A Comparative Study of Changes in Left Ventricular Function after Mitral Valve Replacement in Patients with Severe Rheumatic Mitral Regurgitation with and without Mild Mitral Stenosis

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ABSTRACT

Introduction: Surgical correction is the fundamental strategy for severe rheumatic mitral regurgitation as (MR) as medical management for MR can not prevent the hemodynamic consequences of severe MR in the asymptomatic and minimally symptomatic subjects. The purpose of this study is to assess the impact of duration of progressive rheumatic MR on LVEF, PH, LV and right ventricular dysfunction and decide about the selection of optimal timing for surgical intervention in our patient population.

Material and methods: This study involves the data of 30 patients of MVR divided over 2 groups, from 1st January 2015 to 31st December, 2018 and follow up of the survivors. There were (a) 12 cases of isolated severe MR described as MR and (b) 18 cases of severe MR associated with mild MS described as MS +MR. Changes in echocardiographic parameters in both the groups after MVR, LVEF, LVESD, LV end diastolic diameter (LVEDD), PASP and NYHA functional class were assessed, analyzed and compared at 30 and 180 days.

Results: In the postoperative period after 30 days, improvement of NYHA status were observed to be higher in 13 survivors with MS +MR from III to I while it was 6 in MR group. This improvement noted more in younger group below 40 years. NYHA changes from III to II was observed in 4 in each in both groups more in older group above 40 years. At 180 days, 1 each from NYHA II improved to I in younger group. Out of the 2 post operative mortality, there was 1 in MR group who had post operative RV dysfunction and died after discharge on 29th day and 1 in MS+MR group and who died of respiratory failure after 7 days though the cardiac indices improved and both were in older group.

Conclusion: MVR can reversely remodel hearts and restore LV function with relatively preserved LV

Keywords: Isolated Mitral Regurgitation (MR), Mitral Stenosis (MS) with Mitral Regurgitation (MS +MR), Mitral Valve Replacement (MVR), Pulmonary Hypertension (PH), Pulmonary Vascular Resistance (PVR)

INTRODUCTION

Mitral stenosis (MS) does not induce any volume or pressure overload in left ventricle (LV) unlike aortic stenosis (AS), which induces a pressure overload on the left ventricle resulting in remodeling responses on the LV manifested as concentric hypertrophy of LV myocardium. On the other hand, moderate and severe mitral regurgitation (MR) imposes volume overload and induces growth of cardiomyocytes resulting in eccentric remodeling and LV dilatation[1] while the contractile function is preserved.

During the initial presymptomatic compensated phase of MR (stage B), there is left ventricular eccentric hypertrophy. But the LV contractile function and pulmonary arterial pressures are normal and the patient remains asymptomatic.

During the intervening asymptomatic decompensating phase (Stage C), LV ejection fraction(LVEF) begins to deteriorate but the high preload masks the underlying contractile dysfunction.[2] Left atrial pressure (LAP), which was not substantially elevated in the early compensated phase, may begin to rise due to gradual loss of compliance. There is higher pulmonary artery wedge pressure (PAWP), which results in remodeling of pulmonary venules which gives rise to post-capillary PH[2,3,4] and in this stage it can resolve quickly after successful MVR or mitral valve repair MVr.[2] The left ventricular end systolic volume (LVESD) and left ventricular end diastolic volume (LVEDD) however goes on increasing if MR is neglected.

During the final symptomatic decompensated phase of chronic severe MR, the contractile function or LVEF has declined substantially and the symptoms of heart failure (HF) are prominent (stage D). With further deterioration of LV systolic function (reduced LVEF) and diastolic relaxation due to increased passive stiffness of LV, the rise in LAP causes passive pulmonary venous hypertension or post capillary PH. Pulmonary vasculature can lead to reactive pulmonary arteriolar vasoconstriction or reactive precapillary pulmonary arterial hypertension (PAH) due to pathological remodeling, leading to an elevated pulmonary

