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ORIGINAL RESEARCH

Preprocedural Left Atrial Strain as a Predictor of Long-Term Outcomes Following Mitral Valve Interventions in Rheumatic Severe Mitral Stenosis

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BACKGROUND: This study explores whether preprocedural left atrial (LA) strain predicts outcomes in individuals with rheumatic, severe mitral stenosis undergoing mitral valve (MV) interventions.

METHODS: Data were from the MASTER (Multicenter Mitral Stenosis with Rheumatic Etiology) registry, including patients with severe mitral stenosis who underwent percutaneous mitral valvuloplasty or MV replacement. Participants with moderate or greater dysfunction of other valves or missing strain data were excluded. The primary outcome was a composite of all-cause mortality and heart failure hospitalization. Decreased LA reservoir strain was defined as <12.2%, determined through receiver operating characteristic analysis.

RESULTS: Among 609 individuals (mean age 57.4±12.1 years; 73% women), 424 (69.6%) had MV replacement and 185 (30.4%) underwent percutaneous MV. Those with decreased LA strain (n=307) were older, had more atrial fibrillation, smaller MV area, elevated mean diastolic pressure gradient, and increased right ventricular systolic pressure than those with preserved LA strain (n=302). Over a median follow-up of 6.1 (2.3–10.7) years after MV intervention, 7.7% (n=47) experienced the primary outcome, with significantly higher rates observed in individuals with decreased LA strain (P=0.001). Multivariate analysis showed decreased LA strain (hazard ratio [HR], 2.04 [95% CI, 1.06–3.93]; P=0.001), older age, and higher right ventricular systolic pressure were independent predictors of adverse outcomes.

CONCLUSIONS: Preprocedural decreased LA reservoir strain was associated with adverse clinical outcomes after MV intervention in individuals with severe mitral stenosis. These findings suggest that LA strain could serve as a marker for optimizing the timing of MV intervention.

Key Words: left atrium ■ mitral valve ■ prognosis ■ strain

Rheumatic mitral stenosis (MS) remains the most prevalent form of valvular heart disease, with a particularly high burden in low- and middle-income countries.[1,2] Current guidelines recommend mitral valve (MV) intervention for individuals with severe MS who are symptomatic, asymptomatic but present with

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CLINICAL PERSPECTIVE

What Is New?

- This study represents the first registry-based analysis to evaluate pre-procedural left atrial reservoir strain as a predictive marker for clinical outcomes following mitral valve intervention in individuals with severe mitral stenosis.
- The findings establish left atrial reservoir strain as a novel and clinically relevant prognostic marker for predicting outcomes after mitral valve intervention in individuals with severe mitral stenosis.

What Are the Clinical Implications?

- The study underscores left atrial reservoir strain as a prognostic marker in severe mitral stenosis, suggesting its integration into clinical decisions may help optimize and individualize mitral valve intervention.

Nonstandard Abbreviations and Acronyms

LAVI	left atrial volume index
MDPG	mean diastolic pressure gradient
MV	mitral valve
MVA	mitral valve area
MVR	mitral valve replacement
PMV	percutaneous mitral valvuloplasty
PSM	propensity score matching
RVSP	right ventricular systolic pressure

new-onset atrial fibrillation (AF), or have elevated right ventricular systolic pressure (RVSP) >50 mm Hg.[3,4] With careful selection of candidates, timely MV interventions, whether surgical or percutaneous, have the potential to alleviate symptoms and improve long-term prognosis in this population.[5]

The left atrium (LA) plays a pivotal role in the pathophysiology of rheumatic MS. As MS severity progresses, persistent narrowing of the MV impairs LA function, manifesting as fibrosis, increased stiffness, and reduced contractility. This process of adverse LA remodeling contributes to significant complications, including AF, pulmonary hypertension, and congestive heart failure (HF).[6] Given the critical importance of LA function in the progression of rheumatic MS and its impact on clinical outcomes, identifying individuals with adverse LA remodeling may provide valuable insights for optimizing management strategies and predicting outcomes.

Recent studies have identified LA function, assessed using 2-dimensional speckle-tracking echocardiography, as a strong prognostic indicator for cardiovascular outcomes in individuals with various cardiac diseases such as congestive HF, AF, and mitral regurgitation.[7–9] However, limited data currently exist regarding the association between LA strain and clinical outcomes in individuals with rheumatic MS, particularly following MV interventions. Therefore, this study aimed to evaluate the prognostic impact of preprocedural LA strain on clinical outcomes in individuals with rheumatic MS undergoing MV interventions, including percutaneous mitral valvuloplasty (PMV) or mitral valve replacement (MVR).

METHODS

The data underlying this article, including LA and LV strain, are available upon reasonable request to the corresponding author.

