Outcome after mitral valve replacement in patients with rheumatic mitral valve regurgitation and severe pulmonary hypertension

Shady E. Elwany, Ahmed H. Mohamed, Amany K. Abu El-Hussein

Correspondence to Amany K. Abu El-Hussein, MD
Tel: +20 11 44 33 8 432;
e-mail: dr.amanykhairy@hotmail.com

Received 6 June 2013
Accepted 27 July 2013

The Egyptian Journal of Cardiothoracic Anesthesia 2013, 7:74–78

Objective
The aim of this study was to assess the early outcome after elective mitral valve replacement (MVR) in patients with rheumatic mitral valve regurgitation and severe pulmonary arterial hypertension.
Patients and methods
The study included patients with baseline systolic pulmonary artery pressure (sPAP) of at least 40 mmHg who underwent elective MVR for rheumatic mitral valve regurgitation. The systemic and pulmonary hemodynamic changes and arterial blood gas parameters were reported at baseline, after intubation, after bypass, 30 min after extubation, and 24 and 48 h postoperatively. Preoperative and postoperative transthoracic echocardiography was performed.
Results
Thirty patients (11 men and 19 women), median age 31 years (range: 16–52), were included in the study. The operative mortality rate was 10%. The receiver operating characteristic curves identified sPAP as a good predictor of operative mortality. Postoperatively, there was a significant reduction in left atrial diameter and right ventricular systolic pressure in survivors. The median sPAP and pulmonary capillary wedge pressure decreased significantly after bypass and persisted throughout the study period. Central venous pressure decreased after cardiopulmonary bypass time and remained so for 48 h postoperatively. After intubation, on intermittent positive-pressure ventilation and FiO_2 of 1.0, there was a significant improvement in PaO_2 and SaO_2. pH and HCO_3^- concentration increased significantly postoperatively.
Conclusion
Proper perioperative care and anesthetic techniques resulted in improved left atrial diameter, right ventricular systolic pressure, sPAP, pulmonary capillary wedge pressure, and oxygenation with reduced operative mortality in patients who underwent MVR for mitral valve regurgitation with severe pulmonary hypertension.

Keywords:
mitral valve regurgitation, mitral valve replacement, severe pulmonary hypertension

Egypt J Cardiothorac Anesth 7:74–78

1687-9090

Introduction

Worldwide, rheumatic heart disease remains a major health problem, although its prevalence in the developed countries is much reduced. Involvement of the mitral valve results in mitral regurgitation and/or stenosis. Where surgery is indicated, mitral valve replacement (MVR) is usually necessary [1].

The development of pulmonary arterial hypertension (PAH) has long been considered a risk factor for poor outcome in patients undergoing MVR [2,3]. However, there is no consensus on the outcome of patients with PAH after MVR in the literature; some studies have shown that severe PAH is associated with poorer outcome and higher mortality rate [4,5], whereas others do not agree that severe PAH implies a higher risk during corrective surgery [6–10].

The present study was designed to assess the early clinical, hemodynamic, and echocardiographic changes after elective MVR in patients with severe PAH.

Patients and methods

Patients

The study included 30 patients with a baseline systolic pulmonary artery pressure (sPAP) of at least 40 mmHg (as measured by preinduction transthoracic echocardiography) who underwent elective MVR for rheumatic mitral valve regurgitation between June 2009 and June 2011 at the Nasser Medical Institute and Al-Minia University Hospital. The study protocol was approved by the ethics committee of the authors' institute, and a written informed consent was obtained

from each patient. Patients with significant aortic valve disease or coronary artery disease were excluded from the study.

Preoperative assessment

All preoperative assessments were carried out by two-dimensional transthoracic echocardiography. A thermodilution catheter was placed in the pulmonary artery to measure sPAP and pulmonary capillary wedge pressure (PCWP).

Anesthesia

General anesthesia was induced with fentanyl, 8–10 μg/kg, and thiopental, 3.0 mg/kg. The therapy for PAH was instituted with a nitroglycerin infusion (0.5–1 μg/kg/min), deliberate hypocarbia (arterial carbon dioxide tension £35 mmHg), fractional inspired oxygen concentration (FiO_2) of 1.0, and elective ventilation for at least 12 h in the postoperative period.