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vascular resistance (PVR) and high transpulmonary pressure gradient (TPG). At this stage, this PVR which is still ≤ 3WU (Wood units) is reversible.[2,4] Right heart catheterization (RHC) also allows for differentiation of "passive" and "reactive" pulmonary hypertension by calculation of the TPG, which is defined as the difference between mean (m) PAP and PCWP. In passive pulmonary hypertension due to left heart failure, PCWP is > 15 and the TPG is normal (<12 mm Hg). The term pulmonary artery hypertension (PAH) is defined when mPAP exceeds 25 mm Hg and PCWP is less< 15 or TPG is >12 and is found in WHO group 1 PH like scleroderma. TPG is also elevated (>12 mm Hg) in those with reactive or out-of proportion pulmonary hypertension[4] in patients with LV failure out of proportion to the degree of LV dysfunction or have persistent PAH after therapies that lower their PCWP. The PH, when irreversible, is called out-of-proportion post-capillary or "post-capillary PH with a pre-capillary component" (Cpc-PH) and usually present in those with PVR ≥3 WU (Wood units).[2] This PH is may not be lowered by therapies for PH and by MVR.[2,4,5] Higher PASP greater than 50 mm Hg (resulting in out of proportion PH due to increased PVR) significantly increases impedance to right ventricular (RV) emptying and produces high RV afterload and increased right atrial (RA) pressures resulting in functional tricuspid regurgitation (TR).[2,6] Sustained post capillary PH can lead to disruption of alveolar capillary complex known as alveolar capillary stress failure which can result in leakage causing pulmonary edema. Further elevation of PH leads to deposition of type IV collagen leading to remodeling of arterioles and capillaries leading to reactive precapillary pulmonary arterial hypertension (PAH) and reduction of alveolar diffusion capacity. PVR during this reactive precapillary stage of PAH is still reversible. However, such early changes in pulmonary vascular bed increasing the PVR may be considered to be protective in both MS (PVR appearing early in severe MS) and MR (PVR develops late in MR and mild MS) as because it protects the pulmonary capillary bed from excessive venous pressure and pulmonary edema and episodes of paroxysmal dyspnea decrease. The level of PVR as measured are found to be half in stages of paroxysmal dyspnea when compared to the advanced stage of higher irreversible PH in advanced mitral valve disease (MVD).[7] However, a subset of patients do not develop PH or increased PVR and may continue to remain asymptomatic for longer time.[4] Increased PVR can lead to further rise of PAH, increases symptoms of shortness of breath on exertion and fatigue. Further increase of PVR results in lower cardiac output (CO) and RHF characterized by fluid retention, edema and in severe cases presyncope, chest pain or syncope.[5] The term PH, in a less specific manner, refers to a mean PA pressure (mPAP) >25mmHg due to any cause. PH is regarded as normal, mPAP < 20mm Hg, moderate (mPAP 25 - 40) and severe (mPAP >40).[8] Pulmonary arterial hypertension (PAH) is measured at rest by right heart catheterization (RHC)[2,9] and the calculating the difference PCWP and mPAP and is described before. Normal PASP is approximately 25 mm Hg in normal subjects. But PH as measured by PASP by echocardiography in presence of left heart disease is considered as no PH PASP<40 mm Hg, mild PH (PASP 40 -49), significant or moderate PH (PASP 50 -59) and severe PH (PASP> 60).[4,8] Even the mild PASP of > 40-49 mm Hg caused longer intensive care and hospital stay more than those with no PH after MV surgery.[8]

Changes in the LV myocardium due to volume overload and assessment of LV and RV function

