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Case Report

Correlation between Peak Left Atrial Longitudinal Strain and The Severity of Mitral Valve Disease at Haji Adam Malik General Hospital Medan.

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Introduction: Mitral stenosis and regurgitation, are common throughout the world. Peak Left Atrial Strain (PALS) is a parameter for assessing left atrial deformation in the evaluation of atrial function and a predictor of long-term outcomes of various heart diseases. In this study, we assessed the relationship between PALS and the severity of mitral stenosis and mitral regurgitation.
Methods: AThis is a cross-sectional study on 119 subjects with mitral stenosis and 103 mitral regurgitation who met the inclusion criteria at Haji Adam Malik General Hospital. PALS measurements were taken. Data were analyzed univariate, bivariate, and correlated to assess the relationship between PALS and the severity of mitral valve disease.
Results: 119 patients with severe mitral stenosis. In mitral stenosis, the mean PALS is 8.2 (4.9-22.8). PALS was significantly higher in patients with sinus rhythm than in the group with AF (10.29 ± 3.89 vs 8.63 ± 7.8%; P = 0.002). PALS had a significant correlation with MVA, pressure gradient, and PHT (r = 0.676, P = <0.001; r=-0.594, P= 0.001 and r=-0.594, P= 0.001). Whereas in mitral regurgitation, it has an average PALS of 15.2 (7.8-19.2). PALS was also significantly higher in patients with sinus rhythm than in the group with AF (16.36 ± 2.43 vs 11.64 ± 2.89%, P = 0.001). PALS correlates with VC, PISA, EROA, and RVol (r = -0.533, P=0.001; r=-0.618; r=-0.563, P=0.001; r= -0.528, P=0.001).
Conclusion: PALS has a significant correlation with the assessment of the severity of mitral stenosis and regurgitation.

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Keywords: PALS, mitral stenosis, mitral regurgitation.

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Introduction

Mitral valve disease includes mitral stenosis and regurgitation. Mitral stenosis is an obstruction of the mitral valve that causes blood flow from the left atrium (LA) to the left ventricle disrupted, while mitral regurgitation is caused by the backflow of blood from the left ventricle to the right atrium; both due to arthritis (most often) and non-rheumatism. The prevalence of rheumatic fever in developed countries has declined, with an estimated incidence of 1 in 100,000 rheumatic fever. However, this prevalence is still higher in developing countries.[1,2]

The mitral valve is the most frequently involved in rheumatic heart disease (RHD) and usually presents with complaints such as dyspnoea on exertion, pulmonary hypertension, and right heart failure. The initial diagnosis of suspected valve disease is certainly enforced based on physical examination, history taking, and supporting examinations such as an electrocardiogram or chest X-ray. Echocardiography has a role as a tool to establish a definite diagnosis of valve disease as well as to provide further management directions and determine the patient's prognosis in the future.[3,4,5]

Several studies have shown that left atrial dysfunction in mitral valve disease could be assessed by Left Atrial Strain using speckle tracking echocardiography (STE). Peak Left Atrial Strain is a measurement of LA reservoir function which is calculated based on QRS, and is the most widely used parameter and has stronger evidence compared to LA conduit and contractile strain examinations.[3]

Peak Left Atrial Strain evaluation has practically in mitral regurgitation during preoperative evaluation and to predict postoperative LA improvement and clinical outcome, correlates independently to postoperative success and functional capacity as assessed by the NYHA classification and Borg scale, also be used for postoperative cardiac changes evaluation, which indicates the success of the surgical procedure.[6] Given the function of the Peak Left Atrial Strain parameter which is currently developing and could be used as a basis for evaluating evaluation of mitral valve disease, we aim to find the relationship between peak left atrial longitudinal strain and the severity of mitral valve disease in Haji Adam Malik General Hospital.

Methods

This is a cross-sectional study conducted at Haji Adam Malik General Hospital from January 2021 to July 2023. All samples must meet the inclusion criteria, such as patients with mitral stenosis and regurgitation; the patient's clinical and echocardiographic examination supports severe mitral stenosis and regurgitation; not accompanied by coexistence of significant lesions on other valves with severe degree; non-ischemic mitral regurgitation; not with an ejection fraction <50%; have not undergone prosthetic valve placement surgery; did not have congenital heart defects; did not have cardiomyopathy; and good echocardiography without poor echo window. Patients with incomplete medical record data will be excluded.

