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Original Article

Medium-term follow-up of mechanical valves inserted in children

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Abstract *Objective:* We reviewed our experience with mechanical valves inserted between 1988 and 2002 in children aged 15 years or younger. *Methods:* Hospital files were extracted retrospectively. Follow-up was completed by March 2005. *Results:* Of 41 patients, we inserted a valve in atrioventricular position in 27 children, having a median age of 3.1 years, ranging from 0.4 to 14.5 years, and in aortic position in the remaining 14, having a median age of 13.5 years, and a range from 7.0 to 14.9 years. For the valves inserted in atrioventricular position, the underlying disease was congenital in 23, rheumatic in two, post-endocarditic in one, and Marfan's syndrome in one. Mean follow-up was 7.7 years, with standard deviation of 5.3, giving a total follow-up of 209 patient years. Mortality at 30 days was 7%, and survival was 73% at up to 16 years follow-up. Events related to anticoagulation were seen in 3 patients, corresponding to 1.4% per patient year. In 6 patients (22%), heart block ensued which required implantation of a pacemaker treatment, and 5 patients (19%) had reoperations. For the implantations in aortic position, the underlying disease was congenital in 13, stenosis in 10 and insufficiency in three, and post-endocarditis in one. Mean follow-up was 6.8 years, with standard deviation of 4.6, giving a total of 95 patient years. We lost one patient within 30 days (7.7% mortality), and survival was 77% at up to 13 years follow-up. There were no incidents of thrombosis, nor events related to anticoagulation, but one patient (7%) needed insertion of a pacemaker due to a perioperative heart block, and one (7%) required new valvar replacement. *Conclusions:* Although preferably avoided, mechanical valves can be implanted in children with an acceptable mortality and morbidity, and good long-term results.

Keywords: Mechanical prostheses; congenital heart disease; atrioventricular valve; aortic valve

Reconstructive surgery is preferred in children with severe valvar dysfunction.[1] When this treatment fails, and replacement of the valve is necessary, mechanical prostheses are generally preferred in children because of the well-recognised accelerated calcification and dysfunction of bioprostheses.[2–4] This choice is not without problems. The patients need life-long anticoagulation, and may outgrow the size of the valve. Because diseased valves are infrequently replaced in children, knowledge of the prognosis is limited. In this study, we reviewed retrospectively all patients under the age of 15 years in whom we inserted a mechanical valve between 1988 and 2002.

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Materials and methods

Population studied

Skejby Sygehus covers a population of approximately 3 millions, resulting in a yearly caseload of approximately 145 operations in children less than 15 years of age with congenital cardiac disease. Between

December 1988 and July 2002 we inserted mechanical valves in 41 of these patients. For these patients, we reviewed the hospital files from our institution and the referring centres. In 27 patients, 15 being girls, we inserted valves in atrioventricular position at a median age of 3.1 years, with a range from 0.4 to 14.5 years. The initial disease was congenital in 23, rheumatic in two, post-endocarditic in one, and Marfan's syndrome in one (Table 1). In the other 14 patients, 2 being female, we implantated valves in aortic position at a median age of 13.5 years, with a range from 7.0 to 14.9 years. The initial aortic disease was congenital in 13, due to stenosis in 10 and insufficiency in three, and post-endocarditic in the remaining patient.

Table 1. Underlying cardiac morphology.

	Number of patients
Congenital	23
AVSD	7
Primum defects	4
TGA	4
FUVH	2
MVI	2
Floppy mitral valve	2
HLHS	1
Shones syndrome	1
Rheumatic	2
Endocarditis	1
Marfan's syndrome	1
Total	27

Underlying disease for patients having an atrioventricular valvar implantation
Abbreviations: AVSD: atrioventricular septal defect; TGA: transposition of the great arteries; FUVH: functionally univentricular heart; MVI: unspecified mitral valvar insuffiency; HLHS: hypoplastic left heart syndrome

Table 2. Distribution of sizes of valvar prostheses used for atrioventricular valvar implantations. All inserted valves were St. Jude.

Size	Number
19	4
21	4
23	4
25	6
27	3
29	3
31	3

Table 3. Distribution of sizes of valvar prostheses used for aortic valvar implantations. Of the inserted valves, 11 were St. Jude, and 3 were Carbomedics, the latter all being size 23.

