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Original article

Myocardial Strain in Prediction of Outcomes after Surgery for Severe Mitral Regurgitation

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Abstract:

Background: Severe primary mitral regurgitation (MR) poses a significant clinical challenge, and surgical correction is often necessary to improve outcomes. However, the ability to predict post-surgical results is still a critical concern. This research aimed to investigate the function of myocardial strain, specifically global longitudinal strain (GLS), in predicting outcomes after surgery for severe MR. **Methods:** This prospective cohort research was undertaken on 104 individuals with severe primary MR who had repair or replacement of the mitral valve. Transthoracic echocardiography and speckle-tracking analysis were conducted to assess myocardial strain. **Results:** Patients experiencing the primary endpoint (a composite of re-hospitalization for heart failure, cardiac mortality, and redo surgery) demonstrated significantly lower baseline GLS (-14.1 ± 3.4 vs. -18.3 ± 2.5, P-value < 0.001) compared to those without the endpoint. ROC analysis exhibited that baseline GLS was an excellent predictor of the primary endpoint (AUC = 0.846, P-value < 0.001). Multivariate logistic regression confirmed that baseline GLS was a significant predictor of the primary endpoint (OR = 0.566, 95% CI = 0.445 – 0.719, P-value < 0.001). Kaplan-Meier analysis exhibited that patients with GLS ≤ 17.9 had significantly lower endpoint-free survival rates. **Conclusion:** GLS seems to be a more accurate predictor of cardiac events than all-cause mortality following surgery for severe MR. In patients with severe primary MR, measuring preoperative GLS is useful for predicting postoperative prognosis and deciding the appropriate schedule for surgery.

Keywords: Mitral Regurgitation; Myocardial Strain; Global Longitudinal Strain; Surgical Correction; Echocardiography.

Introduction

Mitral regurgitation (MR) refers to the abnormal reversal of blood flow from the left ventricle (LV) to the left atrium (LA). This condition occurs due to damage to any part of the machinery associated with the mitral valve (MV) [(1)]. The primary factors leading to MR include mitral valve prolapse (MVP), rheumatic heart disease, infectious endocarditis, annular calcification, cardiomyopathy, and ischemic heart disease [(2)].

The second most typical heart valve condition in industrialized nations is MR. Severe MR is related to greater morbidity and mortality without surgical treatment despite most people with the condition being asymptomatic[(3)]. MV repair is considered a better surgical choice than MV replacement in severe MR patients because it prevents LV remodelling dysfunction and enhances clinical results. Although some clinical evidence suggests that early surgery is beneficial, the ideal surgery time in severe MR cases is still unknown [(4)].

Patients with significant MR have reported that measures of myocardial deformation, such as LV strain and strain rate obtained through speckle-tracking imaging, are valuable in detecting early declines in LV function before clinical symptoms emerge and predicting a rapid reduction in LV ejection fraction following surgery [(5)].

Despite the notable success achieved through surgical repair for primary MR, as well as a substantial decrease in operative mortality, the 2017 focused update guidelines for operative criteria continued to uphold the 2006 guidelines [(6)]. The current recommendations endorse surgical intervention for individuals experiencing severe MR symptoms or those who, even in the absence of symptoms, demonstrate early signs of LV failure [(7)]

When the LV ejection fraction (EF) is between 30% and 60% or the LV end-systolic dimension (ESD) is ⩾40 or ⩾45 millimetres, it is said that the LV is dysfunctional [(6)]. The existing rules make it challenging to choose the best time for surgery, though. The hemodynamic environment of MR has an impact on the interpretation of the LVESD and LVEF parameters, which are suggested in the guideline. LVESD is rarely greater than 45 mm in asymptomatic individuals considering operation [(7)].

Furthermore, due to MR's propensity to reduce LV afterload, subclinical LV dysfunction may often escape detection in individuals with severe MR, as their LVEF frequently remains within the normal or elevated range [(8)]. Early-stage LV dysfunction with a normal LVEF indicates a poor prognosis, necessitating surgical LV decompensation. Hence, it can be a complex task to promptly identify potential LV dysfunction and perform timely surgical intervention in individuals with chronic severe MR to prevent the progression of permanent LV dysfunction [(7)].

Longitudinal myocardial function has been shown to be more effective in detecting moderate myocardial injury in MR patients compared to radial myocardial function, making it a suitable method for this purpose. One of the best ways to quantify the longitudinal contraction of the LV is by myocardial strain, and a recently developed technique called speckle-tracking strain analysis has been proven to properly depict LV myocardial function with angle-independent assessment [(9)].

This research aimed to determine whether GLS serves as a more precise predictor of clinical outcomes after MR surgery compared to conventional measures.

Patients and methods:

This prospective cohort research was conducted in the Cardiology Department of the National Heart Institute and Benha University on 104 severe primary MR patients who had undergone surgical correction with either MV repair or MV replacement. The study was done over a period of two years from July 2021 to June 2023.

After receiving written informed consent from each subject, the study was carried out with their permission after receiving approval from the Institutional Review Board (IRB) of the Benha University Faculty of Medicine (Approval number: MD.5.7.2021).

