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RE-INTERVENTIONS AFTER THE ROSS PROCEDURE: REASONS, TECHNICAL APPROACHES, IMMEDIATE OUTCOMES

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Re-interventions after pulmonary autograft aortic valve replacement (Ross procedure) may be associated with dysfunction of the neoaortic, neopulmonary, or both operated valves. Late dysfunction, other than infective endocarditis, is associated with underlying conditions, technical errors, and unsuitable pulmonary trunk replacement materials. Re-interventions are technically complex, while tactical approaches have not been definitively formulated. **Objective:** to analyze re-interventions in patients after Ross procedure, technical approaches and immediate outcomes. **Material and methods.** Between 2001 and 2019, 14 patients were reoperated upon within 2 days to 21 years after primary Ross procedure. Early prosthetic endocarditis (2) and technical errors (1) were the reasons for early postoperative re-intervention. Neoaortic valve insufficiency (7), including pulmonary valve dysfunction (2), pulmonary valve degeneration (2), pulmonary prosthetic valve endocarditis (1), aortic, pulmonary and mitral valve endocarditis (1) were the reasons for late postoperative re-intervention. Based on the lesion volume, neoaortic valve replacement (3), neoaortic root replacement (6), including pulmonary valve/trunk replacement (8), and pulmonary trunk stenting (2) were performed. **Results.** In-hospital mortality was 7.1%. One patient died of early endocarditis after primary procedure. The postoperative period for the remaining patients was uneventful. Microscopic examination of the neoaorta revealed fragmentation of elastic fibers and rearrangement of tissue histoarchitectonics. In the pulmonary position, the aortic allograft and stentless xenograft had severe calcification and valve stenosis. **Conclusions.** Neoaortic valve insufficiency associated with cusp prolapse and neoaortic root dilatation may be the reasons for re-interventions after the Ross procedure. The second reason for re-interventions is valve graft dysfunction in the pulmonary trunk position. Elective reoperations on the neoaortic root and/or lung graft, despite the large volume, can be performed with low mortality and morbidity. Aortic allografts and xenografts for reconstruction of the right ventricular outflow tract (RVOT) is unjustified due to early and more severe dysfunction compared to pulmonary allograft.

Keywords: Ross procedure, autograft, allograft, aortic valve, reoperation.

INTRODUCTION

When replacing the aortic valve (AV) in young patients, surgeons are faced with the challenge of choosing a prosthesis. Biological prostheses have limited durability; mechanical prostheses seriously change the patient's lifestyle, binding him/her to lifelong anticoagulant therapy, which, in a number of patients, does not prevent thromboembolic and hemorrhagic complications [1–5]. In addition, in children with small-diameter implanted prosthesis, a "prosthesis–patient" mismatch develops over time, with the formation of high transvalvular gradients and the need for reimplantation of a larger valve [6]. An alternative to mechanical prosthesis is the aortic valve prosthesis with a pulmonary autograft (Ross procedure). Pulmonary autograft provides long-term stability of outcomes, low probability of dysfunction and reintervention, excellent hemodynamic parameters even with a narrow fibrous ring (FR) and high quality of life for patients; it does not require anticoagulants, is able to grow as the body grows, which is important for children [7, 9]. The restrain among surgeons towards Ross procedure is due to the more complicated implantation technique, as well as a possible need for reintervention for neo-aortic valve dysfunction and/or right ventricular outflow tract (RVOT) prostheses.

MATERIALS AND METHODS

The Department of Emergency Surgery for Acquired Heart Diseases, Bakulev National Medical Research Center for Cardiovascular Surgery performed 80 Ross procedures from November 2001 to March 2019. During this period, 14 repeated interventions were performed again after the Ross procedure. Eight patients had been primarily operated on at other institutions and 6 in our series of 80 operations (7.5%). Of those reoperated, there were 11 men, mean age was 22.5 years (8–47). From medical history and extracts from previous medical records, the main cause of primary surgery was congenital bicuspid aortic valve – 13, including active infective endocarditis (IE) of the AV in 3 patients. By lesion morphology, most patients (13) initially had aortic insufficiency

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(AI), while 1 patient had isolated aortic stenosis (AoS). In 13 cases, a pulmonary autograph was implanted using the free root technique with reimplantation of the coronary artery ostia, while in 1 patient, it was done using the subcoronary technique. A cryopreserved pulmonary allograft was used to restore the integrity of the RVOT in 8 patients, aortic allograft in 3 cases and stentless xenograft in 3 patients (2 xenoaortic, 1 – xenopericardial). The mean time from primary surgery to re-surgery for all reasons was 8 ± 1.9 years (Table 1).