Size	Number
19	1
21	5
23	8

Operative data

Atrioventricular valves. A mechanical valve was inserted in mitral position in 23 patients, including eight with a leaking left-sided atrioventricular valve in the setting of an atrioventricular septal defect with common atrioventricular junction. In the other 3 patients with surgically palliated functionally univentricular hearts, one with hypoplasia of the left heart, the valve was inserted in the tricuspid position. In one patient with atrioventricular septal defect, first the left, and subsequently the right-sided atrioventricular valve was substituted. Prior surgical valvoplasty or valvotomy had been performed in 15 (56%) of the patients.

The prosthesis was placed within orifice of the native valve in all but two patients with a narrow annulus, in whom a supraannular position was chosen to accommodate a larger valve. The prostheses used were all St. Jude Medical Prostheses (St. Jude Medical Inc, St. Paul, Minneapolis, USA). The sizes are given in Table 2.

In 6 (22%) of the patients undergoing atrioventricular valvar implantation, additional surgery was needed during the same procedure, with 2 patients having 2 procedures. This included three replacements of the aortic valve, albeit that these procedures are not included in the section of our review devoted to the aortic valve, two tricuspid valvoplasties, resection of a subvalvar shelf in the left ventricle, and excision of a partition in the left atrium. In addition, one patient had correction of stenosis across a Mustard baffle.

Aortic valves. We placed mechanical aortic valves in 14 patients, 6 of these having undergone prior balloon valvoplasty. Indeed, one patient had undergone three attempts of percutaneous dilation, and two attempts at surgical valvoplasty, before the native valve was replaced. In two patients, surgical valvoplasty were attempted perioperatively, but failed. The prostheses used were 11 St. Jude valves and three Carbomedics valves (Carbomedics Inc, Austin, Texas, USA). The sizes are given in Table 3.

In two patients, the replacement was supplemented with a myectomy due to subvalvar obstruction, while an additional 2 patients had a supravalvar obstruction corrected by insertion of an aortic patch, and one had a perimembranous ventricular septal defect closed through the aortotomy. A patient with a common arterial trunk repaired as a neonate received a mechanical valve due to insufficiency of the native truncal

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Table 4. Mortality.

Patient #	Age at operation (years)	Underlying disease	Valve	Time from operation to death (days)	Cause of death
5	4.4	VSD, TGA, pulm. stenosis	MVR	65	Heart failure
10	0.8	AVSD, Downs	L-AV	107	Sepsis
15	1.1	HLHS	TVR in HLHS	69	Heart failure
18	1.8	AVSD	L- and R-AV	143	Heart failure
20	3.6	Marfan's syndrome	MVR	0	Heart failure
21	1.2	FUVH	TVR in UVH	29	Sepsis, endocarditis
14	10.3	VSD and TGA	MVR	2859	Road accident

Age at operation, underlying disease, time from operation to death and cause of death for patients with an atrioventricular valve
Abbreviations: VSD: ventricular septal defect; TGA: transposition of the great arteries; pulm.: pulmonary; AVSD: atrioventricular septal defect; HLHS: hypoplastic left heart syndrome; FUVH: functionally univentricular heart; MVR: mitral valvar replacement; L- and R-AV: left and right atrioventricular valve; TVR: tricuspid valvar replacement

valve, combined with replacement of a pulmonary homograft.

Anticoagulation

Postoperatively all patients received anticoagulation (coumarins) treatment in order to maintain an international normalised ratio within the range of 2.5 to 3.5 for the patients with a mechanical atrioventricular valve, and within 2.0 to 3.0 for the patients with a mechanical aortic valve. In 26% of those with atrioventricular valves, and 43% of those with aortic valves, oral anticoagulation was self-managed by the patients or their parents as described earlier by Christensen et al.[5] Patients were not advised to avoid physical activities.

Follow-up

The children were checked clinically and by echocardiography at intervals of 3 months to 2 years. Outgrowth in relation to valvar size was judged by the presence of clinical symptoms and supportive echocardiographic findings.

