Original Article

Impact of preoperative pulmonary arterial hypertension on early and late outcomes in patients undergoing valve surgery for rheumatic heart disease

Address for correspondence:
Dr. Deepak Prakash Borde,
Department of Cardiac
Anesthesia, Ozone
Anesthesia Group,
Seth Nandlal Dhoot Hospital,
Aurangabad - 431 001,
Maharashtra, India.
E-mail: deepakborde2482@
gmail.com

Deepak Prakash Borde, Balaji Asegaonkar, Sujit Khade, Manish Puranik[1],
Antony George[2], Shreedhar Joshi[3]

Department of Cardiac Anesthesia, Ozone Anesthesia Group, [1]Department of Cardiac Surgery, Seth Nandlal Dhoot Hospital, Aurangabad, Maharashtra, [2]Department of Cardiac Anesthesia, Lissie Hospital, Kochi, Kerala, [3]Department of Cardiac Anesthesia, Narayana Institute of Cardiac Sciences, Bengaluru, Karnataka, India

ABSTRACT

Background and Aims: There is conflicting evidence on adverse effect of Pulmonary Arterial Hypertension (PAH) on outcomes after cardiac surgery for rheumatic heart disease (RHD). The authors studied Indian patients with RHD and preoperative PAH, who undergo cardiac surgery with a hypothesis that they have poor short and long-term outcomes. **Methods:** This was a retrospective observational study of 407 patients. The patients were divided in three groups based on PAH estimated on echocardiograph as; no or mild PAH (pulmonary artery systolic pressure (PASP) <30 mm of Hg); moderate PAH (PASP 31-55 mm of Hg) and severe PAH (PASP >55 mm of Hg). The primary endpoint was in-hospital mortality and major morbidities; while secondary endpoint was long-term survival. **Results:** In-hospital mortality was 24 (5.9%); and was not different in patients with severe, (9.1%), moderate (4.5%) or mild PAH (2.8%) (P = 0.09). Patients with severe PAH had higher incidence of prolonged ventilation (P = 0.007). Factors independently associated with mortality were; >2-packed cell transfusion, prolonged ventilation and acute kidney injury but not moderate and severe PAH. Patients with mitral stenosis (MS) and severe PAH had significantly higher mortality as compared to no or mild PAH (P = 0.03) on long-term follow-up [81.37% (mean duration 19.40 ± 14.10 months)], mortality was 8% and not statistically different (P = 0.25) across PAH categories. **Conclusion:** Moderate and severe PAH does not affect short and long term outcomes of patients undergoing valve surgery for RHD. Patients with MS with severe PAH had higher mortality compared to those with no PAH.

Key words: Indian, pulmonary hypertension, rheumatic heart disease

INTRODUCTION

Rheumatic heart disease (RHD) is a major burden in developing countries where it causes most of the cardiovascular morbidity and mortality in young people, leading to about 250,000 deaths/year worldwide.[1] Pulmonary arterial hypertension (PAH) is often found in symptomatic patients with left-sided valvular lesions. One of the most commonly used scoring system for mortality prediction after cardiac surgery, European System for Cardiac Operative Risk Evaluation II (EuroSCORE II), identifies moderate [pulmonary artery systolic pressure (PASP) 31–55 mmHg] and severe [PASP more than 55 mmHg] PAH as risk factors for mortality.[2]

Recent studies have indicated improved outcomes in patients with severe PAH, with reduced perioperative mortality rates compared to older studies.[3] Evidence on this topic appears to be controversial, with some studies claiming PAH as independent risk factor, whereas others conclude that mortality is unaffected by severe PAH. Indian studies on this important topic are very limited.[4,5]

The authors report their experience of impact of preoperative PAH on short- and long-term outcomes of patients undergoing mitral ± aortic valve surgery for RHD.

METHODS

This was a retrospective observational data analysis. The Institutional Review Board approved the study with a waiver of consent. Consecutive adult patients, who underwent cardiac surgery at our institute for RHD from January 2010 to August 2016, were considered eligible for inclusion in the study. Exclusion criteria were isolated aortic valve replacement as they have entirely different pathophysiology for PAH, non-availability of preoperative PAH data; and incomplete records.

The primary end points were in-hospital mortality defined as all-cause mortality in the same admission of cardiac surgery and major morbidities like re-exploration for bleeding, prolonged ventilator support (for more than 24 h), cardiac surgery-related acute kidney injury (CSAKI) (defined as more than 50% increase or doubling of preoperative creatinine during 7 days or requirement of renal replacement therapy) and neurologic deficit of more than 24 h. The secondary end point was long-term survival.

