



**Heart-Type Fatty Acid Binding Protein (H-FABP)  
Key Publications**

Full abstracts from peer-reviewed journals



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## Abstract 1

Ann Clin Biochem. 2009 Nov;46(Pt 6):464-7.

### Serum 99th centile values for two heart-type fatty acid binding protein assays

Bathia DP, Carless DR, Viswanathan K, Hall AS, Barth JH.

Department of Clinical Biochemistry, Leeds General Infirmary, UK.

#### Reference

Bathia DP, Carless DR, Viswanathan K, Hall AS, Barth JH. Serum 99th centile values for two heart-type fatty acid binding protein assays. Ann Clin Biochem. 2009 Nov;46(Pt 6):464-7.

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#### BACKGROUND:

We have previously demonstrated that heart-type fatty acid binding protein (H-FABP) is an independent prognostic marker for survival after acute coronary syndrome (ACS). This study aimed to define the 99th centile values for H-FABP as determined with two different assays, and to study the relationship with age, gender and renal function.

#### METHODS

H-FABP was measured on redundant routine outpatient samples using the MARKIT-M (Dainippon) and the Evidence Investigator (Randox) assays.

#### RESULTS

Two hundred and forty-two subjects with Siemens Ultra-Tnl value  $<0.045$  microg/L (99th centile) were studied. In all, 174 subjects had estimated glomerular filtration rate (eGFR)  $>60$  mL/min. The 99th centile values for subjects with eGFR  $>60$  mL/min for the Evidence Investigator H-FABP were 5.3 and 5.8 microg/L and for the MARKIT-M H-FABP were 8.3 and 9.1 microg/L in female and male subjects, respectively. There is an increase in H-FABP with age in subjects with normal renal function for both assays. Gender comparison showed no significant difference for either assay. Comparison of samples showed that subjects with eGFR  $<60$  mL/min showed a median increase of 0.71 microg/L with Evidence Investigator assay and 1.09 microg/L with MARKIT-M assay compared with subjects with eGFR  $>60$  mL/min. Calibration differences were confirmed by cross measurement of calibrators and recombinant H-FABP.

#### CONCLUSION

We have defined the 99th centile values for H-FABP in a population of primary and secondary care outpatients that can be used to risk stratify patients with ACS. We have confirmed that H-FABP increases with renal dysfunction and age, but have not confirmed the gender difference previously reported.

## Abstract 2

Eur Heart J. 2008 Dec;29(23):2843-50.

### Novel biomarkers in early diagnosis of acute myocardial infarction compared with cardiac troponin T.

McCann CJ, Glover BM, Menown IB, Moore MJ, McEnery J, Owens CG, Smith B, Sharpe PC, Young IS, Adgey JA.  
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National Institute of Scientific Investigation, Korea

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#### AIMS

To evaluate the role of novel biomarkers in early detection of acute myocardial infarction (MI) in patients admitted with acute chest pain.

#### METHODS AND RESULTS

A prospective study of 664 patients presenting to two coronary care units with chest pain was conducted over 3 years from 2003. Patients were assessed on admission: clinical characteristics, ECG (electrocardiogram), renal function, cardiac troponin T (cTnT), heart fatty acid binding protein (H-FABP), glycogen phosphorylase-BB, NT-pro-brain natriuretic peptide, D-dimer, hsCRP (high sensitivity C-reactive protein), myeloperoxidase, matrix metalloproteinase-9, pregnancy associated plasma protein-A, soluble CD40 ligand. A > or = 12 h cTnT sample was also obtained. MI was defined as cTnT > or = 0.03 microg/L. In patients presenting <4 h of symptom onset, sensitivity of H-FABP for MI was significantly higher than admission cTnT (73 vs. 55%;  $P = 0.043$ ). Specificity of H-FABP was 71%. None of the other biomarkers challenged cTnT. Combined use of H-FABP and cTnT (either one elevated initially) significantly improved the sensitivities of H-FABP or cTnT (85%;  $P < or = 0.004$ ). This combined approach also improved the negative predictive value, negative likelihood ratio, and the risk ratio.

#### CONCLUSION

Assessment of H-FABP within the first 4 h of symptoms is superior to cTnT for detection of MI, and is a useful additional biomarker for patients with acute chest pain.

#### Reference

Bathia DP, Carless DR, Viswanathan K, Hall AS, Barth JH. Serum 99th centile values for two heart-type fatty acid binding protein assays. *Ann Clin Biochem.* 2009 Nov;46(Pt 6):464-7.

## Abstract 3

Eur J Emerg Med. 2008 Jun;15(3):140-4.

### Clinical assessment of heart-type fatty acid binding protein in early diagnosis of acute coronary syndrome.

Valle HA, Riesgo LG, Bel MS, Gonzalo FE, Sanchez MS, Oliva LI.

