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Biological Valved Reconstructive Surgery of the Aortic Root through the years

Abdullah Kaya

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Biological Valved Reconstructive Surgery of the Aortic Root through the years

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**Biological Valved Reconstructive Surgery of the Aortic Root through the years**

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**Cover**

Ebru artwork by Dr. Mustafa A. Akdemir

Ebru Art: Turkish art of Marbling is the art of creating colorful patterns by sprinkling and brushing color pigments on a pan of oily water and then transforming this pattern to paper. It is believed to be invented in the thirteenth century Turkistan. This decorative art then spread to China, India and Persia and Anatolia. Seljuk and Ottoman calligraphers and artists used marbling to decorate books, imperial decrees, official correspondence and documents. New forms and techniques were perfected in the process and Turkey remained the center of marbling for many centuries. Up until the 1920’s, marblers had workshops in the Beyazit district of Istanbul, creating for both the local and European market, where it is known as Turkish marble paper. In Turkey it continues to be very popular.

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of the Aortic Root through the years

Proefschrift

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Introduction
AORTIC ROOT ANATOMY

The aortic root is an intriguing part of the heart. It provides the supporting structures for the aortic valve leaflets and forms a functional and dynamic connection between the left ventricle and the ascending aorta. It is deeply anchored within the central base of the heart between the pulmonary root anteriorly and the mitral and tricuspid valves posteriorly. Components of the aortic root are the semilunar aortic leaflets, the sinuses of Valsalva and the interleaflet triangles. The boundaries of the root are formed superiorly by the sinotubular junction and inferiorly by the virtual basal ring at the level of the basal attachment points (the nadirs) of the leaflets within the left ventricle, as shown in Figure 1 (1-5). The different leaflets and sinuses are distinguished by the origins of the left and right coronary arteries.

Each leaflet contains a hinge point, a body and a coapting free edge with a thickened central nodule (nodule of Arantius). The hinge point is a condensation of collagenous tissue and is the area where the leaflet is attached to the aortic root. The body is the large weight-bearing surface of the leaflet. The free edge of the leaflet is constructed so that, when closed, the leaflets coapt over several millimeters. This margin of overlap defines the coapting surface of the leaflet. The leaflet itself consists of three distinctive connective tissue layers, including the lamina fibrosa on the aortic side, the lamina spongiosa in the middle and a thin layer of elastin fibers on the ventricular side called the lamina ventricularis (6, 7). The leaflets form a mobile layer of tissue that separate the haemodynamic components of the left ventricle and the aorta and are attached to the wall of the aortic root in a semilunar fashion. This leaflet attachment line has a crown-like shape and the highest points of these attachment lines are at the sinotubular junction level forming the commissures (Figure 2). The leaflet attachment line constitutes the haemodynamic or physiologic ventriculo-arterial junction. This is different from the anatomic ventriculo-arterial junction, which is a virtual horizontal circle (basal ring) where the fibro-elastic aortic wall joins the supporting muscular structures of the left ventricle at the nadir of the left and right leaflets. Beneath the non-coronary leaflet there is no muscular crescent at the base, because it has exclusively fibrous walls, the so-called aortic-mitral fibrous continuity.
Figure 1 (A) The muscular sleeve of the right ventricular outlet (RVOT) has been pulled forward to show the left (L) and right (R) aortic sinuses that give origin to the main coronary arteries. The non-coronary (N) aortic sinus is furthest from the pulmonary trunk. (B) This overview shows the central location of the aortic root and the relationship of the non-coronary aortic sinus to the plane of the atrial septum (double-headed arrow). The open arrow indicates the area of the aortic mound. MV, mitral valve; TV, tricuspid valve. (C) The aortic root has been opened longitudinally to display the level of the sinutubular junction (open arrows), orifices of the coronary arteries (small arrows), and the area of fibrous continuity (broken line) between aortic and mitral valves. The asterisk marks the pale-coloured area that is the membranous septum. (From Ho SY. Eur J Echocardiogr. 2009;10(1):i3-10; reprinted with permission from the author and Oxford Journals)
The sinuses of Valsalva are the expanded portions of the aortic root confined proximally by the attachments of the leaflets and distally by the sinotubular junction. The sinuses are composed primarily of elastic tissue and support the origins of the coronary arteries. They are the anatomical and functional units of the aortic root supporting the opening of the leaflets and allowing formation of vortices, which aid proper valvular closure and enhance coronary artery perfusion during diastole. An interaction of all the components of the aortic root is needed for correct functioning of the aortic valve complex, including the sinotubular junction, which is the upper part of the sinuses of Valsalva and delineates the beginning of the tubular ascending aorta (8-11). The basal parts of the sinuses are separated from each other by the interleaflet triangles.

The interleaflet triangles are positioned subvalvularly and are subjected to the hemodynamics of the left ventricle. They are triangular extensions of the left ventricular outflow tract, which prolong distally to the level of the sinotubular junction. The triangles are fibrous areas of the aortic root. The interleaflet triangle between the non-coronary and left coronary sinus is part of the area of aortic-mitral fibrous
continuity. The triangle between the non-coronary and the right coronary sinuses is directly continuous with the membranous part of the ventricular septum. The bundle of His lies immediately below the membranous ventricular septum. The last triangle, which separates the left and right coronary sinuses, is in continuity with the ventricular septum. The interleaflet triangles are crucial for proper valvular function because when one or more of the triangles are rudimentary, the valve becomes stenotic (1).

The aortic root is a complex hemodynamic unit. Its components are continuously changing and move in harmony during each cardiac cycle. This is due to aortic and ventricular pressures and geometry. In vivo studies with tagged radiopaque material to ovine and canine aortic roots showed the dynamic nature of the valve complex. During systole the diameter of the sinotubular junction increases initially as aortic pressure increases, allowing the leaflets to retract and open, and the diameter at the base of the leaflets decreases so the root adopts a cylindrical shape. During diastole the reverse occurs, the leaflets move towards the ventricle and close so that the root geometry changes to a conical shape (8-11).

AORTIC ROOT DISEASE

Aortic aneurysms and dissections are the most common indications for aortic root surgery. Pathological aortic leaflets are predominantly treated by aortic valve replacement, but when other components of the aortic root are involved, like diseased bicuspid aortic valves with a dilated aortic root, aortic root surgery may be necessary. Endocarditis of the aortic valve with destruction of the annulus can also be an indication for aortic root replacement. There are more pathological conditions of the aortic root, but these are less common and will not be discussed here.

An aneurysm is a dilatation of a blood vessel to more than 1.5 times the diameter expected for sex, age, body weight and height (12). An aneurysm of the aortic root alone is termed as annulo-aortic ectasia and mainly seen with connective tissue disorders (e.g. Marfan syndrome). Most aortic root aneurysms are seen in combination
with ascending aorta aneurysms. In the elderly, aneurysms of the ascending aorta or aortic root are mainly caused by cystic medial degeneration. In younger patients connective tissue disorders, like Marfan syndrome, or a congenital disorder of the aortic valve, like a bicuspid aortic valve, are frequently associated with aneurysmal dilatation of the aortic root. Most aneurysms are asymptomatic and are diagnosed by coincidence. Echocardiography is a frequent mode of diagnosis. Symptomatic patients present with chest pain. This is a surgical indication. Size, etiology and growth rate determine the surgical intervention moment for asymptomatic ascending aorta and aortic root aneurysms. According to guidelines, an asymptomatic degenerative aneurysm of the ascending aorta or aortic root with a diameter of 5.5 cm or greater should be evaluated for surgery. Patients with connective tissue disorders (e.g. Marfan syndrome) or congenital aortic valve disorders (e.g. bicuspid valve) are advised to undergo surgery at smaller diameters (4.5 to 5.0 cm) to avoid acute dissection or rupture in the future (12).

An aortic dissection is an acute condition with an intimal tear that leads to separation of the medial layer of the aortic wall into two layers with the result of a true and a false lumen. The true lumen is delineated by the original intimal layer and the false lumen is located in the media of the aortic wall. Hypertension, connective tissue disorders and cystic medial degeneration are important risk factors for aortic dissection. There are two frequently used classifications for dissections, namely the DeBakey and the Stanford classifications. The more functional Stanford classification is predominantly used in clinics. In Stanford type A, dissection of the ascending aorta is involved. Because of intra-pericardial location and the risk of rupture of the aorta in the pericardium with acute tamponade, resulting in death, an emergency indication for surgical intervention exists. In Stanford type B, the dissection is located beyond the left subclavian artery in the descending aorta. Most patients with type A aortic dissection have severe chest pain and can be in shock. Untreated type A dissection patients have an extremely poor prognosis. If untreated, almost half of the patients are deceased within 48 hours. Surgical treatment has the goal of preventing rupture by exclusion of the entry tear by replacement.
Active endocarditis of the aortic valve is associated with considerable morbidity and mortality, especially if there is destruction of the aortic annulus. Fever, heart murmur, conduction disorders and embolic manifestations like coronary or systemic embolization of vegetations can be present. Clinical suspicion of endocarditis should be followed by echocardiography. Most causes of endocarditis are due to staphylococcal, streptococcal and enterococcal microorganisms. Antimicrobial therapy is the initial treatment after identification of the causative microorganism. In approximately half of the patients with endocarditis surgical treatment is necessary. Heart failure, uncontrolled infection with perivalvular extension and prevention of embolic events (vegetations > 10 mm) are the main indications for surgery (13). The main purpose of surgery in active endocarditis is to remove all infected tissue and reconstruct the affected area.

AORTIC ROOT REPLACEMENT

There are several surgical options for patients with aortic root disease. Replacement of the aortic root and valve with a composite valved graft (conduit) is the most common surgical approach. Beside this option, valve-sparing aortic root replacement has gained widespread use during the past two decades. The choice of aortic valve substitute can be mechanical, biological or, if applicable, the aortic valve leaflets can be spared. This choice is made by the patient, the referring cardiologist and the attending surgeon and depends on various factors: age, the mental capability and preference of the patient (e.g. lifestyle or desire to become pregnant), concomitant disease (e.g. atrial fibrillation, dilated poor left ventricle, or already having a mechanical valve), the morphology of the aortic valve leaflets and the experience of the surgeon with different surgical techniques.

The mechanical valve was the first aortic valve substitute, the main advantage of which was its long durability (14). Mechanical valves, however, require lifelong oral anticoagulation therapy to prevent thromboembolic complications. This is a major disadvantage, because it is associated with an increased risk of bleeding complications.
Oral anticoagulation (i.e. vitamin K antagonists) is difficult to use in clinical practice, because it has a slow onset and offset, narrow therapeutic window, variable dose-response in individuals, and interacts with different food and drugs. These antagonists need to be closely monitored for their anticoagulant effect, which is inconvenient for patients and costly for health-care systems. The estimated risk of thromboembolism after mechanical valve replacement and oral anticoagulation use is 0.2 per 100 patient-years for valve thrombosis, 1.0 per 100 patient-years for major embolism and 1.8 per 100 patient-years for all types of embolism with the risk of major bleeding being 1.4 per 100 patient-years (15, 16). Mechanical valved conduits are not specifically studied in this evaluation and are out of the scope of this thesis, since it concentrates on biological valved reconstructive surgery of the aortic root.

Given the fact that the population in the Western World is ageing, it can be expected that the percentage of biological solutions for aortic valve and aortic root pathology will increase in the future. In fact, the percentage of bioprosthetic valves or biological valved conduits implanted in the last decade is increasing, as illustrated in Figure 3 (17). The biological options discussed in this dissertation are the types of biological valved conduits used in the St. Antonius Hospital, Nieuwegein.

![Figure 3](image)

**Figure 3** Percentage use of bioprosthetic valves relative to mechanical valves from 1997 through 2006. Bioprosthetic valve use increased progressively during 10 years. Asterisk indicates P<0.00001. *(From Brown JM et al., J Thorac Cardiovasc Surg 2009;137:82-90; reprinted with permission from Elsevier)*
In 1962 Donald Ross and Brian Barrat-Boyes reported independently the clinical use of a donor aortic valve homograft (allograft) in an orthotopic subcoronary position (18, 19). Ever since, several changes have taken place with the use of homografts. The subcoronary technique was initially used to implant the homograft in the aortic position, whereby the homograft valve was sewn directly into the aortic root. Because of some extensive aortic root pathology expanding beyond the aortic valvular leaflets, a full aortic root replacement was introduced, in which the complete homograft aortic root is implanted as a functional unit for left ventricular outflow tract reconstruction with reimplantation of the coronary arteries (20-22). This technique has advantages over subcoronary implantation, since the homograft is less likely to be distorted. Matching the homograft size to the host annulus is less critical and is a well-tried, accepted technique (23).

The homografts are usually preserved as a complete aortic root. This includes the aortic valve, the muscular part of the left ventricular outflow tract, the anterior leaflet of the mitral valve and the ascending aorta together with the aortic arch (Figure 4). All these tissues may be applicable, depending on the morphological pathology that is encountered during surgery. In general, a homograft aortic root replacement is considered in aortic valve endocarditis (native and prosthetic) and all aortic valve replacements and left ventricular outflow tract reconstructions where anticoagulation is undesirable (e.g. children and young adults, women of child-bearing age). Homografts have a superior hemodynamic performance, are permeable to serum antibiotics and therefore relatively resistant to endocarditis, have very rare thrombo-embolic events and do not require long-term anticoagulation (20, 24-26). The initial results with cryopreserved homografts are good (27). In Chapter 2 the mid-term results after full root replacement with cryopreserved aortic homografts will be evaluated.
The use of the autologous pulmonary valve (autograft) to replace the diseased aortic valve and a reconstruction of the right ventricular outflow tract with a pulmonary homograft was first described by Donald Ross in 1967 (28). The morphology and function of the aortic and pulmonary valves are similar. The trileaflet pulmonary valves are supported throughout the circumference by the musculature of the infundibulum and by the three sinuses of the pulmonary trunk, which interdigitate with the fibrous extension of the outflow tract as a consequence of the semilunar attachment of the leaflets. This semilunar ventriculo-arterial junction resembles the aortic root, but the main difference is the lack of an anatomic ventriculo-arterial junction, the relatively thin infundibular muscle compared to thick left myocardium and the lack of a sinotubular junction.

Initially the subcoronary implantation technique was used to implant the pulmonary autograft, but after relatively high reoperation rates for severe regurgitation, the autograft aortic full root replacement with reimplantation of the coronary arteries was introduced, also known as the modified Ross procedure (29, 30). This is the favoured technique for implanting a pulmonary autograft in the aortic position and a cryopreserved homograft in the pulmonary position.

The advantages of the pulmonary autograft include the increased cellular viability, the growth potential in children, the avoidance of life-long oral anticoagulation,
superior hemodynamic performance and rare thromboembolic events (31). The modified Ross procedure implies a double valve replacement in patients with univalvular disease, which makes the operation technically more demanding and requires more experience from the surgeon. The modified Ross procedure is currently considered in children and young adults in whom oral anticoagulation is undesirable. Contraindications to this operation exist in patients with connective tissue disorders or patients with anatomic or structural defects of the pulmonary valve.

Since 1990 the modified Ross procedure has been offered to young adults in the St. Antonius Hospital, Nieuwegein. The initial report of aortic root replacement with the pulmonary autograft is promising (32). The mid-term results with the use of the pulmonary autograft in the aortic position and a homograft in pulmonary position are evaluated in Chapter 3. Chapter 4 illustrates a rare complication after pulmonary autograft implantation in a young patient.

**Valve-sparing Aortic Root Replacement with the Reimplantation technique**

After attempts to repair regurgitant aortic valves in the early years of cardiac surgery, valve-sparing aortic root replacement techniques for aortic valve regurgitation regained interest in the eighties and nineties (33-36). These procedures evolved during the years and are nowadays classified as a remodeling (Yacoub) and a reimplantation (David) technique (35, 36). The different modifications of valve-sparing aortic root replacement have been classified by Miller as follows: David-I is the original reimplantation procedure using a cylindrical tube graft, David-II is the original Yacoub remodeling procedure, David-III is the remodeling procedure with an external narrowing annuloplasty strip, David-IV is reimplantation using a 4-mm larger graft size with plication of the graft circumferentially at the sinotubular junction above the tops of the commissures, and David-V is reimplantation using an even larger graft size, which is ‘necked down’ at both the bottom and the top ends to create graft pseudosinuses (37).

In the remodeling procedure the scalloped graft is sewn to residual aortic sinus tissue around the aortic leaflets and commissures proximally. This procedure employs 2 aortic suture lines. The advantage of the remodeling approach is that the graft
billows, thereby mimicking the natural sinuses of Valsalva. Conversely, the drawback of the remodeling procedure is the absence of fixation of the ventriculo-aortic junction, which can predispose to postoperative annular dilatation and recurrent aortic regurgitation.

The reimplantation method preferred in the St. Antonius Hospital, is the initial David-I method in which the proximal suture technique consists of suturing the proximal graft with interrupted, horizontal mattress sutures through the left ventricular outflow tract and continuous sutures in a scalloped fashion immediately above the insertion of the aortic leaflets. This is the predominantly used method of valve-sparing aortic root replacement for different aortic root pathology with preserved, morphologically normal aortic leaflets in the St. Antonius Hospital. The advantage of the reimplantation approach is that this method firmly anchors the aortic graft proximally at the ventriculo-aortic junction below the leaflets with the commissures sewn inside the Dacron graft. The preliminary results of valve-sparing aortic root replacement using the reimplantation technique are promising (38). In Chapter 5 the mid-term results of valve-sparing aortic root replacement with the reimplantation technique are evaluated. Chapter 6 describes a rare traumatic lesion of the aortic valve that is solved by valve-sparing repair of the leaflet.

**Biological Valved Conduits**

The first complete replacement of the aortic root with a conduit was in 1968 and contained a mechanical valve sutured to the end of a Teflon aortic prosthesis (39). The so-called inclusion or wrap technique was used to implant the conduit for aortic root reconstruction. The appreciation of false aneurysms arising at the side to side coronary ostial or distal aortic anastomosis caused this technique to evolve over the years to the button technique. Here, the coronary ostia are dissected as buttons, preserving 5 to 6 mm of native aortic wall, and reimplanting in an end to side fashion to the aortic graft (40, 41). The button technique, also known as the modified Bentall procedure, is the favoured method for aortic root reconstruction.
Biological valved conduits are nowadays commercially available as substitutes for aortic root replacement. These are readily available in all sizes and do not need lifelong oral anticoagulation. Since the nineties many companies began offering biological valved conduits to the market e.g. Medtronic Freestyle (Medtronic, Inc., Minneapolis, MN, USA), Toronto stentless root (St. Jude Medical, Inc., St. Paul, MN, USA) or Edwards prima plus stentless root (Edwards Lifesciences, Corp., CA, USA). Over the years two biological valved conduits have been used primarily in the St. Antonius Hospital, Nieuwegein, namely the Shelhigh BioConduit model NR-2000C (Shelhigh, Inc, Milburn, NJ, USA) and the BioValsalva Conduit (Vascutek Terumo, Renfrewshire, Scotland).

Shelhigh BioConduit model NR-2000C is a bovine pericardial straight graft with an incorporated porcine stentless valve, which is treated with the No-React process (Figure 5). This No-React xenograft pre-treatment involves aldehyde cross-linkage to achieve high resistance to biodegradation, an aldehyde detoxification process, and surface modification with a surfactant (42). This method seems to have beneficial properties above the standard treatment of fresh bioprosthetic leaflet materials of either bovine pericardium or porcine aortic valve with glutaraldehyde (43). Chapter 7 evaluates our initial experience with the use of the Shelhigh BioConduit.

![Figure 5 Shelhigh BioConduit model NR-2000C](image-url)
The BioValsalva conduit is a combination of a Valsalva graft and a stentless porcine valve (Elan, Vascutek, Terumo) (Figure 6). The coated polyester (Dacron) Valsalva graft has to be stored in a dry environment and the biological valve must be stored in glutaraldehyde. This problem is solved by modifying the coated polyester Valsalva graft into a 3-layered graft, which allows storage in glutaraldehyde and preserves its impermeability. This vascular graft is made of an uncoated Gelweave (Vascutek, Terumo) polyester inner layer and a polytetrafluoroethylene outer layer, which are glued together with a central, self-sealing elastomeric membrane that makes the graft impermeable (44). The proximal part of the graft has the Valsalva shape, mimicking the sinuses of the aortic root with reduction of tension on the coronary buttons and improvement of coronary flow and valve hemodynamics (45, 46). In Chapter 8 our experience with the BioValsalva conduit is described.