Demographic and procedural data were abstracted from medical records. It included age, sex and pre-existing comorbidities, including, anaemia as per world health oragnisation (WHO) definition, New York Heart Association (NYHA) functional classification, atrial fibrillation (AF), chronic obstructive pulmonary disease (COPD) that was defined as per X-ray and clinical findings, diabetes mellitus, renal disease (abnormal creatinine level >1.5 mg/dL and/or reduced creatinine clearance <50 ml/min), previous cerebrovascular accident (CVA) as defined as neuro-deficit of >24 h, peripheral vascular disease (PVD) and previous cardiac surgery. The primary predominant lesion and associated tricuspid regurgitation (TR) with its severity were also noted.

Preoperative echocardiography imaging was performed according to guidelines of the American Society of Echocardiography.[6] PASP was estimated by Doppler echocardiography by calculating the right ventricular to right atrial pressure gradient during systole, approximated by the modified Bernoulli equation as $4v^2$, where v is the velocity of the tricuspid regurgitation jet in m/s. The patients were divided in three groups based on PASP which was estimated on latest echocardiograph before surgery as (1) no or mild PAH (PASP less than 30 mmHg), (2) moderate PAH (PASP 31–55 mmHg) and (3) severe PAH (PASP more than 55 mmHg). These cut-offs were based on definitions used in EuroSCORE II system.[2] None of the patients underwent right heart catheterisation (RHC) for estimation of PA pressure or pulmonary vascular resistance (PVR) measurements.

Intraoperative monitoring in addition to standard American Society of Anesthesiology Guidelines consisted of arterial blood pressure monitoring by femoral arterial catheter, arterial blood gas monitoring, central venous pressure monitoring and temperature monitoring at two sites, nasopharynx and skin. Induction of general anaesthesia was done with midazolam, fentanyl and propofol. Vecuronium was used as a muscle relaxant. After induction, intravenous tranexamic acid, 10-mg/kg bolus, was given to all patients. Titrated doses of sevoflurane or isoflurane and titrated boluses of fentanyl and midazolam as per haemodynamic parameters were used for maintenance of anaesthesia. All patients had surgery through median sternotomy. Cardiopulmonary bypass (CPB) was established with aortic and bicaval cannulation after adequate heparinisation (activated clotting time ACT >400 s). Moderate hypothermia (32–34°C) was maintained during conduct of CPB. The extracorporeal circuit consisted of membrane oxygenator, roller pump, tubing and crystalloid prime solution. Blood cardioplegia was used to achieve cardiac arrest and to provide myocardial protection during aortic clamping. At the end of CPB, protamine reversal was given to achieve normal ACT. All patients were transferred to the intensive care unit. Patients were extubated as per standardised institutional protocols. Operative details noted were CPB duration, aortic cross-clamping duration (ACC), concomitant procedure and selection of prosthetic valves.

Data on long-term follow-up were abstracted from hospital record; if the follow-up record was not available, the patients were contacted telephonically. Information on mortality, readmission for cardiac

causes (prosthetic-valve thrombosis, congestive heart failure, arrhythmias resulting in significant haemodynamic disturbances etc.) and non-cardiac causes (anticoagulation related bleeding, neurological complications, respiratory causes etc.) was collected.

Patients were classified in three groups according to the severity of PAH according to EuroSCORE II system. Continuous variables were described as mean with standard deviation and were compared between PAH groups by using analysis of variance. Categorical data were presented as percentage and were compared using Chi-square test. Ordinal data were described as median (interquartile range, range). Univariate and multiple regression analysis were used to identify factors associated with mortality. Crude survival curves were estimated using the nonparametric Kaplan–Meier method. The log-rank test was used to compare survival among groups. All *P* values <0.05 were considered as significant. The Statistical Package for Social Sciences (SPSS) version 16.0.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for analysis.

RESULTS

A total of 482 patients underwent surgery during the study period. Patients excluded as per exclusion criteria were isolated aortic valve replacement (42; 8.7%), non-availability of preoperative PAH data (23; 4.8%) and incomplete records (20; 4.2%). The final analysis included 407 patients. A total of 278 patients underwent isolated mitral valve replacement (MVR), 50 patients underwent MVR + tricuspid valve repair (TV rep), 79 patients underwent double valve replacement (DVR) and 7 patients underwent DVR + TV rep.

Baseline clinical characteristics of patients are summarised in Table 1. Prevalence of preoperative moderate and severe PAH was 32.7% (133/407) and 40.5% (165/407), respectively, in the cohort. The groups had similar demographics and comorbidities except that there were more patients with severe PAH in NYHA III and IV class, more patients with severe PAH had severe TR and fewer patients in severe PAH category underwent concomitant aortic valve surgery. EuroSCORE II was significantly higher in moderate and severe PAH groups. As shown in Table 1, significantly higher number of patients underwent TV repair procedure in severe PAH category, although overall CPB and ACC times were similar in all categories.

