Immediate and Short-Term Outcomes of Percutaneous Transvenous Mitral Commissurotomy on Global and Regional Right Ventricular Strain by Speckle-Tracking Echocardiography

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Abstract

Objectives: The study aimed to determine short- and long-term improvement on global and regional right ventricular (RV) strain after successful treatment by percutaneous transvenous mitral commissurotomy (PTMC). Furthermore, we endeavored to define the normal values of RV strain in a healthy age- and sex-matched population that may serve as reference for future investigators. **Methods:** The interventional case–control study was done on consecutive patients who were admitted in the department of cardiology for balloon mitral valvotomy (BMV) from April 2018 to July 2019. One hundred and forty-eight patients with isolated severe mitral stenosis (MS) in sinus rhythm were assessed for RV function by two-dimensional speckle tracking calculating RV global longitudinal strain (GLS-RV) and longitudinal strain of the free wall (GLS-RVFW) before and after BMV and compared with seventy-two healthy age-matched controls for a 6-month follow-up. **Results:** At baseline, the GLS of the right ventricle and free wall strain was significantly less among cases as compared to controls (GLS-RV median 20 vs. 23.3, $P < 0.0001$ and GLS-RVFW median 23 vs. 27, $P < 0.0001$). Post-PTMC, the global and regional longitudinal RV strain improved significantly at 24 h and 6 months post procedure and became comparable to that of the control population at 6-month follow-up (cases vs. controls: median GLS-RV [23 vs. 23.3, $P = 0.774$] and GLS-RVFW [27 vs. 27, $P = 0.558$]). **Conclusions:** PTMC causes significant immediate and long-term improvement in the RV strain and can serve as a good prognostic marker for the outcomes in patients with isolated MS.

Keywords: Free wall right ventricular strain, global right ventricular strain, mitral stenosis

Introduction

Mitral stenosis (MS) is a common occurrence associated with rheumatic fever (in developing countries) and degenerative diseases (in developed countries). It is due to decreased mitral valve orifice area (MVOA), consequently leading to elevation in the pulmonary artery–venous pressure.[1]

Patients with MS have significant right ventricular (RV) systolic dysfunction,[2] and RV failure plays an important role in the development of clinical symptoms, significantly affecting exercise capacity, prognosis, and survival of patients with pure MS.[3,4] RV function may also be impaired by the direct involvement of myocardial tissue or through the reactive changes of the pulmonary arteriolar vasculature caused by a passive increase in left atrial pressure and pulmonary hypertension.[5,6]

The evaluation of global and regional RV function is difficult because of its asymmetric and complex anatomy.[7,8] Better RV

Received: 19-01-2021 **Revised:** 08-03-2021 **Accepted:** 25-03-2021

Published Online: 05-07-2021

Access this article online

Quick Response Code:

Website: http://www.ijcva.com

DOI: 10.4103/ijca.ijca_5_21

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How to cite this article: Maheshwari D, Sareen S, Mahla H, Sharma SM. Immediate and short-term outcomes of percutaneous transvenous mitral commissurotomy on global and regional right ventricular strain by speckle-tracking echocardiography. Int J Cardiovasc Acad 2021;7:39-44.

function analysis has been obtained by magnetic resonance imaging, but the method is costly and available in few institutions.[9] On the other hand, transthoracic echocardiography is a noninvasive and widely used technique that has reproducible and concordant results with other imaging methods.[10] Until now, tissue Doppler imaging and Doppler-derived strain and strain rate analysis are the most widely used techniques for the evaluation of RV myocardial function.[11-14] However, those measurements have major disadvantages such as angle dependence, limited spatial resolution, and deformation analysis in one dimension.[15]

Two-dimensional (2D) strain and strain rate imaging has been developed for the quantitative assessment of global and regional myocardial function. This technique is based on gray scale images that are analyzed by the dedicated software system. Although 2D strain imaging has been frequently used to investigate left ventricular (LV) function, little is known about global and segmental RV function.[16,17] Various studies have demonstrated the importance of 2D strain and strain rate analysis in assessing RV function in different disorders. However, there are only a few studies, which assessed 2D RV strain and strain rate in patients with isolated MS.[18]

RV dysfunction in isolated severe MS patients has prognostic significance. Among the treatment surgeries, percutaneous transvenous mitral commissurotomy (PTMC) has become established as a safe and effective treatment for MS and remains the treatment of choice in patients with a favorable anatomy.[19-21] Global RV function of the pressure-overloaded right ventricle in patients with MS and pulmonary hypertension after successful PTMC has not been well defined. Strain imaging by speckle-tracking echocardiography is a novel and sensitive technique for determining ventricular function. The global longitudinal strain (GLS) of the left ventricle is now well defined in the normal population by various vendors. However, there is a paucity of data regarding the longitudinal RV strain, both global and regional in the normal population of our country.