Table 1

Clinical characteristics of patients during the first surgery

Age at first operation (years)	22.5 ± 4 (8–47)
≤18 years	8
Gender	
Men	11 (79%)
Women	3 (21%)
Hemodynamic changes in the AV during the first operation	
Stenosis	1
Insufficiency	13
Etiology of AV disorder at the first operation	
Bicuspid AV / tricuspid AV	13/1
Infective AV endocarditis, primary	1
Infective AV endocarditis, secondary	2
RVOT prosthesis	
Lung allograft	8
Aortic allograft	3
Stentless xenograft	3
Autograft implantation technique	
Subcoronary technique	1 (7%)
Free root	13 (93%)

In preparation for surgery, all patients underwent a comprehensive examination, including echocardiography, contrast-enhanced multislice CT (MSCT), and three-dimensional reconstruction of the heart and blood vessels. The diameter of the aorta, pulmonary conduit at different levels, anastomotic zones, the degree of adherence of heart structures to the sternum were determined, which allowed to plan surgical support and safe access. All patients over 40 years of age underwent coronary angiography.

Reintervention technique

12 operations were performed under complete sternotomy, hypothermic (26–28 °C) cardiopulmonary bypass and pharmaco-cold cardioplegia. Central cannulation of the aorta and both vena cavae was used in 10 patients. In two cases, we first cannulated and initiated cardiopulmonary bypass through the femoral vessels, then the arterial cannula was moved into the ascending aorta. Right heart cardiolysis was performed, the aorta and pulmonary trunk were isolated. A conventional technique was used to replace the aortic and pulmonary valves. For aortic root replacement, the pulmonary autograft wall was dissected up to the annulus fibrosus with mobilization of the coronary artery (CA) ostia. A dacron conduit with a mechanical prosthesis and direct implantation of the CA ostia into the conduit wall was used. In the case of pulmonary valve IE and/or pulmonary trunk calcification, the latter was completely excised, and a valve-containing conduit (dacron with mechanical prosthesis or pulmonary allograft) was implanted.

Endovascular intervention for the correction of degenerative pulmonary artery (PA) conduit stenosis in two patients was performed in the X-ray operating room and consisted of PA trunk stenting.

Reasons for re-interventions in the early postoperative period

Three re-interventions were performed in the early postoperative period. One patient showed signs of myocardial ischemia on ECG on day 2 after the primary operation. Coronary angiography revealed left coronary artery (LCA) torsion in the area of implantation into the autograft. On emergency re-intervention, the anastomosis was dissolved and re-applied, and coronary artery bypass grafting of the anterior interventricular branch was performed preventively. The second patient had prolonged fever in the early postoperative period without the effect of antibiotic therapy. EchoCG revealed vegetations on the pulmonary allograft. The patient underwent a pulmonary allograft replacement but died from intractable systemic infection and erosive bleeding from the aortic wall. In the third patient, who was operated on in the active stage of infective endocarditis of the aortic valve with an annulus fibrosus abscess, early prosthetic endocarditis of the pulmonary autograft and pulmonary allograft one month after the Ross procedure was the indication for re-intervention. The patient underwent aortic root replacement with a synthetic valve-containing conduit and pulmonary artery replacement with a pulmonary allograft.

Reasons and volume of re-interventions in the long-term period

Grade 3 neoaortic valve regurgitation was detected in 3 patients. The cause of regurgitation was prolapse of one or all three leaflets without neoaortic root dilatation. The mean time from primary surgery to re-intervention was 10.3 years (9–12 years).

Neo-aortic rook dilatation ≥45 mm with marked AV regurgitation was an indication for re-intervention in 4 patients (Fig. 1, a, b). The mean time from primary surgery to re-intervention was 12.2 years (5–21 years).

The reason for prosthesis replacement in the RVOT in 7 patients with autograft valve failure was moderate lung allograft dysfunction (3 patients), aortic allograft stenosis at the level of the proximal and distal anasto-

mosis (2 patients), calcification and stenosis of stentless aortic xenograft (1 patient) (Table 2).

In 2 patients, the indication for repeated surgical intervention was late prosthetic valve IE. In one case, three years after the Ross procedure, there was an isolated pulmonary allograft lesion. In the second case, the indication for re-intervention was autograft dissection and active IE of the neoaortic, aortic allograft in RVOT and mitral valves 14 years after surgery (Fig. 2).

