CORRELATION BETWEEN HEAT SHOCK PROTEIN (HSP) 70 LEVEL AND LEFT VENTRICULAR DYSFUNCTION AND ITS EFFECT ON CARDIOVASCULAR AND REHOSPITALIZATION INCIDENCE IN PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRAK

Peran protein HSP70 pada penyakit arteri koroner (CAD) masih diperdebatkan. Pandangan studi menunjukkan bahwa HSP70 berperan sebagai sinyal bahaya permulaan respon peradangan yang terlibat dalam ventrikel kiri (LV) hasil renovasi di LV disfungsi dan gagal jantung. Penelitian ini bertujuan membuktikan hubungan tingkat ekstraseluler HSP70 dengan disfungsi LV serta efeknya pada kejadian kardiovaskular dan rehospitalization pada pasien dengan ACS. Enam puluh pasien terdaftar dengan ACS di RSUD Dr. Soetomo antara Juli dan Oktober 2013 diikuti selama 6 bulan. Sesuai nilai median HSP70 pasien digolongkan HSP70 rendah dan tinggi. HSP70 diukur pada awal, fungsi LV dinilai dengan ekokardiografi pada awal dan dibandingkan setelah 3 bulan tindak lanjut. Analisis survival Kaplan-Meier menggambarkan gagal jantung, kematian, dan rehospitalization akibat penyakit kardiovaskuler selama 6 bulan tindak-lanjut pada kedua kelompok. Kadar HSP70 secara signifikan berkorelasi dengan LVEF saat masuk dan setelah 3 bulan (r=-0,689; p<0,001; r=-0,705; p<0,001), LV PW MPI saat masuk dan setelah 3 bulan (r=0,507; p<0,001; r=0,675; p<0,001), LV TDI MPI saat masuk dan setelah 3 bulan (r = 0,588; p<0,001; r=0,672; p<0,001), DT saat masuk (r=-0,322; p=0,012), E/A pada penerimaan (r=0,373; p=0,003), E/E' saat masuk dan setelah 3 bulan (r=324; p=0,011; r=0,382; p=0,006). Kadar HSP70 yang lebih tinggi terkait peningkatan gagal jantung (p<0,001) selama 6 bulan masa tindak lanjut. Analisis survival Kaplan-Meier menunjukkan HR gagal jantung berdasarkan median HSP70 adalah 5,35 (CI 95% (2,25-12,7); p<0,001), HR kematian 3,096 (CI95% (0,838-11,444); p=0,09) dan HR dari rehospitalization 85,685 (CI 95% (0,059-125012,62); p=0,231). Simpulan, tingkat HSP70 ekstraseluler terkait dengan fungsi LV dan gagal jantung pada pasien dengan ACS. ***(FMI 2015;51:125-131)***

Kata kunci: *Sindrom koroner akut, HSP70, fungsi ventrikel kiri (LV), gagal jantung, kematian dan rehospitalization*

ABSTRACT

HSP70 role in coronary artery disease (CAD) is still debated. Some studies showed that it played a role as a danger signal initiates inflammation response involved in left ventricular (LV) remodeling that result in LV dysfunction and heart failure. Our study aimed to prove the association between extracellular HSP70 level and LV dysfunction and its effect on cardiovascular events and rehospitalization in ACS patients Sixty patients with ACS in Dr. Soetomo Hospital between July and October 2013 were followed up for 6 months. The patients were stratified into low and high HSP70 group. HSP70 was measured at the initial admission while LV function by echocardiography was assessed at the initial admission and compared after 3 months of follow up. Kaplan-Meier survival analysis was done to describe heart failure, mortality, and rehospitalization caused by cardiovascular disease during 6 months follow-up in both groups. The HSP70 level was significantly correlated with LVEF at admission and after 3 months (r=-0.689; p<0.001; r=-0.705; p<0.001), LV PW MPI at admission and after 3 months (r=0.507; p<0.001; r=0.675; p<0.001), LV TDI MPI at admission and after 3 months (r=0.588; p<0.001; r=0.672; p<0.001), DT at admission (r=-0.322; p=0.012), E/A at admission (r=0.373; p=0.003), E/E' at admission and after 3 months (r=324; p=0.011; r=0.382; p=0.006). In our study, higher HSP70 levels were associated with an increased heart failure (log-rank test, p<0.001) during the 6 months follow-up period. Kaplan-Meier survival analysis showed HR of heart failure based on the HSP70 median was 5.35 (CI 95% (2.25-12.7); p<0.001), HR of mortality 3.096 (CI95% (0.838-11.444); p=0.09) and HR of rehospitalization 85.685 (CI 95% (0.059-125012.62); p=0.231). In conclusion, extracellular HSP70 level associated with LV function and heart failure in the patients with ACS. ***(FMI 2015;51:125-131)***

