

Diagnostic value of qualitative bedside heart-type fatty acid-binding protein tests compared with cardiac troponin assays in patients with suspected acute coronary syndrome

Valentin A. Kokorin¹, Mikhail N. Arefiev², Nina N. Levchouk², Ivan G. Gordeev¹

¹ Pirogov Russian National Research Medical University, Moscow, Russia

² Filatov Municipal Clinical Hospital No 15, Moscow, Russia

Introduction The early diagnosis of acute coronary syndrome (ACS) in patients with chest pain remains a challenge for internists even in the era of troponins, especially in the case of an atypical clinical presentation and absence of typical electrocardiographic (ECG) signs.

Heart-type fatty acid-binding protein (hFABP) is an early marker of myocardial damage and necrosis. It reaches the diagnostic concentration in blood just within 1 to 2 hours after the onset of clinical symptoms.¹

Several studies have shown high efficacy of the hFABP evaluation in the early diagnosis of ACS; it has a higher sensitivity than cardiac troponins (cTns) and creatine kinase-MB (CK-MB) and higher specificity than myoglobin.²⁻⁴ However, recent meta-analyses have provided controversial results.⁵⁻⁶ Therefore, the role of hFABP in the diagnostic algorithm for ACS remains unclear.

A quantitative assessment of hFABP in early stages of ACS with an enzyme-linked immunosorbent assay is rather complicated, because it requires special laboratory conditions and is time consuming. Therefore, a qualitative bedside hFABP test based on the immunochromatographic method seems to be more practical.⁷ In Russia, 2 qualitative bedside hFABP tests have been approved for use and are available on the market. CardioFABP (Biotest, Russia) is a one-step in-vitro express test for evaluating hFABP levels in whole venous blood, with a diagnostic threshold of 10 ng/ml. This test was examined in more than 3500 patients with ACS included in a noncommercial multicenter GIANT trial. The results showed its high sensitivity (66%–100%), depending on the time since onset of clinical symptoms, and satisfactory specificity (67%–100%) in the early

diagnosis of ACS.⁸⁻¹⁰ The CARD-INFO test (OFK-Cardio, Russia) has been designed to evaluate hFABP levels in capillary blood. Its diagnostic threshold is 7 ng/ml, but there is limited evidence base to support its use.¹¹

We aimed to compare these 2 different hFABP tests and cTn assays (including cTnI and high-sensitivity troponin I [hs-TnI]) in terms of their diagnostic value according to time elapsed since the onset of symptoms and the type of ACS.

Patients and methods A total of 199 patients were included in this prospective single-center study. All patients were admitted to the intensive care unit of Filatov Municipal Clinical Hospital No 15 between June, 2017, and March, 2018, with primary diagnosis of ACS within 1 to 24 hours since the onset of chest pain. The mean (SD) age of participants was 63 (13.7) years, and 131 patients (66%) were male. The exclusion criteria were as follows: myocardial infarction (MI), stroke, surgery, extensive burns, massive wounds and injuries, percutaneous coronary interventions or electrical cardioversion (all within the previous month), pregnancy or lactation, and any metastatic cancer.

All patients underwent routine clinical assessment. In addition, venous and capillary blood samples were collected shortly after admission. HFABP concentrations in whole venous blood were assessed by the qualitative immunochromatographic express test CardioFABP; for capillary blood, the CARD-INFO test was used. A cardiologist who performed both bedside hFABP tests was blinded to the patients' medical history, ECG, and laboratory data. The levels of cTnI were measured quantitatively on admission and at 6 hours

Correspondence to:

Valentin A. Kokorin, MD, PhD,
Pirogov Russian National Research
Medical University, ul. Ostrovityanova 1,
Moscow, 117997, Russia,
phone: +7 495 370 46 90,
email: valentinkokorin@yahoo.com
Received: July 28, 2018.
Revision accepted: August 21, 2018.
Published online: August 22, 2018.
Conflict of interest: none declared.
Pol Arch Intern Med. 2018;
128 (10): 623-625
doi:10.20452/pamw.4319
Copyright by Medycyna Praktyczna,
Kraków 2018

using the TnI assay (Immunolite 2000 Troponin I, Siemens, Germany), with a diagnostic threshold (99th percentile) of 0.5 ng/ml. Hs-TnI (Pathfast cTnI, Mitsubishi Chemical, Japan) was also measured serially on admission and at 3 to 6 hours. The diagnostic cutoff value for the hs-TnI assay was 0.02 ng/ml. Patients were diagnosed and treated according to the guidelines of the European Society of Cardiology.

