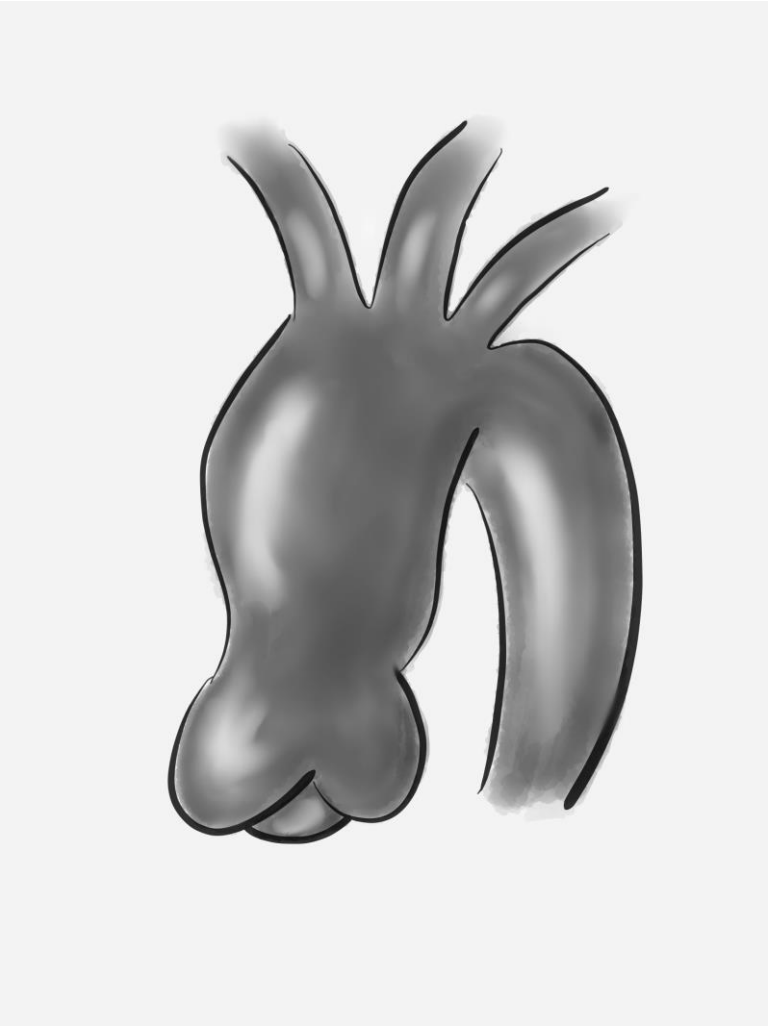
VALVE-SPARING AORTIC ROOT RECONSTRUCTION



Fabrizio Settepani

VALVE-SPARING AORTIC ROOT RECONSTRUCTION

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Valve-sparing aortic root reconstruction
F. Settepani

Thesis, Radboud University Nijmegen
Proefschrift Radboud Universiteit Nijmegen

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VALVE-SPARING AORTIC ROOT RECONSTRUCTION

Proefschrift

ter verkrijging van de graad van doctor

aan de Radboud Universiteit Nijmegen

op gezag van de rector magnificus prof. dr. J.H.J.M. van Krieken,

volgens besluit van het college van decanen

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VALVE-SPARING AORTIC ROOT RECONSTRUCTION

Doctoral thesis

to obtain the degree of doctor

from Radboud University Nijmegen

on the authority of the Rector Magnificus prof. dr. J.H.J.M. van Krieken,

according to the decision of the Council of Deans

to be defended in public on Tuesday, October 17, 2017

at 16.30 hours

by

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To the memory of Professor Angelo Pierangeli,
Master of surgery and sailing companion

