CORRELATION BETWEEN SERUM LEVEL OF HEART TYPE FATTY ACID BINDING PROTEIN (H-FABP) AND N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP) ON ACUTE CORONARY SYNDROME PATIENT

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ABSTRAK

Heart-type fatty acid-binding protein (H-FABP) adalah marker awal dari nekrosis otot jantung dan menunjukkan korelasi yang baik dengan ukuran infark. N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) dilepaskan sebagai respons terhadap stress pada dinding jantung dan regangan sel otot. Penelitian ini bertujuan menganalisis korelasi antara kk\adar H-FABP dan NT-proBNP pada pasien sindroma koroner akut (ACS) (n=34) di UGD dan ICCU RSUD Dr. Soetomo Surabaya. RELIA TM Immunoassay Diagnostic Instrument (SSJ-2) Kit digunakan untuk mengukur konsentrasi H-FABP dan NT-proBNP dengan metode ELISA pada 1 dan 6 jam setelah admisi. Rata-rata konsentrasi H-FABP pada 1 dan 6 jam setelah admisi adalah 35,202882 + 45,0928572 ng/mL (H1) dan 35,907147 + 44,6597609 ng/mL (H6). Rata-rata konsentrasi NT-proBNP pada 1 dan 6 jam setelah admisi adalah 2040,3062 + 4169,89471 pg/mL (N1) and 2683,3376 + 4190,6605 pg/mL (N6). Tidak ada perbedaan signifikan antara H1 dan N1; H6 dan N6. H1, N1, H6, N6 secra signifikan lebih tinggi pada pasien Infark Miokard daripada pasien unstable/stable angina. Terdapat korelasi positif antara konsentrasi H1 dan N1 (p=0,014; r=0,419), H6 dan N6 (p=0,001; r=0,527). Terdapat korelasi positif antara konsentrasi puncak H1 dan N1 (p=0,000; r=0,570) dan antara konsentrasi puncak H6 dan N6 (p=0,027; r=0,378). Terdapat korelasi positif yang kuat antara konsentrasi H-FABP dan NT-proBNP pada pasien ACS. (FMI 2014;50:73-80)

Kata kunci: Sindroma Koroner Akut, H-FABP, NT-proBNP

ABSTRACT

Heart-type fatty acid-binding protein (H-FABP) is an early marker of cardiac necrosis and shows good correlation with infarct size. N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) is released as a response of wall stress and myocyte stretch. This study aims to analyze correlation between serum level of H-FABP and NT-proBNP on acute coronary syndrome (ACS) patients (n=34) in Emergency Department and Coronary Care Unit of Dr. Soetomo General Hospital, Surabaya. H-FABP and NT-proBNP concentration were measured using RELIA TM Immunoassay Diagnostic Instrument (SSJ-2) Kit with ELISA method on 1 and 6 hours after admission. Mean of H-FABP concentration at 1 and 6 hours after admission consecutively were 35.202882 + 45.0928572 ng/mL H(1) and 35.907147 + 44.6597609 ng/mL(H6). Mean of NT-proBNP concentration at 1 and 6 hours after admission consecutively were 2040.3062 + 4169.89471 pg/mL (N1) and 2683.3376 + 4190.6605 pg/mL (N6). No significant differences between H1 and N1; H6 and N6. H1, N1, H6, N6 were significantly higher on myocardial infarct than unstable/stable angina patients. There were positive correlation of H1 and N1 (p=0.014, r=0.419), H6 and N6 (p=0.001; r=0.527). There was a positive correlation between peak H1 and N1 (p=0.000; r=0.570) and between peak H6 and N6 (p=0.027; r=0.378). There was strong positive correlation between levels of H-FABP and NT-proBNP on ACS patients. (FMI 2014;50:73-80)

Keywords: Acute Coronary Syndrome, H-FABP, NT-proBNP

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INTRODUCTION

Coronary heart disease is the leading cause of death in the United States, accounting for 20% of all death (Rosamond et al 2007). In the United States, more than a million people are hospitalized annually with unstable angina or myocardial infarction without ST-segment elevation, so-called acute coronary syndromes (Hillis & Lange 2009). Mortality following acute myocardial infarction has declined by approximately 30% over the past 2 decades (Giugliano & Braunwald 2011).