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#### Reference

Valle HA, Riesgo LG, Bel MS, Gonzalo FE, Sanchez MS, Oliva LI. Clinical assessment of heart-type fatty acid binding protein in early diagnosis of acute coronary syndrome. Eur J Emerg Med. 2008 Jun;15(3):140-4

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#### BACKGROUND

Early identification of acute coronary syndrome (ACS) in the emergency room is still a difficult task. The objective of this study is to estimate the reliability of heart-type fatty acid binding protein (H-FABP) in identifying ACS in the early stage of chest pain onset.

#### METHODS:

In a prospective multicentre study in emergency room patients with suspected ACS lasting less than 3 h, heart heart-type fatty acid binding protein (H-FABP) was compared with conventional biomarkers. Protein levels  $>7$  ng/ml were considered positive results.

#### RESULTS

A total of 419 patients were analyzed. Acute myocardial infarction was diagnosed in 148 patients (35%). H-FABP sensitivity was 60% (89 out of 148 patients), significantly higher than troponin T [19% (28 out of 148 patients);  $P < 0.05$ ]. Specificity of troponin T, however, [99% (270 out of 271 patients)] was better than H-FABP [88% (237 out of 271 patients)], though this was not statistically significant.

#### CONCLUSION

H-FABP can be a useful early diagnostic biochemical marker, particularly within the first 6 h of symptoms, in patients attending the emergency department.

## Abstract 4

Am J Emerg Med. 2011 Jan 3.

### Diagnostic accuracy of heart-type fatty acid-binding protein for the early diagnosis of acute myocardial infarction.

McMahon CG, Lamont JV, Curtin E, McConnell RI, Crockard M, Kurth MJ, Crean P, Fitzgerald SP.  
Emergency Department and Chest Pain Assessment Unit, St. James's Hospital, Dublin 8, Republic of Ireland.

#### OBJECTIVE

The aim of this study was to evaluate the diagnostic efficacy of multiple tests-heart-type fatty acid-binding protein (H-FABP), cardiac troponin I (cTnI), creatine kinase-MB, and myoglobin-for the early detection of acute myocardial infarction among patients who present to the emergency department with chest pain.

#### METHODS

A total of 1128 patients provided a total of 2924 venous blood samples. Patients with chest pain were nonselected and treated according to hospital guidelines. Additional cardiac biomarkers were assayed simultaneously at serial time points using the Cardiac Array (Randox Laboratories Ltd, Crumlin, United Kingdom).

#### RESULTS

Heart-type fatty acid-binding protein had the greatest sensitivity at 0 to 3 hours (64.3%) and 3 to 6 hours (85.3%) after chest pain onset. The combination of cTnI measurement with H-FABP increased sensitivity to 71.4% at 3 to 6 hours and 88.2% at 3 to 6 hours. Receiver operating characteristic curves demonstrated that H-FABP had the greatest diagnostic ability with area under the curve at 0 to 3 hours of 0.841 and 3 to 6 hours of 0.894. The specificity was also high for the combination of H-FABP with cTnI at these time points. Heart-type fatty acid-binding protein had the highest negative predictive values of all the individual markers: 0 to 3 hours (93%) and 3 to 6 hours (97%). Again, the combined measurement of cTnI with H-FABP increased the negative predictive values to 94% at 0 to 3 hours, 98% at 3 to 6 hours, and 99% at 6 to 12 hours.

#### CONCLUSION

Testing both H-FABP and cTnI using the Cardiac Array proved to be both a reliable diagnostic tool for the early diagnosis of myocardial infarction/acute coronary syndrome and also a valuable rule-out test for patients presenting at 3 to 6 hours after chest pain onset.

#### Reference:

McMahon CG, Lamont JV, Curtin E, McConnell RI, Crockard M, Kurth MJ, Crean P, Fitzgerald SP. Diagnostic accuracy of heart-type fatty acid-binding protein for the early diagnosis of acute myocardial infarction. Am J Emerg Med. 2011 Jan 3

## Abstract 5

Circulation. 2006 Aug 8;114(6):550-7.

### Prognostic utility of heart-type fatty acid binding protein in patients with acute coronary syndromes.

O'Donoghue M, de Lemos JA, Morrow DA, Murphy SA, Buos JL, Cannon CP, Sabatine MS. Cardiovascular Division, Brigham and Women's Hospital, 350 Longwood Ave, First Floor, Boston, Mass 02115, USA.

#### Reference

O'Donoghue M, de Lemos JA, Morrow DA, Murphy SA, Buos JL, Cannon CP, Sabatine MS. Prognostic utility of heart-type fatty acid binding protein in patients with acute coronary syndromes. *Circulation*. 2006 Aug 8;114(6):550-7

#### BACKGROUND

Heart-type fatty acid binding protein (H-FABP) is a cytosolic protein that is released rapidly from the cardiomyocyte in response to myocardial injury. Although it has been investigated as an early marker of acute myocardial infarction, its prognostic utility in acute coronary syndromes has not been established.

