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Evaluation of Right Ventricular Function in Patients Undergoing Mitral Valve Replacement with Pulmonary Artery Systolic Pressure of more than 50 mmHg: A Prospective Analysis

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ABSTRACT

Objectives: The severity of pulmonary artery hypertension affects the outcomes of patients undergoing mitral valve replacement (MVR). Speckle-tracking derived strain is a new modality for the assessment of the right ventricular (RV) function as well as the longitudinal contractile pattern.

Our main objective of this study was to evaluate the right ventricular (RV) function in patients undergoing MVR with pulmonary artery systolic pressure (PASP) of more than 50 mmHg at 1 and 4 weeks postoperatively.

Material and Methods: This prospective cohort study included 40 patients with rheumatic heart disease (RHD) (mitral stenosis [MS] and mitral regurgitation [MR]) scheduled to undergo MVR between January 2022 and December 2023 in AIIMS, New Delhi. Serial 2D echocardiography, tissue Doppler imaging, as well as RV speckle-tracking echocardiography were performed, and serum brain natriuretic peptide (BNP) levels were measured during the pre-operative period, 1st week and 4th weeks postoperatively to evaluate RV function.

Results: Tricuspid annular plane systolic excursion (TAPSE) and left ventricular ejection fractions (LVEFs) were significantly lower at 1 week after surgery, compared to pre-operative levels, and reached the pre-operative values at 4 weeks after surgery. The RV fractional area change (RVFAC) at 4 weeks postoperatively significantly increased compared to 1st week and baseline values. The tricuspid valve (TV) tissue velocity in systole (S′), TV velocity in diastole (E′), RV global strain (RVGLS), and RV free wall strain (RVFWLS) at post-operative 4 weeks were lower than pre-operative values, and this difference was statistically significant.

Conclusion: Four weeks after MVR, in adult patients with RHD (MS and MR) having PASP >50 mmHg, it was observed that deformational indices or speckle-tracking echocardiography such as RVGLS and RVFWLS predict better RV dysfunction than linear indices like TAPSE. The BNP, PASP (delta TR), right atrial volume, left atrial volume, LV internal diameter in systole, and LV internal diameter in diastole decreased significantly in these patients. RVFAC increased significantly to compensate for the loss of longitudinal function.

Keywords: Right ventricular function, Rheumatic heart disease, Mitral valve replacement, Pulmonary artery systolic pressure, Speckle-tracking echocardiography

INTRODUCTION

Rheumatic heart disease (RHD) remains a major health problem in developing countries, which causes significant cardiovascular morbidity and mortality.[1] The two most common forms of RHD are mitral stenosis (MS) and mitral regurgitation (MR), or a combination of both. Mitral valve disease is often associated with pulmonary artery hypertension (PAH).[2] The severity of PAH determines the risk and affects outcomes of patients undergoing mitral valve replacement (MVR). Patients with mitral stenosis develop PAH mediated by endothelin 1. The PAH causes right ventricular (RV) dilation, hypertrophy, dysfunction, and ultimately failure. RV helps maintain adequate pulmonary perfusion pressure and delivers deoxygenated venous blood to the lungs, facilitating a low systemic venous pressure, and preventing tissue and organ congestion.[3] The RV dysfunction limits the preload affecting the function of the left ventricle, compromising the systolic and diastolic function due to ventricular interdependence.[4] RV impairment is commonly seen in chronic degenerative MR or in combination with low left ventricular (LV) ejection fraction. It strongly predicts the patient's poor cardiovascular and overall survival.[5] Le Tourneau *et al*. have reported that RV dysfunction quickly improves after mitral valve surgery.[5] However, echocardiographic evaluation of RV is more difficult than LV in both pre- and post-operative periods due to its complex shape and post-operative distortion of the native RV contractile pattern.[6,7] Conventional echocardiography does not accurately measure the longitudinal contractile pattern of the right ventricle (RV).

Speckle-tracking echocardiography is a newer and advance modality for the assessment of RV function as well as the longitudinal contractile pattern.[8] Conventional methods such as tricuspid annular plane systolic excursion (TAPSE), fractional area change (FAC), and tissue Doppler imaging (TDI) tricuspid lateral annulus tissue velocity in systole (TDI RV S') have significant drawbacks such as angle and preload dependency. Two-dimensional (2D) strain imaging by speckle-tracking allows angle independence and has shown that 2D strain imaging is better than conventional Doppler and TDI in evaluating RV function.[9]

Objectives

Primary objective

Our primary objective was to evaluate the right ventricular (RV) function in patients undergoing MVR with pulmonary artery systolic pressure (PASP) of more than 50 mmHg preoperatively, 1st and 4th weeks postoperatively.

