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(RESEARCH ARTICLE)

The Correlation Between Mitral Valve Area (MVA) Assessed Using Planimetry, Mean Trans-Mitral Gradient (MV mean PG) and Pulmonary Artery Systolic Pressure (PASP) on Global Longitudinal Strain (GLS) of The Left Ventricle in Rheumatic Mitral Stenosis

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Abstract

Background: Rheumatic heart disease (RHD) remains a global health issue, especially in developing countries, with mitral stenosis being one of the most common manifestations. Assessment of left ventricular function in patients with mitral stenosis due to rheumatic heart disease is generally performed using conventional echocardiography; however, this method has limitations in detecting subclinical left ventricular dysfunction. Global Longitudinal Strain (GLS) through speckle tracking echocardiography (STE) has been introduced as a more sensitive method in detecting left ventricular contractility disorders. This study aims to examine the relationship between echocardiographic parameters, including MVA calculated with planimetry, MV Mean PG, and PASP, with the left ventricular GLS values in patients suffering from mitral stenosis due to rheumatic heart disease (RHD).

Method: This cross-sectional observational study involved 72 patients diagnosed with mitral stenosis due to rheumatic heart disease treated at RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar. Echocardiographic examination was conducted to assess MVA, MV Mean PG, and PASP in relation with GLS values which is measured using STE.

Results: A total of 74 samples were involved in this analysis. A significant correlation was found between GLS and MV Mean PG ($r = -0.238$, $p = 0.013$), where the higher the mean transmitral gradient, the lower the GLS value. A positive correlation was also found between MVA planimetry and GLS ($r = 0.329$, $p = 0.004$), indicating that the larger the mitral valve area, the better the left ventricular function, but statistically non-significant. Additionally, PASP shows a negative correlation with GLS ($r = -0.17$, $p = 0.031$), which means that the higher the pulmonary artery systolic pressure, the lower the GLS value of the left ventricle.

Conclusion: GLS is a reliable predictor of left ventricular dysfunction in patients with rheumatic mitral stenosis, with PASP and MV Mean PG as significantly influential factors. On the other hand, MVA by Planimetry has been shown a non-significant correlation to LV GLS.

Keywords: Global Longitudinal Strain; Mitral Valve Area; Pulmonary Artery Systolic Pressure; Rheumatic Heart Disease; Speckle Tracking Echocardiography; Mitral Stenosis

1. Introduction

Data released by the Global Burden of Disease in 2015 indicated that 33.4 million individuals globally were afflicted with rheumatic heart disease. Studies in Asia estimates that the prevalence of RHD ranges from 10.8 to 15.9 million people, resulting in 356,000 to 524,000 fatalities annually. In instances of chronic rheumatic heart disease, mitral valve

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abnormalities are the predominant concern, present in around 50-60% of patients, although a mix of mitral and aortic valve diseases is seen in roughly 20% of cases.1–3

The majority of RHD patients have intact left ventricular systolic function (preserved LVEF), with the exception of those with isolated aortic regurgitation and multiple valve lesions (aortic and mitral), who demonstrate a greater incidence of diminished left ventricular contractility. This phenomenon may result from increased haemodynamic stress on the ventricle in cases of numerous valve defects or volume overload in individuals with isolated aortic regurgitation.3Other studies contend that, irrespective of haemodynamic disruptions caused by structural valve defects, a reduction in left ventricular contractility may also arise from intrinsic processes occurring inside the myocardium.4 Findings from a representative research at a national referral centre hospital in Indonesia indicate that left ventricular systolic function below 50% may occur in the isolated mitral stenosis group, where left ventricular systolic function is often maintained.3