Post-operative outcomes are summarised in Table 2. Overall incidence of in-hospital mortality was 5.9% (*n* = 24), although the incidence of mortality was higher in severe PAH patients (9.1%; *n* = 15) as compared to patients with moderate PAH (4.5%; *n* = 6) and no or mild PAH (2.8%; *n* = 3), but it was not statistically significant (*P* = 0.09). As far as post-operative morbidities are concerned, patients with severe PAH had higher incidence of prolonged ventilation (*P* = 0.007) but incidence of other morbidities such as re-exploration for bleeding (*P* = 0.97), CSAKI (*P* = 0.53) and neurologic deficit (*P* = 0.9) was similar in all categories of PAH. Results of univariate and multiple regression analysis for mortality are shown in Table 3. Factors independently associated with mortality were more than two-packed cell transfusion, prolonged ventilation and CSAKI but not moderate (*P* = 0.37) and severe PAH (*P* = 0.43). When we compared mortality rates as per predominant lesion [mitral stenosis (MS) compared with mitral regurgitation (MR)] and PAH category, we found that patients with MS and severe PAH had significantly higher mortality as compared to no or mild PAH (*P* = 0.03); mortality rates were similar in all categories of PAH in patients with MR as predominant lesion (*P* = 0.98) [Table 4].

The long-term follow-up was available in 81.37% patients. Mean long-term follow-up was 19.40 ± 14.10 months. The total patient-years of follow-up were 350 patient-years. The readmission rates for both cardiac and non-cardiac reasons were similar across all PAH categories (*P* = 0.88). The overall mortality of the entire cohort over the follow-up period was 8% and not statistically different (*P* = 0.25) in patients with no or mild PAH (8%), moderate PAH (11%) and severe PAH (6%), as shown in Table 5. Also, long-term survival was not significantly different in the moderate and severe PAH groups compared with the normal and mild PAH groups using the Kaplan–Meier curve analysis (Chi-square value 2.47; *P* = 0.29, log-rank test) [Figure 1].

DISCUSSION

The main findings of this study are that patients with moderate or severe PAH undergoing cardiac surgery for RHD have similar short and long-term mortality and morbidity compared to no or mild PAH. Patients with severe PAH experience higher incidence of prolonged post-operative ventilation. Patients with MS as predominant lesion and with severe PAH have significantly higher mortality as compared to patients with no or mild PAH (*P* = 0.03); mortality rates were

Table 1: Preoperative characteristics and intra-operative variables					
	Total (*n*=407)	None or mild PAH (*n*=109; 26.8%)	Moderate PAH (*n*=133; 32.7%)	Severe PAH (*n*=165; 40.5%)	*P*
Preoperative characteristics					
Age (mean±SD) (years)	38±12	38±13	39±12	38±12	0.85
Sex (female %)	231 (56.8%)	56 (51.4%)	82 (62.1%)	93 (56.4%)	0.24
Height (mean±SD) (cm)	158±9	159±9	158±9	159±9	0.78
Weight (mean±SD) (kg)	48±10	48±11	48±10	47±10	0.37
Haemoglobin (mean±SD) (g%)	12.6±1.7	12.7±1.7	12.3±1.5	12.7±1.9	0.09
Anaemia (yes) (%)	192 (47.2%)	47 (44%)	72 (54%)	73 (44%)	0.17
Creatinine (mean±SD) (mg%)	0.96±0.2	0.96±0.25	0.92±0.2	0.99±0.3	0.09
COPD (%)	8 (2%)	2 (1.9%)	1 (0.8%)	5 (3%)	0.37
DM (%)	7 (1.7%)	2 (1.9%)	3 (2.3%)	2 (1.2%)	0.78
CVA (%)	20 (4.9%)	6 (5.6%)	4 (3%)	10 (6.1%)	0.45
PVD (%)	2 (0.5%)	1 (0.9%)	0	1 (0.6%)	0.57
Redo surgery	31 (7.8%)	5 (4.7%)	11 (8.3%)	15 (9.1%)	0.39
EF (mean±SD) (%)	60±7	60±7	60±8	61±6	0.77
NYHA					0.003
II (%)	115 (28%)	41 (37.6%)	29 (22%)	33 (20%)	
III	279 (67%)	41 (37.6%)	63 (47%)	109 (66%)	
IV	13 (3.2%)	2 (2%)	6 (5%)	5 (3%)	
AF (%)	201 (49%)	46 (42%)	78 (59%)	77 (47%)	0.02
Primary lesion					0.01
MS (%)	301 (74%)	70 (64%)	99 (75%)	132 (80%)	
MR (%)	106 (26%)	39 (36%)	34 (25%)	33 (20%)	
More than mild TR	59 (14.5%)	8 (7.3%)	17 (13%)	34 (20.6%)	0.001
Concomitant aortic valve surgery (%)	79 (19.4%)	24 (22%)	37 (28%)	18 (11%)	0.00
EuroSCORE II	2.2±1.3	1.9±1.1	2.2±1.1	2.4±1.5	0.002
Intraoperative variables					0.000
Surgery	278 (68.3%)	81 (74.3%)	82 (61.7%)	115 (69.7%)	
MVR	50 (12.3%)	4 (3.7%)	14 (10.5%)	32 (19.4%)	
MVR+TV repair	72 (17.7%)	22 (20.2%)	34 (25.6%)	16 (9.7%)	
DVR	7 (1.7%)	2 (1.8%)	3 (2.3%)	2 (1.2%)	
DVR+TV repair					
CPB time (min)	108±45	110±48	117±44	110±42	0.33
ACC time (min)	77±37	83±39	89±34	81±34	0.18
Prosthesis					
Mechanical/Bio-prosthesis (%)	89.4%/10.6%	97%/3%	88.7%/11.3%	90.3%/9.7%	0.89

