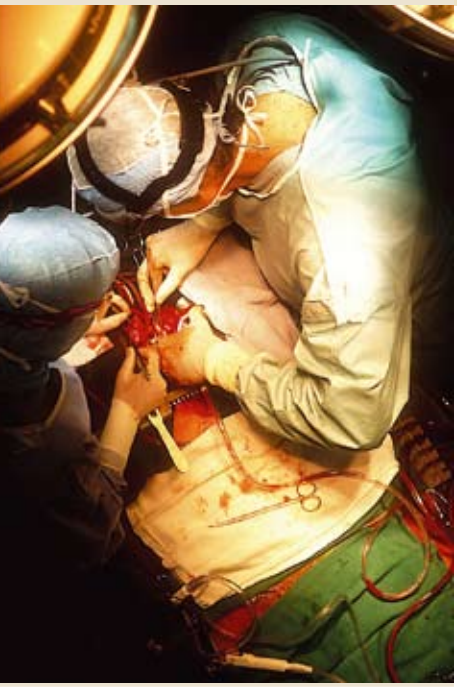
Pulmonary Valve Replacement in Patients With Congenital Heart Disease: Is There Any Place for Mechanical Valves?



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Abstract:

Background: We would report the results of 112 mechanical valve replacements in the position of pulmonary valve during 6 years in the Rajaie Heart Center.

Material & Methods: Between March 2004 and September 2010, 246 patients underwent pulmonary valve replacement for a congenital heart defect. In 112 cases (45.5%) a mechanical valve was implanted in the pulmonary position. These 112 patients were the subject of our retrospective descriptive study. All cases were followed on a predetermined regular interval in our center (2 weeks, 3 & 6 months post-operatively and then every six months). Special attention was paid to RV function and prosthetic valvular performance by trans-thoracic and/or trans-esophageal echocardiography. Statistical analyses were performed using SPSS software (version 19). All data are presented as mean values ±standard deviation (SD) or percentages. The x^2 test or the Fisher's exact test was used for the comparison of categorical variables. Student's T-test or Wilcoxon's signed rank tests were used for the comparison of parametric and non-parametric variables, respectively. Any P value of less than 0.05 was considered statistically significant.

Results: Mean age: 21.8±9.06 yrs (Range: 3.5-58 yr). They consisted of 82 (73.2%) male and 30 (26.8%) female. TF was the most common basic lesion in 89 patients (86.4%). Mean time of follow-up was 27.27±16.16 months, (Range: 6-72 months). Mean duration of ICU and hospital stay was 3.17±3.14 days & 10.12±6.13 days, respectively. A positive past history of Gore-Tex shunt was present in 21 (18.8%) and in 9 patients (8%) PVR was their first operation without prior history of any intervention. Dyspnea on exertion was the most common presenting symptom (82, 73.2%). Severe PI associated with RV-dysfunction was the most common indication for PVR. Ironically in 6 patients (5.4%), PVR was performed due to degeneration of previous biologic valve in the pulmonary position. Most patients had moderate RV dysfunction before operation (44, 39.3%).

Post op hemorrhage requiring re-exploration was noted in 8 (7.2%). Prosthetic valve malfunction was present in 12 cases (10.8%); of whom, 8 (66.6%) improved with SK infusion and did not require re-operation. Redo surgery for valve replacement was required in 4(3.6%). Freedom from re-operation at 1 yr was 100% and at the mean follow-up period (27.27 months) was 96.4%. Mean interval between PVR and malfunction was 19.84±12.11 months. Other complications were as follows: Subdural hematoma in one (0.9%), GI complications in 2 (1.8%), Pulmonary complications in 7 (6.3%), Anticoagulation related hemorrhage in 3 (2.7%), post op arrhythmia in 5 (4.5%), superficial or deep wound infection in 2 (1.8%), HIT in one (0.9%), Warfarin toxicity in 2 (1.8%) patients. There was no evidence of thrombo-embolic

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complications. No post-op renal complication was noted. Post op mortality was observed in 4 (3.6%) which included one intra-operative (0.9%) and 3 in hospital mortality (2.7%).There was no statistically significant relationship between sex and post op complications. Again there was no significant relationship between sex and age with mortality. Post op LVEF as well as post op RV function improved following PVR (P=0.033 and, P=0.004 respectively).