Presently, a technique known as speckle tracking echocardiography (STE) evaluates cardiac function by identifying and monitoring specific points in the myocardium with distinct echocardiographic features within speckle blocks, facilitating the measurement of speckle displacement during the cardiac cycle. Speckle tracking echocardiography (STE) may quantify parameters like longitudinal, radial, or circumferential myocardial strain, global longitudinal strain (GLS), and strain rate. GLS is identified as a superior predictor relative to other cardiac strain parameters.5 GLS may identify early-stage left ventricular disease and subclinical impairment, as well as assess cardiac performance independent of geometric assumptions. GLS may directly assess cardiac deformation using a 16-segment model. GLS may serve as a superior measure compared to LVEF due to its heightened sensitivity in identifying alterations in long axis shortening.6

Currently, there are no studies in Indonesia that evaluate echocardiographic parameters, specifically the severity degree parameters of mitral stenosis such as MVA planimetry, mean transmitral gradient (MV mean PG), and pulmonary artery systolic pressure (PASP) in relation to the GLS values at various degrees rheumatic mitral stenosis.

2. Method

2.1. Study Design

This study is an observational study with a cross-sectional design, aimed at determining the correlation between the global longitudinal strain (GLS) value of the left ventricle and mitral valve stenosis variables (mean trans-mitral gradient, mitral valve planimetry) and pulmonary artery systolic pressure (PASP) in patients with rheumatic mitral stenosis.

2.2. Participants

A total of 74 patients are concecutively recruited for echocardiography assessment. Inclusion criteria included patients aged 18–65 years with patients diagnosed with rheumatic mitral stenosis at the cardiac clinic of RSUP Prof. dr. I.G.N.G. Ngoerah, patients aged 18-65 years, are willing to participate in this study for a non-invasive transthoracic echocardiography examination. Exclusion criteria included patient who does not have other significant heart valve abnormalities (moderate to severe aortic stenosis, moderate to severe aortic regurgitation, moderate to severe mitral regurgitation, severe pulmonary regurgitation, tricuspid stenosis, moderate to severe tricuspid regurgitation), patients with left ventricular systolic dysfunction (LVEF <50%), patients with a history of chemotherapy, patients with CKD with a glomerular filtration rate <30 ml/min, history of heart surgery, data corresponding to the variables sought in this study are incomplete, patients who refuse to participate after being given informed consent.

2.3. Measurements

Global longitudinal strain LV is a 2D echocardiography examination using spectral tracing mode on apical long axis images (4 chamber and 2 chamber view). All image acquisitions were performed during breath-holding and captured in cine-loop format through 3 consecutive beats with a frame rate of 60-90 frames/s used for GLS analysis. GLS is automatically calculated by averaging the strain values from all myocardial segments obtained by the software. This examination uses the GE Health Care Vivid S70N echocardiography machine. The GLS value is low if the value is less than -16.

The planimetry area of the mitral valve (MVA planimetry) is performed through a 2D echocardiographic examination, using short-axis cuts at the level of the mitral valve, and images are taken during 3 consecutive beats. The measurement of MVA planimetry is performed at the end diastolic phase (the moment when the mitral valve is widest open), followed by tracing the area of the mitral valve.

The mean transmitral gradient (MV mean PG) is measured using continuous wave Doppler (CW Doppler) examination on the mitral valve, obtained through two-dimensional echocardiography in the apical 4-chamber and apical 3-chamber views. The trans-mitral CW Doppler values are taken over 3 consecutive beats.

Pulmonary Arterial Systolic Pressure (PASP) is measured using CW Doppler transvalvular blood flow examination on the tricuspid valve by calculating the peak velocity of regurgitant flow. The formula that can be used to estimate PASP $= 4 \times (TRV)^2 + RAP$.

2.4. Statistical Analysis

Data were analyzed using SPSS version 26 software. Pearson correlation test (if all data are normally distributed) or Spearman correlation test (if there is non-normally distributed data) to determine the correlation between mitral stenosis parameters (MV mean PG, MV max PG, and MVA planimetry) and LV GLS values. Linear regression test to determine the parameters that independently affect LV GLS values in patients with mitral stenosis. Statistical significance was set at $p < 0.05$.

