Original Article

Clinical Outcomes of Mechanical and Bioprosthetic Pulmonary Valve Replacement During Mid to Long-term Follow-up in a Single Tertiary Center for Congenital Heart Disease

Zahra Khajali[1], MD; Fateme Jorfi[1*], MD; Niloofar Samiei[1], MD; Majid Maleki[2], MD; Sedighe Saedi[1], MD; Behshid Ghadrdoost[1], PhD; Maryam Keshavarz Hedayati[3], MD

ABSTRACT

Background: Pulmonary valve replacement (PVR) is frequently performed during the correction of various congenital heart disease. Pulmonary valve substitutes include bioprostheses, homografts, and mechanical valves. Among these, bioprosthetic valves are probably the most widely used because they are readily available and they do not need lifelong anticoagulation therapy. However, most of these bioprostheses will fail and require replacement mainly due to structural valve degeneration.

Methods: We retrospectively identified all patients who had undergone PVR at Rajaie Cardiovascular Medical and Research Center between 2010 and 2017. Medical records were reviewed for demographic and clinical information and follow-up imaging results.

Results: A total of 435 patients were eligible, and they had regular follow-ups after PVR based on their medical records. Mechanical valves were used for 66% of the patients (n=288) at first PVR and bioprosthetic valves for 34% of the patients. Forty-five patients with mechanical pulmonary valves (15%) received at least 1 thrombolytic therapy due to prosthetic valve thrombosis. Seventeen patients needed redo PVR, and 28 patients (62%) had successful thrombolytic therapy. There was no significant association between redo PVR and the prosthetic valve size (P=0.7) or the valve type (P=0.07), although the percentage of patients with first bioprosthetic valves who needed redo PVR was almost twice that of patients with first mechanical valves (13.4% vs 5.9%).

Conclusions: A mechanical valve can be a promising option for PVR in selected patients.

(Iranian Heart Journal 2021; 22(4): 66-70)

KEYWORDS: Congenital heart disease, Mechanical valve, Pulmonary valve

[1] Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Cardiovascular Intervention Research Center Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[3] Qazvin University of Medical Sciences, Qazvin, IR Iran.

*** Corresponding Author:** Fateme Jorfi, MD; Rajaie cardiovascular medical and research center, Iran University of Medical Sciences, Tehran, IR Iran.
Email: fajorfi@gmail.com **Tel:** +982156795155

Received: May 16, 2020 **Accepted:** October 5, 2020

The pulmonary valve is the most common heart valve repaired and replaced in the treatment of congenital heart disease (CHD). [1] Life expectancy in patients with CHD has improved over the past decades, increasing the need for a durable pulmonary prosthetic valve. There are limited population-based data about outcomes after pulmonary valve replacement (PVR). [2]

The main differences between valve types (mechanical vs bioprosthetic) relate to durability and the need for anticoagulation. There are no important differences in the incidence of prosthetic valve endocarditis, although some series have demonstrated a higher incidence of early (<1 y) infection with mechanical valves compared with bioprostheses. [3] While the thromboembolic risk after PVR with mechanical valves is thought to be high, recent studies have shown promising short and midterm results. On the other hand, bioprosthetic valve failure is rapid in children and adults younger than 35 to 40 years, and most of the patients who need PVR are within this range of age. Therefore, prosthetic valve type selection is a challenging situation for both patient and physician. [4] We herein describe our experience as a tertiary center for CHD in PVR patients and compare clinical outcomes between mechanical and bioprosthetic pulmonary valves.

METHODS

We retrospectively identified all patients who had undergone PVR at Rajaie Cardiovascular Medical and Research Center between 2010 and 2017. The medical records were reviewed for demographic and clinical information and follow-up imaging results. Categorical variables are expressed as frequencies and percentages, while continuous variables are presented as the mean ± the standard deviation (SD). The Wilcoxon rank-sum test and the Fisher exact test, as appropriate, were applied to compare the demographic variables. For the statistical analyses, SPSS, version 22, for Windows (SPSS Inc, Chicago, IL) was used. A *P*-value of 0.05 or less was considered statistically significant.

The selection of the type of prosthesis at the time of surgery was based on several factors, including patient characteristics and informed patient preferences. Patients who preferred not to be subjected to repeated surgery, patients with a high surgical risk, and patients who already had an indication for permanent anticoagulation therapy were considered candidates for a mechanical prosthesis. Female patients who wished to have a pregnancy and patients who refused lifelong anticoagulation therapy underwent PVR with bioprosthetic valves. Preoperative electrocardiograms at the time of surgery and a postoperative electrocardiogram at least 3 months after surgery were considered for the calculation of the QRS duration. The number of post-PVR hospital admissions, thrombolytic therapies, and surgical redo PVR procedures was obtained using medical records until the last follow-up visit of the patients. Our study was designed with a focus on valvular thrombosis and reoperation as primary endpoints. Death was not chosen as the primary endpoint because mortality is more associated with heart failure than with the prosthetic valve itself. [5] The mortality rate of patients with PVR is low (1%–2%) and almost similar in both mechanical and bioprosthetic valves in the literature. [6]

