, initiation of antithrombotic treatment, and appropriate risk stratification.[2,3] However, early diagnosis in the emergency department remains challenging because symptoms may be atypical, electrocardiographic changes can be non-diagnostic, and biochemical markers may not yet be elevated.[2-4]

Cardiac troponins are the preferred biomarkers for diagnosing myocardial infarction because of their high myocardial specificity.[2,3] Nonetheless, troponin elevation is time dependent, and sensitivity is reduced during the initial hours after symptom onset, particularly in patients presenting early or with smaller infarcts.[3-5] This "troponin-blind" window contributes to diagnostic uncertainty, prolonged observation, repeat testing, and potential delays in treatment. The challenge is especially relevant in high-volume emergency settings and in regions where delayed presentation and constrained resources are common.[6]

Heart-type fatty acid–binding protein (H-FABP) is a low–molecular-weight cytosolic protein rapidly released into the circulation following myocardial ischemia and injury.[7] Its early release kinetics make it a biologically plausible marker for detecting myocardial injury during the hyper-acute phase of ACS. Recent studies have suggested that H-FABP may improve early diagnostic sensitivity when used alongside troponin.[3,8-10] However, published data are heterogeneous with respect to assay methods, cut-off values, and study populations, limiting routine clinical adoption.[7] Moreover, evidence from Indian emergency cohorts—particularly with respect to early time windows and differentiation of cardiac from non-cardiac chest pain—remains limited.

Given these gaps, this study evaluated the diagnostic accuracy of H-FABP for early detection of ACS in patients presenting to the emergency department with acute chest pain and compared its temporal performance with cardiac troponin. We hypothesized that H-FABP would demonstrate superior sensitivity during early presentation and provide incremental diagnostic value when used alongside troponin.

MATERIAL AND METHODS

Study design and setting

This prospective diagnostic accuracy study was conducted in the emergency department of a tertiary care hospital. The study design and reporting adhered to the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines.

Study population

Adult patients presenting with acute chest pain suggestive of ACS within 12 hours of symptom onset were consecutively screened. A total of 245 patients met the inclusion criteria and were enrolled.

Inclusion criteria included acute chest pain consistent with possible myocardial ischemia and presentation within 12 hours of symptom onset. Exclusion criteria were ST-segment elevation myocardial infarction on initial ECG, known renal or hepatic dysfunction, recent trauma, active infection, or other conditions likely to confound biomarker interpretation.

Clinical assessment and electrocardiography

All patients underwent standard clinical evaluation and 12-lead electrocardiography at presentation. ECG findings were recorded and incorporated into routine clinical decision-making.

Biomarker sampling and assays

Venous blood samples were collected at two predefined intervals based on symptom onset: 0–4 hours and 6–10 hours. Plasma heart-type fatty acid–binding protein (H-FABP) levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (BT LAB, Biossaye Technology Laboratory), with results expressed in nanograms per milliliter (ng/mL), in accordance with the manufacturer's instructions.

Cardiac troponin T was measured using a high-sensitivity cardiac troponin T (hs-cTnT) assay (Roche Diagnostics, Mannheim, Germany) on an automated immunoassay platform. Troponin concentrations were reported in nanograms per liter (ng/L), and a value ≥14 ng/L, corresponding to the 99th percentile upper reference limit of the assay, was considered indicative of myocardial injury. An H-FABP cut-off value of 19 ng/mL was determined using receiver operating characteristic (ROC) curve analysis and the Youden index to optimize sensitivity and specificity in the study population. All laboratory personnel were blinded to the final clinical diagnosis.

Reference standard

The reference diagnosis of myocardial infarction was established using serial high-sensitivity cardiac troponin T (hs-cTnT) measurements interpreted in conjunction with clinical presentation and electrocardiographic findings, in accordance with contemporary guideline definitions.

Outcome measures

The primary outcome was the diagnostic accuracy of H-FABP for early detection of myocardial infarction in the 0–4-hour window. Secondary outcomes included comparative diagnostic performance across time windows, ROC–AUC analysis, subgroup analyses, differentiation of cardiac versus non-cardiac chest pain, and evaluation of incremental diagnostic value in troponin-negative early presenters.