2.5. Ethical Considerations

The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants prior to enrollment.

3. Results

3.1. Sample Characteristics

This study involved a total of 74 samples with rheumatic mitral stenosis. The average LV GLS value in all samples of this study is 16.48%, with an average GLS value in the decreased GLS group being 12.81% and in the normal GLS group being 18.98%. No differences were found in age, gender, MVA planimetry, degree of MS severity based on planimetry, atrial fibrillation status, ACE-I/ARB therapy, LAVI, TAPSE, and biplane ejection fraction between the groups of patients with decreased LV GLS and normal LV GLS (p>0.05). The PASP value was higher in the group with decreased LV GLS (44.89 mmHg) compared to the group with normal LV GLS (34.45 mmHg) (p=0.035). The MV mean gradient value was higher in the group with decreased LV GLS (10.70 mmHg) compared to the MV mean gradient in the group with normal LV GLS (8.28 mmHg) (p<0.001). (Table 1)

Table 1 Characteristics of research samples

Kara kteristik	**Total**	**Reduced GLS (n=30)**	**Normal GLS (n=44)**	**p**
Age (mean ± SD) (year)	47.52 ± 12.50	45.23 ± 12.42	49.09 ± 12.45	0.195
Gender (n, %)				
Male	27 (36.5%)	10 (37.0%)	17 (63.0%)	0.642
Female	47 (63.5%)	20 (42.6%)	27 (57.4%)	
AF status (n, %)				
Yes	35 (47.3%)	18 (51.4%)	17 (48.6%)	0.071
No	39 (52.7%)	12 (30.8%)	27 (69.2%)	
ACE-I/ARB treatment (n, %)				
Yes	41 (55.4%)	19 (46.3%)	22 (53.7%)	0.257
No	33 (44.6%)	11 (33.3%)	22 (66.7%)	
MVA planimetry (cm2) (Median-IQR)	0.96 (0.75)	0.75 (0.65)	1.25 (0.73)	0.105
Severity MS by planimetry (n, %)				
Mild	11 (14.9%)	2 (18.2%)	9 (81.8%)	0.069
Moderate	25 (33.8%)	8 (32.0%)	17 (68.0%)	

Severe	38 (51.4%)	20 (52.6%)	18 (47.4%)	
PASP (mmHg) (Median-IQR)	33.50 (19.47)	36.98 (25.53)	29.62 (17.68)	0.035*
MV mean gradient (mmHg) (mean± SD)	9.26 ± 4.66	10.70 ± 4.70	8.28 ± 4.42	0.028*
GLS (%) (mean ± SD)	16.48 ± 3.99	12.81 ± 2.72	18.98 ± 2.48	<0.001*
LAVI (ml/m2) (Median-IQR)	61.50 (43.77)	66.79 (61.21)	58.09 (32.21)	0.072
TAPSE (mm) (Median-IQR)	20 (5.0)	18.50 (6.25)	21 (5.75)	0.055
LV Ejection Fraction Biplane (%) (Median-IQR)	58.53 (6.11)	56.58 (5.93)	59.32 (5.30)	0.061

*Significant (p<0,05)

Table 2 Characteristics of GLS LV, MV gradient, and PASP based on MS severity according to planimetry

Echocardiography Characteristic	Mild MS (n=11)	Moderate MS (n=25)	Severe MS (n=38)	p
PASP	30.87 ± 12.37	30.56 ± 10.11	46.28 ± 33.87	0.005*
GLS	18.48 ± 1.12	17.37 ± 2.89	15.32 ± 4.36	0.025*
MV mean gradient	4.14 ± 1.88	6.59 ± 2.51	12.50 ±3.79	<0.001*

*Significant (p<0,05)

Table 3 Correlation test between MV planimetry, PASP, and MV gradient against GLS LV value

Variable	GLS (%)	
	r	p
MV *mean gradient* (mmHg)	-0.28	0.013*ᶲ
MVA *planimetry* (cm^2)	0.32	0.004*Ψ
PASP (mmHg)	-0.17	0.031*Ψ