Study Population

The MASTER (Multicenter Mitral Stenosis With Rheumatic Etiology) registry is a multicenter, observational registry involving 4 tertiary hospitals in South Korea, with 3140 participants diagnosed with moderate to severe rheumatic MS between January 2001 and December 2020.[1,5,10,11] Among them, we screened 1030 individuals with severe MS who underwent their first MV intervention, either PMV or MVR, during this period. Of these, individuals with significant (moderate or greater) mitral regurgitation, aortic stenosis, or aortic regurgitation (n=343), as well as those with poor-quality echocardiographic images for left chamber strain analysis (n=78), were excluded. Ultimately, 609 individuals who underwent MV intervention for rheumatic severe MS were included in the study cohort (Figure 1).

Treatment strategies were determined by the attending specialized cardiologists based on clinical symptoms, physical activity levels, and indexed transthoracic echocardiographic findings. Following MV intervention, participants attended regular outpatient visits. Baseline clinical characteristics, medication usage, echocardiographic variables, and clinical outcomes were meticulously reviewed using the electronic medical records of each hospital. In patients who underwent PMV, postprocedural echocardiography was additionally analyzed to assess the effectiveness of the procedure and the improvement in echocardiographic parameters. This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Yonsei University Health System (IRB number: 4-2022-0214). The board waived the requirement for informed consent due to the study's retrospective design.

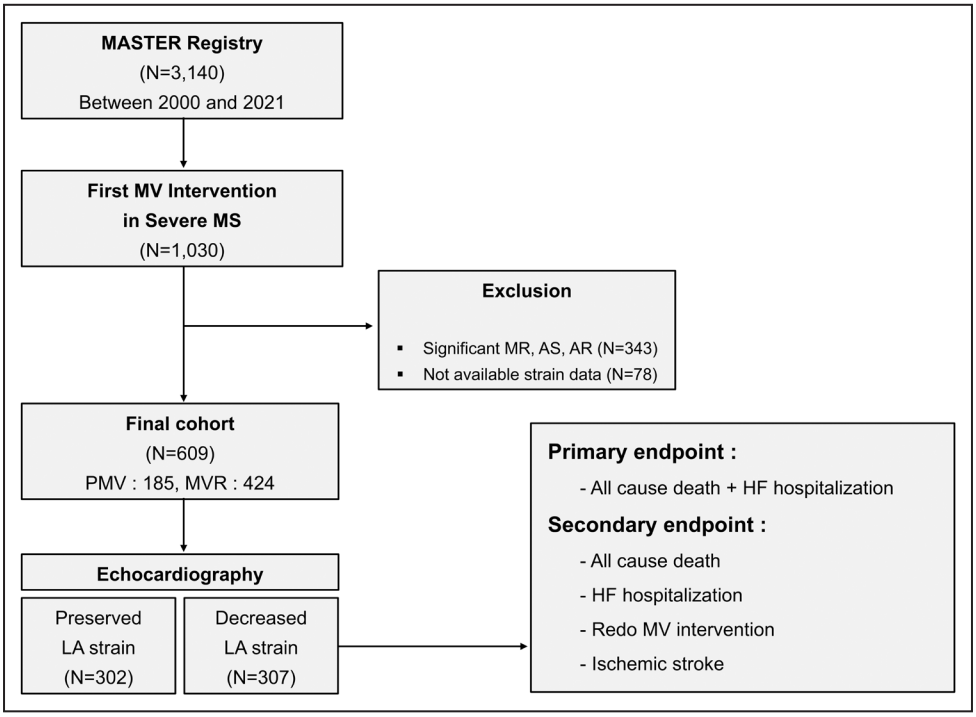

Figure 1. Study flow chart.
Patient inclusion and exclusion flow chart. AR indicates aortic regurgitation; AS, aortic stenosis; HF, heart failure; MASTER, Multicenter Mitral Stenosis with Rheumatic Etiology; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; MVR, mitral valve replacement; and PMV, percutaneous mitral valvuloplasty.

Clinical Outcomes

The primary outcome was defined as a composite of all-cause mortality and HF hospitalization. HF hospitalization was defined based on the following criteria: dyspnea of at least New York Heart Association class III, requirement for intravenous medications such as diuretics or vasodilators, elevated NT-proBNP (N-terminal pro-B-type natriuretic peptide) levels, and evidence of pulmonary congestion or pleural effusion confirmed on chest X-ray. If an individual experienced multiple clinical events during the follow-up period, only the first event was included in the primary outcome analysis.

Secondary outcomes comprised all-cause mortality, HF hospitalization, redo MV intervention, and ischemic stroke. Ischemic stroke was defined as focal neurologic impairment of vascular origin without evidence of primary cerebral hemorrhage on initial imaging modalities. Additionally, PMV success was defined as a postprocedural MV area (MVA) ≥1.5 cm^2, with an increase of at least 0.5 cm^2 compared with the baseline echocardiographic MVA.