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CHAPTER 1

INTRODUCTION

THE AORTIC VALVE-SPARING OPERATIONS: AN OVERVIEW

The definition "aortic-valve sparing operations" was coined in the early '90s to describe procedures developed to preserve the native aortic valve in patients with aortic root aneurysm with or without aortic incompetence (AI). Until then the main procedure to treat this pathology was the Bentall operation consisting in the replacement of the aortic root by means of a valve conduit (1). In very selected cases, the Ross procedure (pulmonary autograft in aortic position) was considered an alternative (2). Although the Bentall operation has been shown excellent short and long-term results, why to replace, in the setting of an aortic root aneurysm, an anatomically normal or nearly normal aortic valve? This is the question that Magdi Yacoub and Tirone David asked themselves about 25 years ago when they developed *"the aortic root remodelling"* and *"the aortic valve reimplantation"*, respectively (3,4). The aortic root remodelling consists, basically, in the excision of the aortic wall to within 2 to 3 mm of leaflet attachment, detachment of the coronary ostia, reconstruction of the aortic root with the aid of a tailored Dacron graft and reimplantation of the coronary ostia. The aortic valve reimplantation differs from the latter because after the excision of the aortic root aneurysm, the native aortic valve is entirely reimplanted within a Dacron graft (figure 1).

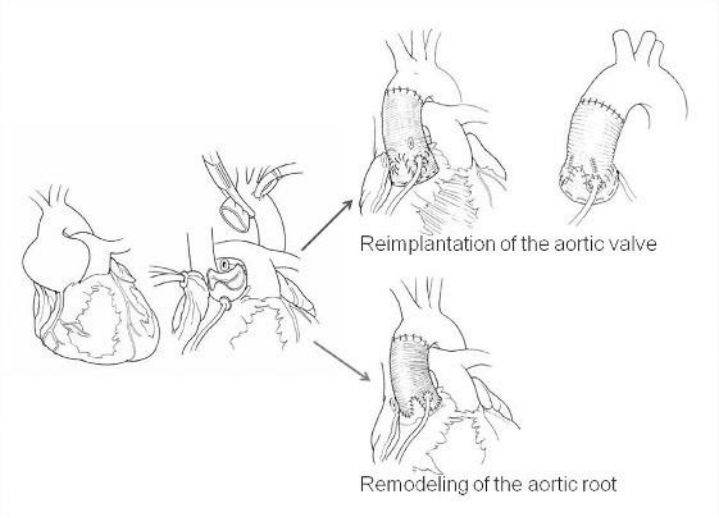

Fig 1. After the excision of the aortic root, the native valve is entirely reimplanted within the Dacron graft (reimplantation of the aortic valve) or, sutured to a tailored graft (remodelling of the aortic root). Reprint with permission form Elsevier.

Remodelling of the aortic root is considered physiologically superior to reimplantation of the aortic valve mainly because the aortic annulus and the *neo*-aortic root seem to maintain their compliance during the cardiac cycle, thereby mimicking the native sinuses of Valsalva (5). The principal criticism to this operation is that it doesn't stabilize the ventriculo-aortic junction, with possible further dilatation and risk for recurrent AI, particularly in patients with connective tissue disorders (6) or in patients with dilated annulus. However, it has provided excellent results in patients with preserved aortic annulus (7). Conversely, the reimplantation of the aortic valve stabilizes the annulus, which is entirely contained within the Dacron graft thus preventing from further dilatation but, however, it doesn't permit the physiological systo-diastolic movement of the annulus and the *neo*-aortic root. Several modifications have been made over the years to overcome the limitations of both techniques. To address the issue of annular dilatation during remodelling of the aortic root several types of internal and external annuloplasty were designed, including the use of strip of Dacron (8), polytetra-fluoroethylene (PTFE) suture (9), and more recently, a commercially available flexible ring (10). On the opposite side, to overcome the lack of compliance at the level of the neo-root during aortic valve reimplantation, in 2000 Ruggero De Paulis introduced the Valsalva graft that, upon implantation and pressurization generates 3 independent *pseudo-sinuses* without the need for any substantial variation in the original reimplantation technique (11). The peculiar design of the Valsalva graft allows for proper root reconstruction by re-establishing the main root characteristics: 2 rings (annulus and ST junction), joined by 3 pillars (the commissures), separating 3 independent bulging sinuses (figure 2).

