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ASSESSMENT OF GLOBAL LONGITUDINAL STRAIN AS A PREDICTOR OF LESION SIGNIFICANCE IN STABLE CORONARY HEART DISEASE PATIENTS WITH PRESERVED EJECTION FRACTION AT ADAM MALIK HOSPITAL MEDAN

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Abstract

Background : Prevalence of coronary heart disease in Indonesia is increasing by age and become the main cause of morbidity and mortality. However, now it has been found that GLS value can reflect the ischemic and infarct area.

Objective : To assessed Global Longitudinal Strain (GLS) as a predictor of lesion significance in stable coronary heart disease patients.

Methods : This research is a cross-sectional study conducted on 28 coronary heart disease patients with preserved EF who underwent coronary angiography examination at Adam Malik Hospital Medan from February 2020 – July 2020. The GLS examination was carried out using speckle tracking software on late diastolic phase. Spearman correlation test was performed to analyze GLS value with coronary angiography results. Bivariate analysis to evaluate GLS value with coronary angiography parameters was carried out with Chi-square and Fisher's Exact test. P value < 0.05 is said to be statistically significant.

Results : After Spearman correlation test, it was found that the correlation coefficient was -0.733, which means that there is a strong relationship between GLS and significant lesions. Calculation of area under the curve (AUC) found value of 0.923 (P = < 0.001, 95% CI 0.885-0.991). The GLS cut off value is -16.4300 with 85,7% sensitivity of 85.7%, 8,6% false positive rate (1-specificity), and 91,4% specificity.

Conclusion : GLS can be used to predict lesions significance in stable coronary heart disease patients and has an inverse relationship with coronary lesions significance.

Introduction

Cardiovascular disease, especially coronary heart disease (CHD) is the leading cause of morbidity and mortality in the world. Reports from World Health Organization (WHO) in 2013, as many as 17.5 million people die each year due to cardiovascular disease, which is 31% of total deaths in the world. (Mozaffarian D, 2015) In Indonesia, the prevalence of CHD based on a doctor's diagnosis or symptoms is 1.5%, and increases with age to 3.6%. (Ministry of Health RI, 2013)

Coronary heart disease itself is based on atherosclerotic plaques that are progressing. This progressive plaque will cause stenosis and even occlusion that impede myocardium perfusion, causing an imbalance between oxygen demand and supply, which can lead to ischemia and myocardial infarction. (Gloekler S, 2007).

Global Longitudinal Strain (GLS) is a direct echocardiographic assessment of myocardial fibers deformation performed by speckle-tracking echocardiography. Strain is the change in length of an object in a certain direction compared to its original length. Myocardial anatomy consists of endocardial fibers arranged longitudinally in an oblique direction, while middle wall fibers are arranged in a circumferential manner. This causes a non-uniform distribution of Wall Stress (WS). Longitudinally oriented myocardial fibers are located in the subendocardium which is an area prone to ischemia. This makes the longitudinal strain examination sensitive to GLS ischemia by echocardiography which is able to reflect ischemia and infarction area with left ventricular function. (Bukberg et al, 2008).

Material and methods

This research is a cross-sectional study conducted on 28 coronary heart disease patients with preserved EF who underwent coronary angiography examination at Adam Malik Hospital Medan from February 2020 – July 2020. The sample was selected based on inclusion criteria, namely coronary heart disease patients with preserved EF with Biplane Simpson method which was examined by echocardography, coronary heart disease patients with

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preserved EF with Biplane Simpson method who underwent coronary angiography examination, LVEF ≥50% and willing to be research sample; and the exclusion criteria which is having history of acute coronary syndrome, primary valvular heart disease, congenital heart disease, history of coronary bypass surgery, and poor coronary angiography or echocardiography images/videos.

Global Longitudinal Strain (GLS) Assessment Procedure

Echocardiographic examination was performed in lateral decubitus position using Vivid GE S6 machine with 3.50 Mhz heart probe sector. EF examination using Biplane Simpson method. GLS examination was carried out using speckle tracking software on 17 segments of three standard apical views (3-chamber, 4-chamber, and 2-chamber), measurements were carried out in end-diastolic phase, the peak of te R wave on electrocardiogram was used as a reference for end-diastolic value. The endocardial boundary then traced automatically by software. The deformity parameter graph display and appears automatically. The GLS value was obtained from average peak systolic strain value on 17 longitudinal strain areas. After that, all research subjects will be subjected to IKP to assess occlusion location.