Thus, the study was conducted with a primary objective to determine short- and long-term improvement on global and regional RV strain after successful treatment by PTMC by speckled echocardiography. The secondary objective of the study was to define the normal values of RV strain in a healthy age- and sex-matched population that may serve as reference for future investigators.

Methods

The interventional case–control study (type) was done on consecutive patients who were admitted in the department of cardiology for balloon mitral valvotomy (BMV) from April 2018 to July 2019.

The sample size calculation was done based on the study of Kumar *et al*.[22] who observed the mean values of mid RV free wall systolic of -1.98 ± 0.76 in controls and -3.21 ± 2.99 in cases and apical RV free wall systolic of -1.04 ± 0.70 in controls and -1.49 ± 0.96 in cases. Taking these values as reference and sample size ratio as 2:1, the minimum required sample size with 90% power of study and 5% level of significance was 66 patients for controls and 132 patients for cases. To reduce margin of error, we have taken almost more than twice the calculated sample size, and the total sample size taken was 218 (148 cases and 70 controls).

The study patients were included as per the inclusion exclusion criteria.

Ethical statement

The study was approved by the insitutional ethical committee of the hospital. (SMS/R/31907).

Inclusion criteria

- Patients with age >18 years
- Isolated severe rheumatic MS who were admitted for BMV and underwent the same during hospital stay
- Patients in sinus rhythm/AF
- New York Heart Association (NYHA) functional class 2/3 pre procedure.

Exclusion criteria

Patients with

- Diabetes mellitus, hypertension, and coronary artery disease
- Pericardial disease
- Atrioventricular conduction abnormalities or any bundle branch blocks on the electrocardiogram (ECG)
- Moderate-to-severe valvular disease other than MS
- Chronic obstructive pulmonary disease
- Abnormal serum electrolyte levels
- Impaired LV systolic function (LV ejection fraction < 50%)
- Pregnancy
- Poor imaging windows or image quality that precluded strain analysis.

After obtaining written informed consent from the patients, details regarding demographic characteristics, symptoms, pulmonary artery hypertension, pulmonary venous hypertension, and NYHA class were recorded. A standard twelve-lead ECG was done for the assessment of cardiac rhythm and features suggesting chamber enlargement and CAD. The left atrial diameter, LV end-systolic and end-diastolic diameters, LV fractional shortening percentage, the thickness of the interventricular septum, and the posterior wall were measured according to the recommendations of the American Society of Echocardiography.[23] The LV ejection fraction was calculated by Simpson's method.

Echocardiography studies were obtained using a Philips iE33 ultrasonographic machine equipped with a 3.5 MHz transducer and interpreted by 2 experienced echocardiographers independently.

Conventional MS indices, such as mean diastolic gradient (MDG), were calculated. MVOA was measured by mitral orifice planimetry in parasternal short-axis view and by the Doppler-derived pressure halftime method, and the average area was calculated by the mean value of the two measurements. MS severity was calculated based on hemodynamic data, using MVOA, MDG, and pulmonary artery systolic pressure (PASP), and severe MS is defined as MVOA <1.5 cm^2. PASP was measured by adding 10 mmHg, considering the diameter of the inferior vena cava and level of its collapse resulting from respiration, to the value measured by evaluating Bernoulli equation, which is simplified from tricuspid insufficiency velocities. The values of PASP >35 mmHg were defined as pulmonary hypertension.[24]

Strain imaging

- Echocardiography images were obtained from the apical four-chamber view. Three stable cardiac cycles were stored for each view (five for patients with AF), and Cineloop formats were recorded on the hard disk of the echocardiography device, then used for off-line analysis
- Frame rates used for analysis were 60–80 frames/s. B-mode gray scale images were used by the system and the activity of the stable acoustic markers, named speckles tracked throughout the myocardial tissue
- After manually defining the endocardial border, the software system constitutes an automatic epicardial tracing for each view. When the regions of interest included the whole thickness of the RV, the process is initiated and the software system advanced the tracking frame-by-frame. If the automatically obtained tracking segments are adequate for analysis, the software system accepts to read each region, whereas in-adequate tracking segments are automatically excluded and the investigator manually corrects the contour to achieve optimal tracking
- The myocardium of the RV was divided into two segments (septum and RV free wall [RVFW]), then subdivided into three segments (apical, mid, and basal) that results in a total of six segments. The longitudinal peak systolic strain and peak systolic strain rates were calculated for each segment
- Free wall longitudinal strain was calculated by taking the arithmetic mean of the three values displayed for the RV free wall
- All measurements were obtained by two separate investigators who were unaware of patient characteristics. Measurements were calculated at least three times and the average of these measurements was determined.