Parameters in determining the severity of mitral stenosis were based on the American Society of Echocardiography 2022, such as planimetry, gradient pressure, Pulmonary Artery Systolic Pressure (PASP), and Pressure Half Time (PHT). Mitral stenosis is considered severe if the mitral valve area (MVA) is <1.5 cm2, the pressure gradient is>10 mmHg, PHT is>150 ms, and PASP is>50 mmHg. Parameters to determine the severity of mitral regurgitation are the width of the vena contract (VC), Effective Regurgitant Orifice Area (EROA), Proximal Isovelocity Surface Area (PISA), and Regurgitant Volume (RVol). VC width >0.7 cm is specific for severe mitral regurgitation, and EROA ≥0.40 also indicates severe mitral regurgitation.

The assessment of peak left atrial longitudinal strain (PALS) was obtained from echocardiographic examination, which was calculated based on the difference in strain results at the opening of the mitral valve minus the end of ventricular diastole. Echocardiography was performed by 2 observers and intraobserver reliability was performed by using the Bland-Altman test. The PALS value is the average of the examination results on the 4-chamber display after tracing the LA limit.

Data with categorical variables are presented with frequency (n) and percentage (%), while numerical variables are presented with mean and standard deviation (SD) or median and interquartile range. Data were analyzed by bivariate analysis, and the correlation between the two variables was calculated using Pearson correlation regression or Spearman correlation. Variables are considered significant if the p-value <0.05.

Table 1. Subject Characteristics.

Variable	Mitral Stenosis (n=119)	Mitral Regurgitation (n-103)	P value
Gender			0.186[1]
Man	45 (20.3%)	48 (21.6%)	
Woman	74 (33.3%)	55 (24.8%)	
Age	41.46 ± 11.81	43.61 ± 14.47	0.528[2]
EKG			0.031[1]
Sinus rhythm	43 (19.4%)	52 (23.4%)	
Atrial fibrillation	76 (34.2%)	51 (23%)	
NYHA			0.856[1]
I	1 (0.5%)	2 (0.9%)	
II	67 (30.2%)	58 (26.1%)	
III	44 (19.8%)	33 (14.9%)	
IV	7 (3.2%)	10 (4.5%)	
Furosemide	115 (51.8%)	94 (42.3%)	0.150[1]
Spironolactone	110 (49.5%)	81 (36.5%)	0.310[1]
Beta Blocker	98 (44.1%)	83 (37.4%)	0.735[1]
ACE/ARB	7 (3.2%)	60 (27%)	<0.001[1]
Digoxin	59 (26.6%)	34 (15.3%)	0.013[1]
Warfarin	86 (38.7%)	52 (23.4%)	0.001[1]
Echocardiography			
LAVI (mm)	86 (40-131.97)	75.4 (40-97)	0.077[3]
LVEF (%)	60 (52-83)	61 (58-83)	0.324[3]
LVEDD (mm)	45 (30-86)	60 (48-93)	<0.001[3]
LVEDV (ml)	61 (15-367)	102 (18-326)	<0.001[3]
LVESV (ml)	25 (5-255)	40 (6-200)	<0.001[3]
TAPSE (mm)	17 (7-32)	19 (8-35)	0.001[3]
PALS (%)	8.2 (4.9-22.8)	15.2 (7.8-19.2)	<0.001[3]
Planimetry (cm2)	0.7 (0.2-2.5)	-	-
Pressure Gradient(mmHg)	13.3 ± 4.28	-	-
PHT (ms)	220 (100-343)	-	-
Vena Contracta (cm)	-	0.8 (0.4-1.5)	-
PISA (cm)	-	1.1 (0.4-3.47)	-
EROA (cm2)	-	0.5 (0.3-2.3)	-
RVol (ml)	-	60 (30-130)	-

[1]Chi-Square; [2]T-independent; 3Mann-Whitney. EKG: Electrocardiogam; NYHA: New York Heart Association; ACE: Angiotensin-converting enzyme; ARB: Angiotensin II receptor blockers; LAVI: Left Atrial Volume Index; LVEF: Left Ventricular Ejection Fraction; LVEDD: Left Ventricular End Diastolic Diameter; LVEDV: Left Ventricular End-Diastole Volume; LVESV: Left Ventricular End-Systole Volume; TAPSE: Tricuspid Annular Plane Systolic Excursion; PALS: Peak Left Atrial Longitudinal Strain; PHT: Pressure Half Time; PISA: Proximal Isovelocity Surface Area; EROA: Effective Regurgitant Orifice area; Rvol: Regurgitant Volume.

Table 2. Association between PALS and Mitral Stenosis Severity.