Figure 6 BioValsalva Conduit
AIM OF THE THESIS

This thesis presents the results of different biological valved conduits for aortic root surgery, performed in the St. Antonius Hospital in Nieuwegein. The aim is to evaluate hospital outcomes and follow-up results. Based on this, the following research questions will be explored in the corresponding chapters:

- Do the mid-term follow-up results support the use of cryopreserved homografts for endocarditis and in relatively young patients who do not want to use anticoagulation (Chapter 2)?
- Is the modified Ross procedure still an option for young adults who prefer not to use anticoagulation (Chapter 3 and 4)?
- Does the mid-term evaluation of valve-sparing aortic root replacement using the reimplantation technique encourage its application (Chapter 5 and 6)?
- What are the initial results with commercially available biological valved conduits (Shelhigh bioconduit and Biovalsalva conduit) (Chapter 7 and 8)?
REFERENCES

Chapter 1


Valve-Related Events after Aortic Root Replacement with Cryopreserved Aortic Homografts

Abdullah Kaya, MD, Marc A. Schepens, MD, PhD, Wim J. Morshuis, MD, PhD, Robin H. Heijmen, MD, PhD, Aart Brutel De La Rivière, MD, PhD, and Karl M. Dossche, MD, PhD.

ABSTRACT

Background. Aortic root replacement with aortic homografts for various pathologic conditions involving the aortic root has yielded good early results. To assess mid-term valve-related events, a follow-up study was conducted.

Methods. From February 1989 through January 2003, 213 patients with a mean age of 51.3 ± 11.8 years underwent aortic root replacement with a cryopreserved aortic homograft. Bacterial endocarditis (58.7%) was the predominant indication for surgery (native valve endocarditis, n = 73; prosthetic valve endocarditis, n = 52). Of the 197 hospital survivors, 194 were entered in the follow-up study (98.5% complete). Endpoints of the study were death, valve-related death, reoperation for valve failure, endocarditis, thromboembolic events and anticoagulant-related bleeding events. Follow-up was conducted between February and April 2003.

Results. Overall hospital mortality was 7.5% (n = 16; 70% confidence limits, 5.6% to 9.4%). Mean follow-up was 5.8 years (range, 0.3 to 14.3). In total, 20 late deaths occurred (10.3%); of these, 5 were valve-related. The overall survival at 5 and 10 years is 87.3% ± 2.4% and 70.8% ± 5.3%, respectively. Twenty-one patients (10.8%) required reoperation, either for structural valve deterioration (n = 12), false aneurysm (n = 3), endocarditis of the homograft (n = 3), or for other reason (n = 3). Mortality for reoperation was 28.6% (n = 6). Five-year and 10-year freedom from reoperation is 94.5% ± 1.8% and 76.4% ± 5.3%, respectively. Endocarditis of the homograft was reported in 4 patients (3.2%), of whom 1 patient was treated medically and 3 required reoperation. Thromboembolic events (n = 1) and anticoagulant-related bleeding events (n = 0) were rarely seen. A recent echocardiographic study was available in 124 patients (71.3%). Aortic regurgitation grade I to II was reported in 121 patients (97.6%).

Conclusions. Cryopreserved aortic homografts function well on mid-term evaluation. The incidence of structural valve failure is acceptable. Reoperations for homograft endocarditis carry a high mortality rate.
INTRODUCTION

Since the publications on the clinical use of homografts for aortic valve replacement, human tissue valves formed their own position in the era of aortic valve substitutes (1,2). As with every valve substitute, the homograft aortic valve has its advantages and disadvantages. Restoration of normal flow in the aortic root and coronary orifice resulting in better hydraulic performance, resistance to endocarditis and rare thromboembolic events without the need for anticoagulation are considered as advantages. Limited donor availability and homograft durability are the serious disadvantages. The long-term performance of homograft aortic valves is profoundly influenced by sterilization and preservation. Early methods like chemical preservation, irradiation (3-5) and freeze drying (6,7) have shown profound deleterious effect on the long-term function of the aortic homografts. The method of preservation that is currently used in most centres is the technique of homograft valve cryopreservation (8,9). It has the advantage of a long shelf half-life time and is readily available for use. After yielding good early results with cryopreserved aortic homografts used as a freestanding aortic root replacement (10), the present purpose is to assess the midterm valve-related events in a retrospective follow-up study.
MATERIAL AND METHODS

Patients
From February 1989 through January 2003, 213 patients with a mean age of 51.3 ± 11.8 years (range 14 to 79) underwent aortic root replacement (ARR) with a cryopreserved aortic homograft. There were 159 (74.6%) male and 54 (25.4%) female patients. The indication for operation was aortic regurgitation in 172 patients of which 125 cases were due to endocarditis (73 native valve endocarditis versus 52 prosthetic valve endocarditis), aortic stenosis in 27 patients, and mixed lesions in 14 patients. Pertinent patient data are given in Table 1.

Table 1. Preoperative and Perioperative Patient Characteristics (n=213)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender (M/F ratio)</th>
<th>NYHA class</th>
<th>Indication</th>
<th>Type of previous cardiac surgery (n=75)</th>
<th>Elective/urgent operation ratio</th>
<th>Concomitant procedure (n=44)</th>
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<tr>
<td>mean (SD;range)</td>
<td>51.3 (11.8;14-79)</td>
<td>159/54</td>
<td>I</td>
<td>21 (9.9%)</td>
<td>1208/33</td>
<td>coronary bypass planned</td>
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<tr>
<td>Gender (M/F ratio)</td>
<td>159/54</td>
<td>72 (33.8%)</td>
<td>II</td>
<td>77 (36.2%)</td>
<td></td>
<td>MVP/R</td>
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<td>NYHA class</td>
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<td>III</td>
<td>7 (2.1%)</td>
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<td>coronary bypass unplanned</td>
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<tr>
<td>Indication</td>
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<td>IV</td>
<td>14 (6.5%)</td>
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<td>8 (9.7%)</td>
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<td>valve operation</td>
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<td>51 (62.2%)</td>
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<td></td>
<td>MVP/R</td>
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<tr>
<td>combination</td>
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<td></td>
<td>19 (23.2%)</td>
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<td>coronary bypass unplanned</td>
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<tr>
<td>other</td>
<td></td>
<td></td>
<td>4 (4.9%)</td>
<td></td>
<td></td>
<td>other</td>
</tr>
</tbody>
</table>

SD = standard deviation; NYHA = New York Heart Association; MVP/R = mitral valve plasty/replacement
Homograft Data

Aortic homograft valves were harvested under sterile conditions from cardiac transplant recipients, beating-heart or nonbeating-heart donors, with a maximum age of 60 years. Dissection of the heart was generally performed within 24 hours after circulatory arrest. After dissection, the valves were decontaminated by incubation in medium with an antibiotic mixture for 5 hours at 37°C. Thereafter, valves were cryopreserved in medium containing 10% dimethylsulfoxide (DMSO) frozen at a controlled rate of -1°C/min up to -100°C and stored on the vapor of liquid nitrogen (-150° to -196°C). All tissues were cryopreserved within 50 hours after circulatory arrest of the donor. All donors were seronegative for human immunodeficiency virus, hepatitis B surface and core antigen, cytomegalovirus or Treponema pallidum. For implantation, ABO compatibility or HLA type matching was not required. In elective operations, mismatch in age of more than 10 years between the donor valve and recipient was avoided; in urgent operations this was possible only occasionally. All homografts were provided by Bio Implant Services Foundation (BIS, Leiden, the Netherlands). The homograft characteristics are displayed in Table 2. Details on the operative technique were described before (10).

Table 2. Cryopreserved Aortic Homograft Characteristics (n=213)

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>mean (SD)</th>
<th>24.0 (1.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 23</td>
<td>24</td>
<td>(11.3%)</td>
</tr>
<tr>
<td>23 – 25</td>
<td>156</td>
<td>(73.2%)</td>
</tr>
<tr>
<td>&gt; 25</td>
<td>33</td>
<td>(15.5%)</td>
</tr>
<tr>
<td>Donor Age (years)</td>
<td>mean / median (SD;range)</td>
<td>44.5 / 46.0 (11.0;13-60)</td>
</tr>
<tr>
<td>Donor-recipient age mismatch (years)</td>
<td>mean / median (SD;range)</td>
<td>7.1 / 5.5 (17.7; 30-58)</td>
</tr>
</tbody>
</table>

SD = standard deviation
Follow-up
Recent information (less than 6 months) about the status of all hospital survivors is collected from the referring cardiologist, by visit at our cardiology department, or by their general physician. April 30, 2003, was the closing date for follow-up and included physical examination, echocardiography, and chest radiography. Endpoints of the study were death, valve-related death, reoperation for valve failure, endocarditis of the homograft, thromboembolic events, and anticoagulant-related bleeding. These endpoints were defined according to the guidelines reported by Edmunds and associates (11). Valve function was determined by echocardiographic Doppler study including colour-flow mapping, as much as available, otherwise by auscultation. Homograft regurgitation was graded on a scale of 0 to 4 on echocardiography, with 0 as no regurgitation, 1 as trivial regurgitation, 2 as mild regurgitation, 3 as moderate regurgitation and 4 as severe regurgitation.

Data Analysis
Retrospective review was done on the data of all consecutive patients who underwent homograft ARR. Quantitative data are presented as mean ± standard deviation. Univariate comparisons between groups were calculated by the unpaired test, Fisher’s exact test, \( \chi^2 \) test, or the one-way or two-way analysis of variance as appropriate. All probabilities are two-tailed. Kaplan-Meier survival curves were used for analysis of survival times, and Tarone or Breslow test for comparisons between survival curves. Precision was indicated by 70% confidence limits (CL).

RESULTS

Patient Survival
Hospital mortality was 7.5% (n=16; 70% CL, 5.6% to 9.4%). There were 197 hospital survivors, of whom 194 were entered in the follow-up study (98.5% complete). Mean and median follow-up times were 5.8 years and 5.4 years, respectively (range 0.3 to 14.3 years). Total follow-up was 1118 patient-years. Three patients were lost to follow-up, 2 patients due to emigration and 1 patient moved to an unknown address. During
follow-up 20 patients (10.3%) died. Five of these late deaths were valve-related. Three patients had endocarditis of the homograft, 1 had structural valve deterioration and 1 patient had a false aneurysm. All valve-related late deaths were reoperated on. Of the other 15 non-valve related late deaths 4 patients died of cardiac failure (heart failure and one myocardial ischemia 79 months postoperatively) and 11 patients died of noncardiac causes. This is summarized in Table 3. The overall survival at five and ten years is 87.3% ± 2.4% and 70.8% ± 5.3% respectively. Survival at five and ten years for the endocarditis group was 82.7% ± 3.6% and 57.1% ± 9.9% respectively, and 91.3% ± 3.7% and 84.3% ± 5.9% for the non-endocarditis group. This is presented in Figure 1.

Table 3. Late Deaths (n=20)

<table>
<thead>
<tr>
<th>Valve-related</th>
<th>Nonvalve-related</th>
</tr>
</thead>
<tbody>
<tr>
<td>- endocarditis</td>
<td>3</td>
</tr>
<tr>
<td>- structural valve disease</td>
<td>1</td>
</tr>
<tr>
<td>- false aneurysm</td>
<td>1</td>
</tr>
<tr>
<td>- cardiac</td>
<td>4</td>
</tr>
<tr>
<td>- noncardiac</td>
<td>11</td>
</tr>
<tr>
<td>pulmonary</td>
<td>4</td>
</tr>
<tr>
<td>neurologic</td>
<td>1</td>
</tr>
<tr>
<td>cancer</td>
<td>1</td>
</tr>
<tr>
<td>unknown</td>
<td>5</td>
</tr>
</tbody>
</table>

Figure 1 Survival curve after homograft aortic root replacement. Open circles = nonendocarditis group; solid circles = overall group; triangles = native valve endocarditis/prosthetic valve endocarditis group.
Reoperation

Twenty-one patients (10.8%) required reoperation for significant homograft valve dysfunction due to structural valve deterioration (n=12), false aneurysm (n=3), homograft valve endocarditis (n=3) or other reason, as displayed in Table 4. Mean length of time between the initial ARR and reoperation was 67.8 months ± 41.6 months. Six patients reoperated on for structural valve deterioration received an aortic valve replacement (mechanical prosthesis, n= 5; biological prosthesis, n= 1), 3 patients had a Bentall procedure, 2 patients an aortic valve and supracoronary ascending aorta replacement, and 1 patient had a second homograft implantation. Patients reoperated on for homograft endocarditis received a second homograft implantation, a Shelhigh bioconduit (Shelhigh, Millbum, New Jersey) and mechanical aortic valve replacement, respectively. Six patients (28.6%) died after reoperation. Three patients died after reoperation for endocarditis of the homograft, 2 patients after reoperation for false aneurysm and one patient after reoperation for structural valve deterioration. Three of these patients underwent a second or third reoperation. Five- and 10-year freedom from reoperation is 94.5% ± 1.8% and 76.5 ± 5.3% as presented in Figure 2.

![Figure 2](image-url)
Table 4. Indication for Reoperation (n=21)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>- structural valve disease</td>
<td>12</td>
</tr>
<tr>
<td>- false aneurysm</td>
<td>3</td>
</tr>
<tr>
<td>- endocarditis homograft</td>
<td>3</td>
</tr>
<tr>
<td>- coronary sclerosis</td>
<td>1</td>
</tr>
<tr>
<td>- mitral valve regurgitation</td>
<td>1</td>
</tr>
<tr>
<td>- pericarditis constrictiva</td>
<td>1</td>
</tr>
</tbody>
</table>

**Endocarditis**

Endocarditis of the homograft valve was reported in 4 patients (3.2%) of whom one was treated with antibiotics for 6 weeks, and three required reoperation. The medically treated patient recovered completely, but all patients reoperated on for endocarditis of the homograft died soon after the reoperation. The indication for the initial ARR was native valve endocarditis for 3 patients and prosthetic valve endocarditis for 1 patient. The recurrent endocarditis developed 4, 20, 92, and 114 months after the initial operation. The microorganism initially found in the blood culture was different in the second blood cultures in all patients with a recurrent endocarditis of the homograft. The actuarial freedom from endocarditis of the homograft at 5 and 10 years was 99.5% ± 0.5% and 93.5% ± 3.5%, respectively.

**Structural valve deterioration**

Reoperation and replacement of the aortic homograft due to structural valve deterioration was reported in 12 patients. Mean length of time between initial ARR and reoperation was 75.3 months (range 16 to 121). One patient was in the process of evaluation for reoperation due to structural valve deterioration at the end of the follow-up period. One patient died after reoperation for structural valve deterioration. Actuarial freedom from structural valve deterioration at 5 and 10 years was 98.1% ± 1.1% and 85.8% ± 4.5%, respectively.

**Thromboembolism**

One patient developed thromboembolism resulting in stroke with permanent sequel after 61 months of the initial operation. Like thromboembolism, anticoagulant-related bleeding events (n=0) were rarely seen.
Other complications
During follow-up 22 patients needed a definitive pacemaker.

Homograft valve function
Echocardiographic evaluation of the homograft function was performed by most cardiologists when there was a clinical indication. Otherwise, this study was repeated once in 24 months, approximately. A recent echocardiographic evaluation is defined as an echocardiographic study within 24 months before April 30, 2003, the closing date for follow-up. A recent echocardiographic assessment of the homograft valve function was available in 124 patients (71.3%). Data from this evaluation are listed in Figure 3. There was 1 patient in the follow-up group period of 0 to 3 years, who had a grade III aortic regurgitation. This patient had no complaints and the clinical situation was acceptable. The follow-up group period of 4 to 6 years had a predominantly favourable result. Most patients with a severe grade III or IV aortic regurgitation were in the group with the longest follow up. All these patients were in the evaluation for a reoperation. Also the percentage of grade II aortic regurgitation was increasing.

Figure 3 Echocardiographic data: aortic regurgitation during follow-up. Open bars = trivial; light shaded bars = mild; dark shaded bars = moderate; black bars = severe. (yrs = years.)
DISCUSSION

Since the beginning of homograft aortic valve replacement in our centre, the freestanding aortic root replacement has been the technique of choice for the reasons previously described (10). In brief, being a geometrically single functional unit of the homograft at the implantation, it is expected to reduce both early and late postoperative regurgitation (12,13). More than half of the patients in our series had active endocarditis (n=125) and we believe that in such complex aortic root disease the aortic root replacement technique offers additional advantages because it can fill subannular defects with the muscular cuff of the soft annulus and help restore atrioventricular continuity. More recently, however, we would also consider implanting a biological valve conduit in aortic valve endocarditis (14). The rationale is based on several observations. Firstly, the promising initial results with the conduit. Secondly, these valves are readily available on the shelf in all sizes, so the operation can be performed immediately if necessary. Finally, the overall results from our series for reoperations on the homograft root are disappointing; a reoperation on the calcified homograft root is not only challenging for the surgeon, but also especially for the patient.

At the evaluation of results of homograft series one must clearly identify whether viable or nonviable valves are being implanted; and when fresh valves are used, how fresh they are, as was pointed out by O’Brien and associates (9). According to this, we have good results of the cryopreserved homografts comparable to those described in other series (15-19). Overall survival at 10 years was 70.8%, similar to the 73% survival at 9 years demonstrated by Takkenberg and associates (15), 74% survival at 10 years reported by Doty and associates (16) and 85% survival at 8 years in the series of Kirklin and associates (17).

Cryopreserved aortic homograft demonstrates excellent freedom from thromboembolism in this series. In the first three months postoperative acenocoumarol is the choice of oral anticoagulation. After this period, it is switched to acetylsalicylic acid. Only one thromboembolic event was reported on a mean follow-up of 5.8 years. It is not clear whether this extremely low rate is reliable. Usually very little information
on minor thromboembolic events is available, be it from the patient or from the patient’s physician. On the other hand, important thromboembolic events tend to be well documented. Anyway, the overall low incidence of thromboembolic events in our series confirms the findings of other groups. Endocarditis of the homograft developed in 4 patients of which 3 were reoperated on, and one patient was medically treated. Doty and associates (16) reported only one case of homograft endocarditis in 117 patients. In their series only 15 (13%) patients had clinical evidence of aortic valve endocarditis, compared to 125 (58.7%) patients with aortic valve endocarditis in our series. Kirklin and associates (17) reported 3 cases of endocarditis of the homograft in 178 patients followed up for 9 years. Endocarditis was reported as preoperative indication in 41 patients (23%) in their series.

To date, with a mean follow-up of 5.8 years there was structural valve deterioration reported in 12 patients. The freedom from structural valve deterioration at 5 years in our series is acceptable and similar to other comparable studies (15-18). From our results, structural valve degeneration occurred early (less than 5 years) in 4 patients. This has influenced considerably our strategy as to which patients should benefit from a homograft valve. In the earlier phase of the study, the homografts were offered to young adults and patients with endocarditis. Nowadays, in our institution, homografts are seldom offered to young adults, but are still considered for endocarditis patients.

Reoperations for homograft dysfunction carried a high mortality in our series. This was particularly so in patients with homograft endocarditis. It has been our strategy to remove the complete homograft root at reoperation for endocarditis. This has proven to be not the simplest of solutions. Reoperation in the non-endocarditis group had a more favourable outcome, because a less aggressive surgery could be performed.

In conclusion, cryopreserved aortic homografts function well on mid-term. The incidence of structural valve failure is acceptable. Reoperations for homograft endocarditis carry a high mortality.
REFERENCES


The Ross Operation: an Evaluation of a Single Institution’s Experience

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Chapter 3

ABSTRACT

Background. Pulmonary autograft aortic root replacement was used in adults. Risk factors for aortic valve incompetence (AI) and pulmonary homograft valve stenosis are indentified.

Methods. From February 1991 through May 2003, 103 patients, with a mean age of 35.2 ± 9.5 years, underwent aortic root replacement with the pulmonary autograft. Annulus reinforcement (reduction annuloplasty or use of root ring) was carried out in 45 patients. In all but 1 patient, the right ventricular outflow tract was reconstructed with a cryopreserved pulmonary homograft. Mean follow-up duration was 6.0 ± 2.8 years (range 0.3 to 11 years).