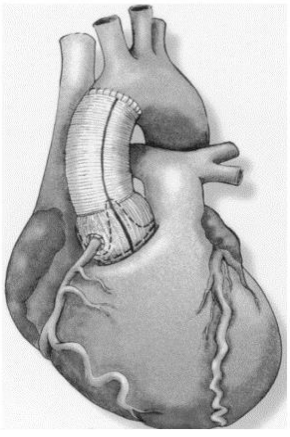

Fig 2: Graft drawing of the Valsalva conduit in a reimplantation type of valve-sparing procedure. *Dotted lines* represent suturing of the patient's own valve to the skirted section of the graft. Note that the top of the commissures reach the new sinotubular junction. After suturing of the valve is completed, the conduit can bulge only at the site of the sinuses whereas it will remain straight behind the commissural posts. Coronary artery is attached at the center of the corresponding sinus.
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Similarly, a few other attempts to reproduce the sinuses of Valsalva by placating a tubular Dacron graft have been carried out in recent years (12,13).
In 2003 Craig Miller proposed a classification of the different techniques as follows (14):

- David I: original reimplantation technique using a cylindrical tubular graft
- David II: classic Yacoub remodelling
- David III: remodelling with an external synthetic strip added between the left and right mitral fibrous trigones
- David IV: reimplantation using a 4-mm larger graft size with plication of the graft circumferentially at the sino-tubular junction above the top of the commissures
- David V: reimplantation using even a larger graft which is necked down at both the bottom and top ends to create pseudo-sinuses.

Nowadays, in literature this group of operations is also identified with the definition "*valve-sparing aortic root replacement*".
The main advantages of the reimplantation technique performed with the Valsalva graft, being ventriculo-aortic junction fixation and recreation of the sinuses of Valsalva, made it the preferred method of aortic-valve sparing operation at Isituto Clinico Humanitas in Milan.

THE ANATOMICAL BASES OF THE VALVE-SPARING AORTIC ROOT SURGERY

In considering the prospect of an aortic valve-sparing procedure a deep knowledge of the surgical anatomy of the aortic root is mandatory. The aortic valve needs to be considered a functional unit composed by three structures: (I) the functional aortic annulus, comprising the ventriculo-aortic junction and the sino-tubular junction, (II) the aortic cusps and (III) the three sinuses of Valsalva. Although the "anatomic" ventriculo-aortic junction seems to be positioned at about a third of height the aortic root, the "surgical" intraluminal ventriculo-aortic junction is a virtual ring formed by joining basal attachment of the aortic cusps (Figure 3) (15,16). On the extraluminal side of the aortic root, the limit of the surgical dissection during valve-sparing aortic root replacement (V-SARR) corresponds to the roof of the left atrium on the side of the non - and left-coronary sinus and to the myocardium coming from the ventricular septum and continuing laterally to the right ventricular outflow tract, on the side of right-coronary

sinus (17). To achieve a proper positioning of the graft during aortic valve reimplantation, the dissection outside the aorta must be at the level just described above, so that the prosthesis can incorporate the entire functional aortic annulus, thus preventing further dilatation. Conversely, during remodelling of the aortic root, a deep dissection outside the aorta is not required as the graft doesn't incorporate the valve but is sutured just above.

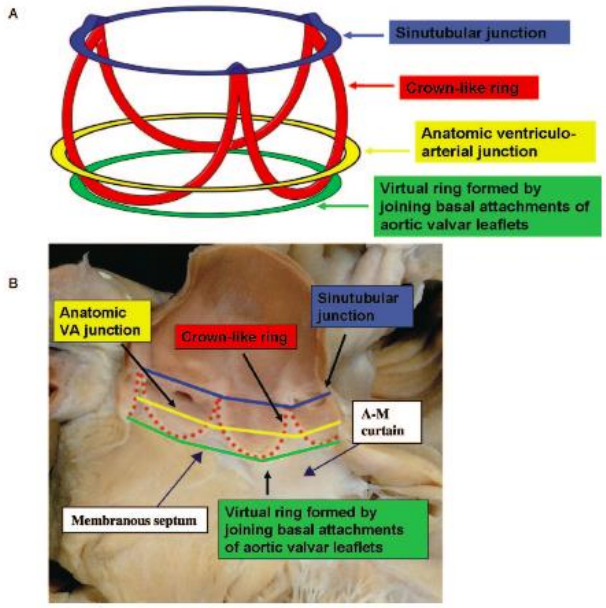

Fig 3: A, Three-dimensional arrangement of the aortic root, which contains 3 circular "rings," but with the leaflets sus-pended within the root in crown-like fashion. B, The leaflets have been removed from this specimen of the aortic root, show-ing the location of the 3 rings relative to the crown-like hinges of the leaflets. VA indicates ventriculoarterial; A-M, aortic-mitral.
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PATIENTS' SELECTION FOR THE AORTIC VALVE-SPARING OPERATIONS