Statistical Analysis

For statistical analysis, Spearman correlation test will be performed to assess GLS values and coronary angiography results to find out the correlation and strength of correlation between these two variables. If the results of the correlation test show a significant relationship, then a cut-off GLS value will be taken using an ROC (Receiver Operating Characteristic) curve analysis, then an analysis GLS diagnostic value will be carried out according to cut-off value to assess lesion size according to coronary angiography.

Bivariate analysis for GLS value with coronary angiography parameters will be tested with Chi-square and Fisher's Exact test. To see the difference in characteristics expressed by numerical variables, the Independent T test was used for normal distribution data, whereas if not normally distributed, Mann Whitney test was used. Statistical data analysis using statistical software, p value <0.05 is said to be statistically significant.

Results

This research included 70 subjects who were divided into two groups with proportion of 35 significant lesions patients and 35 insignificant lesions patients. All research subjects have met the inclusion and exclusion criteria according to the research.

Table 1. Characteristics of Research Subjects

Variable	Significant	Non Significant	p value
Age	53,71±7,987	53,09±8,053	0,744
Gender			
Male	31(64,6%)	17(35,4%)	0,001
Female	4(18.2%)	18(81.8%)	
LVEF	53% (50-75)	58(51-67)	0,03
LVEDD	49(33-58)	48(44-54)	0,323
LVEDS	38(23-50)	39(35-48)	0,238
IVSS	13(10-16)	14(12-17)	0,16
IVSD	11(8-15)	12(8-15)	0,324
TAPSE	19,23±3,1	18,23±2,2	0,127
EA	1,38(0,49-4,4)	1,56(0,49-5,5)	0,738
GLS	-12,34±3,35	-17,92±1,20	<0,001
Hb	12,4±1,21	12,857±1,5	0,224
Leucocyte	7746±1532	7415±1807	0,412

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Trombocyte	185000(156000-321000)	189000(159000-283000)	0,902
Natrium	126,17±5,6	125,7±5,6	0,753
Kalium	3,9(3,0-4,0)	3,9(3,1-4,4)	0,645
Clorida	98(88-110)	95(88-105)	0,327
Ureum	56(12-98)	28(13-63)	<0,001
Creatinin	0,81(0,25-1,95)	0,80(0,31-2,15)	0,698
Dyslipidemia			0,001
Yes	26(37,1%)	11(15,7%)	
No	9 (25,7%)	24(68,6%)	
DM			
Yes	25(71,4%)	10(28,6%)	0,001
No	10(28,6%)	25(71,4%)	
Hipertension			
Yes	29(41,4%)	15(21,4%)	0,001
No	6(17,1%)	20(57,1%)	
Smokers			
Yes	30(85,7%)	13(37,1%)	<0,001
No	5(14,3%)	22 (62,9%	

Analysis Spearman Correlation Test and ROC (Receiver Operating Characteristic) Between Global Longitudinal Strain (GLS) and Significance of Intracoronary Lesions

Spearman correlation test was used to see the extent of relationship between Global Longitudinal Strain (GLS) and Significance of Intracoronary Lesions. From Spearman correlation test, it was found that the correlation coefficient was -0.733, which means that there is a strong relationship between GLS and lesion significance. This negative value indicates an inverse relationship between GLS and lesion significance, meaning that the more negative GLS value, the more significant the lesion.