The final diagnosis was established on the basis of the Third Universal Definition of Myocardial Infarction (2012). MI was diagnosed when at least a single value of cTnI (or hs-TnI) above the 99th percentile was observed in a clinical setting, consistent with myocardial ischemia. Unstable angina was diagnosed based on symptoms accompanied by dynamic ECG changes, signs of ischemia on functional tests, or new coronary angiographic lesions. The final diagnosis was confirmed by an independent cardiologist on the basis of all available clinical, laboratory, and ECG data, coronary angiography, echocardiography, and cardiac exercise test.

To evaluate the diagnostic value of the hFABP tests, we constructed two-by-two tables with the number of true positive, false positive, true negative, and false negative test results, with MI as an outcome. We calculated sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) with 95% CIs, and compared the values between hFABP tests and troponin assays. The first measurement of troponin levels (on admission) was used only to determine the diagnostic efficacy. Subgroup analyses were performed to assess whether the diagnostic values differed according to time since the onset of chest pain (1–3 h, from 3 to 6 h, and >6 h) and type of ACS (with or without ST-segment elevation or a left bundle branch block).

The statistical analysis was performed with Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., United States). The baseline characteristics were assessed with the parametric *t* test and nonparametric Mann–Whitney test for continuous variables, and with the χ^2 test for categorical variables (with the Yates correction in case of small data). Two-tailed *P* values of less than 0.05 were considered significant.

The study was conducted in accordance with the standards of Good Clinical Practice and the principles of the Declaration of Helsinki. The protocol was approved by the ethics committee of Pirogov Russian National Research Medical University. All participants provided written informed consent.

Results Among the 199 enrolled patients, 63 (31.7%) had previous MI and 62 (31.2%), angina pectoris; 168 patients (84.4%) had hypertension; 75 (37.7%), obesity; 36 (18.1%), type 2 diabetes; 39 (19.6%), atrial fibrillation; and 37 (18.6%), symptoms of chronic heart failure. Active smoking was reported in 66 patients

(33.2%); hypercholesterolemia, in 43 (21.6%); history of stroke or transient ischemic attack, in 23 (11.6%); chronic lung diseases, in 15 (7.5%); chronic renal diseases, in 28 (14.1%); and anemia, in 14 (7.0%).

In 66 patients (33.2%), biomarkers were evaluated between 1 and 3 hours since the onset of clinical symptoms; in 68 patients (34.2%), between 3 and 6 hours; and in 65 patients (32.7%), between 6 and 24 hours. ECG on admission revealed ST-segment elevation in 88 patients (44.2%); ST-segment depression, in 49 (24.6%); left bundle branch block or artificial ventricular pace, in 11 (5.5%); and new Q wave without ST-segment deviations, in 7 patients (3.6%). In 44 patients (22.1%), no or nonspecific changes were observed on ECG.

The final diagnosis of MI was confirmed in 111 patients (55.8%); unstable angina, in 69 (34.7%); other heart diseases, in 8 (4%). Clinical symptoms due to noncardiac disorders were reported in 11 patients (5.5%). During hospitalization, echocardiography was performed in 187 patients (94%), and coronary angiography, in 130 (65.3%). Death on admission was reported in 14 patients (7%); in 9 cases, the diagnosis of MI was confirmed on autopsy.

The diagnostic performance of the hFABP tests and troponin assays is presented in [TABLE 1](#). CardioFABP had overall higher sensitivity compared with both cTnI ($P < 0.001$) and hs-TnI ($P < 0.001$) assays. The difference was observed only in patients with ACS with ST-segment elevation. There was no significant difference in sensitivity between hFABP tests and both troponin assays in patients with ACS without ST-segment elevation. The overall specificity of CARD-INFO was superior to cTnI ($P = 0.02$), and lower in the case of CardioFABP versus hs-TnI ($P < 0.001$). The difference was significant only in patients with ACS without ST-segment elevation.

