Original Article

The Diagnostic Role of Speckle-Tracking Echocardiography–Derived Right Ventricular Longitudinal Strain in Determining the Severity of Rheumatic Mitral Stenosis

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Highlights

- 2D STE–derived RVGLS and RVFWLS associate with MS severity in patients with rheumatic MS.
- RVGLS have high sensitivity for ruling out severe MS during routine echocardiographic evaluation.

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ABSTRACT

Introduction: Echocardiographic planimetry is the primary and most available modality for diagnosing rheumatic mitral stenosis (MS). Nonetheless, this approach is highly reliant on the examiner's technique. Echocardiographic evaluation of MS should also include assessment of right ventricular (RV) function because of its prognostic role. We hypothesized that the assessment of RV function via speckle-tracking echocardiography could also have a diagnostic role in determining MS severity.

Methods: This cross-sectional study included 47 patients with a typical diagnosis of rheumatic MS. Echocardiographic data were recorded and evaluated offline by an expert cardiologist. We measured right ventricular global longitudinal strain (RVGLS), right ventricular free-wall longitudinal strain (RVFWLS), mitral valve area (MVA) using 2D planimetry, and other conventional parameters of MS severity. Data were analyzed and visualized utilizing SPSS version 26 (IBM Corp) and Python 3.10.6 (Python Software Foundation).

Results: Our analysis showed that both RVGLS ($R=-0.598$; $P<0.05$) and RVFWLS ($R=-0.620$; $P<0.05$) were significantly correlated with MVA. The mean RVGLS values in patients with severe and progressive MS were -14.44 ± 4.36 and -18.12 ± 3.25, respectively ($P=0.017$). The mean RVFWLS values also demonstrated a significant difference between these two groups (-6.3 ± 4.7 vs -20.8 ± 3.2; $P=0.005$). The area under the curve (AUC) for RVGLS and RVFWLS in detecting severe MS was 0.75 (95% CI, 0.64 to 0.86) and 0.78 (95% CI, 0.66 to 0.90), respectively.

Conclusion: RVGLS and RVFWLS significantly correlate with MVA and may serve as tools to assess the severity of rheumatic MS in daily clinical practice. These strain parameters have high sensitivity for ruling out severe MS during routine echocardiographic evaluation.

Keywords: Mitral Valve Stenosis; Speckle-Tracking Echocardiography; Global Longitudinal Strain; Free-Wall Longitudinal Strain; Right Ventricular Function

Introduction

Rheumatic mitral valve disease is a significant global health issue, affecting approximately 33.4 million people worldwide and leading to 233,000 to 500,000 deaths annually.[1,2] Echocardiography is the primary and most available modality for diagnosing rheumatic mitral stenosis (MS). It provides useful information on the morphology of the mitral valve apparatus, including leaflet mobility and flexibility, leaflet thickness, leaflet calcification, subvalvular fusion, and commissure appearance, as well as hemodynamic changes in MS and their effects on cardiac function.

Two-dimensional planimetry echocardiography is generally considered the gold standard for MS evaluation in routine clinical practice and as the reference method for anatomical measurements of the mitral valve area (MVA).[3,4] Nevertheless, the planimetry approach relies significantly on the examination technique; thus, incorrect receiver gain settings and poor image plane orientation can affect its precision.[5]

During MS, right ventricular (RV) function may also be compromised owing to reactive changes in the pulmonary arteriolar vasculature caused by increased left atrial pressure and pulmonary hypertension (PHTN) or by rheumatic processes directly affecting the myocardium.[6] Assessing RV function is essential for understanding the symptoms and prognosis of patients with valvular and nonvalvular heart disease.[7,8] It has been shown that RV function is a major predictor of prognosis and survival in patients with rheumatic MS, which explains the significance of early identification of RV failure by appropriate imaging modalities.[9]