As the LV volume increases with progressive MR, myocardial fibrosis which has been reported to develop to the extent of 18-40% of LV myocardium[10,11] quantified by cardiac magnetic resonance (CMR). The targeted reverse remodeling after MVR for severe MR is less when the MR is long standing[12] due to increased fibrosis. In some cases of chronically long standing dilated LVESD> 40 or 45 mm, there is irreversible PVR detected by RHC or assessed clinically by RHF and resistance to diuresis. Other echocardiographic parameters for prediction of high PVR are a high LV eccentricity index (a D-shaped LV), a larger RA than LA, and enlarged and apex-forming RV, a low peak early transmitral velocity to peak early mitral annular velocity (mitral E/e'), and a short pulmonary acceleration time which are markers of pre-capillary PH.[2] Tricuspid annulus plane systolic excursion (TAPSE) is a popular measure because of its simplicity and is now becoming a surrogate of RV longitudinal systolic function. It has high prognostic significance in several studies and low TAPSE < 18 mm, increases post operative morbidity and mortality. The absence of improvement in RV size and pulmonary pressure are unequivocally linked with persistence of morbidity-mortality.[2,13,14] Established guidelines[15,16] advocates some of the of the triggers to intervene for mitral valve surgery by MVr when LVESD> 40 -44 in symptomatic or > 45mm in asymptomatic patients, with caution of bad outcome when compared to better outcome when LVESD < 40 mm, and LVEF>60%. But all the western guidelines deal with degenerative MV disease while overwhelming population of MR in our country is rheumatic, which are not often amenable to repair and requires MVR. So, It is necessary to assess the established triggers for MVR in our population of rheumatic MR with deformed valves to correlate with the established norms.

This study was therefore an attempt to compare the perioperative behavior, post operative course, mortality, survival and changes in LV function and dimensions after MVR between the two groups of patients of advanced isolated severe MR and severe MR associated with mild MS, referred for MV surgery after failure of conservative management and decide for optimal criteria and timing for surgical intervention before irreversible PVR develops.

The study includes evaluation of the perioperative behavior and post operative changes of cardiac dimensions, function, mortality and morbidity after elective MVR in between

patients with isolated severe MR and those associated with mild MS (MS+MR). The perioperative characteristics include (1) duration of aortic cross clamp (CC) and cardiopulmonary bypass (CPB) time in both the groups, perioperative and post-operative performances of cardiac function, arrhythmias and need for defibrillation, (2) postoperative ventilator support, stay in intensive therapy unit (ITU), recovery and mortality and improvement of symptoms, (3) changes in the echocardiographic parameters of LVEF, LVEDD, LVESD and PASP before, 30 days and 180 days after MVR.

MATERIAL AND METHODS

This retrospective study was conducted at the Department of Cardiovascular and Thoracic Surgery of Medical College, Kolkata, India after retrieving the records of patients selected for the study from 1st January 2015 to 31st December, 2018. Patients were identified through reviewing of operative and intensive care unit (ICU) notes and medical records and follow up at the OPD. Since it was a retrospective study and no individual patient identifiers used, the patients consent was waived off by the Institutinal Ethical committee, but written consent for the procedure was obtained from all the patients before surgery.

Inclusion criteria

Records of 30 patients who had undergone elective MVR for rheumatic severe isolated mitral regurgitation (MR) or associated with mild mitral stenosis (MS+MR) and LVEF > 30%. The data of some patients who were considered of very high operative risk and some operative findings were only included for discussion.

Exclusion criteria

Those patients of MV disease, who had repairable valves and had mitral valve repair (MVr) or those cases of MVR or MVr who needed additional coronary artery bypass grafting or double valve replacement (DVR) were excluded from this study. Also the cases of MR associated with severe MS, aortic stenosis(AS) and aortic regurgitation(AR) were excluded. The patients of MVR below 30% LVEF who also had been operated were not included.

Our patient population were placed into two groups MR or MS+MR. 18 patients were found to have MS+MR (mitral valve area between 1.6 to 2.0 cm^2) while 12 patients were found to have isolated mitral regurgitation (without MS). All the patients were referred from cardiology department when they did not respond adequately to GDMT directed medications which included diuretics and beta blockers. Severe MR was defined as a ratio of jet area to left atrial area > 40%, a mixed lesion met the criteria for both mild MS and severe MR. Varying degrees of tricuspid regurgitation (TR) from mild to severe, were present in all the patients. All procedures were performed using a standard general anesthesia protocol, median sternotomy, CPB with bicaval cannulation and moderate systemic hypothermia (30 to 31 °C). After the aorta was cross clamped, combined antegrade and retrograde cold cardioplegia at 4°C with del Nido (DN) (1:4 dilution as blood : DN solution) was infused by cardioplegia delivery system at a rate of 20 ml/kg. A second dose (800 to 1000 ml) of DN was infused whenever the cross clamp time exceeded 90 min. Mitral valve replacement (MVR) was done with bileaflet metallic prosthetic valve after completing total chordal preservation using interrupted # 2-0 polyester sutures. Tricuspid annuloplasty (TA) for moderate to severe TR, by De Vaga suture annuoplasty or repair with tricuspid ring was done in 8 cases of MS and 13 cases of MS+MR. Rewarming, de-airing, aortic cross clamp (CC) removal and weaning off bypass were done in the usual manner under Trans esophageal echocardiography (TEE) guidance. Rest of the procedures of decanulation and chest closure were performed in standard fashion.