Follow-up was completed by March of 2005. The mean follow-up for the implantations in atrioventricular position was 7.7 years, with standard deviation of 5.3, giving a total of 209 patient years. The mean follow up for the aortic valves was 6.8 years, with standard deviation of 4.6, giving a total of 95 patient years. Follow up was complete for both groups. Valve-related complications were evaluated according to the guidelines reported by Edmunds et al.[6]

Statistical analysis

Data are presented as frequencies, medians with range, or mean with standard deviation, as appropriate. Survival data are presented using Kaplan-Meier curves. Stata Statistical Software (release 8.0; Stata Corporation, College Station, TX, USA) was used for the analyses.

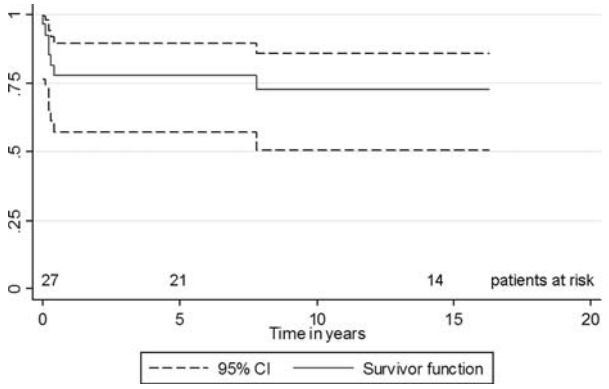

Figure 1.
Kaplan-Meier survival curves for the patients after implantations of valves in atrioventricular position. Numbers under the curve indicate patients at risk.

Results

Mortality

Among the patients with substituted atrioventricular valves, two patients died within 30 days of the operation (7.4%), and five died later (Table 4). Survival at up to 16 years follow-up was 73% (Fig. 1). The first six patients died of cardiac related causes within the first few months, while the last patient died in a road accident seven years after replacement of the valve. An autopsy confirmed that death was unrelated to the mechanical valve.

Following aortic valvar implantation, one patient attended a local hospital on the 27th postoperative day with abdominal pain, and died suddenly a few hours later. Autopsy showed 650 millilitres of clear fluid under pressure in the pericardium. Additionally, there was an embolus in the basilar artery. The international normalised ratio was 4.7 at arrival. This gives mortality at 30 days of 7.7%. Another patient died suddenly seven years after implantation while travelling in Nepal. The cause of death could not be

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determined. Survival at up to 13 years follow-up was 77% (Fig. 2).

Valvar thrombosis and events related to anticoagulation

Among the patients with atrioventricular valves, there were no morbidity caused by thrombosis of the mechanical valve, but there were three episodes of bleeding related to anticoagulation (11%; 1.4% per patient year). In one patient with a high international normalised ratio, bleeding occurred after an operation in the oral cavity, and the patient needed a transfusion. Another patient had two large cerebral bleeds in spite of adequate anticoagulation one year after the implantation. The bleeds originated from a large cerebral arteriovenous malformation, which was subsequently removed surgically. A final patient had major bleedings during her menstruation, requiring hospitalization. The problem was solved with contraceptive pills. Among those with aortic valves, there was no morbidity related to thrombosis of the valve or anticoagulation.

Perioperative heart block

In 6 of the 27 patients (22%) having atrioventricular valvar implantation, perioperative heart block necessitated insertion of a pacemaker (Table 5). Of the 14 patients having aortic valvar implantation, one patient (7%) needed a pacemaker because of perioperative heart block. This patient had a ventricular septal defect closed through the aortotomy at the same procedure as the valvar insertion.

Reoperation

Of the 27 patients undergoing atrioventricular valvar implantation, reoperations were required in five (19%), giving a freedom from reoperation at up to 16 years at 67.2% (Fig. 3). New valves were inserted in 4 patients, one due to outgrowth of the valve, one due to stenosis of the valve by pannus, one due to endocarditis of the prosthetic valve, with all three of these patients receiving a larger valve, and the final patient needing two replacements. In this patient, the mechanical valve was initially replaced with a smaller biological valve due to haemolysis, and this