Two patients with stentless xenografts in the RVOT position and no neoaortic valve dysfunction underwent stenting of narrowed proximal and distal xenograft anastomoses (Fig. 3). As a result of stenting, there was a decrease in right ventricular (RV) pressure, systolic pressure gradients between the RV and PA, and a more than 75% increase in the diameter of the stented segment.

In 4 patients with neoaortic dilatation and neoaortic valve regurgitation, repeated surgery included aortic root replacement with a synthetic valve-containing conduit with mechanical prosthesis (Bentall–De Bono procedure) and valve or pulmonary artery trunk replacement. Implantation of a mechanical prosthesis in AV and RVOT positions was performed in 2 patients. In two cases with severe stenosis and calcification of the prosthesis in RVOT, a synthetic conduit with a mechanical prosthesis was also used for its replacement (Table 3).

In late neo-aortic valve and aortic root replacement, regardless of the function of the neopulmonary valve, we adhered to the tactics of its replacement. Implantation of mechanical prostheses in the position of the aortic and pulmonary valves is the method of choice in our department.

A year after the primary Ross procedure with neoaortic root dilatation with its pronounced insufficiency and enlargement of the proximal aortic arch without pul-

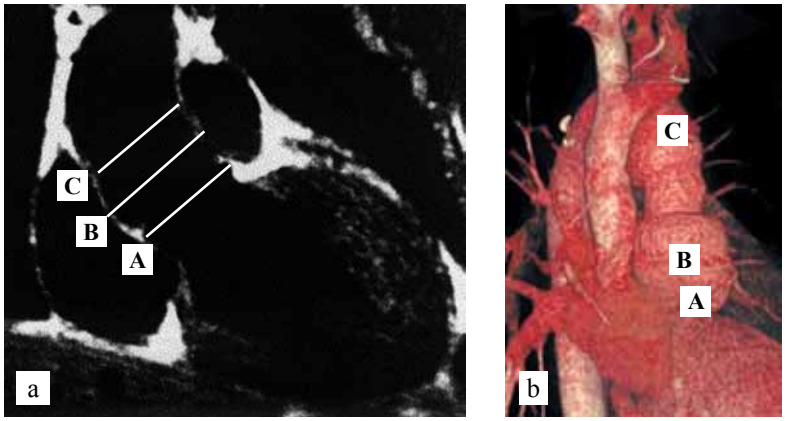

Fig. 1. Cardiac computed tomography: a) patient F., 21 years after surgery (A – aortic annulus – 50 mm, B – sinuses of Valsalva – 55 mm, C – sinotubular junction – 49 mm); b) patient A., 5 years after surgery (A – aortic annulus – 26 mm, B – sinuses of Valsalva – 47 mm, C – ascending aorta – 37 mm)

Table 2

Hemodynamic parameters of RVOT prostheses in patients with autograft and prosthesis replacement in RVOT

	Pulmonary allograft	Aortic allograft	Aortic xenograft
Peak pressure gradient, mm Hg.	19	25	40
Mean pressure gradient, mm Hg.	11	12	18
Regurgitation, degree	<1	<2	3
Diameter at the proximal anastomosis level, mm	21	15	16
Diameter at the distal anastomosis level, mm	26	19	21

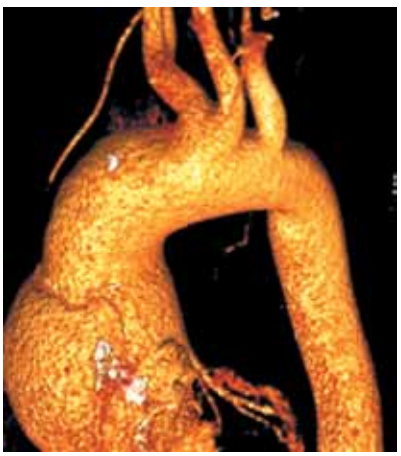

Fig. 2. MSCT of patient R., 14 years after surgery. (34 mm diameter of the aortic annulus, 80 mm at the level of the sinuses of Valsalva, 64 mm at the level of the pulmonary artery trunk)

monary allograft dysfunction in RVOT, in connection with a planned pregnancy, a 31-year-old female patient underwent replacement of the ascending aorta and part of the arch with a synthetic conduit with a stented bioprosthesis without intervention on the prosthesis (pulmonary allograft) in RVOT.