During the period between 1 and 3 hours, CardioFABP showed higher sensitivity compared with both cTnI ($P < 0.001$) and hs-TnI ($P < 0.001$) assays on admission. In the period from 3 to 6 hours, it was higher only in comparison with cTnI ($P = 0.02$), and there were no differences in sensitivity between hFABP tests and cTnI assays after 6 hours since the onset of chest pain.

Both hFABP tests revealed similar diagnostic accuracy to the hs-TnI assay, and it was higher compared with the cTnI assay ($P = 0.03$ and $P = 0.05$, respectively).

The CARD-INFO test had the highest PPV compared with the cTnI assay ($P = 0.03$), while the CardioFABP test demonstrated better NPV compared both with cTnI ($P = 0.005$) and hs-TnI ($P = 0.047$) assays on admission. There were no other significant differences between hFABP and troponin tests.

Discussion This study evaluated the diagnostic value of 2 qualitative bedside hFABP tests in comparison with cTnI and hs-TnI assays in

TABLE 1 Diagnostic value of qualitative bedside heart-type fatty acid-binding protein tests and cardiac troponin assays in patients with suspected acute coronary syndrome at different time periods since the onset of chest pain

Biomarker	Sensitivity, %	Specificity, %	Accuracy, %	PPV, %	NPV, %
HFABP (CARD-INFO test)					
Overall	73.0 (64.7–80.2)	90.9 (84.3–95.2)	80.9 (75.3–85.7)	91.0 (84.5–95.3)	72.7 (64.4–80.0)
1–3 hours	57.9 (43.4–71.4)	96.4 (87.7–99.1)	74.2 (63.6–83.0)	95.7 (85.2–98.9)	62.8 (49.1–75.0)
3–6 hours	84.6 (72.6–92.5)	89.7 (77.2–96.1)	86.8 (78.1–92.7)	91.7 (81.3–96.9)	81.3 (67.2–90.7)
6–24 hours	76.5 (62.1–87.1)	87.1 (74.2–94.5)	81.5 (71.7–88.9)	86.7 (73.5–94.4)	77.1 (63.1–87.5)
HFABP (CardioFABP test)					
Overall	91.9 (86.3–95.6)	64.8 (55.0–73.6)	79.9 (74.2–84.8)	76.7 (69.4–82.9)	86.4 (77.5–92.5)
1–3 hours	94.7 (86.2–98.3)	78.6 (63.1–89.3)	87.9 (79.4–93.6)	85.7 (74.4–93.0)	91.7 (78.9–97.3)
3–6 hours	89.7 (79.1–95.7)	65.5 (49.2–79.3)	79.4 (69.5–87.1)	77.8 (65.4–87.1)	82.6 (66.4–92.5)
6–24 hours	91.2 (80.3–96.7)	51.6 (36.0–66.9)	72.3 (61.5–81.4)	67.4 (54.2–78.6)	84.2 (66.9–93.9)
cTnI					
Overall	67.0 (58.3–74.9)	77.3 (68.4–84.6)	71.6 (65.3–77.3)	78.5 (69.9–85.4)	65.4 (56.4–73.6)
1–3 hours	54.1 (39.5–68.1)	82.1 (67.3–91.7)	66.2 (54.9–76.1)	80.0 (63.9–90.6)	57.5 (43.3–70.7)
3–6 hours	64.1 (49.8–76.6)	82.8 (68.3–92.0)	72.1 (61.4–81.0)	83.3 (69.3–92.3)	63.2 (48.6–76.0)
6–24 hours	84.8 (71.8–93.0)	67.7 (52.0–80.8)	76.6 (66.0–85.0)	73.7 (59.8–84.6)	80.8 (65.1–91.0)
Hs-TnI					
Overall	72.7 (63.9–80.3)	89.6 (82.2–94.5)	80.1 (74.1–85.2)	90.0 (82.8–94.7)	71.9 (62.9–79.7)
1–3 hours	58.3 (43.5–72.1)	100.0 (85.2–99.9)	74.6 (63.4–83.6)	100.0 (83.9–99.9)	60.5 (46.0–73.7)
3–6 hours	72.7 (57.7–84.4)	88.5 (74.9–95.6)	79.7 (69.1–87.7)	88.9 (75.7–95.8)	71.9 (56.6–83.9)
6–24 hours	93.3 (82.8–97.9)	82.1 (67.3–91.7)	87.9 (78.8–93.9)	84.8 (71.8–93.0)	92.0 (79.6–97.5)

Data are presented as percentage (95% CI).