The base line information about the patient's demography, clinical variables like presence of AF, BSA, associated tricuspid regurgitation, perioperative and postoperative variables are summarized in table 1. Changes in several cardiac parameters in both groups of isolated MR, and MS+MR, have been further subdivided into below 40 years age group as <40 and above 40 years age group as >40 age. Like LVEF in %, LVESD, LVEDD in mm, PASP in mm of Hg, were assessed after MVR and summarized in table 2 and the respective units have often been used in this paper without repetitions of the units. The measurements were done after 30 days and 180 days of MVR.

All the data were processed in Microsoft XL tabulation done, and statistical averages, standard deviations and relevant proportion were calculated. No further statistical tests could be done due to small numbers of these rare cases.

RESULTS

The average age in years of patients of MVR for pure MR selected for MVR in our study was also found to be slightly less (32.3 ±10.5), with a range from 26 to 50 years, mostly between 26 to 34. This is in contrast to the MS+MR (36.1 ± 7.2) years with a range from 18 to 50 years, who presented mostly between 18 to 38 years (range 18 to 52 years). The number of patients with MS+MR (n=18) was also larger than the MR (n=12) group. AF, moderate to severe TR, RV>35 mm were more common in the patients having longer duration of MR and having PASP> 50 mm Hg.

The mean age of the patients was 34.9 years± 8.8. The aortic CC time was 108.25 min ±11.17 in MR and 102.8min± 6.8 in MS+MR groups. CPB time were 106.5min ±19.8 in MR and 102.8min ±15.7 in MS+MR group (vide Table No.2). Incidence of post CPB ventricular tachycardia (VT), ventricular fibrillation (VF), and defibrillation were significantly higher in MR in comparison to the MS+MR groups. Higher inotropic support in ITU and post operative ventilation, reintubation rate were slightly more in older >40 years MR than the MS+MR group in the survivors. ITU stays were not significantly different between the two groups being slightly higher in MR groups (11± 2.8 in MR with median10 days vs 9 ± 7.5 days in MS+MR, median 8

days). There were 2 deaths, 1 from each group. Out of the 2, both in >40 years age, there was 1 in MR group who had post operative RV dysfunction and died on 29th day and 1 in MS+MR group died of respiratory failure after 7 days though the cardiac indices improved.

In the postoperative period after 30 days, improvement of NYHA status were observed to be higher in 13 survivors with MS +MR from III to I while it was 6 in MR group, from III to II was observed in 4 each in both groups. At 180 days, 1 each from NYHA II improved to I.

After 30 days in MS+MR group,the mean LVEF (%) was noted to have reduced from 59.1 ±3.1 to 50.9 ±3.8, decrease in LVESD (mm) from 42.3 ±2.1 to 38.4±2, and PASP (mm Hg) from 53.6 ±2.1 to 47.5±3.4. In 30 days in pure MR group, LVEF(%) also decreased from 56.0±1.6 to 51.5±5.3, but, LVESD (mm) decreased a little from 43.0 ±1.4 to 41.6 ± 2.6, and PASP(mm Hg) a little from 53.5 ±9.1 to 48.9±10.4. In MR group >40 years, after 30 days, LVESD increased more from 44.8± 1.7 to 46.6 ±1.4, the PASP decreased from 59.2±1.3 to only 57.2±2.3 in comparison in MR group in <40years LVESD decreased from 44.5±1.6 to 39.6±2.3, and PASP from 52.1±3.6 to 44.7±2.6. In > 40years in MS+MR, after 30 days, decrements in LVESD was from (42.2±1.3 to 40.3±2.0)and PASP from 57.2±2.3 to 52.0±2.5 while in <40 years group the LVESD decreased (42.7±2.0 to 34.9±2.3) and PASP decreased (50.1±6.6 to 43.6±5.7). The degree of improvement of NYHA status within both the groups was observed to be more in the patients with lower preoperative PASP with lower duration of MVD in less than 40 years group and more in patients with MS+MR than pure MR.