The valve-sparing operations were originally designed for young patients with aortic root aneurysm and normal aortic valve cusps. Over the years, the encouraging mid- and long-term results in terms of mortality, morbidity and valve durability, have convinced many surgeons to expand the indication to older subjects (18) and to subjects with more compromised aortic valve, including patients with Marfan syndrome (6), bicuspidity (19), and aortic valve affected by severe incompetence (20). This evolution has resulted in the need to develop a technique that, in addition to the root graft implantation, could correct residual aortic insufficiency due to abnormalities of the aortic valve. Several techniques to correct the residual valve prolapse or to minimize the valve-restricted motion have been introduced. Although the results of valve-sparing

operations in patients with connective tissue disorders and in selective cases of elderly patients seems to be extremely encouraging, especially with the reimplantation technique (21,22), the impact of the additional aortic cusp repair on the recurrent AI is still controversial, particularly in patients with bicuspid aortic valve requiring complex repair (23-25).

Trans-esophageal echocardiography remains the best diagnostic tool to select patients for these operations. All the components of the aortic root need to be investigated, particularly the cusps. Diffusely calcified, sclerotic and stiff cusps are usually considered not suitable for repair. In the setting of significant aortic incompetence, identification of the prolapsing cusp and regurgitant jet direction are of paramount importance.

Angio-CT scan of the chest is also required to precisely measure the root and the ascending aorta and to rule out an involvement of the aortic arch in the aneurysmal pathology.

AORTIC VALVE-SPARING REIMPLANTATION OPERATIVE TECHNIQUE

A median sternotomy is performed and hypothermic cardiopulmonary bypass (32 °C) is instituted with aortic arch, femoral artery or right axillary artery and right atrium cannulation. Myocardial protection is achieved by antegrade or a combination of antegrade and retrograde crystalloid cardioplegic solution. The sinuses and the ascending aorta are excised so that only 3 to 4 mm of the aortic wall is left attached to the annulus. The coronary ostia are prepared for a button reimplantation as for a conventional root-replacement procedure. Then, Ethibond 2/0 with pledgets or alternatively, 4-0 polypropylene sutures are placed from the inside to the outside around the ventriculo-aortic junction along a horizontal plane (basal ring) 2-mm below the valve leaflets level. Prosthesis diameters are calculated from the diameter of the left ventricular outflow tract and/or the height of the aortic cusps. In all the reimplantation procedures the Gelweave Valsalva prosthesis (Sulzer Vascutek, Renfrewshire, Scotland) was implanted. At this point of the operation, it is of crucial importance to make sure that the cusps are coapting at the same level and well above the nadir of the aortic annulus (8–11mm) and the cusps have no 'restricted' motion. If one or both of these conditions are not met, additional cusp repair is needed. The coronary arteries are then implanted and the graft is anastomosed to the distal aorta in a conventional way. In case the aortic arch is involved in the aneurysmal disease, total or partial arch replacement is performed according to dr. Kazui protocol (26).

AIM OF THE THESIS

The aortic valve-sparing reimplantation is a challenging procedure even for experienced aortic surgeons. Preservation of the native valve permits the maintenance of a proper hemodynamic and avoids the lifelong anticoagulation but the risk of recurrent aortic regurgitation remains its Achilles heel.

The aim of this study is to evaluate the results of the aortic-valve sparing reimplantation technique presented both as single and multi -center experience. The impact of several variables on mortality and morbidity has been investigated, focusing particularly on the residual aortic incompetence. Moreover, the outcome of alternative techniques to treat the aortic root aneurysmal pathology, such as the Bentall and the Ross operation, has been explored.