RESULTS

Cardiopulmonary bypass lasted for an average of 278 (160–429) min. The average time of aortic clamping was 156 min (120–265). Intraoperative blood loss was 400 mL (350–550). ICU length of stay was 1.9 ± 0.53 days. Mechanical ventilation lasted for 19 ± 5.9 hours. Length of in-hospital stay was 21 ± 3.1 days.

At the hospital stage, there was 1 death resulting from erosive bleeding from the aorta and unresponsive generalized infection.

The early postoperative period was uneventful for 13 patients. In the late postoperative period (7 ± 3.2 years), patients with mechanical prosthetic valves in the aortic valve position and in the pulmonary artery position (n = 10) followed anticoagulant therapy with target INR values from 2.0 to 3.5. There were no prosthetic thrombosis and no thromboembolic complications. All discharged patients are alive and active. The patients who underwent stenting are dynamically monitored. Given the absence of a valve in the stent, the right ventricular function is assessed in a targeted manner. No thrombosis, stent fracture or restenosis were observed for up to 2 years. Hemodynamic and volumetric parameters of the right ventricle are satisfactory.

Histological picture of explanted prostheses

Histological examination of all explanted bioprosthetic valves was carried out. The pulmonary autograft was characterized by the following changes: in the leaves there are areas of disorganization and fragmentation of elastic fibers, destruction of smooth muscle cells with focal basophilia of the main substance and fibrosis (Fig. 4). In the autograft wall, fibrosis of the middle membrane develops with an increased number of small capillary-type blood vessels in the outer. In some cases, formation of atherosclerotic plaques and acute inflammation areas was found in the autograft.

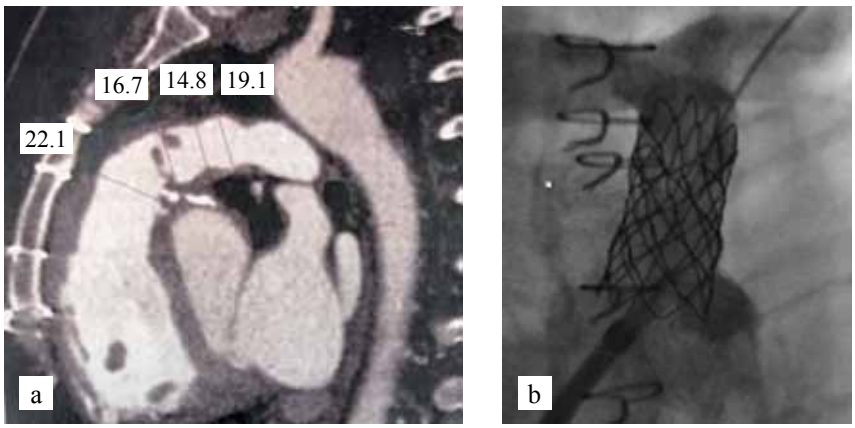

Fig. 3. Patient T., 11 years after Ross procedure: a) MSCT of the RVOT prosthesis (walls are calcified, stenosis in the anastomosis projection); b) angiogram of the implanted stent in the RVOT prosthesis position (xenograft)

Table 3

Types of re-interventions performed

Bentall–De Bono Procedure	PVR (with pulmonary allograft)	2
	PVR (with mechanical prosthesis)	2
	PVR (with conduit)	1
	Pulmonary valve revision	1
AVR + PVR (mechanical prosthesis)		2
AVR + PVR conduit (mechanical prosthesis)		1
PVR with pulmonary allograft		2
RVOT stenting		2
AIV CABG		1

* PVR (pulmonary valve replacement), AVR (aortic valve replacement), RVOT (right ventricular outflow tract), AIV CABG (coronary artery bypass grafting of the anterior interventricular artery).

The histological pictures of the explanted pulmonary and aortic allografts differ. The pulmonary allograft is represented by a thinner wall, absence of cells, and proper arrangement of collagen and elastic fibers.

The aortic allograft is characterized by a denser wall, with petrification areas that create high gradients at the level of the valve, distal and proximal anastomoses (Fig. 5).

Stentless xenografts are characterized by extensive petrificates with the development of tissue ossification (Fig. 6).

DISCUSSION

Excellent long-term survival, low risk of thromboembolic and hemorrhagic complications are the main advantages of the Ross procedure [1–5] (Table 4).