Conclusions: We do not confirm the bad reputation of mechanical valvular prosthesis in the pulmonary position in our center; on the contrary they perform well and potentially results in lower re-operation rate than can be expected after bio-prosthesis usage. No thrombo-embolic complications were noted. Crucial is anti-thrombotic therapy with Coumadin's, maintaining an INR of 2.5-4. Therefore mechanical valvular replacement of the pulmonary valve may be considered as an alternative to biologic valves in patients with multiple previous operations and in patients requiring anticoagulation for other reasons, especially in this young age group.

Key words: TOF: Tetralogy of Fallout, PVR: pulmonary valve replacement, SK: Streptokinase

Introduction:

With the advances in surgical techniques and peri-operative care, complete repair of Tetralogy of Fallout (TOF) is being performed earlier, and in younger age-groups [1-3], with a view to early elimination of hypoxemia and thus promotion of normal growth and organ development [2]. The early mortality of TOF repair in patients beyond infancy is low [4] and many survive to adulthood. Many of them, however, present later in life with increasing exercise intolerance and progressive right ventricular dilatation, dysfunction, or failure [5]. It has been suggested that chronic pulmonary regurgitation (PR) after complete repair of TOF together with myocardial scarring contributes to such deteriorating right ventricular performance [6], many of whom eventually underwent pulmonary valve replacement (PVR), although the timing of such an intervention is still debated. For these patients benefit from PVR may also extend to improved exercise capacity and right ventricular function [11]. Pulmonary regurgitation (PR) is encountered not only after surgical repair of TOF but also following any surgical procedure to relieve pulmonary valve stenosis with or without a trans-annular patch [7].

PR is well tolerated by most patients for many years [8]. However; the chronic effects of long-term volume overload, have deleterious consequences on the RV function. Exercise capacity decreases, and supra-ventricular and ventricular arrhythmia may even lead to sudden cardiac death [9]. An increase in pulmonary micro-vascular resistance combined with restricted RV diastolic physiology and RV dilatation, even with the onset of tricuspid regurgitation, is the most effective predictor of PR and chronically leads to RV fibrosis [10]. Most surgeons replace the pulmonary valve with a bio-prosthesis either xenograft or allograft [12-14]. However; these valvular substitutes both deteriorate over time, making (potentially multiple) reoperations necessary, each associated with morbidity and mortality [15-17]. Additionally, patients usually do not enjoy the prospect of multiple re-operations. Replacement with mechanical valvular prostheses most likely reduces the number of reoperations but has a less favorable reputation.

We offered implantation of a mechanical valvular prosthesis mainly to our adult patients, in order to minimize the expected total amount of operations. Our aim is to report the medium term results of this policy.

Materials and Methods:

Between March 2004 and September 2010, 246 patients underwent pulmonary valve replacement for a congenital heart defect in our center. In 112 cases (45.5%) a mechanical valve was implanted in the pulmonary position. These 112 patients were incorporated into study. Clinical indications for PVR included: (1) Symptomatic patients with right heart failure and moderate-to-severe dysfunction of the pulmonary valve and (2) asymptomatic patients with moderate-to-severe dysfunction of the pulmonary valve and evidence of significant RV dysfunction. In view of sex distribution, they were 82 (73.2%) male and 30 (26.8%) female. Mean age of PVR was 21.8±9.06 yrs (Range: 3.5-58 yr). TOF was the most common primary diagnosis (89, 86.4%). A positive history of Gore-Tex shunt was present in 21 (18.8%) and in 9 patients (8%), PVR was their first operation without prior history of any intervention.

Table 1 and 2 outline some pre-op characteristics of our patients.