Variable	P value	r
LAVI	<0.001	-0.363
LVEF	0.161	-0.129
LVEDD	0.392	-0.079
LVEDV	0.728	-0.032
LVESV	0.552	0.055
TAPSE	0.867	-0.016
MVA Planimetry	<0.001	0.694
Mean PG	<0.001	-0.523
PHT	< 0.001	-0.594

LAVI: Left Atrial Volume Index; LVEF: Left Ventricular Ejection Fraction; LVEDD: Left Ventricular End Diastolic Diameter; LVEDV: Left Ventricular End-Diastole Volume; LVESV: Left Ventricular End-Systole Volume; TAPSE: Tricuspid Annular Plane Systolic Excursion; MVA: Mitral Valve Area; PG: Pressure Gradient: PHT: Pressure Half Time

Table 3. Association between PALS and Mitral Regurgitation Severity.

Variable	Nilai P	r
LAVI	<0.001	-0.434
LVEF	0.392	-0.085
LVEDD	0.062	-0.184
LVEDV	0.228	-0.120
LVESV	0.329	-0.097
TAPSE	0.094	0.166
Vena Contracta	<0.001	-0.533
PISA	<0.001	-0.618
EROA	< 0.001	-0.563
RVol	<0.001	-0.528

LAVI: Left Atrial Volume Index; LVEF: Left Ventricular Ejection Fraction; LVEDD: Left Ventricular End Diastolic Diameter; LVEDV: Left Ventricular End-Diastole Volume; LVESV: Left Ventricular End-Systole Volume; TAPSE: Tricuspid Annular Plane Systolic Excursion; PISA: Proximal Isovelocity Surface Area; EROA: Effective Regurgitant Orifice area; Rvol: Regurgitant Volume.

Results

Subject Characteristics

Of 222 subjects, 119 with mitral stenosis, and 103 with mitral regurgitation. Both groups were dominated by women, with 33.3% and a mean age of 41.46 ± 11.81 years in the mitral stenosis group; and 24.8% with a mean age of 43.61 ± 14.47 years in the mitral regurgitation group **(Table 1)**. Based on electrocardiogram examination, atrial fibrillation (34.2%) was more common in mitral stenosis; and sinus rhythm (23.4%) was more common in mitral regurgitation. There was a significant association between the results of ECG examination and mitral valve disease (p=0.031).

An echocardiographic examination was performed to determine the severity of the mitral stenosis and the size of the mitral valve area. The results showed the median MVA area based on planimetry measurements was 0.7 cm^2, the median pressure gradient was 13.3 mmHg and the average PHT was 220 (100-343). For mitral regurgitation severity, the median VC width was 0.8 cm, and the mean values of PISA and EROA were 1.1 cm and 0.5 cm^2, respectively. In measuring the regurgitant volume, the median value is 60 ml. The median PALS in the mitral regurgitation group was higher than in the mitral stenosis group. There is a significant association between PALS and valvular heart disease (p<0.001). To ensure the reliability of studies, the Bland-Altman test was performed to determine interobserver reliability between 2 operators. The difference in measurement results between the two observers does not exceed 5 so the results obtained were quite indeed reliable. We will provide that in the study manuscript

Correlation between PALS and Mitral Stenosis and Regurgitation Severity

In mitral stenosis **(Table 2 and Figure 1)**, a significant association was found with a strong correlation between PALS and mitral valve area based on planimetric measurements (p < 0.001, r = 0.694). PALS also has a significant association with a fairly strong correlation between gradient pressure and PHT (p<0.001).

In mitral regurgitation (Table 3 and Figure 2), a significant association was found between PALS and LAVI; with sufficient correlation strength (p<0.001, r=-0.434). In addition, a significant association was found

Table 4. PALS with Cardiac Rhythms in Mitral Stenosis and Regurgitation.

PALS	EKG		P value
	Sinus rhythm	Atrial fibrillation	
Mitral stenosis	10.29±3.89	8.63±7.8	0.002
Mitral regurgitation	16.36±2.43	11.64±2.89	<0.001

between PALS and the width of VC, PISA, EROA, and Rvol; with a fairly strong correlation (p<0.001).

Differences between PALS and Heart Rhythms on Electrocardiogram (EKG)

Analysis of the association between PALS and heart rhythm was carried out on patients' ECG with mitral stenosis and regurgitation **(Table 4)**. The mean PALS results were lower in atrial fibrillation in the mitral stenosis and regurgitation group. In addition, there is a statistically significant association between PALS and ECG results for mitral stenosis and regurgitation.