Secondary objective

Comparison of the pre-operative right ventricular (RV) function with post-operative RV function at 1st and 4th weeks and to form correlation among serum brain natriuretic peptide (BNP) levels, TAPSE, RV fractional area change (RVFAC), and echocardiographic indices.

MATERIAL AND METHODS

This prospective cohort single-center study was conducted at the Department of Cardiac Surgical Intensive Care, CTVS, All India Institute of Medical Sciences, New Delhi, between January 2022 and December 2023. Forty patients (>18 years of age) who underwent MVR for RHD (MS or MR) with PASP of more than 50 mmHg were included in this study. Patients with pre-operative hospital stay of more than 7 days, emergency MVR, liver dysfunction (serum bilirubin >2.0 mg/dL), renal dysfunction (serum creatinine >2.0 mg/dL), multi-organ dysfunction (more than two organ dysfunction), poor echo window, and cardiopulmonary resuscitation revived patients and patients on inotropic support preoperatively were excluded from the study.

After obtaining clearance from the Institute Ethics Committee (Ref.no IECPG-788/23.12.21, RT-26/January 27, 2022), the study protocol was explained, and written informed consent was taken from all eligible patients who were fulfilling the inclusion criteria. Serial conventional 2D echocardiography, TDI, as well as RV lateral and septal wall speckle-tracking echocardiography (longitudinal and global strain using dedicated software RV-AFI), were performed using GE-Vivid E 95, an echocardiography system with a 1.7–3.5 MHz adult 4VC transducer and serum BNP levels were measured at the pre-operative period, 1st week, and 4th weeks postoperatively for all the study populations. Echocardiography was performed in the left lateral decubitus position with an apical four-chamber view and parasternal long- and short-axis view. PASP is usually measured from tricuspid regurgitation (TR) peak velocity as PASP = 4 X peak TR velocity^2 + estimated RA pressure. Because measuring the exact right atrial pressures without an invasive line was impossible in pre-operative and 4 weeks postoperatively, the TR gradient calculated as ΔTR = 4 X peak TR velocity[2] was used as a surrogate for PASP. TAPSE was measured by the difference in the displacement of the RV base during systole and diastole. RVFAC was calculated by the difference in the RV end-diastolic and RV end-systolic areas in the apical 4-chamber view. TDI was applied in the pulse-Doppler mode of the tricuspid lateral annulus of RV for measurement of the tissue velocity in systole (S′). 2D echocardiography images were obtained from the four-chamber view for speckle tracking. Digital data were stored and later analyzed in offline mode. After defining the three points (RV apex, septal, and lateral tricuspid annulus), the software automatically traces the endocardial and epicardial borders in a modified four chamber view. The speckle-tracking width was modified to cover the whole RV wall thickness for obtaining strain imaging. After adjusting tracking points manually if required, the longitudinal and global strains were obtained. The area/length method was used to calculate maximum RA and LA volumes from apical four and two-chamber view. Left ventricle's chamber dimensions and ejection fractions were measured using the two-dimensionally guided M-mode method by measuring the LV internal diameter in diastole (LVIDD) and LV internal diameter in systole (LVIDs) from parasternal long axis view (PSLAx). After the surgery (MVR), patients were transferred to the cardiac surgical intensive care unit and placed under continuous and standard monitoring. Indications for tricuspid valve (TV) repair were severe TR (vena contracta width >0.7 cm and TR jet >4 m/s) and organic TR (leaflets structural abnormalities due to RHD).

After extubation, the heart failure management included but was not limited to administering spironolactone up to 1 mg/kg/day (serum potassium <5.5 meq/L), enalapril up to 10 mg/day (systolic blood pressure >100 mm Hg), and furosemide up to 3 mg/kg/day. None of the patients received pulmonary dilators.

Statistical analysis

Sample size

We used repeated measures analysis of variance (ANOVA) to calculate the sample size. A minimum sample size of 33 with a power of 90% and an alpha error of 5% was determined. Three measurements T0, T1, and T2 (mean values of RVSP 49.8, 45.04, and 39.13) based on a previous study by Tejaswi *et al.*, and correlation among repeated measures of 0.7 was considered.[10] We expect a dropout rate of 10%. Thus, we recruited total sample size of n = 40. The sample size was calculated using STATA software.

