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Relationship Between Left Atrium Reservoir Strain and One-Year Mortality After Surgery in Patients with Severe Primary Mitral Regurgitation Undergoing Mitral Valve Replacement at Haji Adam Malik General Hospital, Medan

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ABSTRACT

Introduction: Severe primary Mitral Regurgitation (MR) is a public health program that continues to grow. Echocardiography is still a tool to assess the severity and prognostic of mitral valve disease. LASr assessment has the benefit of assessing the prognostic in patients who have undergone mitral valve replacement surgery. This study aimed to determine the relationship between LASr and mortality one year after surgery for severe primary MR undergoing valve replacement surgery

Methods: This study is an analytic study with a cross-sectional design on 55 subjects with severe primary MR who met the inclusion and exclusion criteria at Haji Adam Malik General Hospital. LASr was measured before surgery and followed by the incidence of mortality one year after mitral valve replacement surgery. Data were analyzed univarite and bivariate as well by correlation tests to assess the relationship between LASr and one-year mortality in severe primary MR undergoing valve replacement surgery

Results: The study subject totaled 55 patients with an average age of 39,35 ± 12,59 years, 28 patients (50.9%) were male and 11 patients (20%) experienced mortality. The main cause of mitral valve abnormalities in this study was rheumatic, namely 39 cases (70.9%). The LASr threshold value was found to be 18.8 (sensitivity: 90.9%; specificity: 70.5%). (AUC: 0.851; P = 0.0001 and 95% CI (0.751 – 0.952).

Conclusion: LASr has a significant correlation to predict one-year mortality in patients with severe primary mitral regurgitation undergoing mitral valve replacement surgery.

Keywords: LASr, Severe Primary MR, Mitral valve replacement surgery, Mortality

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INTRODUCTION

The left atrium (LA) plays a crucial role in left ventricular filling, making its structural and functional evaluation essential for the diagnosis and prognosis of various cardiovascular diseases, including atrial fibrillation (AF), hypertension (HTN), heart failure (HF), valvular heart disease, cardiomyopathy, and coronary artery disease (CAD).[1] Among these conditions, mitral valve disease significantly impacts cardiac function and affects a considerable proportion of the population worldwide.

Mitral valve disease affected approximately 5.8 million adults in the United States in 2016, with 5.49 million cases of mitral regurgitation (MR).[2] The prevalence of MR increases with age, affecting 5.1% of individuals over 65 and 9.3% of those over 75.[3] MR is the second most common valvular disease in high-income countries, after aortic stenosis. It can be classified as primary MR, caused by intrinsic mitral valve abnormalities, or secondary MR, resulting from left atrial or ventricular dysfunction.[4] The most common cause of primary MR is myxomatous degeneration, leading to mitral valve prolapse, with degenerative etiologies such as fibroelastic deficiency and Barlow's disease being prevalent in Western countries.[5] In contrast, rheumatic heart disease remains the leading cause of MR in low-income countries.[6] Another major contributor to MR in the elderly population is mitral annular calcification, a degenerative process that compromises mitral valve function.[7]

Severe primary MR is a growing public health concern.[8] Transthoracic echocardiography (TTE) is the primary diagnostic tool for assessing left ventricular size and function, right ventricular function, left atrial size, pulmonary artery pressure, and the severity and mechanism of MR.[9] When TTE results are inconclusive, transesophageal echocardiography (TEE) is recommended.[10] Diagnosis of severe MR requires meeting more than five specific criteria, including leaflet dilation, vena contracta width >0.7 cm, proximal isovelocity surface area (PISA) radius >1.0 cm, regurgitant jet area >50% of the left atrium, and systolic pulmonary vein flow reversal.[11]

MR-induced volume overload leads to chronic left atrial enlargement and remodeling.[11] Initially, the LA compensates for the increased volume by enhancing its reservoir function. However, in advanced stages, LA remodeling results in dilation, dysfunction, myocardial cell hypertrophy, and interstitial fibrosis, increasing the risk of AF.[12] Two-dimensional speckle-tracking echocardiography (2DSTE) has gained prominence in evaluating LA function.[13] LA function is categorized into reservoir, conduit, and contraction phases, with LA reservoir strain (LASr) being the most reliable prognostic indicator.[14] LA strain assessment provides insights into structural remodeling, with LASr being a superior marker of fibrosis compared to LA size.[15] Myocardial fibrosis precedes LA enlargement in the remodeling process, making LASr a crucial metric for risk stratification, disease progression prediction, and surgical optimization.[16]