Although cardiac magnetic resonance imaging is considered the gold standard noninvasive method for RV function assessment, its limited accessibility and time-consuming nature have affected its use in daily clinical practice.[10,11] Echocardiography, conversely, is the most available tool for assessing RV function. Still, RV function evaluation is complicated due to its intricate geometry and the unique orientation of the RV myocardial fibers. In recent years, RV function assessment has been facilitated by advanced imaging methods, including right ventricular 2D longitudinal strain (RVLS).[12] Since longitudinal contraction accounts for 80% of RV output, this type of contraction has historically been the focus of echocardiographic examination.[13] Right ventricular global longitudinal strain (RVGLS) and right ventricular free-wall longitudinal strain (RVFWLS) are the primary metrics used to measure RVLS and may help diagnose RV dysfunction.[14–16]

Since the echocardiographic evaluation of MS should also include RV function because of its prognostic role, in this study, we hypothesized that the evaluation of RV dysfunction might also play a diagnostic role in determining MS severity. Accordingly, the current study aimed to assess the relationship between RV function measured as RVLS and MVA and other conventional echocardiographic parameters of MS severity. The diagnostic performance of RVGLS and RVFWLS in distinguishing progressive and severe MS was also investigated.

Methods

Study Design and Population

The present cross-sectional study involved adult patients (age ≥18 y) with an established diagnosis of rheumatic MS. Patients were referred to our tertiary center affiliated with Shiraz University of Medical Sciences between January 2020 and January 2022. The study protocol was reviewed and approved by the institutional ethics committee (IR.sums.med.rec.1400.361).

Patients who met the World Heart Federation criteria for rheumatic MS diagnosis, which include anterior mitral valve leaflet thickening of 3 mm or greater, chordal thickening, restricted leaflet motion, and excessive leaflet tip motion during systole, were enrolled in the study.[17] The exclusion criteria were as follows: (1) moderate or more severe mitral regurgitation, aortic stenosis, or aortic regurgitation, and any grade of pulmonary or tricuspid valve stenosis; (2) left ventricular systolic dysfunction (ejection fraction <45%); (3) dysrhythmia or conduction disturbances, such as atrial fibrillation, bundle branch block, or artificial pacing; (4) previously known coronary artery disease; (5) chronic obstructive pulmonary disease; or (6) cardiomyopathy.

Echocardiographic Assessment

All transthoracic echocardiographic assessments were performed by an experienced cardiologist using a GE Vivid E9 ultrasound machine (GE Healthcare). Data were recorded on digital media storage at our center's echocardiography laboratory. Patients were monitored with a single-lead ECG during the examination. A second cardiologist, who was blinded to patients' clinical data and outcomes, performed the offline echocardiographic assessments.

The following parameters were evaluated according to the recommendations of the American Society of Echocardiography (ASE)[18]: left atrial diameter; left ventricular end-systolic and end-diastolic diameters; left ventricular fractional shortening; and the thickness of the interventricular septum and posterior wall. The left ventricular ejection fraction was calculated using the Simpson biplane method of disks. Standard MS severity parameters, including the mean mitral valve pressure gradient MVA, pressure half-time (PHT), tricuspid regurgitation gradient (TRG), and systolic pulmonary artery pressure (SPAP), were also measured according to guidelines.[19] MVA was assessed via 2D planimetry in a parasternal short-axis view at the tip of the leaflets during maximal excursion.[20] Progressive and severe MS were characterized by an MVA greater than 1.5 cm² and an MVA of 1.5 cm² or less, respectively[21] (Table 1). PHTN was defined as an SPAP greater than 35 mm Hg, and RV dilation was defined as an RV basal diameter greater than 41 mm. The RV basal diameter was measured at end-diastole using the apical four-chamber view (RV-focused view)1 (Figure 1).

Two-dimensional speckle-tracking echocardiography (transmit/receive, 1.9/4.0 MHz) was also performed using the apical four-chamber view, with frame rates of 50 to 90 frames per second. The RV endocardial surface was traced manually, and the speckle-tracking width was adjusted to cover the entire RV wall thickness. For the quantification of regional systolic strain, the RV free wall and interventricular septum were each divided into basal, mid, and apical segments. RVGLS and RVFWLS were defined as the mean longitudinal strain of all six segments and the three free-wall segments, respectively (Figure 2).