Echocardiography

Standard 2-dimensional and Doppler measurements were performed using commercially available ultrasound machines, following the current guidelines of the American Society of Echocardiography.[12] Left ventricular (LV) chamber dimensions and ejection fraction (EF) were assessed using the modified Simpson's method and indexed to body surface area. The left atrial volume index (LAVI) was calculated during end-systole using Simpson's method in a biplane, incorporating both apical 4- and 2-chamber views, and indexed to body surface area.

The MVA was evaluated through 2 methods. First, 2-dimensional planimetry was performed at the tips of the MV leaflets during the mid-diastolic phase using the biplane method. Second, MVA was calculated using the pressure half-time method, applying the formula 220/pressure half-time. The mean diastolic pressure gradient (MDPG) was obtained from continuous-wave Doppler signals at the tips of the MV leaflets.

RVSP was calculated by summing the peak systolic pressure derived from the maximal tricuspid regurgitation jet velocity using the modified Bernoulli equation and the estimated right atrial pressure. Right atrial pressure was determined by measuring the diameter of the inferior vena cava and its collapsibility index.[13]

Strain Analysis

We conducted LA and LV mechanical functional analysis using speckle-tracking echocardiography with specialized semiautomated software (AutoSTRAIN,

TOMTEC-ARENA, Munich, Germany).[14] All images were stored offline for at least 3 consecutive cycles at a frame rate of 50 to 70 frames per second. Each participating center transmitted the echocardiographic images on digitally recorded form to the core laboratory by the storage disks, and LA strain measurements were performed by experienced sonographers in the core laboratory (Severance Hospital) who were blind to the information of the study cohorts. Two experts in the core laboratory (I.C. and G.R.H.) checked the quality control of the LA strain by reviewing all images.

To measure LA reservoir strain, the LA endocardial border was traced in apical 4-chamber views, extrapolating across the LA appendage and pulmonary vein orifice.[15] Decreased LA strain was defined as LA reservoir strain <12.2%, determined through receiver operating characteristic analysis for primary outcome (Figure 2). For LV global longitudinal strain, the LV endocardial border was traced in apical 4-, 3-, and 2-chamber views. Strain curves were analyzed by tracking the speckle on the LA and LV endocardial borders, using semiautomatic border tracking with manual adjustments to enhance tracking accuracy. Decreased LV-global longitudinal strain was defined as a value <18.0%, according to the previous study results.[16]

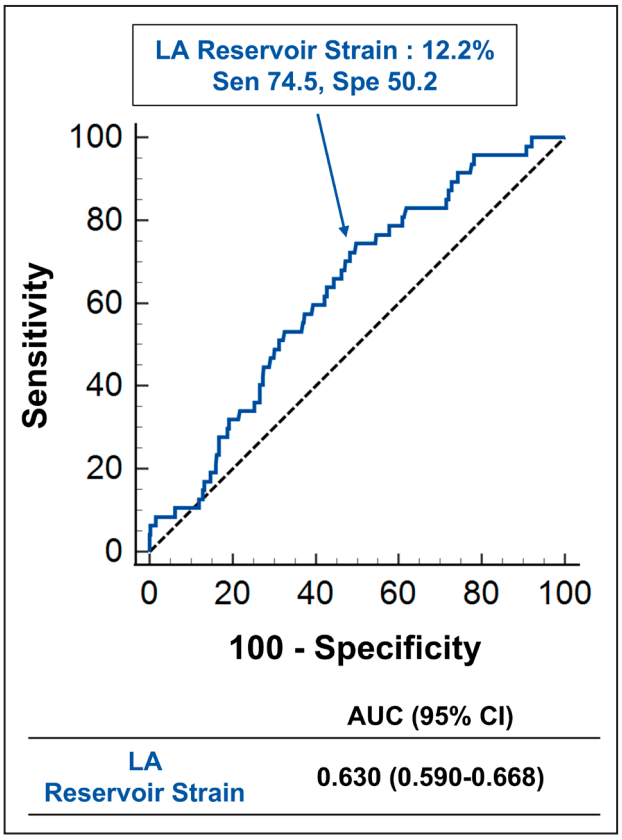

Figure 2. ROC analysis of LA reservoir strain for primary outcome.
AUC indicates area under the curve; LA, left atrium; ROC, receiver operating characteristic; Sen, sensitivity; and Spe, specificity.

Statistical Analysis

Continuous variables are expressed as mean±SD, and categorical variables are presented as frequency and percentages. Differences in continuous variables were analyzed using Student's *t* test, whereas differences in categorical variables were assessed with χ^2 statistics or Fisher's exact test. Clinical outcomes were estimated using Kaplan–Meier methods, and group comparisons were conducted with a log-rank test. The association of LA reservoir strain with clinical outcomes was evaluated using univariate and multivariate Cox proportional regression models.