Abbreviations: cTnI, cardiac troponin I; hFABP, heart-type fatty acid-binding protein; hs-TnI, high-sensitivity troponin I; NPV, negative predictive value; PPV, positive predictive value

patients with suspected ACS. The CardioFABP test showed higher sensitivity, especially during the first 3 hours since MI onset, compared with cTnI and hs-TnI assays, but it had lower specificity than the hs-TnI assay. The CARD-INFO test showed better sensitivity during the period from 3 to 6 hours and better overall specificity compared with the cTnI assay; however, it did not show significant differences with the hs-TnI assay for most diagnostic parameters. We believe that both bedside hFABP tests could have diagnostic value, but more clinical evidence is needed to define their role in the early diagnosis of ACS.

OPEN ACCESS This is an Open Access article distributed under the terms of the Creative Commons AttributionNonCommercialShareAlike 4.0 International License ([CC BY-NC-SA 4.0](https://creativecommons.org/licenses/by-nc-sa/4.0/)), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material, provided the original work is properly cited, distributed under the same license, and used for non-commercial purposes only. For commercial use, please contact the journal office at pamw@mp.pl.

REFERENCES

- 1 Kleine AH, Glatz JF, Van Nieuwenhoven FA, Van der Vusse GJ. Release of heart fatty acid-binding protein into plasma after acute myocardial infarction in man. *Mol Cell Biochem.* 1992; 116: 155-162. [↗](#)
- 2 Nakata T, Hashimoto A, Hase M, et al. Human heart-type fatty acid-binding protein as an early diagnostic and prognostic marker in acute coronary syndrome. *Cardiology.* 2003; 99: 96-104. [↗](#)
- 3 McCann CJ, Glover BM, Menown IB, et al. Novel biomarkers in early diagnosis of acute myocardial infarction compared with cardiac troponin T. *Eur Heart J.* 2008; 29: 2843-2850. [↗](#)
- 4 Hamza M, Demerdash S, Ibrahim M. Heart-type fatty acid-binding protein as a diagnostic biochemical marker for early detection of myocardial infarction. *Acta Cardiol.* 2016; 71: 537-541. [↗](#)
- 5 Carroll C, Al Khalaf M, Stevens JW, et al. Heart-type fatty acid binding protein as an early marker for myocardial infarction: systematic review and meta-analysis. *Emerg Med J.* 2013; 30: 280-286. [↗](#)
- 6 Xu LQ, Yang YM, Tong H, Xu CF. Early diagnostic performance of heart-type fatty acid binding protein in suspected acute myocardial infarction: evidence from a meta-analysis of contemporary studies. *Heart Lung Circ.* 2018; 27: 503-512. [↗](#)
- 7 Seino Y, Ogata K, Takano T, et al. Use of a whole blood rapid panel test for heart-type fatty acid-binding protein in patients with acute chest pain: comparison with rapid troponin T and myoglobin tests. *Am J Med.* 2003; 115: 185-190. [↗](#)
- 8 Zyryanova AV, Yarokhno NN, Nikolaev KY. Immunoassay method for determining the effectiveness of cardiac, fatty acid binding protein (FABP) in early differential diagnosis of acute coronary syndrome [in Russian]. *Circulatory and Cardiac Pathology.* 2010; 4: 12-16.
- 9 Kalinichenko RM, Kopylov FYu, Syrkin AL, et al. The results of application of the rapid quantitative assay for fatty acid-binding protein at the onset of acute coronary syndrome [in Russian]. *Klin Med (Mosk).* 2013; 1: 32-37.
- 10 Martynov AI, Voevoda MI, Arutyunov GP, et al. Clinical effectiveness of early acute myocardial infarction diagnostics, based on the assessment of cardiac fatty acid binding protein levels [in Russian]. *Russian Journal of Cardiology.* 2012; 3: 7-11.
- 11 Kokorin VA, Goncharov AP, Goncharova AY, et al. Effectiveness of the new qualitative express-test for evaluation of heart type fatty acid binding protein in the differential diagnosis of myocardial infarction [in Russian]. *Kazan Medical School Diary.* 2017; 18: 49-53.