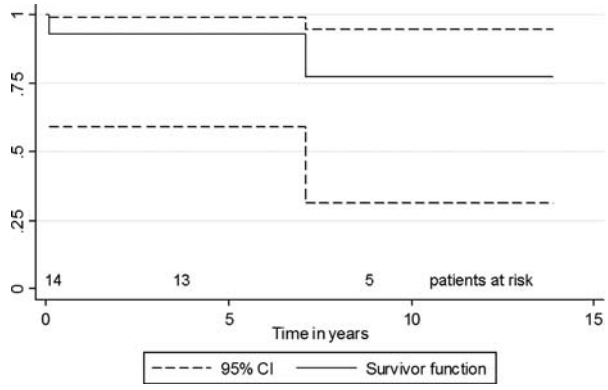

Figure 2.
Kaplan-Meier survival curves for the patients after aortic valvar implantations. Numbers under the curve indicate patients at risk.

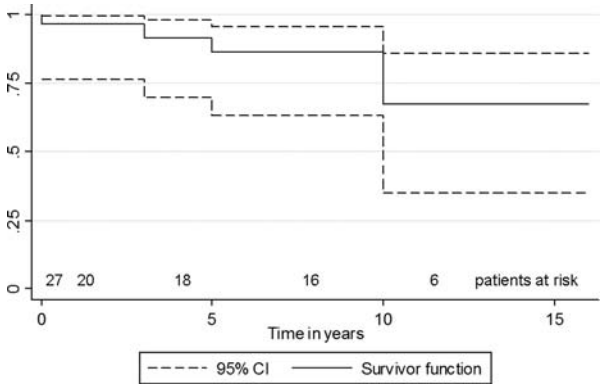

Figure 3.
Freedom from reoperation for patients having valves implanted in atrioventricular position. Numbers under the curve indicate patients at risk.

Table 5. Patients with a mechanical heart valve and subsequent pacemaker implantation.

Patient #	Underlying disease	Type of valve	Mortality
10	AVSD, Downs	Left AVVR	Yes
15	HLHS	TVR in HLHS	Yes
18	AVSD	Left and right AV	Yes
21	FUVH	TVR	Yes
23	FUVH	TVR in FUVH	No
25	AVSD, Downs	Left AV	No

Underlying disease, type of implanted valve and mortality among the pacemaker implantations in patients with a mechanical atrioventricular valve
Abbreviations: AVSD: atrioventricular septal defect; HLHS: hypoplastic left heart syndrome; FUVH: functionally univentricular heart; AVVR: atrioventricular valve; TVR: tricuspid valve

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valve was later replaced with an even smaller mechanical valve due to formation of pannus. No further haemolysis was observed. The fifth patient had excision of a subvalvar shelf in the left ventricle. All five patients survived the operations without complications.

Of the 14 patients having implantation of an aortic valve, one (7%) had a new valve inserted because of haemolysis, giving a freedom from reoperation at up to 14 years of 92.3%. During the operation, a paravalvar leak was found, so the mechanical valve was replaced with a larger biological valve, and no further haemolysis was observed.

Discussion

The major concerns regarding insertion of mechanical valves in children are the perioperative mortality, the risk of outgrowing the mechanical valve, complications related to anticoagulation, and the risk of atrioventricular block. Our study confirms that these risks do exist, but also shows that severe complications are relatively rare.

Mortality

The mortality among our children having insertion of mechanical valves in atrioventricular position resembles the findings from other studies, although our series includes more patients with functionally univentricular hearts than previously reported (Table 6). Like earlier studies, we found that implantation of mechanical valves in children was associated with a high early risk of death, followed by a late phase with low risk, despite the need for subsequent valvar replacement and chronic anticoagulation.[7] Furthermore, the patients who died of cardiac-related causes were under five years of age, and the majority had complex congenital heart defects.

This is somewhat in contrast to the mortality after aortic valvar implantation. The two patients died suddenly, and did not have complex congenital heart defects. In one, death occurred 27 days after operation, due to cardiac tamponade. The described embolus in the basilar artery was not consistent with the high international normalised ratio, and had no clinical correlate. The other patient died while travelling in Nepal seven years after the operation. Since autopsy was not performed, the cause of death was not determined. The low number of children with replaced aortic valves in our population makes it difficult to generalize, however our results still resemble those published by others (Table 6).

Valvar thrombosis and events related to anticoagulation

Another major concern of implanting mechanical valves in children is related to the need of life-long

Table 6. The mortality reported in the literature.