Operative technique

All patients were operated on through a median sternotomy on cardiopulmonary bypass time (CPB) with moderate general hypothermia (28–30°C). The mitral valve was approached through the left atrium (LA) in 24 (80%) patients, through the superior septum in four patients (13.3%), and trans-septally in two patients (6.7%). All patients underwent MVR with a mechanical prosthesis: a Sorin bileaflet mechanical prosthesis (Sorin Biomedica, Vercelli, Italy) in 17 patients (56.7%) and a St Jude Medical (St Jude Medical Inc., St Paul, Minnesota, USA) bileaflet mechanical prosthesis in 13 patients (43.3%).

Data collection

The hemodynamic and arterial blood gas (ABG) parameters were reported at baseline, after intubation, after bypass, 30 min after extubation, and 24 and 48 h postoperatively. Hemodynamic parameters that were recorded included heart rate, mean arterial pressure (MAP), sPAP, PCWP, and central venous pressure (CVP).

Statistical analysis

All data were expressed as median and range or number and percent as appropriate. The preoperative and postoperative echocardiographic parameters, and the hemodynamic and ABG parameters obtained at various time intervals were compared with the baseline values using the nonparametric Wilcoxon test for within-group differences. The receiver operating characteristic (ROC) curves were used to estimate the relationship between sensitivity (proportion of true positive cases) and 1-specificity (proportion of false-positive cases) of sPAP in the prediction of operative mortality. A *P*-value of 0.05 or less was considered significant.

Results

Thirty patients (11 men and 19 women), median age 31 years (range: 16–52), were included in the study. The patients were classified as follows: 14 (46.7%) in NYHA II class and 16 (53.3%) in NYHA III class. All the patients studied had mitral regurgitation. The mean PAP was 62.1 ± 35.2 mmHg (Table 1).

The median CPB was 55 min (range: 30–130) and the median aortic cross-clamp time was 28 min (range: 20–80). De Vega tricuspid annuloplasty was performed in seven (23.3%) patients with severe tricuspid regurgitation. Postoperatively, there was cardiac tamponade in three patients (10%), pleural effusion in one patient (3.3%), inotrope requirement for more than 24 h in nine patients (30%), and hospital stay of more than 10 days in four patients (13.3%).

The operative mortality rate was 10% (Table 2). The ROC curves (Figure 1) identified sPAP as a good predictor of operative mortality (area under the ROC curve: 0.982; $P < 0.001$), and the value greater than 64 mmHg has the highest specificity (93%) and sensitivity (100%) for the risk of operative mortality in those patients. Postoperative evaluation of echocardiographic variables, hemodynamic parameters,

Table 1 Preoperative characteristics of 30 patients with mitral valve regurgitation and severe pulmonary hypertension who underwent mitral valve replacement

Variables	Severe pulmonary hypertension (*N* = 30)
Age (years), median (range)	31 (16–52)
Sex (male/female)	11/19
NYHA II [*n* (%)]	14 (46.7)
NYHA III [*n* (%)]	16 (53.3)
Atrial fibrillation [*n* (%)]	17 (56.7)
Tricuspid regurgitation [*n* (%)]	27 (90)
Mild–moderate	20 (66.7)
Severe	7 (23.3)

Table 2 Intraoperative and postoperative clinical outcome variables of 30 patients with mitral valve regurgitation and severe pulmonary hypertension who underwent mitral valve replacement

Variables	Severe pulmonary hypertension (*N* = 30)
CPB (min), median (range)	55 (30–130)
ACC (min), median (range)	28 (20–80)
De Vega tricuspid annuloplasty [*n* (%)]	7 (23.3)
Cardiac tamponade [n (%)]	3 (10)
Pleural effusion [n (%)]	1 (3.3)
Inotrope requirement for >24 h [*n* (%)]	9 (30)
Hospital stay of >10 days [*n* (%)]	4 (13.3)
Operative mortality [*n* (%)]	3 (10)

ACC, aortic cross-clamp; CPB, cardiopulmonary bypass.

and ABG parameters was performed only for survivors (n = 27 patients) after exclusion of three patients with operative mortality.

