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CLINICAL RESEARCH

The Ross Procedure in Patients among the Pediatric Population, Post Ten Years of Experience

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Abstract

The aim of the study was to analyze the results of the surgical treatment in pediatric patients who had undergone the Ross procedure.

Material and Methods: The study involved 114 patients between 12 days to 18 years in age. The early and late (up to 5 years) results of the treatment were studied. The examination included echocardiography, catheterization of the cardiac chambers and angiocardiography. The case distribution of patients based on diagnosis was as follows: isolated aortic valve stenosis (IAVS) in 38 (33.3%) patients, aortic valve insufficiency (AVI) in 33 (28.9%), and combined heart defects in 56 patients (49.1%).

Results: The death rate was 6.14% during the early postoperative period and 1.14% in the late postoperative period; the actuarial survival in the long-term was 98.86%. The complication rate was 51.5%. The most frequent complication was pericarditis (25.6%), whereas cardiac and respiratory failure occurred in 7.6% of the cases and cardiac arrhythmias in 6.1% of the cases. The average time spent in the intensive care unit was 3.48±2.90 days; the hospitalization period on average was 24.70±10.87 days. After surgery, there was a tendency of the echocardiographic parameters to move toward normalization. The frequency of reoperation in the late period was 23.7%, the main reason for which being the conduit dysfunction in the position of the pulmonary artery (PA).

Conclusion: The clinical efficacy of the Ross procedure in the treatment of aortic valve malformations in the pediatric group was confirmed. However, in some cases, the need to perform repeated operations due to the increase in the ring size and an increase in the neo-aortic insufficiency during the somatic growth process.

Keywords*: pediatric patients, heart defects, Ross procedure, homograft/xenograft.*

Introduction

Among all the valvular heart diseases, aortic valve disease occurred 30-35% of the time; the aortic root pathology of congenital and acquired etiology was identified in 3-18% of all heart diseases. On average, three-quarters of the patients needed re-intervention within 6 years post aortic valve surgery; the frequency of long-term mortality was between 5 and 8.3%. According to several authors, the in-hospital mortality post aortic valve surgery ranged from one to 15%, with an average of 7% [1,2].

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Several authors support pulmonary valve autotransplantation and reconstructive surgery, especially for pediatric patients. This is due, mostly because of the possibility of heart growth without prejudice for hemodynamics, the absence of valve-dependent complications during valve replacement and the non-requirement of anticoagulants, thus avoiding complications related to them [3].

Is the Ross operation a treatment procedure or a temporizing action? This issue is currently being avidly discussed. Some authors consider the Ross procedure the "gold standard" to treat pediatric patients with aortic valve malformations [4,5]. However, there are conflicting opinions. Other authors believe that such an intervention translates the one-valvular malformation in a two-valve malformation, which leads to the development of right ventricular hypertrophy and its diastolic dysfunction [6].

The lack of conventional concepts regarding certain technical features of the Ross procedure should be noted: the

permissibility of size mismatch between the fibrous rings of the aortic valve and PA; reliable techniques to ensure the prevention of injuries and deformities of the coronary arteries; the selection criteria for the size of the valve conduit for the reconstruction of the right ventricular outflow tract (RVOT). In addition, a comparative analysis of the clinical efficacy of different types of grafts is mandatory. A comprehensive assessment of the long-term outcomes of the Ross procedure allows for optimization of the surgical approaches in the treatment of aortic valve disease in the pediatric patient group.

The aim of the study was to study the Ross procedure from a 10-year experience perspective at the Center for Pediatric Cardiac Surgery and Neonatal Surgery of the Academician E.N.Meshalkin NRICP.

Material and Methods

The short- and long-term results of the Ross procedure were analyzed using the data from 114 pediatric patients from the Center, between 2002 and 2012. The patients ranged from 12 days to 18 years in age. The age distribution was as follows: 3 (2.6%) patients between 12 days and 1 year, 18 (15.8%) patients between 1 and 7 years, 72 (63.2%) patients between 7 and 16 years, 21 (18.4%) patients between 16 and 18 years. The average body weight of the patients operated upon was 39.17±17.93 kg (between 2.9 and 87 kg).

The distribution of patients operated based on diagnosis was as follows: IAVS in 38 (33.3%) patients; AVI in 33 (28.9%) patients; combined heart defects in 56 (49.1%) patients.

The following types of conduits were used to replace the valve in the pulmonary position: pulmonary allograft (homograft) in 24 (21.1%) cases and xenografts in 90 (78.9%) cases. The xenografts used included, "Kemerovo AV composite" (diepoxy-treated xenoconduit) in 40 (44.4%) cases, "BioLAB" (glutaraldehyde-treated xenoconduit) in 17 (18.9%) cases, and "Contegra" in 12 (33.3%) cases. The average diameter of the conduit implanted in the pulmonary position was 23.54 mm.