#### METHODS AND RESULTS

We measured H-FABP in 2287 patients with acute coronary syndromes from the OPUS-TIMI 16 trial. H-FABP was elevated ( $> 8$  ng/mL) in 332 patients (14.5%). Patients with an elevated H-FABP were more likely to suffer death (hazard ratio [HR], 4.1; 95% CI, 2.6 to 6.5), recurrent myocardial infarction (HR, 1.6; 95% CI, 1.0 to 2.5), congestive heart failure (HR, 4.5; 95% CI, 2.6 to 7.8), or the composite of these end points (HR, 2.6; 95% CI, 1.9 to 3.5) through the 10-month follow-up period.

H-FABP predicted the risk of the composite end point both in patients who were troponin I negative (HR, 2.1; 95% CI, 1.3 to 3.4) and in those who were troponin I positive (HR, 3.3; 95% CI, 2.0 to 5.3). In a Cox proportional-hazards model that adjusted for baseline variables, including demographics, clinical characteristics, creatinine clearance, ST deviation, index diagnosis, and troponin I, elevated H-FABP remained a significant predictor of the composite end point (HR, 1.9; 95% CI, 1.3 to 2.7), as well as the individual end points of death (HR, 2.7; 95% CI, 1.5 to 4.9) and CHF (HR, 2.4; 95% CI, 1.2 to 5.0). In a multimarker approach, H-FABP, troponin I, and B-type natriuretic peptide provided complementary information.

#### CONCLUSION

Elevation of H-FABP is associated with an increased risk of death and major cardiac events in patients presenting across the spectrum of acute coronary syndromes and is independent of other established clinical risk predictors and biomarkers.



## Abstract 6

Am J Cardiol. 2009 Jan 1;103(1):22-8.

### Prognostic value of a multimarker approach for patients presenting to hospital with acute chest pain.

McCann CJ, Glover BM, Menown IB, Moore MJ, McEnery J, Owens CG, Smith B, Sharpe PC, Young IS, Adgey JA.

To evaluate the prognostic role of novel biomarkers for the risk stratification of patients admitted with ischemic-type chest pain, a prospective study of 664 patients presenting to 2 coronary care units with ischemic-type chest pain was conducted over 3 years beginning in 2003.

Patients were assessed on admission for clinical characteristics, electrocardiographic findings, renal function, cardiac troponin T (cTnT), markers of myocyte injury (heart fatty acid-binding protein [H-FABP] and glycogen phosphorylase BB), neurohormonal activation (N-terminal-pro-brain natriuretic peptide [NT-pro-BNP]), hemostatic activity (fibrinogen and D-dimer), and vascular inflammation (high-sensitivity C-reactive protein, myeloperoxidase, matrix metalloproteinase-9, pregnancy-associated plasma protein-A, and soluble CD40 ligand). A  $\geq$  12-hour cTnT sample was also obtained.

Myocardial infarction (MI) was defined as peak cTnT  $\geq$  0.03 microg/L. Patients were followed for 1 year from the time of admission. The primary end point was death or MI. Elevated fibrinogen, D-dimer, H-FABP, NT-pro-BNP, and peak cTnT were predictive of death or MI within 1 year (unadjusted odds ratios 2.5, 3.1, 5.4, 5.4, and 6.9, respectively).

On multivariate analysis, H-FABP and NT-pro-BNP were selected, in addition to age, peak cTnT, and left ventricular hypertrophy on initial electrocardiography, as significant independent predictors of death or MI within 1 year. Patients without elevations of H-FABP, NT-pro-BNP, or peak cTnT formed a very low risk group in terms of death or MI within 1 year. A very high risk group had elevations of all 3 biomarkers.

In conclusion, the measurement of H-FABP and NT-pro-BNP at the time of hospital admission for patients with ischemic-type chest pain adds useful prognostic information to that provided by the measurement of baseline and 12-hour cTnT.

#### Reference

McCann CJ, Glover BM, Menown IB, Moore MJ, McEnery J, Owens CG, Smith B, Sharpe PC, Young IS, Adgey JA. Prognostic value of a multimarker approach for patients presenting to hospital with acute chest pain. Am. J. Cardiol. 2009;103(1):22-8

## Abstract 7

J Am Coll Cardiol. 2007 Nov 20;50(21):2061-7.

### Heart-type fatty acid-binding protein predicts long-term mortality after acute coronary syndrome and identifies high-risk patients across the range of troponin values.

Kilcullen N, Viswanathan K, Das R, Morrell C, Farrin A, Barth JH, Hall AS; EMMACE-2 Investigators.