Table 1: Mean of pre-op characteristics of patients

	Mean	Min	Max
Age at previous operation (years)	8.03±5.19	2	37
Age at PVR (years)	21.8 ±9.06	3.50	58
Time interval between 2 operations (years)	13.23±5.97	0.3	31
BSA* (m2)	1.56±0.31	0.51	2.02
LVEF (%)	50.18±10.57	30	85
Size of RVOT aneurysm (cm)	4.3±0.84	0.43	7

Table 2: Prevalence of some pre-op characteristics

	N	Percent (%)
Primary diagnosis TF Others	 89 14	 86.4 13.6
Number of sternotomy 1 2 3	 9 98 5	 8 87.5 4.4
CPB before sternotomy	7	6.2
History of Gore-Tex shunt	21	18.8

Surgical technique:

All operations were performed through a median sternotomy and subsequent cannulation of the ascending aorta and caval veins in 105 patients, in the remaining 7 patients cardiopulmonary bypass was established before redo sternotomy with cannulation of femoral artery and vein for increased safety. Aortic cross clamping was performed in all cases and heart was arrested using antegrade injection of cardioplegic solution but it is not mandatory. An incision was made into the right ventricular outflow tract (RVOT), the native pulmonary valve, if present, was resected and valve replacement performed with a mechanical valve. St. Jude Medical mechanical valve was chosen in 95 (84.8%) patients. In the remaining 17 (15.2%) Carbo-Medics mechanical valve was implanted according to the surgeon's preference. Usually about two thirds of the circumference of the prosthetic valve was sutured to the infundibular septum, at the insertion of the original pulmonary valve to allow for insertion of a prosthetic valve of adequate size. The remaining roof was constructed with a diamond shaped patch of Dacron, covering the RVOT, as well as the pulmonary trunk. For the remaining one third of the circumference the patch was sutured to the valve prosthesis. The appropriate concomitant operation was conducted based on pre-op investigations such as repair of residual VSD or relieving PA branch stenosis.

Provided there was no excessive post op bleeding, heparin infusion was commenced for all patients six hours following operation with PTT monitoring in the range of 50-70. They were on warfarin regimen, the day after surgery with the target INR of 2.5-4.

Follow-up: All cases were followed on a pre-determined regular interval in our center (2 weeks, 3 & 6 months postoperatively and then every six months). Special attention

was paid to RV function and prosthetic valve performance by trans-thoracic and/or trans-esophageal echocardiography. Mean time of follow-up was 27.27 months (Range: 6-72 months).

Statistics:

Statistical analyses were performed using SPSS software (version 19). All data are presented as mean values ±standard deviation (SD) or percentages. The x^2 test or the Fisher's exact test was used for comparison of categorical variables. Student's T-test or Wilcoxon's signed rank tests were used as appropriate for comparison of parametric and non-parametric variables, respectively. Any P-value of less than 0.05 was considered statistically significant.

Table 3: Post-op characteristic of patients

Characteristic	Mean	Min	Max
LVEF (%)	51.52±9.49	25	78
ICU stay (days)	3.17±3.14	1	21
Hospital stay (days)	10.12±6.13	1	40
Post-op bleeding (cc)	257.31±263.12	0	1800
Peak trans-valvular gradient (mmHg)	16.62±7.89	5	75
Mean tans-valvular gradient (mmHg)	8.81±4.85	2.5	45
Follow-up period (months)	27.27±16.16	6	72

Results:

Follow-up was completed in 100% of cases. Mean follow-up time was 27.27±16.16 months (Range: 6-72 months). Mean length of ICU and hospital stay was 3.17±3.14 days and 10.12±6.13 days respectively. The amount of post-op hemorrhage within first 24 hr of surgery was 257.3±263.12 cc (Range: 0-1800 cc). Table 3 shows some post-op characteristics of patients.

Isolated PVR was accomplished in 46 patients (41.1%). Repair of residual VSD was the most common concurrent operation (13, 11.6%). In 4 (3.6%) patients, coincident PVR and correction of TOF was conducted.