The total aortic root replacement by the pulmonary autograft with re-implantation of the coronary arteries in the wall of the pulmonary autograft by type «total root replacement» was performed in 105 (88.2%) patients. The subcoronary insertion technique was applied in 14 (15.9%) cases.

We used hypothermic extracorporeal circulation (the average temperature during aortic occlusion was 28.43±3.8°C) and Custodiol cardioplegia with external cooling of the heart with crushed ice. The extracorporeal circulation time lasted from 144 to 730 (244.2±42.7) minutes, whereas the time of the aortic occlusion ranged from 90 to 282 (172.2±42.7) minutes.

Prior to treatment, we conducted a comprehensive survey of the patients. The examination included echocardiography (on the HP Vivid 7 with transthoracic and transesophageal probes; "General Electric", USA), catheterization of the cardiac chambers, angiocardiography and selective aorto-coronary angiography. The angiographic study was performed with mono- and biplane "Advantex" manufactured by "General Electric". On catheterization, the pressure in the cardiac chambers and magistral vessels was determined and the pressure gradients recorded.

The postoperative course was evaluated in terms of mortality and complication rates. In the long-term, we analyzed the frequency of the re-operations and the dynamics of the echocardiographic parameters.

Statistical analysis was performed using the statistical software Statistica 7.0 for Windows. We used the chi-square test with the Yates' correction to compare the frequency of the binary trait in two unrelated groups of paired comparisons. For data with normal distribution, inter-group comparisons were performed using Student's t-test. The Mann-Whitney (U Test) was used to compare the differences between the two independent groups (for non-parametric data). The value of P less than 0.05 was considered significant.

Results

The death rate was 6.14% during the early postoperative period and 1.14% in the late postoperative period; the actuarial survival in the long-term was 98.86%. The complication rate was 51.5%. The most frequent complication was pericarditis (25.6%), whereas cardiac and respiratory failure occurred in 7.6% of the cases and cardiac arrhythmias in 6.1% of the cases. The average time spent in the intensive care unit was 3.48±2.90 days; the hospitalization period on average was 24.70±10.87 days.

The dynamics of the echocardiographic parameters based on the type of heart defect is presented in Tables 1 and 2. After surgery, the tendency of the left ventricle to increase in contractility in all the groups at 1.2-2.2% was identified.

Table 1.

Baseline echocardiographic parameters of patients

Parameters	Groups of patients		
	AVS (n=38)	**AVI** (n=33)	**CHD** (n=56)
LVEF, %	66.7±6.2	62.3±4.9	65.8±5.4
LVEDDI, cm/m^2	3.6±1.1	5.3±1.2	4.2±1.2
LVESDI, cm/m^2	2.06±0.58	3.41±0.82	2.48±0.69
LVEDVI, ml/m^2	60.5±27.9	124.8±33.7	86.5±29.9
LVESVI, ml/m^2	16.6±4.5	49.8±15.5	25.8±7.86
LVSVI, ml/m^2	40.3±17.0	73.7±20.9	54.6±20.1
LVMMI, g/m^2	225.4±81.9	198.6±20.8	206.5±38.6
Systolic transaortic ΔP, mm Hg	96.8±17.3	-	58.6±14.2
Degree of aortic regurgitation/ number of patients	-	II-III/20 III/13	II/40 II-III/16

*Abbreviations: **AVS**, aortic valve stenosis; **AVI**, aortic valve insufficiency; **CHD,** combined heart defects.*

Also, a significant decrease in the indices of the LVEDV (left ventricualar end-diastolic volume) (by 27.31%, 31.07%, and 29%) and the LVESV (left ventricualar end-systolic volume) (by 26.29%, 29.14%, and 27.32 %) were found relative to the initial values for the groups of patients with IAVS, AVI, and combined heart defects, respectively. The tendency for the decrease in the LVMMI (left ventricular myocardial mass index) was noted at the time of discharge from hospital in all the patient groups (Table 2).

The value of the systolic pressure gradient across the implanted autograft valve was noted to be lower in those patients with an initial AVI compared with the corresponding value in patients with AVS.

Table 2.