The centers involved in the clinical study are as follows:

- Humanitas Research Hospital, Humanitas University, Milan, Italy
- S. Orsola Hospital, University of Bologna, Bologna, Italy
- Tor Vergata Hospital, Tor Vergata University, Rome, Italy
- Hospital of the University of Pennsylvania, Philadelphia, USA
- St. Antonius Hospital, Nieuwegein, The Netherlands

The following issues have been explored in details in the corresponding chapters:

- Early and mid-term results of the aortic valve reimplantation technique with reconstruction of the sinuses of Valsalva and compliance of the Valsalva graft pseudo-sinus at mid-term follow-up (Chapter 2-5).
- Results of valve-sparing aortic root replacement in different settings including Marfan patients, bicuspid aortic valve and older patients (Chapter 6-8).
- Impact of additional aortic cusp repair in patients with bicuspid and tricuspid aortic valve including long-term results (Chapter 9,10).
- Outcome of the aortic root replacement with composite valve graft (Chapter 11,12).
- Results of the Ross operation for the aortic root replacement (Chapter 13).

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PART 1

THE ROLE OF THE SINUSES OF VALSALVA IN THE VALVE-SPARING AORTIC ROOT REPLACEMENT: THE RECONSTRUCTION OF THE SINUSES BY MEANS OF THE VALSALVA GRAFT

CHAPTER **2**

Aortic valve-sparing operations in patients with aneurysms of the aortic root or ascending aorta: preliminary results.

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Interact CardioVasc Thorac Surg. 2005; 4: 137 – 9

Abstract

Objective: Aortic valve-sparing operations were developed to preserve the native aortic valve in patients with aneurysms of the aortic root or ascending aorta and normal aortic valve leaflets. This paper describes our initial experience with valve-sparing operations and earlyclinical and echocardiographic results obtained.

Methods: From October 2002 to March 2004, 32 consecutive patients underwent aortic valve-sparing operations at the Istituto Clinico Humanitas, Rozzano, Italy. Preoperative transesophageal echocardiography showed moderate or severe aortic incompetence (AI) in 15 patients (47%). Twenty-nine patients underwent reimplantation of the aortic valve and 3 patients remodeling of one sinus. In 2 cases prolapsing cusp repair was carried out.

Results: There were no intraoperative deaths. At discharge, two-dimensional echocardiogram showed no or trivial aortic incompetence (AI) in 17 (52%) patients and mild AI in 13 (42%); 2 (6%) patients had severe AI requiring reoperation, respectively 4 and 6 weeks later.

Conclusions: The valve-sparing procedures showed good preliminary results, thus encouraging further use of this type of repair. However, further larger studies and long-term results are needed in order to define the durability of these techniques.

Introduction

Aortic valve-sparing operations were developed to preserve the native aortic valve in patients with aneurysms of the aortic root or ascending aorta and normal aortic valve leaflets [1]; in recent years indications have been extended also to valves having cusps without gross structural defects [2,3]. These kind of aneurysms are frequently associated with aortic incompetence (AI) which is caused by loss of the sino-tubular junction, dilatation or distortion of one or more sinuses of Valsalva, annuloaortic ectasia or a combination of these problems [4]. The conventional treatment consists of composite replacement of the aortic valve and the ascending aorta [5]; though it's considered 'safe', it is not free from complications including thromboembolism, endocarditis, and long-term anticoagulation related problems [6]. Then, from October 2002, we have adopted valve-sparing operations to treat patients with root dilatation and aortic cusps without gross structural defects. This paper describes our initial experience with valves-paring operations and early clinical and echocardiographic results obtained.

Material and methods

From October 2002 to March 2004, 32 consecutive patients underwent aortic valve-sparing operations at the Istituto Clinico Humanitas, Rozzano, Italy. Our standard indications have been aneurysms of the aortic root and/or ascending aorta and aortic cusps without gross structural defects. The final decision to preserve the valve was made intraoperatively by the surgeon after inspection of valve cusps and root geometry. When the structural defects of the cusps were considered unsuitable for repair the Bentall procedure was performed. Demographic data are listed in Table 1. Patients were predominantly male and mean age was 58 ±13 (range 28–83). The mean ascending aorta diameter was 5.1±1.1 cm. Among the patients with no, trivial or mild AI the mean ascending aorta diameter was 5.0±1.0 cm and of these 33.3% had a bicuspid aortic valve.