Exclusion criteria: MR resulted from a previous percutaneous mitral valvuloplasty, combined severe aortic regurgitation or aortic stenosis, combined severe mitral stenosis, acute MR brought on by acute infective endocarditis, patients who had undergone CABG for acute coronary syndrome (ACS) or stable angina, and patients who needed to have MV surgery again.

Patients were subjected to the following procedures:

Transthoracic Echocardiography:

The equipment used to collect the echocardiographic data was readily accessible for purchase. A skilled sonographer performed conventional 2-dimensional, M-mode, conventional, and color Doppler ultrasonography on each subject, keeping with the American Society of Echocardiography standards. An integrated method was used to measure the amount of MR, which included looking at the morphology of the valve, measuring the size of the effective regurgitant orifice, calculating the volume of regurgitated blood utilizing the proximal isovelocity surface area method, and analyzing the patterns of pulmonary venous flow. The proximal isovelocity surface area approach confirmed severe MR based on an effective regurgitant orifice area of ≧ 0.40 cm2 and a regurgitant volume of ≧ 60 ml.

Measurements of LV end-diastolic dimension (EDD), ESD, and wall thickness were conducted using M-mode or 2-dimensional imaging. The apical 2-chamber and 4-chamber images were employed to determine LV end-diastolic volume (EDV) and end-systolic volume (ESV), while Simpson's biplane method was used to assess LVEF. The right ventricular systolic pressure calculation was based on the peak velocity of tricuspid regurgitation.

Strain Analysis:

The speckle-tracking methodology enables angle-independent assessment of cardiac deformation by monitoring the frame-to-frame changes in naturally occurring acoustic speckles generated through the scattering of ultrasound beams by tissue. Sonomicrometry and magnetic resonance imaging had shown a correlation with this technique, which had been confirmed. In addition to apical 4-chamber, apical 3-chamber, and apical 2-chamber views, 2-dimensional grayscale pictures were obtained from a parasternal short-axis view at the mid-papillary level for global strain analysis. Software made available for purchase was used to measure strain.

The cardiac picture archiving and communication system's digitally acquired images were downloaded, and after being uploaded, they were analyzed utilizing the TomTec system (Image Arena version 4.6, TomTec, Munich, Germany). The final systolic frame included a hand tracing of the LV endocardial boundary. From the grayscale photos, the software automatically produced a strain curve. Peak strain is the highest negative number on the strain curve throughout the cardiac cycle. The peak value from the three apical images was averaged to determine the GLS. In 15 randomly chosen patients, reproducibility in strain measurement was assessed using the intraclass correlation coefficient.

Sample size:

Based on research conducted previously by another study, the sample size was determined utilizing Power and Sample Size software version 3[(7).] They examined the role of myocardial strain in the prognosis of patients undergoing surgery for severe mitral regurgitation. They reported a mean GLS of -16.5 in those who experienced cardiac events compared to -20.0 in those with no cardiac event. The estimated total sample size was (104 patients, 13 with a cardiac event and 91

without). The adjustments for alpha and power were 0.05 and 0.8, respectively.

Statistical analysis:

We used SPSS version 28 for managing and conducting statistical analysis of the data (IBM, Armonk, New York, United States). To assess the normality of quantitative data, we employed the Kolmogorov-Smirnov test, the Shapiro-Wilk test, and direct data visualization techniques. Quantitative data were summarized using means and standard deviations. Numbers and percentages served as a summary of categorical data. The independent t-test for quantitative variables was utilized to contrast quantitative data based on the 1ry endpoint. Categorical data were contrasted utilizing Chi-square or Fisher's exact test. A repeated-measures ANOVA was utilized to determine echo parameter values across time. All multiple comparisons were adjusted. ROC analysis was done for baseline LVEF and GLS to predict 1ry endpoint. The areas under the curves with their 95% CI, best cutoff points, and diagnostic indices were calculated. Interactions between time and GLS on Echo parameters were assessed using mixed model ANOVA. Multivariate logistic regression analysis was utilized to determine baseline LVEF, GLS, and AF as predictors of the 1ry endpoint and to evaluate the incremental prognostic value of GLS. Odds ratios with 95% CI were calculated. Kaplan Meier analysis was performed to estimate endpoint-free survival according to GLS. Utilizing the Log-rank test, survival curves were contrasted. All statistical tests had two outcomes. Cox regression analysis assessed the hazard ratio (HR) adjusted for other factors. Every statistical test was bi-directional. P-values < 0.05 were considered significant.

Results:

General characteristics:

The mean age of the studied patients was 40 ±14. There was a female predominance (60.7%). The mean BMI was 25.6 ±4.2. About one-third (34.8%) had hypertension, while one-quarter had diabetes (25.9%). Dyslipidemia was reported in 25%. AF was reported in 33%. Only 4.5% had a history of stroke, while 9.8% had a history of coronary revascularization. About half received RAAS blockers (56.3%) or beta-blockers (57.1%). Only 6.3% received CCB. Digoxin and diuretics were used in 23.2% and 68.8%, respectively (Table 1).