In patients with severe primary MR, impaired LASr correlates with worse survival post-mitral valve surgery.[17] A threshold LASr ≤24% is linked to poorer survival over a median follow-up of 6.4 years, and a reduction in LA peak atrial longitudinal strain (PALS) below 35% predicts adverse cardiovascular events such as AF, stroke, and cardiovascular mortality.[15] Studies have demonstrated a significant drop in LASr immediately after mitral valve repair, followed by partial recovery over long-term follow-up.[17] However, patients with persistently low LASr (<22%) postoperatively exhibit significantly higher mortality rates at 1, 3, and 5 years.[6]

The clinical significance of LA reservoir strain is evident in patients with chronic severe MR undergoing surgical correction. Lower LASr values (<23.6%) are associated with a higher risk of cardiovascular events, emphasising the importance of preoperative assessment. Consequently, LA reservoir function assessment is a more reliable prognostic tool than LA volume assessment for determining surgical outcomes. Early mitral valve intervention before significant LASr decline can optimize clinical outcomes, even in symptomatic patients with left atrial volume index (LAVi) max <60 mL/m².[9] This study aimed to determine the relationship between LASr and mortality one year after surgery for severe primary MR undergoing valve replacement surgery

METHOD

This study is an observational analytic study with a cross-sectional design to assess the relationship between left atrial reservoir strain and one-year mortality after surgery in patients with severe primary mitral regurgitation undergoing mitral valve replacement at RSUP H. Adam Malik Medan. Sampling was conducted at RSUP H. Adam Malik Medan from October 2021 to October 2023. The target population included patients with severe primary mitral regurgitation who underwent mitral valve replacement. The sample consisted of patients who met the inclusion and exclusion criteria, with a total of 52 patients selected using consecutive sampling.

The inclusion criteria were adult patients over 18 years of age diagnosed with severe primary mitral regurgitation undergoing mitral valve replacement. The exclusion criteria were as follows: congenital heart disease, hypertrophic cardiomyopathy, baseline left ventricular ejection fraction <50%, coronary artery disease with >50% stenosis, idiopathic myocardial disease, a history of mitral valve surgery, significant mitral stenosis (mean gradient >5 mmHg), significant aortic valve disease (moderate or severe), poor echocardiographic window preventing left atrial and ventricular measurements, mitral valve repair instead of replacement, and incomplete medical records.

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara, and research permission was obtained from the Research and Development Unit of RSUP H. Adam Malik Medan. Subjects undergoing echocardiography at RSUP H. Adam Malik Medan who met the inclusion criteria were included in the study. Patients who met the exclusion criteria were not included in the study. Sampling was conducted using a consecutive sampling method, in which every eligible subject was included until the required sample size was reached. Baseline patient data, including demographic and clinical history, were recorded. Patients were followed up for one year to assess mortality.

Echocardiography was performed by residents specialising in echocardiography under the supervision of an expert. The echocardiography devices used were GE Vivid E9 and GE Healthcare Vivid S60, and image analysis was conducted using EchoPac Software Version 203. The echocardiographic parameters measured included left ventricular end-diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), left atrial volume index (LAVi), tricuspid annular plane systolic excursion (TAPSE), mitral valve area (MVA) via planimetry, regurgitant volume (RVol), vena contracta, and effective regurgitant orifice area (EROA). Left atrial strain was assessed in three phases: reservoir, conduit, and contractile. The left atrial reservoir strain (LASr) was measured based on the difference in strain from the mitral valve opening to the end-diastole of the left ventricle. The LASr value was calculated as the average measurement from the four-chamber view after tracing the left atrial (LA) border.

Categorical variables are presented as frequencies (n) and percentages (%). Numerical variables are presented as mean ± standard deviation for normally distributed data or median (min–max) for non-normally distributed data. Normality testing for numerical variables was performed using the Kolmogorov-Smirnov ($n > 50$) or Shapiro-Wilk ($n < 50$) test. Bivariate analysis was conducted using the Independent T-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Statistical significance was set at $p < 0.05$. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cutoff value of LA reservoir strain (LASr) as a predictor of one-year mortality in patients with severe primary mitral regurgitation undergoing mitral valve replacement. The ROC curve analysis provided the area under the curve (AUC), optimal cutoff value, sensitivity, and specificity.