Subgroup analysis was performed to reduce confounding by comparing individuals with preserved versus decreased LA reservoir strain, matched through propensity score analysis. Propensity scores were calculated using 1-to-1 nearest-neighbor matching, with covariates including age, sex, hypertension, diabetes, chronic kidney disease, AF, MVA, LVEF, MDPG, and RVSP. A maximum caliper width of 0.2 was applied, and absolute standardized mean differences <0.2 were used as indicators of balance and bias reduction. Because age was not balanced between the 2 propensity-matched groups, we performed an additional marginal Cox model, adjusting for age and accounting for the matched-pair design by using a robust sandwich variance estimator. Furthermore, clinical outcomes were also analyzed according to the type of MV intervention.

Statistical significance was defined as $P<0.05$. All analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software, version 19.5.3 (MedCalc Software Ltd., Ostend, Belgium; 2020).

RESULTS

Baseline Characteristics and Echocardiographic Variables

Table 1 presents baseline characteristics stratified by the LA reservoir strain cutoff value of 12.2%. Individuals with decreased LA strain were older (59.1±11.4 versus 55.5±12.4 years, $P<0.001$), had a higher prevalence of AF (94.1% versus 68.5%, $P<0.001$), were more symptomatic with New York Heart Association class ≥III ($P=0.012$), and underwent MVR more frequently (78.5% versus 60.6%, $P<0.001$) compared with those with preserved LA strain (Table 1). On the medication, patients with decreased LA strain had more anticoagulants and antiarrhythmic agents. Regarding MS-related variables, individuals with decreased LA strain showed smaller MVA (0.9±0.2

Table 1. Baseline Characteristics

	Total (n=609)	Preserved LA strain (n=302)	Decreased LA strain (n=307)	*P* value
Demographics				
Age, y	57.4±12.1	55.5±12.4	59.1±11.4	<0.001
Female sex, n (%)	445 (73.1)	229 (75.8)	216 (70.4)	0.128
Body mass index, kg/m^2	22.6±2.9	22.5±2.9	22.6±3.0	0.715
Hypertension, n (%)	276 (45.3)	134 (44.4)	142 (46.3)	0.641
Diabetes, n (%)	139 (22.8)	68 (22.5)	71 (23.1)	0.858
Chronic kidney disease, n (%)	28 (4.6)	11 (3.6)	17 (5.5)	0.264
Atrial fibrillation, n (%)	496 (81.4)	207 (68.5)	289 (94.1)	<0.001
New York Heart Association classification, n (%)				0.012
I	106 (17.4)	57 (18.9)	49 (16.0)	
II	301 (49.4)	161 (53.3)	140 (45.6)	
III	172 (28.2)	76 (25.2)	96 (31.3)	
IV	30 (4.9)	8 (2.6)	22 (7.2)	
Medication				
Anticoagulant, n (%)	564 (92.6)	264 (87.4)	300 (97.7)	<0.001
Warfarin, n (%)	561 (92.1)	261 (86.4)	300 (97.7)	
Novel oral anticoagulant, n (%)	3 (0.5)	3 (1.0)	0 (0.0)	
Antiarrhythmic agent, n (%)	111 (18.2)	39 (12.9)	72 (23.5)	<0.001
MV intervention				<0.001
Percutaneous mitral valvuloplasty, n (%)	185 (30.4)	119 (39.4)	66 (21.5)	
MV replacement, n (%)	424 (69.6)	183 (60.6)	241 (78.5)	
Follow-up duration, ys	6.7±5.0	7.0±5.1	6.5±4.9	0.195

LA indicates left atrium; and MV, mitral valve.

versus 1.0±0.2 cm^2, *P*<0.001), higher MDPG (9.5±4.0 versus 8.4±3.8 mm Hg, *P*<0.001), and elevated RVSP (45.6±17.9 versus 39.9±14.8 mm Hg, *P*<0.001) compared with those with preserved LA strain (Table 2). In terms of left heart chambers, individuals with decreased LA strain showed reduced LVEF (58.5±10.0% versus 63.9±7.3%, *P*<0.001), impaired LV-global longitudinal strain (14.6±3.1% versus 17.4±2.9%, *P*<0.001), and larger LA (LAVI, 105.4±51.7 versus 73.7±30.7 mL/m^2, *P*<0.001). Additionally, they had a higher prevalence of significant (at least moderate) tricuspid regurgitation (40.7% versus 26.8%, *P*<0.001). The proportion of AF before and after MV intervention was also analyzed (Table S1). AF persisted in 71.4% (n=435) of patients across the entire