Results. There were no hospital deaths. Overall patients survival was 98.9 ± 1 % at 1 year and 97.3 ± 1.9 % at 10 years. Autograft function follow-up resulted in 5 patients requiring reoperation for aortic incompetence. The univariate risk factors for aortic incompetence at discharge and during follow-up were respectively annulus reinforcement (p=0.05) and bicuspid aortic valve (p=0.05). Reoperation for homograft failure occurred in 1 patient. During follow-up, 24 patients (25.5%) developed homograft stenosis (gradient > 20 mm Hg). Univariate analysis indicated the diameter of the homograft (p=0.001) as factor associated with stenosis during follow-up. Cox regression identified smaller diameter of the homograft (p=0.001) and older age of donor (p=0.002) as independent risk factor for the development of homograft stenosis.

Conclusions. The Ross operation can be performed with few complications. Although both the aortic autograft and the pulmonary homograft have limited durability, this has not yet resulted in considerable reoperation rates and associated morbidity and mortality.
INTRODUCTION

Ross introduced the replacement of a diseased aortic valve by means of a pulmonary autograft in 1967 (1). Ross’ group identified the advantages of the autograft valve as excellent hemodynamic performance, freedom from anticoagulation and, for children, the potential for growth. Relatively high mortality, early failure rates reported, and the complexity of the procedure have deterred many surgeons from embracing this procedure in the past (2, 3). Recent experience, on the contrary, indicates that this operation can be performed with acceptable risk (4, 5). This can be explained by increasing experience and modification of the surgical technique from an original subcoronary technique toward a full root replacement technique (6). This article describes our medium-term experience with the Ross operation in 103 adult patients (with aortic valve disease) and presents the result of serial echocardiographic study assessing the function of the autograft and the pulmonary homograft.

PATIENTS AND METHODS

From February 1991 through May 2003, 103 selected adult patients with a mean age of 35.2 ± 9.5 years (range 17 to 65 years old) underwent root replacement with the pulmonary autograft. The characteristics of the patients are reported in Table 1. Our operative techniques for the Ross operation and autograft annulus reinforcement and reduction have been previously described (7). Briefly, all operations were performed with the use of mild systemic hypothermia; myocardial protection was provided by low sodium normopotassic cardioplegic solution and topical cooling. In all the patients, the autograft was implanted as a free standing root. The diameter of the aortic annulus and pulmonary autograft was assessed by intraoperative measurement with cylindrical sizers. In 39 patients (37.8%) the proximal autograft suture line was reinforced by a 5-mm large strip of fresh autologous pericardium or prosthetic material (Teflon felt (Impra Inc, subsidiary of C.R. Brand, Temple, AZ), or a woven Dacron ring (C.R. Brand, Haverhill, PA)). In 12 patients (11.6%), significant dilatation of the aortic annulus (diameter exceeding the Z + 2 value for the body surface area), required aortic
annulus reduction. It was carried out by placing two 2-0 polypropylene sutures as a purse-string in a single horizontal plane just below the aortic annulus (8). Homograft reconstruction of the right ventricular outflow tract (RVOT) was accomplished with a cryopreserved pulmonary homograft in 102 patients and with a bovine pericardium mounted xenograft in 1 patient. All cryopreserved pulmonary homografts were provided by Bio Implant Service Foundation (BIS; Leiden, The Netherlands). The donors had a mean age of 45.2 ± 12.9 years (range 9 to 66 years old). Concomitant procedures included mitral valve plasty in 1 patient and open mitral commissurotomy in 1 patient. Mean cardiopulmonary bypass time was 187.8 ± 35.8 min (range 133 to 287 min) and mean aortic cross-clamp time was 137.6 ± 26.5 min (range 98 to 232 min).

Table 1. Preoperative Patient Characteristics (n=103)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>mean (SD)</td>
</tr>
<tr>
<td></td>
<td>35.2 ± 9.5</td>
</tr>
<tr>
<td><strong>Gender (male)</strong></td>
<td>71</td>
</tr>
<tr>
<td><strong>NYHA class</strong></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>59 (57.3%)</td>
</tr>
<tr>
<td>II</td>
<td>27 (26.2%)</td>
</tr>
<tr>
<td>III</td>
<td>17 (16.5%)</td>
</tr>
<tr>
<td>IV</td>
<td>-</td>
</tr>
<tr>
<td><strong>Left ventricular ejection fraction</strong></td>
<td></td>
</tr>
<tr>
<td>&gt; 50%</td>
<td>68 (66.0%)</td>
</tr>
<tr>
<td>30 – 50%</td>
<td>31 (30.1%)</td>
</tr>
<tr>
<td>&lt; 30%</td>
<td>4 (3.9%)</td>
</tr>
<tr>
<td><strong>Predominant lesion</strong></td>
<td></td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>20 (19.4%)</td>
</tr>
<tr>
<td>Aortic incompetence</td>
<td>51 (49.5%)</td>
</tr>
<tr>
<td>Mixed aortic disease</td>
<td>32 (31.1%)</td>
</tr>
<tr>
<td><strong>Aortic valve morphology</strong></td>
<td></td>
</tr>
<tr>
<td>Bicuspid (congenital)</td>
<td>44 (42.7%)</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>59 (57.3%)</td>
</tr>
<tr>
<td><strong>Previous aortic valve surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Valve replacement</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Valvulotomy</td>
<td>5 (4.8%)</td>
</tr>
<tr>
<td>Valvuloplasty</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Enucleation of subvalvular membrane</td>
<td>2 (1.9%)</td>
</tr>
</tbody>
</table>

Values are mean ± 1 standard deviation (SD); NYHA = New York Heart Association
Postoperative Follow-up

Follow up was conducted between June and July 2003 by two investigators and was 97% complete. The 3 patients, whose follow-up was incomplete, were censored at the time of their last follow-up.

Assessment included New York Heart Association (NYHA) functional class, drug therapy, electrocardiogram, chest radiogram and transthoracic M-mode, two dimensional and color-flow Doppler echocardiograms. The echocardiographic examinations were performed at discharge, 3 to 6 months postoperation, 1 year after the operation, and on a regular base thereafter. The mean transvalvular pressure gradient of the aortic and pulmonary valves was calculated (9). Color-flow Doppler was used to detect aortic and pulmonary valvular incompetence, and severity was subjectively graded as trivial (1+), mild (2+), moderate (3+) and severe (4+).

Statistical Analysis

All analyses were performed using SPSS 8.0 for Windows (SPSS Inc, Chicago, IL). Continuous variables were expressed as the mean ± standard deviation (SD) and were analysed by using the unpaired two-tailed t test. Categorical variables were presented as percentage and were analysed with the χ² test or Fischer’s exact test when appropriate. Univariate and multivariate analysis was used to study potential determinants of aortic valve incompetence (AI) grade 2 or more at discharge. The following categorical variables were considered: sex, gender, preoperative AI grade 2 or more, preoperative left ventricle function less than 40 %, annulus reinforcement (reduction annuloplasty or use of root ring), and bicuspid aortic valve. Variables that achieved a p value < 0.2 in the univariate analysis were examined by using multivariate analysis with forward stepwise logistic regression for the developing of AI grade 2 or more. The same variables analysed for AI at discharge were studied for AI grade 2 or more during follow-up. Variables that achieved a p value less than 0.2 in the univariate analysis were examined by using Cox proportional hazard regression for the developing of AI grade 2 or more.

The development of a 20 mm Hg or greater gradient through the pulmonary homograft during follow-up was also investigated. For the univariate analysis the following variables were considered: diameters of the pulmonary homograft (continuous
variable), age of the donor (continuous variable), and donor status (beating heart, non-beating heart; categorical variables). Variables that achieved a p value less than 0.2 in the univariate analysis were examined by using Cox proportional hazard regression for the developing of a 20 mm Hg or greater gradient through the homograft during follow-up. Estimates for long-term survival and freedom from morbid events were made by the Kaplan-Meier method.

RESULTS

Mean follow-up was 6.0 ± 2.8 years (range 0.3 to 11 years).

Mortality

There were no hospital deaths. There were two late deaths. One patient died from bacterial meningitis 1 year postoperatively. The other patient developed pulmonary homograft endocarditis (proven by autopsy) 8 years after the operation and died acutely. Overall patients survival is shown with the Kaplan-Meier analysis in Figure 1, with 98.9 ± 1 % at 1 year and 97.3 ± 1.9 % at 10 years.

![Figure 1. Overall patient survival](image.png)
Morbidity
Eleven patients (10.7 %) required early reoperation (<24 hours) for bleeding. Four patients (3.9 %) developed myocardial infarction (creatine phosphokinase > 300 IU/L, myocardial band > 5 %); 2 of them underwent coronary angiography that revealed a stenosis of the reimplanted right coronary ostium; the lesion was treated in both cases with a stent implantation. Both interventions were done within the same admission, a few days after surgery. The other two patients refused to undergo the coronary angiography, and are actually in NYHA class I. Three patients underwent pacemaker implantation because of permanent atrioventricular block. Two of these patients had extensive annular calcification, and 1 patient was a reoperation.

Reoperations for Autograft Failure
Five patients (4.8 %) have required reoperation on the autograft valve for incompetence. Two patients developed severe aortic incompetence respectively 6 weeks and 15 months after the Ross procedure. In the first patient the pulmonary autograft was quadricuspid and this congenital anomaly was detected only at the end of the initial operation. In the second patient the cause of the autograft failure was unclear. In both cases a mechanical prosthesis was implanted within the autograft. Another patient has undergone aortic valve replacement 4 years after the operation for progressive autograft incompetence due to annular dilatation. The remaining 2 patients were reoperated respectively 3 and 8 years after the initial operation for a dilatation of the autograft root at the sinotubular level and severe AI detected by echocardiogram; in both cases a mechanical composite graft was implanted. Freedom (Kaplan-Meier) from reoperation on pulmonary autograft is 98.7 ± 1.2 % at 5 years, 96 ± 2.9 % at 7 years, and 87.4 ± 6.4 % at 10 years (Fig 2).

Reoperations for Pulmonary Homograft Failure
Reoperation for homograft failure occurred in 1 patient; he developed stenosis of the pulmonary homograft (pulse Doppler gradient of 50 mm Hg) 13 months after the initial operation. The patient, initially treated with patch angioplasty of the pulmonary homograft, had replacement of the homograft 3 years postoperatively. Freedom from reoperation on pulmonary homograft is 98.7 ± 1.2 % at 10 years.
Valvular Endocarditis

Endocarditis occurred in 2 patients. In the first patient the endocarditis was localised on the pulmonary autograft and was successfully treated with antibiotics; a recent echocardiogram of the patient depicts a trivial aortic incompetence. In the second patient, as already described, the endocarditis was localised on the pulmonary homograft and was fatal. Freedom from endocarditis is 98.3 ± 1.6 % at 6 years and 95.7 ± 3 % at 10 years.

Cerebrovascular Accident

Three patients had cerebrovascular accident (CVA) 9 months, 4 years, and 5 years postoperatively, respectively. There was no documented arrhythmia or clot in the heart on echocardiography. Freedom from CVA is 96.7 ± 2.2 % at 6 years and 92.5 ± 4.6 % at 10 years.

When including death of any cause, reoperation, CVA and endocarditis as events, the event-free survival at 1 year is 98.9 ± 1 %, 96.3 ± 2 % at 5 years, 85.5 ± 5.4 at 8 years, and 75.4 ± 7.3 at 10 years (Fig 3).
Figure 3. Event-free survival.

**Autograft Valve Function**

All the patients underwent two-dimensional echocardiogram at discharge. There was no aortic incompetence (AI) in 69 patients (67.0%), 30 patients (29.1%) had a trivial AI; 3 (2.9%) had a mild AI, and 1 (1.0%) had severe AI requiring reoperation 6 weeks after the Ross procedure. The influence of the variables including sex, gender, preoperative AI grade 2 or more, preoperative left ventricular function, bicuspid valve, annulus reinforcement (reduction annuloplasty or use of root ring) on the incidence of early AI grade 2 or more (only 4 patients) was investigated. Regurgitation was central in the majority of patients. At the univariate analysis, annulus reinforcement ($p = 0.05$) was the only factor associated with AI grade 2 or more at discharge. Multivariate analysis failed to show any significant independent risk factor, but numbers in the subgroups were small.

Recent echocardiographic assessment (within 1 year of closing date of the follow-up study) of the pulmonary autograft valve function was available in 73% of patients (excluding 2 deaths and 5 reoperations); in 85% of patients, an echo of less than 2 years old was available. All patients without recent echocardiographic assessment have stable clinical examination. Details are listed in Table 2. None of the patients had aortic valve stenosis. The number of patients with AI grade 2 or more was significantly
(p = 0.03) higher during follow-up compared to discharge (4 of 103 at discharge and 18 of 94 during follow-up). The same variables analysed for their influence on AI at discharge were studied for their influence of AI grade 2 or more during follow-up. At the univariate analysis, bicuspid aortic valve (p = 0.05) was the only factor associated with AI grade 2 or more during follow-up. Cox proportional hazards regression failed to show any significant independent risk factor. Freedom from mild or more AI was 97.8 ± 1.5 % at 1 year, 91.3 ± 3.1 % at 5 years, 76.4 ± 6.1 % at 8 years, and 62.9 ± 8.7 % at 10 years.

Table 2. Aortic valve function during follow-up in the 94 patients who survived with their pulmonary autograft in place

<table>
<thead>
<tr>
<th>Aortic Incompetence</th>
<th>Discharge to 3 years</th>
<th>4 to 6 years</th>
<th>7 to 9 years</th>
<th>&gt; 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>4</td>
<td>13</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Trivial (grade I)</td>
<td>11</td>
<td>19</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Mild (grade II)</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Moderate (grade III)</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Severe (grade IV)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Homograft Valve Function**

None of the patients had pulmonary valve stenosis (gradient > 20 mm Hg, peak velocity across the pulmonary homograft > 1.4 m/s) at discharge, 9 patients (8.7%) had trivial pulmonary regurgitation. During follow-up, 24 patients (25.5%) developed pulmonary homograft stenosis. One patient, as already mentioned, underwent reoperation on the homograft for a stenosis of greater than 50 mm Hg. The influence of the variables including diameter of the pulmonary homograft, age of the donor, and donor status on the development of homograft stenosis was investigated. Univariate analysis indicated that the diameter of the pulmonary homograft (p < 0.001) was the only factor associated with pulmonary stenosis during follow-up. Cox proportional hazards regression identified smaller diameter of the pulmonary homograft and older age of donor as independent risk factor for the development of pulmonary homograft stenosis (Table 3).
Table 3. Cox proportional hazards regression for the development of pulmonary stenosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Range</th>
<th>Multivariate p value</th>
<th>Multivariate risk ratio per unit increase (95% Confidence Limit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homograft Diameter (increasing)</td>
<td>20 – 30 mm</td>
<td>0.001 (-)</td>
<td>0.6 (0.4-0.8)</td>
</tr>
<tr>
<td>Donor age (increasing)</td>
<td>9 – 66 years old</td>
<td>0.002 (+)</td>
<td>1.05 (1.02-1.09)</td>
</tr>
</tbody>
</table>

* The p value is followed by (-) to indicate increased risk with smaller values or (+) to indicate increased risk with larger values. Gradient > 20 mmHg, peak velocity across the pulmonary homograft > 1.4 m/s.

**Functional Status**

At the closure of the study, 94 patients were alive with their pulmonary autograft in place. Of those, 84 patients (87.2%) had no cardiac symptoms and were in NYHA functional class I, 11 (11.7%) were in functional class II, and 1 (1.1%) was in functional class III. In this patient, a recent echocardiogram revealed a severe AI and a pseudoaneurysm of the autograft at the distal suture line. He is scheduled for reoperation.

**DISCUSSION**

Our 11-year experience with the autograft root replacement confirms that the Ross procedure can be performed with low mortality and morbidity. This has only been possible by careful selection of the patients: only adults with few comorbidity were scheduled for the operation.

Autograft failure necessitating reoperation occurred in only 5 patients. In 1 patient the pulmonary homograft was quadricuspid and this congenital malformation was detected only at the end of the initial operation. The quadricuspid pulmonary valve is a rare congenital heart anomaly; the reported incidence ranges from 1 in 400 to 1 in 1000 autopsies (10). The rapid progression of regurgitation of a quadricuspid pulmonary valve in aortic position has already been described in literature (11) and this graft must be considered, therefore, an inadequate candidate for use as an autograft in the Ross procedure.
Aortic insufficiency during follow-up was mainly caused by dilatation at the annular level (1 patient) or at the sino-tubular level (2 patients). The annular dilatation can cause AI because it flattens the scalloped shape of the annulus, preventing coaptation of the cusps (12). Reinforcement of the annulus or adjustment of the diameter to the body surface area of the patient has been recommended for prevention of AI (12, 13). Therefore, in all procedures since 1997 we invariably use a reinforcement ring or a reduction annuloplasty if the aortic annular diameter exceeds the Z + 2 value. In 2 patients the cause of the AI was dilatation of the pulmonary arterial wall at the sinotubular junction. Dilatation of the sinotubular junction cause AI because it pulls the commissures of the aortic valve away from the center of the aortic root, preventing coaptation of the cusps (12). Both patients had an bicuspid aortic valve. The relationship between bicuspid aortic valve and aortic wall abnormalities has been widely described (14, 15). Given the common embryogenesis of the aorta and pulmonary artery (16), Sa and colleagues (15) hypothesized that similar histologic lesions could exist also in the pulmonary wall of patients with bicuspid aortic valve. They found, in fact, a greater prevalence of degenerative changes of the media of the pulmonary artery of patients with an bicuspid aortic valve. We do not routinely reinforce the distal suture line, but are considering it.

The results of our study, in terms of autograft competence, are consistent with the outcomes of other studies using the autograft as a free standing root (17, 18). Over the last few years, the implantation technique has been addressed; in our opinion the free standing root technique is critical to achieve and maintain consistent autograft competence. There is some evidence that the long-term results, in term of valve competence, are superior after root replacement than after cylindric and subcoronary techniques (19). The advantages of the freestanding aortic root over the other two techniques has also been shown by Elkins and associates (13) and is probably due to the fact that the geometry of the autograft, and therefore the coaptation of the cusps, is better preserved. In contrast with this theory is the study of Sievers and associates (20) that shows good mid-term results with subcoronary or root inclusion technique; however, long-term results are needed.

The present series is of particular interest as 79.8 % of the patients with a recent echocardiogram have an AI less than grade 2, and continue to maintain the benefits
of their pulmonary autograft. The majority of them are in NYHA class I and conduct a normal life without anticoagulation.

Right ventricular outflow tract reconstruction, in our series, was routinely done with a cryopreserved homograft. We, and others (18, 19) have noticed a significant increase in pulmonary flow velocities during follow-up. Pulse-wave Doppler indicated that the gradient was located directly at the homograft leaflets and not at the anastomosis. We are inclined to think, therefore, that the increased flow velocities are valve related and on the base of the results of the multivariate analysis, we support the current practice of oversizing the homograft by at least 2 to 3 mm (21); usually this results in a pulmonary homograft with a minimum internal diameter of 28 mm.

The influence of immune activation on human valve homograft deterioration remains unclear. Nevertheless, Oei and associates (22) reported that in rats, aortic valve homografts are able to induce a donor reactive immune response that is related to early graft destruction and incompetence. Further studies are needed to fully understand the role of immunologic factors in human valve homograft deterioration. Older age of donor was identified as independent risk factor for the development of pulmonary homograft stenosis ($p = 0.002$); Lund and coworkers (23) found, in a large series of patients, that donor age above 65 years old was a significant risk factor for homograft failure. According to previous studies (23, 24), however, we keep the donor-patient age mismatch within 10 years.