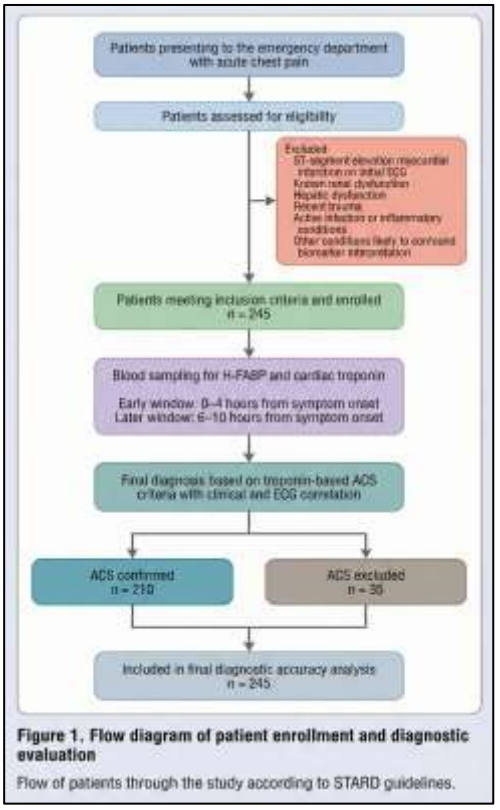

Figure 1. Study flow diagram

Statistical analysis

Diagnostic performance indices—sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy—were calculated using contingency tables. ROC curves were generated and AUC values computed with confidence intervals. Subgroup analyses were performed based on major cardiovascular risk factors. A two-sided p value <0.05 was considered statistically significant. Confidence intervals for diagnostic accuracy measures were calculated using standard binomial methods.

Ethical considerations

The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants. The study complied with the Declaration of Helsinki.

RESULTS

Study population

A total of 245 patients presenting with acute chest pain within 12 hours of symptom onset were included in the final analysis. Based on the reference standard, 210 patients (85.7%) were diagnosed with myocardial infarction, while 35 patients (14.3%) were classified as ACS-negative.

Patients with ACS were significantly older than those without ACS, with a mean age of 59.1 ± 12.0 years compared with 49.2 ± 10.2 years in the non-ACS group. The overall cohort demonstrated male predominance (64.5%). Major cardiovascular risk factors were highly prevalent: type 2 diabetes mellitus (63.3%), hypertension (48.6%), dyslipidemia (49.4%), and active smoking (34.3%). ST-segment deviation on electrocardiography was observed in 43.3% of patients, reflecting a high-risk emergency department population.

Table 1. Baseline clinical characteristics of patients presenting with acute chest pain

Characteristic	Number (n)	Percentage (%)
Male	158	64.5
Female	87	35.5
Type 2 Diabetes	155	63.3
Hypertension	119	48.6
Family history of ACS	20	8.2
Smoker	84	34.3
Dyslipidemia	121	49.4
ST deviation on ECG	106	43.3

Biomarker distribution by time window

In the 0–4-hour window, H-FABP levels were significantly higher in ACS patients than in non-ACS patients, whereas troponin levels showed limited early discrimination. H-FABP levels were 34.2 ng/mL in the ACS group compared with 9.6 ng/mL in the non-ACS group. Troponin levels showed limited early discrimination, with median values of 8.96 ng/L in ACS-positive group and 5.20 ng/L in ACS-negative group.

At 6–10 hours, troponin levels rose markedly in ACS patients (median 68.5 ng/L vs 6.9 ng/L in non-ACS), while H-FABP levels declined (median 19.1 ng/mL vs 8.3 ng/mL), reflecting expected biomarker kinetics.

Table 2. Distribution of H-FABP and troponin levels by time from symptom onset

Biomarker	ACS Status	Mean	Median	SD	Min	Max
H-FABP H1 (0–4h)	Negative	16.6	9.60	26.4	0.20	100
	Positive	39.1	34.2	21.4	1.00	100
H-FABP H2 (6–10h)	Negative	13.1	8.30	18.2	1.10	87.6
	Positive	23.9	19.1	16.9	1.20	100
Troponin T1 (0–4h)	Negative	5.77	5.20	3.19	1.10	12.2
	Positive	57.6	8.96	148	0.12	1088
Troponin T2 (6–10h)	Negative	7.16	6.90	3.66	0.88	13.4
	Positive	120	68.5	173	14.3	1393

Diagnostic accuracy of H-FABP for myocardial infarction compared with troponin

Early diagnostic performance (0–4 hours)

Using predefined cut-off values of Troponin- greater than or equal to 14 ng/L (Positive) and H-FABP - greater than or equal to 19 ng/mL (Positive), H-FABP demonstrated high diagnostic accuracy in the early window, with a sensitivity of 89.5%, specificity of 91.4%, positive predictive value (PPV) of 98.4%, negative predictive value (NPV) of 59.3%, and an overall accuracy of 89.8%.