Table 2. Echocardiographic Variables

	Total (n=609)	Preserved LA strain (n=302)	Decreased LA strain (n=307)	*P* value
MVA by 2 dimensions, cm^2	0.9±0.2	1.0±0.2	0.9±0.2	<0.001
MVA by pressure half time	1.0±0.3	1.0±0.3	1.0±0.3	<0.001
Mean diastolic pressure gradient, mm Hg	9.0±4.0	8.4±3.8	9.5±4.0	<0.001
Right ventricular systolic pressure, mm Hg	42.8±16.6	39.9±14.8	45.6±17.9	<0.001
LV ejection fraction, %	61.2±9.1	63.9±7.3	58.5±10.0	<0.001
LV end-diastolic diameter, mm	48.0±5.1	47.7±4.8	48.3±5.4	0.140
LV end-systolic diameter, mm	33.0±4.8	32.1±4.4	34.0±5.0	<0.001
LV mass index, mL/m^2	87.7±25.0	85.0±22.3	90.3±27.2	0.008
LV global longitudinal strain, %	–16.0±3.3	–17.4±2.9	–14.6±3.1	<0.001
LA volume index, mL/m^2	89.7±45.4	73.7±30.7	105.4±51.7	<0.001
LA reservoir strain, %	13.0±5.4	17.1±4.4	8.9±2.2	<0.001
At least moderate tricuspid regurgitation, n (%)	206 (33.8)	81 (26.8)	125 (40.7)	<0.001

LA indicates left atrium; LV, left ventricle; and MVA, mitral valve area.

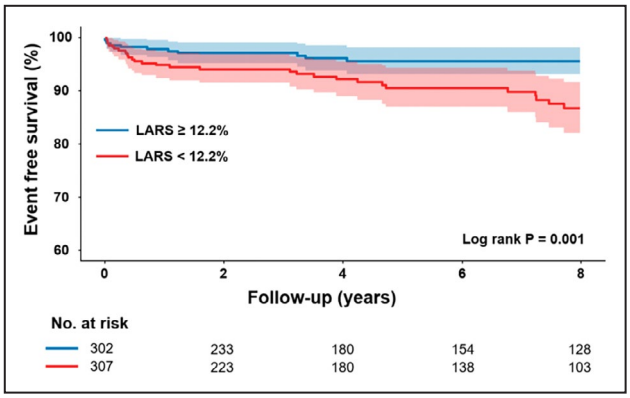

Figure 3. Kaplan–Meier analysis of primary outcomes according to cutoff value of LA reservoir strain.
LA indicates left atrium; and LARS, left atrial reservoir strain.

cohort following MV intervention. Among patients who underwent PMV, 12 received concurrent direct current cardioversion, with 58.3% (n=7) remaining in AF after the procedure. In the MVR group, 172 patients underwent concurrent MAZE surgery, and 72.4% (n=124) continued to exhibit AF postoperatively.

Clinical Outcomes

During a median follow-up of 6.1 [2.3–10.7] years after MV intervention among 609 individuals (mean age 57.4±12.1 years; 73.1% female), 47 individuals (7.7%) experienced primary outcomes, including 19 cases of all-cause mortality and 29 cases of HF hospitalization. Additionally, 40 individuals (6.6%) experienced ischemic stroke within the total study cohort. Individuals with decreased LA strain had a significantly higher incidence of primary outcomes compared with those with preserved LA strain (log-rank test, *P*=0.001) (Figure 3). We further analyzed the prognosis according to the LA strain value in the MVR and PMV groups separately. In the MVR group, patients with decreased LA strain had significantly poorer outcomes compared with those with preserved LA strain (*P*=0.001). In contrast, no significant difference was observed in the PMV group (*P*=0.657) (Figure S1).

The results for secondary outcomes, including comparisons for each event within the primary outcomes, are shown in Figure 4. Individuals with decreased LA strain had significantly more cases of all-cause mortality (Figure 4A) and HF hospitalization (Figure 4B) compared with those with preserved LA strain (*P*=0.037