RESULTS

A total of 55 patients with severe primary mitral regurgitation who underwent mitral valve replacement at RSUP H. Adam Malik Medan were included in this study. All participants met the inclusion and exclusion criteria and underwent comprehensive clinical assessments, including anthropometric indices, risk factors, baseline ECG rhythm, previous cardiac medication history, laboratory tests, and echocardiographic evaluations. Laboratory parameters included complete blood count and renal function tests, while echocardiographic parameters included left ventricular ejection fraction (LVEF), left atrial volume index (LAVi), and right ventricular contractility using TAPSE.

The mean age of the study participants was 39.35 ± 12.59 years, with a male predominance of 28 patients (50.9%). The most common aetiology of mitral valve disease was rheumatic heart disease, which was found in 39 cases (70.9%). Atrial fibrillation was the predominant ECG rhythm, observed in 33 (60%) patients, whereas sinus rhythm was observed in 22 (40%) patients. Tricuspid regurgitation was the most frequently associated valvular abnormality in 16 patients (29.1%), followed by moderate mitral stenosis in 5 patients (9.1%) and mild aortic regurgitation in 5 patients (9.1%). Hypertension, type 2 diabetes mellitus, and COPD were comorbidities found in two (3.6%), seven (12.7%), and two (3.6%) patients, respectively. Beta-blocker use was recorded in 47 patients (85.5%), whereas 41 patients (74.5%) received ACE inhibitors. The median systolic and diastolic blood pressures were 110 mmHg (90-140) and 70 mmHg (50-80), respectively. The laboratory findings showed a mean haemoglobin level of 13.1 ± 1.37 g/dL. The mean preoperative and postoperative creatinine clearance values were 81 ± 31.83 mL/min and 83 ± 43.88 mL/min, respectively.

Table 1. Clinical Characteristics of Study Subjects

Parameter	n (55)
Male Gender, n (%)	28 (50.9)
Age (years)	39.35 ± 12.59
Body Weight (Kg)	56.09 ± 13.52
Height (cm)	160.11 ± 7.43
Body Surface Area (m²)	1.55 ± 0.29
Systolic Blood Pressure (mmHg)	110 (90 – 140)
Diastolic Blood Pressure (mmHg)	70 (50 – 80)
ECG Findings, n (%)	
Sinus Rhythm	22 (40)
Atrial Fibrillation	33 (60)
Comorbidities, n (%)	
Type 2 Diabetes Mellitus	7 (12.7)
Chronic Obstructive Pulmonary Disease (COPD)	2 (3.6)
Hypertension	2 (3.6)
Medication History, n (%)	
ACE Inhibitors	41 (74.5)
Beta-Blockers	47 (85.5)
Mitral Valve Etiology, n (%)	
Degenerative	15 (27.3)
Rheumatic	39 (70.9)
Infective Endocarditis	1 (1.8)
Associated Valvular Involvement, n (%)	
Moderate Mitral Stenosis	5 (9.1)
Moderate to Severe Tricuspid Regurgitation	16 (29.1)
Moderate Aortic Regurgitation	5 (9.1)
Laboratory Findings	
Hemoglobin (g/dL)	13.1 ± 1.37
Creatinine Clearance Pre-Op (mL/min)	81 ± 31.83
Creatinine Clearance Post-Op (mL/min)	83 ± 43.88
Surgical Procedure Details	
Procedure Duration (minutes)	161.04 ± 65.46
Cardiopulmonary Bypass Duration (minutes)	97.31 ± 31.45
Aortic Cross-Clamp Duration (minutes)	77.49 ± 28.63
Postoperative Outcomes	
ICU Stay Duration (days)	2 (1 – 19)
Total Hospital Stay Duration (days)	5 (1 – 18)
High-Dose Hemodynamic Support, n (%)	18 (32.7)
Postoperative Heart Failure, n (%)	16 (29.1)
Postoperative Complications, n (%)	27 (49.1)
One-Year Postoperative Mortality, n (%)	11 (20)

Postoperative outcomes showed that 11 patients (20%) died within one year of surgery, with two deaths occurring after hospital discharge. Acute heart failure developed in 16 patients (29.1%), and no patient required repeat surgery. The median intensive care unit (ICU) stay was 2 days (1-19), and the median total hospitalisation duration was 5 days (1-18). Postoperative complications were observed in 27 patients (49.1%), including bleeding (5 patients, 29.4%), arrhythmia (4 patients, 28.5%), shock (5 patients, 29.4%), coagulation abnormalities (3 patients, 21.4%), acute kidney injury (1 patient, 7.1%), and adhesiolysis (1 patient, 7.1%). Haemodynamic support with high-dose inotropes, such as dobutamine, milrinone, norepinephrine, epinephrine, and dopamine, was required in 18 patients (32.7%).