Study	Valve	N	Age at VR (mean ± SD)	Follow-up (years ± SD)	Survival (%)						
					Op.	Hosp.	30 days	5 years	10 years	15 years	20 years
Alexiou[2]	MVR	44	6.8 ± 4.7	6.4 ± 4.8	86			81 ± 6 (1)	78 ± 7 (1)		
Caldarone[7]	MVR	139	1.9 ± 1.4	6.2 (2)			82	75	74		
van Doorn[10]	MVR	54	3.3 (2)	4.1 (2)			79.7	68 (3)	68 (3)		
Günther[3]	MVR	35	1.9 ± 1.7	4.2 ± 4.7		82.9					51.2 ± 13.3
Kojori[16]	MVR	104	7.4 (2)				84	70		62	
Masuda[15]	MVR	32	10.3	6.8 ± 4.8	100					63 ± 19	
Yoshimura[14]	MVR	56	5.7 ± 5.0	7.7		100			90.3		
Ibrahim[17]	MVR, TVR, AVR	20	10.3	5.3 ± 0.78		95		95 ± 5 (4)			
Lubiszewska[18]	AVVR, AVR	44	8.9 ± 3.9	6.8 ± 3.5	100	100				93.4	
Alexiou[12]	AVR	56	11.2	7.3	94.7				91		84.9
Champsaur[11]	AVR	54	12.8 ± 4	4.8 (5)			87	84.5 ± 0.61	70.2 ± 0.91		
Lupinetti[13]	AVR	50	12.1 ± 4.6	5.4	90			83 (6)	79		
Mazzitelli[4]	AVR	30	11.6	6.6		100					90 (7)

Abbreviations: MVR: mitral valvar replacement; AVR: aortic valvar replacement; TVR: tricuspid valvar replacement; AVVR: atrioventricular valvar replacement; N: number of patients having mechanical valve replacement; VR: valve replacement; Op.: operative survival; Hosp.: hospital survival
(1) overall survival; (2) median; (3) including 30 day mortality and transplantation; (4) survival at six years; (5) 261 patient years; (6) survival at four years; (7) max follow-up 21.6 years

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anticoagulation to prevent thromboembolism, but at the same time to avoid bleeding events. This can at times be a difficult balance, especially in children due to lack of compliance in puberty.[8,9] We found complete freedom from thromboembolic events, and 88% freedom from bleeding at up to 16 years following implantation of valves in atrioventricular position. The absence of thromboembolism, and the low rate of bleedings, are encouraging since previous studies reported higher rates, with freedom from bleeding at 10 years varying between 65% and 90%.[2,3,10] Furthermore, the bleedings that occurred in our study were minor in two, and associated with a cerebral vascular malformation in one. Although there is still a substantial risk related to implantation of mechanical valves, the outcome seems to have improved in the current era. This is also encouraging taking into account that these patients have not been restrained from normal physical activities. The reason might be better control of anticoagulation.

Among patients having replacement of an aortic valve, there were no clinically relevant thromboembolic or bleeding events that resembled the findings reported in other studies.[4,11–13]

Perioperative heart block

Of the patients requiring insertion of a permanent pacemaker, 4 had complex heart defects. Of these, one had an atrioventricular septal defect where both the left- and the right-sided atrioventricular valves were replaced, and three had functionally univentricular hearts. Thus, it seems as if atrioventricular valvar replacement in the setting of a functionally univentricular heart carries a high risk of block. Of these patients, three died within a few months after surgery, indicating the severity of their disease.

Reoperation

Freedom from reoperation in our study was in accordance with previously reported series.[4,7,12] Of our four patients having second replacements, one was due to outgrowth, which is a relatively low frequency compared with results reported by others.[2,3,10,14,15] Furthermore, in accordance with other studies,[7,10,14] we found that the second replacement could be performed with a low mortality and morbidity.

The low rate of second replacements in patients having diseased aortic valves could be due to a slightly older age at the initial operation, thereby making it possible to place a larger valve. This older age at first operation could reflect that we perform balloon valvoplasty as primary treatment for congenital aortic valvar stenosis.