In conclusion, our long-term experience with the Ross operation has confirmed the suitability and safety of this operation for patients with aortic valve disease. Although both the aortic autograft and the pulmonary homograft have limited durability, this has not yet resulted in considerable reoperation rates and associated morbidity and mortality.
REFERENCES


Chronic Type A Dissection in a Pulmonary Autograft

Abdullah Kaya MD, Robin H. Heijmen MD, PhD, Willem Vreuls MD, Cornelis A. Seldenrijk MD, PhD, Marc A. Schepens MD, PhD

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ABSTRACT

A 37-year-old patient presented with severe aortic valve insufficiency due to massive dilatation of the neo-aortic root (77 mm diameter) 14 years after a Ross procedure. Intraoperatively, the dilatation appeared to be caused by a localized chronic dissection of the pulmonary autograft. Surgery consisted of a modified Bentall procedure with a mechanical composite valve, with an uncomplicated postoperative course.
INTRODUCTION

In experienced hands, the Ross operation shows minimal perioperative complications. Although both the autograft and the allograft have demonstrated limited durability, this has not yet resulted in considerable reoperation rates [1]. In the long term, however, dilatation of the pulmonary autograft root may occur [2, 3]. Histopathological investigations have identified the presence of cystic medial necrosis, elastic fragmentation and findings indicative of chronic media rupture, which may have been the cause of progressive dilatation [4]. Herein is reported a rare case of chronic type A dissection in a pulmonary autograft, identified 14 years after the initial Ross procedure.

Case report

In 1991, a 23-year-old man with severe insufficiency of a tricuspid aortic valve underwent elective aortic root replacement with the pulmonary autograft and implantation of a pulmonary allograft (24 mm) in the right ventricular outflow tract (i.e. the Ross procedure). The patient had suffered from rheumatic fever as a child. The postoperative period was uncomplicated, and pre-discharge echocardiography showed trivial neo-aortic valve insufficiency and pulmonary valve stenosis, with a peak pressure gradient of 18 mmHg. At two years after surgery, the aortic root appeared thickened on echocardiography, and the diameter had slightly dilated (38 mm). The trivial aortic valve insufficiency persisted, and the pulmonary valve stenosis peak pressure gradient remained at 19 mmHg (mean 12 mmHg). In 1998, the patient was still symptom-free, and echocardiography revealed identical findings as described previously; consequently, the patient withdrew from further medical attention. In April 2005, the patient reported to a local hospital with acute palpitation, dyspnea and fatigue; he was examined but, without any conclusive diagnosis, was discharged with medical therapy. One month later, transthoracic echocardiography revealed a left ventricular end-diastolic dimension of 78 mm with massive aortic insufficiency, normal myocardial thickness, and contractility. The mechanism of the aortic insufficiency was not clear on echocardiography or subsequent angiography, though the latter technique showed an asymmetrically dilated proximal ascending aorta (Figure 1 A). Under the
suspicion of severe autograft degeneration, the patient was referred to the present authors’ institution. A repeat echocardiography showed severe left ventricle dilatation, good left ventricular function, and massive aortic insufficiency with a severe aortic root aneurysm (maximum diameter 77 mm). Following preoperative screening and acquisition of consent, the patient was reoperated on in August 2005. During surgery, and following redo sternotomy and extensive adhesiolysis, the asymmetrically dilated aortic root was evident. The right posterior side of the aortic root and ascending aorta was densely adherent to the superior vena cava and right atrium. Therefore, cardiopulmonary bypass was instituted through the groin. The distal ascending aorta was cross-clamped at the base of the innominate artery, and aortotomy performed. Myocardial arrest was achieved with antegrade Bleese cardioplegia until the septal temperature was 10 °C. Upon inspection of the root, there appeared to be an intimal rim that commenced at the lateral side of the left coronary ostium and extended circumferentially approximately 1 cm distal to the non-coronary annulus (Figure 1 B). The distal anastomosis of the autograft, as well as the ascending aorta, was free of dissection and the aortic leaflets appeared normal. No valve-sparing procedure was performed as the patient had strictly requested the implantation of a mechanical aortic valve prosthesis. Therefore, a Bentall procedure was performed, re-implanting the left coronary ostium as an inlay (due to severe adhesions posteriorly) and the right coronary ostium as a button. The graft used as replacement was a mechanical composite of 29 mm diameter (Carboseal® Valsalva; CarboMedics Inc., Austin, Texas, USA). The patient was successfully and uneventfully weaned from extracorporeal circulation. Histologic examination of the explanted pulmonary autograft revealed degeneration of the elastic fibers of the media due to cystic medial necrosis (Figure 2). There was a sparse chronic inflammatory infiltrate in the pulmonary autograft, and no acute infiltrate or fibrin deposition, which confirmed chronic pulmonary autograft dissection. The leaflets showed normal histological findings. The hospital stay was uneventful and the patient discharged on day 7 after surgery. At a 16-month follow-up examination the patient remained asymptomatic.
Chronic Type A Dissection in a Pulmonary Autograft

Figure 1. (A) Aortic angiogram showing asymmetric root dilatation without a definite intimal flap. (B) The aortic root as viewed from the operating surgeon. An intimal rim (arrow) is present in the pulmonary autograft.

Figure 2. (A) Histology of the resected pulmonary autograft root wall transition, showing a dissection (asterisk) in the lower media of the autograft. (B) The autograft wall has a marked degeneration of the elastic fibers of the media due to cystic medial necrosis, with deposition of mucopolysaccharide material. Staining: (A) elastic van Gieson, original magnification x50; (B) hematoxylin and eosin, original magnification x400.

DISCUSSION

Pulmonary autograft root dilatation is one of the most common late complications seen after the Ross procedure [2, 3]. Likewise, it is well known that the majority of patients with bicuspid aortic valves have histological abnormalities in the aortic and the pulmonary artery wall, such as cystic medial necrosis, elastic fragmentation, and changes in smooth muscle cell orientation [4]. In theory, a combination of pulmonary
autograft dilatation and abnormal histology might lead to dissection within the autograft, but this long-term complication is rarely described. To the present authors’ knowledge, only three reports have been made regarding dissection in a dilated pulmonary autograft with initially a bicuspid aortic valve [5-7]. The present patient had a tricuspid aortic valve and had developed a chronic type A dissection in the dilated pulmonary autograft 14 years after the Ross procedure, with a histological finding of cystic medial necrosis and degeneration of the elastic fibers of the media. This proved that root dilatation and even dissection late after autograft root replacement is not only related to bicuspid aortic valve disease (which is supported by histopathologic studies [8, 9]), but also to other variables such as operative technique and hemodynamic condition, which are associated factors for root dilatation following the Ross procedure.

The present case illustrates that aortic dissection may occur as a long-term complication in a pulmonary autograft, even with an initially tricuspid aortic valve. A high degree of suspicion is warranted in evaluating acute symptoms in a patient following the Ross procedure. Strict monitoring, for example with computed tomography, is advised to follow the dimensions of the autograft root. In view of the life-threatening aspect of this late complication, it is worth considering reoperation in an early dilated phase (prophylactic), as would occur in a patient with a collagen disease such as Marfan syndrome.
REFERENCES


Valve-Sparing Aortic Root Replacement using the Reimplantation Technique: Single Center Experience

Abdullah Kaya, MD, Robin H. Heijmen, MD, PhD, Johannes C. Kelder, MD, Wim J. Morshuis, MD, PhD.

Submitted
Chapter 5

ABSTRACT

Objective: We retrospectively evaluated our results with the valve-sparing aortic root replacement using the reimplantation technique.

Methods: From January 1998 through March 2010, 81 patients with a mean age of 51.9 years (range 19 to 75 years) underwent the reimplantation technique. Indication for surgery was aneurysmal disease of the aorta in 65 patients (80.2 %), acute type A aortic dissection in 14 patients (17.3 %) and pending aortic rupture in 2 patients (2.5 %).

Results: There was no hospital mortality. New neurological symptoms were observed in 2 patients (2.5 %) and were temporary. Mean follow-up was 65.2 months (range 8.1 – 144.8 months). During follow-up 9 deaths occurred (11.1 %), mainly because of a neoplasm (n = 6). The overall survival at 1 and 5 years is 97.5 % (95 % CL, 94.2 % - 99.9 %) and 94.4 % (95 % CL, 89.1 % - 99.9 %) respectively. No tromboembolic events were reported. Nine patients (11.1 %) required a reoperation due to recurrent severe aortic valve regurgitation (n = 7) or endocarditis of the reimplanted aortic valve (n = 2). Echocardiographic follow-up showed mild or no aortic valve regurgitation in most patients (n = 57), mild to moderate regurgitation in 5 patients and one patient with moderate aortic valve regurgitation.

Conclusions: Retrospective analysis of valve-sparing aortic root replacement with the reimplantation technique demonstrated excellent in-hospital results, as well as good medium-term follow-up mortality and tromboembolic rates and an acceptable reoperation percentage, but close follow-up is mandatory.
INTRODUCTION

The gold standard for patients with aortic root aneurysms is implantation of a valved conduit for aortic root replacement and re-implantation of the coronary buttons, first described by Bentall and de Bono (1). Initially these conduits contained a mechanical valve, but subsequently there were biological options, like the allograft and recently there are also biological valved conduits commercially available. These are designated substitutes when the aortic valve is involved in the aortic root pathology. When there is no valvular disease or the aortic valve regurgitation is secondary to the aortic root aneurysm, the morphologically normal aortic cusps can be retained. After attempts of repair of regurgitant aortic valves in the early years of cardiac surgery, valve-sparing aortic root replacement techniques for aortic valve regurgitation gained recurrent interest in the eighties and nineties (2-5). These procedures evolved during the years and are nowadays classified in a remodeling (Yacoub) and a reimplantation (David) technique (4,5). In our center we have used the reimplantation procedure more than the remodeling technique for different aortic root pathology. In this report we describe and analyse our experience with the reimplantation technique.

PATIENTS AND METHODS

Patients

From January 1998 through March 2010, 81 consecutive patients with a mean age of 51.9 years (range 19 to 75 years) underwent valve-sparing aortic root replacement using the reimplantation technique. There were 52 male (64.2 %) and 29 female (35.8 %) patients. The Ethics Committee approved this retrospective cohort study and waived the need for patient consent. Aortic root pathology treated using the reimplantation technique consisted of 65 aneurysms (80.2 %), 14 acute type A aortic dissections (17.3 %) and 2 pending aortic ruptures (2.5 %). The intervention was a reoperation after previous cardiac surgery in 2 patients (2.5 %). Eighteen patients (22.2 %) were treated under emergent or urgent conditions, because of type A aortic dissection, pending aortic rupture or symptomatic, rapidly dilating aortic aneurysms.
One patient was preoperatively on the ventilator. Comorbid medical conditions consisted of hypertension (n = 47, 58.0 %), Marfan syndrome (n = 13, 16.1 %), chronic obstructive pulmonary disease (n = 10, 12.4 %), renal dysfunction (n = 7, 8.6 %; serum creatinine > 120 μmol/L, one patient on hemodialysis), previous cerebrovascular accident or transient ischemic attack (n = 7, 8.6 %) and diabetes (n = 5, 6.2 %). Mean aortic diameter for aneurysmatic disease was 59.8 ± 9.8 mm (range 44 - 90 mm). Concomitant aortic valve pathology consisted of severe aortic regurgitation (grade ≥ 3) in 43 patients (53.1 %). A bicuspid aortic valve was present in 2 patients (2.5 %). Preoperative mitral valve regurgitation (grade ≥ 3) as a comorbid cardiac lesion was present in 2 patients (2.5 %) and coronary artery disease in 7 patients (8.6 %). Pertinent patient data are given in Table 1.
Table 1. Patient characteristics (n = 81)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean (SD ; range)</td>
<td>51.9 (12.4 ; 19-75)</td>
<td></td>
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<table>
<thead>
<tr>
<th>Gender</th>
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</thead>
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<tr>
<td>male</td>
<td>52</td>
<td>64.2</td>
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<table>
<thead>
<tr>
<th>NYHA class</th>
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</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>47</td>
<td>58.0</td>
</tr>
<tr>
<td>II</td>
<td>21</td>
<td>25.9</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>6.2</td>
</tr>
<tr>
<td>IV</td>
<td>8</td>
<td>9.9</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Indication</th>
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<td>Aneurysmatic disease</td>
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<td>80.3</td>
</tr>
<tr>
<td>- degenerative</td>
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<td></td>
</tr>
<tr>
<td>- annuloaortic ectasia</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>- post-dissection</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Acute type A dissection</td>
<td>14</td>
<td>17.3</td>
</tr>
<tr>
<td>Pending aortic rupture</td>
<td>2</td>
<td>2.5</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Valvular disease</th>
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</thead>
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<tr>
<td>Aortic valve regurgitation</td>
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<td>19.7</td>
</tr>
<tr>
<td>- grade I</td>
<td>20</td>
<td>24.7</td>
</tr>
<tr>
<td>- grade II</td>
<td>23</td>
<td>28.4</td>
</tr>
<tr>
<td>- grade III</td>
<td>20</td>
<td>24.7</td>
</tr>
<tr>
<td>- grade IV</td>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>2</td>
<td>2.5</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Reoperation</th>
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<th>%</th>
</tr>
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<tr>
<td>Previous mitral valve</td>
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<tr>
<td>Previous ascending aorta</td>
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<table>
<thead>
<tr>
<th>Comorbid medical conditions</th>
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<th>%</th>
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<tbody>
<tr>
<td>Hypertension</td>
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<td>58.0</td>
</tr>
<tr>
<td>Marfan</td>
<td>13</td>
<td>16.1</td>
</tr>
<tr>
<td>COPD</td>
<td>10</td>
<td>12.4</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>7</td>
<td>8.6</td>
</tr>
<tr>
<td>CVA</td>
<td>7</td>
<td>8.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5</td>
<td>6.2</td>
</tr>
</tbody>
</table>

SD = standard deviation; NYHA = New York Heart Association; COPD = Chronic Obstructive Pulmonary Disease; CVA = Cerebral Vascular Accident.
Procedure

Standard cardiopulmonary bypass was used in all operations and carbon dioxide insufflation in the operation field since 2005. The aortic cannulation site was mainly the distal ascending aorta (n = 52) or the common femoral artery (n = 29) in case of a reoperation or a type A aortic dissection. Cold crystalloid antegrade cardioplegia was administrated through the aortic root or coronary ostia selectively with intermittent cardioplegic reinfusion if needed. During cardioplegic arrest, the myocardial septal temperature was measured and kept around 10 °C using cold saline. Depending on the aortic pathology, the location and extension of the lesion, a distal clamp could be used in 26 cases (32.1 %). If the lesion extended to the aortic arch necessitating open distal anastomosis, deep hypothermic circulatory arrest was used in 18 cases (22.2 %) and antegrade selective cerebral perfusion with mild hypothermia was used in 37 cases (45.7 %) (6, 7). The root was circumferentially dissected down to the nadir of the aortic annulus. All abnormal sinus tissue was excised, leaving a 5 to 6 mm rim of aortic tissue along the annulus. The coronary ostia were dissected in the form of a button and mobilized in all patients. The diameter of the aortic graft was determined using the David-Feindel formula: graft diameter = \[2 \times (H_{\text{cusp}} \times 2/3)\] + 5 mm (5). A ruler was used to measure the height of the cusp (H_{\text{cusp}}) in mm from the deepest point of the nadir to the free edge at the nodule of Arantius. The proximal suture technique was the same in all cases and consisted of suturing the proximal graft with interrupted, horizontal 4-0 polypropylene mattress sutures through the left ventricular outflow tract and continuous 5-0 polypropylene sutures in a scalloped fashion immediately above the insertion of the aortic cusps. Only in one patient aortic cusp repair was done in terms of primary closure of a fenestration.

A straight Dacron graft (Intergard, Maquet, Rastatt, Germany) was used in 46 patients (56.8 %) and a Valsalva graft (Gelweave Valsalva, Vascutek, Renfrewshire, Scotland) in 35 patients (43.2 %) and the choice was based on surgeon preference. The diameter of the implanted straight Dacron grafts ranged from 24 to 32 mm with a median of 30 mm and the diameter of the Valsalva grafts ranged from 26 to 30 mm with a median of 28 mm. Aortic root and distal ascending aorta replacement was done in 38 patients (46.9 %). Root replacement and ascending aorta with partial arch replacement was effectuated in 33 patients (40.7 %). Finally, aortic root, ascending aorta and total
arch replacement with or without elephant trunk was performed in 10 patients (12.4 %). Concomitant procedures included planned coronary artery bypass grafting in 7 patients (8.6 %), coronary artery bypass grafting due to peroperative technical problems in 1 case (1.2 %) and mitral valve repair or replacement in 2 patients (2.5 %). Operative data are given in detail in Table 2.

Table 2. Operative characteristics (n = 81)

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
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<tr>
<td>Emergency</td>
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<td></td>
</tr>
<tr>
<td>Elective</td>
<td>63</td>
<td>77.8</td>
</tr>
<tr>
<td>Emergent</td>
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<td>22.2</td>
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<tr>
<td>Cannulation site</td>
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<td></td>
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<tr>
<td>Ascending aorta</td>
<td>52</td>
<td>64.2</td>
</tr>
<tr>
<td>Common femoral artery</td>
<td>29</td>
<td>35.8</td>
</tr>
<tr>
<td>Perfusion data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPB and distal clamp</td>
<td>26</td>
<td>32.1</td>
</tr>
<tr>
<td>DHCA</td>
<td>18</td>
<td>22.2</td>
</tr>
<tr>
<td>ASCP</td>
<td>37</td>
<td>45.7</td>
</tr>
<tr>
<td>CPB time min, mean (SD ; range)</td>
<td>214.0 (59.9 ; 117 - 474)</td>
<td></td>
</tr>
<tr>
<td>Aortic clamp time</td>
<td>152.0 (36.7 ; 66 - 230)</td>
<td></td>
</tr>
<tr>
<td>DHCA time</td>
<td>21.0 (5.1 ; 15 - 30)</td>
<td></td>
</tr>
<tr>
<td>ASCP time</td>
<td>45.0 (20.1 ; 18 - 90)</td>
<td></td>
</tr>
<tr>
<td>Extent of aorta replacement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Ascending</td>
<td>38</td>
<td>46.9</td>
</tr>
<tr>
<td>+ Ascending and partial Arch</td>
<td>33</td>
<td>40.7</td>
</tr>
<tr>
<td>+ Ascending and total Arch</td>
<td>2</td>
<td>2.5</td>
</tr>
<tr>
<td>+ Ascending, total Arch and ET</td>
<td>8</td>
<td>9.9</td>
</tr>
<tr>
<td>Concomittant procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG planned</td>
<td>7</td>
<td>8.6</td>
</tr>
<tr>
<td>CABG unplanned</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>Mitral valve repair or replacement</td>
<td>2</td>
<td>2.5</td>
</tr>
</tbody>
</table>

CPB = cardiopulmonary bypass; DHCA = deep hypothermic circulatory arrest; ASCP = antegrade selective cerebral perfusion; SD = standard deviation; ET = elephant trunk; CABG = coronary artery bypass grafting.
Follow-up
Recent (< 6 months) information about the status of all hospital survivors was collected from the referring cardiologist, by visit at our outpatient clinic, our cardiology department or by their general physician. The closing interval for follow-up was between February and May 2011 and included physical examination, computed tomography scan, echocardiography and chest radiography, if available. End-points of the study were death, valve-related death, reoperation for valve failure and endocarditis of the aortic valve. These end-points were defined according to the guidelines reported by Akins and associates (8).

Data Analysis
Retrospective review was done on the data of all consecutive patients who underwent valve-sparing aortic root replacement using the reimplantation technique. Quantitative data are presented as mean ± standard deviation. Odds Ratio’s (OR) and Fisher’s exact p-value were used for comparison. Kaplan-Meier survival curves were used for analysis of survival times. Precision was indicated by 95 % confidence limits (CL). All statistical analyses were done by R (version 2.9 www.r-project.org).

RESULTS
Early Results
There were no hospital deaths. Median intensive care unit stay was 3 days (range 1–52 days). Six patients (7.4 %) needed ventilatory support for > 48 hours and a tracheostomy was inserted in 2 patients (2.5%). A rethoracotomy was performed in 14 patients (17.3 %), mostly for excessive bleeding (n = 8), because of leakage from the coronary reattachment line (n = 3), from the distal suture line (n = 3) or cannulation site (n = 2). Clinical signs of tamponade (n = 6) were also a predominant reason for rethoracotomy. There was no permanent pacemaker implantation. Postoperative temporary hemodialysis was necessary in 2 patients (2.5 %) and both recovered without need for long-term dialysis.

New neurological symptoms were observed in 2 emergently operated patients (2.5 %) after a type A dissection. Ischemic cerebral accident occurred in 1 patient and critical
illness polyneuropathy in 1 patient. The neurological symptoms were all temporary and resolved completely.