Table 1: Preoperative patients characteristics

Characteristics	n=32
Age (years)	58±13
Sex (male)	25 (78)
NYHA functional class	
• I	22 (69)
• II	8 (25)
• III	2 (6)
• IV	-
Left ventricular ejection fraction	
• >60%	22 (78)
• 40-59	5 (18)
• <39	1 (4)
Aortic incompetence	
• None/trivial	10 (31)
• Mild	7 (22)
• Moderate	7 (22)
• Severe	8 (25)
Marfan syndrome	1 (3)
Aortic Valve Morphology	
• Bicuspid (congenital)	7 (22)
• Tricuspid	25 (78)
Coronary artery disease	4 (13)
Mitral regurgitation	3 (9)
Diameter of aneurysm (cm)	
1. Aortic root	4.6±0.6
2. Ascending aorta	5.1±1.1

Values are mean ±1 S.D.
Numbers in parentheses are percent.

Operative techniques

A median sternotomy was performed and hypothermic cardiopulmonary bypass (32 °C) was instituted with femoral artery and right atrium cannulation. Femoral artery cannulation was preferred in order to achieve a more distal cross-clamping site on the ascending aorta. Myocardial protection was achieved by combination of antegrade and retrograde Custodiol® cardioplegic solution and topical cooling with 4 °C saline solution. All patients but three, underwent the reimplantation of the aortic valve according to the technique described by David [1]. The sinuses and the ascending aorta were excised so that only 3 to 4 mm of the aortic wall were left attached to the annulus. The coronary ostia were prepared for a button reimplantation as for a conventional root-replacement procedure [5]. In the presence of a bicuspid valve, radial tension was placed on the 2

commissures by means of two sutures in order to assess leaflet prolapse. The free margin of congenital fusion of the left and right coronary leaflets was found to be elongated in 2 cases. Shortening of the free margin was achieved by a plication of the margin itself with a Gore-Tex® 6-0 running suture. Shortening of the leaflet margin was considered adequate if both leaflets were at identical heights after applying radial tension on the two commissures. Then, 4-0 polypropylene sutures were placed from the inside to the outside around the aortic annulus along a horizontal plane below the valve leaflets level. Prosthesis diameters were calculated from the diameter of the left ventricular outflow tract and the height of the aortic cusps. In all the 29 reimplantation procedures the Gelweave Valsalva™ prosthesis (Sulzer Vascutek, Renfrewshire, Scotland) [7,8] was implanted. The diameter of the graft was equal or slightly smaller than the average length of the free margins of the aortic cusps [1]. The coronary arteries were then implanted and the graft was anastomosed to the distal aorta in a conventional way.

Three patients with ascending aorta aneurysms and isolated non-coronary aortic sinus dilatation underwent the remodeling procedure [4]. The non-coronary sinus and the ascending aorta were replaced by a scalloped shape dacron tubular graft (Sulzer Vascutek, Renfrewshire, Scotland).

The graft size was 28 millimetres (mm) in 4 (13%) patients, 30 mm in 13 (40%) and 32 mm in 15 (47%). A transesophageal echocardiogram (TEE) was carried out intraoperatively in all the patients after the cardiopulmonary bypass weaning in order to evaluate the competence of the aortic valve. None of the patients showed AI grater than mild.

Table 2 shows the operative data.

Table 2: Operative data

Characteristic	n=32
Cardiopulmonary bypass time (min)	126±21
Cross clamping time (min)	109±16
Root procedure	
• Reimplantation	29 (91)
• Remodeling of noncoronary sinus	3 (9)
Prolapsing cusp repair	2 (6)
Coronary artery bypass grafting	4 (13)
Mitral valve plasty	2 (6)
Mitral valve replacement	1 (3)
Stay in the intensive care unit (days)	1.4±0.9
Intubation time (hours)	15.5±5.5

Values are mean ±1 S.D. Numbers in parentheses are percent

Results

All patients underwent the operation during a recent 18- month period. There were no intraoperative deaths. One patient showed ischemia at the electrocardiogram soon after the cardiopulmonary bypass weaning; an intraoperative TEE showed a hypokinetic left ventricular posterior wall. A kinking at the right coronary ostium site was noted. After a venous graft on the right coronary was performed, the patient recovered completely and did not develop myocardial infarction (creatinine phosphokinase<300 IU/l, myocardial band < 5%). Three patients required early reoperation (<24 h) for bleeding. Two patients underwent pacemaker implantation because of permanent atrioventricular block.

