Early Hemodynamic Changes after Mitral Valve Replacement in Patients with Severe and Mild Pulmonary Artery Hypertension

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Purpose: to assess the early hemodynamic changes after elective mitral valve replacement (MVR) in patients with severe and mild pulmonary arterial hypertension (PAH).

Methods: a total of 45 consecutive patients, who were candidate for elective MVR, were enrolled in this prospective observational study. Patients were divided into two groups based on the absence (group A, 20 patients) or presence (group B, 25 patients) of severe pulmonary artery hypertension (PAH) defined as systolic pulmonary artery pressure ≥50 mmHg measuring by catheterization. MVR was performed using standard cardiopulmonary bypass (CBD) technique. The hemodynamic and arterial blood gas assessments were carried out at baseline before the induction of general anesthesia, in the operating room immediately after MVR, and then continued after stabilization of hemodynamic status with 2 hr interval up to 24 hours.

Results: The mean CPB and aortic cross-clamp times were similar in two groups (95.3 ± 49.5 and 61.8 ± 36.3 minutes in group A and 103.1 ± 34.7 and 61.9 ± 20.0 minutes in group B). In group A, the mean PAP showed an increase immediately after the operation (from 40.4 ± 7.3 to 43.10 ± 6.2 mmHg) and then decreased significantly to 32.5 ± 3.9 mmHg (P <0.05). In group B, the mean PAP showed no significant reduction immediately after MVR, but it decreased significantly below the range of severe PAP over the first 24 hours.

Conclusion: MVR is safe and effective even in patients with severe PAH. The anesthetic technique and postoperative cares can be useful in improving the outcome in such patients.

Keywords: pulmonary hypertension, mitral valve replacement, hemodynamic, Iran

Introduction

Pulmonary arterial hypertension (PAH) has been recognized as a known risk factor for poor outcome in patients undergoing mitral valve replacement (MVR). The mortality rate of MVR in such patients has been reported up to 31%, and even some authors considered severe PAH as an absolute contraindication for MVR. Pulmonary hypertension at the initial stages may only involve pulmonary venous, but after a while developing of pul-
monary arterial hypertension and accompanying morphologic changes in pulmonary vasculature may lead to subsequent increase in the pulmonary vascular resistance (PVR) and further complications.

However, there is no consensus about the outcome of patients with PAH after MVR in the literature, some studies have revealed that severe PAH is associated with poorer outcome and higher mortality rate while some others do not agree with this and believed that severe PAH do not imply the greater risk in corrective surgery, but the point is that the definition of PAH varies across studies, pulmonary artery pressure >40, 50, 70 and 110 have been considered as severe PAH in various studies.

To our knowledge, there is no related study about this issue in Iran, and most of the previous, related works are not so recent and had been conducted with a small sample size. A major proportion of related studies has assessed the late outcome of MVR in patients with severe PAH. A study with adequate sample size that investigates the outcome of MVR in these patients with new operative techniques and improved postoperative care seems necessary. This study is designed to assess the early hemodynamic changes after elective mitral valve replacement in patients with severe and mild pulmonary arterial hypertension and to diagnose the potential hemodynamic problems in patients with severe PAH to prepare necessary preambles to encounter with them in the future.

Materials and Methods

In this prospective observational study between March 2009 and August 2010 all consecutive patients undergoing elective MVR in Shahid Rajaei Hospital, Tehran, Iran were enrolled the study. The study protocol was approved by ethics committee of Tehran University of Medical Sciences and each patient gave informed consent before enrollment in the study. Those without an informed consent were excluded from the study.

Among these patients, those with, chronic obstructive airway disease (FEV1/FVC <0.70), coexisting coronary artery disease, congestive heart failure (presence of basal crepitations and peripheral edema), systemic hypertension (consistently elevated blood pressure exceeding 140/90 mmHg), aortic valve dysfunction, primary pulmonary hypertension, renal dysfunction (serum creatinine ≥2.0 mg/dL), hepatic dysfunction (serum bilirubin ≥3.0 mg/ dL), or central nervous system dysfunction and those undergoing reoperation were taken apart.

After applying exclusion criteria patients were divided into two groups based on the baseline pulmonary artery pressure (PAP); group A with baseline systolic PAP ≥50 mmHg (20 patients)

(measured by pre-induction pulmonary artery catheterization ) (25 patients) and group B with systolic PAP ≥50 mmHg with the same measurement by catheterization. All hemodynamic and arterial blood gas measurements were taken at baseline, in the operation room and then with 2 hr intervals with continuous electrocardiographic monitoring and invasive arterial blood pressure recording. Systolic PAP and ejection fraction (EF) were measured preoperatively using pulmonary artery catheterization and angiography and they were repeated after operation using 2-dimensional trans-thoracic echocardiography.