DISCUSSION

It was exactly sixty years ago that the first MVR was performed in March 11, 1960 at the National Heart Institute by Nina Starr Braunwald, the first woman to perform cardiac surgery on a 44 year old woman having severe MR. Modeling anatomy, she designed the valve using flexible polyurethane with Teflon chordae. The patient was discharged from the hospital after 2 months and did well clinically for several months before having a sudden death due to arrhythmia.[17,18] The timing and proper intervention for successful mitral valve surgery is still evolving at present era with the objective that MVR should be associated with clinical improvement, augmented stroke volume,regression of LV hypertrophy and smaller LV end-diastolic dimension.[19] However, certain facts need be discussed before arriving at a certain conclusion to reduce morbidity and mortality after MVR.

Pathogenesis of rheumatic heart valve disease (RHD) and PH

Rheumatic fever (RF) is the most common etiology of valvular heart disease (64.3%) in the Indian subcontinent and most other developing countries[20,21,22,23] with low-resource

Groups of severe MR				**MR**	**MS+MR**
Total No of patients			30	12 of 30	18 of 30
Age (years,mean ± SD			34.61±7.49	32.3±10.65	36.1 ± 7.2
MR	n, 7age <40	n,12 age>40			
MS+MR	n,12,age <40	n,6 age>40			
Male, n (%)			9(30.0%)	3(10.0%)	6 (20.0%)
Female, n (%)			21(70.0%)	9 (30.0%)	12 (40.0%)
BSA (mean ± SD)			1.38 ± 0.14	1.3 ±0.1	1.3 ± 0.1
PASP	mm Hg	± SD		53.5±5.1	53.6±2.1
RV basal diameter		>35 mm	n=12	5(31.6-34.3)	7(33.4-37.4)
TR			30	12	18
TR repair				8	13
AF				6 out of 12	11 out of 18
Intra operative variables					
Time taken for cardioplegic arrest			SEC (mean± SD)	24.5 ±4.07	20.5± 3.8
Integrated cardioplegia					1
Chordal preservation				12(100%)	18 (100%)
CC time	min	(mean % ± SD)		64.6 ±10.3	63.6± 8.4
CPB time	min	(mean % ± SD)		106.5±19.8	102.8 ±15.7
Time of return of impulse after CC			SEC (mean± SD)	62±10.1	38±5.1
Arrhythmias		(%)		11(36.6)	6(20.0)
Defibrillation		(%)		5(16.6)	3(10.0)
Post operative ITU course					
Mechanical ventilation		mean± SD		22±4.6	18 ±5.6
Mean ICU stay		mean± SD		4 ± 2.7	3.5 ± 2.5
Low cardiac Output state (LCOS)				5(16.6)	4(13.3)
Hospital stay in days		mean± SD		11 ± 2.8	9 ± 7.5
		Median		10	8
Mortality	30 days		n=2	1in >40 age	1in>40age

Table-1: Base line demography, clinical, intra operative variables during MVR, post operative variables