Keywords: *Acute coronary syndrome, HSP70, LV function, heart failure, mortality and rehospitalization*

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INTRODUCTION

Coronary heart disease (CHD) is one of the major chronic diseases that until now responsible for the majority of morbidity, mortality, and health care costs in both the developed and developing countries (Roger et al 2011). National census data of 2001 showed that the prevalence of CHD tend to increase and 26.4% of deaths caused by cardiovascular diseases, including coronary heart disease. Acute coronary syndrome

(ACS) is part of the clinical manifestations of acute coronary heart disease with a spectrum of clinical presentations include acute myocardial infarction ST-elevation (STEMI), acute myocardial infarction non-ST-elevation (NSTEMI), and unstable angina pectoris. In terms of pathology, SKA is caused primarily by atherosclerosis (Strodter 2010).

Until now it has collected evidence that immunological mechanisms involved in the pathogenesis of atherosclerosis, including autoimmune reactions against heat shock proteins (HSPs). Nevertheless, the relationship between HSP70 and CHD is still a conflict. The study by Zhang et al (2010) showed that high levels of HSP70 Associated with increased risk and severity of SKA. Cardioprotective effect of HSP70 is also shown in an experimental trial, it was found that increased expression of HSP70 led to an increase in resistance to ischemic injury, myocardial function, metabolic function recovery, and reduce infarct size after reperfusion. Significant inverse relationship is still unexplained and possibly into therapeutic targets HSP70 also still to be investigated (Bielecka-Dabrowa et al 2009).

Therefore, further research on the role of HSP70 associated with atherosclerosis, in particular on the SKA are still poorly investigated urgently needed. This study aims to prove the relationship between the levels of extracellular HSP70 with left ventricular dysfunction and its effect on cardiovascular events (heart failure and death) and rehospitalisasi in patients with ACS.

MATERIALS AND METHODS

This type of research is analytic observational prospective cohort design and internal comparison group. This research was conducted in the emergency department (IRD), ICCU, and inpatient cardiac dr. Soetomo during July 2013-April 2014.

Affordable population is patients who underwent inpatient SKA. Purposive sampling method of consecutive sampling, met the inclusion criteria that all patients diagnosed with ACS and willing to comply with study procedures by signing the informed consent. Exclusion criteria include pregnant or breastfeeding, have a history of myocardial infarction, heart failure, systemic infections in the last 3 months, oncology disease or undergoing radio or chemotherapy, autoimmune, endocrine, except diabetes mellitus (DM), severe liver abnormalities, severe kidney, heart congenital, and echocardiography difficult or assessed.

Levels of HSP70 and supporting basic laboratory diagnosis be taken upon arrival. HSP70 levels measured from venous blood sampling by ELISA using Stressgen. Echocardiographic measurements performed upon arrival and after 3 months of observation with Echo Vivid 7. Mayor and rehospitalisasi Cardiovascular events were evaluated during the first 6 months after hospital admission.

Parameters examined included echocardiographic systolic function, diastolic and left ventricular Tei index. Left ventricular systolic function in the form of left ventricular ejection fraction (LVEF). Diastolic function in the form of deceleration time (DT), the ratio E/A, and the ratio E/E'. Tei index measured by traditional (pulsedwave (PW) and tissue Doppler (TDI). Output is measured clinical and rehospitalisasi major cardiovascular events. The incidence of major cardiovascular events include heart failure and death.

RESULTS

The total sample in this study analyzed are 60 people with a range of ages ranging from 29-76 years (mean 54.41 $\pm$ 9.73 years). The number of subjects showed predominantly male gender is 48 people (80%) and 12 people (20%) are women. Based SKA category, 78.3% of total subjects categorized as ACS STEMI, NSTEMI 16.7%, and 5.0% is UA. Among cardiovascular risk factors was found that smoking and dyslipidemia are the highest risk factors, namely 78.30%, while the next is hypertension and obesity, respectively amounted to 51.70% and 40.00%.

