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Association between Arterial Stiffness and Left Ventricular Diastolic Dysfunction in Stable Coronary Heart Disease

Running head: Arterial Stiffness dan Cardio-Ankle Vascular Index

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Abstract*---*Background *Arterial stiffness is one of coronary heart disease risks that exacerbates vascular and myocardial function. Arterial stiffness causes an increase in systolic pressure and decreases diastolic in the left ventricle. Cardio-ankle vascular index (CAVI) is a new tool used to detect arterial stiffness.*

Objectives

Analyzing the correlation between arterial stiffness using cardio-ankle vascular index with left ventricular diastolic dysfunction in patients with stable coronary heart disease

Method

The study was conducted from March to May 2015. Data collected were age, gender, laboratory examination, echocardiography for diastolic function, ejection fraction, and CAVI. The data then were analyzed using SPSS (SPSS, Inc., Chicago, IL).

Result

The samples were 32 respondents (78.1% of males, average age of 58.22±7.6 years). The result of CAVI statistic test with diastolic dysfunction was r =0.394 and p value =0.026 (α =0.05).

Conclusion

There was a significant positive correlation between Arterial stiffness using CAVI with left ventricular diastolic dysfunction.

Keywords*---*Arterial stiffness, Cardio-ankle vascular index, Diastolic, Left ventricular

I. BACKGROUND

The National Center for Health Statistics in 2011 mentioned that in the United States, cardiovascular disease was the death leading cause of coronary heart disease, and as the most common type of cadavascular disease causing deaths of 405 thousand three hundred and nine in 2008. Each year 785 thousand people had heart attacks for the first time, and 470 thousand people suffered a re-attack (1).

Arterial stiffnes is associated with atherosclerotic risk factors and is a marker of the development of cardiovascular disease (2). Patients with coronary heart disease showed an increase in arterial stiffness, compared to non- coronary heart disease patients. Arterial stiffness is also associated with the severity of coronary atherosclerosis (3, 4). Arterial

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stiffnes also occurs in hypertensive patients, diabetes mellitus, dyslipidemia, obesity and metabolic syndrome. Evaluation of arterial stiffness is widely used to determine cardiovascular risk and monitor the success of therapy based on these relationships (5, 6).

Enhanchment of arterial stiffness increases systolic pressure and decreases diastolic pressure, induced ventricular hypertrophy or increased cardiac stiffening (7). Increased systolic pressure will increase left ventricular pressure and cause left ventricular hypertrophy which is a major determinant of left ventricular diastolic dysfunction. Arterial stiffness contributes to the occurrence of diastolic dysfunction through increased pulse pressure and left ventricular afterload, which can aggravate sub-endocardial ischemia, interfere myocardial relaxation and cause interstitial fibrosis, all of which will decrease left ventricular compliance. Further, coronary artery supply is decreased due to decreased diastolic pressure, then this cardiac fibrosis can be more significant in patients with coronary heart disease (8). The process of vascular stiffening and left ventricular diastole dysfunction occurs prior to the onset of symptoms. Therefore, early detection of arterial changes and ventricular performance may be useful for the prevention of cardiovascular complications (9).

Some parameters are used to measure arterial stiffness such as pulse pressure, pulse wave velocity, β parameters and so on. Each parameter has advantages and disadvantages. Measurement used is CAVI. CAVI is developed to measure arterial stiffness precisely, based on the theory of β stiffness parameters that are theoretically independent through changes in blood pressure. CAVI, with these special advantages has been widely used to determine arterial stiffness in people with cardiovascular disease, including patients with coronary heart disease, and stroke, as well as individuals with cardiovascular risk factors such as hypertension, diabetes, old age, and obesity (8, 10).

The ability of CAVI to measure can be used to prevent cardiovascular disease risk. CAVI can also be used for early detection of arteriosclerosis and preventive action to change lifestyle. In addition, CAVI is also used to evaluate quantitatively the progression of disease and the effectiveness of therapy given (8). Diastolic dysfunction is a significant determinant of functional capacity in patients with stable coronary heart disease. Coronary heart disease is also common in patients with heart failure with favorable fraction ejection, and contributing to the occurrence of heart failure, thereby it is one of targeting therapies (11).

Research (4) mentioned a relationship between CAVI with left ventricular diastolic dysfunction in patients with coronary heart disease. Previous studies conducted (12, 13) also showed an association between arterial stiffness and the occurrence of diastolic dysfunction in the general population. Studies in populations with cardiovascular risk factors also showed the same (14). Parameters used to measure arterial stiffness and diastolic function also vary with various advantages and disadvantages. CAVI as one of measuring arterial stiffness method is a relatively new, easy, cheap, operator-dependent free, and superior compared to other arterial stiffness measurement that have not been widely used (8).

Based on these things, this study evaluated the correlation between arterial stiffness measured by CAVI in the presence of left ventricular diastolic dysfunction in patients with stable coronary heart disease.