However, the operation remains technically more complicated than the standard aortic valve replacement with stented prosthesis. The correctness of the anastomosis between the autograft and the left ventricular outflow tract (LVOT), anastomoses with the coronary arteries, as well as the duration of aortic clamping and cardiopulmonary bypass play a role in immediate mortality and survival. Even Donald Ross noted that with increasing experience, the initial problems of compression, kinking,

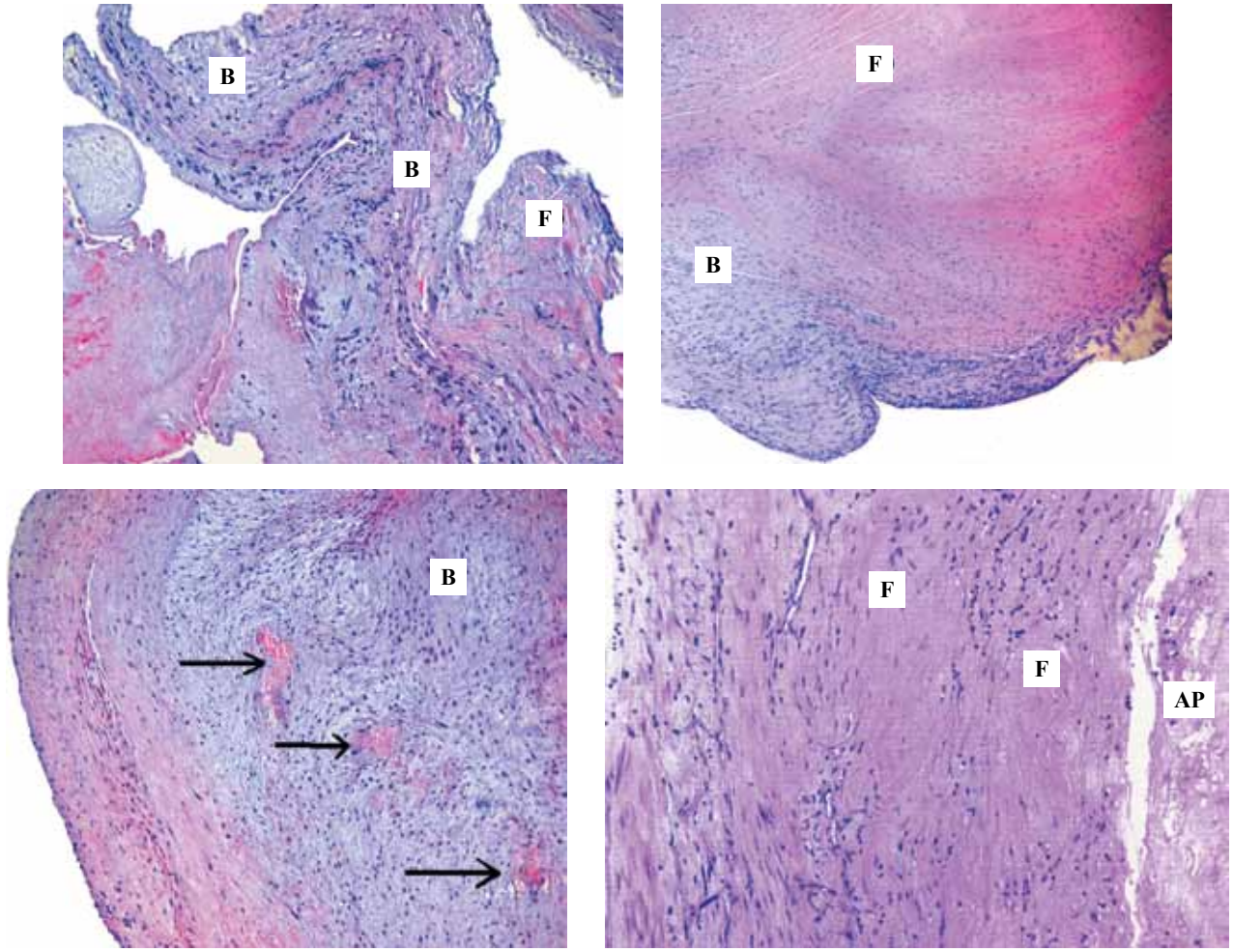

Fig. 4. Autograft leaflets. Micrograph. H&E stain. 100× magnification. In the valves of the pulmonary autografts, there is a picture of focal basophilia (B), fibrosis (F). Area of tissue destruction and eosinophilia (indicated by an arrow). Atherosclerotic plaque (AP)