In comparison, troponin measured in the same window showed markedly lower sensitivity (25.7%), despite perfect specificity (100%), resulting in poor overall early diagnostic performance.

Importantly, among 156 ACS patients who were troponin-negative at 0–4 hours, 153 (98.1%) were correctly identified as positive by H-FABP, indicating a substantial early diagnostic "rescue effect."

Table 3. Diagnostic performance of H-FABP h1 and troponin by T1 time window 0-4hr

Marker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
HFABP H1	89.5	91.4	98.4	59.3	89.8
Troponin T1	25.7	100.0	100.0	18.3	36.3

Later diagnostic performance (6–10 hours)

At 6–10 hours, the diagnostic performance of troponin improved substantially, achieving 100% sensitivity and specificity, confirming its established role as the definitive biomarker at later time points. Conversely, H-FABP sensitivity declined to 51.0%, while specificity remained high (91.4%), reflecting its early-peaking kinetics.

Table 4. Diagnostic performance of H-FABP H2 and troponin by T2 time window 6-10hr

Marker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
HFABP H2	51.0	91.4	97.3	23.7	56.7
Troponin T2	100.0	100.0	100.0	100.0	100.0

Receiver operating characteristic (ROC) curve analysis

ROC analysis demonstrated distinct temporal performance patterns for both biomarkers.
In the early window, H-FABP achieved an AUC of 0.874 (95% CI: 0.781–0.966), significantly outperforming troponin (AUC 0.689; 95% CI: 0.614–0.764).

In the later window, troponin achieved perfect discriminative ability (AUC 1.000), while H-FABP maintained moderate accuracy (AUC 0.803; 95% CI: 0.712–0.894).

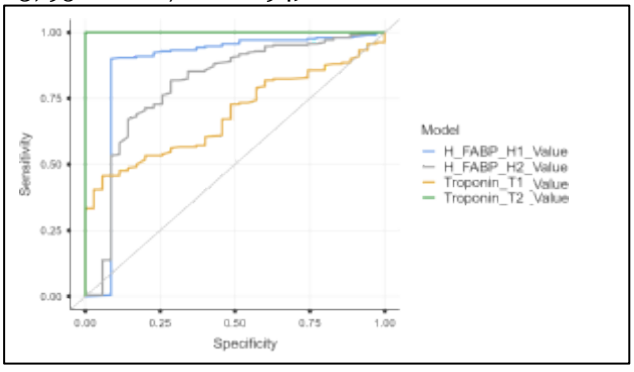

Figure 2. ROC curves for H-FABP and troponin in the early window (0–4 h)

Comparative temporal performance and biomarker kinetics

Direct comparison of biomarkers across time windows highlighted complementary diagnostic roles. H-FABP exhibited high sensitivity and specificity in the hyper-acute phase, while troponin performance improved progressively with time. Correlation analysis showed strong within-marker correlations over time (H-FABP H1–H2 and troponin T1–T2), with weak cross-marker correlations, reflecting divergent release kinetics.

