The value of point-of-care fatty acid binding protein in patients with chest pain in determining myocardial infarction in the emergency setting

在急症環境下以護理點脂肪酸結合蛋白決定胸痛病人心肌梗塞之價值

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Introduction: Detecting patients in the early hours of acute myocardial infarction is still a challenge for emergency physicians. Fatty acid binding protein (FABP) was thought to be released into the intravascular space earlier than cardiac troponins. The aim of this study was to determine the diagnostic value of point-of-care FABP test either in diagnosing or excluding myocardial infarction during the initial admission of patients presenting with typical chest pain to the emergency department. ***Methods:*** This study was performed in a tertiary care emergency department. Patients with typical chest pain were included into the study. Point-of-care FABP was studied during the initial admission and two hours after admission. Patients were diagnosed as myocardial infarction or not ultimately by ECG and troponin levels. ***Results:*** A total of 224 patients were included into the study, 73 of them (32.6%) were diagnosed as acute myocardial infarction. FABP had a sensitivity and specificity of 41.0% (95%CI 29.7 to 53.2) and 100% (95%CI 97.6 to 100) and myoglobin had a sensitivity and specificity of 57.5% (95%CI 45.4 to 69.0) and 90.7% (95%CI 85.0 to 95.0) during the initial admission. Cardiac troponin T had a sensitivity of 45.2% (95%CI 33.7 to 57.2) and specificity of 100% (95%CI 97.0 to 100) during the initial admission. Two hours after admission, FABP had a sensitivity of 56.0% (95%CI 40.0 to 71.0) and specificity of 99.0% (95%CI 96.4 to 100) respectively. ***Conclusions:*** Point-of-care FABP is good at diagnosing acute myocardial infarction in patients presenting with chest pain. However, FABP was found to be not better than either myoglobin or cardiac troponin T in excluding acute myocardial infarction in patients presenting with chest pain. (*Hong Kong j.emerg.med.* 2010;17:224-229)

引言：查出早期心肌梗塞的病人仍是急症科醫生的一個挑戰。脂肪酸結合蛋白被認為較心肌鈣蛋白更早被釋出至血管內腔。本研究旨在確定有典型胸痛到急症室求診的病人中，護理點脂肪酸結合蛋白測試於早期斷定或排除心肌梗塞之診斷價值。**方法：**本研究在一所高等護理急症室內進行，包括典型胸痛的病人。入院時及入院後 2 小時，化驗護理點脂肪酸結合蛋白。最終以心電圖及肌鈣蛋白的水平診斷病人有否心肌梗塞。**結果：**本研究共包括 224 名病人，其中 73 名（32.6%）診斷為急性心肌梗塞。入院時，脂肪酸結合蛋白的敏感度為 41.0%（95% 置信區間 29.7 至 53.2）而特異性為 100%（95% 置信區間 97.6 至 100），肌紅蛋白的敏感度為 57.5%（95% 置信區間 45.4 至 69.0）而特異性為 90.7%（95% 置信區間 85.0 至 95.0），入院早期的心肌鈣蛋白 T 的敏感度為 45.2%（95% 置信區間 33.7 至 57.2）而

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特異性100%（95%置信區間97.0至100）。入院2小時後，脂肪酸結合蛋白的敏感度為56.0%（95%置信區間40.0至71.0）而特異性為99.0%（95%置信區間96.4至100）。**結論：**護理點脂肪酸結合蛋白為呈現胸痛病人診斷急性心肌梗塞是有效的。然而，於呈現胸痛病人中排除急性心肌梗塞方面，脂肪酸結合蛋白並不優於肌紅蛋白或心肌鈣蛋白T。

Keywords: Fatty acid-binding proteins, hospital emergency service, myocardial infarction, myoglobin, troponin

關鍵詞：脂肪酸結合蛋白、醫院緊急服務、心肌梗塞、肌紅蛋白、肌鈣蛋白

Introduction

Chest pain is one of the leading complaints of emergency department (ED) visits. Despite 24 hours electrocardiogram (ECG) and cardiac markers, 2-5% of acute myocardial infarctions (AMI) are discharged from the ED inappropriately.[1-4] Because of the high mortality and morbidity of the acute coronary syndrome, management of these patients is still a challenge for ED physicians. Moreover, the efforts in diagnosing acute coronary syndrome can pose an economic burden.[5,6]

Cardiac troponins may be accepted as the gold standard for detecting myocardial injury. However, cardiac troponins elevate 4-6 hours after the beginning of myocardial injury. Although cardiac troponins are very sensitive and specific after 4-6 hours, they do not have sufficient sensitivity in the early hours of myocardial injury. Myoglobin has been thought to increase earlier than cardiac troponins, but it also does not have sufficient sensitivity during the initial presentation.[7] Both troponin and myoglobin have high specificity but low sensitivity at the initial admission.[7] It is not possible to exclude myocardial infarction in the emergency department in the early hours for patients with chest pain using the currently available cardiac markers.

Human heart-type fatty acid binding protein (FABP) is a low molecular weight protein found in the cytoplasm of cardiac myocytes that has been thought to be rapidly released into the circulation after myocardial injury.[8] However, the diagnostic ability of FABP either for detecting or excluding myocardial infarction during the initial ED admission has not been validated yet.