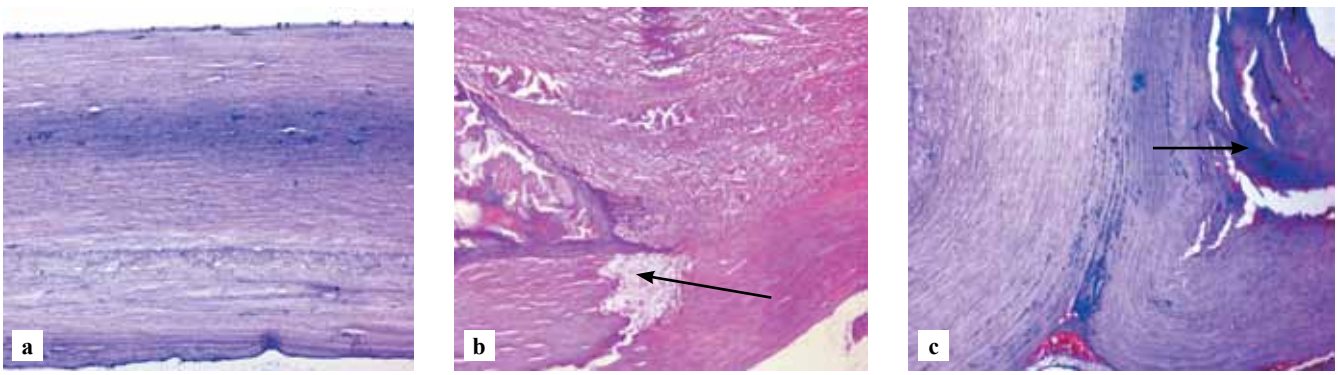

Fig. 5. Wall of grafts in the pulmonary artery position. Micrograph. H&E stain. 100× magnification: a) pulmonary allograft, built from collagen and elastic fibers; b–c) aortic allograft with a tissue petrification focus (indicated by an arrow)

torsion of the coronary arteries and complete heart block have been largely overcome [10]. We had one case of torsion of the LCA ostium, which was diagnosed on time and eliminated.

Re-interventions are characterized by prolonged aortic torsion, blood loss, high risk of injury to the structures of the heart and coronary arteries, and should be provided with adequate anesthetic and perfusion support, performed in a specialized center with a wide arsenal of techniques and means to eliminate sudden fatal complications.

Pulmonary autograft dilatation is one of the reasons for neoaortic valve reinterventions. Dilation of the sinotubular junction causes tension in the neovalve cusps with the development of central regurgitation. We found this phenomenon in 5 patients, one of whom even developed autograft wall dissection. Studies show that autograft dilatation occurs regardless of the implantation method and is due to the inability of the pulmonary trunk and valve to adapt to systemic arterial pressure [10, 11]. The process of remodeling has been demonstrated in explanted pulmonary autografts that have been subjected to systemic circulation for more than a decade [12]. Histological examination of the explants revealed the destruction of elastic fibers, smooth muscle cells with replacement of the extracellular matrix with connective tissue. Similar results have been obtained in the study of our material. For the prevention of neoaortic dilatation, some authors suggest the use of autologous tissues or synthetic materials, which serve as an external sheath for an autograft [5, 13, 14].

To prevent neoaortic dilatation, Magdi Yacoub suggests implanting the autograft subannularly for proximal support with the aortic annulus fibrosus, and perform the