Table 1. Mitral stenosis classification according to the 2020 ACC/AHA guideline

	Mitral Valve Area	Diastolic Pressure Half-Time	Systolic Pulmonary Artery Pressure
Progressive MS	>1.5 cm^2	<150 ms	Normal pulmonary pressure at rest
Severe MS	≤1.5 cm^2	≥150 ms	SPAP >50 mm Hg

MS: mitral stenosis

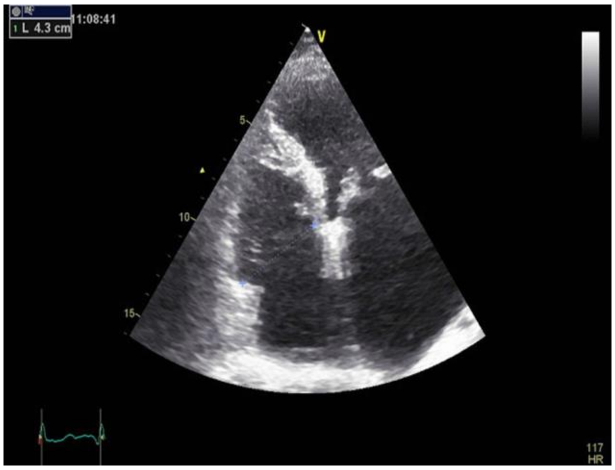

Figure 1. The image shows the measurement of the right ventricle base diameter at end-diastole.

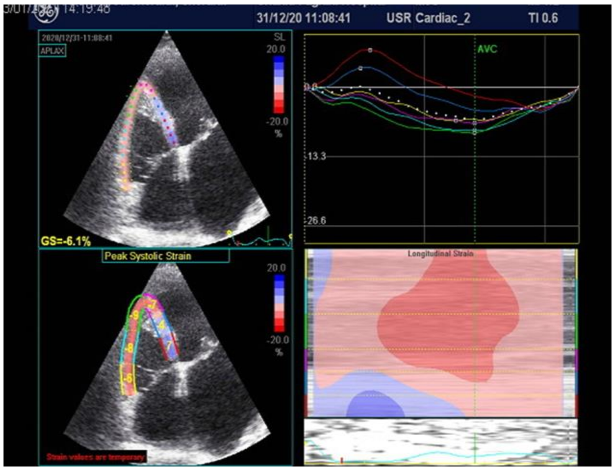

Figure 2. The images present the measurement of right ventricular global longitudinal strain in all six segments.

Study Endpoints

The primary outcome of this study was to determine the relationship between MVA and RVLS. We also investigated the association between RVLS and other conventional echocardiographic parameters in MS, including TRG, SPAP, RV size, PHT, and the mean mitral valve gradient. The secondary outcome was to determine the diagnostic performance of RVGLS and RVFWLS in differentiating severe MS from progressive MS.

Statistical Analysis

Quantitative variables are expressed as mean values (SD), and categorical variables are expressed as frequencies and percentages. The Pearson correlation test was employed to determine the correlation between RVGLS and RVFWLS and TRG, SPAP, MVA, RV size, PHT, and the mean mitral valve gradient. Correlations were defined as strong (correlation coefficient [r]>0.5), moderate (r=0.3–0.5), or weak (r<0.3).

Patients were divided into progressive and severe MS groups based on MVA. Additionally, RVGLS and RVFWLS were compared between these groups using an independent-samples t test. The diagnostic performance of RVGLS and RVFWLS in distinguishing severe from progressive MS was assessed by means of receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) was computed to evaluate diagnostic performance. The statistical significance of the difference between AUC values was evaluated with the DeLong test, and the optimum cutoff values were identified using the Youden index. Data were analyzed and visualized with the aid of SPSS version 26 (IBM Corp) and Python 3.10.6 (Python Software Foundation). A P value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics of The Studied Patients

A total of 47 patients, with a mean age of 42.29±5.26 years, were enrolled in the study. Men accounted for 53.2% (n=25) of the study population. The mean left ventricular ejection fraction was 53.6%±4.5%, ranging from 45% to 60%. Thirty-seven patients (78.7%) were found to have severe MS, and 10 (21.3%) were classified as having progressive MS. The mean RVGLS and RVFWLS values were −15.22±4.39 and −17.68±5.07, respectively (Table 2).