The mean hemoglobin was 12.9 ±1.5 gm/dl. The mean creatinine was 1 ±0.3 mg/dl. The mean total cholesterol was 189 ±39 mg/dl. The most frequent NYHA class was II (44.6%), while the least frequent was I (7.1%). Rheumatic disease was the most frequent etiology of MR (69.6%). Most patients underwent mitral valve replacement (83%), while the remaining 17% underwent valve repair. Only 4.5% needed concomitant CABG (Table 1).

Patients were classified according to the occurrence of 1ry endpoint at one year. Those with the 1ry endpoint demonstrated significantly higher diabetes (40.5% vs. 17.1%, P = 0.006), history of MI (16.7% vs. 4.3%, P = 0.026), history of coronary revascularization (19% vs. 4.3%, P = 0.011), calcium channel blockers use (14.3% vs. 1.4%, P = 0.011), and diuretics use (81% vs. 61.4%, P = 0.031). No significant variations were noticed regarding other parameters (Table 1, Figure 1).

Baseline Echo findings:

Patients who experienced the 1ry endpoint at one year had significantly lower LVEF (57.1 ±8.9 vs. 60.7 ±8.6, P = 0.038) and GLS (-14.1 ±3.4 vs. -18.3 ±2.5, P < 0.001) but higher LVESD (47.8 ±5.3 vs. 44.5 ±5.1, P = 0.001), LVESV (82.6 ±17.6 vs. 72.5 ±23, P = 0.016), LVEDD (63.84 ±5.08 vs. 61.05 ±5.14, P = 0.006), and RVSP (53.6 ±9.8 vs. 49.9 ±9.1, P = 0.049) in contrast to those who was not affected by the 1ry endpoint. Additionally, those with the 1ry endpoint had significantly higher GLS ≤ 17.9 (90.5% vs. 34.3%, P-

value < 0.001) than those who did not experience the 1ry endpoint (Table 2).

No significant differences were reported concerning LVEDV (P = 0.083) and LA diameter (P = 0.225) (Table 2).

Echo findings at baseline and follow-up:

LVEF significantly differed between baseline and follow-up (P-value <0.001). Post hoc analysis showed that it was noticeably greater at baseline (59.4 ±8.8) than immediately postoperative (46.6 ±7.9) and at one year (55 ±10.1). Additionally, it was significantly higher at one year than immediately postoperative (Table 3).

LVEDD significantly differed between baseline and follow-up (P-value <0.001). Post hoc analysis exhibited that it was significantly greater at baseline (62.09 ±5.27) than immediately postoperative (59.8 ±5.5) and at one year (57.8 ±5). Additionally, it was significantly higher immediately postoperative than at one year (Table 3).

LVEDV significantly differed between baseline and follow-up (P-value <0.001). Post hoc analysis showed that it was significantly greater at baseline (188.7 ±37.1) than immediately postoperative (165.6 ±40.9) and at one year (150.1 ±30.2). Additionally, it was significantly higher immediately postoperative than at one year **(**Table 3).

LVESD significantly differed between baseline and follow-up (P-value <0.001). Post hoc analysis exhibited that it was significantly greater immediately postoperative (48.4 ±5.6) than at baseline (45.7 ±5.4) and one year (44.1 ±5.6). Additionally, it was significantly greater at baseline than at one year (Table 3).

LVESV significantly differed between baseline and follow-up (P <0.001). Post hoc analysis exhibited that it was significantly greater immediately postoperative (89.4 ±33.9) than at baseline (76.3 ±21.6) and one year (69.4 ±29.7), with no significant difference between baseline and 1-year measure (Table 3).

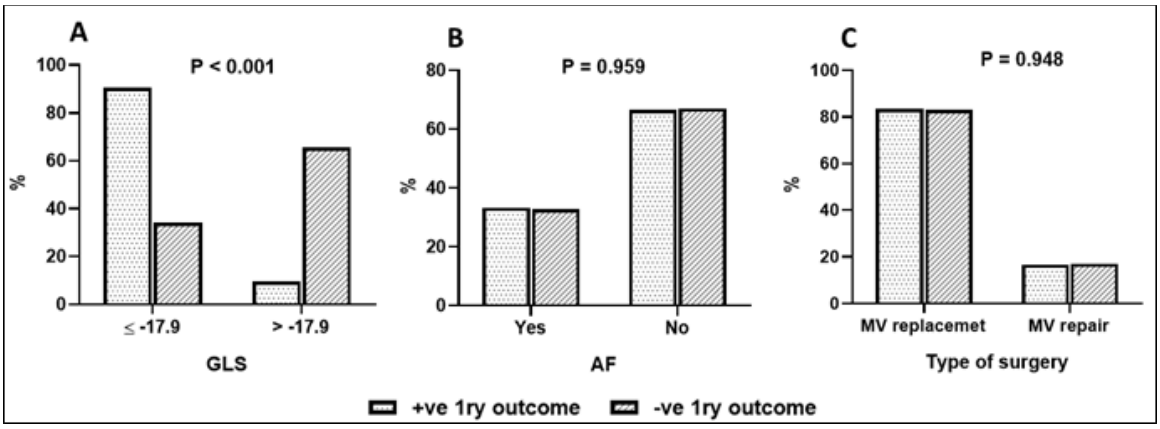

Figure 1. GLS, AF, and type of surgery according to the occurrence of the 1ry endpoint