Table 2. Echocardiographic Characteristics Before and After Surgery

Parameter	n (55)
LVEF (%)	42.84 ± 10.95
LAVi (mL/m²)	120.5 (46–496)
TAPSE (mm)	17 (12–28)
LVEDD (mm)	61.55 ± 10.64
MR VC (cm)	0.84 ± 0.26
MR PISA (cm)	0.99 ± 0.35
MR ERO (cm²)	0.6 (0.2–2.3)
MR Rvol (mL)	88.79 ± 33.82
LASr	20.79 ± 7.45

Table 3. Differences in Clinical Characteristics of Study Subjects Based on Mortality

Parameter	Mortality		P-value
	Yes (n=11, 20%)	No (n=44, 80%)	
Gender, n (%)			
Male	5 (45.5)	23 (52.3)	0.686a
Age and Anthropometric Data			
Age (years)	41 ± 9.35	38.93 ± 13.33	0.636c
Body Weight (Kg)	56.27 ± 19.10	56.05 ± 12.03	0.961c
Height (cm)	157.09 ± 7.88	160.86 ± 7.21	0.133c
Body Surface Area (m²)	1.56 ± 0.28	1.54 ± 0.302	0.876c
Systolic Blood Pressure (mmHg)	100 (90–120)	110 (90–140)	0.244d
Diastolic Blood Pressure (mmHg)	70 (50–80)	70 (60–80)	0.806d
ECG Findings, n (%)			
Sinus Rhythm	7 (63.6)	26 (59.1)	1.000b
Atrial Fibrillation	4 (36.1)	18 (40.9)	
Comorbidities, n (%)			
Type 2 Diabetes Mellitus	1 (9.1)	6 (3.6)	1.000b
Chronic Obstructive Pulmonary Disease (COPD)	0 (0)	2 (4.5)	1.000b
Hypertension	0 (0)	2 (4.5)	1.000b
Medication History, n (%)			
ACE Inhibitors/ARBs	8 (72.7)	33 (75.0)	1.000b
Beta-Blockers	8 (72.7)	39 (88.6)	0.335b
Mitral Valve Etiology, n (%)			
Degenerative	3 (27.3)	12 (27.3)	
Rheumatic	8 (72.7)	31 (70.5)	0.880b
Infective Endocarditis	0	1 (2.3)	
Other Valvular Involvement, n (%)			
Moderate Mitral Stenosis	1 (9.1)	4 (9.1)	1.000b
Moderate to Severe Tricuspid Regurgitation	3 (27.3)	13 (29.5)	0.259b
Moderate Aortic Regurgitation	2 (18.2)	3 (6.8)	
Laboratory Findings			
Hemoglobin (g/dL)	13.51 ± 1.41	13.00 ± 1.35	0.277c
Creatinine Clearance Pre-OP (ml/min)	86.36 ± 29.97	88.98 ± 32.59	0.131c
Creatinine Clearance Post-OP (ml/min)	66.09 ± 44.43	88.49 ± 43.08	0.810c
Surgical Procedure Parameters			
Procedure Duration (minutes)	193.00 ± 92.55	153.05 ± 55.34	0.078c
Cardiopulmonary Bypass Duration (minutes)	114.55 ± 32.55	93.00 ± 30.01	0.043c
Aortic Cross-Clamp Duration (minutes)	92.09 ± 26.42	73.84 ± 28.26	0.058c
Hospital Stay			
ICU Stay (days)	2 (1–19)	2 (1–6)	0.120d
Total Hospital Stay (days)	5 (1–12)	6 (2–18)	0.068d
Postoperative Outcomes, n (%)			
High-Dose Hemodynamic Support	10 (90.9)	8 (18.2)	0.001b
Postoperative Heart Failure (NYHA Class III-IV)	9 (81.8)	7 (15.9)	0.001b
Postoperative Complications	9 (81.8)	18 (40.9)	0.015a

Noted**:** a, Fisher Exact Test; b, Mann-Whitney Test; c, Independent T-test; d, Mann-Whitney Test

Table 4. Differences in Echocardiographic Characteristics of Study Subjects Based on Mortality