The mean levels of HSP70 in this study, amounted to 0.153 $\pm$ 0.02 ng/mL. Therefore, up to now there is no cut-off point value for HSP70, HSP70 levels of the classification in this study using the median value. Based on median values, the classification of HSP70 divided by 2 is: low (< 0.147 ng/mL) and high (> 0.147 ng/mL).

Systolic function parameters measured include LVEF with Simpson's method or equation (by Biplane). Diastolic function parameters using transmitral and tissue Doppler mitral inflow, covering DT, the ratio E/A ratio and E/E'.

A total of 10 patients died during treatment in hospital, so that only 50 research subjects to do a re-examination echocardiography at follow-up after 3 months. Mean LVEF values on admission lower and obtained significant improvement at follow-up after 3 months (52.50 $\pm$ 56.02 $\pm$ 7.6% vs 7.8%; $p = 0.002$). Also found a significant decrease in the value of PW-MPI (0.50 $\pm$ 0.1 $\pm$ 0.1 vs. 0.42; $p < 0.001$) and TDI-MPI (0.53 vs. 0.45 $\pm$ 0.1 $\pm$ 0.1; $p < 0.001$) of the left ventricle at

follow-up after 3 months. DT mean not increased significantly between when the MRS and the follow-up after 3 months (55.1 ms vs 210.10 ± 214.76 ± 49,1ms; p = 0.637). The mean ratio E/A between the time of admission and follow-up after 3 months found a significant reduction (0.98 ± 0.97 ± 0.6 vs. 0.4, p = 0.002), while the average ratio E/E 'not found a significant decrease (11.19 ± 9.95 ± 6.0 vs 5.1; p = 0.484).

This study shows a significant correlation between serum levels of HSP70 with LVEF on admission (r = -0.689; p < 0.001) and after 3 months (r = -0.705; p < 0.001), LV PW-MPI on admission (r = 0.507 ; p < 0.001) and after 3 months (r = 0.675; p < 0.001), LV TDI-MPI on admission (r = 0.588; p < 0.001) and after 3 months (r = 0.672; p = 0.000), DT on admission (r = -0.322; p = 0.012), the ratio E/A on admission (r = 0.373; p = 0.003), the ratio E/E' on admission (r = 324; p = 0.011) and after 3 months (r = 0.382; p = 0.006).

Based on the grouping of HSP70, found significant differences between the groups HSP70 high and low on the assessment of LVEF parameters on admission (p < 0.001) and after 3 months (p < 0.001), LV PW-MPI on admission (p < 0.001) and after 3 months (p < 0.001), TDI-MPI on admission (p < 0.001), DT on admission (p = 0.001) and after 3 months (p = 0.035), the ratio E/A on admission (p < 0.001), the ratio E/E' on admission (p = 0.001) and after 3 months (p < 0.001). Conversely, diastolic function parameters E/A after 3 months of follow-up showed no significant difference between high and low HSP70 group.

From all subjects traced up to 6 months, obtained a cardiovascular event such as the death of as many as 12 patients (20%) with a mean survival time of 19.40 (IC 95% from 17.072 to 21.728) and heart failure by 33 patients (55%) with a mean survival time 12.35 (95% KI 9.563 to 15.138). Therefore, 10 subjects experienced the first death while being treated in hospital, the observation of the events conducted on 50 subjects rehospitalisasi remaining studies. Rehospitalisasi only occurred in 5 patients (9.3%) with a mean survival time of 23.02 (IC 95% from 22.069 to 23.971). Death and heart failure occurred in the first week of treatment while in hospital. Heart failure and most deaths occurred in the group of high HSP70 is a row of 26 patients (78.8%) and 9 patients (75%). Total rehospitalisasi entirely in the category of high HSP70.

Analysis of survival by Kaplan-Meier method against heart failure showed that there were significant differences between the two groups with the log rank p < 0.001. Bivariate analysis using Cox's proportional hazards models regressionmenunjukkan Hazard Ratio (HR) groups HSP70 high and low on the incidence of heart failure by 95% CI 5.35 (2.25 to 12.7) and p value < 0.001. Thus, any time a group HSP70 high of 5.35 times as likely to develop heart failure than the low HSP70 group. Mortality and rehospitalisasi between the two groups showed no significant differences, respectively HR 95% CI 3.096 (0.838 to 11.444) and p = 0.090 and 85.685 HR CI 95% (from 0.059 to 125102.62) and p = 0.231. It can be concluded that there was no correlation between the levels of HSP70 with the occurrence of death and rehospitalisasi in patients with ACS.