Dyspnea on exertion was the most common presenting symptom, (82, 73.2%). 12 (10.7%) of the patients were asymptomatic at the time of operation and discovered based on routine follow-up incidentally. Severe PI associated with RV dysfunction was the most common indication for PVR (71, 63.4%). Ironically, in 6 (5.4%) PVR was performed due to degeneration of previous biologic valve in the pulmonary position.

Most patients had moderate RV dysfunction before operation (44, 39.3%).

With respect to the size of mechanical valve, 25 was the most commonly used valve size; (57, 50.9%), followed by size 23; (38, 33.9%).

In view of post-op complications; post op hemorrhage requiring re-exploration was noted in 8 (7.2%). Prosthetic valve malfunction was present in 12 (10.8%); of whom, 8 (66.6%) improved with SK infusion and did not require re-operation. Redo surgery for valve replacement was required in 4 (3.6%). Freedom from re-operation at 1 yr was 100% and at the mean follow-up period (27.27 months) was 96.4%. Mean interval between PVR and malfunction was 19.84±12.11 months. Other complications were as follows: Subdural hematoma in one (0.9%), GI complications in 2 (1.8%), Pulmonary complications in 7 (6.3%), Anticoagulation related hemorrhage in 3 (2.7%), post op arrhythmia in 5 (4.5%), superficial or deep wound infection in 2 (1.8%), HIT in one (0.9%), Warfarin toxicity in 2 (1.8%) patients. There were no evidence of thrombo-embolic complications. No post-op renal complication was noted. Post op mortality was observed in 4 (3.6%) which included one intra operative (0.9%) and 3 in hospital mortality (2.7%).

Using statistical methods and calculation of P value, no statistically significant relationship was detected between sex and post op complications. Again there was no significant relationship between sex and age with mortality. Post op LVEF as well as post op RV function improved following PVR (P=0.033 and, P=0.004 respectively).

Discussion

Pulmonary valve replacement is performed in an increasing number of patients for pulmonary regurgitation causing right ventricular failure, mostly late after the correction of Tetralogy of Fallot [18]. These patients have right ventricular failure and often have ventricular rhythm disturbances, but can be treated easily by pulmonary valve replacement. Studies have shown that early restoration of pulmonary valve competence can result in restoration of the right ventricular function and exercise capacity, but the exact timing of such intervention remains controversial [19]. The traditional method for restoration of pulmonary valve competence is by surgical PVR using a mechanical, or bioprosthetic valve, jugular vein valved conduit, or homograft.

Pulmonary homograft has the advantage of providing low trans-valvular gradient, and good long-term outcomes without the need for anticoagulation. In many centers, however their cost and availability may prevent their use [20-21]. A mechanical prosthesis has the advantages of a low re-operation rate, but the need for long-term anticoagulation and potential thrombo-embolic complications and risk of bleeding are drawbacks. The majority of our patients had bioprosthetic PVRs. These valves are readily available and require only short-term anticoagulation.

In our center from 2004 to 2010 during 6 years, of 246 patients, PVR was performed with bioprosthesis in 134 (54.5%) and mechanical valve in the remaining 112 (45.5%) of the patients.

Despite the unfavorable reputation, we showed that mechanical pulmonary valvular replacement can be performed with promising early and mid term results. These results are not surprising from a theoretical stand point, since flow through these prostheses is essentially the same as through an aortic valvular prosthesis, although that pressures are obviously much lower [22].

Why mechanical pulmonary valve replacement has such an unfavorable status is somewhat of a mystery. Until recently there was almost no support for this strategy in the literature, on the contrary implantation of mechanical valves is advised against because of hearsay evidence of pulmonary thrombo-embolic complications [23].

Reviewing the literature reveals that most studies especially more recent ones, have emphasized on mechanical valves as an alternative to bio-prosthesis in the pulmonary position [22, 24-29].

On the other hand, if we pay attention to the studies that discourage the use of mechanical valves in the right side of the heart, it will be clarified that most of these, have performed during 1989-91 i.e. Nearly two decades ago and mainly in one country (Japan) and they lack sufficient samples and acceptable follow-up period [30-32].

Furthermore, in some studies there was no statistically significant difference between mechanical and bio-prosthesis outcomes, nonetheless, the use of mechanical valve has been discouraged relying on theoretical points [33].