Table 2 Global Longitudinal Strains and Significance of Intracoronary Lesions

Variable	Significant Coronary Lesion	r	P value
GLS	53,71±7,987	- 0.733	0.000

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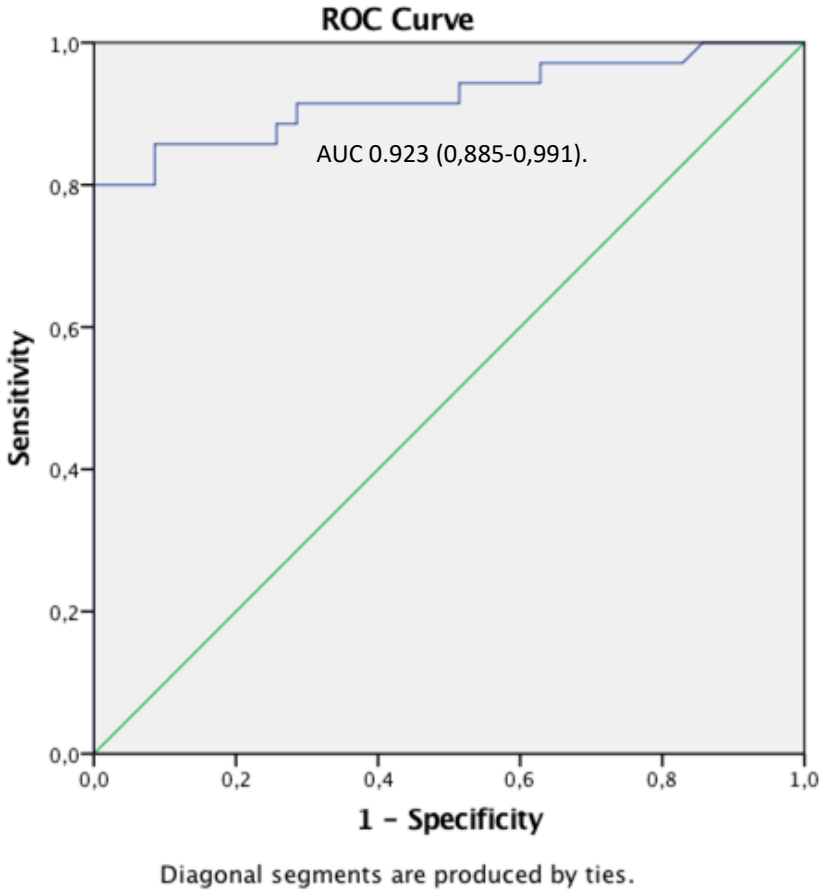

Gambar 1. ROC Curve (Receiver Operating Characteristic)

From Area Under the Curve (AUC) calculation it was found that AUC value was 0.923 (P = < 0.001, 95% CI 0.885-0.991). With AUC values greater than 0.7 and almost touching 1, it can be concluded that GLS is a good method for screening and predicting the incidence of significant lesions on angiography.

From the ROC curve, we get a table containing threshold values along with sensitivity and 1-specificity for each of these cut off. It can be concluded that GLS cut off -16.4300 can be used as a threshold for possibility of significant lesions on coronary angiography with a sensitivity of 85.7%, false positive rate (1-specificity) of 8.6%, and specificity of 91.4%.

Table 3. GLS Intersection Values with Coronary Lesion Significance

Coordinate Point of GLS Value		
Positive if greater than or equal to	Sensitivity	1- Specificity
- 17.2050	0.886	0.257
-17.100	0.857	0.257
-16.8100	0.857	0.200
-16.6100	0.857	0.114
-16.4300	0.829	0.086
-16.1800*	0.829	0.086
-15.9600	0.800	0.086

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Discussions

The Relationship Between GLS (Global Longitudinal Strain) and the Significance of Obstructive Lesions in Coronary Arteries

Global Longitudinal Strain has proven to be the most accurate measurement of strain parameter compared to others which is defined as mean peak systolic strain value of all left ventricular segments from apical imaging (Sjoli et al, 2009). GLS is an excellent parameter for detecting signs of heart disease. GLS is also an excellent predictor of heart failure and ischemic heart disease, apart from being a predictor of ejection fraction. If the ejection fraction is < 35%, it is better to add GLS information, but if Ejection Fraction (EF) > 35% there is still a place to add GLS information even though it is more meaningful in the case of EF < 35% (Evardsen and Haugaa, 2011). Another benefit of the GLS is being able to identify a large subgroup of non-elevation myocardial infarction patients with total occlusion requiring urgent revascularization. Electrocardiography (ECG) examination in this group did not show ST-segment elevation, so this indicates the low sensitivity of ECG in identifying patients with coronary occlusion. (Eek et al, 2010)