Aortic valve function

All the patients underwent two-dimensional echocardiogram at discharge. Colour flow Doppler was used to detect AI, and severity was subjectively graded as trivial (1+), mild (2+), moderate (3+) and severe (4+). There was no or trivial (1+) AI in 17 (52%) patients; 13 (42%) had a mild (2+) AI and 2 (6%) had severe (4+) AI requiring mechanical aortic valve replacement respectively 4 and 6 weeks after the aortic valve reimplantation procedure. The first patient was a 28-year-old man with Marfan syndrome, the second, with a bicuspid aortic valve, had during the first operation a prolapsing cusp repair by shortening of the free margin. Two more patients required reoperation for non-valve related complications. One patient developed a pseudoaneurysm for a leak at the left coronary anastomosis 1 month after the first operation; the second developed a constrictive pericarditis three months after the first procedure. Both of them recovered completely after the reoperation.

Discussion

The mechanisms that lead to AI in patients with aortic root and/or ascending aorta aneurysms are nowadays well known [9–11]. The conventional treatment of these patients consists of aortic root replacement with a composite graft. Many series [12,13] showed that this operation is safe and has a low mortality and morbidity rate. However, most of these patients arrive for the operation with intact or minimally stretched aortic

cusps. Why should one remove an anatomically normal aortic valve? This is the question that Sarsam, Yacoub and David asked themselves approximately a decade ago. Sarsam and Yacoub [14] proposed the remodeling technique of the aortic root to achieve cusps coaptation by reduction of the sinotubular junction. This approach preserves the anatomy and the function of the sinuses of Valsalva; this step is considered essential in order to avoid cusps trauma and degeneration, but does not provide stabilization of the annulus with a tendency towards progressive AI [15]. We did not use this technique in our series. This aspect was addressed by David and Feindel [1]; they found that in many patients with sinotubular dilatation, it also co-exists annulus dilatation. This is particularly evident in patients with connective tissues disorders, such as the Marfan syndrome [16]. They proposed the reimplantation technique to provide stabilization of the aortic annulus, better support of the aortic wall and less chance of suture bleeding.

Nevertheless, we have to admit that one of the two patients of our series, a young man with Marfan syndrome, who underwent reoperation for severe AI, had originally a reimplantation procedure and did not benefit from it. This technique, however, does not preserve the anatomy and the function of the sinuses of Valsalva. This issue was addressed by De Paulis [7,8], introducing modified Dacron conduit (Gelweave Valsalva™, Sulzer Vascutek, Renfrewshire, Scotland) that on implantation recreates sinuses of Valsalva of normal shape and dimension, providing a sufficient gap that should avoid any contact between the open leaflet and the Dacron wall. Longer follow-up is needed in order to assess the cusps preservation. We used this prosthesis in all the patients who underwent aortic valve reimplantation in our series.

Langer and colleagues [17] showed that the addition of leaflet prolapse repair to root replacement does not result in increased morbidity or hospital mortality. Our experience in cusp repair is very limited; we used the free margin shortening technique just in two patients, but one of them, with a bicuspid aortic valve, rapidly developed severe AI and underwent reoperation. The TEE carried out before reoperation showed a central jet through the valve. The valve, in fact, turned out to have a central gap caused by the retraction of the cusp presenting a raphe. Was the raphe fibrosis the cause of the cusp retraction? Was our approach in shortening the free margin too aggressive? We are still not able to answer these questions, but since our approach consists of triangular resection of the raphe [18] in case of prolapsing bicuspid aortic valve. It has been shown that reconstruction of the regurgitant bicuspid valve by means of triangular resection of a median raphe, in combination with proximal aortic replacement provides good midterm results [2]. Although the current results are promising, further follow-up will

be required in order to determine the reliability of this technique in the long term. In our series there were no deaths and the freedom from moderate or severe AI at discharge was 94%; we thus conclude that the valve-sparing operations have, in our short experience, a low morbidity rate especially in patients with tricuspid aortic valve. We moreover think that the optimal technique of leaflet repair is still open to controversy.