			MR, 7	MR, 5	MR, 12		MS+MR,18	MS+MR,12	MS+MR,6
			age<40	age>40				age<40	age>40
LVESD pre			44.5.0±1.6	44.8±1.7	43.0 ±1.4		42.3 ±2.1	42.7±2.0	42.2±1.3
LVESD post		After 30 days	39.6±2.3	46.6±1.4	41.6 ± 2.6		38.4±2.4	34.9±2.3	40.3±2.0
LVESD post		After 180 days	34.2±1.3	44.3±2.2	40.4±1.1		35.2±1.7	32.3±1.3	38.3±1.4
LVEDD pre			63.2±2.4	59.3±1.2	58.8±1.1		59.4 ± 3.1	64.1±4.6	59.2±2.4
LVEDD post		After 30 days	56.3±2.7	56.4±1.7	59.7±2.7		55.1± 3.6	55.2±3.2	58.2±1.7
LVEDD post		After 180 days	54.3±1.8	57.4±2.8	59.7±2.7		50.3± 2.8	49.2±2.2	53.2±1.6
			age<40	age>40				age<40	age>40
Pre OP LVEF			59.1±1.3	54.9±1.8	56.0±1.6		59.1±3.1	59.5±3.7	58.2±1.2
Post OP LVEF		After 30 days	51.8±2.1	49.8±1.2	51.5±5.3		50.9±3.8	51.0±2.7	52.4±1.6
Post OP LVEF		After 180 days	56±2.5	52.3±1.6	55.6±2.8		57.5±3.6	59±2.7	54.4±2.8
Pre OP PASP			52.1±3.6	59.2±1.3	53.5±5.1		53.6±2.1	50.1±6.6	57.2±2.3
Post OP PASP		After 30 days	44.7±2.6	57.2±2.3	48.9±10.4		47.5±3.4	43.6±5.7	52±2.5
Post OP PASP		After 180 days	40.1±2.7	53.4±1.5	44.2±2.9		42.3±2.3	39.4±3.2	46.3±2.2
30 day mortality			2/30(6.7%)		1/12(8.3%)		1/18(5.6%)	0	n=1
NYHA class	III to II	8/27,	0	n=1	n4	8/27,29.6%	n,4	n 2	n 2
NYHA class	III to I	19/27,	n 2	n 2	n6	19/27,70.3%	n13	n 10	n3
NYHA class	II to I	*6/8	30 days	n 1	n3	6/8,75%	n,3	n 2	n 1
			n 5	n 1					
			n 2	180days					

*In the MR and MS+MR group 180 days 1 each from remained in NYHA II

Table-2: Changes of cardiac dimensions and function after mvr

settings. Factors that consistently predispose patients to the development of chronic RHD include first episode of RF in a younger age, more severe carditis at first episode of RF, and frequency and number of RF recurrences.[24] Sometimes, children who do not have clinical carditis during initial RF, develop chronic RHD and absence of RF was also observed in the history of a few patients in this series. RHD involves the mitral valve almost 100% of the time, a aortic valve in 20–30%, and tricuspid valves are affected histologically in 15–40%[20] though functional TR is more common. Rheumatic pancarditis with valvulitis results in appearance of MR earlier than MS which develops later due to repeated attacks of RF at the rate of 0.1 to 0.3 cm^2 per year due to cumulative damage of the mitral valve.[20,25,26] Moderate MR like moderate MS remains asymptomatic for a longer period of time when compared to severe MS.[4] With the development of PH in severe MR (stage C) patients can remain asymptomatic for a further period of time before it produces features of decompensated LV failure with higher PASP and PVH at a later age in 4th or 5th decade and it was observed in our study too. With the progression of PVR, the the symptoms of pulmonary venous congestion are replaced by fatigue and edema[7] due to RHF. Accelerated forms of rheumatic MR also occur in the some geographic areas like the Indian subcontinent with high incidence of recurrent RF in age group below 20 years.[27] Except in the young teens and early 20s, where pure MR dominates, mixed valvular pathology of MS+MR is the most common finding in chronic RHD referred for surgical intervention[28] and is also most common in our series for MVR. Patients with severe MR who are also found in the younger age group in early 20s or late teens, in our hospital referred for surgery are mostly surgically managed by MVr and are not included in this series. All the patients in both groups for MVR had deformed valve leaflets not amenable to repair.

The effect of duration of RHD, age and preoperative LV function on survivability and mortality in our experience