PAH – Pulmonary arterial hypertension; COPD – Chronic obstructive pulmonary disease; DM – Diabetes mellitus; CVA – Cerebrovascular accidents; PVD – Peripheral vascular disease; EF – Ejection fraction; NYHA – New York Heart Association; AF – Atrial fibrillation; MS – Mitral stenosis; MR – Mitral regurgitation; TR – Tricuspid regurgitation; EuroSCORE II – European System for Cardiac Operative Risk Evaluation II; MVR – Mitral valve replacement; DVR – Double valve replacement; CPB – Cardiopulmonary bypass; ACC – Aortic cross clamp

Table 2: Early post-operative outcomes					
Variables	Total (*n*=407)	No or mild PAH (*n*=109; 26.8%)	Moderate PAH (*n*=133; 32.7%)	Severe PAH (*n*=165; 40.5%)	*P*
Re-exploration (%)	5 (1.2%)	1 (0.9%)	2 (1.5%)	2 (1.8%)	0.97
Prolonged ventilation (%)	55 (13.5%)	6 (5.5%)	18 (13.5%)	31 (18.3%)	0.007
CSAKI (%)	198 (24.1%)	21 (19.3%)	34 (25.7%)	43 (26.1%)	0.38
Neurologic deficit (%)	6 (1.5%)	1 (0.9%)	2 (2.2%)	3 (2.1%)	0.82
Mortality (%)	24 (5.9%)	3 (2.8%)	6 (4.5%)	15 (9.1%)	0.09

PAH – Pulmonary arterial hypertension; CSAKI – Cardiac-surgery-related acute kidney injury

similar in all categories of PAH in patients with MR as predominant lesion (*P* = 0.98).

The RHD is major burden on health care in developing countries affecting mainly young population.[1] The development of PAH frequently complicates left-sided valve disease and is usually most pronounced in those with long-standing rheumatic mitral valve involvement. PAH reflects not only passively transmitted backpressure from left atrial (LA)

hypertension but also an active increase in PVR caused by a combination of pulmonary vasoconstriction and obliterative changes in the pulmonary vascular bed.[7] The pressure in a relatively thin-walled chamber like LA depends on several factors such as its stiffness, mechanical effects of its rhythmic contraction and relaxation, diastolic period, the quantity of blood entering and exiting it, and the net atrio-ventricular compliance which include compliance of LA and left ventricle (LV), and compliance of the pulmonary venous system. Schwammenthal *et al.* in a study of 20 patients reported a significant increase in PA pressure on exercise in a subgroup of patients with low

atrio-ventricular compliance.[8] Apparently, in patients of MS, a wide spectrum of atrio-ventricular compliance exists – patients with low compliance and patients with normal compliance. Patients with low compliance develop significant PAH, severe increase in LA pressure and symptoms of MS on exercise or in situations of increased cardiac output, whereas patients with normal compliance remain asymptomatic in situations of increased cardiac output as the increased RV stroke volume is accommodated in the compliant pulmonary venous bed.[9] This probably explains that even though all patients had severe mitral valve disease, only 40% patients in our cohort developed severe PAH.