Indonesian Health Profile 2009 issued by the Ministry of Health showed that cardiovascular diseases are a common cause of death in the hospital. Early diagnosis and intervention would improve the prognosis of acute myocardial infarction. However, there are no satisfactory markers for the early diagnosis of AMI (Kim et al 2010)

Biochemical markers have played an increasingly important role in the diagnosis of acute coronary syndrome (ACS). Currently, the cardiac troponins

remain the most widely used biomarkers for the diagnosis of ACS. Their widespread recognition was supported by the inclusion of cardiac troponin as the preferred biomarker in the diagnosis of ACS both in the New Definition of MI (1999) and further reinforced in the Universal Definition of Myocardial Infarction (2007) (Viswanathan et al 2012). Biomarkers should provide important information related to the early detection of subclinical disease, risk stratification, selection of treatment options, monitor disease progression and therapeutic efficacy (Vasan 2006).

Heart-type fatty acid binding protein/H-FABP is a 15 kDa protein thought to be involved in myocardial lipid homeostasis, and is present in substantial amounts in the cytoplasm of myocardial tissue, but is also expressed in tissues outside the heart. Early release of H-FABP into the bloodstream during ischemia has been known for many years. Glatz and collaborators reported as early as in 1994 that H-FABP is detectable earlier than CK-MB and demonstrated a good correlation to infarct size. H-FABP can be detected as early as 1 h and peaks at 6–8 h after an acute coronary occlusion. The role of H-FABP in early diagnosis of AMI is also supported by other previous, comparable studies. Although the prognostic utility of H-FABP in long-term follow-up is not confirmed in this prospective report, an analysis of plasma from 2287 patients in the OPUS-TIMI 16 trial disputed H-FABP as a marker of death and major cardiac events among ACS patients. Among these patients, H-FABP was an independent predictor of adverse outcome and gave additional prognostic information to that provided by cTnI and BNP (Gravning & Kjekshus 2008).

H-FABP, and several markers of myocardial injury may be useful as powerful markers for determining the severity of CHF. Concentration of H-FABP and CK-MB in plasma correlated with BNP in patients with heart failure group. After treatment, the decrease in H-FABP and CK-MB levels correlated with the decrease in BNP levels (Goto et al 2003). Natriuretic peptides, have primarily been use to diagnose of congestive heart failure (CHF) , have also been found to be elevated in the setting of ACS (McCullough et al 2002). Recent evidence suggests that the use of BNP may contribute to both the diagnosis and prognostic outcome in patients with MI (Carreiro-Lewandowski 2006). Natriuretic peptides are vasoactive hormones secreted by the heart as part of a systemic response to cardiac stress and ventricular dysfunction. The precursor peptide of brain natriuretic peptide (BNP) is stored in granules of ventricular myocytes. There, it is cleaved into an amino-terminal product (NT-proBNP) and the physiologically active BNP. Release of BNP and NT-proBNP are regulated by wall stress and myocyte stretch. The BNP

levels trend upward to a peak between 14 and 40 h after an ischemic event. Elevated BNP and NT-proBNP levels at admission in the setting of ACS are associated with poor prognosis, including increased mortality, development of CHF, and recurrent ischemic events (Kwan et al 2007).