Table 2. The demographic and echocardiographic characteristics of the studied patients

		Mean±SD	Maximum	Minimum
Sex	Male: 25 (53.2%) Female: 22 (46.8%)			
Age		42.29 ± 5.26	30	50
LVEF		53.61 ± 4.50	45	60
MVA		1.22 ± 0.36	0.60	2.20
RVGLS		-15.22 ± 4.39	-24.40	-6.10
RVFWLS		-17.68 ± 5.07	-28.06	-7.01
RV size		3.78 ± 0.48	2.70	4.80
SPAP		42.93 ± 12.57	30.00	70.00
Mean gradient		7.77 ± 4.57	1.40	25.00
TRG		36.08 ± 11.62	20.00	65.00
PHT		183.74 ± 55.94	100.00	378.00

SD: standard deviation; LVEF: left ventricular ejection fraction; MVA: mitral valve area; SPAP: systolic pulmonary artery pressure; RV size: right ventricular size; TRG: tricuspid regurgitation gradient; RVGLS: right ventricular global longitudinal strain; RVFWLS: right ventricular free-wall longitudinal strain; PHT: pressure half time

RVLS and MS Severity

Our analysis showed both RVGLS (r=−0.598; P<0.05) and RVFWLS (r=−0.620; P<0.05) correlated with MVA, one of the principal indicators of MS severity. The mean RVGLS in patients with severe and progressive MS was −14.44±4.36 and −18.12±3.25, respectively, indicating a significant difference between these two groups (P=0.017).

The mean RVFWLS also demonstrated a significant difference between patients with severe MS (−16.3±4.7) and those with progressive MS (−20.8±3.2) (P=0.005). RVGLS had a moderate positive correlation with TRG (r=0.414; P=0.004) and SPAP (r=0.428; P=0.003). A weak correlation was also found between RVGLS and PHT (r=0.310; P=0.034) and the mean gradient of MV (r=0.302; P=0.039). Notably, no significant correlation was observed between RVGLS and RV size (r=0.084; P=0.574). A positive correlation was also found between RVFWLS and TRG (r=0.328; P=0.024), SPAP (r=0.365; P=0.012), PHT (r=0.366; P=0.011), and the mean gradient of MV. Similar to RVGLS, RVFWLS did not correlate with RV size (r=0.113; P=0.448) (Table 3 and Figures 3 and 4).

Table 3. Correlations between RVLS parameters and conventional echocardiographic indices in MS

	RVGLS		RVFWLS	
	Correlation coefficient (R)	P	Correlation coefficient (R)	P
MVA	-0.598*	0.000	-0.620*	0.000
PHT	0.305*	0.037	0.366*	0.011
Mean gradient	0.356*	0.014	0.336	0.021
SPAP	0.390*	0.007	0.365*	0.012
TRG	0.353*	0.015	0.328*	0.024
RV size	0.048	0.751	0.104	0.487

* Correlation is significant at the 0.05 level (two-tailed).
RVGLS: right ventricular global longitudinal strain; RVFWLS: right ventricular free-wall longitudinal strain; MVA: mitral valve area; RV size: right ventricle size; PHT: mitral valve pressure half-time; Mean gradient: mean Gradient of mitral valve; SPAP: systolic pulmonary artery pressure; TRG: tricuspid regurgitation gradient