PAH has been defined as an increase in mean pulmonary arterial pressure more than 25 mmHg at rest as assessed by RHC.[10] Echocardiography is a convenient screening tool for PAH.[11] EuroSCORE II identifies moderate (PASP 31–55 mmHg) and severe (PASP more than 55 mmHg) PAH as risk factors for mortality.[2] In a recent meta-analysis of 32 studies, 2604 Doppler–RHC pairings were studied. The authors concluded that correlation between echo-based and RHC assessment of PAH is high particularly in patients with left-sided heart pathology and elevated PA pressures.[12] Echocardiography is also non-invasive, convenient and practical approach. Hence, the authors used values based on latest preoperative echocardiography with EuroSCORE II cut-offs. Like present study, previously published studies also have
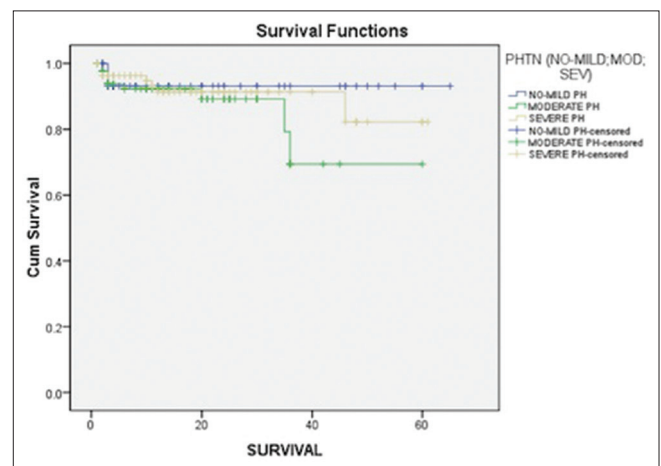
Table 3: Univariate and multiple logistic regression analysis for in-hospital mortality						
Variables	Univariate analysis			Multivariate analysis		
	OR	CI	P	OR	CI	P
Creatinine clearance	1.01	0.96-1.06	0.64			
Anaemia	0.74	0.12-4.39	0.74			
NYHA III	0.84	0.13-5.34	0.86			
NYHA IV	6.78	0.27-168.8	0.24			
Mod PAH	0.36	0.003-3.4	0.37			
Severe PAH	2.26	0.13-5.34	0.43			
Lesion MS vs. MR	5.0	0.59-42	0.14			
EuroSCORE II	1.11	0.6-1.9	0.69			
CPB time	0.97	0.9-1.03	0.36			
ACC time	1.03	0.95-1.1	0.41			
>2 PC transfusion	13.47	1.7-106.5	0.01	10.76	1.97-58.6	0.006
Re-exploration	0.89	0.09-8.75	0.92			
CSAKI	11.89	2.5-54.1	0.001	8.26	2.2-30.93	0.002
Prolonged ventilation	31.57	6.1-161	0.000	20.86	5.75-75.55	0.000

NYHA – New York Heart Association; MS – Mitral stenosis; MR – Mitral regurgitation; CPB – Cardiopulmonary bypass; ACC – Aortic cross clamp; PC – Packed cell; CSAKI – Cardiac surgery-related acute kidney injury; PAH – Pulmonary arterial hypertension;

Table 4: Mortality rates as per predominant lesion and severity of PAH			
Predominant lesion	PAH category	Mortality (%)	P
Mitral stenosis (*n*=301)	No or mild	1/70 (1.4%)	0.03
	Moderate	4/99 (4%)	
	Severe	13/132 (9.8%)	
Mitral regurgitation (*n*=106)	No or mild	2/39 (5.1%)	0.98
	Moderate	2/34 (5.9%)	
	Severe	2/33 (6.1%)	

PAH – Pulmonary arterial hypertension

Figure 1: Long term Survival by Kaplan-Meier curve analysis

Table 5: Long-term outcomes					
Parameter	Total (*n*=331)	No/Mild PAH (*n*=84)	Moderate PAH (*n*=111)	Severe PAH (*n*=136)	P
No readmissions	191 (58%)	50 (60%)	60 (54%)	81 (60%)	0.88
Readmissions for cardiac cause	42 (13%)	11 (13%)	15 (14%)	16 (12%)	
Readmission for non-cardiac cause	70 (21%)	16 (19%)	23 (21%)	31 (23%)	
Mortality	28 (8%)	7 (8%)	13 (11%)	8 (6%)	0.25

utilised echo-based measurements for estimation of PAH.[3,13]

Large body of literature is available on impact of PAH on outcomes in valve surgeries. These studies have studied various patient populations and used different methods for assessment of PAH with variable cut-offs and variable follow-up[3-5,13-25] [Table 6]. Present study

assessed impact of PAH as measured by Doppler echocardiography on patients undergoing cardiac surgery exclusively for RHD as per EuroSCORE II cut-offs. The incidence of severe PAH in our study was 40%, which is in accordance to previous studies.[13] Overall incidence of in-hospital mortality of 5.9% and 9.1% in moderate and severe PAH, respectively, are comparable to the recently published literature of