General anesthesia was induced using fentanyl 8–10 µg/kg, and thiopental 1.0 mg/kg. Rocuronium 0.6–0.9 mg/kg was administrated for muscle relaxation, except in those with heart rate (HR) 100/min in whom vecuronium 0.15 mg/kg, was used. Subsequently, patients were manually ventilated by bag and mask, and laryngoscopy and tracheal intubation were performed by two trained anesthesiologists using tracheal tubes no. 6.5–7 for women and no. 7–7.5 for men. Then, patients were mechanically ventilated using a Siemens Servo 900C ventilator (Siemens-Elema, Solna, Sweden) with inspiratory:expiratory ratio of 1:2, rate, 14–18/min; tidal volume, 7–10 mL/kg; and positive end expiratory pressure, 5 cmH2O. Then, anesthesia was maintained with intermittent doses of fentanyl, midazolam, isoflurane, and muscle relaxant. FIO2 1.0 was maintained throughout the surgical period.

All patients underwent a median sternotomy on CPB with moderate general hypothermia (28°C–30°C). Mechanical prosthesis of bileaflet tilting-disk valve prosthesis such as the bileaflet St. Jude cardiac valve and Bileaflet carbomedic valve used for MVR. Narcotic analgesics and vasodilator therapy in the form of nitroglycerine infusion were applied in all the patients until the stabilization of hemodynamics and the possibility of extubation. The use of milrinone and inotropic agents (dopamine, adrenaline, and dobutamine) was determined by the patient’s hemodynamic status, and they were discontinued when the hemodynamics became stable , and the patient was extubated. Acetaminophen IV and coumarin or warfarin was administrated in patients when they were extubated , and it was given through a nasogastric tube for those with long-term ventilation.

After the operation, all patients were transferred to the
intensive care unit (ICU) and monitored until their discharge.

The hemodynamic and ABG assessments were carried out at baseline before the induction of general anesthesia, in the operating room immediately after MVR, and then continued after stabilization of hemodynamic status with 2 hr interval in the intensive care unit (ICU) up to 24 hours. All the hemodynamic and ABG parameters including systolic PAP, EF, heart rate (HR), duration of mechanical ventilation, use of inotropes, systolic and diastolic blood pressure were recorded and compared for within- and inter-group differences at various times before and after the operation.

Statistical analysis

Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using the Student’s t- test for continuous variables and the chi-square test (or Fisher’s exact test if required) for categorical variables. The hemodynamic and ABG parameters obtained at various time intervals were compared with the baseline values using a paired t test for within-group differences. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16 (SPSS Inc, Chicago, IL, USA) for Windows.

Results

A total number of 45 consecutive patients with the mean age of 51.5 ± 8.6 years (range: 29–69 years) who were candidate for elective MVR were enrolled the study. Among them 25 patients (55.6%) had severe PAH and other 20 ones (44.4%) had mild PAH. Most of these patients had severe mitral stenosis (MS) (60%), followed by moderate MS (20%) and combined severe MS with left atrial appendage clot (11.1%), moderate TR (4.4%) and moderate (2.2%) and severe mitral regurgitation (2.2%).

Comparison of baseline hemodynamic and ABG parameters between two groups has been shown in Table 1. Among these parameters, a significant difference was found about baseline PAP between two groups (P = 0.04). Table 2 shows the operative data and inotropic requirements in each group. Changes in these parameters at various stages in each group has been summarized in Figs. 1 and 2.

In group A the mean PAP showed an increase immediately after the operation (from 40.4 ± 7.3 to 43.10 ± 6.2 mmHg) and then decreased significantly to 32.5 ± 3.9 mmHg (P <0.05). The mean EF decreased significantly after the surgery (50.8 ± 5.3 to 46.7 ± 6.4, P = 0.02). The means of HR and systolic blood pressure remained stable in this group, but there were significant changes in some stages about diastolic BP compared to the baseline values.

<table>
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<tr>
<th>Table 1</th>
<th>Comparison of baseline hemodynamic and ABG parameters between two groups.</th>
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<tbody>
<tr>
<td>Variable</td>
<td>Mild PAH (n = 20)</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>85.4 ± 15.5</td>
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<tr>
<td>Mean PAP (mmHg)</td>
<td>40.4 ± 7.3</td>
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<tr>
<td>EF</td>
<td>50.8 ± 5.3</td>
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<tr>
<td>Mean SBP (mmHg)</td>
<td>109.2 ± 22.7</td>
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<tr>
<td>Mean DBP (mmHg)</td>
<td>68.7 ± 9.4</td>
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<tr>
<td>pH</td>
<td>7.4 ± 0.4</td>
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<tr>
<td>PaO2 (mmHg)</td>
<td>74.0 ± 9.0</td>
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<tr>
<td>PaCO2 (mmHg)</td>
<td>34.6 ± 5.7</td>
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PAH: pulmonary artery hypertension; HR: heart rate; PAP: pulmonary artery pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure

<table>
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<tr>
<th>Table 2</th>
<th>Operative data, duration of elective ventilation and inotropic requirement in each group</th>
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<tr>
<td>Variable</td>
<td>Mild PAH (n = 20)</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>103.1 ± 34.7</td>
</tr>
<tr>
<td>Aortic cross-clamp time (min)</td>
<td>61.8 ± 36.3</td>
</tr>
<tr>
<td>Elective ventilation (hour)</td>
<td>14.3 ± 17.1</td>
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<tr>
<td>Mean Inotropic use</td>
<td>0.71 ± 0.81</td>
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PAH: pulmonary artery hypertension
The mean arterial pressure of O2 (PaO2) was higher in the each stage postoperatively compared to its preoperative values (P < 0.05) while PaCO2 did not change during the first 24 hr after the operation (except 6th hour after the surgery) (P > 0.05) (Fig. 1).