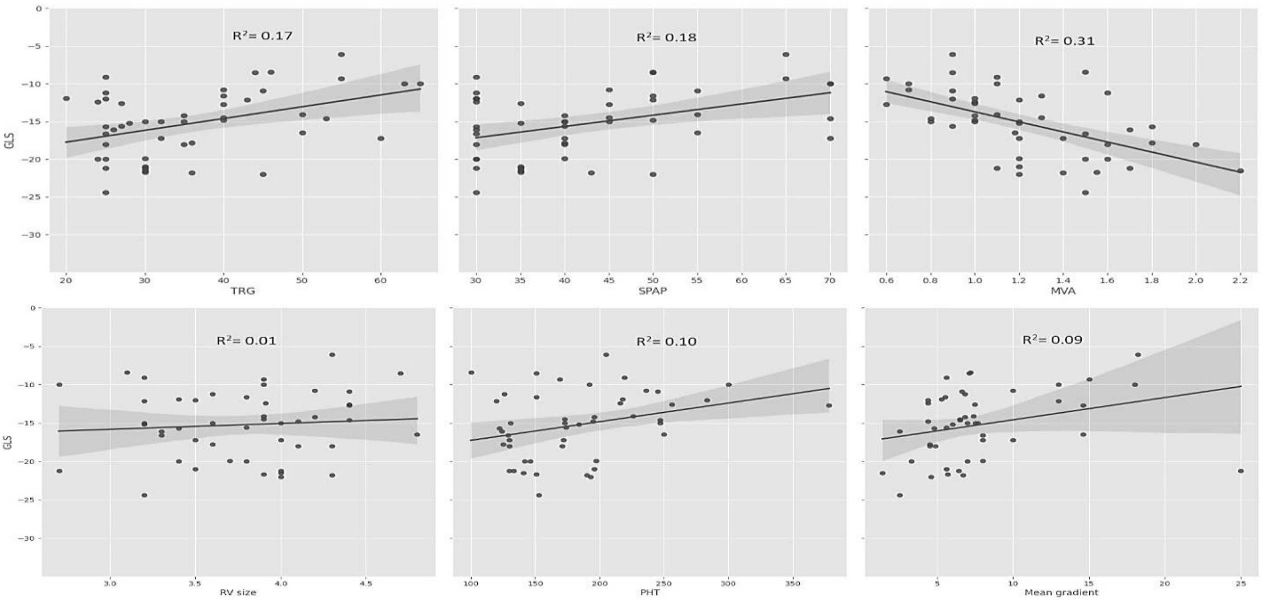

Figure 3. The images illustrate the correlations of right ventricular global longitudinal strain (RVGLS) with tricuspid regurgitation gradient (TRG), systolic pulmonary artery pressure (SPAP), mitral valve area (MVA), right ventricular (RV) size, mitral valve pressure half-time (PHT), and mean gradient of mitral valve.