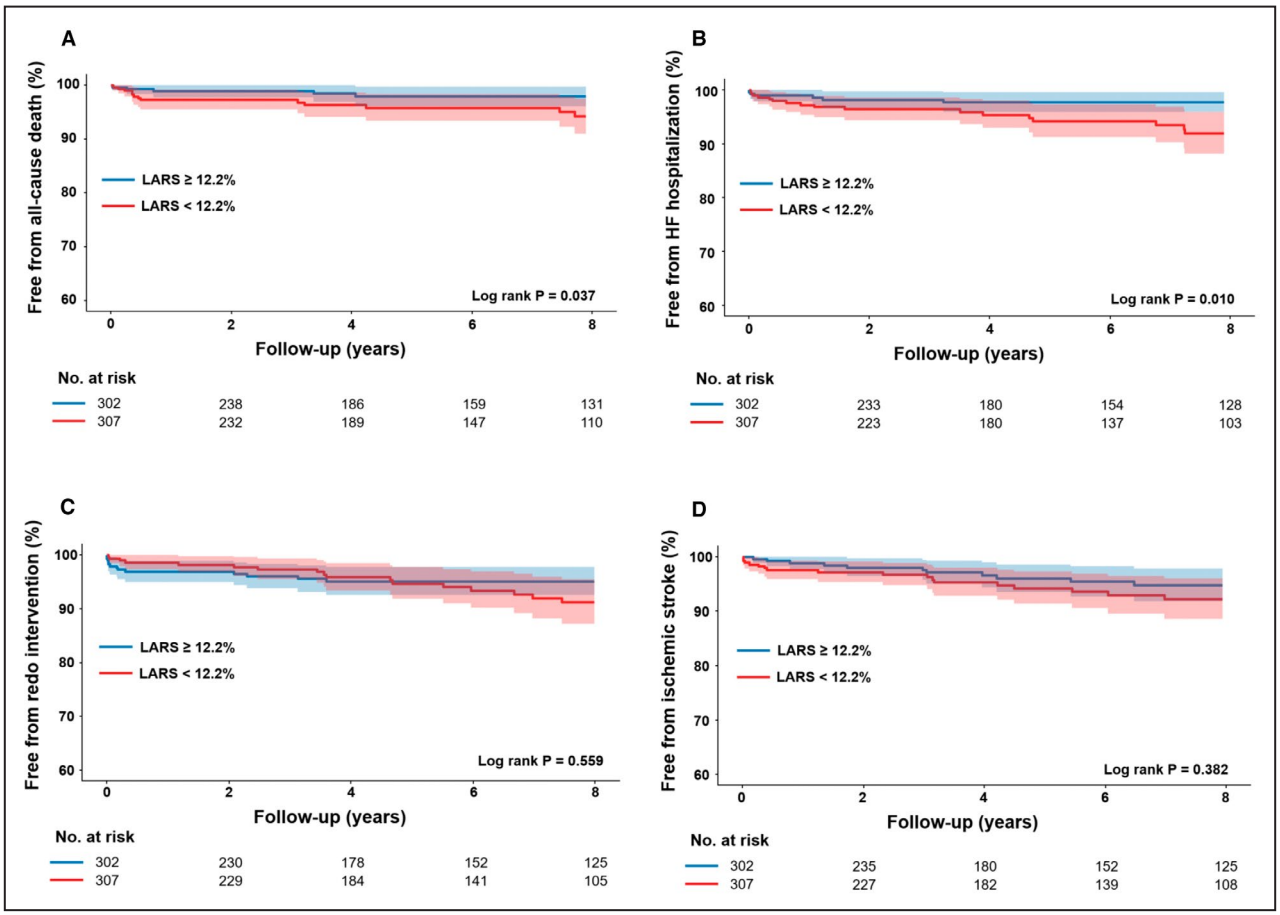

Figure 4. Kaplan–Meier analysis of secondary outcomes according to cutoff value of LA reservoir strain.
A, All-cause death; **B**, HF hospitalization; **C**, redo MV intervention; **D**, ischemic stroke. HF indicates heart failure; LA, left atrium; LARS, left atrial reservoir strain; and MV, mitral valve.

Table 3. Cox Regression Analysis for Clinical Outcomes

	Univariate			Multivariate		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age	1.07	1.04–1.11	<0.001	1.07	1.04–1.10	<0.001
Atrial fibrillation	5.45	1.32–22.5	0.019	2.02	0.46–8.95	0.354
Mean diastolic pressure gradient, mm Hg	0.98	0.91–1.06	0.650			
Right ventricular systolic pressure, mm Hg	1.02	1.01–1.03	0.004	1.02	1.01–1.04	0.008
Decreased left ventricle-global longitudinal strain	1.43	0.73–2.81	0.304			
Decreased left atrial reservoir strain	2.75	1.45–5.22	0.002	2.04	1.06–3.93	0.034
Significant tricuspid regurgitation	1.90	1.07–3.36	0.028	0.94	0.50–1.75	0.834
Mitral valve area, cm^2	0.74	0.21–2.57	0.633			

HR indicates hazard ratio.

and *P*=0.010, respectively). However, the incidence of redo MV intervention (Figure 4C) and ischemic stroke (Figure 4D) did not differ significantly between the 2 groups (*P*=0.566 and *P*=0.382, respectively). In multivariate Cox regression analysis, older age (hazard ratio [HR], 1.07 [95% CI, 1.04–1.10], *P*<0.001), higher RVSP (HR, 1.02 [95% CI, 1.01–1.04], *P*=0.008), and decreased LA reservoir strain (HR, 2.04 [95% CI, 1.06–3.93], *P*=0.034) were identified as significant independent predictors of primary outcomes (Table 3). The Schoenfeld residuals test indicated that the proportional hazards assumption was satisfied. (Table S2) We also analyzed the association between procedural success and improvements in echocardiographic parameters among patients who underwent PMV, as presented in Table S3, with comparisons based on LA strain values. Of the 185 patients who underwent PMV, 88 (47.6%) achieved procedural success. This cohort demonstrated significant improvements, including a mean MVA increase >0.5 cm^2, and reductions in MDPG, RVSP, and LA size. However, these improvements did not significantly differ according to the level of LA strain.