Table 1: General characteristics according to the occurrence of the 1ry endpoint

		1ry endpoint at one year		
	Total (n = 112)	**Yes (n = 42)**	**No (n = 70)**	**P-value**
Age (years)	40 ±14	43 ±13	38 ±14	0.052
Gender				
Males	44 (39.3)	16 (38.1)	28 (40)	0.842
Females	68 (60.7)	26 (61.9)	42 (60)	
Body mass index (kg/m^2)	25.6 ±4.2	26.3 ±3.9	25.2 ±4.4	0.167
Hypertension	39 (34.8)	16 (38.1)	23 (32.9)	0.573
Diabetes mellitus	29 (25.9)	17 (40.5)	12 (17.1)	**0.006***
Dyslipidemia	28 (25)	12 (28.6)	16 (22.9)	0.499
Atrial fibrillation	37 (33)	14 (33.3)	23 (32.9)	0.959
History of stroke	5 (4.5)	0 (0)	5 (7.1)	0.155
History of MI	10 (8.9)	7 (16.7)	3 (4.3)	**0.026***
History of coronary revasc.	11 (9.8)	8 (19)	3 (4.3)	**0.011***
RAAS blocker	63 (56.3)	27 (64.3)	36 (51.4)	0.184
Beta-blockers	64 (57.1)	23 (54.8)	41 (58.6)	0.693
CCB	7 (6.3)	6 (14.3)	1 (1.4)	**0.011***
Digoxin	26 (23.2)	6 (14.3)	20 (28.6)	0.083
Duiretics	77 (68.8)	34 (81)	43 (61.4)	**0.031***
Hemoglobin (gm/dl)	12.9 ±1.5	12.8 ±1.2	13 ±1.6	0.421
Creatinine (mg/dl)	1 ±0.3	1 ±0.3	1 ±0.3	0.993
Total cholesterol (mg/dl)	189 ±39	190 ±38	188 ±40	0.835
NYHA class				
I	8 (7.1)	4 (9.5)	4 (5.7)	0.697
II	50 (44.6)	16 (38.1)	34 (48.6)	
III	30 (26.8)	12 (28.6)	18 (25.7)	
IV	24 (21.4)	10 (23.8)	14 (20)	
Etiology of MR				
Degenerative	34 (30.4)	16 (38.1)	18 (25.7)	0.168
Rheumatic	78 (69.6)	26 (61.9)	52 (74.3)	
Congenital	0 (0)	0 (0)	0 (0)	
Type of mitral surgery				
MV replacement	93 (83.0)	35 (83.3)	58 (82.9)	0.948
MV repair	19 (17.0)	7 (16.7)	12 (17.1)	
Concomitant CABG	5 (4.5)	4 (9.5)	1 (1.4)	0.065

Data were displayed as mean ± standard deviation (SD) and frequency (%), *Significant P-value; MI: Myocardial infarction; RAAS: Renin-angiotensin-aldosterone system; CCB: Calcium channel blockers; NYHA; New York heart association; MR: Mitral regurgitation; CABG: Coronary artery bypass graft.

Table 2: Baseline Echo findings according to the occurrence of the 1ry endpoint

		1ry endpoint at one year		
	Total	**Yes (n = 42)**	**No (n = 70)**	**P-value**
Baseline LVEF (%)	59.4 ±8.8	57.1 ±8.9	60.7 ±8.6	**0.038***
Baseline LVESD (mm)	45.7 ±5.4	47.8 ±5.3	44.5 ±5.1	**0.001***
Baseline LVESV (ml)	76.3 ±21.6	82.6 ±17.6	72.5 ±23	**0.016***
Baseline LVEDD (mm)	62.09 ±5.27	63.84 ±5.08	61.05 ±5.14	**0.006***
Baseline LVEDV (ml)	188.7 ±37.1	196.6 ±38.4	184 ±35.7	0.083
Baseline LA diameter (mm)	57.2 ±7.2	58.2 ±7	56.5 ±7.3	0.225
Baseline RVSP (mmHg)	51.3 ±9.5	53.6 ±9.8	49.9 ±9.1	**0.049***
Baseline GLS (%)	-16.7 ±3.5	-14.1 ±3.4	-18.3 ±2.5	**<0.001***
GLS cutoff				
≤ -17.9	62 (55.4)	38 (90.5)	24 (34.3)	**<0.001***
> -17.9	50 (44.6)	4 (9.5)	46 (65.7)	

Data were displayed as mean ± standard deviation (SD) and frequency (%), *Significant P-value; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic diameter; LVESV: Left ventricular end-systolic volume; LVEDD: Left ventricular end-diastolic diameter; LVEDV: Left ventricular end-diastolic volume; RVSP: Right ventricular systolic pressure; GLS: Global longitudinal strain.