Coronary Artery Disease Clinical Research Network Group, Leeds Institute for Genetic, Health & Therapeutics, Leeds, United Kingdom. [niamhkilcullen@doctors.org.uk](mailto:niamhkilcullen@doctors.org.uk)

#### Reference

Kilcullen N, Viswanathan K, Das R, Morrell C, Farrin A, Barth JH, Hall AS; EMMACE-2 Investigators. Heart-type fatty acid-binding protein predicts long-term mortality after acute coronary syndrome and identifies high-risk patients across the range of troponin values. *J. Am. Coll. Cardiol.* 2007;50(21):2061-7

#### OBJECTIVES

Our aim was to determine if a high-performance assay for heart-type fatty acid-binding protein (H-FABP) has a role in predicting all-cause mortality after acute coronary syndrome (ACS).

#### BACKGROUND

Heart-type fatty acid-binding protein is released into the circulation following myocardial ischemia and necrosis and therefore may be of value to physicians when caring for patients admitted to hospital with a clinical diagnosis of ACS.

#### METHODS

This was a prospective observational study with a follow-up of 12 months. The H-FABP was measured 12 to 24 h after onset of symptoms in 1,448 patients admitted to hospital with ACS. The main outcome measure was all-cause mortality 1 year after index hospital admission. Multivariable analyses were conducted using the well validated GRACE (Global Registry of Acute Coronary Events) variables together with troponin I and highly sensitive C-reactive protein (hs-CRP).

#### RESULTS

After 12 months of follow-up, 296 patients had died. Multivariable analysis demonstrated that H-FABP quartiles were strongly predictive of outcome: Q1 hazard ratio (HR) 1.0; Q2 HR 2.32 (95% confidence interval [CI] 1.25 to 4.30;  $p = 0.007$ ); Q3 HR 3.17 (95% CI 1.73 to 5.82;  $p < 0.001$ ); Q4 HR 4.88 (95% CI 2.67 to 8.93;  $p < 0.001$ ). The crude all-cause 1-year mortality for unstable angina patients with H-FABP  $< 5.8$  microg/l was 2.1% compared with 22.9% for patients above this cutoff. The adjusted all-cause mortality HR in this group was 11.35 (95% CI 2.00 to 64.34;  $p = 0.006$ ).

#### CONCLUSION

Heart-type fatty acid-binding protein predicts long-term mortality after ACS and identifies high-risk patients in a manner that is additive to the GRACE clinical risk factors, troponin, and hs-CRP, possibly as a result of identifying the occurrence of myocardial ischemia with or without necrosis.

## Abstract 8

Circulation. 2010;122:A11374

### Abstract 11374: In Acute Coronary Syndromes, Heart-type Fatty Acid Binding Protein is a More Accurate Predictor of Long Term Prognosis than Troponin.

Ian R Pearson; Alistair S Hall; Christopher P Gale; Mohan U Sivananthan; Karthik Viswanathan; Niamh Kilcullen; Julian H Barth Leeds Teaching Hosps NHS Trust, Leeds, United Kingdom

#### INTRODUCTION

We have previously shown that heart-type fatty acid binding protein (H-FABP) has a role in predicting all-cause mortality after acute coronary syndromes (ACS) and, after multivariable analysis, provides additional information to that gained from the GRACE clinical risk factor score, troponin and highly sensitive CRP. H-FABP is released into the circulation during myocardial ischemia and after myocardial necrosis, in contrast to troponin which is released after myocardial necrosis only. We have also shown that there is a group of ACS patients who are at high risk of cardiac events and death despite normal troponin levels on admission. This group may benefit from an early invasive strategy.

#### HYPOTHESIS

Plasma H-FABP level, taken between twelve and twenty-four hours after admission, can identify troponin negative ACS patients who are at a high long-term risk of death.

#### METHODS

Six year mortality data is now available for patients enrolled in the FAB I study, for which one year mortality data was published in 2007. In this study, 1 448 unselected patients admitted to hospital with ACS had serum H-FABP level measured in addition to usual care. Mortality was tracked by the UK Office of National Statistics.

#### RESULTS

At six years overall all-cause mortality, available for 1421 patients (98.1%), was 43.5%. If troponin -ve/H-FABP -ve mortality was 20.9%; troponin -ve/H-FABP +ve 56.4%; troponin +ve/H-FABP -ve 20.2%; troponin +ve/H-FABP +ve 49.1%. Mortality rate was independent of troponin status but strongly related to H-FABP status.

#### CONCLUSION

The current system of stratification of ACS patients for early invasive management if troponin positive will miss a cohort of patients who are at high risk of death despite being troponin negative, and who may benefit from invasive investigation. Conversely, it is likely that some ACS patients undergo angiography based on a false positive troponin level. The addition of H-FABP measurement to the management of ACS could avoid this.

#### Reference

Ian R Pearson; Alistair S Hall; Christopher P Gale; Mohan U Sivananthan; Karthik Viswanathan; Niamh Kilcullen; Julian H Barth. Abstract 11374: In Acute Coronary Syndromes, Heart-type Fatty Acid Binding Protein is a More Accurate Predictor of Long Term Prognosis than Troponin. Circulation. 2010;122:A11374. Presented at AHA Scientific Sessions 2010.