Therefore, we hypothesized that H-FABP level is correlated with NT-proBNP level in Acute Coronary Syndrome Patients. This study is conducted to analyze the correlation between serum level of Heart Type Fatty Acid Binding Protein (H-FABP) and N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) on Acute Coronary Syndrome patients

MATERIALS AND METHODS

This was an observational study of 34 consecutive patients of acute coronary syndromes admitted to the Emergency Department and Coronary Care Unit Dr Soetomo General Hospital. We excluded patients with creatinin serum level > 2mg/dl, septicemia, hepatic cirrhosis, hemoglobin level <8 mg/dl, acute stroke, malignancy, previous history of heart failure, and critically ill patients. We examined plasma level of H-FABP and NT-proBNP at 1 hour and 6 hour after admission. The local scientific ethical committee has approved the study and each participant gave written informed consent.

All protocols of Acute Coronary Syndrome management of Dr Soetomo General Hospital were performed to each participant, including 12 lead ECG, Chest X Ray, laboratory examination and echocardiography. At the time of enrollment, blood specimens were collected in citrate treated tubes and were centrifuged at 3000 rpm for at least 15 minutes. The plasma component was frozen. After the procedures were completed, all available plasma specimens were analyzed. RELIA TM Immunoassay Diagnostic Instrument (SSJ-2) Kit was used to measure H-FABP and NT-proBNP levels with ELISA method. Results were presented as mean (+SD). Correlation between plasma level of H-FABP and NT-proBNP were examined by Pearson correlation test if the distribution of data were normal or Spearman correlation test if data distribution was abnormal. The p value of <0.05 was considered significant.

RESULTS

This study was carried out on 34 patients, 19 men and 15 women, suffering from acute coronary syndromes consisting of 17 patients suffering from ST Elevation

myocardial infarction (STEMI), 3 patients suffering from non-ST elevation myocardial infarction (NSTEMI) and 14 patients suffering from unstable angina (UA). Based on Killip class classification there were 23 patients (67,6%) suffering Killip I, 6 patients (17.6 %) suffering Killip II, 3 patients (8.8%) with Killip III, and 2 patients (5.9%) with Killip IV. 15 patients (67,6%) were smokers, 10 patients (29,4%) in infarct group (NSTEMI/STEMI) and 5 patients (14,7%) in UA group. 11 patients (32,4%) have history of Diabetes Mellitus, 8

patients (23.5%) in infarct group and 3 patients (8.8%) in UA group. 23 patients (67,6%) with history of hypertension, 15 patients (44,1%) in infarct group and 8 patients (23,5%) in UA group. Baseline characteristic of participant is given in Table 1. Table 1 showed that the Mean value of Random Plasma Glucose, Leukocyte count, ALT, AST, CK-MB, Troponin T were higher in infarct patients than UA patients. The mean value of Left Ventricular Ejection Fraction was lower in infarct group.