Table 3: Echo findings at baseline and follow-up of the studied patients

	Mean ±SD	P-value
LVEF (%)		
Baseline	59.4 ±8.8 [a]	**<0.001***
Immediate post-op	46.6 ±7.9 [b]	
At 1-year	55 ±10.1 [c]	
LVEDD		
Baseline	62.09 ±5.27 [a]	**<0.001***
Immediate post-op	59.8 ±5.5 [b]	
At 1-year	57.8 ±5 [c]	
LVEDV		
Baseline	188.7 ±37.1 [a]	**<0.001***
Immediate post-op	165.6 ±40.9 [b]	
At 1-year	150.1 ±30.2 [c]	
LVESD		
Baseline	45.7 ±5.4 [a]	**<0.001***
Immediate post-op	48.4 ±5.6 [b]	
At 1-year	44.1 ±5.6 [c]	
LVESV		
Baseline	76.3 ±21.6 [a]	**<0.001***
Immediate post-op	89.4 ±33.9 [b]	
At 1-year	69.4 ±29.7 [a]	

Data were displayed as mean ± standard deviation (SD), *Significant P-value; Small letters indicate a significant pair if different and a non-significant pair if similar; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic diameter; LVESV: Left ventricular end-systolic volume; LVEDD: Left ventricular end-diastolic diameter; LVEDV: Left ventricular end-diastolic volume.

ROC analysis for LVED and GLS to predict 1ry endpoint:

ROC analysis was done for baseline LVEF and GLS to predict the occurrence of 1ry endpoint. For baseline LVEF, a significant AUC of 0.621 was observed, with a 95% CI ranging from 0.514 – 0.727 (P = 0.033), indicating fair discrimination ability. The best cut-off point was ≤ 56, at which sensitivity, specificity, PPV, and NPV were 42.9%, 75.7%, 51.4%, and 68.8%, respectively (Figure 2).

For baseline GLS, ROC analysis revealed a significant AUC of 0.846, with a 95% CI ranging from 0.773 – 0.920 (P < 0.001), indicating excellent discrimination ability. The best cut-off point was ≤ -17.9, at which sensitivity, specificity, PPV, and NPV were 90.5%, 65.7%, 61.3%, and 92%, respectively. There was a significant difference between the two ROC curves (P < 0.001) (Figure 2).

Interaction between time and GLS on Echo parameters

LVEF, LVEDD, and LVEDV were assessed at baseline, immediately postoperative, and at one year, according to the cut-off of GLS. As shown in Figure 3, no interactions were observed between the effect of time of follow-up and GLS on these parameters (Figure 3).

Primary endpoint:

The primary endpoint was reported in 37.5% of the studied patients. The most common endpoint was re-hospitalization for HF (64.3%), followed by cardiac mortality (26.2%) and redo surgery (9.5%) (Table 4).

Prediction of the 1^{ry} endpoint:

Multivariate logistic regression analysis was performed to anticipate the occurrence of the 1ry endpoint. Baseline GLS, LVEF, and AF were assessed as predictors, controlling for age, gender, BMI, DM, hypertension, and dyslipidaemia. Baseline GLS was a significant predictor of the 1ry endpoint at one year; a one percent rise in GLS was linked to 43.4% risk reduction of the 1ry endpoint (OR = 0.566, 95% CI = 0.445 – 0.719, P < 0.001) (Table 5).

Incremental prognostic value of GLS:
The incremental prognostic value of GLS in predicting 1ry endpoint was assessed. The 1st model included age and AF only. The global X^2 value was 3.789. After adding AF, the global X^2 value increased to 5.611. When GLS was added, the global X^2 increased to 49.032 (Figure 4).

Endpoint-free survival according to GLS:
Kaplan Meier analysis was done to ascertain endpoint-free survival according to the cut-off point of GLS. At six months, the endpoint-free survival was 87.1% for those with GLS ≤ 17.9 compared to 98% for those with GLS > 17.9. After six months, the curves greatly diverged until the end of the study. At the end of the study, the endpoint-free survival was 16.2% for those with GLS ≤ 17.9 compared to 91.5% for those with GLS > 17.9. A significant variation was reported between the two survival curves (Log-rank P < 0.001, adjusted HR = 11.118, 95% CI = 3.811 – 32.439). The HR was modified for age, gender, BMI, diabetes, hypertension, and dyslipidaemia (Figure 5).

Table 4: Primary endpoint and its type in the studied patients

	n (%)
Primary endpoint	42 (37.5)
Type of 1ry endpoint*	
Cardiac mortality	11 (26.2)
Rehospitalization for heart failure	27 (64.3)
Redo surgery	4 (9.5)

*Percentages were calculated according to a total of 42 patients with 1ry endpoint.

Table 5: Multivariate logistic regression analysis for baseline GLS, LVEF, and AF to predict 1ry endpoint

	OR (95%CI)†	P-value
Baseline GLS	0.566 (0.445- 0.719)	**<.001***
Baseline LVEF (%)	0.958 (0.909 - 1.011)	0.117
Atrial fibrillation	1.182 (0.494 - 2.829)	0.707

*Significant P-value; †Adjusted for age, gender, BMI, DM, HTN, and dyslipidemia; OR: Odds ratio; 95% CI: 95% Confidence interval

