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ASSOCIATION BETWEEN LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AND SEVERITY OF CORONARY ARTERY DISEASE IN NSTEMI PATIENTS

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Abstract

Background : Myocardial ischemia caused by coronary artery lesion can cause systolic and diastolic dysfunction. Diastolic dysfunction is a result from ineffective left ventricle relaxation. Early identification of extensive ischemia based on diastolic function parameters through echocardiography is very useful. This can provide clinicians with knowledge about the severity of coronary artery lesions so that they can help determine more appropriate treatment strategies.

Methods : A cross-sectional study of NSTEMI patients who underwent coronary angiography were included. LV diastolic dysfunction was assessed by echocardiographic parameters. LV diastolic dysfunction was divided into 3 groups (Grade I, Grade II, and Grade III). Severity of coronary artery lesions were analysed by SYNTAX score, which was further divided into 3 groups (low, moderate, and high SYNTAX score).

Results : A total of 110 patients presented with NSTEMI were included in this study (88 males and 22 females, with mean age 56.9 ± 9.6 years old). Bivariate analysis between SYNTAX scores and baseline characteristics found a significant relationship in age and echocardiographic characteristics such as LVEF, LVEDD, E/A ratio, average E/e' ratio, TR maximum velocity and LA volume index. On the analysis between LV diastolic dysfunction and SYNTAX score resulted in significant relationship with p value <0.001.

Introduction

Coronary artery disease is a leading cause of death worldwide. WHO records the death of as many as 17 million people each year due to coronary artery disease. An estimated 84 million Americans died of cardiovascular disease. This number is expected to increase along with the high rates of obesity and diabetes in the world population. [1,2]

Ischemia that occurs can cause systolic dysfunction and diastolic dysfunction. Diastolic dysfunction occurs due to the ineffectiveness of left atrial emptying to the left ventricle. [3] Early identification of extensive ischemia based on diastolic function parameters through echocardiography is very useful in patients treated with acute myocardial infarction. Echocardiographic assessment has the advantage in terms of efficiency, with a quick and easy examination to do. The combination of parameters E velocity, A velocity, E / A ratio, deceeration time (DT), isovolumic relaxation time (IVRT), and tissue Doppler imaging (TDI) can evaluate overall diastolic function. [3,4]

One marker or predictor in determining the prognosis in patients is the degree of diastolic dysfunction. This is because it is associated with the heavier degree of diastolic dysfunction, the more severe myocardial infarction occurs and the larger infarct area.[5,6,7,8]

This study aims to determine whether there is a relationship between the degree of diastolic dysfunction and severity of coronary artery lesions. This study also aims to determine whether there is a relationship between the characteristics of both risk factors and echocardiographic characteristics with the severity of coronary artery lesions.

Methods

This cross-sectional study was conducted at Haji Adam Malik General Hospital from December 2018 to June 2019. Subjects was all patients diagnosed with NSTEMI and underwent coronary angiography. Patients with poor accoustic window, poor angiography documentation, previous history of CABG and patients with atrial fibrillation were excluded. Patients with history of mitral valve disease, pericardial disease, congenital heart disease were also excluded. Echocardiography was done within 12 hours of admission. LV diastolic dysfunction was analysed and further cathegorized into 3 groups, according to the 2016 ASE/EACVI guideline using the algorithm "Assessment of Diastolic Function in Patients with Depressed LVEF or Underlying Myocardial Disease", which is grade I diastolic dysfunction, grade II diastolic dysfunction, and grade III diastolic dysfunction. Coronary angiography was performed to evaluate the coronary lesion. Severity of coronary lesions were calculated with SYNTAX Score, which were analysed by two interventional cardiologist. SYNTAX score were divided into 3 groups; low (≤22), intermediate (23-32), and high (≥33).