Follow-up

Follow-up was done after 6 months of the intervention where patients' MVOA, MDG, PASP, TAPSE, and RV strain were recorded. The data were entered into MS EXCEL spreadsheet and analysis was done using Statistical Package for the Social Sciences, IBM manufacturer, Chicago, USA, version 21.0.

Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± standard deviation and median. Normality of data was tested by Kolmogorov–Smirnov test. If the normality was rejected, nonparametric test was used.

Statistical tests were applied as follows:

1. Quantitative variables were compared using Mann–Whitney test (as the data sets were not normally distributed) between the two groups and Wilcoxon signed-rank test between pre and post
2. Qualitative variables were correlated using Chi-square test.

$P < 0.05$ was considered statistically significant.

Results

The mean age of the cases was 29.82 years and of the controls was 30.2 years with an almost 1:1 M: F gender distribution in both groups ($P > 0.05$) [Table 1]. Majority of the cases belonged to NYHA Class 2 (47.97%) and Class 3 (49.32%) with 2 (1.35%) cases each of NYHA Class 1 and 4.

At baseline, the GLS of the right ventricle and free wall strain was significantly less among cases as compared to controls (GLS-RV median 20 vs. 23.3, $P < 0.0001$ and GLS-RVFW median 23 vs. 27, $P < 0.0001$) as shown in Table 2.

After the treatment, a significant improvement was noted in MVOA, MDG, PASP, TAPSE, GLS-RV, and GLS-RVFW

Table 1: Comparison of demographic characteristics between case and control

Demographic characteristics	Case (*n*=148)	Control (*n*=70)	*P*
Age (years)			
Mean±SD	29.82±7.22	30.2±6.52	0.499
Median (IQR)	29 (24.500-33)	29.5 (25-34)	
Range	18-65	19-49	
Gender, *n* (%)			
Female	76 (51.35)	30 (42.86)	0.241
Male	72 (48.65)	40 (57.14)	

SD: Standard deviation, IQR: Interquartile range

Table 2: Comparison of baseline characteristics between case and control

Baseline characteristics	Case (*n*=148)	Control (*n*=70)	*P*
GLS-RV			
Mean±SD	19.41±1.84	23.35±0.8	<0.0001
Median (IQR)	20 (18-20.700)	23.3 (22.900-24)	
Range	14.8-24	21-25	
GLS-RVFW			
Mean±SD	22.57±1.98	26.97±0.69	<0.0001
Median (IQR)	23 (21-24)	27 (26.600-27.300)	
Range	18-27	24.7-28.6	

GLS-RV: Right ventricular global longitudinal strain, GLS-RVFW: Right ventricular free wall longitudinal strain, SD: Standard deviation, IQR: Interquartile range at 24 h and 6 months as compared to the baseline ($P < 0.0001$) as shown in Table 3.

Due to the significant improvement after the intervention, as compared to controls, the cases had comparable median GLS-RV (23 vs. 23.3, P = 0.774) and GLS-RVFW (27 vs. 27, P = 0.558) at 6 months of follow-up [Table 4].

Discussion

The measurement of RV function does not have a single validated echocardiographic indicator. Literature suggests assessment of various parameters, but the index study selected the improvement in the RV strain as a marker for RV systolic dysfunction since (1) it is a global parameter, (2) encompasses the myocardial contractility of the free wall, (3) has better prognostic power, and (4) correlates with other parameters such as TAPSE, PASP, RV ejection fraction, RV Tei index, and tricuspid S' velocity.[25]

In this study, comparing nearly 150 patients of rheumatic MS with about half the number of age- and sex-matched controls, we found that the mean global and regional RV strain was significantly lower at baseline in the patient cohort. This was more evident in patients who had longstanding mitral valve stenosis like the ones who had undergone PTMC earlier. The decreased myocardial contractility as seen in the index study with strain imaging has also been seen in previous studies who assessed an association of RV strain and CV outcomes.[26-32]