Table 1. Baseline Characteristic

	Total (n =34)	Infarct (NSTEMI/STEMI)	UA
Age	55.76 $\pm$ 11.322	52.25 $\pm$ 11.346	60.79 $\pm$ 9.545
Sex :			
Male	19 (55.9%)	12 (35.3%)	7 (20.6%)
Female	15 (44.1%)	8 (23.5%)	7 (20.6%)
Risk Factors :			
Smoking	15 (44.1%)	10 (29.4%)	5 (14.7%)
Hypertension	23 (67.6%)	15 (44.1%)	8 (23.5%)
Diabetes	11 (32.4%)	8 (23.5%)	3 (8.8%)
UA	14 (41.2%)		
NSTEMI	3 (8.8%)		
STEMI	17 (50%)		
Killip 1	23 (67.6 %)		
Killip 2	6 (17.6 %)		
Killip 3	3 (8.8%)		
Killip 4	2 (5.9 %)		
Systolic blood pressure	124.88 $\pm$ 24.070	122 $\pm$ 20.700	128.36 $\pm$ 28.678
Diastolic blood pressure	76.12 $\pm$ 10.887	74.50 $\pm$ 11.910	78.43$\pm$ 9.154
Hemoglobin	13.49 $\pm$ 2.054	13.8950$\pm$ 2.45389	12.9143 $\pm$ 1.14210
Leukocyte count	12532.06 $\pm$ 5157.346	15200 $\pm$4874	8714.29 $\pm$2479.720
Thrombocyte	286176.47 $\pm$ 77774.916	289000 $\pm$84106.551	282000$\pm$70567.402
Random plasma glucose	182.79 $\pm$ 111.538	225.10 $\pm$ 124.848	122.36 $\pm$45.958
BUN	14.9176 $\pm$ 9.91331	14.8950 $\pm$ 5.80022	14.9500 $\pm$14.15245
Creatinine	0.9406 $\pm$ 0.35960	0.9810 $\pm$ 0.36109	0.8829$\pm$ 0.36276
AST	69.62 $\pm$ 93.591	103.60 $\pm$ 110.596	21.07 $\pm$ 6.627
ALT	27.82 $\pm$ 19.220	37.20 $\pm$ 19.814	14.43 $\pm$ 5.958
CKMB hour-1	99.4206 $\pm$ 145.84275	149.21 $\pm$ 174.39	28.2929 $\pm$ 16.84721
CKMB hour-6	120.4147 $\pm$ 156.01615	190.86 $\pm$ 171.95	19.7786 $\pm$ 5.94270
Troponin T hour-1	0.4424 $\pm$ 0 .61906	0.7510 $\pm$ 0.64967	0.0014 $\pm$ 0.00363
Troponin T hour-6	0.7168 $\pm$ 0. 81502	1.2175 $\pm$ 0.71604	0.0014$\pm$ 0.00363
Total Cholesterol	193.50 $\pm$ 41.735	193.55 $\pm$ 52.171	193.57 $\pm$21.063
LDL cholesterol	137.71 $\pm$ 35.732	130.85 $\pm$ 38.5	147.50 $\pm$29.984
HDL cholesterol	33.32 $\pm$ 9.344	30.40 $\pm$ 9.528	37.50 $\pm$ 7.552
Triglyceride	179.79 $\pm$ 48.462	166.05 $\pm$ 45.475	199.43 $\pm$47.260
Ejection Fraction	55.71$\pm$ 10.053	52.95$\pm$ 10.49047	59.6429$\pm$ 8.20513
NT-proBNPhour-1	2040.3062 $\pm$ 4169.89471	3182.1 $\pm$5163.07232	409.22 $\pm$554.50214
NT-proBNP hour-6	2683.3376 $\pm$ 4190.66055	4142.1 $\pm$ 4971.40194	600.10 $\pm$712.53186
H-FABP hour-1	35.202882 $\pm$ 45.0928572	57.966 $\pm$46.914268	2.68393$\pm$ 2.973824
H-FABP hour-6	35.907147 $\pm$ 44.6597609	58.158 $\pm$46.416289	4.12021$\pm$ 8.017324

NT-proBNP level based on clinical spectrum of Acute Coronary Syndrome
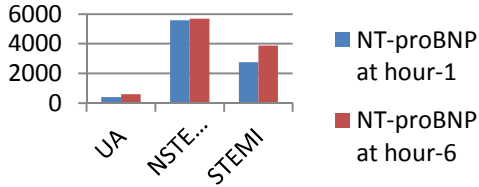

Figure 1. Mean value of NT-pro BNP level were higher in STEMI and NSTEMI patients. The highest mean value was in NSTEMI patients. The figure showed that the mechanical stress in infarct group was higher than UA group.