Data processing and analysis of statistical data using SPSS version 22-23. Categorical variables are represented by the number or frequency (n) and percentage (%). Test data normality using Kolmogorov-Smirnoff. To assess the hypothesis whether there is a relationship between the degree of left ventricular diastolic dysfunction through echocardiography and the SYNTAX score obtained from coronary angiography in patients with acute myocardial infarction using the Chi squared test with Yates correction if x2 conditions are met, but if these conditions are not met then the test is used Fisher exact test. P value less than 0.05 is proven to be statistically significant relationship. Research data were tested and analyzed statistically using the help of available statistical tools. The interobserver variability assessment of echocardiographic results and the SYNTAX score will be assessed using the Kappa test (Cohen's Kappa Coefficient).

Results

This research was conducted at the Department of Cardiology and Vascular Medicine of Haji Adam Malik General Hospital by taking data on patients diagnosed and treated with Non-ST Elevation Myocardial Infarction (NSTEMI) from December 2018 to June 2019. This study involved a sample of 110 people from a population with subjects with a diagnosis of Non-ST Elevation Myocardial Infarction (NSTEMI) who underwent echocardiographic examination and coronary angiography that met the inclusion and exclusion criteria so that they could be included in the study.

From the total sample, data collected from history taking, physical examination, echocardiography were done as soon as possible after the patient was treated or within 12 hours of treatment, laboratory examination and coronary angiography examination. Echocardiographic examination results in the form of the degree of left ventricular diastolic dysfunction which will then be recorded. From coronary angiography examination will then be assessed severity of coronary artery lesions using the SYNTAX score. Then the relationship between the degree of left ventricular diastolic dysfunction and the severity of coronary artery lesions will be assessed using the SYNTAX score.

Tabe l. Baseline Characteristics of Research Subjects

Variable	**n=110**
Age (y.o)	56.9 ± 9.6
Sex	
Female	22 (20%)
Male	88 (80%)
Smoker	82 (74.5%)
Hypertension	78 (70.9%)
Diabetes Mellitus	42 (38.2%)
Family History	10 (9.1%)
Laboratory results	
Hb	13.4 ± 2.3
Creatinine	1.3 (0.5-4.4)
Troponin I	1.54 (0.17-32)

CK-MB	67 (17-528)
Random Blood Glucose	145 (80-483)
Echocardiography results	
LVEF	45 (20-69)
Grade I diastolic dysfuction	50 (45.5 %)
Grade II diastolic dysfuction	30 (27.3 %)
Grade III diastolic dysfuction	30 (27.3 %)
Coronary angiography	
CAD 1VD	12 (10.9%)
CAD 2VD	39 (35.5%)
CAD 3VD	53 (48.2%)
Normal	6 (5.5%)
SYNTAX Score	
Low (≤22)	45 (40.9 %)
Intermediate (23-32)	21 (19.1%)
High (≥33)	44 (40 %)

From the bivariate analysis of demographic characteristics with SYNTAX scores grouped into mild and moderate-high SYNTAX scores, a significant relationship was found in age, and echocardiographic parameters such as LVEF, LVEDD, E / A ratio, average E / e ', LAVI, and maximum TR velocity. In the medium-high SYTNAX score group, older patients were found with mean age 58 (± 9) (p value 0.019), lower LVEF with a median value of 41 (20-69%) (p value <0.001), greater LVEDD with a mean of 54 (± 7.0) (p value <0.001), a higher E/A ratio with a median value of 1.8 (0.4 - 3.3) (p value <0.001), a higher mean E/e' with a median value of 1.8 (0.4 - 3.3) (value <p 0.001), greater LAVI with a median value of 33 (18-42) (p value <0.001), higher maximum TR velocity with a median of 2.9 (1.0 - 3.4) (p value <0.001)). The results of the bivariate analysis are attached in table 2.