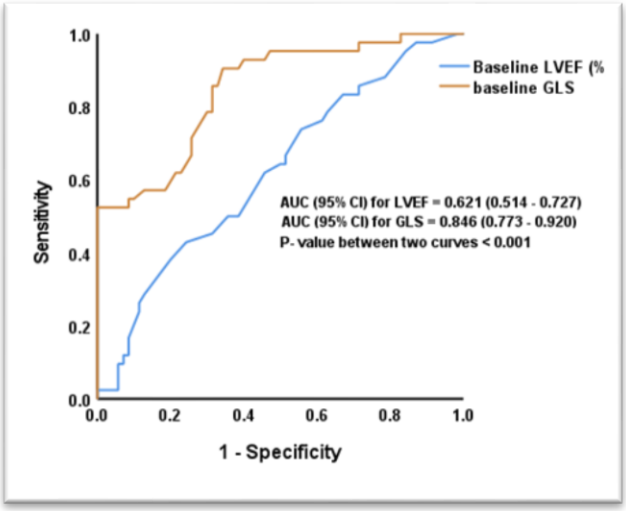

Figure 2. ROC analysis for LVED and GLS to predict 1ry endpoint

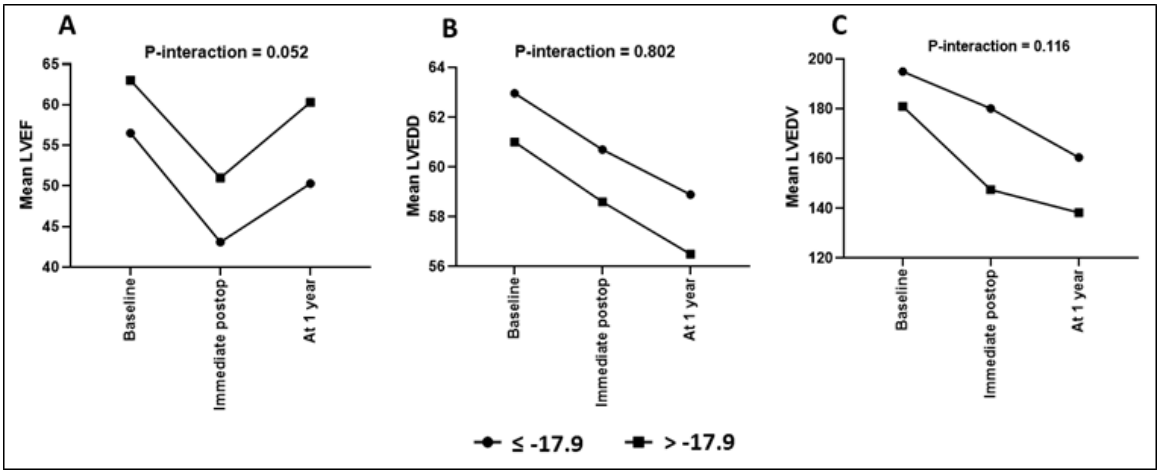

Figure 3. LVEF, LVEDD, and LVEDV at baseline, immediately postoperative, and at one year according to the cutoff of GLS