II. METHOD

Respondents were stable coronary heart disease patients who underwent treatment in Dr. Soetomo General Hospital Surabaya, Indonesia. Inclusion criteria of respondents was male or female aged >40 years. The exclusion criteria of respondents were having ejection fraction <50%, restrictive cardiomyopathy and hypertrophic

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cardiomyopathy, having severe valvular disease, acute coronary heart disease, atrial fibrillation, chronic kidney disease, peripheral arterial disease with ABI value <0.9, and congenital heart abnormalities.

This research was conducted from March to May 2015. Before the research, it was done an ethical test and respondents filled out informed consent. The data collected were age, gender, laboratory examination, echocardiography for diastolic function, ejection fraction, and CAVI. The cardio-ankle vascular index examination was performed automatically using VS-1500 VA Sera (Fukuda Denshi, Tokyo, Japan) machine by lying down the subjects, after 5-10 minutes, a blood pressure monitor, electrocardiography, and cardiographic phonography were turned on. On CAVI examination, an ECG electrode was placed on both wrists, a microphone for phonography placed in the sternum of the second intercostal space area, 4 cuffs of blood pressure placed on all four extremities. In this way the ankle-brachial index, toe-brachial index, augmentation index, aortic pulse wave velocity and blood pressure in the upper arm and ankle could be measured by plethysmography.

The collected data were then analyzed in accordance with the independent and dependent variables to enforce the hypothesis. Statistical analysis used was spearman correlation test with α =0.05 using SPSS program (SPSS, Inc., Chicago, IL).

III. RESULT

Respondent's Characteristic

The samples chosen in this study consisted of 25 males (78.1%) and 7 females (21.9%). The average age was 58.22±7.6 years with average time of suffering stable coronary heart disease for 49.8±18 months. The average body mass index was 25.0±4, which meant included in overweight. The average systolic blood pressure was 129.9±21.47 and diastolic blood pressure was 77.56±12.49 mmHg that was within normal limits (table 1).

The most modifiable risk factors found were hypertension as much as 53%, then dyslipidemia as much as 50%, smoking as much as 50% and diabetes mellitus as much as 25%. There were 46.9% of subjects having 1 risk factor, 34.4% having 2 risk factors, 15.6%, having 3 risk factors and 3.1% having 4 risk factors (table 2).

Research subjects with stable coronary heart disease who also suffered hypertension received ACE inhibitor or ARB therapy and 100% calcium channel blocker. Research subjects with coronary heart disease who sufferedd diabetes mellitus received glimepirid and metformin therapy as much as 100%. Coronary heart disease therapy obtained by all research subjek included beta blockers, aspirin, isosorbid dinitrat and simvastatin. Clopidogrel was consumed by 4 subjects (table 3). Subjects with CAVI >9 was 8 people, with CAVI 8-9 was 9 people and with CAVI <8 was 15 people (table 4).

IV. Data Analysis

The correlation test results showed a significant positive correlation between CAVI and left ventricular diastolic function, with r =0.394, and p value =.026 (α = 0.05; table 5). Diastolic parameters of other dysfunction had significant correlation between CAVI and E/A with p = .03 and r =0.38 and decelaration time with p =0.04 and r =-0.36. However CAVI showed no significant correlation with E 'septal, E' lateral and E/E '(Table 6). No significant correlation between CAVI or diastolic dysfunction with clinical characteristics such as age, duration of illness, BMI, systolic and diastolic blood pressure, and risk factors (Table 7).

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V. DISCUSION

Among some arterial stiffness parameters, pulse wave velocity is the most commonly measurement method used in studies, although there are some problems with the use of this tool, such as technical complications. CAVI is a new tool using β and pulse wave velocity parameters that has shown accuracy in detecting arterial stiffness and atherosclerosis, therefore in this study CAVI was chosen as a tool to measure arterial stiffness. Another thing is that CAVI assesses arterial stiffness in the aorta, femoral artery and overall tibial artery (4).

Previous studies have shown that CAVI as a relatively new parameter for the measurement of higher arterial stiffness in patients with coronary heart disease compared to patients without coronary heart disease (15). Arterial stiffness in patients with coronary heart disease is higher than patients without coronary heart disease, and is associated with the severity of coronary atherosclerosis (16). Previous studies have also suggested that CAVI increased with the increasing of affected coronary arteries (17). CAVI as an arterial stiffness parameter is also associated with cardiovascular incidence, and is an important predictor for recurrence of cardiovascular in post-myocardial infarction patients with impaired left ventricular systolic function. Thus determining arterial stiffness value is useful for risk stratification (4).

CAVI is associated with left ventricular diastolic dysfunction, which is assessed using echocardiography (15). CAVI is significantly higher in patients with left ventricular diastolic dysfunction, than in patients with normal diastolic function (14). The relationship of CAVI and left ventricular diastolic function had been discussed in several studies, in patients with cardiovascular risk. As previously mentioned, left ventricular diastolic dysfunction occured prior to left ventricular systolic dysfunction in patients with cardiovascular risk (15). Increased arterial stiffness changes the shift pressure wafe reflection from diastole to systole, thereby causing an increase in systolic pressure and decreasing diastolic pressure (4).