*Significant (p<0,05); ϕcorrelation Pearson; Ψcorrelation Spearman

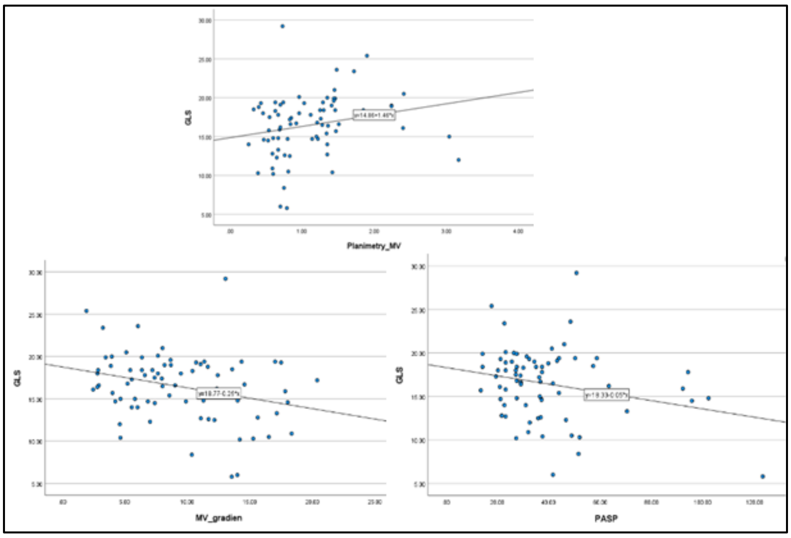

Figure 1 *Scatter plot* graphic that shows correlation between Koreas Antara GLS LV denga MVA planimetry, MV mean gradient and PASP

Table 4 Multiple Linear Regression analysis between MV gradient, PASP, and MV planimetry on LV GLS

Variable	B	Coefficient std. error	p
Constant	18.786	2.184	<0.001*
MV Planimetry	0.369	0.974	0.076
PASP	-0.031	0.023	0.038*
MV mean gradient	-0.162	0.133	0.023*

*Significant (p<0,05); R-square = 0,309

Characteristics based on the severity of rheumatic mitral stenosis, the highest PASP value was found in the severe MS group (46.28 mmHg) compared to the mild MS group (30.87 mmHg) and the moderate MS group (30.56 mmHg). The highest GLS value was found in the mild MS group (18.48%), while the highest MV gradient was found in the severe MS group (Table 2). The normality tests using the Kolmogorov Smirnov-Z test shows that age, LV GLS, and MV mean gradient have a normal distribution (p>0.05), while PASP, ejection fraction, LAVI, TAPSE, and planimetry have a non-normal distribution (p<0.05).

3.2. Correlation between MV mean gradient and LV GLS

Correlation analysis used the Pearson test on the LV GLS and MV mean gradient variables. There is a significant weak negative correlation (r = -0.238; p = 0.013) between the MV mean gradient and LV GLS value, meaning that the higher the MV mean gradient, the lower the GLS value tends to be.

3.3. Correlation between MVA Planimetry and LV GLS

The analysis of MVA planimetry and LV GLS used the Spearman correlation test. There is a significant moderate positive correlation between MVA planimetry and LV GLS value (r=0.329; p=0.004), the larger the MV planimetry, the higher the LV GLS value will be.