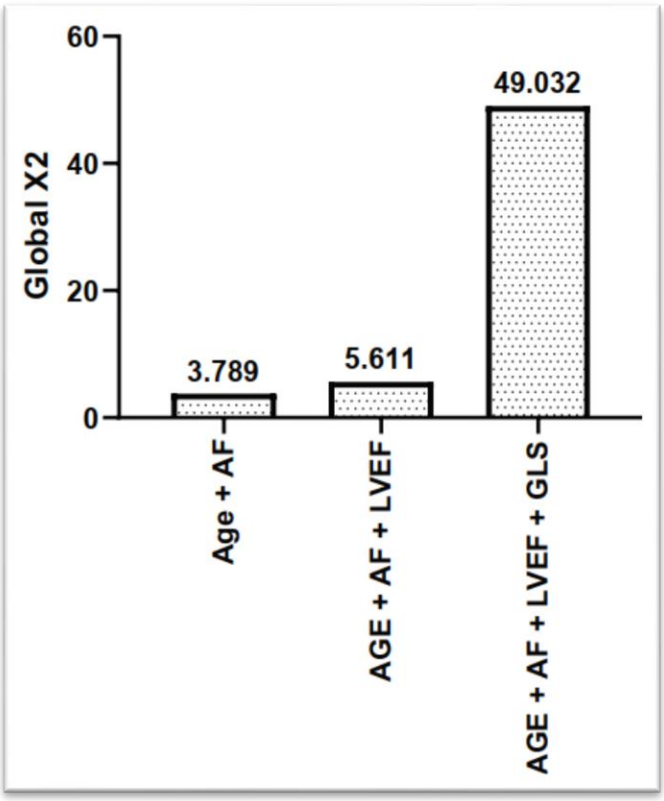

Figure 4. Incremental prognostic value of GLS in predicting 1ry endpoint

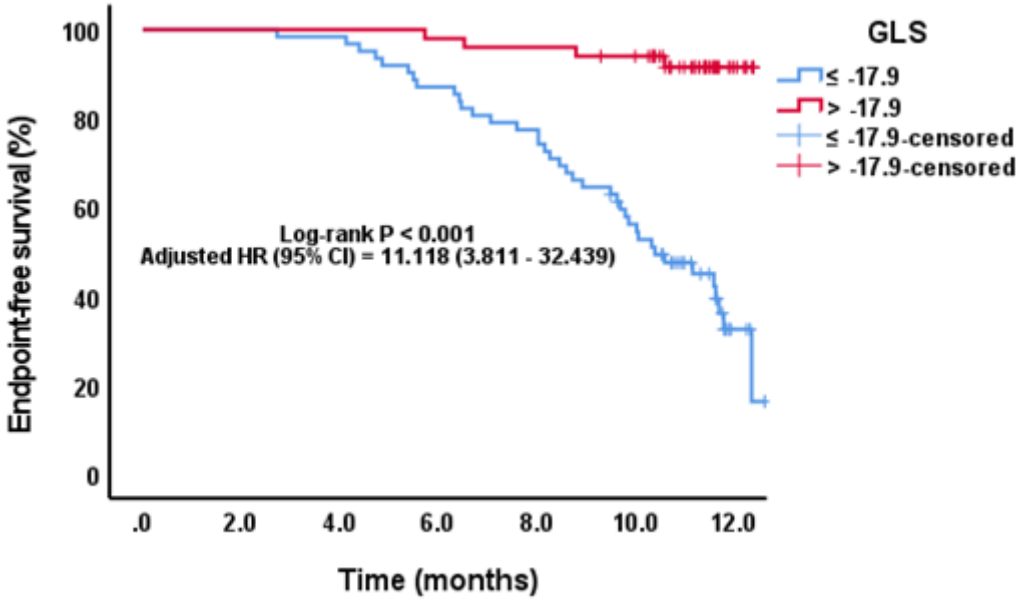

Figure 5. Kaplan Meier analysis for endpoint-free survival according to the cutoff point of GLS

Discussion:

In the current study, the mean age of studied patients was 40 ±14. There was a female predominance (60.7%). Patients were classified based on the prevalence of 1^{ry} endpoint at one year. Those with the 1^{ry} endpoint demonstrated significantly higher diabetes, history of MI, history of coronary revascularization, CCBs use, and diuretics use. A study found that patients with cardiac events were older (63.6 ± 13.3) years and had a greater prevalence of AF, stroke, and previous revascularization. However, no major differences existed between the groups concerning sex, hypertension, DM, and hypercholesterolemia. They also noted lower hemoglobin and total cholesterol levels and higher creatinine levels in the group that experienced cardiac incidents. Interestingly, there were no variations in cardiovascular drugs, such as renin-angiotensin system blockers, beta-blockers, CCBs, and diuretics, between the two groups. These differences could result from variations in sample size and also the patient characteristics [7].

Our study revealed that patients who experienced the primary endpoint exhibited lower GLS but higher LVESD, LVESV, LVEDD, and RVSP compared to those without the endpoint. At the same time, no significant differences were observed for LVEDV and LA diameter. Conversely, a study observed LV reverse remodeling after surgery, where LV parameters adapt to new loading conditions. Before surgery, compensatory mechanisms maintain normal LVEF despite increased preload and LV volume, while post-surgery, LV size decreases due to reduced preload. This reveals the complex nature of LV adaptation to surgical interventions [7].

Furthermore, other studies have shown a reduction in LVEF after MV surgery, primarily due to a smaller decrease in preload-dependent LVEDV than afterload-dependent LVESV [10, 11]. Some patients experience significant LVEF reduction, indicating LV dysfunction [12-14]. Of note, these studies showed the role of GLS in detecting postoperative LV dysfunction, which aligns with our finding that GLS

was significantly less in patients experiencing the primary endpoint.

The primary endpoint in our study was reported in 37.5% of the studied patients. The most common endpoint was re-hospitalization for HF (64.3%), followed by cardiac mortality (26.2%) and redo surgery (9.5%). Consistent with our findings, a study reported over a median follow-up period of 3.5 years that 56 (11.1%) patients died, 41 (8.1%) were hospitalized for heart failure, and 10 (2.0%) required reoperation [(7)].

In the current analysis, multivariable logistic regression revealed that baseline GLS was a significant predictor of the primary outcome at one year (OR = 0.566, 95% CI = 0.445 – 0.719, $p < 0.001$), controlling for age, gender, BMI, DM, hypertension, and dyslipidemia.

Some researchers studied 593 patients (64% men, age 65 ± 12 years) with severe primary MR who had MV surgery and reported that LV-GLS (HR: 1.13; 95% CI: 1.06 to 1.21; $p < 0.001$) were independently linked to all-cause death [(15)]. According to a study, the authors used multivariate Cox models to find that age (HR: 1.429, 95% CI: 1.116 to 1.831; $p = 0.005$), left atrial dimension (HR: 1.034, 95% CI: 1.006 to 1.063; $p = 0.019$), and GLS (HR: 1.229, 95% CI: 1.135 to 1.331; $p < 0.001$) were independent predictors of cardiac events. They also noted that LV GLS was a significant predictor of cardiac outcomes across different patient subgroups, irrespective of LV dysfunction, atrial fibrillation, or the type of surgery [(7)]. Also, a study reported that on multivariable Cox survival analysis, LV-GLS ([HR]: 1.11) was linked to a higher risk of death over time (all $p < 0.001$) [(16)].