The aim of this study was to determine the diagnostic value of point-of-care FABP test either in diagnosing or excluding myocardial infarction in the early hours after patients presented with typical chest pain to the ED.

Material and methods

Study design

This cross sectional study was conducted between December 2008 and March 2009 in a four-month period at an academic emergency department with 50,000 visits annually. The local ethics committee had approved the study.

Study setting and population

All patients over 18 years presenting to the ED with typical chest pain were included into the study. Typical chest pain was defined as squeezing pain over the precordial area radiating to the neck, arm, back or epigastric region accompanied by sweating, nausea, vomiting or syncope. Furthermore, chest pain induced by exercise and relieved by rest or sublingual nitroglycerin or associated symptoms similar to those of documented coronary artery disease were accepted as typical chest pain. Atypical chest pain was defined as pleuritic, induced by palpation, confined to one point of the anterior chest wall, lasting only a few seconds or lasting for many hours.

Patients with atypical chest pain, musculoskeletal trauma such as intramuscular injection, electrical cardioversion within the last 24 hours, musculoskeletal disease, acute or chronic renal failure, liver disease and those without consent were excluded from the study.

Study protocol

Patients included into the study were admitted to the telemetry unit of the ED. During the admission, bedside point-of-care FABP test (Cardiodetect©: Med-Rennessens, Niemcy, Poland) which was based on a fast chromatographic immunoassay qualitative method was performed. Point-of-care FABP test was found to have a positive line when the serum FABP concentration was over 6.2 ng/ml. Three drops of blood were dripped to the test strip and 15 minutes later, a second line adjacent to the control line would appear if the test was positive.

Venous blood samples from the patients were also taken for myoglobin and troponin T (cTnT) analysis. Levels greater than 0.1 ng/ml was accepted as positive for cTnT; 52 mg/dl for women and 81 mg/dl for men were accepted as positive for myoglobin.

If the patient had a positive initial FABP test, no other point-of-care test would be performed. Otherwise, an additional FABP would be studied two hours later. In order to diagnose myocardial infarction, serial ECG measurements and 6th hour cTnT levels after admission were also implemented if the diagnosis was not ST segment elevation myocardial infarction (STEMI). Patients with STEMI were transferred to the angiography laboratory for primary percutaneous coronary intervention 24 hours a day. The second point-of-care FABP test was performed in the cardiology ward by cardiology residents if the first test was negative in these patients.

Study patients were diagnosed to have acute myocardial infarction on the basis of at least two of the following World Health Organization criteria:

A. Chest pain over 20 minutes
B. ≥1 mm ST segment elevation in at least two consecutive leads or ≥2 mm in V_1-V_3.
C. Elevated cardiac enzymes (cTnT ≥0.1 ng/ml)

Statistical analysis

The study data were analysed by the Medcalc 10.4.0.0 software. Continuous data were presented as means with standard deviation and categorical data as rates. The diagnostic value of FABP and the other cardiac markers were determined by calculating the sensitivity, specificity, positive likelihood ratio and negative likelihood ratio with 95% confidence intervals (95%CI).

Results

A total of 224 patients were included into the study. The study patients had a mean age of 56.8±12 years and 72.8% (n=163) of them were male; 38 patients (17.0%) were diagnosed as STEMI, 35 (15.6%) as NSTEMI and 102 (45.5%) as unstable angina pectoris. The demographic features of the study patients are displayed in Table 1.

FABP had a sensitivity and specificity of 41.0% (95%CI: 29.7-53.2) and 100% (95%CI: 97.6-100) during the initial admission. Myoglobin had a sensitivity and specificity of 57.5% (95%CI: 45.4-69.0) and 90.7% (95%CI: 85.0 to 95.0) during the initial admission. However two hours after admission, the

Table 1. Demographic features of study patients

Variable	n (%)
Age	56.8±12
Gender	
Male	163 (72.8)
Female	61 (27.2)
Diabetes mellitus	46 (20.5)
Hypertension	79 (35.3)
Coronary artery disease	92 (41.1)
Smoking	54 (24.1)
Diagnosis	
STEMI	38 (17.0)
NSTEMI	35 (15.6)
UAP	102 (45.5)
SAP	29 (12.9)
Atypical chest pain	20 (8.9)

NSTEM=non-ST segment elevation myocardial infarction; SAP=stable angina pectoris; STEMI=ST segment elevation myocardial infarction; UAP=unstable angina pectoris.

sensitivity and specificity of FABP did not change significantly – sensitivity 56.0% (95%CI: 40.0 to 71.0) and specificity 99.0% (95%CI: 96.4 to 100). Table 2 displays the diagnostic value of FABP and myoglobin during the initial admission and two hours after admission.

Discussion

This study showed that point-of-care FABP is a reliable tool for detecting myocardial infarction during admission. However, the ability of point-of-care FABP to exclude these patients during the initial admission was found to be insufficient. Point-of-care FABP was found to have a higher specificity and positive likelihood ratio than myoglobin on initial admission. However, myoglobin still seems better in excluding myocardial infarction than FABP. Even though troponin is believed to increase 4-6 hours after myocardial injury, the values of the initial FABP and troponin measurements in the ED were found to be similar in our study.