Statistical analysis was done using STATA V. 14. Data were summarized as the mean and standard deviation for numerical variables and frequency/percentages for categorical variables. Shapiro–Wilk test was used for normal distribution. Comparison among the groups was done by repeated measures ANOVA followed by multiple comparisons by Bonferroni test. Friedman test was used for non-normal variables followed by *post hoc* comparison using the Wilcoxon signed-rank test. Pearson correlation coefficient/Spearman correlation coefficient was calculated to find the correlation among BNP, TAPSE, RVFAC, and echocardiography variables with each other. $P \leq 0.05$ was considered for statistically significant.

RESULTS

Out of 40 patients enrolled, 37 completed the study. The demographic data are detailed in Figure 1, Table 1.

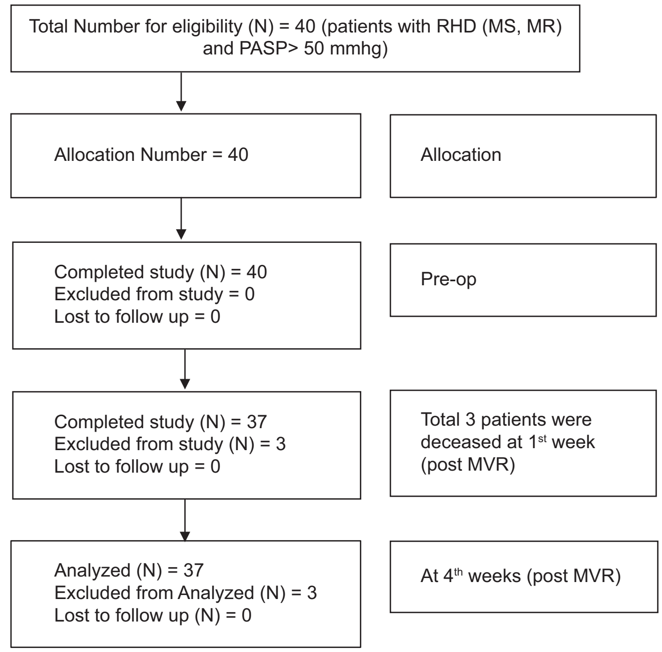

Figure 1: (Consort statement) study design and participant flowchart. MS: Mitral Stenosis, MR: Mitral Regurgitation, MVR: Mitral valve Regurgitation, PASP: Pulmonary Artery Systolic Pressure.

Table 1: Demographic variables (n=37).

Variables	Number of patients
Age (years)	40.1 ± 13.3
Sex (M/F)	15/22
Diagnosis:	
Mitral stenosis (MS)	19 (51.33%)
Mitral regurgitation (MR)	8 (21.62%)
Mitral stenosis plus Mitral regurgitation (MS + MR)	10 (27.02%)
Tricuspid valve repair	3 (8.1%)
Atrial fibrillation	9 (24.32%)

After 1 week of surgery, BNP levels increased to 202.1 ± 165.02 pg/mL from 173.7 ± 114.7 pg/mL ($P = 0.24$). However, 4 weeks after surgery, the BNP levels (89.30 ± 79.25 pg/mL) were significantly lower than pre-operative ($P < 0.0001$) and BNP levels at 1 week postoperatively ($P < 0.0001$) [Table 2].

The ΔTR (PASP), right atrial volume (RAV), left atrial volume (LAV), LVIDD, and LLVIDs significantly decreased after surgery at 1 week and 4 weeks postoperatively [Table 1]. TV tissue velocity in systole (S′), TV tissue velocity in diastole (E´), RV global strain (RVGLS), and RV free wall strain (RVFWLS) were significantly reduced at 1 week postoperatively but increased at 4 weeks after surgery. The TV s´ velocity, TV e´ velocity, RVGLS, and RVFWLS at post-operative 4 weeks were lower than pre-operative values, and this difference was statistically significant [Table 2].

Table 2: Comparison between different echocardiographic and BNP mean values at different time intervals in the study (n=37).