The incremental prognostic value of GLS in predicting 1^{ry} endpoint was assessed. The 1st model included age and AF only. The global X^2 value was 3.789. After adding AF, the global X^2 value increased to 5.611. When GLS was added, the global X^2 increased to 49.032.

Speckle-tracking enables angle-independent evaluation, while LV GLS helps assess LV long-axis operation [(12)]. Due to the subendocardial placement, it has been proposed that cardiac diseases cause longitudinal myocardial function to be decreased more quickly than circular function [(21, 22)]. Consequently, evaluation of longitudinal function may aid in the early detection of LV failure [(22)]. Patients with MR also experienced earlier longitudinal function impairment. Longitudinal motion, being more adept at identifying mild LV dysfunction compared to radial contraction, becomes compromised as the left ventricle (LV) undergoes dilation and transitions towards a spherical shape with the progression of MR [(11)]. In contrast to left ventricular ejection fraction (LVEF), which predominantly evaluates radial contraction, global longitudinal strain (GLS) exhibited superior additional predictive value for cardiac events in this study. In another study, the incremental prognostic value of GLS for cardiovascular events was assessed. Model 3, modified for age, LA dimension, and AF, demonstrated higher predictive value with GLS (global X^2 from 31.926 to 59.246; $p < 0.001$). Model 4, which added LVEF to Model 2, also showed enhanced predictive power with GLS (global X^2 from 36.008 to 60.467; $p < 0.001$). GLS provided stronger incremental predictive capability compared to LVEF, beyond traditional risk factors [(7)]. In another study, the addition of LV-GLS to a clinical model (which also included age, AF, New York Heart Association functional class≥ II, estimated glomerular filtration rate, LVEDD, LVEF, and systolic pulmonary artery pressure) resulted in a substantial enhancement of the prognostic model (p 0.001) with a rise in C-statistic from 0.74 to 0.77 [(15)].

These findings underscore the clinical value of global longitudinal strain (GLS) in patients with severe MR who are scheduled for surgery, as it provides a

valuable contrast to LVEF and LVESD, which are the metrics recommended in the current guidelines. Setting the surgical timing based on the strain may, therefore, be beneficial. To ascertain the crucial function of GLS calculation in selecting the ideal timing of surgery, more prospective clinical trials are required.

In the present study, Kaplan-Meier analysis revealed a significant difference between survival curves based on a GLS cut-off 17.9. At six months, survival was 87.1% (GLS ≤ 17.9) vs. 98% (GLS > 17.9), and this difference continued until the end of the study. At the study's conclusion, survival was 16.2% (GLS ≤ 17.9) and 91.5% (GLS > 17.9). Log-rank test exhibited a significant variation ($p < 0.001$), with an adjusted HR of 11.118 (95% CI: 3.811 – 32.439), adjusted for age, gender, BMI, diabetes, hypertension, and dyslipidaemia.

Compatibly, a study observed that lowered GLS was connected to all-cause mortality (HR: 1.068, 95% CI: 1.003 to 1.136; $p = 0.040$) [7]. Interestingly, their study showed that patients with LV-GLS >–20.6% (more impaired) demonstrated noticeably lower survival than patients with LV-GLS ≤–20.6% [15]. A study revealed that patients with LV-GLS worse than the median (-19.5%) died at a considerably higher rate than patients with LV-GLS better than the median (log-rank P = 0.01) (86 of 513 [17%] vs. 60 of 550 [11%]). With an LV-GLS of worse than -19%, the chance of death at five years was dramatically elevated [16].

In a systematic review, the results show that baseline GLS, which ranges from -17.9 % to -21.7 % GLS, acts as an independent predictor of postoperative outcomes. Furthermore, they observed that impaired baseline GLS was linked to greater mortality rates. Notably, patients who underwent early surgery exhibited more favorable long-term survival rates [17]. In patients with primary MR, preoperative GLS is predictive of long-term survival and postoperative LVEF, as determined by a meta-analysis comprising eight studies that examined survival and postoperative LVEF outcomes according to preoperative GLS. They discovered that patients with a lower GLS percentage had a poorer prognosis after MV repair. (HR = 1.13, 95% [CI]: 1.02-1.26). Patients with preoperatively decreased GLS percent had postoperatively diminished LVEF (mean difference [MD] = -5.06%, 95% CI: -8.97-1.16%). Moreover, individuals with surgical LVEF dysfunction exhibited poorer preoperative GLS (MD = 4.33, 95% CI: 3.89-4.76) [17].

Finally, this study had some limitations. The study has a relatively small sample size, which could potentially limit the statistical power of the research. Secondly, the success of strain measurements is contingent on the quality of acquired images. We included patients with severe MR and AF to assess the prognostic value of GLS. Many prior clinical studies on GLS ruled out patients with AF owing to the variation in ventricular cycle length from beat to beat. Nevertheless, current guidelines recommend conducting several measures in AF patients [18]. Lastly, considering that the optimal cutoff value for GLS may differ in various populations of severe MR, it would be prudent to seek external validation in larger patient cohorts.

Conclusion:

Preoperative GLS is more accurate than standard parameters for predicting cardiac events in severe primary MR patients undergoing MV surgery. It aids in determining postoperative outcomes and timing the surgery optimally.

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