After undergoing successful PTMC, the global and free wall strain tended to improve even after just 24 h of the procedure, reiterating a possibility that this immediate improvement in global RV function is due to improved hemodynamics, better LV filling, and RV emptying after BMV. Our findings were in line with other studies.[3,33-35]

Table 3: Comparison of parameters between baseline with 24 h and 6 months in cases

Variables	Baseline	24 h	6 months
MVOA	1 (0.800-1.200)	1.8 (1.600-2)*	1.8 (1.600-2)*
MDG	11 (10-15)	6 (5-7)*	6 (5-7)*
PASP	50 (40-59)	31 (27-40)*	31 (27-40)*
TAPSE	17 (16-19)	18 (17-20)*	18 (17-20)*
GLS-RV	20 (18-20.700)	21 (20-22)*	23 (22.500-24)*
GLS-RVFW	23 (21-24)	24 (23-25)*	27 (26-27.700)*

*P<0.0001. Median values (IQR). MVOA: Mitral valve orifice area, MDG: Mean diastolic gradient, PASP: Pulmonary artery systolic pressure, TAPSE: Tricuspid annular plane systolic excursion, GLS-RV: Right ventricular global longitudinal strain, GLS-RVFW: Right ventricular free wall longitudinal strain, IQR: Interquartile range

The greater immediate improvement of global RV strain than RV free wall strain may be because of enhanced LV filling and LV contractility post BMV. However, the strain was still significantly lower at 24 h post PTMC as compared to the control population values.

On long-term follow-up done at 6 months, despite 4 patients being lost to follow-up, both global and free wall RV strain tended to reach values comparable to the control population. This shows that BMV causes significant improvement in the RV systolic function over time, which may be due to the increased contractility of the longitudinal fibers of RV, which constitutes around 80% of the RV contraction.

We also observed that there was significant improvement in the MVOA, MDG, PASP, and TAPSE at 24 h and 6 months of follow-up after the intervention. This further corroborates with the fact that these parameters correlate with the improvement in the RV strain as done by strain echocardiography. Among previous studies also, RVGLS was found to be significantly correlated with RV ejection fraction ($r = -0.50$–-0.80),[31,36-38] TAPSE (r = −0.547–−0.83), RVFAC (r = −0.213–−0.73), tricuspid S' velocity (r = 0.718), RV Tei index (r = 0.590),[27,31,32,36,39] and PASP (r = 0.56, $P < 0.001$).[40]

In this study, we have also tried to determine the normal range and the usefulness of RV global and free wall systolic strain to detect subtle RV systolic abnormalities that has not been done in any Indian study to the best of our knowledge. Literature shows that there are vendor differences and gender and age differences in strain values among different population,[41-44] and thus, each region/ethnicity should consider their own reference values for estimating the RVGLS total and RVGLS-FW strain.

This study has some limitations. First, the cases and controls were known to the operators, so a bias may be present. Second, exclusion of CAD was not done by CT/conventional angiography and LV dysfunction was not ruled out using GL/radial/circumferential strain but by the ejection fraction calculated by various standardized methods. Third, a longer follow-up may be required to assess the impact of pre PTMC strain or its lack of improvement on the survival of these

Table 4: Comparison of follow up variables between case and control

Follow up variables	Case (n=148)	Control (n=70)	P
GLS-RV (24 h post-PTMC)	21 (20-22)	23.3 (22.900-24)	<0.0001
GLS-RVFW (24 h post-PTMC)	24 (23-25)	27 (26.600-27.300)	<0.0001
GLS-RV (6 months post-PTMC)	23 (22.500-24)	23.3 (22.900-24)	0.774
GLS-RVFW (6 months post-PTMC)	27 (26-27.700)	27 (26.600-27.300)	0.558

Median values (IQR). GLS-RV: Right ventricular global longitudinal strain, GLS-RVFW: Right ventricular free wall longitudinal strain, IQR: Interquartile range, PTMC: Percutaneous transvenous mitral commissurotomy patients. Fourth, in keeping with the current guidelines,[45] only apical view was used to calculate the RV strain, so some areas of RV may be underrepresented.

Conclusions

RV systolic function is impaired in patients with severe MS and can be accurately assessed by global and segmental RV strain. Impaired global and segmental RV strain values in these patients are primarily due to increased after load which improve after BMV with reduction in RV afterload. In addition, the study may help foster clinical studies using the normal values of RV GLS in comparing the abnormal GLS of the right ventricle in pulmonary hypertension, congenital heart diseases, and heart failure with reduced ejection fraction in Indian population.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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