Sr. No.	Author Journal Year of publication	Study period	n	Patient population	PAH criteria	Early mortality	Late mortality	Conclusions
	Table 6: Studies published on impact of PAH on outcomes in valve surgeries							
1	Jiang *et al.* BMJ 2017[13]	2009-2013	1639	RHD	Echo-based 4 groups PAP <30, PAP 30-50, PAP 50-70, PAP>70	Overall: 3.84% <30: 1.9% 30-50: 2.3% 50-70: 4.7% >70: 10.2%	1 year; 5.14%	PAP is a predictor of post-operative and 1-year mortality
2	Yang *et al.* JTCVS 2016[14]	1992-2014	317	Mitral stenosis	RHC-based mild=35-44 moderate=45-59 Severe = >60	Overall: 9% Mild: 6% Moderate: 15% Severe: 9%	12 years, worse long-term outcomes when mod and severe PH combined	Acceptable 30-day mortality but poor long-term survival in moderate and severe PAH
3	Enter *et al.*; JTCVS 2016[3]	2004-2013	1571	All patients: mitral valve surgery	Echo/RHC-based None: <35, moderate: 35-49, severe 50-79, extreme: >80	Overall: 2.86% None: 1.2% Moderate: 2.8% Severe: 3.8% Extreme: 12%	2 years	Mortality unaffected by severe PHT, extreme PHT remains a risk factor
4	Gosain *et al.* ICVTS 2016[15]	2011-2014	569	Minimally invasive mitral and or aortic	Swan-Ganz catheter-based; mPAP Mild: 25-29, moderate: 30-39, severe: >40	Overall: 3.51% mild, moderate: 4%, severe: 3%	N.A.	Minimally invasive approach is safe even in patients with severe PAH
5	Castillo-Sang *et al.* Innovations 2015[16]	1996-2010	138	Redo mitral valve surgery	Swan-Ganz catheter based; PH-mean PAP >25 mmHg or sPAP >40 mmHg	10.1%	5 years survival rates 55.9%	The severity of PAH does not affect operative mortality rates, but it may decrease 1-, 3- and 5-year survival
6	Coutinho *et al.*; EJCTS 2015[17]	1992-2012	382	Asymptomatic severe degenerative MR	RHC or echo based; two groups presence or absence of atrial fibrillation and or PH	Overall: 0.8%, presence of AF±=0.9% Absence of AF±PH=0.7%	15 years survival; 84.35% for no or mild PH vs. 62% in severe PH	Asymptomatic or mildly symptomatic patients with severe MR, preserved LV function and AF/PHT had poorer long-term survival and event-free survival
7	Song *et al.* JCTS 2015[18]	2010-2012	32	RHD mitral valve disease with severe PH (sPAP >80 mmHg)	Echo	3.6%	26±10 months; 96.9% survival rate	MVR can be safely performed even in severe PAH
8	Paras *et al.* Pak Heart J 2015[19]	2012-2014	30	MVR in MS patients	Echo; moderate PH (30-60 mmHg) severe PH (>60 mmHg)	N.A.	N.A.	Mitral valve replacement should be offered even in presence of severe PAH

Contd...

Sr. No.	Author Journal Year of publication	Study period	n	Patient population	PAH criteria	Early mortality	Late mortality	Conclusions
9	Bayat *et al.*; *Ann Thorac Cardiovasc Surg*; 2013[20]	2009-2010	45	MVR	Swan-Ganz catheter based; PAP >50	N.A.	N.A.	MVR is safe and effective even in patients with severe PAH
10	Nirmal Kumar *et al.* *WJCS* 2013[21]	2009-2010	68	MVR in severe mitral valve disease	Echo; severe PH-sPAP >50 mmHg; two groups; sub-systemic PH or supra-systemic PH	Overall: 5.8% sub-systemic: 3.5% supra-systemic: 16.6%	12 months	MVR is safe and effective at the presence of severe PAH; with supra-systemic PAP, MVR carries a high risk of mortality
11	Elwany *et al.* *EJCA* 2013[22]	N.A.	30	RHD with MR	Echo; severe PH, sPAP >40 mmHg	10%	N.A.	MVR can be offered in patients with severe MR and severe PAH with proper perioperative and anaesthetic care
12	Tempe *et al.* *JCVA* 2009[4]	May-Dec. 2004	60	RHD with severe mitral valve disease	Swan-Ganz catheter based	N.A.	N.A.	PAP returns to near-normal values in patients with severe preoperative PAH after MVR. The outcome after surgery in patients with severe PAH is comparable to those with mild PAH
13	Mubeen *et al.*; *ACTA* 2008[5]	2000-2001	43	RHD	N.A.; mPAP >50 mmHg	Overall: 9.3 Sub-systemic: 5.5% Supra-systemic: 28.5%	14±10 months, no late deaths	Mitral valve replacement is safe even in the presence of severe PAH as long as pulmonary arterial pressures are sub-systemic
14	Cesnjevar *et al.*; *EJCTS* 1998[23]	1963-1993	382	MVR patients	RHC; severe PH, PAP >50 mmHg, PVR 690±46 dyn/s/m^2	10.5%	8.4±2 years	Recommend MVR in severe PAH even in the elderly, with a high but acceptable risk and good long-term results
15	Vincent *et al.* *Circulation* 1995[24]	1981-1992	42	MVR patients	RHC; severe PH sPAP >60 mmHg, mPAP >50 mmHg	11.6%	10 years	Cardiac surgery can be successfully performed with acceptable mortality in severe PAH patients
16	Camara *et al.* *EJCTS* 1988[25]	1976-1986	88	MVR	RHC; sPAP>50 mmHg	5.6%	44 months	Patients with mitral valve disease may benefit from surgical treatment regardless of degree of PAH