Parameter	Yes (n=11)	No (n=44)	P-value
Preoperative Echocardiography			
Left Ventricular Ejection Fraction (LVEF, %)	60 ± 8.29	62.57 ± 8.52	0.373c
Left Atrial Volume Index (LAVi, ml/m²)	150 (80–273)	119 (46–496)	0.214d
Tricuspid Annular Plane Systolic Excursion (TAPSE, mm)	17 (12–24)	17 (14–28)	0.558d
Left Ventricular End-Diastolic Diameter (LVEDD, mm)	65 (46–88)	62 (43–88)	0.405d
Mitral Regurgitation Vena Contracta (MR VC, cm)	0.85 ± 0.21	0.84 ± 0.28	0.840c
Mitral Regurgitation PISA (cm)	1.07 ± 0.50	0.97 ± 0.31	0.388c
Mitral Regurgitation Effective Regurgitant Orifice Area (MR ERO, cm²)	0.6 (0.4–2)	0.6 (0.3–2.3)	0.251d
Mitral Regurgitation Regurgitant Volume (MR Rvol, ml)	93.82 ± 36.00	87.52 ± 33.56	0.586c
Left Atrial Reservoir Strain (LASr)	11.86 ± 2.77	22.51 ± 7.24	0.001c
Postoperative Echocardiography			
Left Ventricular Ejection Fraction (LVEF, %)	49 (25–54)	45 (23–58)	0.697d
Left Atrial Volume Index (LAVi, ml/m²)	81 (41–453)	96.5 (40–453)	0.712d
Tricuspid Annular Plane Systolic Excursion (TAPSE, mm)	11.91 ± 3.7	13.59 ± 2.69	0.092c

Noted: Statistical Tests: * Fisher Exact Test; ** Mann-Whitney Test; *** Kruskal-Wallis Test

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal LASr cutoff for predicting one-year mortality. The ROC curve demonstrated a strong predictive value (P = 0.0001, AUC = 0.851, 95% CI = 0.751–0.952). An LASr cutoff of 18.8 showed a sensitivity of 90.9% and a specificity of 70.5% for predicting mortality (Table 5).

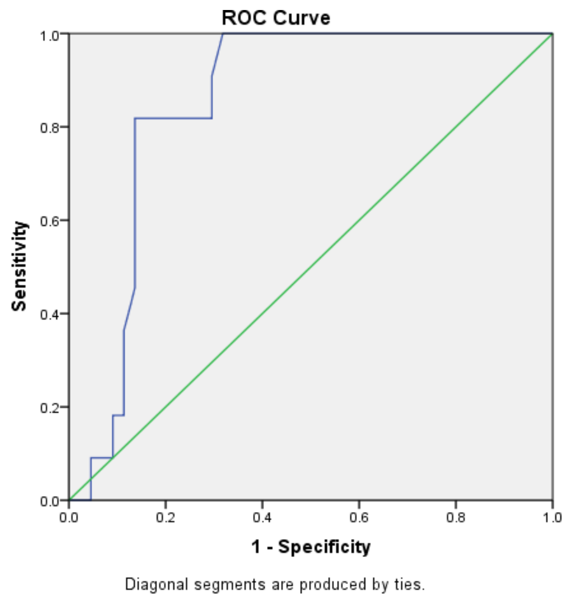

Figure 1. ROC Curve of LASr Parameter as a Predictor of One-Year Mortality After Mitral Valve Replacement in Patients with Severe Primary Mitral Regurgitation.

Table 5. ROC Analysis of LASr as a Predictor of One-Year Mortality

Parameter	Cutoff Value	AUC	P-value	Sensitivity	Specificity	95% CI
LASr	18.8	0.851	0.0001	90.9%	70.5%	0.751–0.952

Bivariate analysis confirmed that patients with a preoperative LASr ≤18.8 had significantly higher mortality rates (90.9%) than those with LASr >18.8 (9.1%) (P = 0.0001; OR = 23.85, 95% CI: 2.763–205.789). These findings highlight the prognostic significance of LASr in predicting one-year mortality following mitral valve replacement in patients with severe primary mitral regurgitation. These results suggest that early assessment and stratification based on LASr may help optimise surgical timing and improve clinical outcomes (Table 6).