RESULTS

A total of 454 patients underwent PVR in our center between 2010 and 2017. From this total, 435 patients were eligible, and they had regular follow-ups after PVR based on their medical records. Thus, the study population consisted of 272 male (62.5%) and 163 female (37.4%) patients at a mean

age of 21.6±9.2 years (range =1–55 y) at the time of PVR. Mechanical valves were used for 66% of the patients (n=288) at first PVR and bioprosthetic valves for 34% of the patients. Follow-up was calculated from the date of PVR to the date of the last contact and redo PVR. The median follow-up duration was 6.4±3.9 years (range =1–26 y). Tetralogy of Fallot was the most common underlying etiology for PVR, with a subgroup of 81%, followed by pulmonary stenosis (Table 1). The mean interval between the first corrective procedure and the first surgical PVR was 14±6.5 years.

Table 1. Underlying heart diseases

Variable: Diagnosis	n (%)
TOF	345 (81%)
PS	25 (5.9%)
PS + ASD	26 (6.1%)
PS + VSD	13 (3.1%)
Double-outlet right ventricle	8(1.9%)
TOF + ASD	6 (1.4%)
Tricuspid stenosis + PS	2 (0.4%)

TOF, Tetralogy of Fallot; PS, Pulmonary stenosis; ASD, Atrial septal defect; VSD, Ventricular septal defect

Mechanical valves were implanted in 288 patients (64.1%): St Jude Medical in 160 (55%), On-X in 58 (20%), CarboMedics in 60 (20%), and ATS in 7 (2.4%). The mean labeled size of the prostheses was 24.0±1.6 mm (range =16–38 mm). Bioprosthetic valves were used in 147 patients (32.7%): Hancock II in 46 (31.3%), Carpentier–Edwards porcine in 18 (12.2%), Carpentier–Edwards PERIMOUNT in 16 (10.9%), Epic in 11 (7.5%), and Mitroflow in 10 (6.8%).

The QRS duration was 137±73 ms before PVR and 137±23 ms after PVR, with no significant change. The mean pressure gradient and the peak pressure gradient of the pulmonary prosthetic valves at baseline, following PVR, and 6 months and 1 year after PVR are shown in Table 2.

Table 2. Pressure gradient of the pulmonary prostheses

Valve Type	Mechanical	Bioprosthetic
Baseline post PVR	PPG:17±7 MPG:9±4	PPG:23±10 MPG:12±5
6 months post PVR	PPG:18± 6 MPG:10± 4	PPG:25± 12 MPG:15± 8
1 year post PVR	PPG:20± 8 MPG:11± 5	PPG:27± 12 MPG:16± 8

PVR, Pulmonary valve replacement; PPG, Peak pressure gradient; MPG, Mean pressure gradient

Pre-PVR cardiac magnetic resonance imaging of the patients was reviewed, and the results showed a median left ventricular ejection fraction of 50±7%, a median right ventricular ejection fraction of 39±18%, and a right ventricular end-diastolic volume index of 166±48 mL/m^2.

Forty-five patients with mechanical pulmonary valves (15%) received at least 1 thrombolytic therapy due to prosthetic valve thrombosis, and 19 patients had more than 1 hospital admission for thrombolytic therapy. Seventeen patients needed redo PVR, and 28 patients (62%) had successful thrombolytic therapy. The median international normalized ratio (INR) at the time of valve thrombosis was 1.9±0.6 (range =1–3.1). There was no significant association between valve thrombosis and valve size (P=0.4) or the patients' sex (P=0.4). Hospitalization due to bleeding events occurred in 19 patients with mechanical valves, with a median INR of 4.6±3 (range =1.2–11).

Redo PVR was done for 38 patients: 17 patients with first mechanical valves and 21 patients with first bioprosthetic valves. There was no significant association between redo PVR and the prosthetic valve size (P=0.7) or the valve type (P=0.07), although the percentage of patients with first bioprosthetic valves who needed redo PVR was almost twice that of patients with first mechanical valves (13.4% vs 5.9%). There seemed to be a relationship between redo PVR and patients' sex and age. More female

patients underwent redo PVR than male patients (23 female patients vs 15 male patients; *P*<0.005). Patients in the redo PVR group were younger than those who did not need redo PVR (18 vs 22 y; *P*=0.01). The median interval between the first and second PVR procedures was 5.5±2.8 years (range =1–11 y).

Valve-related hospital admission occurred in 135 patients, and 62 patients were admitted more than once. Patients with first mechanical pulmonary valves had more hospitalization than patients with first bioprosthetic valves (*P*=0.001). The indications for admission included valve thrombosis, bleeding, low INR, dental procedures, bridging therapy, and redo PVR.