Average was found to be slightly less (32.3 ±10.5), with a range from 26 to 50 years, mostly between 26 to 34 in MR group. This is in contrast to the MS+MR (36.1 ± 7.2) years with a range from 18 to 50 years, who presented mostly between 18 to 38 years (range 18 to 52 years). The number of patients with MS+MR (n=18) was also larger than the MR (n=12) group. The same preponderance of rheumatic MS+MR patients were also observed to be more in other Western surgical series[29] reported more than 55 years back in comparison to MR in present Western study and was probably due to repeated episodes of RF in that era which is still prevalent in our country. The cohort with late presentation of MR in our surgical series was higher in contrast to those presenting earlier with MR for medical management in cardiology

practice.[19] The reason for this discrepancy is that our patient population of MR were referred for MVR after being either non responsive to GDMT for long periods for cardiac failure which is associated with increase of LVESD over 40 mm and decreasing LVEF (below 60%), progression of PVH which raised PASP more than 50 mm Hg and sometimes are found to be inoperable due to presence of higher irreversible PVR. Preoperative response to decongestant therapy were observed in the majority of the patients with MS+MR where the decrease of TR ranged from severe to moderate or even mild. So actually, these TRs were masked, would have been all moderate or severe without diuretics and betablockers. Appearance of atrial fibrillation was observed in majority of the patients over 40 years in both groups. It was observed that the Mild MS in our series of severe MR had probably developed later in the course of MR due to repeated RF as which exacerbated the symptoms of dyspnea and fatigue at a relatively younger age group below 40. All these patients had almost equal LVEDD 64.1±4.6 in MS+MR comparison to 63.2±2.4 in MR group in the <40 age group. In comparison, patients from 20 to 40years, with severe MS referred for surgery, in our department, not included in this study usually had lower LVIDD around 44-46, LVESD of 29-33 mm, higher LVEF above 55% and a higher PASP >60-70 mm Hg. In MR group >40 years a higher LVEDD, was observed in a few of the patients and were associated with RHF and more severe PVR with systemic hypotension, as demonstrated by late response to diuretic and decongestant therapy. In contrast, in >40 years in MS+MR group, an earlier response to diuretics were denoted. The list does not include the preoperative patients with high PVR in both the groups who did not respond to decongestant therapy with oral or parenteral diuretics, sildenafil and were not considered for MVR in our set up as previous experience have shown such patients to suffer from RV failure after MVR and tricuspid annuloplasty, with difficulty to wean off from CPB. One such a patient in the MR group aged 43 years, responded to intravenous diuretics along with milrinone over two weeks, hepatomegaly subsided and MVR with ticuspid annuloplasty were done.Though the CC time was 89 minutes,there was prolonged CPB time over 180 minutes. She was on post operative prolonged ventilation for over a week and sent to ward after 3 weeks in NYHA class III status from preoperative class IV. She succumbed to systemic hypotension on 29th post operative day and was included in our mortality list. Preoperative LVESD was 47 mm,LVEDD 64mm, LVEF was 37% and PASP of 63 mm Hg after pre treatment with Sildenafil and diuretics and was a class I indication for MVR. Though there was no preoperative RHC, her PVR was obviously much higher in comparison to the PASP pretreated with sildenafil. On post operative death review, the preoperative TAPSE was found to be <15 mm, which was missed. The cause of mortality in the other male, non smoker patient of 48 years within the MS+MR group, was due to respiratory failure. He had preoperative LVESD of 44mm, LVEDD of 62mm, LVEF 43%, PASP of 62 mm Hg and also had MVR with TA for severe TR. Probably he had high PVR with irreversible remodelling of alveolar capillary unit leading to reduced alveolar diffusion capacity.[4] He died after 5 days of ventilary support from which he could not be weaned off though the inotrope requirements were minimal. TA has sometimes reversed the outcome after MVR. In one such a patient, a 40 years Female, (not in this series) reportedly was operated by one of our authors(4), MVR for MS and reportedly having grade I TR. After after CC release (CC time-45 minutes), several episodes of VF and inability to wean off from CPB after several attempts, the tense RA was was stabbed open and soon spontaneous rhythm returned. De Vaga TA was done in beating heart and patient had uneventful recovery.