A comparison of preoperative and postoperative echocardiographic variables is presented in Table 3. Postoperatively, there was a significant reduction in LA and right ventricular systolic pressure (RVSP; $P < 0.05$).

The hemodynamic parameters at various stages in the studied patients are shown in Table 4. The median baseline heart rate was 92.5 beats/min (range: 77–146), which remained stable until postextubation, after which it decreased to 85 beats/min (range: 75–115) 48 h postoperatively ($P < 0.05$). The median of MAP decreased from 87 mmHg (range: 75–95) to 75 mmHg (range: 70–90) at 24 h postoperatively ($P < 0.05$) and it remained so for 48 h ($P < 0.05$). The median sPAP and PCWP decreased significantly after bypass, and this change remained throughout 48 h postoperatively ($P < 0.05$). CVP decreased after CPB and remained so for 48 h postoperatively ($P < 0.05$).

Table 3 Comparison of preoperative- and postoperative echocardiographic variables in 27 patients with severe pulmonary hypertension who survived after mitral valve replacement

Variables	Preoperative	Postoperative	*P*-value
LA (mm)	70 (40–120)	65 (20–85)	0.0001*
LVEDD (mm)	57 (30–70)	59 (35–60)	0.62
LVESD (mm)	26 (20–46)	26 (20–50)	0.06
RVSP (mmHg)	90 (40–110)	68 (25–75)	0.0001*
EF (%)	50 (40–70)	51.5 (42–68)	0.42

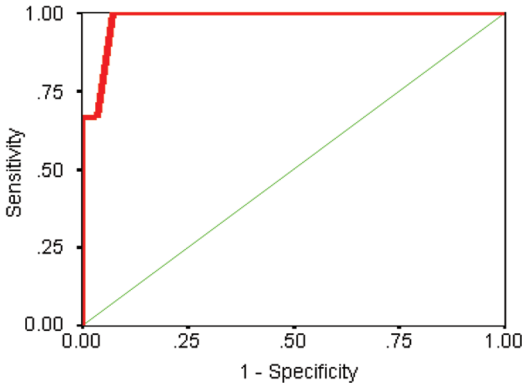
EF, ejection fraction; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; RVSP, right ventricular systolic pressure.

ABG parameters observed at various stages in patients with severe PAH are shown in Table 5. After intubation, on intermittent positive-pressure ventilation and an FiO_2 of 1.0, there was a significant improvement in partial pressure of oxygen (PaO_2) and SaO_2. pH and HCO_3^- concentration increased significantly at 48 h postoperatively ($P < 0.05$).

Discussion

The development of PAH is usually associated with a poor prognosis in mitral valve diseases, but it is doubtful whether it should be considered as a contraindication for MVR or not [11,12]. The increased LA pressure in mitral valve disease is passively transmitted to the pulmonary vasculature and can lead to an increase in

Figure 1



The receiver operating characteristic curve of systolic pulmonary arterial hypertension as a predictor of operative mortality in patients who underwent mitral valve replacement.

Table 4 Hemodynamic parameters observed at various stages in 27 patients with severe pulmonary hypertension who survived after mitral valve replacement

Variables	Baseline	Postintubation	Postbypass	Postextubation	24 h postoperation	48 h postoperation
HR (beats/min)	95 (77–146)	96 (80–140)	96 (80–140)	95 (90–130)	90 (78–120)	85 (75–115)[a]
MAP (mmHg)	87 (75–95)	87 (65–100)	87 (67–95)	87 (75–95)	75 (70–90)[a]	70 (65–88)[a]
sPAP (mmHg)	55 (44–85)	50 (37–79)	22 (15–30)[a]	22 (15–30)[a]	18 (15–30)[a]	17 (15–30)[a]
PCWP (mmHg)	37 (28–52)	33 (27–45)	23 (8–40)[a]	16 (11–20)[a]	14 (10–20)[a]	14 (9–20)[a]
CVP (mmHg)	11 (4–18)	11 (6–18)	7 (4–12)	5 (4–12)	5 (2–12)	4 (2–12)

CVP, central venous pressure; HR, heart rate; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; sPAP, pulmonary systolic arterial pressure. aSignificant difference.