Incremental Prognostic Value of LA Reservoir Strain

The incremental prognostic value of the LA reservoir strain is illustrated in Figure S2. Incorporating decreased LA reservoir strain into a model that included clinical variables and echocardiographic factors related to MV severity, such as MVA, MDPG, and RVSP, significantly enhanced the model's ability to predict primary outcomes (*P*=0.028).

Propensity-Matched Comparison: Subgroup Analysis

To minimize bias introduced by clinical and echocardiographic variables, a propensity score matching (PSM) analysis was performed. This yielded a matched cohort of 194 individuals with decreased LA strain and 194 individuals with preserved LA strain. After PSM, no significant differences were observed in clinical and echocardiographic characteristics between the 2 groups, except for age (Table 4). Kaplan–Meier analysis of primary outcomes after PSM (Figure S3) revealed that individuals with decreased LA strain experienced a significantly higher incidence of primary outcomes than those with preserved LA strain (log-rank test, *P*=0.036). Furthermore, in the Cox proportional hazards regression adjusted for age, decreased LA strain showed a trend toward association with the primary outcome, although this did not reach statistical significance (HR, 1.90 [95% CI, 0.92–3.90], *P*=0.081).

DISCUSSION

This multicenter study, conducted on individuals with rheumatic MS undergoing their first MV intervention, identified several key findings. Decreased preoperative

Table 4. Baseline Characteristics and Echocardiographic Variables of the Propensity-Matched Cohort

	Preserved LA strain (n=194)	Decreased LA strain (n=194)	SMD
Age, y	57.0±12.0	59.9±12.0	0.232
Female sex, n (%)	52 (26.8)	58 (29.9)	0.057
Hypertension, n (%)	92 (47.4)	81 (41.8)	0.104
Diabetes, n (%)	53 (27.3)	51 (26.3)	0.012
Chronic kidney disease, n (%)	10 (5.2)	10 (5.2)	<0.001
Atrial fibrillation, n (%)	177 (91.2)	176 (90.7)	0.018
Mitral valve area by 2 dimensions, cm^2	0.9±0.2	0.9±0.2	0.025
Left ventricular ejection fraction, %	62.0±7.1	62.1±7.3	0.020
Mean diastolic pressure gradient, mm Hg	8.4±3.8	8.6±3.8	0.055
Right ventricular systolic pressure, mm Hg	41.8±16.1	42.5±16.4	0.046

LA indicates left atrium; and SMD: standardized mean difference.

LA function, as assessed by LA reservoir strain, along with older age and higher RVSP, was significantly associated with poor clinical outcomes, including all-cause mortality and HF hospitalization, over long-term follow-up after MV intervention. These results remained consistent even in the propensity-matched sample, which accounted for confounding factors among all individuals. These findings highlight the potential utility of serial LA functional assessments using LA reservoir strain in guiding clinical decisions for individuals with rheumatic MS undergoing MV interventions, such as PMV or MVR. Incorporating LA reservoir strain into routine evaluations would be beneficial in determining the optimal timing for MV intervention and improving the prediction of clinical outcomes.

Associated Prognostic Factors in Severe MS

Although prognoses are expected to improve with optimal interventional treatment for severe rheumatic MS, not all individuals achieve favorable outcomes due to varying hemodynamic profiles.[17] In our study, older age, elevated RVSP, and decreased LA reservoir strain were associated with poorer outcomes after MV intervention. Following the revised 2014 guideline defining severe rheumatic MS as MVA ≤1.5 cm^2, several studies have evaluated prognostic factors influencing clinical outcomes in severe MS. In a study of 436 individuals with severe MS, Ko et al. identified RVSP, particularly its rapid progression, as a prognostic marker for rheumatic MS.[18] This aligns with our findings, as increased RVSP reflects the hemodynamic severity of MS, where disease progression elevates LA pressure and, subsequently, RVSP. Regarding other indices, El Sabbagh et al. investigated low-gradient MS and reported that a low MDPG (<10 mm Hg) in individuals with severe MS was linked to less symptomatic improvement after PMV compared with those with a high MDPG.[19] Traditionally, MDPG has been used as a marker of MS severity. In our study, higher MDPG was observed in groups with poorer outcomes, such as those with decreased LA strain. However, El Sabbagh et al.'s study noted that low MDPG was associated with complex hemodynamic profiles, including older age, higher LV afterload, and lower LV compliance. Further comprehensive, prospective studies are needed to clarify the implications of MDPG on clinical outcomes in severe MS.