Echocardiographic parameters in patients after the Ross procedure

Parameters	Groups of patients		
	AVS (n=36)	AVI (n=32)	CHD (n=52)
LVEF, %	69.2±8.2	63.3±6.4	66.7±6.2
LVEDDI, cm/m^2	3.2±0.6	5.6±0.9	3.6±1.1
LVESDI, cm/m^2	1.91±0.42	3.11±1.02	2.06±0.58
LVEDVI, ml/m^2	44.3±12.8	86.1±16.1	60.5±27.9
LVESVI, ml/m^2	12.3±3.7	35.2±20.3	16.6±4.5
LVSVI, ml/m^2	32.8±10.8	50.7±7.9	40.3±17.0
LVMMI, g/m^2	210.5±76.5	185.3±24.6	198.6±20.8
Systolic transaortic ΔP, mm Hg	13.4±4.3	6.6±3.4	11.7±3.6

Abbreviations as in Table 1.

The study of the uniqueness of the long-term period post surgery showed that the frequency of the repeated operations was at 23.7%, where conduit dysfunction in the PA position was the primary cause. The average peak gradient at the time of reoperation was 62.8±17.02 mmHg.

The PTCA with stenting of the left main coronary artery due to stenosis of the main *trunk* of the left coronary artery was performed in two cases (1.76%). No autograft dysfunctions requiring reoperation during the period of observation were noted.

Conduit dysfunction in right-sided positions occurred due to the following reasons: calcification of the valve in 12 (52%) cases, calcification of the conduit walls with stenosis development in 7 (30%) cases, and calcification of the distal anastomosis in 4 (17%) cases.

Table 3 reveals the conduits, which required replacement. As shown, the conduit "Kemerovo AV", with the maximum diameter, was replaced most often (in 52% of cases). At the same time, the period prior to the replacement for this graft was higher than for the others. This indicator showed a minimal value for "Contegra", although only one case of replacement was recorded for this conduit. Conduit "BioLAB" required replacement more often, in 43% of the cases.

Table 3.

Conduit characteristics

Type of conduit	Number (abs, %)	Diameter (mm)	Period prior to the replacement (y)
Kemerovo AV	12 (52.0)	24.6±1.2	4.08±1.3 (1; 6)
BioLAB	10 (43.0)	24.0±2.9	3.2±2.0 (1; 6)
Contegra	1 (5.0)	20.0	2.0

Evaluation of the increasing graft root diameter and the degree of its impact on aortic regurgitation revealed that children who underwent the Ross procedure, had the age-appropriate size of the neo-aortic root. Increasing the size of the ring was also consistent with the somatic growth of the children surveyed. Increasing the size of the ring also matched with the somatic growth of the children surveyed. Increasing the diameter of the sinus and the sino-tubular junction slightly outpaced the somatic growth during the observation period. As evident from Table 4, the average compliance coefficient between the fibrous rings of the aortic valve and the pulmonary autograft was 1.19±0.10 in 1-2 years; later, it increased to 1.28±0.14 in 3-4 years post surgery; and after 5 years or more, the index value was 1.32±0.18.

Table 4.

Hemodynamic parameters in the long-term period after surgery

Parameters	Period after surgery		
	1-2 years	3-4 years	≥5 years
Degree of aortic regurgitation	0	0	0.50
Gradient LV/Ao	6.1±1.2	6.3±1.3	8.5±2.5
Z score Ao valve	1.19±0.10	1.28±0.14	1.32±0.18

Estimation of the patients over a long-term period, based on the type of the heart defect, showed that the left ventricle parameters changed in accordance with the somatic growth during the first 5 years in all the groups; however, further, the intensity of the changes began to reduce in patients with the initial AVI.

The study of the dynamics of the right ventricle (RV)/PA gradient in the long-term period post the Ross procedure showed that, in some cases, an increase in this indicator was observed after 3 or more years after surgery. As seen from Table 5, this tendency is most marked for conduit "Kemerovo AV". Such an increase was observed to a lesser extent for the other xenografts. For the "Contegra" and "BioLAB", a more pronounced increase in this parameter was observed after 5 or more years, post surgery. In the case of the allografts, the increase in this parameter was observed after an increase in the RV/LA gradient (on average 3 years after the Ross procedure), following which, it decreased again.

Table 5.

Dynamics of RV/PA gradient (mm Hg) after the Ross procedure

Period after surgery, (y)	Type of conduit			
	Kemerovo AV (n=12)	BioLAB (n=7)	Contegra (n=8)	Pulmonary allograft (n=7)
1	23.6±9.5	28.8±15.3	20.6±6.5	17.1±4.7
3	35.1±14.7	31.5±16.0	20.0±1.4	25.8±8.5
≥5	51.9±20.4	31.9±9.0	36.8±4.2	27.5±3.7

Discussion

Studies over the recent decades have confirmed the importance of the Ross Procedure as one of the most appropriate options for aortic valve replacement (AVR) in children, younger and older age groups. Thus, the study of Hörer J. et al. [7] showed that the mortality rate in this group was 2.6% (for a 6.1 year follow-up), whereas 5 - and 10-year survival rates were 93.9% and 90.4%, respectively. Seven patients required re-intervention (explantation - 7 and reconstruction -1). The 5- and 10-year freedom from graft re-intervention was 99.3% and 95.5%,

respectively.

