Diagnostic Value of The Heart-Type Fatty Acid-Binding Protein (h-FABP) in Diagnosing Acute Myocardial Infarction

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Diagnostic Value of The Heart-Type Fatty Acid-Binding Protein (h-FABP) in Diagnosing Acute Myocardial Infarction

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Abstract

Objective: Coronary Heart Disease (CHD) remains understudied, underdiagnosed, and undertreated in women. Sex differences in clinical presentation have consequences for timely identification of ischemic symptoms, appropriate triage, and judicious diagnostic testing and management. Timely diagnosis and prompt treatment is critical in acute myocardial infarction (AMI). This research aimed to assess the diagnostic value of h-FABP in diagnosis AMI within 6 hours onset.

Methods: This is a diagnostic study performed in 39 patients with 6 hours chest pain onset in 2015. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the h-FABP and troponin T were calculated and compared.

Results: In this study, the sensitivity, negative predictive value, and accuracy of the h-FABP were higher than the troponin T (87.5% vs 41.6%, 80% vs 51.7%, and 84.5% vs 64.1%, respectively).

Conclusion: In patients with early onset chest pain with non-ST elevation in ECG and negative troponin T, the h-FABP could be used to diagnose AMI.

KEYWORDS : Acute Myocardial Infarction, h-FABP, troponin T, woman

Introduction

Acute coronary syndrome (ACS) is a spectrum of clinical syndromes ranging from unstable angina pectoris, acute myocardial infarction (ST elevation and non-ST elevation) to sudden death. Diagnosis of acute myocardial infarction is enforced based on WHO criteria, including complaints of typical chest pain, changes in ECG, and an increasing in cardiac biomarkers (1). The incidence of ACS is increasing from year to year. In the United States, more than 13 million people had coronary heart disease (CHD), and about 1.4 million people with ACS must be hospitalized every year (2). In Indonesia, based on Basic Health Research in 2007, mortality due to cardiovascular disease (stroke and coronary heart disease) is in the first rank (3). Cardiovascular disease (CVD) is the leading cause of mortality for women in the United States

and globally. Despite stunning improvements in cardiovascular mortality for women in the past 2 decades, CHD remains understudied, underdiagnosed, and undertreated in women. Sex differences in clinical presentation have consequences for timely identification of ischemic symptoms, appropriate triage, and judicious diagnostic testing and management. The detrimental consequences for women are misdiagnosis, delayed revascularization, and higher AMI mortality rates (4). Early diagnosis of ACS patients was challenging for doctors, especially doctors who work in the emergency department. Mistakes or delays in ACS diagnosing can result in increased morbidity and mortality(5). Conversely, early diagnosis of ACS will reduce morbidity and mortality. Most ACS patients coming to the ER with complaint of chest pain, which occupies about 5% of all visits in the ER. (6). Although an electrocardiogram (ECG) is the most advanced diagnostic tool for detecting ACS, it has a low sensitivity (35-50%), so that a normal ECG result does not necessarily rule out ACS (7, 8). In these conditions, cardiac biomarkers (troponin T or I and CKMB) play an important role in diagnosing ACS. However, these biomarkers have not increased significantly at onset less than 4-6 hours, so clinicians need time to wait until blood samples are adequate for the assessment of these biomarkers. Most of these cases must be observed for 10-12 hours and causing accumulation of patients in the ER, late diagnosis will also cause greater complications for the patient (9). Therefore, a biomarker is needed as a marker of necrosis that is more sensitive and can be detected more quickly in the blood so that it can diagnose ACS more quickly. To answer this challenge, in the last 20 years many researches have been carried out on heart-type fatty acid-binding protein (h-FABP) as a biomarker for cardiac muscle ischemic markers. Glatz et al. introduced h-FABP as a new biomarker for acute myocardial infarction (10). Heart-type fatty acid-binding protein is a small cytosolic protein which is abundant in cells with active fatty acid metabolism such as heart muscle (11). Levels of h-FABP begin to increase after 30 minutes to 1 hour since ischemic onset and peak within 3-6 hours, then return to normal within 24-30 hours (12, 13). The process of examining h-FABP is also quite simple. It can be done next to patient by using a strip and the results can be obtained in less than 10 minutes. This study aimed to evaluate the diagnostic value of h-FABP in diagnosing AMI in patients with chest pain onset ≤ 6 hours.

Method

Research location

This research was conducted at the Emergency Unit of Dr. Wahidin Sudirohusodo Hospital Makassar, from February 2015 to March 2015. This study was a diagnostic test study to evaluate the diagnostic value of h-FABP in diagnosing AMI in patients with chest pain onset ≤ 6 hours.