Limitations

Our study has some inherent limitations in being retrospective, with the potential of reporting error and bias during the collection of the date. Furthermore, the limited number of patients, combined with diverse diagnoses, makes it difficult to compare our population with those of other published studies.

Conclusion

Implantation of mechanical valves in the left atrioventricular and aortic positions can be performed with acceptable mortality, low occurrence of adverse events, and good long-term results. Our data suggests, nonetheless, that substitution of valves in children with functionally univentricular hearts carries an increased risk of need for implantation of pacemakers and death.

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References

1. Chauvaud S, Fuzellier JF, Houel R, Berrebi A, Mihaileanu S, Carpentier A. Reconstructive surgery in congenital mitral valve insufficiency (Carpentier's techniques): long-term results. J Thorac Cardiovasc Surg 1998; 115: 84–92.
2. Alexiou C, Galogavrou M, Chen Q, et al. Mitral valve replacement with mechanical prostheses in children: improved operative risk and survival. Eur J Cardiothorac Surg 2001; 20: 105–113.
3. Gunther T, Mazzitelli D, Schreiber C, et al. Mitral-valve replacement in children under 6 years of age. Eur J Cardiothorac Surg 2000; 17: 426–430.
4. Mazzitelli D, Guenther T, Schreiber C, Wottke M, Michel J, Meisner H. Aortic valve replacement in children: are we on the right track? Eur J Cardiothorac Surg 1998; 13: 565–571.
5. Christensen TD, Andersen NT, Maegaard M, Hansen OK, Hjortdal VE, Hasenkam JM. Oral anticoagulation therapy in children: successfully controlled by self-management. Heart Surg Forum 2004; 7: E321–E325.
6. Edmunds LH, Jr., Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. The American Association for Thoracic Surgery, Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity. Ann Thorac Surg 1996; 62: 932–935.
7. Caldarone CA, Raghuveer G, Hills CB, et al. Long-term survival after mitral valve replacement in children aged <5 years: a multi-institutional study. Circulation 2001; 104: I143–I147.
8. Stewart S, Cianciotta D, Alexson C, Manning J. The long-term risk of warfarin sodium therapy and the incidence of thromboembolism in children after prosthetic cardiac valve replacement. J Thorac Cardiovasc Surg 1987; 93: 551–554.
9. Buck ML. Anticoagulation with warfarin in infants and children. Ann Pharmacother 1996; 30: 1316–1322.

10. van Doorn C, Yates R, Tsang V, deLeval M, Elliott M. Mitral valve replacement in children: mortality, morbidity, and haemodynamic status up to medium term follow up. Heart 2000; 84: 636–642.
11. Champsaur G, Robin J, Tronc F, et al. Mechanical valve in aortic position is a valid option in children and adolescents. Eur J Cardiothorac Surg 1997; 11: 117–122.
12. Alexiou C, McDonald A, Langley SM, Dalrymple-Hay MJ, Haw MP, Monro JL. Aortic valve replacement in children: are mechanical prostheses a good option? Eur J Cardiothorac Surg 2000; 17: 125–133.
13. Lupinetti FM, Duncan BW, Scifres AM, et al. Intermediate-term results in pediatric aortic valve replacement. Ann Thorac Surg 1999; 68: 521–525.
14. Yoshimura N, Yamaguchi M, Oshima Y, et al. Surgery for mitral valve disease in the pediatric age group. J Thorac Cardiovasc Surg 1999; 118: 99–106.
15. Masuda M, Kado H, Tatewaki H, Shiokawa Y, Yasui H. Late results after mitral valve replacement with bileaflet mechanical prosthesis in children: evaluation of prosthesis-patient mismatch. Ann Thorac Surg 2004; 77: 913–917.
16. Kojori F, Chen R, Caldarone CA, et al. Outcomes of mitral valve replacement in children: a competing-risks analysis. J Thorac Cardiovasc Surg 2004; 128: 703–709.
17. Ibrahim M, Cleland J, O'Kane H, Gladstone D, Mullholland C, Craig B. St. Jude Medical prosthesis in children. J Thorac Cardiovasc Surg 1994; 108: 52–66.
18. Lubiszewska B, Rozanski J, Szufladowicz M, et al. Mechanical valve replacement in congenital heart disease in children. J Heart Valve Dis 1999; 8: 74–79.