Table 2. Bivariate Analysis of Demographic Characteristics with SYNTAX Score

Variable	**SYNTAX Score**		**p Value**
	Low (n=45)	**Intermediate-High (n=65)**	
Age	54 (± 10)	58 (± 9)	0.019*
Sex			
Male, (%)	35 (77.7 %)	53 (81.5 %)	0.629***
Female, (%)	10 (22.2 %)	12 (18.4 %)	
Smoker	34 (75.5 %)	48 (73.8%)	0.840***
Hypertension	32 (71.1%)	46 (70.7 %)	0.969***
Diabetes Mellitus	13 (68.8%)	29 (44.6%)	0.095***
Family History	5 (11.1%)	5 (7.6 %)	0.738***
Laboratory results			
Troponin I	1.3 (0.22 - 32)	1.4 (0.17 – 32)	0.525**
CK-MB	64 (18 – 409)	64 (17 – 528)	0.939**
Creatinine	1.4 (0.5 – 4.4)	1.6 (0.8 – 3.1)	0.220**
Echocardiography results			
LVEF (%)	56(38-68 %)	41 (20-69%)	<0.001**
LVEDD	46 (± 6.2)	54 (± 7.0)	<0.001*
E/A Ratio	0.8 (0.6 – 2.2)	1.8 (0.4 – 3.3)	<0.001**
Averaged E/e' Ratio	9.5 (6.1 - 17)	14.5 (5.5 – 31.5)	<0.001**
Maximum TR velocity	1.9 (1.1 – 3.2)	2.9 (1.0 – 3.4)	<0.001**
LAVI	30 (18 – 36)	33 (18 – 42)	<0.001**

Note: * T-test, ** Mann Whitney Test, *** Chi Square

In this study, an analysis of the relationship between the degree of left ventricular diastolic dysfunction and SYNTAX score was evaluated. The relationship was found significant with p value <0.001. The results of the analysis are shown in table 3.

Table 3. Relationship between the degree of left ventricular diastolic dysfunction with the SYNTAX Score

LV Diastolic Dysfunction	SYNTAX Score			p Value
	Low (≤22)	Intermediate (23-32)	High (≥33)	
Grade I	34	11	5	<0.001
Grade II	8	9	13	
Grade III	1	3	26	

Discussion

This study is a cross-sectional study to assess the relationship between the degree of left ventricular diastolic dysfunction and the severity of coronary artery lesions assessed using the SYNTAX score. This study involved 110 patients with diagnoses of Non-ST Elevation Myocardial Infarction who were treated at Haji Adam Malik General Hospital Medan from December 2018 to June 2019 who met the inclusion and exclusion criteria. The patient underwent echocardiographic examination to assess the degree of left ventricular diastolic dysfunction and then performed coronary angiography to assess coronary artery lesions. The severity of coronary artery lesions will then be assessed using the SYNTAX score.

In the moderate-high SYNTAX score group, there was an older age than the low SYNTAX score group. Other characteristics studied such as sex, risk factors for diabetes mellitus, hypertension, and family history of coronary artery disease were not found to have a significant relationship with the SYNTAX score. In a study conducted by Du et al, 2015 which assessed the relationship between LVEDP and severity of coronary artery disease showed a significant relationship on the basic characteristics of patients with coronary heart disease. In this study found a significant relationship in age, male sex, and risk factors for diabetes mellitus with a p value <0.001. Another study assessed the correlation between diastolic dysfunction and coronary artery severity via CT angiography also found a significant relationship between baseline characteristics, risk factors for hypertension and diabetes mellitus for a higher Calcium score.[9]

In the bivariate analysis between demographic characteristics and the degree of diastolic dysfunction also found a significant relationship in age, risk factors for hypertension, LVEF and LVEDD. However, no significant relationship was found in sex, risk factors for diabetes mellitus and smoking. This is consistent with previous research which also found a significant relationship between diastolic dysfunction with age and hypertension risk factors, but not with risk factors for diabetes mellitus.[9]

In the analysis of the relationship between the degree of diastolic dysfunction with the SYNTAX score found a significant relationship with a value of p <0.001. Analysis of the relationship between the degree of diastolic dysfunction with a qualitative assessment of vessel involvement also found a significant relationship with a value of p <0.001. A previous study also proved a positive correlation between severity of coronary artery lesions using the SYNTAX score with diastolic function parameters namely E/A ratio, E/e 'ratio, and LAVI.[10] In a study conducted by Teixeira et al, increased LVEDP have a significant relationship to decreased LVEF and greater LVEDD, with a negative correlation to LVEF and LVEDP of -0.324 (p value <0.01). In this study also found a high LVEDP associated with worse survival for 1 month, 6 months, and 12 months post hospitalization. In this study, LVEDP ≥ 26.5 mmHg had a significant relationship with 1 year mortality after hospitalization.[7]