The death rate was 6.14% during the early postoperative period and 1.14% in the late postoperative period; the actuarial survival in the long-term was 98.86%. The complication rate was 51.5%. The most common complication encountered was pericarditis (25.6%), which was typical for the 8- to 12-year age group; for the 1- to 7-year age group and 12- to 18-year age group this complication was noted significantly less often; for age group below 1 year, this complication was not observed. At the same time, cardiac and respiratory failure, the frequency of which reached to 7.6%, was typical for the younger age group (between 0 and 2 years). In the same group, however, the frequency of the cardiac arrhythmias was 6.1%.

The results of this study are consistent with those authors who contend that the Ross procedure is the best option for children requiring AVR. We demonstrated the clinical efficacy of the Ross procedure in the treatment of aortic valve defects both in the early and late postoperative periods. Patients in the early postoperative period revealed a reduction in the left ventricular cavity, an increase in the contractility of the left ventricle, a reduction in the stroke volume of the left ventricle, a reduction of the systolic pressure gradient between the left ventricle and the ascending aorta, the absence of hemodynamically significant systolic gradients of pressure and the degrees of regurgitation across the implanted valves in the left and right positions. However, clinical experience has revealed that implementation of the reoperation is inevitable due to the increase in the ring size and the increase in the neo-aortic insufficiency during the somatic growth process.

According to our data, the frequency of the reoperation was 23.7%, the main reason for this being conduit dysfunction in the position of the PA.

Currently, researchers believe that the autograft dysfunctions, which may require graft replacement in the early postoperative period or re-operation after 6 months, are rare in clinical centers experienced in this procedure. According to the International Registry of Ross procedure, the frequency of such complications is less than 1% of all the cases [8]. In our study, these autograft dysfunctions were not observed.

The pulmonary autograft is recognized as the best long-term option of AVR [9]. According to the data presented in the International Register of the Ross procedure, the frequency of the autograft decompensation with its replacement within one year after surgery is 2.5%. The actuarial graft survival for 19 years is 48% [10].

The research conducted among patients of younger and older age groups who underwent echocardiography after the Ross procedure was consistent with the finding that the progressive extension of the neo-aortic root was not proportional to the somatic growth of the patients [11]. Researchers emphasized the expansion of the neo-aortic root because of the Ross procedure, in which there was a progression of the aortic regurgitation, which was more pronounced at the geometric mismatch of the aortic and pulmonary roots [12]. At the same time, the results of this study showed no tendency to the passive dilatation of the pulmonary autograft valve ring and the development of aortic insufficiency in the long-term period after intervention in pediatric patients.

Recent data indicate that the replacement of the homograft was usually necessary during the patient's lifetime. The factors contributing to the development of the homograft dysfunction include: use of the aortic homograft; its small size; recipient age below 10 years; the time of homograft storage; blood type mismatch and the development of immune-mediated reactions [3,11].

Estimating the increase in the diameter of the graft root and the degree of its impact on aortic regurgitation, Hörer J. et al. [7] found that the size of the neo-aortic root was more enlarged in the children who underwent the Ross procedure than in healthy children. The increase in the ring size was shown to correspond to the somatic growth of the children surveyed. At the same time, the increase in the diameter of the sinus and the sino-tubular junctions were significantly higher, relative to the degree of somatic growth which, perhaps, explains the development of the aortic regurgitation [7].

The results of this study concur with the data of other authors [13,14] and confirm that the Ross procedure has several advantages, in particular, it ensures normalization of the hemodynamic flow and the growth potential for the autograft in proportion to the somatic growth of the child. The Ross procedure has favorable long-term results, in particular, the length of the lifetime and the minimal frequency of embolic complications. Repeated operations on the RVOTO for the homograft replacement are rarely done and accompanied by a low operative risk. The definite advantages of the Ross procedure, despite some limitations, make it a main priority intervention for AVR in children.

Further studies are warranted to assess the risk factors for death and complications from the Ross procedure; it is essential to identify the predictors of the complications during the surgery and in the short-term postoperative period. The results of these studies will contribute greatly to the optimization of patient selection, the treatment tactics and postoperative management of the patients who had undergone the Ross procedure.

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