Table 6. Bivariate Analysis of Preoperative LASr Values and One-Year Mortality After Surgery

LASr	Mortality	No Mortality	P-value	OR	95% CI
≤ 18.8	10 (90.9%)	13 (29.5%)	0.0001*	23.85	2.763 – 205.789
> 18.8	1 (9.1%)	31 (70.5%)			

Statistical Test: * Fisher Exact Test

DISCUSSION

This study highlights the prognostic significance of left atrial reservoir strain (LASr) in patients undergoing mitral valve replacement for severe primary mitral regurgitation (MR). Among the 55 patients, 11 (20%) did not survive, whereas 44 (80%) survived. Preoperative echocardiographic evaluation revealed that the majority of patients had preserved left ventricular ejection fraction (LVEF), with an average preoperative LVEF of 42.84 ± 10.95 and an LASr of 20.79 ± 7.45. Notably, the mean LASr was significantly lower in patients who did not survive (11.86 ± 2.77 vs. 22.51 ± 7.24, P = 0.001).

Speckle-tracking echocardiography (STE) is a novel non-Doppler-based method that enables the objective quantification of left atrial (LA) myocardial deformation, making it useful for functional LA analysis. Cameli et al. demonstrated a strong inverse correlation between peak atrial longitudinal strain (PALS) and LA myocardial fibrosis (r = -0.82, P < 0.0001), establishing PALS as a superior predictor compared to LA volume index (r = 0.51, P = 0.01) and LA ejection fraction (r = 0.61, P = 0.005) (34). Mandoli et al. further demonstrated that PALS <21% was associated with significantly worse five-year event-free survival (30 ± 9% vs. 90 ± 5%, P < 0.0001) (31).

LASr has also been linked to atrial remodeling and adverse clinical outcomes. Yang et al. found that lower baseline LASr was associated with increased LA remodeling and a higher likelihood of mitral valve intervention (β = -0.424, P = 0.002) (37). Stassen et al. confirmed that preoperative LASr <22% was independently associated with increased all-cause mortality at 1, 3, and 5 years (P < 0.001) (6). Additionally, Oh et al. found that LASr <23.6% was predictive of major cardiovascular events within five years (AUC = 0.736, P < 0.001) (9).

Sugimoto et al. demonstrated that LASr >16% during exercise was predictive of three-year event-free survival in MR patients (41). Ring et al. found that LA function independently predicted survival in patients with moderate-to-severe MR, supporting early surgical intervention in high-risk patients (39). Kim et al. also showed that LASr <15.5% was associated with significantly worse postoperative clinical outcomes (AUC = 0.661, P = 0.003) (30).

Our ROC curve analysis revealed an AUC of 0.851 for LASr, with an optimal cutoff of 18.8, showing 90.9% sensitivity and 70.5% specificity for predicting mortality. Among patients with LASr ≤18.8, 90.9% (10 out of 11) died, while only 9.1% (1 out of 11) with LASr >18.8 died (P = 0.0001; OR = 23.85; 95% CI: 2.763 – 205.789). These findings underscore the potential role of LASr in stratifying high-risk patients who require closer monitoring or early surgical intervention.

Stassen et al. demonstrated that LASr significantly declines immediately after mitral valve repair (23.6 ± 9.4% preoperatively to 11.5 ± 5.0%, P < 0.001) but partially recovers during long-term follow-up (17.3 ± 7.5%, P < 0.001) (6). Patients with persistent LASr decline during follow-up exhibited significantly higher mortality, emphasising its prognostic significance.

These findings suggest that LASr is a crucial parameter in the management of MRA, providing valuable insights for risk stratification and early surgical intervention. In asymptomatic patients with severe MR, LASr evaluation may help identify candidates for early mitral valve surgery, preventing adverse left ventricular remodelling, new-onset atrial fibrillation, and irreversible pulmonary vascular remodelling (6). Conversely, patients with left atrial dilation but preserved LASr may benefit from conservative treatment.

CONCLUSION

LASr has a strong predictive value for one-year mortality in patients with severe primary mitral regurgitation undergoing mitral valve replacement. The study population consisted predominantly of young patients, with rheumatic heart disease as the leading cause of death. Atrial fibrillation was a common finding, and postoperative echocardiography revealed a decline in left ventricular ejection fraction and atrial function. Lower LASr values were associated with higher mortality, prolonged cardiopulmonary bypass time, increased need for inotropic support, postoperative heart failure, and complications. These findings highlight the importance of LASr in risk stratification and the optimisation of surgical timing for better clinical outcomes.

DECLARATIONS

Ethics approval and consent to participate were obtained. Permission for this study was obtained from the Ethics Committee of the Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare no conflicts of interest in this study.

AUTHORS' CONTRIBUTIONS

All authors significantly contributed to the work reported in the execution, acquisition of data, analysis, and interpretation, or in all these areas. Contributed to drafting, revising, or critically reviewing the article. Approved the final version for publication, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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