DISCUSSION

The optimal pulmonary valve prosthesis has not yet been clearly defined. Large studies evaluating long-term valve-related complications are missing. In the present study, we sought to compare outcomes between mechanical and bioprosthetic valves in our tertiary CHD center. The literature contains reports on PVR with mechanical and bioprosthetic valves. Nonetheless, by comparison with our study, all of them have included small samples, patients with only mechanical or bioprosthetic valves, and short follow-ups. The controversy over biologic versus mechanical valve replacement of the pulmonary valve is unbalanced in favor of biologic substitutes. [1] Despite small series showing favorable results, mechanical valves are typically not used in the pulmonary position because of the increased risk of thrombosis. [7]

Although the thromboembolic risk after PVR with mechanical valves is presumed to be high, our data suggested a 15% rate of valve thrombosis during a mean follow-up of 6.4±3.9 years, with successful thrombolytic therapy in 28 of 45 patients. There was no association between valve thrombosis and the labeled valve size or the patients' sex. The median INR was 1.9±0.6 in patients with valve thrombosis and 4.6±3 in patients with bleeding events leading to hospitalization. It is of great importance to inform patients that incorrect INR levels can result in such severe complications as bleeding complications and redo PVR because of valvular thrombosis.

Most centers prefer biologic valve prostheses in the pulmonary position as the risk of thrombosis is low and no anticoagulation is needed. Cheul Lee et al [7] reported that the durability of bioprosthetic valves in the pulmonary position was suboptimal and that valve function was maintained stable until 5 years after surgery. A total of 147 patients had undergone PVR with bioprostheses in our center, and 21 (14.2%) patients needed redo PVR due to valve degeneration. The interval between the first and second PVR procedures was 5.5±2.8 years. Redo PVR was done for 17 patients with mechanical pulmonary valves. A relationship seemed to exist between redo PVR and patients' sex and age. Redo PVR was done more on younger and female patients. The labeled valve size had no significant association with redo PVR. The results of our multivariable correlation analysis in our patients with redo PVR are presented in Table 3.

Table 3. Multivariable correlation analysis in patients with redo pulmonary valve replacement

Variables	B	Odds Ratio	Confidence Interval	*P*-value
Age	0.049	0.95	(0.90 - 1.00)	0.04
Sex	- 0.86	0.92	(0.18 – 0.94)	0.03
Valve type	0.129		(0.5 - 2.56)	0.75

Information on the long-term behavior of different pulmonary prosthetic valves, especially mechanical valves, is scarce. With this study, we highlight the medium- to long-term performance of mechanical and biologic valves in the pulmonary position. Although the nonrandomized and retrospective nature of this study including a number of heterogeneous patients are its major limitations, our results show an acceptable risk of valvular thrombosis and promising results for thrombolytic treatment. It is essential to assess thromboembolic and bleeding risks before implanting a mechanical valve prosthesis.

CONCLUSIONS

A mechanical valve can be a promising option for PVR in selected patients and medical centers of countries with limited access to cardiac surgeons or high operation mortality, while biological valves are susceptible to degeneration and patients might require 1 or more reoperations.

Conflict of Interest

The authors declare that there are no conflicts of interest.

REFERENCES

1. Husain SA, Brown J. Biologic versus Mechanical Valve Replacement of the Pulmonary Valve After Multiple Reconstructions of the RVOT Tract. Operative Techniques in Thoracic and Cardiovascular Surgery. 2006 Sep 1; 11(3):207-15.

2. Freling HG, van Slooten YJ, van Melle JP, Ebels T, Hoendermis ES, Berger RM, Hillege HL, Waterbolk TW, van Veldhuisen DJ, Willems TP, Pieper PG. Pulmonary valve replacement: twenty-six years of experience with mechanical valvar prostheses. The Annals of thoracic surgery. 2015 Mar 1; 99(3):905-10.

3. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. Elsevier Health Sciences; 2018: pp.3657.

4. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. Elsevier Health Sciences; 2015: pp.1507.

5. Pragt H, van Melle JP, Javadikasgari H, Seo DM, Stulak JM, Knez I, Hörer J, Muñoz-Guijosa C, Dehaki MG, Shin HJ, Dearani JA. Mechanical valves in the pulmonary position: An international retrospective analysis. The Journal of thoracic and cardiovascular surgery. 2017 Oct 1; 154(4):1371-8.

6. Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. Elsevier Health Sciences; 2018: pp. 3901.

7. Chen XJ, Smith PB, Jaggers J, Lodge AJ. Bioprosthetic pulmonary valve replacement: contemporary analysis of a large, single-center series of 170 cases. The Journal of thoracic and cardiovascular surgery. 2013 Dec 1; 146(6):1461-6.

8. Lee C, Park CS, Lee CH, Kwak JG, Kim SJ, Shim WS, Song JY, Choi EY, Lee SY. Durability of bioprosthetic valves in the pulmonary position: long-term follow-up of 181 implants in patients with congenital heart disease. The Journal of thoracic and cardiovascular surgery. 2011 Aug 1; 142(2):351-8.