Types and sources of data

The collected data were patient's current medical history, previous medical history, risk factors for CHD, family history of suffering from CHD, demographic data, and clinical data. Demographic and clinical data including age, gender, risk factors for CHD, supporting laboratory tests, including Random Blood Glucose (RBG), SGOT / SGPT, urea, creatinine, lipid profile. The data were obtained from comprehensive interview with patient or patient's family, laboratory examination, and physical examination.

Data collection techniques

All chest pain patients with suspected ACS of ≤ 6 hours had routine triage examinations as soon as possible. An ECG is done in less than 10 minutes. Patients who met the inclusion criteria were then given informed consent. Three ml of venous blood samples were taken for h-FABP and troponin T tests. Patients with negative troponin T test results would undergo serial examinations within 6-12 hours later. The final diagnosis of unstable AMI or angina pectoris using WHO criteria was established within 12 hours after the patient entered the emergency room. Patients were then divided into two gruops (based on WHO criteria), the IMA patient group (myocardial infarction with ST segment elevation and myocardial infarction without ST segment elevation) and the non-AMI group (unstable angina pectoris).

Results

During the study period 42 samples met the inclusion criteria, but 3 samples were excluded because of impaired renal function (eGFR <60 ml / hour). From 39 samples, 24 samples (61.5%) were AMI patients and 15 samples (38.5%) were non AMI patients (unstable angina pectoris). Thirty one subjects entered the emergency room with ≤ 3 hours onset (79.5%), while onset> 3-6 hours was only 8 subjects (20.5%). Thirty six subjects were male, 21 subjects in the AMI group and 15 subjects in the non-AMI group. Most of the subjects were ≤ 55 years old (59%), both in AMI group (62.5%) and non-AMI group(53.3%). Twenty two subjects suffered from hypertension, 12 subjects in the AMI group and 10 subjects in the non-AMI group. Thirty one subjects (79.5%) had no previous history of CHD. The majority of subjects (97.4%) did not have a family history of CHD, both in the AMI group (100%), and the non-AMI group (93.3%). Most of the subjects also did not have a history of Diabetes Mellitus (DM) (76.9%), but more than half (51.3%) of the subjects admitted to the hospital with RBG> 140 mg / dL, with a mean RBG 178.5 ± 98.2 mg/dL, with range between 87 mg/dL - 405 mg/dL. The mean LDL was 133.7 ± 30.3 mg/dL, with a range between 67 mg/dL-224 mg/dL, as many as 20 subjects had LDL levels ≤ 130 mg/dL and 19 subjects had LDL levels> 130 mg/dL. The mean HDL levels were 42 ± 12.6 mg/dL, with a range of values between 15 mg/dL - 97 mg/dL, 32 subjects had HDL levels ≤ 50 mg/dL and only 7 subjects had HDL levels> 50 mg/dL. The mean serum creatinine was 1.04 ± 0.2 mg/dL with a range of values between 0.6 - 1.7 mg/dL, the majority of subjects (84.6%) had serum creatinine levels ≤ 1.2 mg/dL. From 24 subjects with AMI, 7 subjects showed ST elevation ECG (STEMI diagnosis) and 17 subjects showed non-ST elevation ECG (NSTEMI diagnosis). All samples with a STEMI diagnosis showed positive h-FABP test results and only 3 samples showed positive troponin T test results. In the samples with final diagnosis of NSTEMI, only 7 samples (41.1%) showed positive troponin T test results, while 10 samples (58.9%) showed negative troponin T test results. From that 10 samples, there are 7 samples (70%) that have negative troponin T test results but positive h-FABP test result. The Sensitivity value, Negative Predictive Value(NPV), and accuracy of h-FABP were higher than troponin T in chest pain patients with suspected acute coronary syndrome ≤ 6 hours of onset (87.5% vs 41.6%, 80.0% vs 51.7%, and 84.6% vs 64.5%). However, specificity and Positive Predictive Value(PPV) of troponin T were higher than h-FABP (80% vs 100% and 87.5% vs 100%).(see Figure 1)