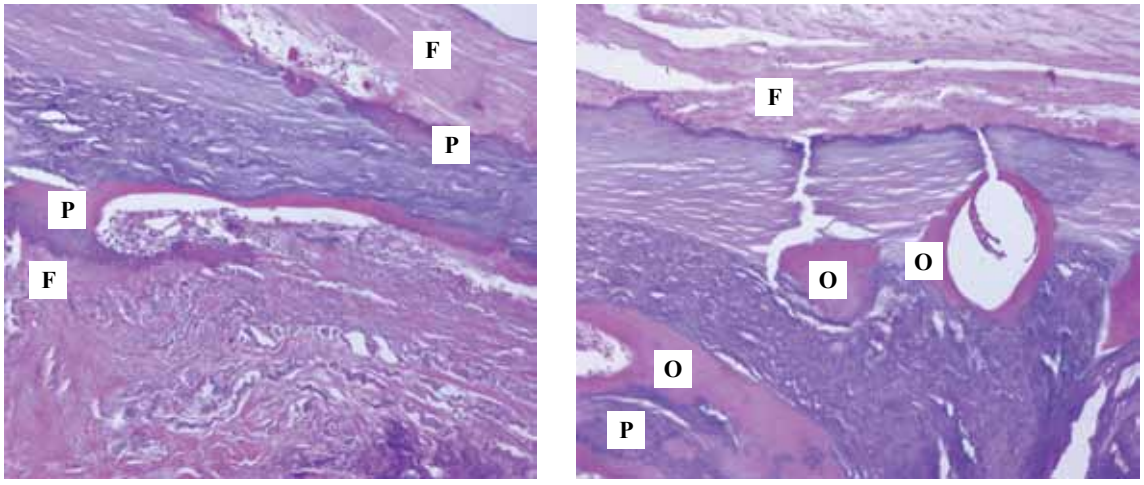

Fig. 6. Xenograft wall in the pulmonary artery position. Micrograph. H&E stain. 100× magnification. Xenograft with areas of fibrosis (F), pertrification (P), tissue ossification (O)

Table 4

Freedom from re-interventions on the neoaortic valve and RVOT prostheses in the long-term postoperative period

Author	Number of cases	Autograft	RVOT prostheses
Bogers A.J., 2004	123	89% (10 years)	91% (10 years)
Kouchoukos N.T., 2007	119	75% (10 years)	86% (10 years)
Elkins R.C., 2008	489	90% (10 years) 83 % (16 years)	90% (10 years) 82 % (16 years)
Mokhles M.M., 2012	161	84% (10 years) 51% (18 years)	90% (10 years) 81% (18 years)
Da Costa F., 2014	414	90.7% (15 years)	92.5% (15 years)
Weimar T., 2014	645	91.6% (12 years)	95% (12 years)
Martin E., 2017	310	96% (10 years) 90% (15 years) 76% (20 years)	96.6% (10 years) 92.1% (15 years) 82.3% (20 years)
Sharifulin R., 2018	793	91.4 (10 years)	91.4% (10 years)
Sievers H.H., 2018	630	96.4% (10 years) 89.8% (20 years)	96.5% (10 years) 91.0% (20 years)
David T.E., 2018	212	83.2% (20 years)	91.8% (20 years)

distal anastomosis at or slightly above the sinotubular ridge [15].

One of the factors for neoaortic dilatation and stratification may consist of a technical error when a long pulmonary artery autograft is used without strengthening the proximal and distal anastomoses areas. In our practice, to support an autograft implanted using the free root technique, we bring the diameters of the annulus fibrosus and the native aorta into full compliance, create the distal anastomosis 1 cm above the sinotubular ridge of the autograft, and also stabilize the proximal and distal anastomosis using synthetic strips (PTFE, Teflon).

A number of researchers believe that the possible predictors of neoaortic dilatation are male gender, mismatch in the size of the aortic root and pulmonary autograft, aortic annulus larger than 25 mm, and aortic insufficiency. T. David suggests reducing the diameter of the aortic annulus and ascending aorta to the size of the pulmonary artery to prevent dilatation. However, this does not always prevent long-term dysfunction in patients with congenital AV abnormalities. Pulmonary autograft dilatation was observed in 9 of 10 patients, all had a wide aortic annulus (≥27 mm) before surgery. Before 15 years, there were no neoaortic reinterventions in patients with an aortic annulus less than 27 mm and in women. The author concluded that women with AoS are ideal candidates for surgery; secondly, a dilated aortic annulus is a marker of connective tissue dysplasia, which may also be present on the pulmonary valve, which can cause premature neoaortic dysfunction [16, 17]. Similar figures are reported by Elkins and colleagues. In this study, the Ross procedure was performed in 487 patients, 197 of whom were younger than 18 years of age. At 16 years after surgery, 164 patients with AI were 59% free of neo-aortic dysfunction, which was significantly less than in 304 patients with AoS, in whom this indicator was 82%. The risk of autograft dysfunction in men was 3 times higher than in women. Annulus reduction and fixation was performed using synthetic material or autopericardium (FR >27 mm) in 96 patients with primary AI, for whom actuarial freedom from autograft valve failure was 87% at 10 years [7]. Weimar T. and colleagues have shown that reinterventions are performed 6 times more often in men than in women. Multivariate analysis showed that AI and aortic annulus of at least 26 mm are predictors of reinterventions [18].

We consider congenital AV defect with AI and ascending aorta aneurysm as one of the contraindications for Ross's procedure.