Table 1. Characteristics of the study subjects echo-cardiography

Variables	Hospitalization (Mean ± SB)	3 m follow-up (Mean ± SB)	*P**
E/A ratio	0.98 ± 0.6	0.97 ± 0.4	0.002
E/E' ratio	11.19 ± 6.0	9.95 ± 5.1	0.484
DT (ms)	210.10 ± 55.1	214.76 ± 49.1	0.637
TDI- MPI	0.53 ± 0.1	0.45 ± 0.1	< 0.001
PW MPI	0.50 ± 0.1	0.42 ± 0.1	< 0.001
LVEF	52.50 ± 7.6	56.02 ± 7.8	0.001

LVEF: left ventricular ejection fraction; DT: deceleration time; MPI: myocardial performance index; MRS: hospital admission; *Wilcoxon test.

DISCUSSION

Most of the study subjects (80%) male sex. This is consistent with the theory and previous research, men 2-3 times greater risk than women to suffer from SKA (Morrow 2010). Risk factors of smoking and dyslipidemia highest ranks respectively by 78.30%, followed by hypertension (51.70%), obesity (40.0%), and diabetes (31.7%). Data from studies evaluating risk factors coronary heart disease in patients aged <45 years were carried out in RS Kariyadi, Semarang, showed that the risk factors of smoking and dyslipidemia tops, namely dyslipidemia (p = 0.029; OR = 2.8; 95% CI = 1, 1 to 7.1) and smoking (p = 0.028; OR = 2.3; 95% CI = 1,1- 5.0 (Supriyono et al 2008). Smoking synergistically plus other risk factors will increase the incidence CHD (Falk & Fuster 2001).

Most of the subjects (60%) were obese and central obesity. According to the IDF central obesity increases the risk of cardiovascular disease. Studies by Hariadi and Ali in 2005 found a significant relationship to obesity CHD events were accompanied by DM (p 0.018), hypertension (p 0.007), and there is no significant correlation between the incidence of CHD in obesity is accompanied by dyslipidemia.

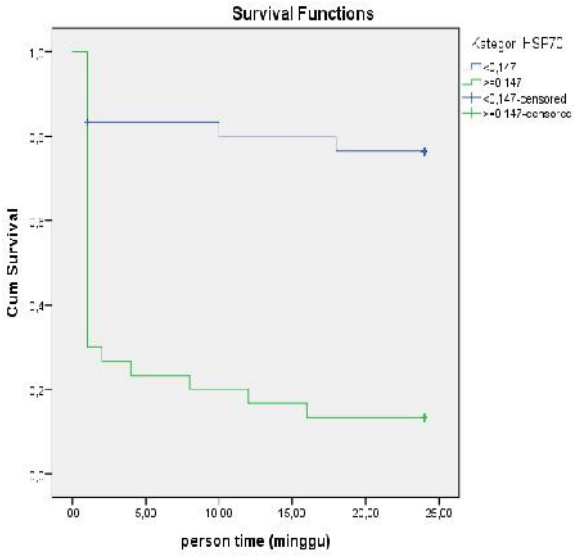

Figure 1. Survival HSP70 against heart failure within 6 months of observation

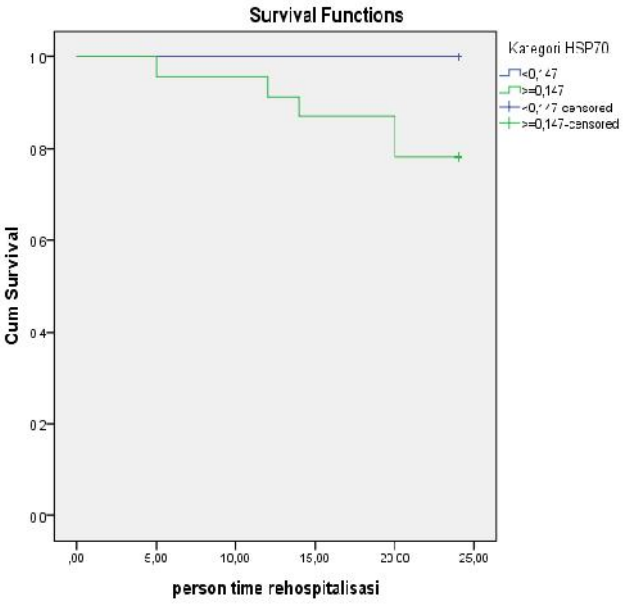

Figure 2. Survival HSP70 against rehospitalization within 6 months of observation

Mean values increased CKMB and troponin obtained from the normal value. CKMB and troponin have a positive correlation with the degree of cell necrosis and myocardial ischemia. Increased troponin levels was associated with a worse prognosis (Dybdahl et al 2005, Satoh et al 2006, Haan et al 2013).