Table 5 Arterial blood gas parameters observed at various stages in 27 patients with severe pulmonary hypertension who survived after mitral valve replacement

Variables	Baseline (on room air)	Postintubation (on FiO2 = 1.0)	48 h postoperatively (on O2 by nasal prongs)
pH	7.4 (7.36–7.44)	7.7 (7–8)	7.6 (7.17–7.77)[a]
PaCO2 (mmHg)	33 (30–42)	33 (30–44)	33 (30–42)
PaO2 (mmHg)	70 (51.5–85.5)	400 (322–520)[a]	150 (90–230)[a]
K+ (mEq/l)	4 (3.3–4.7)	4 (3.2–4.6)	4 (3.4–4.5)
HCO3– (mEq/l)	22 (19.6–26)	22 (19.9–25.7)	27 (24.3–30.3)[a]
SaO2 (%)	97.5 (96.8–98.2)	99.5 (99.2–100)[a]	99.2 (97.6–99.6)[a]

[a]Significant difference.

PVR. Some other factors such as reactive pulmonary vasoconstriction and organic changes in pulmonary vasculature are also responsible for this increase in PVR [13]. Following mitral valve surgery, LA loading can be adequately decompressed. This decompression is very influential in the regression of pulmonary hypertension [14].

Our results showed a significant decrease in PAP and PCWP after bypass, and this change persisted throughout 48 h postoperatively. These findings are in agreement with some investigators who have reported hemodynamic changes in patients with rheumatic mitral valve disease at different intervals after MVR, with an immediate reduction in PAP.

In the study by Tempe *et al.* [6], the mean PAP, PCWP, and pulmonary vascular resistance decreased significantly soon after CPB in patients with severe pulmonary hypertension. The mean PAP approached near-normal values (23 ± 8 mmHg) immediately postoperatively. The study by Mubeen *et al.* [7] showed that the mean PAP decreased by 38% from a mean preoperative level of 59.8 to 37.1 mmHg immediately following MVR. Although it continued to decrease over the next 24 h, this further decrease was not statistically significant. In a recent study by Bayat *et al.* [12], PAP in patients with severe PAH showed no significant reduction immediately after MVR, but it decreased significantly below the range of severe PAP over the first 24 h.

The present study shows that MVR can be performed in patients with rheumatic valvular disease and severe pulmonary hypertension with an acceptable operative mortality of 10%. The early studies showed higher operative mortality and considered pulmonary hypertension as a risk factor for poor outcome in patients undergoing MVR, with operative mortality rates ranging from 15 to 31% [3,10]. Other reports have shown improved outcome in patients with PAH undergoing MVR, with perioperative mortality ranging from 2.3 to 10% [8,15,16]. The improved outcome in these reports was attributed to better myocardial preservation, preservation of the subvalvular apparatus, and improved postoperative care.

The study by Mubeen *et al.* [7] showed that the operative mortality was 5.5% in patients with subsystemic PAP, with a mean of 58.1 mmHg and 28.5% in patients with a suprasystemic PAP of 83.2 mmHg. Also, the recent study by Ghoreishi *et al.* [17] showed that operative mortality was correlated with the degree of preoperative pulmonary hypertension (2, 3, 8, and 12% for none, mild, moderate, and severe pulmonary hypertension, respectively).

In the present study, sPAP was identified as a good predictor of operative mortality (area under the ROC curve: 0.982; $P<0.001$), and the value greater than 64 mmHg has the highest specificity and sensitivity for the risk of operative mortality in those patients. Similarly, the recent study by Corciova *et al.* [18] identified sPAP value greater than 65 mmHg to have the highest specificity and sensitivity for the risk of perioperative death in mitral regurgitation patients (area under the ROC curve: 0.782; $P<0.001$). Also, the recent study by Ghoreishi *et al.* [17] concluded that preoperative sPAP is a powerful predictor of early and late survival after mitral valve operation for mitral regurgitation. Even modest increases in sPAP affect outcomes adversely.