In group B, the mean PAP decreased from 61.8 ± 8.0 to 46.1 ± 28.1 twenty four hours after the operation while the mean EF did not change. Systolic and diastolic BPs remained relatively stable after MVR (except at ICU for diastolic BP) (P >0.05). The mean HR shows some fluctuation in various stages postoperatively compared to its baseline values. The pattern of changes in ABG parameters were to some extent similar to its trend in severe PAH group (Fig. 2).

Discussion

The development of PAH is usually associated with poorer prognosis in mitral valve diseases, but it is under doubt whether it should be considered as a contraindication for MVR or not. The increased left atrium (LA) pressure in mitral valve diseases is passively transmitted to the pulmonary vasculature and can lead to increase in PVR. Meanwhile, some other factors such as reactive pulmonary vasoconstriction and organic changes in pulmonary vasculature are also responsible for this increase in PVR.20

In our study, despite the significant difference in baseline PAP between two groups, both groups showed a significant decrease in PAP in the first 24 hours after the operation. In patients with severe PAH, the mean PAP showed no significant reduction immediately after MVR, but it decreased gradually below the range of severe PAP.
over the first 24 hours, and the fall was significant at 24 hours, when compared to baseline values. There is not a consensus in the literature about the reversibility of severe PAH; some authors showed a significant short term or long term regression in the mean PAP after MVR in patients with severe PAH9–19) while some others failed to confirmed this.3–8)

In patients with mild PAH, the mean PAP showed an increase immediately after MVR, but it decreased significantly from 40.4 ± 7.3 to 32.5 ± 3.9 mmHg over the first 24 hours. The main reason of this finding is not clear, but the reactive component of pulmonary arterial vasoconstriction might be responsible for the disproportionate elevation in PAP and PVR, in patients undergoing MVR.

The operation mortality rate in patients with severe PAH undergoing MVR has been reported up to 31%.1,2) Recent studies have confirmed improved outcomes and lower mortality rate (2.3%–10.0%) as a result of better myocardial preservation and improved postoperative care.11,12,21,22)

In our study, the overall mortality rate was 0.0%, and this is counted a great outcome in comparison to the previous works. The myocardial preservation, anesthetic technique and postoperative managements can have considerable impacts on improving the outcome of MVR in patients with severe PAH.

The cardiopulmonary bypass time, aortic cross-clamp time and elective ventilation duration did not differ between our two groups (P >0.05). The favorable effects of Nitroglycerin,23,24) dobutamine and milrinone25) in decreasing PVR and obtaining better outcome have been reported in several studies. We used these drugs for all patients, and the inotropic requirement was the same in both groups (P >0.05).

A relative improvement in arterial oxygenation postoperatively was observed in both patients with and without severe PAH. Tempe DK et al in an assessment of sixty patients with (30 patients) and without (30 patients) severe PAH found that the improvement in arterial oxygenation was significantly more in patients with severe PAH than those with mild PAH.

They attributed this to the fact that patients with severe PAH were sicker preoperatively, and the reversed process of the disease after MVR led to significant improvement in oxygenation in comparison to patients with mild PAH who had better baseline oxygenation.9) The baseline oxygenation did not differ between our two groups and the mean baseline PAP was considerably higher in our patients with mild PAH compared to their patients (40.4 ± 7.3 vs. 29 ± 6 mmHg) and these could explain the significant improvement in our both groups especially patients with mild PAH. Except for some fluctuation in HR in some stages postoperatively compared to the baseline in group B, other hemodynamic parameters remained relatively stable in various stages of the study, in both groups.

The severity of mitral valve stenosis highly affects pulmonary pressure; thus it is recommended to evaluate pulmonary wedge pressure and pulmonary vascular resistance before and after the operation. These variables have not been registered for all participants, and our data base was incomplete. Therefore, they were not entered in the final analysis. The lack of follow up of pulmonary vascular dynamics by catheterization because of economic problems is one limitation of this study. The small sample size may limit the statistical significance of the study. Further large-scaled studies are required to obtain a clearer view from this issue.

**Conclusion**

Finally, it can be concluded that MVR is safe and effective even in patients with severe PAH.

The anesthetic technique and postoperative cares can be useful in improving the outcome in such patients.

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**Disclosure Statement**

Authors declare any conflicts of interests.

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