PAH – Pulmonary arterial hypertension; RHD – Rheumatic heart disease; RHC – Right heart catheterisation; MR – Mitral regurgitation; AF – Atrial fibrillation; MVR – Mitral valve replacement; PHT – Pulmonary hypertension PASP – pulmonary artery systemic pressure PH – Pulmonary artery hypertension mPAP – Mean pulmonary artery pressure sPAP – Systolic pulmonary artery pressure LV – Left ventricle, NA – Not available

cardiac surgery in RHD patients.[13,14,22] The mortality in severe PAH was not statistically different than in moderate and no or mild PAH patients. Factors significantly associated with mortality were more than two-packed cell transfusion, prolonged ventilation and CSAKI. Majority of previous studies in various patient populations have concluded that mitral valve surgery can be performed with acceptable perioperative mortality in patients with severe PAH.[3-5,22-24] Our findings are similar to previous studies. In contrast, a recent large study of 1639 RHD patients undergoing cardiac surgery demonstrated that PASP >70 mmHg

was an independent risk factor for in-hospital mortality (OR 2.93, 95% CI 1.61–5.32, $P < 0.001$), and patients with PASP >52 mmHg experienced higher 1-year mortality.[13] Another interesting finding in our study was that when we separated patients based on predominant lesion as MS or MR, patients with MS and severe PAH had significantly higher mortality as compared to no or mild PAH in contrast to MR in which mortality was similar in all categories of PAH.

The improved survival rates in severe PAH patients can be multi-factorial. There is better understanding of pathophysiological changes due to PAH resulting in improved anaesthetic, surgical and CPB techniques and materials. Special anaesthetic considerations apply to patients with PAH in order to avert the risk of right ventricular failure. It consists of balanced anaesthetic technique, avoidance of hypoxia, hyper-carbia, avoidance of use of nitrous oxide, judicious use of vasodilator and inotrope therapy and use of post-operative ventilator support.[4] There is realisation that PAH decreases significantly immediately after repair or replacement of diseased mitral valve.[4,20] One of the important findings of our study was that patients with severe PAH experienced higher rates of post-operative mechanical ventilation. The exact reasons for prolong ventilation were not available for detailed analysis. This appears to be more likely an association rather than causative effect.

There are many reports that severe PAH returns to normal after MVR.[4,20,26] This can be one of the important reasons for similar long-term outcomes in patients with severe and mild PAH. The long-term survival was comparable across all categories of PAH. This finding is in contrast to some of the previously published reports claiming reduced survival in severe PAH patients.[12,14] Also, we assessed patients for incidence of readmissions for both cardiac (prosthetic valve thrombosis, congestive heart failure, arrhythmias resulting in significant haemodynamic disturbances etc.) and non-cardiac (anticoagulation related bleeding, neurological complications, respiratory causes etc.) reasons and found no significant difference in rates of readmissions.

There are various important limitations to the present study, most important being retrospective nature and single centre study. The study duration was long which might likely change the management practices related to PAH. We evaluated PA pressure based on Doppler echocardiography and not RHC, which is

gold standard for its assessment. Certain patients who did not follow with our hospital were followed up by telephonic call, which is prone for some errors.

CONCLUSION

Moderate and severe PAH does not affect short and long-term outcomes of patients undergoing mitral ± aortic valve surgery for RHD. Patients with MS with severe PAH had higher mortality compared to those with no PAH, whereas mortality in patients with MR as primary pathology was not different across PAH categories.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. Lancet 2012;379:953-64.
2. Nashef SAM, Roques F, Sharples LD, Nilson J, Smith C, Goldstone AR, et al. EuroSCORE II. Eur J Cardiothorac Surg 2012;41:734-45.
3. Enter DH, Zaki A, Duncan BF, Kruse J, Anderi AC, Li Z, et al. A contemporary analysis of pulmonary hypertension in patients undergoing mitral valve surgery: Is this a risk factor? J Thorac Cardiovasc Surg 2016;151:1288-99.
4. Tempe DK, Hasija S, Datt V, Tomar AS, Virmani S, Banerjee A, et al. Evaluation and comparison of early hemodynamic changes after elective mitral valve replacement in patients with severe and mild pulmonary arterial hypertension. J Cardiothorac Vasc Anesth 2009;23:298-305.
5. Mubeen M, Singh AK, Agarwal SK, Pillai J, Kapoor S, Srivastava AK. Mitral valve replacement in severe pulmonary arterial hypertension. Asian Cardiovasc Thorac Ann 2008;16:37-42.
6. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quanti cation Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440-63.
7. Groves P. Surgery of valve disease: Late results and late complications. Heart 2001;86:715-21.
8. Schwammenthal E, Vered Z, Agranat O, Kaplinsky E, Rabinowitz B, Feinberg MS. Impact of atrioventricular compliance on pulmonary artery pressure in mitral stenosis: An exercise echocardiographic study. Circulation 2000;102:2378-84.
9. Neema PK, Rathod RC. Pulmonary artery hypertension in mitral stenosis: Role of right ventricular stroke volume,

atrio-ventricular compliance, and pulmonary venous compliance. J Anaesthesiol Clin Pharmacol 2012; 28:261-2.