Clinical Implication of the LA Remodeling

In individuals with MS, LA remodeling plays a central role in the disease's pathophysiology. This remodeling, encompassing both structural and functional changes, has been strongly correlated with the development of AF, stroke, acute myocardial infarction, congestive HF, and all-cause mortality, all of which are linked to poor clinical outcomes.[20–24] Over time, the progression of MS increases LA workload through pressure overload, leading to structural changes and functional impairment.[25]

Even within the same severity of MS, the extent of LA remodeling varies between individuals due to differences in how pressure overload affects the LA. Consequently, individuals with severely impaired LA remodeling are likely to have poorer prognoses, even after successful MV intervention, as the degree of LA reverse remodeling may be insufficient to restore its function. Recent studies have highlighted the impact of LA remodeling on clinical outcomes in rheumatic MS. For instance, Cho et al. demonstrated that an increased LA size, measured as a LAVI >57 mL/m^2 in individuals with rheumatic MS, was independently associated with poor outcomes, including death, HF hospitalization, stroke, and repeat MV intervention.[26]

Many studies have investigated the role of LA strain in predicting clinical outcomes. Figueiredo et al. demonstrated the prognostic value of LA reservoir strain in 493 individuals with MS, showing that a decreased LA reservoir strain with a threshold of 13% significantly predicted poorer outcomes, including all-cause mortality and MV replacement, over a mean follow-up of 3.8 years.[27] Another study examined LA strain rate in 53 individuals with asymptomatic MS and found that, after 3 years of follow-up, those with decreased LA peak strain rates had higher incidences of symptoms or AF occurrence, hospitalization for cardiac causes, thrombosis, and MV intervention.[28] The consistent finding across these studies that lower LA strain values predict poorer prognoses, regardless of symptoms, aligns with the data from our study. However, there remains a lack of sufficient evidence on the role of LA strain in determining outcomes after MV intervention. Despite undergoing PMV or MVR at guideline-recommended times, many individuals still experience adverse outcomes. Based on our results, the pre-procedural LA strain cutoff value presented could serve as a novel parameter to help determine the optimal timing for MV intervention in individuals with severe rheumatic MS.

LA Strain Value as a Sensitive Prognostic Marker in Severe MS

Our study demonstrates that preprocedural LA strain is closely associated with clinical outcomes in severe MS, establishing its role as a sensitive prognostic marker. As LA remodeling is central to MS pathophysiology, parameters with greater sensitivity than conventional echocardiographic variables are essential for predicting outcomes. Traditionally, LAVI has been used to estimate elevated LV filling pressure and has demonstrated prognostic value in cardiovascular diseases. However,

LAVI has limitations, such as its inability to detect early myocardial deformation and its reliance on static geometry. Additionally, LAVI is not solely dependent on the severity of MS. Other confounding factors, such as AF or diastolic dysfunction, also contribute to the further enlargement of LA. Meanwhile, LA strain as a modality for assessing LA remodeling offers significant advantages over conventional parameters. It does not rely on geometric assumptions or angle alignment and is less affected by pre-load conditions.[29] LA strain has shown greater sensitivity than LA volume for predicting prognosis in conditions such as HF with preserved EF, hypertension, diabetes, and AF.[7,30,31] Thus, this result again highlights the value of LA strain as an invaluable tool for routine echocardiographic investigation in patients with MS.

It was confirmed in our study that the decreased LA strain had an incremental prognostic value. (Figure S2) Therefore, this can be considered to have a role of independent prognostic factor. However, validation is required in more study cohorts, and the difference in weight from other prognostic factors related to MV intervention in patients with MS should be considered. Therefore, it is worth developing a risk score or classification system through a validation study in the future.

As the prevalence of nonrheumatic MS, usually degenerative, has increased over time, it is important to consider whether our results could also be applied to this cohort.[32] Nonrheumatic MS typically occurs in older patients with multiple comorbidities. As calcification of the mitral annulus progresses in degenerative MS, LA pressure increases, and it causes functional impairment of the LA. However, confounders such as diastolic dysfunction, myocardial stiffness, and other valvular dysfunction might substantially influence clinical outcomes beyond the effect of MS itself. With careful consideration of these confounders, the impact of the LA strain itself on the outcome in degenerative MS would likely be weaker than in pure rheumatic cohorts, and more comprehensive prospective studies would be needed to clearly address this problem.

Study Limitations

This study has some limitations. First, its retrospective design introduced potential variations in clinical outcomes due to inconsistent follow-up durations across patients. Additionally, as this was a multicenter study, variations in treatment timing and the absence of a uniform standard for selecting treatment methods may have influenced the results. Second, the area under the curve value (0.630) of the LA strain cutoff in the receiver operating characteristic analysis was relatively low. Subsequent Cox regression and PSM analyses revealed its utility as an independent predictor in this cohort, but the lack of statistical significance in the additional analysis adjusting for age after PSM may be partly attributable to the limited sample size and residual variability. It might suggest the need for a more robust and comprehensive prospective study in the future. Third, invasive cardiac catheterization was not performed to assess MS severity, which may have resulted in unrecognized comorbidities affecting the outcomes.

CONCLUSIONS

Preprocedural decreased LA reservoir strain was strongly associated with poor clinical outcomes following MV intervention in individuals with MS. This parameter could serve as a valuable marker for determining the optimal timing for intervention in this population.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S3
Figures S1–S3

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