NT-proBNP level based on Killip class classification

NT-proBNP levels increase with increasing Killip class, either at first or at the sixth hour. The highest mean value of NT-proBNP levels found in Killip class 3. It can be concluded the more severe the Killip class the higher NT-proBNP level, which indicates a more severe mechanical stress (Figure 2.)
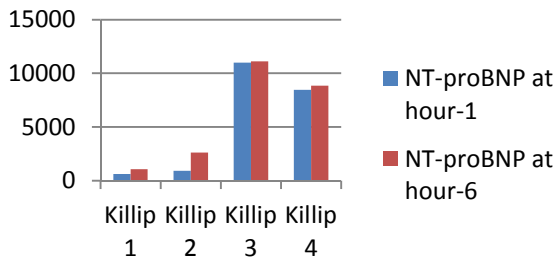
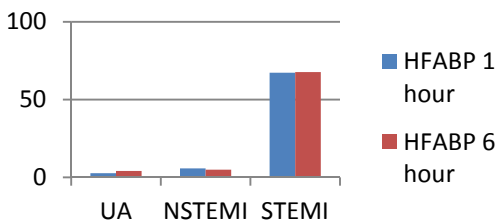Figure 2. Mean value NT-proBNP level based on Killip class classification

Figure 3. Mean value H-FABP level based on clinical spectrum of Acute Coronary Syndrome

H-FABP levels based on the clinical spectrum of Acute Coronary Syndrome

The mean value H-FABP was higher in Infarct patients than UA patients. The highest mean value was in the STEMI patients. It can be concluded that patients with STEMI has the most extensive areas of myocardial necrosis or ischemia (figure 3).

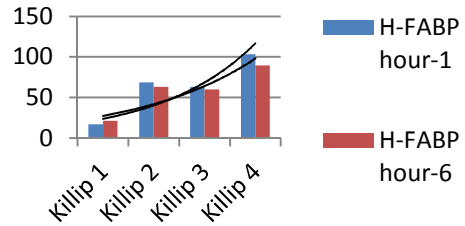## H-FABP level based on Killip class classification

Figure 4. Mean value of H-FABP increased along with the increase in Killip class. With the highest mean value of H-FABP found in patients with Killip IV. It can be concluded that higher Killip class have more extensive myocardial necrosis or ischemia.

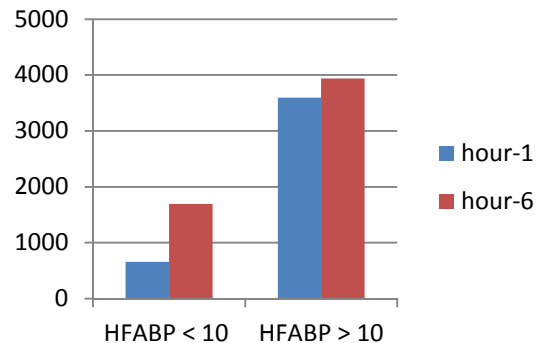## NT-proBNP levels based on the levels H-FABP

Figure 5. Mean value of NT-proBNP level in patients with HFABP levels >10 ng/mL higher than patients with H-FABP levels <10 ng/mL, both in the first hour or 6 hour. It was shown that patients with H-FABP levels >10 ng/mL had greater mechanical stress.

H-FABP levels based on levels of NT-proBNP

Figure 6 and 7 indicates that the mean value of H-FABP level increasing in accordance with NT-proBNP levels, either in the first hour and sixth hour. This shows that the extensive areas of myocardial necrosis, in this case that the higher the value H-FABP, will experience

greater biomechanical stress, in this case indicated by the higher value of NT-proBNP.
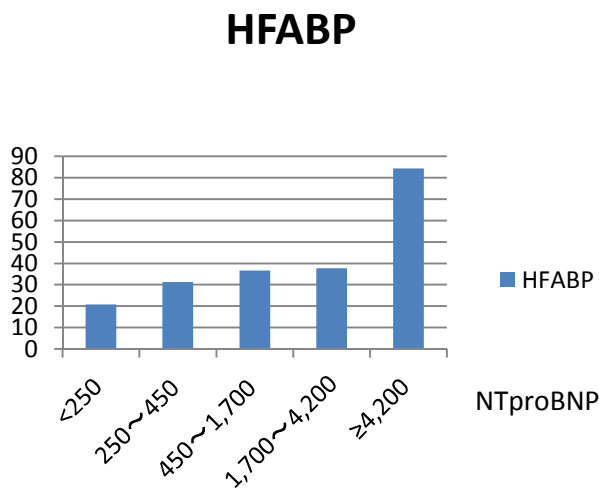