The medical literature on the diagnostic value of FABP in patients presenting with chest pain to emergency departments is limited. Valle et al studied point-of-care FABP on 419 patients who were suspected for acute coronary syndrome. However, the inclusion criteria were not defined clearly in their study. They reported the sensitivity and specificity of FABP for myocardial infarction as 60% and 88%, and for cTnT 19% and 99% respectively during the admission.[9] Their results were similar to the findings of our study. Seino et al studied on 371 consecutive patients presenting with acute chest pain or symptoms related to myocardial infarction to the ED. They categorised the patients according to the onset of symptoms differently from our study. They also excluded patients with ST segment elevation myocardial infarction and 71 patients with unclear onset of symptoms. They reported the sensitivity and specificity of FABP as 89% and 52%, 22% and 94% for cTnT, 38% and 71% for myoglobin within two hours of symptom onset in 68 patients. Furthermore, they found the sensitivity and specificity of FABP similar if the onset of symptom was between 2-4 hours (103 patients), but the sensitivity and specificity of cTnT were 57% and 70%, and of myoglobin 63% and 64%.[10] The findings of Seino et al do not correlate with our findings and those of Valle et al. Furthermore, high sensitivity and low specificity are not expected in the early hours of myocardial infarction and they also found low sensitivity and higher specificity of myoglobin and troponin compared to FABP. This discordance requires further evaluation.

Ruzgar et al studied 40 consecutive patients admitted to the coronary care unit with acute chest pain suggestive of acute coronary syndrome. Notwithstanding the small sample size, they reported the sensitivity and specificity of point-of-care FABP and cTnT within six hours of symptoms onset (n=26 patients) as 95.2%, 100% and 38.1%, 100%, respectively.[11] Ishii et al studied 165 patients admitted to the coronary care unit within six hours of onset of chest pain (99 with AMI). After taking the cut-off value as 12 μg/L, they reported the sensitivity and specificity for FABP and myoglobin as follows: 81.8%, 86.4% and 72.7%, 75.8%, respectively.[12] Seino et al studied

Table 2. Diagnostic value of FABP and myoglobin during initial admission and two hours after admission.

Variable	Sensitivity (95%CI)	Specificity (95%CI)	Positive LR (95%CI)	Negative LR (95%CI)
FABP*	41.0 (29.7-53.2)	100 (97.6-100)	Infinity (5.0-∞)	0.59 (0.49-0.71)
FABP†	56.0 (40.0-71.0)	99.0 (96.4-100)	56.0(7.9-397)	0.45 (0.36-0.60)
Myoglobin*	57.5 (45.4-69.0)	90.7 (85.0-95.0)	6.2 (5.0-7.8)	0.47 (0.40-0.55)
Troponin*	45.2 (33.7-57.2)	100 (97.0-100)	Infinity (5.7-∞)	0.55 (0.52-0.58)

*At initial admission; †Two hours after admission

FABP=fatty acid binding protein; LR=likelihood ratio

on 129 patients presenting with chest pain or dyspnoea. They reported the sensitivity and specificity of point-of-care FABP and cTnT within three hours after symptom onset as follows: 100%, 63% and 50%, 96.3%, respectively (n=35 patients). The overall sensitivity and specificity without regard to time were 90.3%, 77.5% and 67.7%, 94.9% for FABP and cTnT respectively.[13]

Although both myoglobin and FABP are found in skeletal muscle, concentrations of myoglobin from cardiac myocytes are higher than FABP. After excluding related factors leading to increases, a cardiac marker is expected to have high specificity in the early hours of presentation of acute coronary syndrome. The comprehensive systematic review by Balk et al[7] illustrated that both myoglobin and cardiac troponins had high specificity but low sensitivity on initial admission. High specificity represents low probability of false positive results and low sensitivity represents high probability of false negative results during the initial admission. However, as in the studies mentioned above, high sensitivity but low specificity indicates low false negative but high false positive results which can be related to inappropriate patient selection.

The levels of FABP two hours after admission are noteworthy. The sensitivity of FABP increased from 41% to 56% and the specificity remained the same two hours after admission. This indicates that FABP levels increase with time but still do not have sufficient sensitivity two hours after admission.

Limitation

This study has several limitations. Patients with typical chest pain were included into the study. Although the rate of AMI is low, atypical chest pain may also be related to AMI. However, we used this approach in order to recruit more AMI from the study patient population. Including all patients with chest pain might result in a much bigger sample size for this study. We only studied the 6th hour troponin levels in order to diagnose AMI other than STEMI. This may also be a limitation for the present study. Levels of myoglobin and cTnT were not studied with FABP two hours after admission.

Conclusion

Point-of-care FABP is good at diagnosing acute myocardial infarction during the initial presentation of chest pain patients. However, it does not have enough sensitivity to exclude myocardial infarction in these patients either at the initial presentation or two hours after admission. Further studies are needed in order to determine the diagnostic value of FABP in emergency departments.

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