In this research, it was found that mean GLS values difference in obstructive CHD lesions was -12.34±3.35 compared to controls with -17.92±1.20, this was significantly significant (P = <0.001). This is in line with other studies that analysis this topic. Radwan, et al, 2016 showed a lower mean GLS score with -11.86 ± 2.89 in group 1, which had obstructive CHD compared to group 2, which did not have obstructive CHD with -18.65 ± 0.79 and this is significant (P < 0.000). Another study, by Choi et al., 2009 also showed similar results, which in its publication stated that GLS >-18% was found mostly in 216 patients who underwent invasive coronary angiography to detect CHD (P < 0.0001). The GLS is also used in studies that measure its correlation with a score called SYNTAX Score, a scoring system used to estimate the benefit of coronary bypass surgery over percutaneous coronary intervention. A high score (>22) indicates more coronary involvement and lesions, so that consideration for coronary bypass surgery is preferable. The study by Vrettos, et al, 2016 showed that GLS had an inverse correlation with SYNTAX score (r2 = 0.38, p < 0.001), where the GLS cut off value > 13.95% had a sensitivity of 71% and a specificity of 90% (P < 0.001) to detect severe coronary stenosis. Biering-Sørensen et al. 2014 studied 296 patients who had stable angina pectoris, without history of CHD, normal LVEF, showing that GLS was an independent predictor of CHD after multivariate analysis (OR = 1.25, p = 0.016 per 1% reduction in GLS).

Ability of GLS to predict Significant Obstructive Lesions on Invasive Coronary Angiography

From Spearman correlation test, it was found that correlation coefficient was -0.733, which means that there is a strong relationship between GLS and significant lesions. This negative value indicates an inverse relationship between GLS and lesion significance, meaning that the more negative the GLS value, the more significant the lesion will be. From the ROC curve, it is found that the line is located on upper left, where the Area Under the Curve (AUC) is found to be 0.923 (P = < 0.001, 95% CI 0.885-0.991). With AUC values greater than 0.7 and almost touching 1, it can be concluded that GLS is a good method for screening and predicting the incidence of significant lesions on angiography. This is in line with previous studies. Radwan, et al, 2016 showed the AUC for GLS was 0.88, 95% CI 0.78–0.96 P< 0.000. In another study, GLS had an AUC for detecting significant coronary lesions of 0.95 for GLS> -18.44% for a single lesion, AUC 0.9 for GLS> -17.35% for lesions in two coronary vessels, and AUC 0.68 for GLS> -15.33% for three coronary vessels (Moustafa, et al, 2018). A study by Zuo, et al, 2018 showed an AUC value of 0.818 for GLS in detecting circumflex coronary artery lesions, and AUC of 0.723 for detecting right coronary branch lesions. Biering-Srensen et al. 2014 showed that the AUC was higher when the GLS was combined with the treadmill test (AUC = 0.84) than the AUC for the treadmill test alone which is 0.78 (P = 0.007).

From ROC curve, we get a table containing cut off values along with sensitivity and 1-specificity of each of these cut off. It can be concluded that the GLS cut off value of -16.4300 can be used as a threshold for significant lesions possibility on coronary angiography with a sensitivity of 85.7%, false positive rate (1-specificity) of 8.6%, and specificity of 91.4%. Other studies show threshold value that are not much different from this study. Radwan, et al., 2016 showed that GLS cut off value of -15.6 had a sensitivity, specificity, and accuracy of 93.1%, 81.8%, and 90%. Choi, et al., 2009 also showed that GLS >-18% had a sensitivity of 91.1%, specificity of 80 .4%, Positive Predictive Value (PPV) 80.4%, and Negative Predictive Value (NPV) 80.5%. Vrettos, et al, 2016 showed a GLS threshold value > 13.95% having a sensitivity of 71% and a specificity of 90% (P < 0.001) for detecting severe

coronary stenosis. Overall, both the results of this research, and those of previous studies, show that GLS has good sensitivity and specificity in detecting significant obstructive coronary arteries lesions.

Conclusion

GLS can be used to predict lesions significance in patients with stable coronary heart disease and has an inverse relationship with coronary lesions significance. The GLS cut off value of -16.4300 can be used as a threshold for significant lesions possibility on coronary angiography with a sensitivity of 85.7%, a false positive rate (1-specificity) of 8.6%, and a specificity of 91.4%.

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