Sampling was performed at a mean onset HSP70 7.43 ± 6.2 hours. Therefore, normal value HSP70 in Indonesia or Asian populations has not been found, then the researchers used an internal comparator using the median value. Group I or HSP70 HSP70 low with serum levels < 0.147 ng/dl and group II or HSP70 high with serum HSP70 levels ≥ 0.147 ng/dl.

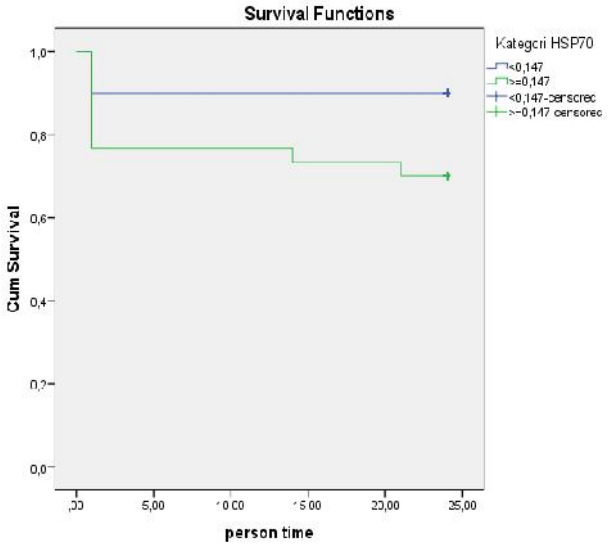

Figure 3. Survival HSP70 to death within 6 months of observation

The average value of total serum levels of HSP70 subject of 0.153 ± 0.02 ng/dl, smaller than the results Satoh et al (2006), namely 1.254 ± 0.102 ng/mL in patients with AMI 24 hours after onset of chest pain. Similarly, by Dybdahl et al (2005) obtained a mean serum HSP70 levels of 0.868 ng/ml in patients with AMI 6 hours after the onset of chest pain, as well as by Zhang et al (2010) is 3.77 ng/mL in patients with ACS who were taken 12 hours after the onset of chest pain. The value difference can be due to differences in onset time of sampling HSP70.

There are two kinds of mechanisms that release of HSP70 in the circulation of passive and active mechanisms. Passive mechanisms include cell necrosis, severe blunt trauma, surgery, and infection by the virus lytic. Active mechanisms involving non classical releasepathway. HSP70 is released in the form of free HSP and in lysosomes. Haan et al (2013) suggested HSP70 issued by myocardial cells undergo "stressed" in the form of ischemia. Research Dybdahl et al (2005) states that the levels of HSP70 in patients with AMI peaked at 6 hours after the onset of chest pain and decreased significantly in the next day. HSP70 sample inspection method together with research and Satoh

Dybdahl is by ELISA. Unlike the case with research data Satoh et al. namely serum HSP70 levels be kept high up to 14 days. Some things that can affect the kinetics of serum HSP70 has been excluded in this study, which is an infection, malignant disease, was in chemotherapy and or radiotherapy, severe liver function impairment, severe renal function disorders and autoimmune disease (Dybdahl et al 2005, Satoh et al 2006, Zhang et al 2010, Haan et al 2013) This fact has conformity with theory and previous research. Theory immunopathogenesis of inflammatory response after acute myocardial infarction state that HSP70 plays a role as a 'danger signal' issued by myocardial cells undergo "stressed". Research conducted by stating dybdahl peak levels of HSP70 correlated with peak levels of troponin T and CKMB (Dybdahl et al 2005, Satoh et al 2006, Haan et al 2013).

