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Program and Abstract Book





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CORRELATION BETWEEN PLASMA APELIN LEVEL AND DIASTOLIC DYSFUNCTION IN PATIENTS HEART FAILURE WITH PRESERVED EJECTION FRACTION

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INTRODUCTION

Heart failure is one health problem with high morbidity and mortality worldwide. Epidemiological survey of heart failure in Asia, said that the prevalence of heart failure in China is 1.26% of the entire population, in Malaysia stated that the figure of 1,435 hospital visits, 6.7% were patients with heart failure, in Japan mentioned that there is 1 million people who suffer from heart failure in 2012 (0.7% of the population). Indonesia does not have exact data on the prevalence of heart disease, at Harapan Kita Heart Hospital, every day there are about 400-500 people with outpatient and approximately 65% are patients with heart failure. Registry in Asia, which in Japan say that more than half (65.2%) patients with heart failure have a left ventricular ejection fraction that normal or near normal and is known as heart failure with preserved ejection fraction (HFPEF), with hypertension and old age as a major risk factor. Large-scale research on heart failure in Europe mentioned that heart failure patients with normal ejection fraction have the same mortality rate as in patients with heart failure with reduced ejection fraction.

Hypertension is a risk factor that most often found in cases of heart failure with preserved ejection fraction, which almost all patients with heart failure with preserved ejection fraction appeared to have a progression hipertensi.^{4,6-8} In hypertensive patients, there was a condition of pressure overload or chronic tension loads that cause structural changes and functional cardiac

preceded by left ventricular hypertrophy, diastolic dysfunction, failed heart with normal ejection fraction, or often referred to as diastolic heart failure, and when it happens cardiac chamber dilatation may occur a heart failure with systolic dysfunction.

Significant differences both structurally and functionally found in heart failure with systolic and diastolic dysfunction, but clinical presentation between the two are the same, the presence of signs and symptoms of heart failure.^{6,8} The process of fibrosis and damage to the heart muscle cells occurs in both heart failure with normal ejection fraction or decrease with different.

Apelin is the endogenous ligand of the APJ receptor which is one of a group of G protein coupled receptors (GPCRs) that play a role in the control of cardiac function.^{20,21} Apelin is produced by cardiac muscle cells and has a beneficial effect on the heart as a vasodilator, increase myocardial contractility, increase cardiac output and maintain cardiac performance during a cardiovascular stress such as at a state of pressure overload or chronic pressure load.

Apelin increased significantly in conditions of chronic pressure load than normal and significantly reduced systolic dysfunction with a significant decrease occurred in cardiac fibrosis and suffered damage to the most severe heart muscle.

METHODOLOGY

Subjects were hypertensive patients with heart failure and preserved ejection fraction at dr. Hasan Sadikin Hospital who meet the inclusion and exclusion criteria. Inclusion criteria for the study are hypertension with heart failure and left ventricular ejection fraction $\geq 40\%$. The exclusion criteria of the study are atrial fibrillation, coronary heart disease, diabetes mellitus, obesity and chronic renal failure.

This research is the type of clinical epidemiology with the cross-sectional design, descriptive data analysis followed by correlation and regression analysis.

The data are in the form of apelin levels that taken from peripheral blood parameters associated with diastolic dysfunction, namely tissue Doppler imaging (TDI) or the ratio of E / e 'and the relationship was assessed by correlation and regression analysis. The experiment was conducted at the Outpatient Installation Noninvasive Cardiac Diagnostic Department and Division of Cardiology and Vascular Medicine, HasanSadikin Bandung. This study was conducted from January to April 2014.

RESULT

Characteristics of the study subjects are listed in Table 1.

Table 1 General Characteristics of Research Subjects

Characteristics	Average	Median (range) or number (%)
Age	58.72(11,02)	
Gender		
Male – (%)		24(48%)
Female– (%)		26 (52%)
Systolic blood pressure		130 (120-180)
Diastolic blood pressure		90 (70-100)
Heart frequency		80 (70-91)
IMT	24,14 (3,88)	
Hypertension length		5 (1-30)
EF		65(49-77)
Diastolic function		
TDI	10,32 (2,40)	
E/A		0,775 (0,43-1,53)

Dec Time	228,2 (33,82)	
IVRT		94,5 (70-177)
Apelin level		1080,5 (999,3-1113)
Drugs used		
ACE Inhibitor		42 (84%)
ARB		3 (6%)
Beta Blocker		6 (12%)
CCB		27 (54%)
Diuretics		1 (2%)

In the characteristic data table above, the subject of the research presented 50 samples studied, obtained male subjects were 24 (48%) and women were 26 (52%), the average age of the study subjects was 58.72 (11.02) years , body mass index, an average of 24.14 (3.88) kg / m². Systolic blood pressure obtained median 130 (120-180) mmHg and diastolic blood pressure to the median of 90 (70-110) mmHg. The frequency of cardiac is median 80 (70-91) x per minute. The median ejection fraction 65 (49-77)%. Long suffered from hypertension median of 5 (1-30) years. The drugs used were angiotensin converting enzyme inhibitors (ACEI) as many as 42 (84%), calcium channel blockers (CCB) by 27 (54%), beta-blockers were 6 (12%), angiotensin II receptor blocker (ARB) as 3 (6%) and diuretics 1 (2%). The results of measurements of diastolic function on the subject of this study is to measure the average TDI with 10.32, deceleration time average of 228.2 seconds, the ratio of E / A median of 0.77 (0.43 to 1.53), IVRT median 92 (59-177) seconds. Apelin levels in subjects of this study is the median 1080.5 (993.2 to 1113) pg / ml.