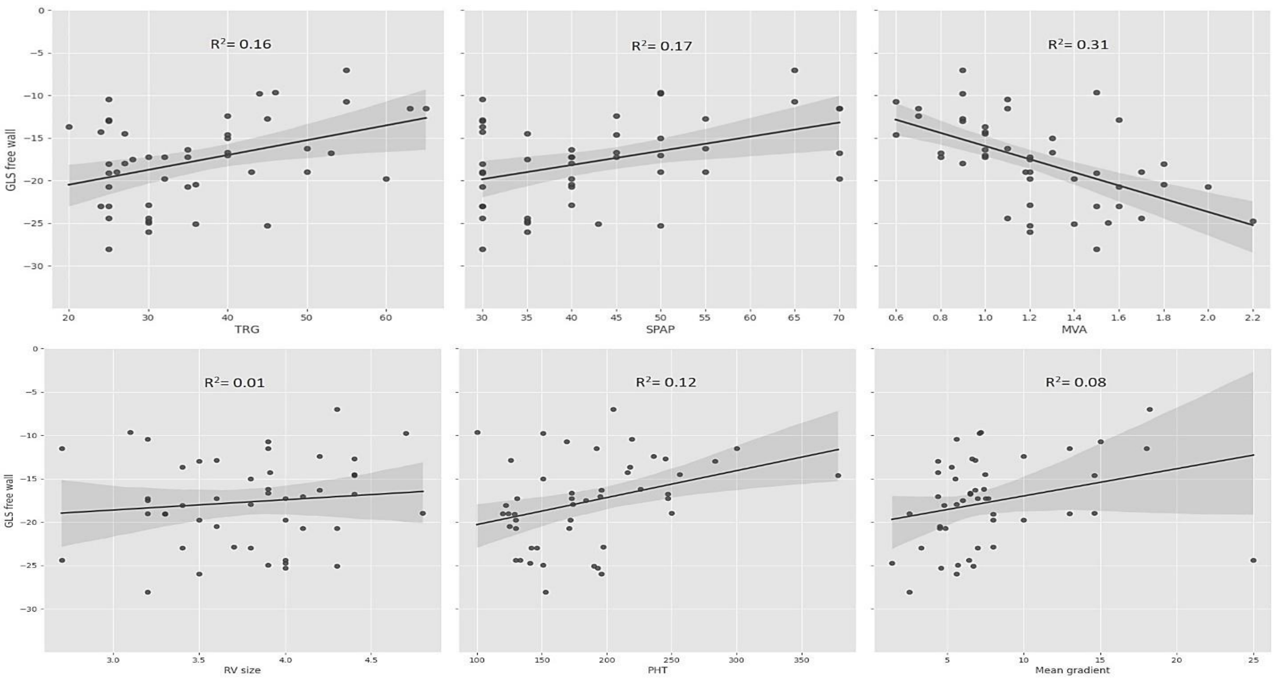

Figure 4. The images depict the correlations of right ventricular free wall longitudinal strain (RVFWLS) with tricuspid regurgitation gradient (TRG), systolic pulmonary artery pressure (SPAP), mitral valve area (MVA), right ventricular (RV) size, mitral valve pressure half-time (PHT), and mean gradient of mitral valve.

RVLS in Diagnosing Severe MS

At the identified optimal cutoffs, RVGLS of −15.2% achieved a sensitivity of 81.6% (95% CI, 65.3% to 92.8%) and a specificity of 56.9% (95% CI, 38.5% to 73.0%) in identifying patients with severe MS. RVFWLS demonstrated a sensitivity of 82.7% (95% CI, 67.1% to 93.5%) and a specificity of 62.6% (95% CI, 45.9% to 78.6%) at a cutoff of −17.8%. The AUC values for RVGLS and RVFWLS for detecting severe MS were 0.75 (95% CI, 0.64 to 0.86) and 0.78 (95% CI, 0.66 to 0.90), respectively (Figure 5). Although RVFWLS demonstrated a slightly higher AUC, the difference was not statistically significant (Z=0.03; P=0.97).