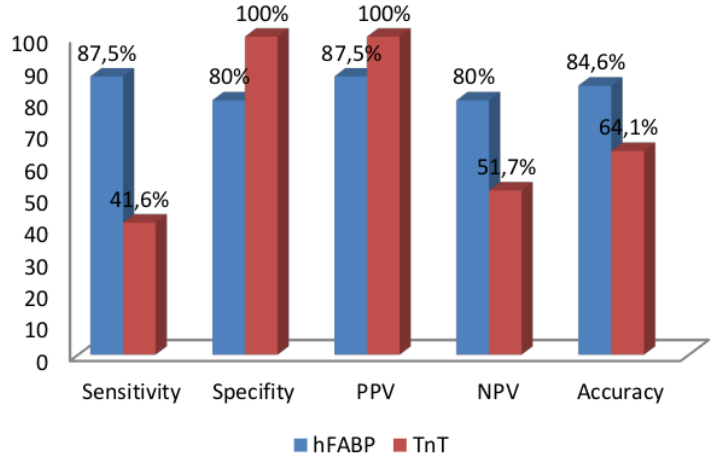

Figure 1. Comparison of diagnostic value between h-FABP and TnT in suspected ACS patient ≤ 6 hours onset

Discussion

This study shows that the sensitivity, NPV, and accuracy of the h-FABP test to diagnose AMI in chest pain ≤ 6 hours onset are higher than the troponin T test. These results same as study conducted by Hisamuddin and Suhailan (14), which also reported higher sensitivity and NPV of h-FABP than TnT in patients with chest pain ≤ 4 hours onset (50.0% vs 10.0% and 73.6% vs 70.9%) but the specificity and PPV of h-FABP were lower than TnT (63.6% vs 100.0% and 38.4% vs 100%). The study conducted by Chao YT et al. also showed that the sensitivity, specificity, PPV, NPV, and the accuracy of the h-FABP were higher than the TnT to diagnose AMI in chest pain ≤ 6 hours onset (15). Nakata et al. also reported that h-FABP has a greater diagnostic ability compared to other cardiac biomarkers for AMI diagnosis in ≤12 hours onset of chest pain(16). In this study only 3 female subjects had AMI. Although most patients with AMI present with typical chest pain or chest discomfort, women often present with atypical chest pain and angina equivalent symptoms. A number of studies have shown that women present later to treatment for AMI than men. Delays in seeking medical care for symptoms plausibly contribute to poorer outcomes for women. Delay in seeking treatment for AMI is often due to lack of awareness of risk, passivity, inaccurate symptom attribution, and barriers to selfcare (4).

H-FABP is a cytoplasmic protein with a low molecular weight (15 kDa) which is abundant in the cytosol of heart muscle cells. The low molecular weight and abundance of these proteins causes h-FABP to be quickly released into the cytoplasm compared to other cardiac biomarkers when cardiac muscle ischemia occurs (17). Levels of h-FABP begin to increase within 30 minutes to 1 hour of ischemic onset, peak within 6-8 hours, and will return to normal within 24-36 hours of ischemic onset. Meanwhile, troponin T begins to increase within 3-6 hours and reaches a peak within 14-18 hours from the ischemic onset. This condition causes the sensitivity of troponin T to be lower than h-FABP in the first hours of ischemic onset (18). Early detection of h-FABP in patients with suspected ACS provides better diagnostic capability compared to other cardiac biomarkers, such as myoglobin, CKMB, and TnT, especially in patients admitted to hospital with chest pain onset ≤ 6 hours.

Early diagnosis of AMI patients is necessary for early treatment. In patients with chest pain with ST elevation ECG, the diagnosis of AMI can be made early without having to wait for biomarkers of myocardial infarction markers. However, about 40% of AMI patients are admitted to the hospital with an atypical ECG. In these patients the role of biomarkers is very important. The problem is the biomarkers (troponin or CKMB) take about 3-4 hours from the onset of chest pain to increase. Because of that, we need biomarkers that can detect AMI more quickly. The results of this study indicate that h-FABP is quite sensitive in detecting non-ST elevation AMI with onset of chest pain ≤ 6 hours and negative troponin T. A study by Alhashemi also showed the same result, where h-FABP is very useful for AMI diagnosis in atypical chest pain patients with non-ST elevation ECG and negative troponin T (19).

Conclusion

Despite stunning improvements in cardiovascular mortality for women in the past 2 decades, CHD remains understudied, underdiagnosed, and undertreated in women. Sex differences in clinical presentation have consequences for timely identification of ischemic symptoms, appropriate triage, and judicious diagnostic testing and management. The detrimental consequences for women are misdiagnosis, delayed revascularization, and higher AMI mortality rates. The sensitivity, NPV, and accuracy of h-FABP were higher than troponin T to diagnose AMI with chest pain ≤ 6 hours onset. In patients with early onset chest pain with non-ST elevation ECG and negative troponin T, h-FABP could be used to diagnose AMI.

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