Parameters	Pre-operative (Mean±SD)	Post-operative 1st week (Mean±SD)	Post-operative 4th week (Mean±SD)	Pair1: comparison b/w pre-operative and post-operative 1st week	Pair2; comparison b/w post-operative 1st and 4th week-	Pair3: comparison b/w pre-operative and post-operative 4th week
				P-value	*P*-value	*P*-value
BNP (pg/mL)	173.7±114.7	202.1±165.02	89.30±79.25	0.248	<0.0001	0.001
TAPSE (mm)	16.24±2.60	13.73±1.74	16.16±1.89	<0.0001	<0.0001	0.854
RVFAC (%)	32.76±6.19	31.60±3.36	38.66±4.0	0.221	<0.0001	<0.0001
TV-systolic velocity S′ (cm/see)	11.0±1.66	8.62±0.86	9.89±1.1	<0.0001	<0.0001	0.001
TV-peak E′ velocity (cm/see)	13.95±2.05	10.49±1.42	11.92±1.57	<0.0001	<0.0001	<0.0001
ΔTR (mm Hg)	52.447±9.885	28.007±9.41	20.94±6.47	<0.0001	<0.0001	<0.0001
RVGLS (%)	−15.332±−2.69	−12.01±−2.206	−14.15±2.48	<0.0001	<0.0001	0.004
RVFWLS (%)	−17.78±6.64	−11.53±6.94	−15.66±2.99	<0.0001	<0.0001	0.008
RA volume (mL)	84.81±64.9	60.96±41.3	52.63±39.7	<0.0001	<0.0001	<0.0001
LA volume (mL)	247.37±139.6	175.5±75.4	141.4±57.3	<0.0001	<0.0001	<0.0001
LVIDS (mm)	33.03±7.62	28.86±6.08	25.14±5.52	<0.0001	<0.0001	<0.0001
LVIDD (mm)	46.68±8.91	40.27±7.53	34.81±5.86	<0.0001	<0.0001	<0.0001
LVEF (%)	54.11±5.86	47.43±4.26	53.35±4.77	<0.0001	<0.0001	0.496

BNP: Brain natriuretic peptide, TAPSE: Tricuspid annular plane systolic excursion, RVFAC: Right ventricular fractional area change, TV-S′: Tricuspid valve lateral annulus systolic velocity, TV-E′: Tricuspid valve lateral annulus diastolic velocity, ΔTR: Gradient of tricuspid regurgitation, RVGLS: Right ventricular global strain, RVFWLS: Right ventricular free wall strain, RA: Right atrium, LA: Left atrium, LVIDS: Left ventricular internal diameter in systole, LVIDD: Left ventricular internal diameter in diastole, LVEF: Left ventricular ejection fraction, SD: Standard deviation

TAPSE and LV ejection fraction (LVEF) were significantly lower at 1 week after surgery compared to pre-operative levels. However, both variables reached the pre-operative values at 4 weeks after surgery (TAPSE, 16.24 ± 2.60 vs. 16.16 ± 1.89 mm, P = 0.85 and LVEF, 54.11 ± 5.86 vs. 53.35 ± 4.77%, P = 0.49). After 1 week of surgery, the RVFAC was lower than the pre-operative RVFAC, but this decrease was not statistically significant. The RVFAC at 4 weeks postoperatively significantly increased compared to 1st week and baseline values [Table 2].

Neither the BNP levels nor the RVFAC correlated with other echocardiographic indices before, 1 week, and 4 weeks after surgery.

TAPSE significantly correlated with TV s′ velocity, RVGLS, and RVFWLS at baseline. TAPSE correlated with RVGLS 1 week after surgery and 4 weeks after surgery with TV s′ velocity. There was no significant correlation between TAPSE and RVFWLS at 1 or 4 weeks after surgery [Table 3].

Table 3: Correlation between TAPSE with RV Echocardiographic parameters at different time intervals in the study populations (n=37).

Time	TV-TDI, S`-velocity (cm/sec)		RVGLS (%)		RVFWLS (%)	
	R	*P*	r	*P*	R	*P*
Pre-op	0.441	0.006	−0.355	0.030	−0.387	0.017
1st week	0.109	0.51	−0.368	0.024	−0.299	0.07
4th week	0.380	0.020	−0.112	0.505	−0.035	0.835

r: Pearson correlation coefficient, *P*: *P* value, TAPSE: Tricuspid annular plane systolic excursion, TV-TDI: Tricuspid valve tissue Doppler imaging, RVGLS: RV global strain, RVFWLS: RV free wall strain

DISCUSSION

The normal value for TAPSE is 17 mm. TAPSE has been shown to decrease immediately after cardiac surgery and to remain lower than the baseline levels even 6 months later. TAPSE can be overestimated in the presence of significant TR. In the presence of mild-to-moderate TR, TAPSE and TV tissue velocity in systole (S′) correlate well with cardiac magnetic resonance imaging (CMR)-calculated RV ejection fraction (RVEF). However, with severe TR, there is no correlation between CMR-calculated RVEF and either TV S′ velocity or TAPSE.[11] RVFWLS correlates better with CMR-calculated RVEF than TAPSE and RVFAC and is less influenced by TR.