**Follow-up results**

All hospital survivors (n = 81) were entered in the follow-up study (100 % complete). Mean follow-up was 65.2 months (range 8.1 – 144.8 months). Total follow-up was 440 patient-years. During follow-up 9 patients (11.1 %) died. Cause of death during follow-up was neoplasm in 6 patients, cardiac failure in 1 patient and unknown in 2 patients. The mean period between initial valve-sparing aortic root replacement and death was 53.1 months (range 2.1 – 114.6 months). The last echocardiography available before death showed predominantly a mild aortic valve regurgitation (grade I/IV n = 7) and two patients had mild to moderate aortic valve regurgitation (grade II/IV n = 2). The overall survival at 1 and 5 years is 97.5 % (95 % CL, 94.2 % - 99.9 %) and 94.4 % (95 % CL, 89.1 % - 99.9 %) respectively. This is presented in Figure 1.

**Figure 1.** Kaplan-Meier survival curve after valve-sparing aortic root replacement with the reimplantation technique.
Seven patients (8.6 %) required a reoperation for recurrence of severe aortic valve regurgitation and two patients (2.5 %) underwent a reoperation, because of endocarditis of the spared aortic valve. These reoperated patients had an aortic regurgitation at discharge of trivial to mild (grade ≤ I/IV) on echocardiography. Mean period between the initial reimplantation procedure and reoperation was 43.3 months (range 20.5 – 102.8 months). One patient received a homograft and the rest of the patients an aortic valve replacement with a mechanical valve. None of the patients died after a reoperation. Two other patients underwent descending aorta replacement, because of an aneurysm. The 1 and 5 years freedom from reoperation is 100 % (95 % CL, 96.0 % - 100 %) and 86.8 % (95 % CL, 78.7 % - 95.8 %) respectively. This is presented in Figure 2.

![Figure 2](image-url)
New onset endocarditis of the reimplanted aortic valve was reported in 2 patients (2.5 %) and both were reoperated as described above and survived. Both patients had Streptococcus as a cultured microorganism. No late thromboembolic or bleeding events were reported and also no false aneurysms were seen.

Follow-up imaging was done by echocardiography. This showed severe aortic valve regurgitation in 7 patients en endocarditis in 2 patients, who were reoperated as described above. Beside these patients the majority of the follow-up patients had mild aortic valve regurgitation (grade I/IV n = 57), 5 patients had mild to moderate aortic valve regurgitation (grade I-II/IV) and in one patient moderate aortic valve regurgitation (grade II/IV) was observed. The last patient had no symptoms and is being followed up.

DISCUSSION

Aortic regurgitation can be the result of disease from the aortic valve, the ascending aorta or both. When there is no valvular disease or the aortic valve regurgitation is secondary to the aortic root pathology (aneurysm), the morphologically normal aortic cusps can be retained. In our institution the reimplantation technique for valve-sparing aortic root replacement, first described by David and Feindel in 1992, is most commonly used (5). After reports with promising mid-term results in 1997 we started to use the aortic valve reimplantation technique (9, 10). Initially, aortic root or ascending aorta aneurysms were the primary indication for this reimplantation technique. After gaining more experience the indication expanded to type A dissections if the aortic valves were unaffected.

In this retrospective analysis of 81 patients with a mean age of 51.9 years, with predominantly an aneurysm or a type A dissection, who underwent valve-sparing aortic root replacement with the reimplantation technique, there was no hospital mortality. There were 2 major adverse events in terms of ischemic cerebral accident in 1 patient and critical illness polyneuropathy in another patient. Both patients were emergently operated after a type A dissection. These new neurological symptoms were temporary and resolved completely. These short-term results are excellent and similar to other reports about the reimplantation technique (11-14).
During a mean follow-up of 65.2 months, 9 patients (11.1%) died, mainly because of a neoplasm (n = 6). These patients had predominantly mild aortic valve regurgitation before death. The overall survival at 5 years is 94.4% (95% CL, 89.1% - 99.9%), which is comparable with other reports on the reimplantation technique (11-14). The 5 years survival of our mechanical Bentall group (mean age 54 years) is 87% (15). A direct comparison between these groups would not be correct, because the patient groups are not comparable.

Reoperation for recurrence of severe aortic valve regurgitation was necessary for 7 patients (8.6%) after a mean period of 43.3 months between the initial reimplantation procedure and reoperation. Half of the patients (n = 4) who needed a reoperation were initially operated in the ‘learning curve’ phase at the beginning of the reimplantation technique in our institution. Five reoperated patients had a straight Dacron graft and 2 patients a Valsalva graft, but univariate analysis showed no significance between the type of graft and reoperation (HazardRatio = 0.88, 95% CL, 0.21 - 3.69, p = 0.86). Only one reoperated patient was a Marfan patient. There were 2 other patients who were reoperated because of endocarditis of the reimplanted aortic valves. The 5 years freedom from reoperation is 86.8% (95% CL, 78.7% - 95.8%). Compared to other reimplantation technique reports our reoperation percentage (11.1%) is acceptable (12-14). Only the group of David and associates has an excellent rate of reoperation of the reimplantation procedure of 0.9% (2/228) (11). The risk of a reoperation in the future for recurrence of aortic regurgitation should be weight preoperatively together with the patient to the risk of anticoagulation related complications, when a mechanical conduit is used or even if a biological valved conduit is chosen (16).

Nowadays, some biological valved conduits have good clinical results and these should be considered in elderly (> 70 years) patients instead of valve-sparing aortic root replacement, which is surgically more demanding with longer aortic cross clamp times and the chance to be reoperated in the future (17).

In our institution, after valve-sparing aortic root replacement, patients get only the first 3 months acetyl salicylic acid. Thereafter, anticoagulation is stopped, unless there is another indication. During the follow-up of 440 patient-years no thromboembolic or bleeding events were reported. In this view the valve-sparing aortic root replacement with the reimplantation technique is superior to mechanical and biological valved conduits (15-17).
In conclusion, our results of valve-sparing aortic root replacement with the reimplantation technique show excellent in-hospital morbidity and mortality rates as well as good medium-term follow-up mortality and tromboembolic rates. The reoperation percentage for recurrent aortic regurgitation is acceptable, but close follow-up is mandatory and long term results are to be awaited for.
REFERENCES


Traumatic Aorto-Right Ventricular Fistula

with Aortic Insufficiency

Abdullah Kaya MD, Paul Dekkers MD, Antonino Loforte MD, Wybren Jaarsma MD, PhD, Wim J. Morshuis MD, PhD

ABSTRACT

We present a case of a traumatic aorto-right ventricular fistula coexistent with aortic insufficiency due to perforation of the left coronary leaflet, which is a lesion rarely described in the literature. We compare our experience with reports from the literature.
INTRODUCTION

Since the first case report of traumatic aorto-right ventricular fistula in 1958, there have been 42 case reports in literature [1-3]. Only 17 of these describe the combination of traumatic aorto-right ventricular fistula with aortic insufficiency [2, 3]. We present a case of an aorta to the right ventricular fistula combined with aortic insufficiency after a penetrating trauma. The aim is to compare our experience with the various approaches described in the literature.

Case report

A 19-year-old man was stabbed with a small bladed stiletto knife in the left third intercostal space adjacent to the sternum. On admission, the patient was alert and responsive with stable vital signs. There was no significant past medical history or medication. There was no thrill or murmur heard on examination. Chest roentgenogram showed fluid in the left hemithorax. A mild to moderate amount of pericardial effusion associated with left sided-pleural fluid was detected by transthoracic echocardiography. Mild aortic valve insufficiency and a small ventricular septal defect was also seen (Fig 1). Unfortunately the patient refused transesophageal echocardiography, which could give more detailed information about the pathology. A left-sided chest drain produced 1270 ml of serosanguineous fluid over a 2-day period. At re-evaluation by transthoracic echocardiography the findings were unchanged. The patient was hemodynamically stable and maintained adequate oxygen saturation. He had no complaints and was optimally mobilized. He made an uneventful recovery and insisted on being discharged against medical advice. He did not report for follow-up at the outpatient clinic. A month later he was urgently readmitted due to severe dyspnea. A continuous pre-cordial murmur was heard on auscultation and congestion of his jugular veins was evident. Pericardial tamponade was confirmed by transthoracic echocardiography and subxiphoid pericardiocentesis was performed with 1060 ml of blood evacuated. Re-evaluation with transthoracic echocardiography confirmed moderate aortic valve regurgitation, an increased left to right shunt between the aortic root and right ventricular outflow tract, and a moderately dilated right ventricle (Fig 1).
Figure 1. Parasternal short axis view showing increased left to right shunt (arrow) after 1 month. (Ao = Aorta; RA = Right Atrium; RV = Right Ventricle; RVOT = Right Ventricular Outflow Tract)

At surgery, a median sternotomy was performed, the pericardium was opened, and the epicardial adhesions were released. On cardiopulmonary bypass with double venous cannulation, cold crystalloid cardioplegia was selectively infused through the coronary ostia until a septal temperature of 10 °C was achieved. The aorto-right ventricular communication was exposed through the transverse aortotomy. An imaginary line could be drawn from the lacerated left coronary cusp, crossing the interleaflet triangle between the left and right coronary cusp, penetrating the right ventricular outflow tract (Fig 2). A small opening was also noticed in the pericardium covering the right
ventricle, thus confirming the trajectory of the penetrating injury. No superficial entry wound was found on the right ventricle, probably due to the adhesions. The septal communication was closed through the aortotomy with continuous 5-0 polypropylene suture. A small (5 mm) clean cut longitudinal laceration at the base of the left coronary cusp of the aortic valve could be repaired primarily with a double layer continuous 7-0 polypropylene suture (Fig 2). Postoperatively to the repair, an intraoperative transesophageal echocardiographic evaluation showed no evidence of aortic valve insufficiency or left to right shunt. The postoperative course was uneventful and the patient was discharged on postoperative day 5. To our disappointment, thus far the patient has continued to abstain from following up at the outpatient clinic.

Figure 2. Artist impression of an intracardiac direction of penetrating injury (arrow). Inset: postoperative repair diagram of left coronary cusp (asterisk). (LCC = Left Coronary Cusp; LCO = Left Coronary Ostium; RVOT = Right Ventricular Outflow Tract.)
DISCUSSION

Traumatic aorto-right ventricular fistulas with aortic insufficiency are rare lesions after penetrating thoracic injuries. According to the literature this specific lesion has been reported 17 times previously [2, 3].

The time interval between injury and surgical intervention is variable. Some patients require immediate surgical management due to instable hemodynamics, but others may have a delayed clinical presentation and therefore delayed repair [3-5]. The interval until definitive repair could be as long as 17 years, as reported by Ehrenstein and colleagues [6]. In this case, the time interval between injury and repair was 56 days. The propensity for shunts in aorto-right ventricular fistulas to increase in size with time may explain the delayed time interval to definitive repair as reported by some authors [3-5, 7]. All patients with a traumatic aorta to right ventricular fistula combined with aortic insufficiency (except for one patient) were operated on sooner or later, as reported in the review by Samuels and colleagues [2]. Our experience confirms that a traumatic aorto-right ventricular shunt with aortic insufficiency has a tendency to increase in size with time. Therefore it is advisable that these patients be operated on at an early stage.

Although patients with aorto-right ventricular fistula combined with aortic insufficiency after a penetrating trauma may have no cardiac symptoms, they should be thoroughly evaluated, preferably by transesophageal echocardiography and operated on during the same admission. If left untreated, congestive heart failure will invariably develop.
REFERENCES

Stentless Biological Valved Conduit for Aortic Root Replacement: Initial Experience with the Shelhigh BioConduit model NR-2000C

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Chapter 7

ABSTRACT

Objectives: We retrospectively evaluated our results with the Shelhigh biological conduit model NR-2000C (Shelhigh, Inc, Millburn, NJ).

Methods: From November 1998 through December 2007, 175 patients with a mean age of 71.1 ± 7.4 years underwent aortic root replacement with a Shelhigh biological conduit. Indication for surgery was aneurysmal disease of the aorta in 120 (68.6 %) patients, aortic valve endocarditis in 20 (11.4 %), acute type A aortic dissection in 11 (6.3 %), and other in 24 (13.7 %) patients.

Results: Overall hospital mortality was 13.7 % (n=24; 95% confidence limits, 9.0 % - 19.7 %). Cause of death was cardiac failure in 12 patients, central neurological damage in 5 patients, pulmonary in 3 patients, gastrointestinal ischemia in 2 patients, and aorta-related in 2 patients. Mean follow-up was 3.1 years (range 0.2 - 9.9 years). In total, 50 (33.1%) late deaths occurred; of these 7 were valve-related. The overall survival at 1 and 5 years is 77.6 % ± 3.2 % and 54.6 % ± 4.6 % respectively. Six (4.0 %) patients required reoperation, either for endocarditis of the bioconduit (n=5) or for false aneurysm (n=1). Endocarditis of the bioconduit was reported in 11 (7.3 %) patients, of whom 6 were treated nonoperatively and 5 required reoperation.

Conclusions: Midterm results of the implantation of the Shelhigh biological valved conduit are worrisome. The relatively high incidence of endocarditis of the Shelhigh bioconduit has forced us to look for other alternatives.
INTRODUCTION

Bentall and DeBono described the first complete replacement of the aortic root with a conduit in 1968 (1). The initial composite valved graft contained a mechanical valve, but nowadays there are also complete biological conduits as substitute for aortic root replacement. The homograft or autograft is an alternative but has the disadvantage of limited donor availability and durability (2). Aortic valve-sparing surgery may not be applicable for all pathologic situations of the aortic root and in particular the aortic valve (3, 4). Nowadays, only a few biological valved conduits are readily available off the shelf in all sizes and without the need for lifelong oral anticoagulation. At the end of the nineties, a new stentless biological valved conduit, Shelhigh bioconduit, model NR-2000C (Shelhigh, Inc, Millburn, NJ), was introduced. This is a bovine pericardial straight graft with an incorporated porcine stentless valve, which is glutaraldehyde cross-linked, detoxified, and heparin-treated (No-React process). Since 1998 we have used this biological valved conduit for aortic root replacement in the elderly patients or for specific indication, such as infective aortic root abscesses. In this report we describe and analyse our initial results.

PATIENTS AND METHODS

Patients

From November 1998 through December 2007, 175 patients with a mean age of 71.1 years (range 31-84 years) underwent aortic root replacement with a Shelhigh bioconduit model NR-2000C. Fifty-two (29.7 %) patients were 75 years or older. There were 102 (58.3%) male and 73 (41.7%) female patients. The Ethics Committee approved this retrospective cohort study and waived the need for patient consent. Aortic root diseases treated with this complete biological conduit consisted of the following: aneurysm, n = 120 (68.6 %); aortic valve endocarditis, n = 20 (11.4 %); acute type A aortic dissection, n = 11 (6.3 %), calcified (‘porcelain’) aortic root, n = 8 (4.6 %); and other, for example, small aortic annulus or aortic stenosis owing to pannus formation after previous aortic valve replacement, n = 16 (9.1 %). The intervention
was a reoperation after previous cardiac surgery in 45 patients (25.7 %) of whom the majority (33 patients) had previous aortic valve surgery. Twenty-two (12.6 %) patients were treated under emergency conditions. Four (2.3 %) patients were preoperatively supported with the ventilator, mainly owing to complicated type A aortic dissection or prosthetic valve endocarditis. Comorbid medical conditions consisted of hypertension (n = 123, 70.3 %), renal dysfunction (n = 25, 14.3 %; serum creatinine > 120 μmol/L among whom 2 required hemodialysis), chronic obstructive pulmonary disease (n = 23, 13.1 %), previous cerebrovascular accident or transient ischemic attack (n = 16, 9.1 %), diabetes (n = 13, 7.4 %) and Marfan syndrome (n = 3, 1.7 %). Mean aortic diameter for aneurysmatic disease was 59.7 ± 10.1 mm (range 43-108 mm). Concomitant aortic valve disease consisted of severe aortic regurgitation (grade ≥ 3) in 88 patients (50.3 %), moderate to severe aortic valve stenosis (mean gradient 65.6 ± 25.6 mmHg) in 54 patients (30.9 %) and mixed aortic valve lesion in 26 patients (14.9 %). A bicuspid aortic valve was present in 16 patients (9.1 %). Preoperative mitral valve regurgitation (grade ≥ 3) as a comorbid cardiac lesion was present in 8 patients (4.6 %) and coronary artery disease in 46 patients (26.3 %). Pertinent patient data are given in Table 1.
Table 1. Patient characteristics (n=175)

| Age (years) mean (SD ; range) | 71.1 (7.4 ; 31-84) |
| Gender | male 102 58.3 |
| NYHA class | I 30 17.1 |
| | II 62 35.5 |
| | III 53 30.3 |
| | IV 30 17.1 |
| Indication | Aneurysmatic disease 120 68.6 |
| | - degenerative 110 |
| | - false 6 |
| | - post dissection 4 |
| | Aortic valve endocarditis 20 11.4 |
| | - prosthetic 16 |
| | - native 4 |
| | Acute type A dissection 11 6.3 |
| | Calcified aortic root 8 4.6 |
| | Other 16 9.3 |
| Valvular disease | Aortic valve regurgitation  |
| | - grade I 55 31.4 |
| | - grade II 32 18.3 |
| | - grade III 55 31.4 |
| | - grade IV 33 18.9 |
| | Aortic valve stenosis 54 30.9 |
| | mean gradient, mmHg (SD;range) 65.6 (25.6 ; 20-135) |
| | Mixed aortic valve lesion 26 14.9 |
| | Bicuspid aortic valve 16 9.1 |
| Reoperation | 45 25.7 |
| | Previous aortic valve surgery 33 |
| Comorbid medical conditions | Hypertension 123 70.3 |
| | Renal insufficiency 25 14.3 |
| | COPD 23 13.1 |
| | CVA 21 12.0 |
| | Diabetes 13 7.4 |
| | Marfan 3 1.7 |

SD = standard deviation; NYHA = New York Heart Association; COPD = Chronic Obstructive Pulmonary Disease; CVA = Cerebral Vascular Accident.
Chapter 7

**Procedure**

Full aortic root replacement for composite valve graft insertion with the button technique for reattachment of the coronary ostia was used in all patients in combination with standard cardiopulmonary bypass (5). The aortic cannulation site was mainly the distal ascending aorta or the common femoral artery in case of a reoperation or a type A dissection. Cold crystalloid cardioplegic solution was administrated antegrade through the aortic root or coronary ostia selectively with intermittent cardioplegic reinfusion if needed. During cardioplegic arrest, the myocardial septal temperature was measured and kept around 10 °C using a Shumway cold line. Depending on the aortic disease, the location and extension of the lesion, a distal clamp could be used in 67 (38.3 %) patients. If the lesion extended to the aortic arch necessitating open distal anastomosis, deep hypothermic circulatory arrest was used in 63 (36.0 %) patients and antegrade selective cerebral perfusion with mild hypothermia was used in 45 (25.7 %). The latter technique was used when a circulatory arrest period of more than 30 minutes was anticipated (6, 7). The proximal suture technique was by preference of the surgeon and consisted of three separate, continuous 4-0 polypropylene sutures (n = 108, 61.7%) for the attachment of the bioconduit sewing ring to the aortic annulus or interrupted pledget-supported 2-0 braided polyester mattress sutures (n = 67, 38.3 %). In recent years a continuous 5-0 polypropylene suture was used to reinforce the proximal annular anastomosis against anastomotic leakage.

The diameter of the implanted biological conduits ranged from 21 to 27 mm with a median of 25 mm. Aortic root replacement solely was done in only 12 patients (6.9 %). Aortic root and distal ascending aorta replacement was realized in 72 patients (41.1 %). Root replacement and ascending aorta with partial arch replacement was effected in 68 patients (38.9 %). Finally, aortic root, ascending aorta and total arch replacement with or without elephant trunk was performed in 23 patients (13.1 %). In 99 patients (56.6 %) a woven vascular graft was used as an extension of the bioconduit and the native downstream aorta. The graft diameter ranged from 22 to 32 mm with a median of 26 mm.