We believe that there is insufficient evidence against the use of mechanical pulmonary valve prostheses, although the experimental work of kiyota et al must be taken into account. [34] This study reports in vitro experiments on leaflet closure of mechanical bi-leaflet valves in low-pressure circumstances and conclude that forces in the pulmonary system are insufficient to close both semi-discs at all times and that as a result, pulmonary regurgitation remains in this experimental setting. Although the authors advocate in vivo assessment of mechanical valves in a low-pressure system, we could not find any subsequent report on these views. On the contrary, our clinical echocardiography studies did not show any evidence of regurgitation of the mechanical valvular prosthesis, apart from the normal early diastolic jets, that also can be seen after placement of a mechanical valve in the aortic position.

The drawback of the need for anticoagulation is counterbalanced by the prospect of the likely absence of re-operations due to valve malfunction as compared to biological valvular substitutes.

The reported freedom from reoperation of allograft in the right ventricular outflow tract varies in different papers. The most favorable figures are 89% actuarial freedom from reoperation at 10 years and 80% at 20 years [35]. Other papers report 81% at 5 years and 70% at 7 years [16]. Second and third replaced allograft fare worse [15], so that the interval between reoperations becomes shorter over time. Preservation techniques of allograft and subsequent rejection-like phenomena play a role, as yet not fully elucidated [36]. Multiple re-operations are to be anticipated in this strategy, when taking the otherwise good life expectancy of these patients into account, a prospect most patients do not relish.

Xenografts can also be used in the right ventricular outflow tract, and have a reported 10 year survival of 85% [17]. Essentially, Xenografts have the same drawback as allograft do, resulting in multiple reoperations. Patients with an allograt or Xenografts therefore have an estimated risk of re-operation of 15-20% in 10 years [37]. Mean age of our patients was 21.8 years, taking into account their normal life expectancy; multiple reoperations could be expected with the use of tissue valves.

In our study of 112 patients with mechanical valvular PVR, six cases were due to degeneration of previous biologic valve within less than 5 years of their implantation. Out of the total 112 patients who underwent PVR with mechanical valve, prosthetic valve malfunction was observed in 12

(10.8%) during follow-up period with the mean interval of 27.27±16.16 months following PVR, most of whom improved with streptokinase and did not require reoperation. Reoperation was needed in 4 (3.6%) patients with the minimum interval of 14 months & maximum, 48 months,thus freedom from reoperation within one year of operation was 100% and during mean follow-up of 27.27 months was 96.4%

The risk of thrombo-embolic and bleeding complications in patients on oral anticoagulant therapy for mechanical heart valves has been thoroughly analyzed by Cannegieter et al [38]. The linear risk of cerebral emboli was 0.68 per 100 patient- years, whilst the risk of peripheral emboli was much lower at 0.03 per 100 patient years, most likely due to the lack of detection of the latter. These embolic risks must theoretical be similar for pulmonary valvular prostheses. Thus the embolic risk of a mechanical pulmonary valvular prosthesis seems to be slight. The risk of thrombosis of the valve must also be minimal when anticoagulation is adequate.

Bleeding complications, in the Cannegieter paper [37], whether intracranial or spinal, were reported to be 0.57 per 100 patient years.

It is difficult to compare these risks because of their disparate nature. In our opinion, mechanical PVR and bioprosthetic PVR probably do not differ in the incidence of complications, but do, in mode of complication. Where patients that need re-do operations risk mortality, patients that use anti-coagulant medication, suffer more from morbidity, albeit during entire lifetime. Furthermore we do realize that fatal thrombo-embolic or bleeding complications do occur occasionally. We advocate maintaining an INR of 2.5-4.

In our study of the total 112 patients who underwent PVR with mechanical valve, 4 (3.6%) mortality was noted which included 1 intra-operative (0.9%) and 3 (2.7%) during hospitalization. None of the fatalities could be attributed to the type of prosthesis used (mechanical valve).

As previously described, no statistically significant relationship was noted between sex and age of the patients with mortality.