Extracellular HSP70 levels and left ventricular diastolic function

Data from this study showed significant differences in left ventricular diastolic function, namely DT on admission ($p = 0.001$) and after 3 months ($p = 0.035$), the ratio E/A on admission ($p < 0.001$) and the ratio E/E' on admission ($p = 0.001$) and after 3 months ($p < 0.001$) based on serum levels of HSP70. Almost all parameters of diastolic function were significantly different based on the levels of HSP70 unless the ratio E/A after 3 months. Not all echocardiographic parameters of diastolic function had a significant correlation with the levels of HSP70. There is a weak positive correlation between the levels of extracellular HSP70 with the ratio E/A on admission ($r = 0.373$; $p = 0.003$), the ratio E/E' on admission ($r = 0.324$; $p = 0.011$) and after 3 months ($r = 0.382$; $p = 0.006$), and a weak negative correlation with DT on admission ($r = -0.322$; $p = 0.012$). This happens because the parameters of diastolic function is influenced by many factors such as age, gender, presence or absence of diabetes, hypertension, and treatment status. Results of this study have conformity with the study of Li et al (2013) which analyzed the effect of HSP70 on the incidence of heart failure in rats. The study mentions significant correlation between plasma HSP70 levels LA diameter ($r = 0.202$, $p = 0.05$) and LA pressure ($r = 0.279$, $p = 0.01$) but there is no significant correlation between plasma levels of HSP70 with LVEF.

The research data on the relationship of HSP70 with left ventricular diastolic function is very limited. Several studies have been done revealed a correlation ratio E/E', deceleration time and LA volume with troponin T and CKMB as well as the incidence of heart failure in patients with AMI. Several previous studies demonstrate the value of DT < 130 ms an independent predictor of the incidence of heart failure and mortality for 14 days in patients with AMI (Moller et al 2006).

Left ventricular diastolic dysfunction in patients with ACS is not known with certainty. Some conditions may explain the mechanism of occurrence of left ventricular diastolic dysfunction include myocardial ischemia, fibrosis, and scarring due to extensive myocardial infarction. Myocardial ischemia will issue a "danger alarmin" one of which is HSP70. The HSP70 binds to pattern recognition receptors (PRR) on myocardial cells around it so it activates immunological response. Immunological response that occurs in the form of the release of several inflammatory mediators that TNF-α, IL-6 dan IL-1β. The inflammatory mediators play a role in the occurrence of left ventricular remodeling after AMI. Remodelling occurs in the acute phase and latency. The conditions resulted in a slowdown in relaxation, distensibility disorders, and increased passive stiffness which result in left ventricular diastolic dysfunction. Diastolic dysfunction can be identified by abnormalities of left ventricular filling dynamics through noninvansif namely echocardiography examination (Poulsen 2001, Persson et al 2007, Ohara & Little 2010).

Extracellular HSP70 levels and left ventricular MPI

This study showed significant differences in left ventricular MPI on admission ($p < 0.001$) and after 3 months ($p < 0.001$) based on the levels of HSP70. MPI value larger group II which despite a decline in the value of MPI after 3 months the value is still above the normal values. The phenomenon indicates that the group is still going on HSP70 high systolic and diastolic dysfunction globally after 3 months. By contrast, in the group of HSP70 low, after 3 months of follow-up its value becomes normal MPI well with PW and TDI method. This study showed a significant positive correlation strong between serum HSP70 levels with left ventricular MPI both PW and TDI at the first admission and after 3 months of post-attack SKA.

MPI has been demonstrated as an independent prognostic factor in the initial phase of myocardial infarction associated with heart failure. This index is significantly highly sensitive in predicting patients with clinical output ugly and become independent predictors for cardiac events when hospitalization. In the later phase of this index became independent predictor of death, heart failure and new cardiac events. Facts obtained from this study have conformity with theory. In the event of IMA, there will be changes in myocardial relaxation and contraction. Myocardial contraction and relaxation depend on the energy that myocardial dysfunction causes elongation of

isovolumetric contraction time (iVCT) and the shortening of the ejection time (ET). Elongation isovolumetric relaxation time (IVRT) indicates diastolic dysfunction. When the systolic and diastolic dysfunction that can simultaneously generate value MPI. From this fact HSP70 serum can be used as one of the possible biological marker of prognosis of the left ventricular MPI in patients with ACS.

Levels of HSP70 and left ventricular systolic function

This study shows there is a strong negative correlation between the levels of HSP70 significant serum with LVEF by Simpson's biplanes during the first admission measurements ($r = -0.689$; $p < 0.001$) and after 3 months of post-attack SKA ($r = -0.705$; $p < 0.001$). This negative correlation indicates the higher levels of serum HSP70 then LVEF further down. This has the conformity with the results of previous studies.