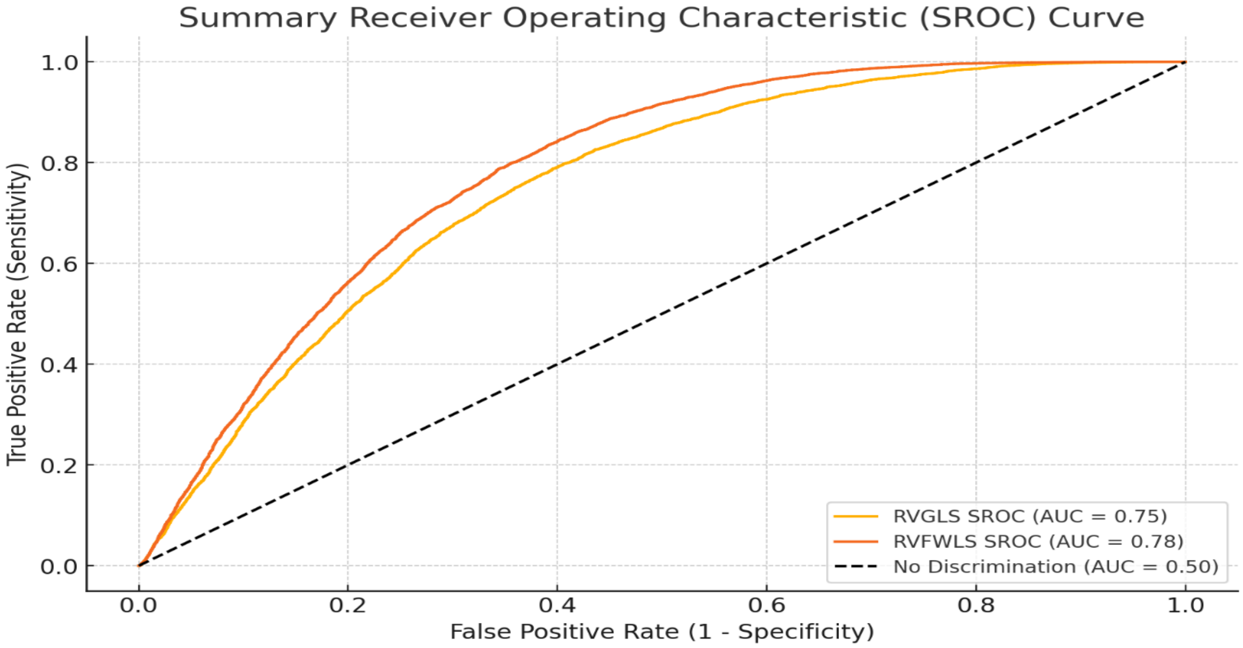

Figure 5. Area under the curve of the summary receiver operating characteristic curve (SROC) for right ventricular global longitudinal strain (RVGLS) and right ventricular free wall longitudinal strain (RVFWLS) in differentiating severe and progressive mitral stenosis (MS).

Discussion

The current study aimed to investigate the relationship between 2D STE–derived RVLS and MVA in patients with rheumatic MS. We found significant correlations between RVLS (RVGLS and RVFWLS) and MS severity parameters, including MVA, the mean mitral valve gradient pressure, and PHT. There was a significant difference in RVGLS and RVFWLS between patients with progressive or severe MS. RVGLS and RVFWLS also demonstrated high sensitivity in differentiating severe and progressive MS at the cutoff points of −15.2% and −17.8%.

Mechanism of RV Dysfunction in MS

RV dysfunction is common in MS and plays a critical role in the onset of clinical symptoms and the progression of the disease. It can be attributed to two distinct mechanisms. The notable hemodynamic effect of MS is observed in the right heart chambers and pulmonary circulation. MS leads to elevated left atrial pressure and subsequently pulmonary venous pressure (postcapillary), as a result of which pulmonary capillary wedge pressure and pulmonary arterial pressure (PAP) increase. The progression of this situation induces pulmonary vascular remodeling, accompanied by thrombotic and fibrotic alterations, resulting in abnormal vasoconstriction. Reactive vascular changes lead to a disproportionate increase in PAP compared with pulmonary capillary wedge pressure, resulting in both precapillary and postcapillary pulmonary hypertension.[22,23]

Endothelial dysfunction finally results in irreversible pulmonary hypertension. This condition results in RV dysfunction in the absence of systemic congestion indicators. An elevation in PAP and RV afterload results in gradual remodeling of the RV, ending in RV hypertrophy, RV dilation, or a combination of both conditions. Consequently, tricuspid valve annular dilation and regurgitation develop. Decreased RV systolic function results in a diminished RV ejection fraction, which reduces forward blood flow and causes significant retrograde flow into the right atrium. This creates a vicious cycle that leads to RV volume overload and further deterioration of RV function.[24,25] Prior investigations have demonstrated that rheumatic involvement of RV myocytes contributes to RV dysfunction by myocyte necrosis, fibrosis replacement, and calcification.[9]

Clinical Significance of Current Findings

Echocardiography plays a crucial role in the decision-making process for patients with MS by confirming the diagnosis, evaluating valve structure, and determining the degree of stenosis and its hemodynamic effects. According to the European Association of Echocardiography/American Society of Echocardiography (EAE/ASE) guidelines, the use of the mean mitral valve gradient, MVA by planimetry, and PHT is recommended for the echocardiographic assessment of MS.[26] Although these indices for assessing MS severity have a class I recommendation, their application has limitations. The assessment requires substantial technical proficiency and may be impractical, even for skilled echocardiographers, in patients with a poor acoustic window or significant distortion of the valve structure, particularly from severe calcification of the leaflet tips.

In this study, we found that RVGLS and RVFWLS might be viable and accurate tools for the daily clinical evaluation of MS. These parameters provide prognostic data for patients with MS and may be useful as simple, complementary methods to mitral valve planimetry for distinguishing between severe and progressive MS.