Theoretically, examination with mitral inflow is easy to do, well described, and as a basic pattern of diastolic function categorization. Tissue dopler imaging has an advantage unaffected by various ventricular loading conditions compared to mitral inflow. However tissue doppler imaging has technical and clinical limitation. Technical limitation includes sampling. It is needed to be noted location, filters, and minimal angulation with anular motion to get reliable measurements. Clinical limitation, E/E’ parameter is inaccurate in some conditions where E' septal is higher than E 'lateral, for example in a localized disease process such as myocardial infarction, on severe lateral anular calcification or in mitral valve disease. The value of E 'will be higher in moderate to severe mitral regurgitation. It is preferable to use the average of E 'if there is a suspected regional dysfunction(18, 19).

The study (20) reported that arterial stiffness associated with diastolic dysfunction. This study used baPWV to measure arterial stiffness and E/A values as a measuring parameter of diastolic dysfunction. A research (4) using CAVI and E/A values in patients with coronary heart disease also showed similar correlations. Another study (21) reported that the arterial stiffness relationship was measured by augmentation index with diastolic dysfunction using tau index in the coronary heart disease population meanwhile this research (14) found a significant correlation between arterial stiffness using CAVI with diastolic dysfunction as measured by E/A in population with cardiovascular risk. Only this study (13) that used E/E 'and showed the same level of correlation as previous research.

The weakness of this cross-sectional study can not determine the exact mechanism, which underlies the relationship between arterial stiffness and diastolic dysfunction. Research on the association of both has been done

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worldwide and biologically reasonable although its mechanism has not been clear yet. A theory stated that arterial stiffness which is a coronary heart disease risk factor will cause changes in wave propagation during systolic and diastolic. Fast-propagation of waves in stiff arteries lead to increase systolic pressure and lower aortic pressure at diastolic time. The result is an increase in systolic afterload and decrease coronary perfusion when diastolic, leading to a decrease in left ventricular relaxation. Supply of the coronary artery also decreases because of a decrease in diastolic pressure, and this decrease is more significant in patients with coronary heart disease, leading to myocardial fibrosis (20).

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VII. CONFLICT OF INTEREST

No conflict of interest was anticipated. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Table 1: Descriptive data

Variable	Mean
N	32
Age (year)	38.21±7.6
IMT (Kg/m^2)	25±4
Disease duration (month)	49.8±18
Sistolic TD (mmHg)	129.9±21
Diastolic TD (mmHg)	77.56±12.5
Hypertension (%)	53.1
Smoking (%)	50
Diabetes mellitus (%)	25
Dislipidemia (%)	50
Ejection Faction (%)	57.18±2.3

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CAVI	7.8±1.17
E/A	0.91±0.34
E/E'	7.7±1.2
E' (septal)	6.7±0.6
E' (lateral)	8.4±1.34
Deceleration time	238±51.95

Table 2: Total of Risk Factor

Risk Factor	Mean
1	15 (46.9%)
2	11 (34.4%)
3	5 (15.6%)
4	1 (3.1%)

Table 3: Distribution of IL-6 and EF values before and after therapy

Risk factors and therapy	Mean
Hypertension	17 (53.1%)
- ACE inhibitor/ARB	17 (100%)
- CCB	17 (100%)
Diabetes mellitus	8 (25%)
- Glimepirid	8 (100%)
- Metformin	8 (100%)
Smoking	16 (50%)
Dislipidemia	16 (50%)
- Statin	32 (100%)

Table 4: Risk factor frequency based on CAVI

	CAVI <8	CAVI 8-9	CAVI >9
Total	15 (46.9%)	9 (28.1%)	8 (25%)
Hypertension	8 (53.3%)	7 (77.8%)	2 (25%)
Smoking	8 (53.3%)	2 (22.2%)	6 (75%)
Diabetes mellitus	3 (20%)	3 (33.3%)	2 (25%)
Dislipidemi	4 (26.7%)	9 (100%)	3 (37.5%)

Table 5: Results of spearman correlation analysis

	CAVI Score
Diastolic dysfunction score	r=0.394
	p=0.026

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n=32

Table 6: Correlation of CAVI and echocardiographic parameters of diastolic dysfunction

	CAVI	
	R	p
E/A	0.38	0.03
E/e’	0.13	0.49
E’ septal	0.024	0.89
E’ Lateral	0.11	0.56
Decelation time	-0.36	0.004

Table 7: Correlation between CAVI or dysfunction and clinical characteristics

	CAVI		Diastolic Dysfunction	
	r	P	r	p
Hypertension	-0.14	0.43	-0.17	0.33
Smoking	0.08	0.66	0.27	0.14
Diabetes mellitus	0.07	0.7	-0.08	0.67
Dislipidemia	0.24	0.17	-0.27	0.14
Age	0.20	0.26	-0.01	0.95
Disease Duration	0.13	0.48	0.1	0.58
IMT	0.01	0.95	-0.11	0.53
TDS	0.16	0.38	-0.23	0.20
TDD	0.14	0.46	-0.11	0.53

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