## Abstract 9

J Am Coll Cardiol. 2010 Jun 8;55(23):2590-8.

### Heart-type fatty acid-binding protein predicts long-term mortality and re-infarction in consecutive patients with suspected acute coronary syndrome who are troponin-negative.

Viswanathan K, Kicullen N, Morrell C, Thistlethwaite S, Sivananthan MU, Hassan TB, Barth JH, Hall AS. C-NET Group, Multidisciplinary Cardiovascular Research Centre, The LIGHT Institute, University of Leeds, Leeds, United Kingdom.

#### Reference

Viswanathan K, Kicullen N, Morrell C, Thistlethwaite S, Sivananthan MU, Hassan TB, Barth JH, Hall AS. heart-type fatty-acidbinding-protein (H-FABP) predicts long-term mortality and re-infarction in consecutive patients with suspected acute coronary syndrome who are troponin negative. J. Am. Coll. Cardiol. 2010;55(23): 2590-

#### OBJECTIVES

The purpose of this study was to establish the prognostic value of measuring heart fatty acid-binding protein (H-FABP) in patients with suspected acute coronary syndrome (ACS) (in particular, low- to intermediate-risk patients), in addition to troponin measured with the latest third-generation troponin assay.

#### BACKGROUND

We have previously shown that H-FABP is a useful prognostic marker in patients with proven ACS.

#### METHODS

Patients (n = 1,080) consecutively admitted to the hospital with suspected ACS were recruited over 46 weeks. Siemens Advia Ultra-Tnl (Siemens Healthcare Diagnostics, Newbury, United Kingdom) and Randox Evidence H-FABP (Randox Laboratories, Ltd., Co., Antrim, United Kingdom) were analyzed on samples collected 12 to 24 h from symptom onset. After exclusion of patients with ST-segment elevation and new left bundle branch block, 955 patients were included in the analysis.

#### RESULTS

The primary outcome measure of death or readmission with myocardial infarction after a minimum follow-up period of 12 months (median 18 months) occurred in 96 of 955 patients (10.1%). The H-FABP concentration was an independent predictor of death or myocardial infarction, after multivariate adjustment. Patients with H-FABP concentrations >6.48 microg/l had significantly increased risk of adverse events (adjusted hazard ratio: 2.62, 95% confidence interval: 1.30 to 5.28, p = 0.007). Among troponin-negative patients (which constituted 79.2% of the cohort), the aforementioned cutoff of 6.48 microg/l identified patients at very high risk for adverse outcomes independent of patient age and serum creatinine.

#### CONCLUSION

We have demonstrated that the prognostic value of elevated H-FABP is additive to troponin in low- and intermediate-risk patients with suspected ACS. Other studies suggest that our observations reflect the value of H-FABP as a marker of myocardial ischemia, even in the absence of frank necrosis.

## Abstract 10

Eur Heart J. 2007 Jan;28(2):224-9.

### Heart-type fatty acid-binding protein permits early risk stratification of pulmonary embolism.

Puls M, Dellas C, Lankeit M, Olschewski M, Binder L, Geibel A, Reiner C, Schäfer K, Hasenfuss G, Konstantinides S.  
Department of Cardiology and Pulmonology, University of Goettingen, Germany.

#### AIMS

We investigated the value of a novel early biomarker, heart-type fatty acid-binding protein (H-FABP), in risk stratification of patients with acute pulmonary embolism (PE).

#### METHODS AND RESULTS

We prospectively included 107 consecutive patients with confirmed PE. The endpoints were (i) PE-related death or major complications and (ii) overall 30-day mortality. Overall, 29 patients (27%) had abnormal (>6 ng/mL) H-FABP levels at presentation. Of those, 12 (41%) had a complicated course, whereas all patients with normal baseline H-FABP had a favourable 30-day outcome (OR, 71.45;  $P<0.0001$ ). At multivariable analysis, H-FABP ( $P<0.0001$ ), but not cardiac troponin T ( $P=0.13$ ) or N-terminal pro-brain natriuretic peptide ( $P=0.36$ ), predicted an adverse outcome.

Evaluation of a strategy combining biomarker testing with echocardiography revealed that patients with a negative H-FABP test had an excellent prognosis regardless of echocardiographic findings. In contrast, patients with a positive H-FABP test had a complication rate of 23.1% even in the presence of a normal echocardiogram, and this rose to 57.1% if echocardiography also demonstrated right ventricular dysfunction (OR vs. a negative H-FABP test, 5.6 and 81.4, respectively).

#### CONCLUSION

H-FABP is a promising early indicator of right ventricular injury and dysfunction in acute PE. It may help optimize risk stratification algorithms and treatment strategies.