Another important point which deserves mentioning was the significant relationship between pre & post-op myocardial performance, so that both ventricles showed improved function following operation. In the case of RV, owing to relieving PR and consequent volume overload, this is predictable, however concerning LV, it could be interpreted that RV distention due to PR leads to deviation of interventricular septum toward LV and results in decreasing LVEF, However ameliorating the distention of RV, resulted from PVR might potentially be responsible for improved post-op LVEF.

We confess to special limitations in our study. In addition to defects in medical records of patients in some instances, insufficient follow-up period could not be overlooked; so that only mid-term results (maximum 6 yrs) were evaluated. It's obvious that studies with more samples and longer follow-up are needed to investigate the long-term results of mechanical valves in the pulmonary position. Furthermore studies incorporating two groups of patients are required to compare special valve-related outcomes between commonly used bio-prostheses and mechanical valves in the RVOT position.

Conclusion

Replacement of pulmonary valve with mechanical valve prosthesis can be performed with promising early and mid-term results. The unfavorable reputation of PVR with mechanical bi-leaflet valve prosthesis must be reconsidered in the light of our findings. Our experience is in keeping with that of others, but consists of more patients and a longer follow-up. Anti-thrombotic therapy with coumadines is critical, maintaining an INR of 2.5-4. On the condition that this can be managed, fewer reoperations can be expected. Patients that fulfill with this condition can safely be offered replacement of their pulmonary valve with mechanical valve prosthesis. Complications due to anti-thrombotic therapy will occur but must be weighed against the complications of multiple re-operations. Therefore, mechanical valve replacement in the position of pulmonary valve could be considered as an alternative to bio-prostheses especially in patients with multiple prior operations or when there is another need for warfarin anticoagulation as in rhythm disturbances.

References

1. Hirsch JC, et al. Complete repair of tetralogy of fallot in the neconate: results in the modern era. Ann surg 2000; 232:508-14.
2. Derby CD, et al. Roatine primary repair of tetralogy of fallot in the neconate. Expect Rev Cardiovasc ther 2005; 3:857-63.
3. Kolcz J, et al. Neonatal repair of Thetralogy of fallot results in improved