Concomitant procedures included planned coronary artery bypass grafting in 41 patients (23.4 %), coronary artery bypass grafting owing to peroperative technical problems in 6 patients (3.4 %), mitral valve repair or replacement in 5 patients (2.9 %),
combination of planned coronary artery bypass grafting and mitral or tricuspid valve surgery in 5 patients (2.9 %) or other procedures in 7 patients (4.0 %), like Morrow procedure or closure of an atrial septal defect. Operative data are given in detail in Table 2.

Table 2. Operative characteristics (n=175)

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td><strong>Emergency</strong></td>
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<td></td>
</tr>
<tr>
<td>Elective</td>
<td>153</td>
<td>87.4</td>
</tr>
<tr>
<td>Emergent</td>
<td>22</td>
<td>12.6</td>
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<tr>
<td><strong>Cannulation site</strong></td>
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<tr>
<td>Ascending aorta</td>
<td>134</td>
<td>76.6</td>
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<tr>
<td>Common femoral artery</td>
<td>39</td>
<td>22.3</td>
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<tr>
<td>Axillary artery</td>
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<td>1.1</td>
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<tr>
<td><strong>Perfusion data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPB and distal clamp</td>
<td>67</td>
<td>38.3</td>
</tr>
<tr>
<td>DHCA</td>
<td>63</td>
<td>36.0</td>
</tr>
<tr>
<td>ASCP</td>
<td>45</td>
<td>25.7</td>
</tr>
<tr>
<td>CPB time; min, mean (SD; range)</td>
<td>190.4 (53.6; 117-376)</td>
<td></td>
</tr>
<tr>
<td>Aortic clamp time</td>
<td>125.1 (30.2; 73-228)</td>
<td></td>
</tr>
<tr>
<td>DHCA time</td>
<td>24.5 (5.9; 17-40)</td>
<td></td>
</tr>
<tr>
<td>ASCP time</td>
<td>57.1 (14.8; 38-79)</td>
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<tr>
<td><strong>Conduit suture technique</strong></td>
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<tr>
<td>Continuous polypropylene sutures</td>
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<tr>
<td>Interrupted pledgeted polyester sutures</td>
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<tr>
<td><strong>Extent of aorta replacement</strong></td>
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<tr>
<td>Root only</td>
<td>12</td>
<td>6.9</td>
</tr>
<tr>
<td>+ Ascending</td>
<td>72</td>
<td>41.1</td>
</tr>
<tr>
<td>+ Ascending and partial Arch</td>
<td>68</td>
<td>38.9</td>
</tr>
<tr>
<td>+ Ascending and total Arch</td>
<td>6</td>
<td>3.4</td>
</tr>
<tr>
<td>+ Ascending, total Arch and ET</td>
<td>17</td>
<td>9.7</td>
</tr>
<tr>
<td><strong>Concomittant procedure</strong></td>
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<td></td>
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<tr>
<td>CABG planned</td>
<td>41</td>
<td>23.4</td>
</tr>
<tr>
<td>CABG unplanned</td>
<td>6</td>
<td>3.4</td>
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<tr>
<td>Mitral valve repair or replacement</td>
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<td>2.9</td>
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<tr>
<td>Combination</td>
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<td>2.9</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>4.0</td>
</tr>
</tbody>
</table>

CPB = cardiopulmonary bypass; DHCA = deep hypothermic circulatory arrest; ASCP = antegrade selective cerebral perfusion; SD = standard deviation; ET = elephant trunk; CABG = coronary artery bypass grafting.
Follow-up
Recent (< 6 months) information about the status of all hospital survivors was collected from the referring cardiologist, by visit at our outpatient clinic, our cardiology department, or by their general physician. December 31, 2008 was the closing date for follow-up and included physical examination, computed tomography scan, echocardiography, and chest radiography, if available. Endpoints of the study were death, valve-related death, reoperation for valve failure, and endocarditis of the bioconduit. These endpoints were defined according to the guidelines reported by Akins and associates (8).

Data Analysis
Retrospective review was done on the data of all consecutive patients who underwent aortic root replacement with the Shelhigh bioconduit. Quantitative data are presented as mean ± standard deviation. Odds Ratio’s (OR) and Fisher’s exact p value were used for comparison. Kaplan-Meier survival curves were used for analysis of survival times. Precision was indicated by 95 % confidence limits (CL). All statistical analyses were done by R (version 2.9 www.r-project.org).

RESULTS

Early Results
Overall hospital mortality was 13.7 % (n = 24; 95 % CL, 9.0 %- 19.7%), of which 8.5 % was for elective and 50.0 % for emergency cases (p < 0.0001). All the patients undergoing emergency surgery who died had acute type A dissection or endocarditis, and the predominant cause of death were ischemic cardiac or severe neurological causes. There were 3 intraoperative deaths (1.7 %). All patients who died intraoperatively had poor left ventricular function (ejection fraction ≤ 25 %), 2 had emergency operations and the causes of death were cardiac failure, myocardial infarction, and electromechanical dissociation after ventricular fibrillation. Causes of in-hospital death are summarized in Table 3. Univariate analysis showed acute type A dissection (OR 9.7; 95 % CL, 2.7 - 35.2; p = 0.0005), endocarditis (OR 4.4; 95 % CL, 2.5 – 7.7;
p = 0.0058) and emergency operation (OR 10.8; 95 % CL, 6.4 – 18.1; p < 0.0001) as important variables for hospital mortality. Multivariate analysis did not produce any independent predictor. Especially, there was no independent association between indication type and emergency operation on hospital mortality. The hospital mortality for patients with an aortic aneurysm (non-dissection and non-endocarditis) having elective surgery was 4.2 % (n = 5). In 6 patients (3.4 %), intra-operative problems required a second cardiopulmonary bypass run and in 5 of these patients a second crossclamp of the aorta with cardioplegic arrest was necessary. Main cause was to obtain control of bleeding from the proximal suture line or left coronary ostium anastomosis.

Mean and median intensive care unit stay was 6 days and 3 days respectively (range 1 – 60 days). Thirty-one patients (18.0 %) needed ventilatory support for more than 48 hours and a tracheostomy was inserted in 9 patients (5.2 %). A rethoracotomy was performed in 48 patients (27.9 %), mostly for excessive bleeding (n = 18), because of diffuse leakage (n = 8), from the coronary reattachment line (n = 4), distal bioconduit suture line (n = 2), proximal bioconduit suture line (n = 2) or other (n = 2). Signs of tamponade (n = 17) were also a predominant reason for rethoracotomy and only half of these patients (n =9) did have a clear tamponade during the rethoracotomy. A planned rethoracotomy in the next few days for removal of gauzes (n =12) was the third major cause of rethoracotomy. Perioperative myocardial damage (serum creatinine kinase level > 300 IU/L, with a creatinine kinase MB isoenzyme fraction > 5 %) occurred in 14 patients (8.1 %). Permanent pacemaker implantation was necessary in 17 patients (9.9 %). Postoperative temporary hemodialysis was necessary in 7 patients (4.1 %). Three of these patients died in the hospital, the others recovered without the need for long-term dialysis.

New neurological symptoms were observed in 23 patients (13.1 %). Ischemic cerebral accidents occurred in 19 patients, critical illness polyneuropathy in 2 patients and transient peripheral neuropathy in 2 patients. In the stroke group 7 patients died in the hospital, 2 of non-neurological causes, and permanent neurological damage was manifest in 6 patients (3.4 %). The odds radio for ischemic stroke in the group having deep hypothermic circulatory arrest was 4.6 (95 % CL, 1.7 – 12.8, p = 0.0035) in comparison with the group having antegrade selective cerebral perfusion and distal clamping.
Table 3. Causes of Early and Late death (n=74)

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early: In hospital Operative</td>
<td>24</td>
<td>13.7</td>
</tr>
<tr>
<td>- Elective: - arrhythmia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- Emergent: - heart failure</td>
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<tr>
<td>- late (&gt; 1 year)</td>
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<td>- ruptured aneurysm</td>
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<tr>
<td>Sudden, unexplained</td>
<td>14</td>
<td>9.3</td>
</tr>
</tbody>
</table>

MV = mitral valve.
**Late results**

There were 151 hospital survivors and all were entered in the follow-up study (100 % complete). Mean and median follow-up was 3.1 years and 2.9 years respectively (range 0.2-9.9 years). Total follow-up was 543 patient-years. During follow-up, 50 (33.1 %) patients died, and 15 of these deaths occurred in the first postoperative year. Causes of death during follow-up are summarized in Table 3. Seven of these late deaths were prosthesis-related owing to endocarditis of the bioconduit. Among the other 43 patients with non-prosthesis related late deaths, 8 patients died of cardiac causes, 1 of whom had recurrent endocarditis of the mitral valve prosthesis (Shelhigh) with vegetations on echocardiography. The overall survival at 1 and 5 years is 77.6 % ± 3.2 % and 54.6 % ± 4.6 % respectively. This information is presented in Figure 1 for the total group and selectively for the patients having elective and emergency operations. For the complete follow-up period, there is a significant difference between the elective and emergency groups (p = 0.003). After exclusion of the first 30 postoperative days, this difference disappears (p = 0.679).

![Figure 1. Survival curve after aortic root replacement with a Shelhigh bioconduit for the elective, emergency and total group.](image)
Six (4.0%) patients required reoperation for significant prosthesis dysfunction owing to endocarditis of the bioconduit (n = 5) and false aneurysm (n = 1). Mean length of time between the initial aortic root replacement and reoperation was 21.7 months ± 22.1 months. Three patients underwent reoperation within one year after the initial root replacement, and in all these cases the cause of reoperation was endocarditis. During reoperation most patients received a second Shelhigh bioconduit, except one patient who received a homograft. One patient, known to have a false aneurysm, is being followed up conservatively because she underwent multiple sternal wound explorations, and a reoperation for false aneurysm correction is estimated to be too high a risk. One patient died after reoperation for endocarditis. One- and five-year freedom from reoperation is 76.4% ± 3.2% and 50.8 ± 4.6% as presented in Figure 2.

![Figure 2. Freedom from reoperation after aortic root replacement with a Shelhigh bioconduit](image)

Endocarditis of the Shelhigh bioconduit was reported in 11 patients (7.3%). Five of these patients were reoperated on and only one patient died 3 months after the reoperation, as described earlier. Six patients were not referred for surgery by their
cardiologist and were treated medically, and all these patients died subsequently. Two of them had autopsy, which confirmed endocarditis of the bioconduit. The indication for the initial aortic root replacement was prosthetic valve endocarditis for one patient, and the rest of the patients had new-onset endocarditis of the bioconduit with Staphylococcus and Enterococcus as predominant microorganism. The incidence of late endocarditis was lower in the rethoracotomy group (2.1 %) than in the non-rethoracotomy group (7.9 %; p = 0.2297). Nine (81.8 %) of the 11 patients who had new onset endocarditis received the implant after the year 2003. Mean interval between initial aortic root replacement and new onset endocarditis was 18.9 months ± 20.4 months, with a median of 9.3 months.

Follow-up imaging was mostly done by computed tomography scan. This was available for 82 patients (81.2%) and showed the 2 cases of false aneurysm as described earlier. Distal native aorta diameter increased in 5 patients without indication for reoperation. Dilatation or calcification of the pericardial tube was not observed. Echocardiographic evaluation of the bioconduit function was performed by most referring cardiologists when there was a clinical indication. A recent echocardiographic assessment of the bioconduit function was available in 43 survivors (42.6%). Apart from adequate valve function, this showed previously mentioned vegetations and false aneurysms. Besides, there were 2 patients with moderate aortic regurgitation and 3 patients with moderate aortic stenosis (mean gradient 50.7 ± 12.9 mmHg) during a mean follow-up of 3.1 years.

**DISCUSSION**

The aortic homograft was the first complete biological composite valved graft used in our center, predominantly for endocarditis and for relatively young patients. Its limited donor availability and suboptimal long-term durability has made us less enthusiastic to use this graft (2). As an alternative, commercially available stentless biological valved conduits were introduced, which have the benefit of being readily available off the shelf in all sizes. The Shelhigh bioconduit is such a biological composite valve graft. We used this bioconduit predominantly in the elderly patient (mean age 71 years) with
degenerative aortic root disease, but also in patients with aortic valve endocarditis (mean age 64 years), because of its complete biological aspect.

The limited initial results about the Shelhigh bioconduit in the literature were promising with good clinical and echocardiographic results, even in patients with active infective endocarditis (9-11). Recently, the US Food and Drug Administration (FDA) published a preliminary public health notification on possible contamination and malfunction of devices manufactured by Shelhigh, Inc. (12). After this, Carrel and associates reported several precarious cases of reoperations and unexplained deaths occurring after implantation of the Shelhigh bioconduit (13, 14). In their total group of 115 patients who received a Shelhigh bioconduit, 7 patients (6.1 %) had ‘sudden disastrous findings’ and 4 of them required emergency reoperation. In our series 11 patients (7.3 %) had blood culture positive endocarditis and 5 of them required reoperation. Patients with endocarditis of the bioconduit who were not referred for surgery all died, and in 2 of these patients endocarditis was proven by autopsy. Our aggressive rethoracotomy policy did not have a significant effect on late endocarditis because the incidence of late endocarditis was lower in the rethoracotomy group than in the non-rethoracotomy group (2.1 % vs 7.9 %; p = 0.2297).

Beside endocarditis of the bioconduit, there were 2 patients with false aneurysm formation at the bioconduit and the number of patients with sudden, unexplained death was relatively high (9.3 %). Unfortunately, we could not find detailed information about the cause of death of these patients (mean age, 75.8 ± 8.4 years). It is conceivable that there might be some sudden, unexplained deaths because of endocarditis of the bioconduit. If we look at the 7.3 % incidence of endocarditis of the Shelhigh bioconduit in this study and in our previous homograft series, we note that the incidence of endocarditis of the homograft was only 3.2 %, despite a higher number of patients with endocarditis as the initial indication for surgery (2). A true comparison, however, is not valid, because the patient groups are not comparable. It is important to note that most of the endocarditis of the bioconduit cases (81.8 %) were Shelhigh conduits implanted after 2003. In 2007 the Food and Drug Administration published its preliminary public health notification. As a consequence, we have now strictly limited the implantation of the Shelhigh bioconduit for extensive aortic valve
endocarditis complicated by annular abscesses. In elective setting, we are in search of an alternative for the Shelhigh bioconduit.

Because of the lack of published clinical experience reports specifically about the Shelhigh bioconduit, we sought literature concerning other stentless biological conduits (15-19). Compared with these reports, our operative mortality of 1.7% and hospital mortality of 13.7% satisfies in a group with a mean age of 71 years, extended graft repair of the ascending aorta (41%) and involved aortic arch repair (52%) with aortic valve endocarditis (11.4%) or acute type A dissection (6.3%) in 17.7% of the patients. The incidence of endocarditis of the stentless biological conduits in these reports is lower than our 7.3%. The freedom from reoperation is comparable with these reports.

In conclusion, although perioperative results are satisfactory, the follow-up results are worrisome and the relatively high incidence of endocarditis of the Shelhigh bioconduit in our retrospective single center analysis has led us to change our policy. There is a need for other centers to report their experiences as well, in order to draw more solid conclusions. Patients who have received the Shelhigh bioconduit should be monitored closely and long-term results should be evaluated.
REFERENCES


First 102 Patients with the BioValsalva Conduit for Aortic Root Replacement

Abdullah Kaya, MD, Robin H. Heijmen, MD, PhD, Johannes C. Kelder, MD, Wim J. Morshuis, MD, PhD

The Annals of Thoracic Surgery 2012;94:72-7
ABSTRACT

Objective: We retrospectively evaluated our results with the BioValsalva conduit (Vascutek Terumo, Renfrewshire Scotland), a stentless porcine valve incorporated in a three-layered prosthetic graft.

Methods: From July 2008 through April 2011, 102 patients with a mean age of 70.9 ± 7.3 years underwent aortic root replacement with a BioValsalva conduit. The indication for surgery was aneurysmal disease of the aorta in 81 patients (79.4 %), aortic valve endocarditis in 15 patients (14.7 %), acute type A aortic dissection in 4 patients (3.9 %) and other causes in 2 patients (2.0 %). In 26 patients (25.5 %) the intervention was a reoperation.

Results: Overall hospital mortality was 4.9 % (n = 5; 95 % confidence limit (CL), 1.6 %- 11.1 %). Cause of death was cardiac failure in 2 patients, multiple organ or renal failure in 2 patients and tamponade in 1 patient. Mean follow-up was 8.1 months. During follow-up 3 deaths occurred (3.1 %), because of mediastinitis, cardiac ischemia and arrhythmia. The overall survival at 3 and 12 months was 95.9 % (95 % CL, 92.0 %- 99.9 %) and 92.1 % (95 % CL, 85.7 %- 98.9 %) respectively. Three patients (3.1 %) had new-onset endocarditis of the BioValsalva conduit; 2 of these patients required a reoperation and 1 patient received antibiotic treatment only.

Conclusions: Retrospective analysis of the BioValsalva conduit for aortic root replacement in more than 100 consecutive patients demonstrated satisfactory initial results, with low mortality and acceptable low morbidity rates. Follow-up is mandatory and long-term results are to be awaited.
INTRODUCTION

The composite valved graft used at the first aortic root replacement contained a mechanical valve; currently there are also biological valved conduits that can be used for aortic root replacement (1). The increasing age of patients and the thromboembolic complication risk because of the necessary use of a vitamin K antagonist along with mechanical valves advanced the need for biological valved conduits in the treatment of aortic root pathology conditions. Currently, a few biological valved conduits are available; they have the benefit of being readily available off the shelf in all sizes and do not require lifelong oral anticoagulation and subsequently present a lower thromboembolic risk (2). After disappointing results with the Shelhigh bioconduit (Shelhigh, Millburn, NJ), the BioValsalva conduit (Vascutek Terumo, Renfrewshire Schotland) was introduced in our center (3-5). This conduit is a combination of a Valsalva graft, already introduced in 2000, and a stentless porcine valve (Elan, Vascutek, Terumo) (6). The coated polyester (Dacron) Valsalva graft has to be stored in a dry environment and the biological valve must be stored in glutaraldehyde. This problem is solved by modifying the coated polyester Valsalva graft into a three-layered graft, which allows storage in glutaraldehyde and preserves its impermeability (Figure 1). This vascular graft is made of an uncoated Gelweave (Vascutek, Terumo) polyester inner layer and a polytetrafluoroethylene outer layer, which are glued together with a central, self-sealing elastomeric membrane that makes the graft impermeable (7). The proximal part of the graft has the Valsalva shape, mimicking the sinuses of the aortic root with reduction of tension on the coronary buttons and improvement of coronary flow and valve hemodynamics (8, 9). This new composite bioprosthetic valve has been used for various aortic root pathologic conditions. In this article, we describe and analyse our initial experience in 102 patients.
Figure 1. (A) BioValsalva conduit: a stentless porcine valve incorporated in a 3-layered prosthetic graft. (B) View from inside.
PATIENTS AND METHODS

Patients
From July 2008 through April 2011, 102 consecutive patients with a mean age of 70.9 years (range 34 - 85 years) underwent aortic root replacement with a BioValsalva conduit. There were 69 male (67.6 %) and 33 female (32.4 %) patients. The Ethics Committee at our institution approved this retrospective cohort study and waived the need for patient consent. The aortic root pathologic conditions treated using this composite bioprosthetic valve consisted of 81 aneurysms (79.4 %), 14 cases of prosthetic valve endocarditis (13.7 %), 4 acute type A aortic dissections (3.9 %), 2 false aneurysms after previous aortic root replacement (Shelhigh) (2.0 %) and one native valve endocarditis with root abscess (1.0 %). The intervention was a reoperation after previous cardiac operations in 26 patients (25.5 %) the majority of whom (23 patients) had previous aortic valve operations. Twelve patients (11.8 %) were treated under emergency conditions because of type A aortic dissection or prosthetic valve endocarditis. Comorbid medical conditions consisted of hypertension (n = 64, 62.8 %), chronic obstructive pulmonary disease (n = 16, 15.7 %), diabetes (n = 12, 11.8 %), renal dysfunction (n = 10, 9.8 %; serum creatinine level > 120 μmol/L), previous cerebrovascular accident or transient ischemic attack (n = 7, 6.9 %) and Marfan syndrome (n = 2, 2.0 %). Mean aortic diameter for aneurysmal disease was 54.8 ± 8.3 mm (range 40 - 85 mm). Concomitant aortic valve pathologic conditions consisted of severe aortic regurgitation (grade ≥ 3) in 43 patients (42.2 %), moderate to severe aortic valve stenosis (mean gradient, 67.4 ± 35.7 mmHg) in 24 patients (23.5 %). A bicuspid aortic valve was present in 16 patients (15.7 %). Preoperative mitral valve regurgitation (grade ≥ 3) as a comorbid cardiac lesion was present in 7 patients (6.9 %) and coronary artery disease was seen in 25 patients (24.5 %). Pertinent patient data are given in Table 1.
Table 1. Patient characteristics (n = 102)

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<tr>
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<td><strong>Gender</strong></td>
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<tr>
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<tr>
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<td>- false</td>
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<td>Marfan syndrome</td>
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SD = standard deviation; NYHA = New York Heart Association; COPD = Chronic Obstructive Pulmonary Disease; CVA = Cerebral Vascular Accident.
**Procedure**

Full aortic root replacement for composite valve graft insertion with the button technique for reattachment of the coronary ostia was used in all patients in combination with standard cardiopulmonary bypass and carbon dioxide insufflation in the operative field. The aortic cannulation site was mainly the distal ascending aorta (n = 68) or the common femoral artery (n = 33) in case of a reoperation or a type A aortic dissection. Cold crystalloid antegrade cardioplegia was administrated through the aortic root or coronary ostia selectively with intermittent cardioplegic reinfusion if needed. During cardioplegic arrest, the myocardial septal temperature was measured and kept around 10 °C using a Shumway cold line. Depending on the pathologic condition of the aorta and the location and extension of the lesion, a distal clamp could be used in 62 cases (60.8 %). If the lesion extended to the aortic arch, necessitating open distal anastomosis, deep hypothermic circulatory arrest was used in 11 patients (10.8 %) and antegrade selective cerebral perfusion with mild hypothermia was used in 29 patients (28.4 %), by surgeon preference (10,11). The proximal suture technique was the same in all cases and consisted of suturing the prosthetic sewing ring to the annulus with interrupted pledgeted 2-0 braided polyester mattress sutures, and a continuous 5-0 polypropylene suture was used to reinforce the proximal annular anastomosis against anastomotic leakage. After measuring the appropriate position for the coronary ostia, an opening was made with a blade and not with cautery, because of the polytetrafluoroethylene outer layer. Afterward, circular holes were created with a 4-mm punch and the coronary ostia were reattached with a continuous 6-0 polypropylene suture.