#### Reference

Puls M, Dellas C, Lankeit M, Olschewski M, Binder L, Geibel A, Reiner C, Schäfer K, Hasenfuss G, Konstantinides S. Heart-type fatty acid-binding protein permits early risk stratification of pulmonary embolism. Eur Heart J. 2007 Jan;28(2):224-9.

## Abstract 11

J Am Coll Cardiol. 2010 May 11;55(19):2150-7.

### Elevated heart-type fatty acid-binding protein levels on admission predict an adverse outcome in normotensive patients with acute pulmonary embolism.

Dellas C, Puls M, Lankeit M, Schäfer K, Cuny M, Berner M, Hasenfuss G, Konstantinides S.  
Department of Cardiology and Pulmonology, Georg August University of Goettingen, Goettingen, Germany.

#### Reference

Puls M, Dellas C, Lankeit M, Olschewski M, Binder L, Geibel A, Reiner C, Schäfer K, Hasenfuss G, Konstantinides S. Heart-type fatty acid-binding protein permits early risk stratification of pulmonary embolism. *Eur Heart J*. 2007 Jan;28(2):224-9.

#### OBJECTIVES

We assessed the predictive value of heart-type fatty acid-binding protein (H-FABP) in normotensive patients with acute pulmonary embolism (PE).

#### BACKGROUND

Risk stratification of initially normotensive patients with PE on the basis of right ventricular dysfunction or injury remains controversial. Previous studies investigating biomarkers or imaging modalities included unselected patients, some of whom presented with cardiogenic shock.

#### METHODS

We included 126 consecutive normotensive patients with confirmed PE. Complicated 30-day outcome was defined as death, resuscitation, intubation, or use of catecholamines. Long-term survival was assessed by follow-up clinical examination.

#### RESULTS

During the first 30 days, 9 (7%) patients suffered complications. These patients had higher baseline H-FABP values (median, 11.2 ng/ml [interquartile range: 8.0 to 36.8 ng/ml]) compared with patients with an uncomplicated course (3.4 ng/ml [2.1 to 4.9 ng/ml];  $p < 0.001$ ). H-FABP values were above the calculated (by receiver operating characteristic curve analysis) cutoff value of 6 ng/ml in 29 patients. Eight (28%) of them suffered complications versus 1 of 97 patients with low H-FABP (negative predictive value, 99%;  $p < 0.001$ ).

By logistic regression, elevated ( $>$  or  $=$  6 ng/ml) H-FABP was associated with a 36.6-fold increase in the death or complication risk. The combination of H-FABP with tachycardia was a particularly useful prognostic indicator: H-FABP also predicted long-term mortality over 499 (interquartile range: 204 to 1,166) days (hazard ratio: 3.6; 95% confidence interval: 1.6 to 8.2;  $p = 0.003$ ).

#### CONCLUSION

The H-FABP might be a useful biomarker for risk stratification of normotensive patients with acute PE.

## Abstract 12

Eur Respir J. 2008 May;31(5):1024-9.

### Heart-type fatty acid-binding protein for risk assessment of chronic thromboembolic pulmonary hypertension.

Lankeit M, Dellas C, Panzenböck A, Skoro-Sajer N, Bonderman D, Olschewski M, Schäfer K, Puls M, Konstantinides S, Lang IM.  
Dept of Cardiology and Pulmonology, University of Goettingen, D-37099 Goettingen, Germany.

Heart-type fatty acid-binding protein (H-FABP) is a reliable marker of myocardial injury and was recently identified as a predictor of outcome in acute pulmonary embolism. The aim of the present study was to investigate the prognostic value of H-FABP in chronic thromboembolic pulmonary hypertension (CTEPH).

In total, 93 consecutive patients with CTEPH were studied. During long-term follow-up (median duration 1,260 days, interquartile range (IQR) 708-2,460 days), 46 (49%) patients had an adverse outcome, defined as CTEPH-related death, lung transplantation or persistent pulmonary hypertension after pulmonary endarterectomy (PEA). Baseline H-FABP levels in plasma ranged from 0.69-24.3 ng x mL(-1) (median (IQR) 3.41 (2.28-4.86) ng x mL(-1)).

Cox regression analysis revealed a hazard ratio of 1.10 (95% confidence interval 1.04-1.18) for each increase of H-FABP by 1 ng x mL(-1), and continuous elevations of H-FABP emerged as an independent predictor of adverse outcome by multivariable analysis. PEA was performed in 52 patients and favourably affected the long-term outcome.

Kaplan-Meier analysis revealed that patients with baseline H-FABP concentrations >2.7 ng x mL(-1), the median value of the biomarker in the surgically treated population, had a lower probability of event-free survival after PEA. Heart-type fatty acid-binding protein is a promising novel biomarker for risk stratification of patients with chronic thromboembolic pulmonary hypertension.