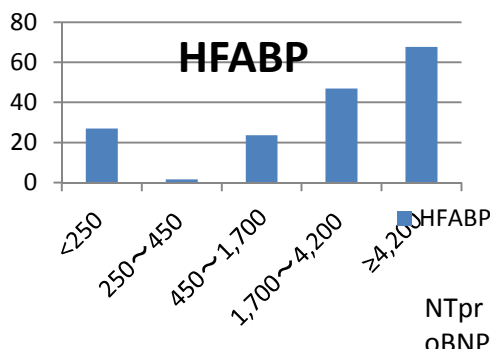Figure 6. H-FABP level based on NT-proBNP level at 1st hour

Figure 7. H-FABP level based on NT-proBNP level at 6th hour

Correlation between H-FAB and NT-proBNP

Kolmogorov Smirnov or Shapiro Wilks test results concluded that the data distribution was abnormal. The Pearson correlation test was used to measure correlation between H-FABP and NT-proBNP. There was strong correlation between H-FABP & NT-proBNP concentration at first hour (p=0.014; r=0.419) and H-FABP & NT-proBNP concentration at sixth hour (p=0.001; r=0.527). There was correlation between Peak H-FABP & NT-proBNP concentration (p=0.000; r=0.570) and Peak H-FABP concentration & increase NT-proBP concentration (p=0.031; r=0.370)

DISCUSSION

Early diagnosis of acute MI facilitates rapid and appropriate triage of patients within the Accident and Emergency department, helping to prevent inadvertent discharge of patients with acute MI. It also avoids delay in administering treatment for acute MI, and reduces the possibility of patients without acute MI given treatments from which they will not benefit, and which have the potential to cause significant harm. The 12-lead ECG is an important tool for early detection of acute MI, but it has significant limitations, e.g. LBBB or a permanent pacemaker, etc. may make interpretation impossible. Another significant factor is that interpretation of the 12-lead ECG is dependent on the experience of the physician (McCann et al 2008).

Diagnosis of acute myocardial infarction can be made if there is biochemical evidence of myocardial necrosis. The preferred biomarker—overall and for each specific category of MI—is cTn (I or T), which has high myocardial tissue specificity as well as high clinical sensitivity. Detection of a rise and/or fall of the measurements is essential to the diagnosis of acute MI. An increased cTn concentration is defined as a value exceeding the 99th percentile of a normal reference population [upper reference limit (URL)] (Thygesen et al 2012). Cardiac troponin rises with a time course similar to CK-MB but can remain increased for up to 4–7 days for cTnI and 10–14 days for cTnT (Morrow et al 2007).

H-FABP is a small cytosolic protein (14 to 15 kDa) that is present in abundance in both skeletal and cardiac muscle. Because of its small size, H-FABP is released quickly into the circulation when membrane integrity is compromised in response to cardiac ischemia. Levels of H-FABP are detectable as early as 2 to 3 hours after injury, with a return to baseline levels typically within 12 to 24 hours of the initial insult (McCann et al 2008, O'Donoghue et al 2006).The measurement of infarct size after Acute Myocardial Infarction can have prognostic implication. Sohmiya et al. (1993) showed good correlation between myocardial infarct size measured from plasma HFABP and infarcted myocardium estimated from triphenyl tetrazolium chloride (TTC) staining. A study by Glatz et al. (1994), as cited in Alhadi & Fox (2004), showed a good correlation between HFABP, CKMB, and α-hydroxybutyrate dehydrogenase (α-HBDH) for estimation of infarct size (Alhadi & Fox 2004).