pulmonary artery development without increased need for reintervention. Eur J Cardiothorac surg 2005; 28:394-9.
4. Ammash. NM, et al. Pulmonary regurgitation after tetralogy of fallot repair: Clincical features, sequelae, and timing of pulmonary valve replacement. Congenital Heart Dis 2007, 2:386-403.
5. Bouzas B, et al. Pulmonary regurgitation: not abenign lesion. Eur Heart J 2005; 26:433-9.
6. Graham TP Jr, et al. Right ventricular volume characteristics before and after palliative and reparative operation in tetralogy of fallot. Circulation 1976; 54:417-23.
7. Wiliams RG, et al. Repart of the National Heart, Lung and Blood institute working group on research in adult congenital heart disease. J Am Coll Cardiol 2006; 47:701-707.
8. Dave HH, et al. Early insertion of a pulmonary valve for chronic regurgitation helps restoration of ventricular dimensions. Ann thorac surg 2005; 80:1615-1620.
9. Gatzoulis MA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of fallot: a multicenter study. Lancet 2000; 356: 975-981.
10. Redington A, et al. Congenital disease in the right heart New York: Springer 2009:337.
11. Kostolny M, et al. Rescue surgery following percutaneous pulmonary valve implantation. Eur J Cardiothorac surg 2008; 33:607-12.
12. Yemets LM, et al. Pulmonary valve replacement late after repair of tetralogy of fallot. Ann thorac surg 1997; 64(2): 526-30.
13. Bonow RO, et al. Acc/AHA guidelines for the management of patients with valvular heart disease. Circulation 1998; 98:1949-84.
14. Corno AF, et al. Bovine valved xenograft in pulmonary position: medium-term follow-up with excellent hemodynamics and freedom from calcification. Ann thorac surg 2004; 78(4): 1382-8.
15. Stark J, et al. Fate of subpulmonary homograft conduits: determinants of late homograft failure. J thorac cardiovasc surg 1998; 115:506-16.
16. Forbess JM, et al. Cryopreserved homografts in the pulmonary position: determinants of durability. Ann thorac surg 2001; 71:54-60.
17. Fukada J, et al. Influence of pulmonic position on durability of bioprosthetic heart valves. Ann Thorac surg 1997;64:1678-81.
18. Kliner PJ, et al. Pulmonary regurgitation. Eur Heart J 2005; 26(5):433-9.
19. Eysken SB, et al. Homograft insertion for pulmonary regurgitation after repair of tetralogy of fallot improves cardiorespiratory exercise performance. Am J Cardiol 2000; 85:221-5.
20. Balaguer JM, et al. Orthotoic pumonic valve replacement with a pulmonary homograft as an interposition graft. J Card surg 1996;11:417-20.
21. Oosterhof T, et al. Long-term follow-up of homograft function after pulmonary valve replacement in patients with tetralogy of fallot. Eur Heart J 2006;27:1478-84.
22. Tjalling W. Waterbolk, et al. Pulmonary valve replacement with a mechanical prosthesis. Promising results of 28 procedures in patients with congenital heart disease. Eur J Cardio Thorac surg 2006; 30 (28-34).
23. Haas F, et al. Is there a role for mechanical valved conduits in the pulmonary position? Ann Thorac surg 2005; 79(5):1662-7.
24. Stulak JM, et al. The increasing use of mechanical pulmonary valve replacement over a 40-year period. Ann Thorac surg 2010; 90(6):2009-14.
25. Martinez E. et al. Chronic pulmonary insufficiency after tetralogy of fallot and pulmonary stenosis intervention. Pulmonary valve replacement with mechanical prosthesis. An pediatr (Barc) 2008; 69(3): 215-20.
26. Deorsola L, et al. Pulmonary valve replacement with mechanical prosthesis: Long term results in 4 patients. Ann Thorac surg 2010; 89(6):2036-8.
27. Dos L, et al. Long term outcome of mechanical valve prosthesis in the pulmonary position. Int J Cardiol 2010.
28. Horer J, et al. A comparative study of mechanical and homograft prosthesis in the pulmonary position. Ann Thorac Surg 2009: 88(5):1534-9.
29. Ismar ovcina, et al. Pulmonary valve replacement with mechanical prosthesis in re-do fallot patients. Interactive cardiovasc & Thorac surg 2011; 1:20-25.
30. Miyamura H, et al. Long term results of valve replacement in the right side of the heart in congenital heart disease- comparative study of bioprosthetic valve and mechanical valve. Nippon Kyoba 1990; 38(8):1298-303.
31. Kawachi Y, et al. Comparative study between St. Jude medical and bioprosthetic valves in the right side of the heart. JPn Circ J 1991; 55(6):553-62.
32. Fleming WH, et al. Valve replacement in the right side of the heart in children: Long-term follow-up. Ann Thorac surg 1989; 48(3):404-8.
33. Takunaga S, et al. Isolated pulmonary valve replacement analysis of 27 years of experience. J Artif organs 2008; 11(3):130-3.
34. Kiyota Y, et al. In vitro closing behaviour of the St. Jude medical heart valve in the pulmonary postion. Valve incompetence originating in the prosthesis itself. J Thorac Cardiovasc Surg 1992; 104:779-85.
35. Chambers JC, et al. Pulmonary antograft procedure for aortic valve disease: Long-term results of the pioneer series. Circulation 1997; 96 (7):2206-14.
36. Hoekstra FM, et al. Immunogenic human leukocyte antigen class II antigens on human cardiac valves induce specific allo antibodies. Ann thorac surg 1998; 66(6):2022-6.
37. Hazekamp MG, et al. Pulmonary valve insertion late after repair of fallot's tetralogy. Eur J Cardio-thorac surg 2001; 19:667-70.
38. Cannegieter SC, et al. Optimal oral anticoagulant therapy in patients with mechanical heart valves. N Engl J Med 1995; 333:11-17.