#### Reference

Lankeit M, Dellas C, Panzenböck A, Skoro-Sajer N, Bonderman D, Olschewski M, Schäfer K, Puls M, Konstantinides S, Lang IM. Heart-type fatty acid-binding protein for risk assessment of chronic thromboembolic pulmonary hypertension. Eur Respir J. 2008 May;31(5):1024-9.

## Abstract 13

Am Heart J. 2010 Aug;160(2):294-300.

### Correlation of heart-type fatty acid-binding protein with mortality and echocardiographic data in patients with pulmonary embolism at intermediate risk.

Boscheri A, Wunderlich C, Langer M, Schoen S, Wiedemann B, Stolte D, Elmer G, Barthel P, Strasser RH. Medical Clinic, Department of Cardiology, University of Technology Dresden, Dresden, Germany. aboscheri@hotmail.com

#### Reference

Boscheri A, Wunderlich C, Langer M, Schoen S, Wiedemann B, Stolte D, Elmer G, Barthel P, Strasser RH. Correlation of heart-type fatty acid-binding protein with mortality and echocardiographic data in patients with pulmonary embolism at intermediate risk. Am Heart J. 2010 Aug;160(2):294-300.

#### BACKGROUND

The management strategy in patients presenting with pulmonary embolism at intermediate risk still remains controversial. Our aim was to determine the role of heart-type fatty acid-binding protein (H-FABP) in this patient population.

#### METHODS

One hundred one consecutive patients with confirmed pulmonary embolism and echocardiographic signs of right ventricular overload but without evidence for hypotension or shock, referred to as pulmonary embolism at intermediate risk, were included in the study. Heart-type fatty acid-binding protein and other biomarkers were measured in all patients upon arrival in the emergency department.

#### RESULTS

Of the included 101 patients, 14 had positive H-FABP tests. Ten patients with positive H-FABP (71%) had clinical deterioration during the hospital course and required inotropic support and 8 of these patients died. None of the 87 patients with a negative test worsened or needed inotropic support or died during hospital stay ( $P < .005$ ). In the H-FABP-positive group, right ventricular function on echocardiography was more impaired (tricuspid annular plane systolic excursion  $13 \pm 4$  vs  $18 \pm 4$  mm, RV/LV ratio  $1.1 \pm 0.2$  vs  $0.9 \pm 0.2$ , presence of paradoxical septal movement 79% vs 46%, presence of McConnell sign 100% vs 60%, respectively, all  $P < .05$ ) compared to the H-FABP-negative group. After adjusting for potential confounding parameters, in multivariate analysis, H-FABP was the only independent predictor of mortality.

#### CONCLUSION

Heart-type fatty acid-binding protein significantly predicts mortality in patients with pulmonary embolism at intermediate risk. Furthermore, it is significantly associated with impaired right ventricular function and shows better correlation with mortality than troponin I. It may be a novel prognostic parameter enabling the optimization of management strategy in the very difficult population of pulmonary embolism at intermediate risk.



## Abstract 14

Anesth Analg. 2010 Nov;111(5):1101-9.

### Heart-type fatty acid binding protein is an independent predictor of death and ventricular dysfunction after coronary artery bypass graft surgery.

Muehlschlegel JD, Perry TE, Liu KY, Fox AA, Collard CD, Sherman SK, Body SC.

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#### BACKGROUND

Heart-type fatty acid binding protein (hFABP) functions as a myocardial fatty acid transporter and is released into the circulation early after myocardial injury. We hypothesized that hFABP is superior to conventional cardiac biomarkers for predicting early perioperative myocardial injury after coronary artery bypass graft (CABG) surgery.

#### METHODS

A prospective cohort study of 1298 patients undergoing primary CABG with cardiopulmonary bypass (CPB) was performed at 2 institutions. Four plasma myocardial injury biomarkers (hFABP; cardiac troponin I [cTnI]; creatine kinase, MB [CK-MB] fraction; and myoglobin) were measured at 7 perioperative time points. The association among perioperative cardiac biomarkers and ventricular dysfunction, hospital length of stay (HLOS), and up to 5-year postoperative mortality (median 3.3 years) was assessed using Cox proportional hazard models. We defined in-hospital ventricular dysfunction as a new requirement for 2 or more inotropes, or new placement of an intraaortic balloon pump, or ventricular assist device either during the intraoperative period after the patient separated from CPB or postoperatively in the intensive care unit.