Comparison of the levels of H-FABP showed a significant increase of mean H-FABP (ng/ml) in STEMI patients (29.64±10.21), NSTEMI patients (24.54±8.40) and UA patients (21.07±4.66) than controls (8.92±3.92)

and also NCCP (11.77±5.60). Ischii et al. (2005) reported that serum concentration of H-FABP and cTnT on admission was significantly higher in STEMI patients than NSTEMI/UA. In this study there were increasing mean value of H-FABP level in clinical spectrum of ACS, on UA patients were (2.683 + 2.973) , NSTEMI (5.780 + 6.365) and STEMI (67.175 + 44.80). This study showed that STEMI patients had greater myocardial damage than NSTEMI/UA (Gururajan et al 2010).

An analysis of plasma from 2287 patients in the OPUS-TIMI 16 trial disputed H-FABP as a marker of death and major cardiac events among ACS patients. Among these patients, H-FABP was an independent predictor of adverse outcome and gave additional prognostic information to that provided by cTnI and BNP (Gravning & Kjekshus 2008). Patients with H-FABP levels >6.48 µg/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 cut off of 6.48 µg/l identified patients at very high risk for adverse outcomes independent of patient age and serum creatinine (Viswanathan et al 2010). Patients with elevated H-FABP more commonly presented with STEMI as their index diagnosis or had signs of CHF (Killip class II through IV), but were found to have a similar angiographic burden of disease. Patients with elevated serum H-FABP >6.08 ng/ml were more likely to be older and female, and to have DM, hypertension, HF defined as Killip class 2 on admission, and multivessel disease compared to those with H-FABP 6.08 ng/ml (Matsumoto et al 2013). In this study, H-FABP level was increase with increasing Killip class classification.

BNP and NT-proBNP are released from cardiac myocytes in response to increases in ventricular wall stress (Morrow et al 2007). The earliest manifestation of myocardial ischemia is a transient increase in LV wall tension. In patients with chest pain syndromes, both plasma BNP and NT-proBNP levels are found to be significantly higher in the unstable angina group than in the atypical or stable angina groups (Tang & Francis 2005). Salama et al (2011) showed that NT-proBNP was significantly higher in NSTE-ACS patients than in STE-ACS patients despite lower values of the conventional cardiac markers CK-MB and Tn-T in NSTE-ACS patients. NT-proBNP levels increased during the hyperacute phase in NSTE-ACS patients, and weren't raised by the process of myocardial necrosis but the ischemic insult per se. In this study, the mean value of NT-proBNP was higher in infarct patient than UA

patients, and the highest mean value was in the NSTEMI group (Salama et al 2011).

Clinical heart failure is a poor prognostic sign in patients with ACS and is commonly regarded as a sign of significant ventricular dysfunction. LVEF is a frequently used index of left ventricular systolic function and a powerful prognostic indicator. Interestingly, LVEF and clinical classification of heart failure (ie. Killip classification) provide independent prognostic information, suggesting that factors other than systolic function are of importance for prognosis in these patients. Circulating natriuretic peptide levels are elevated both in patients with low ejection fractions and in patients with clinical heart failure (Omland et al 2002).