The anesthetic technique and the postoperative management can adversely influence the favorable changes and hence assume importance. Manners *et al.* [19] attributed the improved outcome in their patients to better surgical and CPB techniques and materials, judicious use of inotropes and vasodilators, and postoperative mechanical ventilation.

Special anesthetic considerations apply to patients with PAH in order to avert the risk of right ventricular failure. In the present study, deliberate hypocarbia (arterial carbon dioxide tension ≤35 mmHg) was used. It is well established that the $PaCO_2$ is an important physiologic determinant of pulmonary vascular tone [20]. Hypercarbia can affect hemodynamics adversely. Even mild hypercarbia significantly increases RVSP, right ventricular end-diastolic pressure, and PCWP after CPB [21]. Drummond *et al.* [22] reported that reducing $PaCO_2$ produced a consistent and reproducible reduction in pulmonary vascular resistance in infants with pulmonary hypertension. As reviewed by Laffey and Kavanagh [23], hypocapnia can have an impact on the balance between cerebral oxygen supply and demand. In a recent study by Mahdi *et al.* [24], moderate hypocapnia was effective in decreasing pulmonary vascular tone in adults following MVR. The application of this maneuver in the immediate postoperative period may provide a bridge until pulmonary vascular tone begins to normalize following surgery.

In the present study, the therapy for pulmonary hypertension was instituted with a nitroglycerin infusion. In agreement with our findings, the study by Yurtseven *et al.* [25] showed that inhalation of nitroglycerin decreases PAP without affecting systemic blood pressures in the early postoperative period in patients who underwent MVR. Nitroglycerin and sodium nitroprusside produce sustained vasodilatation in the pulmonary circulation in a dose-dependent

manner [26]. Nitroglycerin decreases PAP, PCWP, CVP, MAP, and PVR and increases cardiac output in patients with elevated pulmonary vascular resistance secondary to mitral valve disease [27].

Conclusion

MVR is safe and effective even in patients with severe pulmonary hypertension and rheumatic mitral valve regurgitation, with acceptable operative mortality, and a significant improvement in echocardiographic parameters (LA diameter and RVSP), pulmonary hemodynamics (sPAP, PCWP), and oxygenation. The anesthetic technique and perioperative care can be useful in improving the outcome in such patients.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Zakkar M, Amirak E, Chan KM, Punjabi PP Rheumatic mitral valve disease: current surgical status. Prog Cardiovasc Dis 2009; 51:478–481.

2 Ward C, Hancock BW Extreme pulmonary hypertension caused by mitral valve disease. Natural history and results of surgery. Br Heart J 1975; 37:74–78.

3 Chaffin JS, Daggett WM Mitral valve replacement: a nine-year follow-up of risks and survivals. Ann Thorac Surg 1979; 27:312–319.

4 Simonsen S, Forfang K, Andersen A Hospital mortality after mitral valve replacement. Prognostic significance of preoperative clinical and hemodynamic factors. Acta Med Scand 1974; 195:243–2436.

5 Datt V, Tempe DK, Geelani MATomar ASVirmani SGoel M *et al.* Atrial septostomy for acute right ventricular failure following mitral valve replacement – a case report. Ann Card Anaesth 2004; 7:62–66.

6 Tempe DK, Hasija S, Datt VTomar ASVirmani SBanerjee 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.

7 Mubeen M, Singh AK, Agarwal SKPillai JKapoor SSrivastava AK Mitral valve replacement in severe pulmonary arterial hypertension. Asian Cardiovasc Thorac Ann 2008; 16:37–42.

8 Jegaden O, Rossi R, Delahaye FMontagna PDelaye JDelahaye JP *et al.* Mitral valve replacement in severe pulmonary hypertension. Long-term results. Arch Mal Coeur Vaiss 1991; 84:1297–1301.

9 Cámara ML, Aris A, Padró JM Long-term results of mitral valve surgery in patients with severe pulmonary hypertension. Ann Thorac Surg 1988; 45:133–136.

10 Zener JC, Hancock EW, Shumway NE Regression of extreme pulmonary hypertension after mitral valve surgery. Am J Cardiol 1972; 30:820–826.