Analysis to determine the relationship between apelin levels with diastolic dysfunction performed using the Spearman rank correlation test because the data were not normally distributed. The results that obtained as shown in Table 2, 3 and Figure 1 that mapped in scatter plots.

Table 2 Correlation Levels of Apelin with Diastolic Dysfunction (TDI)

characteristics	Mean (SD)	Median (range)	Coerelation coefisien (r)	P value
Apelin levels (pg/ml)		1080,5 (993,2-1113)	0,345	0.14
Diastolic dysfunction (TDI)	10,324 (2,40)			

Remarks: Correlation analysis using Spearman rank test, significant if $P < 0.05$

From Table 2 it can be concluded that there is a positive correlation between apelin levels with diastolic dysfunction (TDI) with a value of $r = 0.345$ and $p = 0.014$ (< 0.05). This means that the higher levels of apelin, the more severe diastolic dysfunction (TDI).

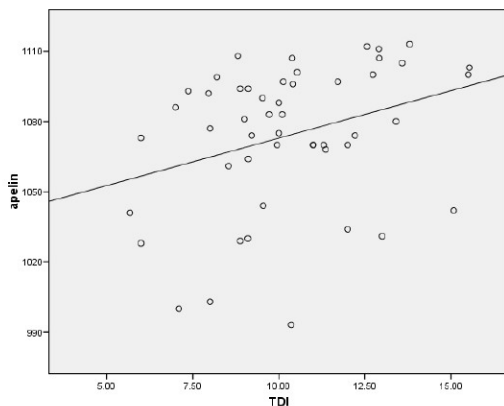


Figure 1 Relationship between Levels of Apelin and Diastolic Dysfunction

Table 3 shows that the significant correlation between apelin levels with diastolic dysfunction is only happened if measured by TDI method, while the method of examination of diastolic

function such as IVRT, mitral inflow (E / A) and deceleration time showed no significant correlation.

Table 3 Correlation with Various Levels of Apelin Parameter Diastolic Dysfunction

Parameter	Correlation Coefficient (r)	P value
TDI	0,345	0,014
E/A	-0,27804	0,0506
IVRT	-0,0160	0,912
Dec Time	0,0208	0,885

Remarks: Correlation analysis using Spearman rank test, significant if $P < 0.05$

DISCUSSION

The result of this study is that there is a positive correlation between apelin levels with diastolic dysfunction as measured by the method of TDI (septal). This is consistent with the hypothesis of this study states that there is a positive correlation between apelin levels with diastolic dysfunction which means that the higher levels of apelin, the more severe diastolic dysfunction were assessed by examination of TDI.

Research that supports this research is a research by Cuban and friends conducted in rats treated by chronic pressure load, the results of these studies indicate that there is an increase in apelin levels in mice with chronic pressure load, accompanied by changes in its structure in the form of heart muscle hypertrophy heart and apelin levels decreased when there has been a

decline in cardiac systolic function characterized by decreased fractional shortening in the rat heart.

Process that can explain the increased levels of apelin on heavy pressure load conditions described by research conducted by Scimia and friends stating that the APJ receptor that is active on the apelin receptor is a receptor that is sensitive to mechanical stimuli (mechanosensor). It is based on the results of research that says that apelin released by heart muscle cells when there is stimulation in the form of high pressure loads and APJ activation causes an increase in the size of these cardiomyocyte cells and induces molecular marker for hypertrophy.

Other studies that give different results and it is important to be discussed is the research conducted by Kosmala and friends which were performed on a population similar to this study which are hypertensive patients with heart failure, but has the opposite result with this research that there is a negative correlation between the levels of apelin with dysfunction diastolic strain measured by the method, which means that apelin levels were significantly decreased in hypertensive patients with diastolic and systolic dysfunction were more severe.

Different measuring devices to measure diastolic dysfunction may be the cause of the different results in these two studies. TDI method and strain method to measure diastolic dysfunction mention that the TDI is more sensitive to assess the pressure load on the left ventricle, while the strains is more sensitive to assess interstitial fibrosis and myocardial viability. This supports the notion that the research subjects Kosmala and friends study may have broader process of fibrosis compared to subjects in this study so as to produce the final result with a different and even opposite conclusions.

The research of Kosmala and friends also examined the correlation between apelin levels with diastolic dysfunction that were examined with TDI method, but the results showed no

significant correlation. Further analysis showed that the value of TDI in subjects of Kosmalaad friends study had relatively higher results than the value of TDI on the subject of this research. This raises the suspicion that there is a possibility the TDI value of certain positive correlation between apelin levels and diastolic dysfunction will disappear even turn out to be negative, especially when there is a high pressure load and accompanied by extensive fibrosis process and characterized by decreasing levels of apelin despite the higher TDI values. The cut off point when there is a loss of correlation between apelin levels with diastolic dysfunction and later turned into a negative is not known so far.

Clinically the meaning of apelin associated with this research is the diastolic dysfunction, apelin levels assessment may have a greater potential to be used as a prognostic parameter than the TDI because the results show that apelin levels were positively correlated with the TDI value, but the value of a particular TDI correlation this positive will disappear even turn out to be negative which occurs when a high pressure load but with a fairly extensive fibrosis process. The cut off point apelin which showed correlation with changes in diastolic dysfunction (TDI) is still unknown until today and requires further research with a larger sample size to represent the entire clinical picture of heart failure with normal ejection fraction.

CONCLUSION

The results of this study showed a positive correlation between the levels of apelin with diastolic dysfunction that is assessed with TDI.

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