In our study, the TAPSE and TV S′ velocity declined 1 week after surgery, but RV FAC increased significantly in our patients. The loss of TAPSE (longitudinal systolic function) is compensated by an increase in RV FAC (radial systolic function).[12]

The TV S´ decreases with the opening of the pericardium in patients undergoing CABG. Unsworth *et al*. reported a 54 ± 11% decrease in TV S´ velocity 5 min after pericardial opening.[13] One month after surgery, the TV S´ velocity was still 55 ± 12% < the pre-operative values. However, our patients showed a decrease of only 10% at the 1-month follow-up. In our patients, the pericardium was closed postoperatively, which may have improved TV S´ velocities. The TAPSE correlated well with TV S´ velocity before and 4 weeks after surgery but not at 1 week postoperatively. Even when the pericardium was closed in all our patients, complete fibrosis requires 4–6 weeks. Therefore, at 1 week postoperatively, the pericardium was not as effective as at 4 weeks after surgery.

The RVGLS is largely modified from LV speckle tracking, whereas RVFWLS is calculated by RVFWLS-specific tracking and is less sensitive to residual TR after surgery. Only GLS has been associated with patient outcomes.[14] In our patients, the RVGLS and RVFWLS were less than normal (−15.33 ± −2.69 and −17.78 ± 6.64, respectively), establishing RV dysfunction in the pre-operative period. Although the TAPSE and LVEF reached their baseline values at 4 weeks, the RVGLS and FWLS were significantly lower at 4 weeks than their baseline values. RVGLS and RVFWLS are pre- and afterload dependent.[15] Both preload and afterload decreased consistently in our patients 4 weeks after surgery. A decreased preload at 4 weeks may have prevented the RVGLS and RVFWLS from reaching their baseline values. Another reason for significantly lower RVGLS and RVFWLS compared to baseline may be an intrinsic decrease in the RV myocardial function, which may persist up to 6 months post-surgery.[16]

Four weeks after surgery, there was no correlation of TAPSE with either RVGLS or RVFWLS, suggesting deformational indices predict RV dysfunction better than linear indices.[17] There was a significant correlation between TAPSE and RVGLS 1 week after surgery but not RVFWhLS. The RVGLS consists of an RV-free wall and septal deformation. The TAPSE appears to be influenced by septal deformation due to LV contraction. Although the interventricular septal deformation is not affected by cardiopulmonary bypass.[17]

Cardiac magnetic resonance imaging (MRI) and right heart catheterization (RHC) can be used to assess the RV function early and accurately.[18] MRI is considered the gold standard for the assessment of RV size and function (RVEF). RHC is the gold standard for the diagnosis of pulmonary hypertension. It can also estimate cardiac output, RV contractility, and RV–PA coupling.[19] Three-dimensional (3D) echocardiography is a novel imaging modality to assess several aspects of the right heart, including volumes, function, and ejection fraction. 3D Echocardiography-derived RVEF closely correlates with MRI results.[18] However, this was not our objective; therefore, these modalities were not included in the study. In this study, we used conventional as well as speckle-tracking echocardiography for the assessment of RV function.

Limitation

Our study is a prospective cohort study from a single tertiary center. It has a short-term (4 weeks) follow-up period which may not be sufficient to assess RV function completely or more precisely. Patients with atrial fibrillation were included in our study, which might have impacted the evaluation of RV function. Few of our patients had poor acoustic windows and improper visualization of RV free wall in perioperative periods which limited the accurate measurement of the RV strain. We also have not measured RV afterload in the study.[20]

CONCLUSION

Four weeks after MVR, in adult patients with RHD (MS and MR) having PASP >50 mm Hg, it was observed that deformational indices or speckle-tracking echocardiography such as RVGLS and RVFWLS predict better RV dysfunction than linear indices like TAPSE. The BNP, PASP (delta TR), RAV, LAV, LVIDS, and LVIDD decreased significantly in these patients. RVFAC increased significantly to compensate for the loss of longitudinal function.

Ethical approval

The authors declare that they have taken the Institutional Ethics Committee approval and the approval number is Ref. no IECPG-788/23.12.21, RT-26/January 27, 2022.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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