3.4. Correlation between PASP and LV GLS

The analysis of PASP and LV GLS used the Spearman correlation test. There is a significant weak negative correlation between PASP and LV GLS values (r = -0.17; p = 0.031), the higher the PASP value, the lower the LV GLS value will be. (Table 3)

The scatter plot curve shows a line towards the upper right (positive correlation), while the curve towards the lower right shows a negative correlation. (Picture 1)

3.5. Multiple Linear Regression analysis between MV gradient, PASP, and MV planimetry on LV GLS

Multiple linear regression analysis shows a significant relationship between PASP, MV Gradient, and LV GLS values (p<0.05). However, no significant relationship was found between MV Planimetry and LV GLS. Through the R-square value showing a figure of 0.309, which means that MV mean gradient, PASP, and MV planimetry can explain their role in LV GLS by 30.9%, while there are still 69.1% of variables affecting GLS outside of the variables in this study. (Table 4)

3.6. Summary of Findings

There is a significant negative correlation between MV gradient and PASP on LV GLS. On the other hand No. there is no significant correlation between MVA planimetry and LV GLS.

4. Discussion

The majority of the samples were female, with 47 (63.5%) patients, while the remaining 27 (36.5%) patients were male. This is consistent with epidemiological data from eight studies showing a predominance of female patients with rheumatic heart disease, which correlates with poor long-term outcomes. There is no specific explanation regarding the pathogenesis of women being more frequently affected by rheumatic mitral stenosis compared to men.7 The average age of patients with rheumatic mitral stenosis in this study is 47.5 years, and this result is not significantly different when compared to national data in Indonesia, which shows an average age of around 42.6 ± 12.50 years.

Compared to other types of heart diseases, the prevalence of rheumatic heart disease affects a relatively younger age group due to the disease's progression starting from an early age.3

There is a significant weak negative correlation (r=-0.238; p=0.013), which means that the higher the MV gradient value, the lower the GLS LV value tends to be. The average MV mean gradient value in patients with decreased GLS LV is 10.7 mmHg. In the group with severe mitral stenosis, a higher MV mean gradient value was found compared to mild and moderate mitral stenosis, which was 12.5 mmHg. In rheumatic mitral stenosis, the increase in MV gradient has been proven to correlate with the mechanism of long-term excessive pressure load and the occurrence of progressive cardiac remodeling. With the passage of time, the consistent condition of this pressure load will cause diastolic dysfunction, disrupting the ability to relax and fill the ventricle.4,8,9

A significant weak negative correlation was found between PASP and GLS LV values (r = -0.17; p = 0.031). This indicates that the higher the PASP value, the lower the GLS LV value will be. In rheumatic mitral stenosis, PASP is related to GLS LV due to the hemodynamic load placed on the left ventricle because of pulmonary hypertension. With the progressive worsening of mitral stenosis caused by the process of fibrosis and commissural fusion, the left atrium will experience chronic overload, leading to increased left atrial pressure and eventually increased pulmonary pressure. As time goes by, chronic pulmonary hypertension will cause right ventricular dysfunction and interventricular septal shift, which negatively impacts left ventricular function and filling leading to a decrease in LV GLS even though LVEF remains within the normal range.8–10

The results of multiple linear regression test showed a significant relationship between PASP and MV mean gradient with LV GLS values ($p<0.05$) but not significant with the MVA planimetry parameter (p = 0.076). These results indicate that hemodynamic parameters appear to have a more significant correlation value compared to the 2D anatomical parameters. The quality of 2D planimetric MVA measurements highly depends on how the image is taken, the position of the transducer, and the precise tracking of the mitral valve orifice (valve tip) in the parasternal short axis view. Suboptimal image acquisition affects inconsistent measurements. Additionally, in the condition of the mitral valve being overly calcified, it will cause an overestimation of the measurement due to shadow artifacts caused by the calcium. Therefore, if the ideal measurement cannot be performed in 2D, it is recommended to use 3D measurements such as direct 3D echocardiography and 3D MPR planimetry.11

5. Conclusion

The results of this study indicate that although LVEF shows normal values in patients with rheumatic mitral stenosis, the global longitudinal strain method reveals a high proportion of patients with subclinical left ventricular dysfunction. The MV mean gradient and PASP parameters significantly correlate with the LV GLS results, but not with the MVA planimetry, where hemodynamic factors play an important role in the occurrence of left ventricular dysfunction in patients with rheumatic mitral stenosis.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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