Evaluation of BNP and NT-proBNP values show good correlation between other assessment criteria schemes used by physicians (eg. New York Heart Association functional class, Framingham score, and echocardiogram results) in assessing dyspnea and CHF, and as good predictors of future adverse cardiac events (Carreiro-Lewandowski 2006). In terms of index presentation, higher baseline NT-proBNP levels were significantly associated with increasing time from symptom onset to initiation of fibrinolytic therapy, anterior location of the MI, and Killip class II to IV (P= 0.001 for all) but not peak CK (P=0.91) (Sabatine et al 2008). The concentration of NT-proBNP in patients with ACS was dramatically correlative with the severity of the diseases: with the upgrading of Braunwald classes, the concentration of NT-proBNP in patients with UA increased gradually; in patients with AMI it also raised gradually with the upgrading of Killip classes; furthermore, the plasma concentration of NT-proBNP in patients with AIM increased much more than that in patients with UA when they are at the similar NYHA functional class (Cao et al 2005). In this study, mean value of NT-proBNP levels was increase with increasing Killip class classification. The mean value of NT proBNP levels in Killip I was 588.84 + 765 031; Killip II 905.58 + 585.50; Killip III 10988 + 6931.60; Killip IV 8459 + 9250.34. The highest mean value was in patients with Killip III. However, a diagnostic NT-proBNP cut-off value in ACS has proved difficult to establish as NT-proBNP levels are influenced by various factors including sex, age, renal function, HF severity and obesity. The normal values tend to increase with age and to be higher in women than in men (Choi et al 2010).

Modest correlations were observed between H-FABP and serum myoglobin (r = 0.46, P=0.001) and BNP (r=0.23, P=0.001). When analyses were restricted only to patients with elevated levels of H-FABP, the

correlation between H-FABP and myoglobin was strengthened (r=0.58, P=0.001), whereas the correlation between H-FABP and BNP was attenuated (r=0.063, P=0.25) (O'Donoghue et al 2006). In this study, there was strong correlation between H-FABP and NT-proBNP level at first hour (r = 0.419, p <0.014) and sixth hour after admission (r = 0.527, p <0.001). There was strong correlation between peak level of H-FABP and NT-proBNP (r = 0.570, p <0.000). There was correlation between peak level H-FABP and amount of increasing NT-proBNP level (r = 0.378, p <0.027). From these evidences it can be concluded that HFABP, an early marker for the diagnosis of acute myocardial infarction, correlated with NT-proBNP, a prognostic marker. So H-FABP may also have prognostic value in patients with ACS.

This study result was similar to the conclusions of study by O'Donoghue et al (2006), in a multimarker analysis and found that H-FABP may provide incremental information for risk stratification beyond that seen with existing risk markers, including troponin, BNP, or myoglobin. Importantly, H-FABP may be useful for identifying patients at increased risk of death or CV events despite having a negative serum troponin or BNP.Limitation of this study is the difficulty to determine the actual onset of AMI, because the chief complaints were subjective, so the peak concentration H-FABP could not be detected. Careful history taking is necessary to distinguish the chief complaints of AMI (the heaviest chest pain) with chest pain in the UA phase. NT-proBNP concentration before ischemia events is unknown. And the history of ventricular dysfunction and hypertrophy were unknown. An increase of NT-proBNP level and the adverse outcomes were not only caused by ischemia alone. Small sample size and high α value greatly affects the results of this study.

CONCLUSIONS

In this study it can be concluded that the mean H-FABP and NT-proBNP in patients with myocardial infarction (STEMI and NSTEMI) were significantly higher than in patients with stable angina/UA. Increase of HFABP and NT-proBNP mean value matches the severity of the patient. It shows that the higher the value of H-FABP and NT-proBNP the more extensive myocardial necrotic areas. The stretch of the left ventricle walls will increase and myocardial dysfunction was more severe. The mean value of NT-proBNP levels in patients with H-FABP >10ng/mL is significantly higher than in patients with H-FABP levels <10ng/mL. The mean value of H-FABP level would elevate along with the increased level of NT-proBNP. And the statistical analysis showed strong correlation between H-FABP and NT-proBNP level on

Acute Coronary Syndrome patient. H-FABP can be used as an additional marker in diagnosing and determining the prognosis of patients with Acute Coronary Syndrome. H-FABP is detected in the circulation earlier so the diagnosis and prognosis can be determined more quickly, and appropriate interventions can be done to prevent morbidity and mortality. Further research is needed with larger sample sizes and better research design. And to assess the prognostic benefits of H-FABP, a prospective cohort studies for major adverse cardiac event (MACE) need to be done.

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