11 Barclay RS, Reid JM, Stevenson JG Long-term follow-up of mitral valve replacement with Starr–Edwards prosthesis. Br Heart J 1972; 34:129–133.

12 Bayat F, Aghdaii N, Farivar F, Bayat A, Valeshabad AK Early hemodynamic changes after mitral valve replacement in patients with severe and mild pulmonary artery hypertension. Ann Thorac Cardiovasc Surg 2013; 19:201–206.

13 Braunwald E in Braunwald E (ed) Valvular heart disease. Heart disease 7th ed. 2005; Philadelphia, PA: Saunders.

14 Lafci G, Diken AI, Gedik HS, Korkmaz K, Ozcan F, Tasoglu I, *et al.* Alterations in pulmonary artery pressure following mitral valve replacement. Turk Kardiyol Dern Ars 2012; 40:235–241.

15 Vincens JJ, Temizer D, Post JR, Edmunds LH Jr, Herrmann HC Long-term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension. Circulation 1995; 92(Suppl II):137–142.

16 Cesnjevar RA, Feyrer R, Walther F, Mahmoud FO, Lindemann Y, von der Emde J High-risk mitral valve replacement in severe pulmonary hypertension – 30 years experience. Eur J Cardiothorac Surg 1998; 13:344–352.

17 Ghoreishi M, Evans CF, DeFilippi CR, Hobbs G, Young CA, Griffith BP, Gammie JS *et al.* Pulmonary hypertension adversely affects short- and long-term survival after mitral valve operation for mitral regurgitation: implications for timing of surgery. J Thorac Cardiovasc Surg 2011; 142:1439–1452.

18 Corciova FC, Corciova C, Georgescu CA, Enache M, Anghel D, Bartos O, Tinica G Echocardiographic predictors of adverse short-term outcomes after heart surgery in patients with mitral regurgitation and pulmonary hypertension. Heart Surg Forum 2012; 15:E127–E132.

19 Manners JM, Monro JL, Ross JK Pulmonary hypertension in mitral valve disease: 56 surgical patients reviewed. Thorax 1977; 32:691–696.

20 Manners JM Nunn's applied respiratory physiology 1993; Oxford, UK: Butterworth-Heinemann.

21 Tempe D, Cooper A, Mohan JC Nigam M Tomar AS Ramesh K *et al.* Closed mitral valvotomy and elective ventilation in the postoperative period: effect of mild hypercarbia on right ventricular function. J Cardiothorac Vasc Anesth 1995; 9:552–557.

22 Drummond WH, Gregory GA, Heymann MA, Phibbs RA The independent effects of hyperventilation, tolazoline, and dopamine on infants with persistent pulmonary hypertension. J Pediatr 1981; 98:603–611.

23 Nishio K, Suzuki Y, Takeshita K, Aoki T, Kudo H, Sato N, *et al.* Effects of hypercapnia and hypocapnia on $[Ca^{2+}]i$ mobilization in human pulmonary artery endothelial cells. J Appl Physiol 2001; 90:2094–2100.

24 Mahdi M, Joseph NJ, Hernandez DP, Crystal GJ, Baraka A, Salem MR Induced hypocapnia is effective in treating pulmonary hypertension following mitral valve replacement. Middle East J Anesthesiol 2011; 21:259–267.

25 Yurtseven N, Karaca P, Uysal G, Ozkul V, Cimen S, Tuygun AK, *et al.* A comparison of the acute hemodynamic effects of inhaled nitroglycerin and iloprost in patients with pulmonary hypertension undergoing mitral valve surgery. Ann Thorac Cardiovasc Surg 2006; 12:319–323.

26 Schütte H, Grimminger F, Otterbein JSpriestersbach RMayer KWalmrath D *et al.* Efficiency of aerosolized nitric oxide donor drugs to achieve sustained pulmonary vasodilation. J Pharmacol Exp Ther 1997; 282:985–994.

27 Ziskind Z, Pohoryles L, Mohr R Smolinsky A Quang HT Ruvolo G *et al.* The effect of low-dose intravenous nitroglycerin on pulmonary hypertension immediately after replacement of a stenotic mitral valve. Circulation 1985; 72:164–169.