AI development with autograft cusp prolapse in our material was observed in 3 cases. On histological examination of the autograft cusps, we found basophilia of the main substance, reflecting the processes of intercellular synthesis. On one hand, these changes may be due to a nonspecific response of the connective tissue structures of the pulmonary valve to systemic arterial pressure; on the other hand, they may be associated with connective tissue dysplasia of the valve apparatus in patients with aortic defect. The ischemic nature of degeneration cannot be ruled out, since blood supply to the wall and cusps is disrupted at the time of transplantation. Basophilia of the main substance leads to thickening, prolapse of the cusps and valve dysfunction. Besides, pulmonary autograft can undergo the same changes (atherosclerosis, infective endocarditis) as the native AV.

Most authors use cryopreserved pulmonary allografts for RVOT reconstruction during the Ross procedure. However, some surgeons allow the use of stentless aortic allografts, xenoaortic, xenopericardial conduits, and engineered PTFE conduits. In our material, aortic allograft and stentless xenograft were implanted in 6 patients. We do not use aortic allograft for the right heart because it degenerates much more often than pulmonary allograft. According to James Albert e. al., the freedom from dysfunction 5 years after surgery for aortic allograft in RVOT was 76% compared to 94% for pulmonary allograft [19]. Similar results were presented by Yankah A. When comparing the function of aortic and pulmonary allografts, freedom from degeneration was 18% and 75%, freedom from dysfunction was 62% and 93%, respectively [20]. Perhaps this is related to the thicker wall of aortic allografts, which, when remodeled and replaced by connective tissue, creates a narrower lumen and higher gradients on RVOT.

The use of xenografts for pulmonary artery reconstruction in young patients is undesirable. Xenograft degeneration develops 10 times more often than pulmonary allograft degeneration [21–24]. In adult patients, xenograft dysfunction occurs less frequently, and they can be used in the absence of allografts. Moreover, in this era of rapid development in percutaneous technologies, endovascular intervention in dysfunction can become a low-traumatic temporary solution to the problem. In two of our patients with pulmonary xenograft calcification and stenosis, the use of stents significantly reduced the systolic gradient and led to clinical improvement.

Reinterventions due to IE were performed in 4 patients, 2 patients at the hospital stage, 1 in the midterm (IE allograft in RVOT after 3 years), 1 in the long term after surgery (neoarticular dissection and IE after 14 years).

Infective endocarditis in AV with abscess formation and aortic root destruction presents difficulties in surgical treatment and is associated with high mortality rates [25, 26]. In the case of IE with infection spreading to paravalvular structures (FR, mitral-aortic contact), allografts or autografts are preferred [25–29]. On the other hand, it has been shown that the rate of recurrent infection in patients with active IE does not depend on the type of prosthesis used, but on the radicality of removal of infected tissues [26, 27, 30, 31]. As our experience also shows, in case of extensive destruction of the aortic root structures or mediastinal infection, even considering

structural dysfunction in the late postoperative period, allografts should be preferred since structural degeneration is a much less complicated problem than recurrent IE.

The choice of a pulmonary valve prosthesis remains important in reintervention after the Ross procedure. This issue is overlooked by most authors. Any biological valve can undergo late degeneration. If the Ross procedure makes it possible to avoid anticoagulants, then during the second operation, a mechanical prosthesis is most often implanted in the aortic position and warfarin therapy is administered. In our opinion, keeping any valve graft in the pulmonary position carries the risk of another reoperation. Therefore, mechanical bicuspid prostheses were implanted in 4 patients in the aortic and pulmonary valve positions. Follow-up showed normal prosthetic function at standard INR (2.0–3.5).

CONCLUSION

Autograft dysfunction in the late postoperative period is a consequence of cusp prolapse and/or with autograft remodeling and dilation at different levels. To increase the autograft lifespan, it is necessary to ensure a match between the diameter of the pulmonary trunk and the aorta, which is achieved using the free root technique; using external support for the proximal and distal anastomoses. Planned repeated neoaortic root and/or pulmonary graft surgery, despite the large volume, can be performed with low mortality and complication rates. Implantation of aortic allografts and xenografts in young patients for RVOT reconstruction is unjustified due to the development of earlier and more severe dysfunction in comparison to pulmonary allografts. The use of an endovascular aid for isolated dysfunction of RVOT prostheses allows delaying the reintervention. It is necessary to strive towards making the repeat operation the "last" one; implantation of mechanical prosthetic valves in the aortic and pulmonary valve position is the most justified.

The authors declare no conflict of interest.

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