Effect of MVR on pulmonary hypertension (PH) and cardiac function

In patients with long duration MR with probably compromised myocardium[30], there is little change in LV size after MVR, which do not result in much improvement of cardiac output when the PH is very high>70 mm Hg with high probability of high PVR and RHF. The compromised fibrotic LV can not reduce the LVESD and LVEDD thereby little reduction in LAP and PASP. At best the fall in LAP results in some relief of dyspnea[31] but NYHA status may not improve much. In contrast, in cases short duration of MR, though they had large LV dimensions there was earlier fall of PH because not only of mechanical elimination of LAP but relatively preserved LV had good contractile force reducing LVESD and LVEDD thereby reducing the PASP and has been observed in our series and is also comparable to similar other observations after MVR.[29]

Pulmonary vascular resistance (PVR) and its effect on LVEF, LVEDD and LVESD and LV function and our experience

LV function often remain poor after MVR which suggests that earlier MVR could have relieved the symptoms.[6,8] One of the young women with large LVESD of 47 mm under <25 years age, in our MS+MR group when the PASP was 50 mm Hg and LVEDD of 68mm, and LVEF of 62% after MVR and TA, the preoperative dimensions had reduced to 34mm, 42 mm Hg, and 51 mm but LVEF was also seen to have decreased to 50% respectively 1 month after MVR with TA. Such post operative drop of LVEF is quite common after MV surgery and was noted in other patients too, but improved gradually unless the PVR was high. But, in the > 40 age group, such preoperative figures of large LVESD >45, and LVEDD >60, with sever MR usually had PASP> 70 mm Hg and LVEF< 40%, and MVR would pose a prohibitive surgical risk because of severe comorbidities and in many such patients conservative management was continued after counselling. A typical patient of MR who was referred as a class I indication[15,16] for MVR had LVESD of 52 mm, LVEDD of 61 mm, PASP of 80 mm Hg and LVEF of 34%. This patient had further echocardiography and TAPSE was measured to be 17.6 mm and was considered not to be operated in our set up. Investigators from Mayo Clinic demonstrated that LV functional recovery is impaired

if the LVESD is> 36 mm and It was was also noted that if postoperative EF was less than 40%, the LVESD was also noted to have increased postoperatively and there was a higher hazard of late death.[32,33] Such increase of LVESD was noted in our >40 age group and were probably due to higher PVR. Others have demonstrated too that 33% of post operative LV dysfunction to have occurred even when LVESD was barely ≥ 37mm with LVEF was ≤ 64%.[34] In a recently analyzed results in Cleveland Clinic review, with an LVEF > 60% the authors[12] demonstrated threshold for baseline RV systolic pressure (RVSP) of ≥ 35 mm Hg, (approximate PASP of ≥ 45), to discriminate the risk of long term mortality while others[8,12] have demonstrated even mild PH (RVSP of > 40 mm) was associated with operative and long term mortality and impact of PH was progressive and higher values of RVSP >50 mm Hg was associated with longer duration of MR. So, these data and our findings show that during the watchful waiting for such patients of MR, caution must be exercised on false reassurance of preserved preoperative LVEF when the LVESD goes on increasing[31] till it reaches the trigger for guideline[13,14] directed surgical intervention when LVESD is ≥40 mm (I B))[13] or ≥ 45mm (IB).[14] In such patients,higher duration of MR, higher age of patient, higher PASP>60mm Hg and lower TAPSE ≤ 18 mm[13,14] should be considered as risk factors. The paradox about the implementation of class IIa indication for surgical intervention in asymptomatic patient when the LVESD is <40mm, whether watchful waiting or active intervention, an observation which was made almost 50 years back, that such patients tended to be too fit in asymptomatic stages "until their ventricles become unfit" for surgical intervention[31] still exists and the dilemma continues even in present day.

CONCLUSION

The present study has described the temporal response of extent of reverse ventricular remodeling after surgical correction of MR in rheumatic severe MR and correlated the response after MVR with preoperative risk factors. The patients most likely to achieve favorable reverse remodeling were those who do not exhibit large preoperative LVESD above 40 mm and higher PASP > 50 mm Hg, consistent with long-standing MR and other risk factors like RV dysfunction in addition to LV dysfunction. The early management of less-than-severe disease, before the onset of symptoms and irreversible LV/RV dysfunction is probably the key for improving prognosis. The TR should be tested intraoperatively in every patient despite it being reported as non significant preoperatively and there should be lower threshold for tricuspid annuloplasty. Reversibility of underlying PVR can be judged clinically by positive response to preoperative decongestant therapy and also by echoscreening for TAPSE>18 mm for better prognosis.

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