The diameter of the implanted BioValsalva conduits ranged from 21 to 27 mm with a median of 25 mm. Aortic root and distal ascending aorta replacement was done in 64 patients (62.8 %). Root replacement and ascending aorta with partial arch replacement was effectuated in 32 patients (31.4 %). Finally, aortic root, ascending aorta, and total arch replacement with or without elephant trunk was performed in 6 patients (5.9 %). In 37 patients (36.3 %) a woven vascular graft was used as an extension of the BioValsalva conduit and the native downstream aorta. The graft diameter ranged from 24 to 32 mm with a median of 26 mm.
Chapter 8

Concomitant procedures included planned coronary artery bypass grafting in 25 patients (24.5 %), coronary artery bypass grafting because of technical problems in 5 patients (4.9 %), mitral valve repair or replacement in 4 patients (3.9 %), combination of planned coronary artery bypass grafting and mitral or tricuspid valve procedures in 3 patients (3.6 %) or other procedures such as carotid endarterectomy or rhythm procedures, in 3 patients (3.6 %). Operative data are given in detail in Table 2.

Table 2. Operative characteristics (n = 102)

<table>
<thead>
<tr>
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<td>88.2</td>
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<td>Emergent</td>
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<tr>
<td>** Cannulation site**</td>
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<tr>
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<tr>
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<td>32.4</td>
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<tr>
<td><strong>Perfusion data</strong></td>
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<tr>
<td>CPB and distal clamp</td>
<td>62</td>
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</tr>
<tr>
<td>DHCA</td>
<td>11</td>
<td>10.8</td>
</tr>
<tr>
<td>ASCP</td>
<td>29</td>
<td>28.4</td>
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<tr>
<td>Aortic clamp time</td>
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<tr>
<td>DHCA time</td>
<td>20.6 (4.5; 15-30)</td>
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<tr>
<td>ASCP time</td>
<td>37.8 (33.3; 19-194)</td>
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<tr>
<td>+ Ascending</td>
<td>64</td>
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</tr>
<tr>
<td>+ Ascending and partial Arch</td>
<td>32</td>
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<td>+ Ascending and total Arch</td>
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</tr>
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<td>4.9</td>
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<tr>
<td>Other</td>
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<td>2.9</td>
</tr>
</tbody>
</table>

CPB = cardiopulmonary bypass; DHCA = deep hypothermic circulatory arrest; ASCP = antegrade selective cerebral perfusion; SD = standard deviation; ET = elephant trunk; CABG = coronary artery bypass grafting.
Follow-up
Recent (< 6 months) information about the status of all hospital survivors was collected from the referring cardiologist, from visits to our outpatient clinic or our cardiology department, or from their general physicians. February 1 and May 1, 2011 was the closing interval for follow-up and included physical examination, computed tomography, echocardiography and chest radiography, if available. Endpoints of the study were death, valve-related death, reoperation for valve failure, and endocarditis of the BioValsalva conduit. These endpoints were defined according to the guidelines reported by Akins and associates (12).

Data Analysis
Retrospective review was performed on the data of all consecutive patients who underwent aortic root replacement with the BioValsalva conduit. Quantitative data are presented as mean ± standard deviation. Odds ratio’s (OR) and Fisher’s exact p value were used for comparison. Kaplan-Meier survival curves were used for analysis of survival times. Precision was indicated by 95% confidence limits (CL). All statistical analyses were done by R (version 2.9 www.r-project.org).

RESULTS

Early Results
There were no intraoperative deaths. Overall hospital mortality was 4.9% (n = 5; 95% CL, 1.6% - 11.1%), 3.3% (n = 3/90) of which was for elective procedures and 16.7% (n = 2/12) was for emergent procedures (p = 0.104). The emergent cases in which the patients died were initially operations for acute type A aortic dissection or prosthetic valve endocarditis, and the cause of death was ischemic cardiac failure for both. They died within 3 postoperative days. The cause of in-hospital deaths in elective operations (mean age of patients, 78 years, died after a mean postoperative period of 65 days) included multiple organ failure, renal failure, and tamponade. Cause of in-hospital death is summarized in Table 3. The hospital mortality for patients with aortic aneurysm (non-dissection and non-endocarditis) who underwent elective operations
was 3.7% (n = 3). In six patients (5.9%), intraoperative problems required a second cardiopulmonary bypass run and in 4 of these patients a second crossclamp of the aorta with cardioplegic arrest was necessary. The main reason was to obtain control of bleeding from the proximal suture line or coronary ostium anastomosis.

Table 3. Causes of Early and Late death (n = 8)

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early: In hospital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Postoperative, hospital</td>
<td>5</td>
<td>4.9</td>
</tr>
<tr>
<td>Elective:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- cardiac tamponade</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- multiple organ failure</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- renal failure</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Emergent:</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>- ischemic cardiac failure</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Late: Follow-up</td>
<td>3</td>
<td>3.1</td>
</tr>
<tr>
<td>Mediastinitis/False aneurysm</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Cardiac</td>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>- ischemic cardiac failure</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>- arrhythmia</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

The median intensive care unit stay was 3 days (range 1 – 65 days). Fourteen patients (13.7%) needed ventilatory support for more than 48 hours, and a tracheostomy was performed in 3 patients (2.9%). A rethoracotomy was performed in 20 patients (19.6%), mostly for excessive bleeding (n = 9) diffuse oozing (n = 4), or leakage from the coronary reattachment line (n = 2), cannulation site (n = 2) or the distal suture line (n = 1). Clinical signs of tamponade (n = 8) were also a predominant reason for rethoracotomy. A planned rethoracotomy within a few days after operation for removal of gauzes (n = 3) was the third reason for rethoracotomy. Postoperative temporary hemodialysis was necessary in 4 patients (3.9%). One of these patients died in the hospital; the others recovered and 1 patient needed long-term dialysis.

New neurologic symptoms were observed in 6 patients (5.9%). Ischemic cerebral accidents occurred in 5 patients and critical illness polyneuropathy was seen in 1
patient. The neurologic symptoms were all temporary and resolved completely. No patients in the stroke group died in the hospital.

**Follow-up results**

There were 97 hospital survivors and all except 1 patient were entered in the follow-up study (99 % complete). The reason for lost to follow-up of 1 patient was emigration to another continent. Mean and median follow-up was 8.1 months and 4.6 months, respectively (range 1.8 - 31.5 months). Total follow-up was 67 patient-years. During follow-up 3 patients (3.1 %) died and all deaths occurred in the first postoperative year. Causes of death during follow-up are summarized in Table 3. One of these late deaths was after mediastinitis with involvement of the composite bioprosthetic valve and signs of a false aneurysm at the aortic root on computed tomography. The reoperation risk was too high for this 79-year-old patient because he was in poor clinical condition and it would be his third reoperation. He received great omentum plasty, refixation of the sternum, and antibiotic treatment, but unfortunately died 4 months later. The second patient died suddenly after ventricular tachycardia 12 months after the initial aortic root replacement, and the third patient after acute coronary syndrome during atrial fibrillation 6 months after the BioValsalva conduit implantation. Unfortunately there was no permission for autopsy. The overall survival at 3 and 12 months was 95.9 % (95 % CL, 92.0 % - 99.9 %) and 92.1 % (95 % CL, 85.7 % - 98.9 %) respectively. This is presented in Figure 2. Univariate analysis showed a better overall survival for the aortic aneurysm group than for the other indications for operation ( HazardRatio = 0.16; 95 % CL 0.04 - 0.67; p < 0.01). Multivariate analysis was not performed because overfitting would occur with this relatively low total number of endpoints.

Two patients (2.1 %) required reoperation for significant prosthesis dysfunction due to endocarditis of the composite bioprosthetic valve and three patients (3.1 %) needed a reoperation for mitral valve procedures. One patient had endocarditis of the composite bioprosthetic valve after percutaneous coronary intervention and received a new aortic root replacement with a composite bioprosthetic valve and the other patient had healed endocarditis after tooth extraction, with severe aortic regurgitation for which he received a biological aortic valve replacement. None of the patients died after a reoperation. Three- and 12-month freedom from reoperation for aortic valve or conduit was 100 % and 97.0 % (95 % CL, 91.2 % - 100 %).
Endocarditis of the BioValsalva conduit was reported in 3 patients (3.1%). Two of these patients underwent reoperations as described and survived. One patient received antibiotic treatment for 6 weeks and recovered with good aortic valve function. The indication for the initial aortic root replacement was aortic aneurysm, and all these patients had new-onset endocarditis of the composite bioprosthetic valve, with Streptococcus and Enterococcus as predominant microorganisms. The interval between initial aortic root replacement and new-onset endocarditis was 22, 8 and 3 months, respectively.

Follow-up imaging was mostly done by computed tomography and showed growth of descending aorta diameter in 3 patients; 2 patients underwent endovascular intervention. There were no pathologic signs on the Biovalsalva prosthesis. Echocardiographic evaluation of the composite bioprosthetic valve function was performed by most referring cardiologists when there was a clinical indication. Apart from adequate valve function, this showed previously mentioned aortic valve dysfunction and new-onset mitral valve regurgitation. There was no moderate or severe aortic regurgitation observed and most patients had no aortic regurgitation.
DISCUSSION

Both the increasing age of patients and the lowered threshold for biological valves will advance the need for biological valved conduits in aortic root pathologic conditions. These biological conduits have the advantage of being readily available off the shelf in all sizes and do not require lifelong oral anticoagulation resulting in low thromboembolic complication risk (2). A number of biological valved conduits are commercially available. Initially we used the Shelhigh bioconduit, but after a disappointing incidence of endocarditis with this graft (7.3 %), we switched to the BioValsalva (Vascutek Terumo) conduit (3-5). This is a stentless porcine valve incorporated into a three-layered graft with a Valsalva shape at the proximal part. The limited initial results with the BioValsalva conduit in the literature are promising, with good clinical and echocardiographic results, but there are only a small number reports (9, 13-16). In this retrospective initial evaluation, we observed that the overall hospital mortality is 4.9 % and for patients undergoing elective procedures, the hospital mortality is 3.3 %. We lost 2 patients who underwent emergent operations because of ischemic cardiac failure and 3 patients who underwent elective operations because of multiple organ failure, renal failure and, unfortunately, a late recognised tamponade in the last patient. Compared with our Shelhigh (13.7 %) or mechanical composite valve group (3.2 %) it is an acceptable number of hospital mortality (3, 17). However a direct comparison between these reports would not be fair because the patient groups are not comparable. Maybe the Shelhigh bioconduit group is most comparable. Other, smaller series of Biovalsalva conduit reported a hospital mortality rate of 4.7 to 8.0 %, which is comparable to our 4.9 % (9, 13-16). Compared with other reports on biological valved conduits, our hospital mortality is satisfactory in a group with a mean age of 71 years, extended graft repair of the ascending aorta and involved aortic arch repair (37.3 %) with aortic valve endocarditis (14.7 %) (18-21). Again, one should note that the patient groups in these comparisons may be different.

There were 5 patients with postoperative ischemic cerebral accidents. During their operations, a distal aortic clamp was used most often and the arterial cannulation site was predominantly in the distal ascending aorta, but 2 patients had peripheral arterial
cannulation. All patients had only ascending aorta replacement, with the exception of 1 patient who also received an aortic arch replacement. Fortunately, all neurological symptoms resolved completely before discharge. During follow-up there were no thromboembolic events reported.

Reoperation for BioValsalva conduit dysfunction was needed in 2 patients because of endocarditis. Endocarditis of the BioValsalva conduit developed after a procedure (tooth extraction, percutaneous coronary intervention) in these patients, despite prophylactic antibiotics, and created severe aortic regurgitation for which reoperation was necessary. The reoperations were uneventful. Compared with other series of Biovalsalva conduit use, the reoperation percentage is acceptable (9, 13-16). Severe mitral valve regurgitation developed during follow-up in 3 other patients, for which they needed mitral valve procedures. One of these patients had moderate mitral valve regurgitation before aortic root replacement, which was aggravated postoperatively. The other 2 patients had new-onset mitral valve regurgitation, and 1 of these patients was initially operated on for prosthetic valve endocarditis with root abscess.

Endocarditis of the BioValsalva conduit was diagnosed in 3 patients (3.1 %). Two patients needed a reoperation as described. The last patient received antibiotic treatment for 6 weeks and recovered. The control echocardiography showed a good functioning composite bioprosthetic valve without aortic regurgitation. The incidence of endocarditis of the BioValsalva conduit (3.1 %) is comparable to the incidence of endocarditis in our homograft (3.2 %) (n = 213), Ross procedure (1.9 %) (n = 103), and mechanical valve conduit groups (3.8 %) (n = 528) (17, 22, 23). In our institution we use the homograft conduit only for patients with extensive aortic root abscess; for all other aortic root pathologic conditions, the BioValsalva conduit is our preferred graft for patients older than 65 years and when the patient’s preference is a biological valve.

As with every initial evaluation report the follow-up period is relatively short and the brief echocardiographic data are the limiting factor in this retrospective study.

In conclusion, the preliminary initial results of the BioValsalva conduit in our series of 102 patients are satisfactory. The relatively low mortality and morbidity numbers are promising, but close follow-up is mandatory and long-term results are awaited.
REFERENCES


Discussion
The aortic root is a complex hemodynamic unit consisting of different components, like the semilunar valvular leaflets, the sinuses of Valsalva and the interleaflet triangles. These are continuously changing and moving in harmony during each cardiac cycle (1). Its function is to connect the left ventricle with the ascending aorta and direct the blood in a unidirectional way and promote coronary artery perfusion. This function can be disturbed at different levels of the aortic root by different pathological processes, like degenerative valvular disease, aneurysm of the aortic root, dissection of the aortic wall with destruction of the aortic root or aortic valve endocarditis with root abscess. In most situations the diseased aortic root is replaced together with the aortic leaflets by a valved conduit. Specific pathological conditions of the aortic root, like aneurysmal dilatation, have less effect on the aortic leaflets and these morphologically normal appearing leaflets can be spared.

The need for biological valved reconstructions of the aortic root is increasing since the patient population is ageing. These biological valved solutions for aortic root replacement avoid the need for permanent oral anticoagulation. This is a major advantage in terms of bleeding, risk of thromboembolism and patient convenience.

This dissertation contains the results of aortic root reconstructions with different biological valved substitutes and valve-sparing aortic root replacement with the reimplantation technique practiced in the St. Antonius Hospital, Nieuwegein. These studies are retrospective cohort evaluations and have the disadvantage of possible bias, such as selection or information bias. The aim of this thesis is to present the hospital outcomes and examine follow-up results in order to answer the previously mentioned research questions.

In Chapter 2 we studied the mid-term results of aortic root replacement with cryopreserved homografts. This biological conduit was predominantly implanted in patients with aortic valve endocarditis (native and prosthetic) and in young patients with aortic valve or root pathology who preferred not to use life-long anticoagulation. In the beginning of aortic homograft use in our institution, the aim was to avoid a prosthetic conduit in active endocarditis, because of the higher rate of recurrent
endocarditis when mechanical or xenograft valves were used (2, 3). Nowadays, the choice of valve prosthesis in native and prosthetic valve endocarditis remains controversial (4, 5). Several reports have shown that the type of prosthesis used is not an important factor in achieving good early and long-term results if radical excision of all infected and necrotic tissue can be achieved and appropriate antibiotic treatment is administered (6-10). Nonetheless, in patients who have periannular abscess and annular destruction, homografts are still our choice of conduits, because of the pliable nature of the homograft that makes it easier to handle than other materials, and its additional periannular tissue that can be used to patch defects created by the resection of the abscesses and help restore atrioventricular continuity (11-13). It has also been reported that aortic homografts reduce the risk of recurrent endocarditis (12). Our mid-term evaluation supports the low recurrence rate of endocarditis of homografts (3.2 %). In contrast, recent reports show no significant difference in recurrent endocarditis rates between different types of prostheses (9, 10).

With a mean follow-up of nearly six years, our mid-term results are comparable to other reports (14-16). We observed that the survival curve declines after 8 to 10 years and is worse in the endocarditis group. Further follow-up of our data is needed to present the exact long-term results of our aortic homografts. Literature reports on long-term results (mean follow-up > 10 years) of homografts show comparable survival curves, with a decline of survival after 10 years (14-16). The initial expectation of life-long durability of aortic homografts has not been achieved according to these long-term studies.

During follow-up, 9.3 % of the hospital survivors required a reoperation for significant homograft dysfunction. This was predominantly for structural valve deterioration. One third of these patients required a reoperation within five years after implantation of the aortic homograft. These ‘early’ reoperations, in a patient group with a mean age of 51 years, and the limited durability of homografts have changed our indication to use an aortic homograft in young patients. In our review, reoperations for homograft dysfunction carried a high mortality risk (28.6 %), especially in cases of homograft endocarditis. Our aggressive strategy to remove the complete homograft...
conduit might be the cause of this. Recent reports show that the mean period of initial homograft implantation and reoperation is around 8 to 10 years (14-16). The reoperation risk is acceptable according to these reports (3.8 %) (17-19). It is not clear if this reoperation risk is due to a less aggressive surgical approach, such as replacement of the deteriorated valves, instead of the whole aortic root. Either way, a reoperation on a calcified homograft root is a challenge for the surgeon and a risk for the patient. All this has influenced our strategy for aortic homograft use. Nowadays, we only implant an aortic homograft in aortic valve endocarditis with annular abscesses. Aortic homografts are no longer advised for young patients with aortic root disease, because of their limited durability and high reoperation risk.

In Chapter 3 the medium-term outcome of aortic full root replacement with the pulmonary autograft and implantation of a homograft in the right ventricular outflow tract, the so-called modified Ross procedure is studied. This is accomplished in young patients (mean age 35 years) with aortic valve or root pathology and the wish not to use oral anticoagulation. There was no hospital mortality and the morbidity rate was low and satisfactory, despite the extensive double valve surgery. Strict patient selection and young patient age with low comorbidity played an important role in these rates. The overall survival at 10 years was 97.3 %, which is satisfactory. El-Hamamsy et al. and Bekkers et al. reported studies with a mean follow-up of more than 10 years and both had comparable survival rates at 10 years (97 % and 95 %) (16, 20). The El-Hamamsy group demonstrated that the survival of the autograft group was even comparable with the matched population for age and sex.