Taamallah et al[27] found that RV dysfunction could be present even in subclinical MS. They reported that patients with MS exhibited decreases in RV fractional area change, tricuspid annular plane systolic excursion, tissue Doppler and pulsed wave Doppler parameters, RV myocardial performance index, and peak systolic velocity (S′). Consistent with our findings, patients with MS in their study exhibited lower RVGLS and RVFWLS. Be that as it may, they did not observe a substantial difference in RVGLS or RVFWLS between patients with severe MS and those with moderate MS.

In a case-control study of 65 patients, Mehrabi-Pari et al[28] found that the absolute global longitudinal strain was lower in patients with severe rheumatic MS and preserved ejection fraction than in healthy controls. Additionally, segmental strain values of the left ventricle were considerably lower in most basal and some mid-myocardial segments.

Kumar et al[29] evaluated RV function using 2D longitudinal strain and strain rate imaging in 25 patients with isolated severe MS in sinus rhythm. RV function was evaluated before and after balloon mitral valvuloplasty and compared with that of 12 age-matched healthy individuals. Patients with severe MS exhibited a notable decrease in RVGLS. Segmental strain at the basal, mid, and apical septum and the basal RV free wall was also significantly lower in patients than in the control group. Nonetheless, strain at the mid and apical RV free wall was similar between the groups. Only the mid-septum showed a substantial decrease in the systolic strain rate. A statistically significant increase in RVGLS and segmental strain at the basal, mid, and apical septum was observed after balloon mitral valvuloplasty.

Another study by Lupi et al[30] showed that cumulative event-free survival was lower in patients with secondary mitral regurgitation who underwent transcatheter edge-to-edge repair and had RVFWLS values of –18% or greater than in those with RVFWLS values of less than –18% (44.0% vs 85.4%). Similarly, patients with RVGLS values of –15% or greater had lower cumulative event-free survival than those with RVGLS values of less than –15% (54.9% vs 81.7%).

To the best of our knowledge, this is the first study to evaluate the diagnostic performance of RVGLS and RVFWLS in differentiating severe and progressive MS. At our proposed cutoff values, both RVGLS and RVFWLS had high sensitivity, which helps rule out severe MS during routine RV assessment when used alongside other conventional parameters of MS severity.

Of note, most studies have shown that RVFWLS has superior diagnostic and prognostic performance to RVGLS.[16,30] This finding can be explained by the fact that RVGLS reflects abnormalities from both the free wall and interventricular septum and may, therefore, be influenced by concomitant left ventricular dysfunction. The similar performance of RVGLS and RVFWLS in our study might be attributable to our exclusion of patients with other left-sided heart diseases.

A correlation was also observed between RVLS and both TRG and SPAP. This finding is consistent with the pathophysiology of MS, in which pressure is transmitted to the pulmonary vasculature and right heart. Still, these correlations were not as strong as those with MVA, underscoring that TRG and SPAP are primarily indicators of PHTN, whereas RVGLS and RVFWLS are indicators of RV function, which can be affected by both PHTN and non-PHTN causes.

Challenges and limitations

Although the findings of this study are promising, several limitations must be acknowledged. The limited sample size, especially in the progressive MS group (n=10), may restrict the generalizability and statistical power of the findings. A larger cohort would strengthen the reliability of cutoff determinations and yield more accurate estimates of sensitivity and specificity.

Furthermore, future studies can focus on the prognostic implications of RVLS in patients with MS concerning survival rate and cardiovascular events.

Conclusion

Our study demonstrated a correlation between 2D STE–derived RVGLS and RVFWLS and MS severity in patients with rheumatic MS. Moreover, RVGLS and RVFWLS exhibited high sensitivity for ruling out severe MS and assessing the severity of MS during routine echocardiographic evaluation. However, further studies with larger sample sizes are warranted to confirm these findings and explore their clinical implications in decision-making for patients with MS.

Declarations:

Ethical Approval

This study was conducted in accordance with the ethical principles of Shiraz University of Medical Sciences (IR.sums.med.rec.1400.361) and the Declaration of Helsinki. Written informed consent was obtained from all participants.

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Conflict of Interest

The authors report no conflict of interest.

Acknowledgment

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