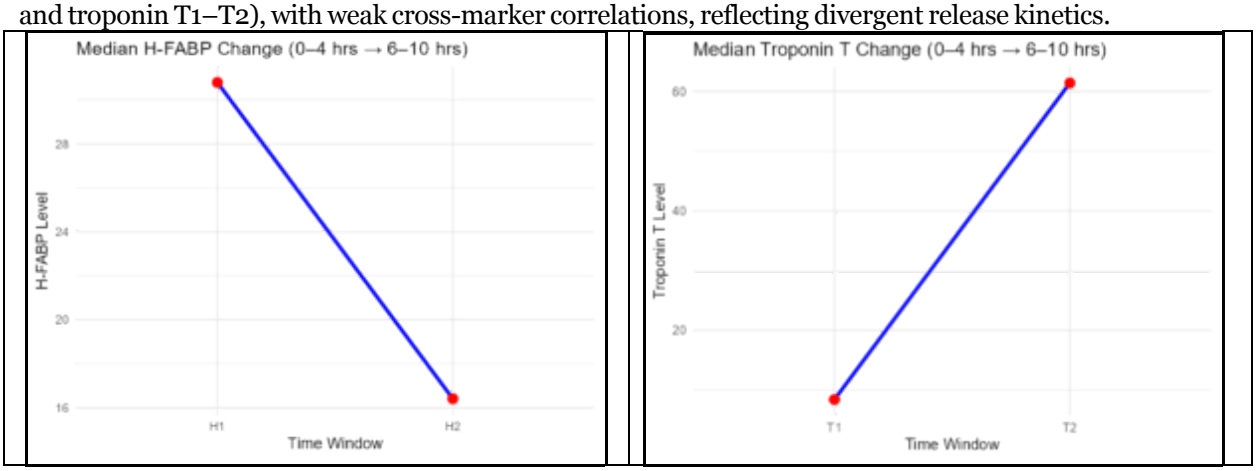

Figure 3. Temporal biomarker kinetics of H-FABP and Troponin

Subgroup analyses

H-FABP demonstrated consistent diagnostic performance across clinically relevant subgroups during the early window. Sensitivity and specificity remained high among patients with diabetes mellitus, hypertension, dyslipidemia, and smoking history. Although minor variations in negative predictive value were observed—particularly in dyslipidemic patients—the overall accuracy remained robust across subgroups, supporting the generalizability of early H-FABP performance in high-risk populations.

Table 5. Subgroup diagnostic performance of H-FABP in the early window (0–4 h).

Subgroup	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Diabetic	90.5	88.2	98.4	53.6	90.3
Non-diabetic	89.0	94.4	98.5	68.0	90.1
Hypertensive	89.9	100	100	47.6	90.8
Non-hypertensive	90.1	88.0	96.8	68.8	89.7
Dyslipidemia	88.8	80.0	99.0	23.5	88.4
No Dyslipidemia	91.5	93.3	97.7	77.8	91.9
Smoker	93.8	90.0	96.8	81.8	92.9
Non-smoker	88.4	93.3	99.2	45.2	88.8

DISCUSSION

H-FABP demonstrated superior diagnostic performance during the hyper-acute phase of ACS presentation, addressing the critical limitation of early troponin insensitivity. These findings are consistent with prior reports describing early H-FABP release kinetics and support its role as an adjunct marker rather than a replacement for troponin.13-16

Our findings align with contemporary evidence that H-FABP is an early-rising marker with potential value in the initial evaluation of suspected ACS/AMI. A comprehensive 2020 review emphasized that H-FABP rises rapidly after myocardial injury and may improve early diagnostic sensitivity, while also noting limitations in specificity in certain clinical contexts (notably renal dysfunction

and non-cardiac injury).13 The temporal behavior observed in our cohort—strong early discrimination with reduced later sensitivity—is also consistent with reports that H-FABP peaks early and clears relatively quickly.13,14

In an East Asian emergency cohort, Moon et al. (2021) evaluated H-FABP in patients suspected of ACS and reported that H-FABP offered clinically meaningful diagnostic and prognostic information, supporting its role as an adjunct marker during early evaluation.15 Our study extends this by explicitly quantifying early-window superiority over troponin and demonstrating a marked rescue effect among early troponin-negative presentations, which is the subgroup of highest operational relevance in emergency triage.

Indian data published in recent years similarly support an early diagnostic advantage. Tarapur et al. (2021) reported that H-FABP values are highest in the earliest symptom-duration strata and decline with time, while troponin demonstrates the opposite pattern, reinforcing the concept of complementary kinetics.16 Our results are concordant and strengthen the argument by demonstrating high early sensitivity and specificity in a real-world emergency cohort.

Further, Kulshrestha et al. (2022) evaluated a dual-marker strategy combining H-FABP with high-sensitivity troponin at presentation as an alternative to serial sampling and reported improved early triage performance compared with relying on a single marker alone.17 This supports the interpretive framework of our findings: H-FABP can bridge the troponin-blind interval, while troponin remains the confirmatory marker as time progresses, consistent with contemporary guideline-based serial testing approaches.18,19

From a clinical perspective, incorporation of H-FABP into early emergency evaluation pathways may reduce diagnostic delay and support more rapid decision-making, particularly in settings where rapid serial troponin testing is logistically challenging.18,20

This single-center study may limit generalizability. Troponin-based criteria were used as the reference standard, potentially underestimating very early myocardial injury. H-FABP is not fully cardiac specific and may be influenced by non-cardiac conditions. The apparent perfect diagnostic performance of troponin at later time points should be interpreted in the context of troponin-based adjudication, which may favor troponin performance by design. Long-term outcomes were not assessed, and assay-specific variability may affect reproducibility across platforms.

CONCLUSION

H-FABP provides significant diagnostic advantage during the early hours of myocardial infarction presentation among patients with suspected ACS and complements troponin-based evaluation in the emergency department. A time-dependent, dual-marker strategy incorporating H-FABP may enhance early triage and reduce diagnostic delay. Further multicenter studies are warranted to define standardized integration of H-FABP into contemporary ACS diagnostic algorithms.

Funding and Conflict of Interest

No external funding was received. The authors declare no conflicts of interest.

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