Discussion

Rheumatic etiology is one of the causes of cardiovascular disease death and disability in low- and middle-income countries. In developing countries, mitral stenosis caused by rheumatic is the most common valvular heart disease. This study is similar to Castro et al, patients with mitral stenosis were dominated by women with an average age older than this study (59 ± 12 years). In this study, there was a strong correlation between PALS and the severity of mitral stenosis; which is in line with previous studies, patients with mitral stenosis had a larger left atrial diameter and a larger volume. Patients with mitral stenosis also had lower PALS compared to the control group.[7]

According to Mehta et al, all LA strain parameters (reservoir strain (LASr), conduit strain (LAScd), and contractile strain (LASct)) were significantly decreased in patients with mitral stenosis.[6] One study conducted on 52 asymptomatic mitral stenosis patients obtained an average MVA of 1.38 ± 0.36 cm^2 and an average transmitral gradient of 7.9 ± 2.8 and reported a decrease in LA reservoir and conduit strain.8 Shojaeifard showed the left atrial strain measurement has a significant correlation with MVA and has a reversal correlation with the Left Atrial Volume Index (LAVI). In line with this study, where PALS correlates with MVA and LAVI; concluded that the smaller the area of the mitral valve, the left atrial function will decrease.[9]

LA strain scores correlate with symptom severity and long-term outcomes in patients with mitral stenosis. In asymptomatic mitral stenosis patients, decreased PALS predicts the incidence of atrial fibrillation at 4 years of follow-up. PALS is also a predictor of symptom severity, the need for hospitalization, atrial fibrillation (AF), thromboembolic events, and the need for surgical procedures or commissurotomy.[9] PALS is a good indicator of left atrial function even 1 day after intervention for mitral stenosis, regardless of the type of treatment modality.[10]

AF is a common complication of RHD and occurs in 30-40% of patients with rheumatic mitral stenosis. Previous studies have shown that LA strain is useful as a diagnostic technique in predicting the onset of AF in patients with heart failure. Vriz et al stated that PALS, age, and mean mitral valve gradient are independent predictors of AF in mitral stenosis.[11] In mitral stenosis, there is a combination of increased right atrial pressure and a vigorous atrial inflammatory response, followed by a progressive increase in atrial wall fibrosis resulting in right atrial dysfunction and right atrial dilatation. The occurrence of this remodeling will disrupt the atrial electrical process which results in AF.[12]

One of the other heart valve diseases that is often found is mitral regurgitation. In line with Lisi et al, patients with mitral regurgitation had lower PALS than the control group. PALS also has a strong negative correlation with EROA.[13] Camelli et al, showed that global PALS was lower in moderate mitral regurgitation and even lower in the severe group. The greater severity of mitral regurgitation is associated independently with lower left atrial reservoir strain.[14]

In the mitral regurgitation group, patients with a history of paroxysmal AF showed significantly decreased global PALS and had an independent association.[14] These findings are similar to this study, the group with

AF had a lower mean PALS than the sinus rhythm group. Lisi et al also showed that global PALS was an independent predictor of postoperative AF mitral valve repair (MVR).[13] Stessen stated that left atrial reservoir strain was independently related to all causes of death in patients with severe primary mitral regurgitation undergoing MVR. Left atrial reservoir strain also has prognostic value and echocardiographic risk factors for long-term survival.[15]

Progressive reduction of PALS in moderate and severe mitral regurgitation is caused by structural abnormalities of the LA due to chronic mitral regurgitation; such as myocyte hypertrophy, interstitial fibrosis, decreased metalloproteinase expression and electrical dissociation occurs between muscle bundles resulting in atrial fibrillation. Strain parameters are not determined by fibrosis, but influenced by filling conditions and irregular rhythms.[16]

Atrial strain analysis has proven useful in a variety of clinical settings. Previous studies have shown a strong association between decreased LA myocardial function and various cardiovascular events.[16] In postoperative mitral valve repair, LA strains were significantly lower in the group with cardiovascular events. Patients with left atrial reservoir strain <9.8% had lower survival rates at 1 year, 2 years, and 5 years follow-up. In mitral valve prolapse, atrial strain examination is an independent predictor of severe mitral regurgitation requiring surgery. PALS, pre-operative LAVI, and age are predictors of LA repair in patients with severe mitral regurgitation who undergo surgical procedures.[17]

Several studies have reported that quantitative assessment based on atrial function as an additional examination has benefits in determining the optimal time for mitral regurgitation surgery. PALS examination could also determine risk stratification in patients with asymptomatic chronic mitral regurgitation. In asymptomatic severe mitral regurgitation, decreased PALS in the LA filling phase predicts a poorer prognosis. These could be additional information in considering early surgery.[16,18]

The limitation of our studies is the lack of multivariate analysis. The multivariate analysis would allow clinicians to determine other variables' ability to affect the correlation between independent and dependent variables.

Conclusion

PALS is associated with the severity of mitral valve stenosis and regurgitation, PALS is also useful in predicting the incidence of atrial fibrillation in mitral stenosis and regurgitation. Thus, PALS could be used as an echocardiographic indicator in assessing the severity of mitral stenosis and regurgitation and could be used as a consideration for clinicians in selecting appropriate actions and therapies for this case.

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