#### RESULTS

The positive and negative predictive values of mortality for hFABP are 13% (95% confidence interval [CI], 9%-19%) and 95% (95% CI, 94%-96%), respectively, which is higher than for cTnI and CK-MB. After adjusting for clinical predictors, both postoperative day (POD) 1 and peak hFABP levels were independent predictors of ventricular dysfunction ( $P < 0.0001$ ), HLOS ( $P < 0.05$ ), and 5-year mortality ( $P < 0.0001$ ) after CABG surgery. Furthermore, POD1 and peak hFABP levels were significantly superior to other evaluated biomarkers for predicting mortality. In a repeated-measures analysis, hFABP outperformed all other models of fit for HLOS. Patients with POD2 hFABP levels higher than post-CPB hFABP levels had an increased mortality compared with those patients whose POD2 hFABP levels decreased from their post-CPB level (hazard ratio, 10.9; 95% CI, 5.0-23.7;  $P = 7.2 \times 10^{-10}$ ). Mortality in the 120 patients (10%) with a later hFABP peak was 18.3%, compared with 4.7% in those who did not peak later. Alternatively, for cTnI or CK-MB, no difference in mortality was detected.

#### CONCLUSION

Compared with traditional markers of myocardial injury after CABG surgery, hFABP peaks earlier and is a superior independent predictor of postoperative mortality and ventricular dysfunction.

#### Reference

Muehlschlegel JD, Perry TE, Liu KY, Fox AA, Collard CD, Sherman SK, Body SC. Heart-type fatty acid binding protein is an independent predictor of death and ventricular dysfunction after coronary artery bypass graft surgery. *Anesth Analg.* 2010 Nov;111(5):1101-9.

## Abstract 15

Clin Biochem. 2010 Oct;43(15):1241-5.

Heart-type fatty acid binding protein is an early marker of myocardial damage after radiofrequency catheter ablation.

Giannessi D, Piacenti M, Maltinti M, Rossi A, Di Cecco P, Startari U, Cabiati M, Panchetti L, Del Ry S, Morales MA. CNR Institute of Clinical Physiology and Fondazione Toscana G. Monasterio, Pisa, Italy. danielag@jfc.cnr.it

### Reference

Giannessi D, Piacenti M, Maltinti M, Rossi A, Di Cecco P, Startari U, Cabiati M, Panchetti L, Del Ry S, Morales MA. Heart-type fatty acid binding protein is an early marker of myocardial damage after radiofrequency catheter ablation. Clin Biochem. 2010 Oct;43(15):1241-5.

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### OBJECTIVES

Radiofrequency (RF) ablation of arrhythmias induces myocardial damage and release of biomarkers. This study aimed to assess the kinetics of heart-type fatty acid-binding protein (h-FABP), a cytosolic protein released after myocardial injury incurred by both atrial and ventricular RF ablation, compared to other markers of myocardial injury.

### DESIGN AND METHODS

h-FABP, cTnI, CK-MB(mass) and myoglobin were evaluated in 30 patients with atrial or ventricular tachyarrhythmias before, immediately after and at 3, 6 and 24h after the procedure.

### RESULTS

h-FABP increased immediately after the procedure in all subjects ( $6.6 \pm 1.2 \mu\text{g/L}$  vs  $2.7 \pm 0.3$ ,  $p < 0.001$ ) but increased significantly only in ventricular ablations. The peak of h-FABP significantly correlates with the values of time for mean power of RF application in both the entire patient cohort and in ventricular ablations.

### CONCLUSION

h-FABP may be an early parameter for monitoring RF-induced lesions and the site of ablation was relevant for biomarker increase.

## Abstract 16

Cardiology, 2007;108(1):4-10.

### Heart fatty acid binding protein in the diagnosis of myocardial infarction: where do we stand today?

Colli A, Josa M, Pomar JL, Mestres CA, Gherli T.

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Heart fatty acid binding protein (hFABP) is a novel small cytosolic protein that is abundant in the heart. It is highly cardiac-specific (i.e. expressed primarily in cardiac tissue), but is also expressed at low concentrations in tissues outside the heart.

After myocardial ischemic damage, hFABP can be detected in the blood as early as 1-3 h after onset of chest pain, with peak values reached at 6-8 h and plasma levels returning to normal within 24-30 h. hFABP's clinical diagnostic value is very limited in the presence of renal failure and skeletal muscle diseases as it is completely renally eliminated. In these conditions, the diagnosis of acute myocardial infarction (AMI) may be overestimated.

The combination of initial hFABP release after symptom onset, rapid kidney clearance from the circulation and high cardiac specificity suggests great potential for clinical use.

Serial measurements of hFABP in the first 24 h after onset of symptoms in AMI patients can: (a) identify patients who are susceptible to reperfusion strategies, (b) detect perioperative AMIs, (c) distinguish patients who reperfuse their infarct-related artery from those who do not, as early as 30 min after starting thrombolytic treatment, (d) detect re-infarction if it occurs within 10 h after symptom onset, and (e) permit an accurate estimation of myocardial infarct size providing important prognosis information.

#### Reference

Colli A, Josa M, Pomar JL, Mestres CA, Gherli T. Heart fatty acid binding protein in the diagnosis of myocardial infarction: where do we stand today? Cardiology. 2007;108(1):4-10.

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