Previous study also found a significant relationship between SYNTAX scores with echocardiographic parameters such as LVEF, LVEDV, LVESV, E wave, deceleration time (DT), and S' septal wave with a p value <0.005. Multivariate analysis was also carried out in this study and E / A, DT, and S' septal annular waves were obtained as strong predictors of high SYNTAX scores. The E/A ratio greater than 2 has a specificity of 93.9% in predicting a high SYNTAX score.[2]

Acute myocardial infarction accompanied by both diastolic dysfunction and systolic dysfunction has worse prognosis. This has been the focus of study in the past few decades. Studies conducted are to improve strategies for treating acute myocardial infarction better, thus not to fall in the condition of heart failure. If there are clinical and radiographic signs and symptoms of heart failure, this is very consistent with poor outcomes.[11]

Acute myocardial infarction will cause myocardial ischemia, cell necrosis, microvascular dysfunction, and abnormalities in movement of the ventricle wall. These things will disrupt the speed of active relaxation of the heart muscle. In addition, interstitial edema, fibrocellular infiltration, and scar tissue formation will cause myocardial stiffness. This will lead to impaired left ventricular filling.[11]

Early detection of severe myocardial ischemia based on diastolic dysfunction via echocardiography is very important to predict the severity of coronary artery lesions even before doing coronary angiography. Assessment of diastolic dysfunction in patients with acute myocardial infarction can also determine the patient's prognosis.[2] In the initial phase of ischemic heart disease, diastolic dysfunction can be detected using transthoracal echocardiographic examination, long before systolic dysfunction occurs. The E/A ratio as a traditional marker in assessing diastolic function can be assessed using pulsed-wave Doppler on the mitral valve from 4 chamber view on transthoracal echocardiography. As coronary artery disease progresses, the left ventricular wall will become stiffer and will cause impaired LV relaxation. The stiffer left ventricular wall will produce a higher E/A ratio. This will trigger heart failure due to abnormality of left ventricular filling.[2,11]

Tissue Doppler imaging (TDI) can provide comprehensive information on evaluating diastolic function based on the movement of the myocardial segment. Myocardial movements during the heart cycle will be displayed in the spectral pulsed-wave Doppler image. Because the left ventricular apex is relatively fixed, the evaluation of left ventricular basal movement reflects the longitudinal vector of contraction and relaxation of the left ventricle. A condition that causes impaired myocardial relaxation and slowed ventricular filling will produce abnormal movement patterns in the mitral annulus, which will be detected by TDI.[2,11,12]

E/e' ratio greater 15 identifies a left ventricular filling pressure that is more than 12 mmHg when measured using a microcatheter. Increased left ventricular filling pressures indicate ventricular stiffness caused by extensive myocardial infarction in patients with acute myocardial infarction.[8,11,13]

Heart disease progression is a continuum that starts from risk factors. This must be considered early and affect the handling strategies of acute myocardial infarction patients.

Conclusion

Based on data analysis in this study, it was found that there was a significant relationship between the degree of left ventricular diastolic dysfunction and the severity of coronary artery lesions assessed by SYTNAX score. In this study also found a significant relationship between age and severity of lesions based on the SYNTAX score. Patients with a higher SYNTAX score have older age. In the analysis of basic characteristics also found a significant relationship between echocardiographic characteristics with SYNTAX score. Basic echocardiographic characteristics that are significantly related to SYNTAX scores are LVEF, LVEDD, E/A ratio, averaged E/e' ratio, maximum TR velocity, and LAVI.

There was no significant correlation between some risk factors and SYNTAX score; such as diabetes melitus, smoker, and family history of coronary artery disease. However, a near significant p value was found for diabetes melitus. For this reason, the need for further research with a larger sample size to reassess the significance of the relationship between baseline characteristics, including risk factors, and the SYNTAX score.

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