During a mean follow-up of six years, 4.8 % of the patients with a modified Ross procedure needed a reoperation for secondary regurgitation of the autograft, due to dilatation at the sinotubular junction or annular dilatation. These dilatation levels emphasize the weak points of the pulmonary autograft with a lack of a sinotubular junction and an anatomic ventriculo-arterial junction. Reinforcement of the annulus or adjustment of the diameter to the body surface area of the patient has been recommended for prevention of autograft regurgitation (21, 22). Since these recommendations a reinforcement ring or a reduction annuloplasty is used when the
annulus is dilated. Most of the reoperated autografts did not have a reinforcement ring. Recent evaluation of the German-Dutch Ross Registry showed that surgical autograft stabilization techniques preserve autograft function and result in significantly lower reoperation rates (23). In this registry, the autograft root replacement without reinforcement was associated with a six times increased reoperation rate compared to the autograft root replacement with reinforcement (p < 0.001).

A reoperation for pulmonary homograft dysfunction was necessary in only one patient, because of significant stenosis. Echocardiographic follow-up showed significant increase in pulmonary flow velocities at the level of the homograft leaflets, without clinical symptoms. Systematic oversizing of the pulmonary homograft, low (< 10 years) donor-patient age mismatch and the use of anti-inflammatory drugs have been recommended to reduce the risk of pulmonary homograft stenosis (16).

A rare complication after autograft dilatation is illustrated in Chapter 4 with a chronic type A dissection secondary to pulmonary autograft root dilatation, because of patient delay. This case underlines the importance of periodic and systematic echocardiographic evaluation of the autograft and the pulmonary homograft for prevention of severe late events.

Literature reports with long-term results after the modified Ross procedure show an increase in the reoperation rate in the second decade, after the initial operation (16, 20, 24). Although our reoperation rate is acceptable for now, we need further follow-up to assess the long-term reoperation rate of our modified Ross group. Bekkers et al. demonstrated that reoperations on the autograft can be done with low mortality and morbidity (20). El-Hamamsy et al. have demonstrated in a unique randomized controlled trial of autograft versus homograft aortic root replacement that the freedom from need of aortic root reoperation and freedom from need of any reoperation supported (p = 0.0003) the autograft group (16). This approves the use of a modified Ross procedure in young patients in comparison to aortic homografts.
In conclusion, the modified Ross procedure is still an option for young patients since the early and mid-term results are good, with the majority of patients having a normal life without anticoagulation. According to literature, long-term survival is excellent (16, 20, 24). Nevertheless, young patients have to be informed that a reoperation may become necessary in the future. The rate of reoperation can be reduced by using annular or sinotubular reinforcement of the autograft. It is therefore mandatory for strict follow-up of Ross patients with repeat echocardiographic evaluations of the autograft and the pulmonary homograft.

In some pathological conditions of the aortic root, like aneurysmal dilatation, the aortic valve leaflets are morphologically normal. These patients have aortic regurgitation secondary to dilatation of the ventriculo-aortic junction and/or sinotubular junction. In these situations the morphologically normal aortic leaflets can be spared using the reimplantation method. Chapter 5 evaluates our results with valve-sparing aortic root replacement with the reimplantation technique. Although there were some modifications of this technique over the years, especially modifications to mimic the sinuses of Valsalva, we continued using the first method described (25). In almost half of the cases the prosthetic Dacron graft type was a Valsalva graft (Gelweave Valsalva, Vascutek, Renfrewshire, Scotland), because there are finite element studies and magnetic resonance imaging reports illustrating the importance of neosinuses of Valsalva in a prosthetic graft in terms of reduced stress on the leaflets and reduced stress at the coronary button anastomoses and a near physiologic flow pattern in the neo aortic root (26-29). These neosinuses of Valsalva are presumed to improve the spared valve function and durability and decrease the incidence of postoperative complications, such as bleeding from the reimplanted coronary ostia and late pseudoaneurysm formation. In our mid-term evaluation, with a mean follow-up of more than five years, there was no significant difference between the type of graft and reoperation for recurrent aortic regurgitation. Further follow-up is needed to demonstrate a potential benefit of neosinuses of Valsalva.
This technique was used mainly in aneurysmal aortic root pathology. After gaining experience, the indication was expanded to type A aortic dissection (17.3%) with unaffected aortic leaflets. Although we had no hospital deaths and the morbidity rate was low, it is a subject of debate whether a longer and more complex operation, like valve-sparing aortic root replacement with the reimplantation technique, should be used in high risk patients with acute type A aortic dissection. However, numerous reports show that valve-sparing aortic root reconstruction does not compromise survival or perioperative risk in acute type A aortic dissection (30-34). Our results also indicate the safe use of this technique in type A dissection patients.

This technique is also used in patients with Marfan syndrome (16.1%). Initially there were concerns regarding the appropriateness of aortic valve-sparing in these patients with connective tissue disorder, but the experiences of several investigators suggests that valve-sparing aortic root replacement in Marfan patients is safe and durable (35-37). Our cohort also showed a good survival of Marfan patients after valve-sparing aortic root replacement with the reimplantation technique. Only one Marfan patient needed a reoperation for recurrent aortic regurgitation.

In our series, the freedom from reoperation at five years was 86.8% (95% CI, 78.7% - 95.8%). During follow-up 8.6% of the patients with valve sparing aortic root replacement with the reimplantation technique needed a reoperation for recurrent severe aortic regurgitation. Half of these reoperated patients were initially operated in the early, learning curve phase of valve sparing aortic root replacement with the reimplantation technique. Compared to the results with high volume centres with longer follow-up, our freedom from reoperation at five years is similar and satisfactory (38-41). Only the group of David reports an excellent rate of freedom from reoperation at 5 years of 99.7% (38).

If permanent oral anticoagulation is undesirable then valve-sparing aortic root replacement with the reimplantation technique is a good option in relatively young patients (mean age 51.9 years) with preserved aortic leaflets. Our mid-term evaluation encourages the use of the reimplantation technique. Long-term results are to be awaited, but literature reports with long-term results are promising (38-40).
Stentless aortic valves have comparable hemodynamic performances like the homograft or autograft (42-44). They become more durable and are readily available in various sizes. The increasing age of the Western population is also increasing the need for biological valved solutions for aortic root pathology. Therefore, a stentless biological valved conduit seems to be the next step in the evolution of biological valved aortic root reconstruction. Chapter 7 evaluates our experience with the totally biological Shelhigh conduit. After limited, but good initial reports in the literature, the Shelhigh conduit was used in our centre predominantly in elderly patients (mean age 71 years) with aortic root pathology and as an alternative to aortic homograft in cases of aortic valve endocarditis (45, 46). The results showed an overall in-hospital mortality of 13.7 %. For elective surgery of aortic root aneurysms this was 4.2 %. Univariate analysis revealed acute type A dissection, endocarditis and emergency operation as significant variables for hospital mortality.

Follow-up results were unsatisfactory. During a mean follow-up of 3.1 years the mortality was 33.1 % of the hospital survivors and the number of endocarditis of the Shelhigh bioconduit (7.3 %) was higher compared to our aortic homograft series and to other stentless biological conduits (44, 47, 48). In addition, the percentage of patients with sudden, unexplained death (9.3 %) was also high. Endocarditis of the Shelhigh bioconduit among these sudden, unexplained deaths could not be ruled out. After several warnings, the US Food and Drug Administration (FDA) published a preliminary public health notification on possible contamination and malfunction of devices manufactured by Shelhigh Inc in 2007 (49). The FDA recommended a voluntary recall, but the company declined, after which the FDA seized all medical products from the device manufacturer. Soon after this Carrel and associates reported a worrying rate of deleterious outcome (50). They experienced “sudden disastrous findings” in 6.1 % of their Shelhigh bioconduit group with disintegration of the graft and rupture of the aortic root. Although they could not find any causative microorganism, their patients experienced persistent fever or subfebrile temperatures for months. In our Shelhigh group microorganisms were isolated from blood cultures or tissue material collected during reoperation. Carrel and associates described a brownish gelatinous material at the native annulus during reoperation and we also had a comparable observation during reoperation.
Beside these two reports with unsatisfactory experiences with the Shelhigh bioconduit, there were also two reports with satisfactory results (51, 52). Musci and associates reported a reinfection after Shelhigh implantation of 8.6 % in a group of 255 endocarditis patients of which 26 received a Shelhigh bioconduit and the other patients a Shelhigh aortic bioprosthesis (51). There was no specification whether the reinfection cases were Shelhigh conduits or bioprostheses. They concluded that their reinfection rate is comparable to the results achieved with their treatment of aortic valve endocarditis with cryopreserved homografts. In our series, the aortic homografts had a lower reinfection rate (3.2 %) compared to our Shelhigh bioconduits (7.3 %). Galinanes and associates reported two (3.0 %) reinfections after Shelhigh bioconduit implantation from a total group of 67 implantations with a mean follow-up of 7.1 years (52). They did not show an increased endocarditis rate after implantation of a Shelhigh conduit. Consequently, it is debatable whether the bioconduit is the cause of endocarditis or if other factors play a role, such as patient-related mechanisms (inflammatory reaction), operation-related factors (use of glue) or other variables. Unfortunately, based on our results and those from the literature the answer remains unclear and more studies are needed from centres with their Shelhigh bioconduit experiences.

Based on our follow-up results with the Shelhigh bioconduit we have stopped using this bioconduit for aortic root reconstruction. Patients with a Shelhigh bioconduit are closely monitored with repeat computed tomography scans and/or echocardiographic evaluation.

As a successor to the Shelhigh bioconduit the BioValsalva conduit was introduced as a biological valved conduit for different aortic root pathology in the elderly. This conduit consists of a stentless porcine valve incorporated in a triple layered Valsalva prosthetic graft with a sinus-like shape at the proximal part of the prosthetic graft. Chapter 8 presents our initial experience with this new conduit. Hospital mortality was comparable to other reports on this conduit and satisfactory in a patient group with a mean age of 70.9 years and 25.5 % of the aortic root replacements being a reoperation after previous cardiac surgery (53-56). During implantation of this conduit
it is important to measure the appropriate location for the coronary ostia because of the position of commissures of the stentless porcine valve. The opening for the coronary ostia should be made with a blade and a punch and not with electrocautery, because of the polytetrafluoroethylene (PTFE) outer layer, as recommended by the manufacturer. Despite this there have been few reported cases of blood between the Dacron inner layer and the PTFE outer layer mimicking a dissection (57-59). Their hypotheses was that the dissection may have been caused by separation of the layers when a scalpel has been used for coronary ostia openings. They recommended soldering the layers together at the coronary button openings with electrocautery. To date, we have followed the recommendations of the manufacturer and have not seen this complication, but it is something to be aware of in a triple-layered graft.

During follow-up the reoperation rate was low (2.1%). Both patients were reoperated on because of endocarditis of the BioValsalva conduit and survived. In one patient the affected stentless porcine valve in the BioValsalva conduit could be replaced without removing the entire BioValsalva conduit. This illustrates the possibility for aortic valve re-replacement of a degenerated porcine valve in a BioValsalva conduit. Baraki and associates have demonstrated the surgical feasibility of aortic valve re-replacement in sheep after a BioValsalva conduit implantation (60). They found slight adhesions of the vascular prosthesis to the surrounding tissue. They concluded that a degenerated stentless biological valve inside the BioValsalva conduit could be replaced with a new tissue valve, without having to remove the entire conduit. We also observed slight adhesions during aortic valve re-reoperation on a BioValsalva conduit. This is advantageous compared to a calcified homograft often found during reoperation. For relatively young patients (> 50 years) who want to avoid the drawbacks of systemic oral anticoagulation and accept the risk of a reoperation, the BioValsalva conduit can be an option. When the stentless valve of the BioValsalva is degenerated and the patient is suitable for a reoperation, this patient can then have a less extensive reoperation by only replacing the biological aortic valve.

Our preliminary results with the BioValsalva conduit are satisfactory. During the initial short follow-up period the reoperation rate is low. Valve failure in a BioValsalva
conduit can be resolved by replacement of the porcine valve only, without having to remove the whole conduit, which is advantageous. Follow-up is mandatory as long-term results of the BioValsalva conduit are awaited.

CONCLUSIONS

Based on mid-term follow-up results, aortic homografts are no longer recommended to young patients (< 65 years) with aortic root disease. In aortic valve endocarditis the indication to use a homograft is limited to endocarditis with annular abscesses only. Long-term follow-up is necessary to draw final conclusions and to clarify the use of aortic homografts in the future.

Young patients with aortic root disease and the desire not to use oral anticoagulation have the option of undergoing a modified Ross procedure. Mid-term results justify the use of this procedure, but the autograft needs an annular or sinotubular reinforcement in order to reduce the reoperation risk. Further follow-up is needed to elucidate the long-term durability of the autograft and the pulmonary homograft.

In some pathological conditions of the aortic root the aortic leaflets may be preserved. These preserved aortic leaflets can be spared by using the reimplantation technique. Mid-term evaluation of this technique encourages its use in aortic root aneurysms, aortic dissections and Marfan patients with aortic root aneurysms. Long-term results are awaited.

Commercially available stentless biological valved conduits are known for their good hemodynamic features. Our experience with the totally biological Shelhigh conduit had unsatisfactory follow-up results with a relatively high rate of follow-up mortality and endocarditis. We have therefore stopped using this bioconduit for aortic root reconstruction and patients with a Shelhigh bioconduit are closely monitored.
The BioValsalva conduit is the successor of the Shelhigh bioconduit and is a unique combination of porcine biological leaflets in a triple layered vascular graft. The preliminary results with the BioValsalva conduit are promising and further follow-up is needed for long-term evaluation.
REFERENCES


Summary
Chapter 1 reports the follow-up results of aortic root replacement with an aortic homograft in 213 patients. During a mean follow-up of almost 6 years 10.3% of the hospital survivors died and a fourth of these were valve-related late deaths. Structural valve deterioration was the predominant cause of reoperation. The incidence of endocarditis of the homograft was studied and echocardiographic assessment of aortic homograft function was analyzed.

Chapter 3 discusses the results of aortic root replacement with the pulmonary autograft in 103 adult patients. Mid-term follow-up showed an excellent overall survival. Dilatation of the autograft was the primary cause of reoperation and reinforcement of the autograft is discussed. Autograft valve function was analyzed by echocardiography and majority of patients had no or trivial aortic regurgitation. The importance of periodic echocardiographic evaluation of the autograft is illustrated in Chapter 4. It describes a rare case of a chronic type A aortic dissection in a pulmonary autograft.

Chapter 5 is a retrospective analysis of valve-sparing aortic root replacement using the reimplantation technique in 81 consecutive patients between 1998 and 2010. There was no hospital mortality. Follow-up mortality (11.1%) was studied and was mainly due to neoplasm. During follow-up, the incidence of reoperation (11.1%) was studied as well as the incidence of endocarditis (2.5%) and echocardiographic imaging was evaluated. A rare case of valve-sparing surgery is illustrated in Chapter 6 in which a traumatic lesion of the left coronary cusp is repaired.

Chapter 7 evaluates the initial experience with the totally biological Shelhigh bioconduit. Aneurysmal disease of the aorta was the primary indication for aortic root replacement. Hospital and follow-up mortality were studied. The incidence of reoperation and endocarditis of the Shelhigh bioconduit during follow-up were
shown. Notable was the follow-up mortality (33.1 %) and the endocarditis rate (7.3 %) of this bioconduit.

Chapter 8 describes the results with the Biovalsalva conduit for aortic root replacement in 102 patients. The predominant use of this conduit was for aneurysmal disease of the aorta. Overall hospital mortality was 4.9 % and for elective procedures this was 3.3 %. Follow-up showed a reoperation rate of 2.1 % and endocarditis of the Biovalsalva conduit was observed in 3.1 %. Further follow-up is necessary.

Chapter 9 provides a general discussion.
Samenvatting
Hoofdstuk 1 geeft een algemene inleiding. De functionele anatomie van de aortawortel, meest voorkomende pathologie en verschillende biologische alternatieven voor aortawortelvervanging worden besproken en het doel van de dissertatie wordt uiteengezet.

Hoofdstuk 2 beschrijft de follow-up resultaten van aortawortelvervanging door middel van een menselijk donor aortaklep in 213 patiënten. Gedurende een gemiddelde follow-up van bijna 6 jaar stierven 10.3% van de ziekenhuis overlevenden en een vierde daarvan waren klepgerelateerde sterfgevallen. Structureel klep falen van de donor aortaklep was de voornaamste oorzaak van reoperatie. De incidentie van endocarditis van de donor aortaklep werd bestudeerd en het echocardiografisch functioneren van de donor aortaklep werd onderzocht.

In Hoofdstuk 3 worden de resultaten van het gebruik van de pulmonalis autograft voor aortawortelvervanging in 103 volwassen patiënten geëvalueerd. Mid termijn follow-up liet een uitstekende overleving zien. De voornaamste oorzaak voor reoperatie was dilatatie van de pulmonalis autograft en versteviging van de autograft wordt bediscussieerd. Autograft klepfunctie werd geanalyseerd middels echocardiografie en de meerderheid van de patiënten had geen of triviale regurgitatie. Het belang van periodieke echocardiografische evaluatie van de pulmonalis autograft wordt geïllustreerd in Hoofdstuk 4, waarin een zeldzaam geval van chronisch type A dissectie in de pulmonalis autograft wordt beschreven.

Hoofdstuk 5 is een retrospectieve analyse van klepsparende aortawortelvervanging met de reimplantatie techniek in 81 opeenvolgende patiënten tussen 1998 en 2010. Er was geen ziekenhuissterfte. Follow-up mortaliteit (11.1%) werd onderzocht en was voornamelijk door een neoplasma. Gedurende de follow-up werd de incidentie van reoperatie (11.1%) en endocarditis (2.5%) onderzocht en de echocardiografische resultaten geëvalueerd. Een zeldzame casus van klepsparende chirurgie wordt in Hoofdstuk 6 geïllustreerd, waarin een traumatisch laesie van de linker coronaire cusp is gerepareerd.
Hoofdstuk 7 evalueert de initiële ervaringen met de volledig biologische Shelhigh bioconduit. Aneurysmata van de aortawortel waren de voornaamste indicaties voor aortawortelvervangingen. Ziekenhuis en follow-up mortaliteit werd onderzocht. De incidentie van reoperatie en endocarditis van de Shelhigh bioconduit werd getoond. Opvallend was de follow-up mortaliteit (33.1 %) en de endocarditis percentage (7.3 %) van deze bioconduit.

Hoofdstuk 8 beschrijft de resultaten met de Biovalsalva conduit voor aortawortelvervanging in 102 patiënten. De voornaamste indicatie voor gebruik van deze conduit was een aneurysma van de aortawortel. Algehele ziekenhuissterfte was 4.9 % en voor electieve procedures was dit 3.3 %. Follow-up toonde een reoperatie percentage van 2.1 % en endocarditis van de Biovalsalva conduit werd geobjectiveerd bij 3.1 %. Verder follow-up is noodzakelijk.

Hoofdstuk 9 bevat een algemene discussie.
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LIST OF PUBLICATIONS

List of publications

CURRICULUM VITAE

Abdullah Kaya was born on November 19, 1976 in Çalapverdi / Boğazliyan, Turkey. In 1978 he emigrated with his family to the Netherlands. He obtained his secondary school certificate in 1995 at the Oude Hoven Lyceum in Gorinchem. He received his medical degree at the University of Utrecht in 2001. During his internships he got deeply interested in cardiac surgery after meeting Prof. Dr. J.F. Hitchcock and Prof. Dr. A. Brutel de la Rivière.

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Uitnodiging

Voor het bijwonen van de openbare verdediging van het proefschrift

Biological Valved Reconstructive Surgery of the Aortic Root through the years

Op dinsdag 19 augustus 2014 om 10.30 uur in de Aula van de Radboud Universiteit Nijmegen, Comeniuslaan 2 te Nijmegen,

Receptie na afloop ter plaatse

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