10. Galiè N, Hoeper MM, Humbert M. Guidelines for the diagnosis and treatment of pulmonary hypertension: The Task Force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009;30:2493-537.

11. McGoon M, Gutterman D, Steen V, Barst R, McCroy DC, Fortin TA, *et al.* Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest 2004;126:14S-34S.

12. Finkelhor RS, Lewis SA, Pillai D. Limitations and strengths of Doppler/Echo pulmonary artery systolic pressure–right heart catheterization correlations: A systematic literature review Echocardiograpahy 2015;32:10-8.

13. Jiang L, Wei XB, He PC, Feng D, Liu YH, Liu J, *et al.* Value of pulmonary artery pressure in predicting in-hospital and one-year mortality after valve replacement surgery in middle-aged and aged patients with rheumatic mitral disease: An observational study. BMJ Open 2017;7:e014316.

14. Yang B, DeBenedictus C, Watt T, Farley S, Salita A, Hornsby W, *et al.* The impact of concomitant pulmonary hypertension on early and late outcomes following surgery for mitral stenosis. J Thorac Cardiovasc Surg 2016;152:394-400.

15. Gosain P, Larrauri-Reyes M, Mihos CG, Escolar E, Santana O. Aortic and/or mitral valve surgery in patients with pulmonary hypertension performed via a minimally invasive approach. Interact CardioVasc Thorac Surg 2016;22:668-70.

16. Castillo-Sang M, Guthrie TJ, Moon MR, Lawton JS, Maniar H, Damiano RJ, *et al.* Outcomes of repeat mitral valve surgery in patients with pulmonary hypertension. Innovations 2015;10:120-4.

17. Coutinho GF, Garcia AL, Correia PM, Branco C, Anyunes MJ. Negative impact of atrial fibrillation and pulmonary hypertension after mitral valve surgery in asymptomatic patients with severe mitral regurgitation: A 20-year follow-up. Eur J Cardiothorac Surg 2015;48:548-56.

18. Song X, Zhang C, Chen X, Chen Y, Shi Q, Niu Y, *et al.* An excellent result of surgical treatment in patients with severe pulmonary arterial hypertension following mitral valve disease. J Cardiothorac Surg 2015;10:70.

19. Paras I, Azam H, Khaki AB. Effects of pulmonary hypertension on early outcomes after mitral valve replacement. Pak Heart J 2015;48:96-100.

20. Bayat F, Aghdaii N, Farivar F, Bayat A, Valeshbabad AK. Early hemodynamic changes after mitral valve replacement in patients with severe and mild pulmonary artery hypertension. Ann Thorac Cardiovasc Surg 2013;19:201-6.

21. Kumar N, Sevta P, Satyarthy S, Agrawal S, Betigeri VK, Satsangi DK. Early results of mitral valve replacement in severe pulmonary artery hypertension—An institutional prospective study. World J Cardiovasc Surg 2013;3:63-9.

22. Elwany SE, Mohamed AH, Abu El-Hussain AK. Outcome after mitral valve replacement in patients with rheumatic mitral valve regurgitation and severe pulmonary hypertension. Egypt J Cardiothorac Anesth 2013;7:74-8.

23. Cesnjevar RA, Feyrer R, Walther F. High-risk mitral valve replacement in severe pulmonary hypertension—30 years experience. Eur J Cardiothorac Surg 1998;13:344–52.

24. Vincent J, Dogan T, James R. Long term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension. Circulation 1995;92:137-42.

25. Camara ML, Aris A, Padro JM. Long term results of mitral valve surgery in patients with severe pulmonary hypertension. Ann Thorac Surg 1988;45:133-6.

26. Parvathy UT, Rajan R, Faybushevich AG. Reversal of abnormal cardiac parameters following mitral valve replacement for severe mitral stenosis in relation to pulmonary artery pressure: A retrospective study of noninvasive parameters – Early and late pattern. Interv Med Appl Sci 2016;8:49-59.

Central Journal of ISA

Now! Opportunity for our members to submit their articles to the Central Journal of ISA (CJISA)! The CJISA, launched by ISA covering the central zone of ISA, solicits articles in Anaesthesiology, Critical care, Pain and Palliative Medicine. Visit http://www.cjisa.org for details.

Dr. Syed Moied Ahmed, Aligarh
Editor In Chief