Compared with diastolic function, LVEF had a stronger correlation to the levels of HSP70 in patients with ACS. This is consistent with the theory that the extracellular HSP70 is a 'danger alarmin' that initiate the inflammatory process and result in better left ventricular remodeling in the early phase and further. HSP70 indirectly lead to an influx of excessive intracellular Ca2+ thereby inducing myocardial cell death. Myocardial contractility disrupt cell death of myocardial cells were assessed via LVEF. This fact allows HSP70 serum is used as a biological marker for prognostic against left ventricular systolic function (Dybdahl et al 2005, Satoh et al 2006, Haan et al 2013).

Levels of HSP70 and clinical exodus of patients with SKA at xix onths observation

During the 6-month observation period, there are 33 subjects who had heart failure, 5 subjects had rehospitalisasi, and 12 subjects with Olehkarena cardiac death. Exodus clinically assessed by analysis of survival by Kaplan-Meier method showed the form of the presence of extracellular HSP70 significant influence on the incidence of heart failure denganHR HSP70 high and low groups on the incidence of heart failure by 5.35 on the CI 95% (2.25 to 12.7) and p value < 0.001. May mean that any time a group HSP70 high of 5.35 times as likely to develop heart failure than the low HSP70 group. In contrast, this study can not prove a link between levels of extracellular HSP70 on the incidence and mortality due rehospitalisasi cardiac. Until now, studies evaluating the effect of extracellular HSP70 on clinical output ACS patients followed for up to 6 months is very limited. Research by Satoh et al (2006) evaluated the effect of serum levels of HSP70 on the incidence of heart failure for 14 days after the onset of chest pain. The study showed that heart failure occurred in 15 of 52 patients with AMI during the observation period of 14 days after onset. HSP 70 levels were significantly higher in patients with heart failure. There is a significant negative correlation between serum HSP70 levels with the incidence of heart failure during the 14-day observation period after the onset of chest pain. The study by Li et al (2013) involving rats mentioned that increased HSP70 levels correlated with the progression of heart failure and possible can be used as a potential biomarker for early screening for heart failure.

Based on existing theories, extracellular HSP70 acts as a 'danger alarmin' which will activate the inflammatory response through TLR-4. Activation of TLR-4 will increase the release of inflammatory cytokines, namely TNF-alpha, IL-6 and IL-1β which play a role in the remodeling of the left ventricle. Previous studies stated that HSP70 correlates with extensive myocardial infarction. Wide degree of myocardial infarction effect on left ventricular function, heart failure incidence, mortality, and rehospitalisasi due to cardiac (Dybdahl et al 2005, Satoh et al 2006, Haan et al 2013).

Analysis of survival in this study showed that there was no correlation between the levels of HSP70 with clinical output in the form of death and rehospitalisasi. Studies conducted by Jenei et al (2013) on patients postcardiac successful arrest resuscitation, useful extracellular HSP70 as a new biomarker for estimating prognosis and predicts mortality for 30 days regardless of age, gender, complications, and APACHE II score. Different studies but by the same researchers mentioned that HSP70 levels above the median is an independent predictor of mortality within 5 years, the incidence of heart failure regardless of age, gender, body mass index, creatinine, and NT proBNP. Ektraselular concluded that HSP70 is useful to estimate survival in patients with heart failure (Jenei et al 2013). Studies by Eapen et al (2012) involving 3763 subjects with CHD as evidenced by coronary angiography, mentioning that the FDP, CRP, and extracellular HSP70 useful as a strong predictor of the risk of death and myocardial infarction over the next 2.5 years. Differences in the results obtained in this study may be due to small sample size and the influence of some prognostic factors associated with mortality and morbidity in ACS that are not controlled in this study.

CONCLUSION

There is a relationship of extracellular HSP70 levels with left ventricular systolic function were assessed with LVEF at admission and after 3 months of

observation; HSP 70 levels of correlation with left ventricular diastolic function parameters based on the ratio E/A, DT time of admission, and the ratio E/E' on admission and after 3 months of observation; there is a relationship in the form of a positive correlation was between systolic and diastolic function of the left ventricle were assessed globally with LV MPI both traditional and Doppler on admission and after 3 months of observation with extracellular HSP70 levels in patients with ACS; there is a relationship between the levels of extracellular HSP70 with clinical output in the form of heart failure, while the death and rehospitalisasi no significant association.

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