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CHAPTER 3

Early results of valve-sparing reimplantation procedure using the Valsalva conduit: a multicenter study.

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Abstract

Background: This study evaluates the midterm clinical results of valve-preserving aortic root reconstruction by means of a modified conduit incorporating sinuses of Valsalva.

Methods: During a 5-year period, 151 patients with aneurysm of the aortic root underwent a reimplantation type of valve-sparing procedure using the Gelweave Valsalva™ prosthesis that incorporates sinuses of Valsalva. There were 121 males (80.1%), and the mean age was 56.4 ± 14.4 years (range, 14 to 83). Fourteen percent of the patients had Marfan syndrome and 8.6% had bicuspid aortic valve. Seven patients (4.6%) suffered from acute aortic dissection. Aortic replacement was extended to the arch in 14 patients (9.3%). Sixteen patients (10.6%) had associated cusp repair.

Results: In-hospital mortality was 3.3%, and it was significantly higher among patients operated on for acute dissection ($p = 0.001$) and in symptomatic patients (III–IV New York Heart Association class; $p = 0.021$). Follow-up (mean, 18 months; range, 1 to 60) was 100% complete. There were 2 late deaths. Ten patients (6.8%) had 3 to 4+ aortic regurgitation, and 8 of these required late aortic valve replacement. Cusp repair was associated with a high incidence of late aortic valve replacement ($p = 0.005$). At 5 years, freedom from aortic valve replacement and freedom from grade 3 to 4 aortic insufficiency was 90.8% ± 3.3% and 88.7% ± 3.6%, respectively.

Conclusions: The reimplantation valve-sparing procedure with the Gelweave Valsalva prosthesis provides satisfactory results for patients with aortic root aneurysm. Aortic cusp repair may lead to late aortic insufficiency. Proper leaflet evaluation is of paramount importance in preventing residual valve regurgitation.

The use of aortic valve-sparing operations has increased in the last years owing to a better understanding of anatomy, function and pathology of the aortic root. The two main surgical procedures adopted are the remodeling and the reimplantation techniques. While the remodeling technique allows a certain reconstruction of the sinuses, it does not stabilize the annulus and carries an higher incidence of residual aortic insufficiency. Conversely, the classical reimplantation prevents progressive annular dilatation but completely abolishes the sinuses. In fact, the cylindrical shape of the tube has been demonstrated to be a cause of increased stress motion of the valve leaflets, and it might lead to sudden cusps deterioration [1–3]. As it is well known that the sinuses of Valsalva are important in assuring normal function of the aortic valve, many technical changes in the original reimplantation procedures have been suggested to create a sort of pseudosinuses [4, 5]. In 2000, it became available as a modified Dacron (C. R. Bard, Haverhill, Pennsylvania) tube, the Gelweave Valsalva graft (Vaskutek; Renfrewshire, Scotland), designed to recreate sinuses of Valsalva of normal shape and dimensions [6]. The advantages of this conduit have been already reported [7–9], not only for valve-sparing procedures but also in cases of Bentall procedures [10]. In the current paper, we describe the combined experience of three cardiac surgery departments in the reimplantation type of valve-sparing procedure using this conduit and analyse the clinical results of the first 151 patients.

Patients and Methods

Between May 2000 and August 2005, 151 patients with aneurysm of the aortic root underwent a valve-sparing operation according to reimplantation procedure using the Gelweave Valsalva prosthesis at S. Orsola Hospital (University of Bologna, Italy), at Istituto Clinico Humanitas (Rozzano, Italy), and at the Tor Vergata University of Rome (Rome, Italy). The study was approved by the Institutional Review Board of each institute, and informed consent was obtained from all patients.

Patients' age ranged from 14 to 83 years (mean, 56.4 ± 14.4). There were 121 male (80.1%) and 30 female (29.9%) patients. All patients were preoperatively evaluated with transthoracic or transesophageal echocardiography. Angiography was performed in patients older than 50 years of age or with a history of coronary artery disease. The clinical and demographic profile of patients is described in Table 1.

Table 1: Clinical Data

Characteristic	Value
Number of patients	151
Sex, male (%)	121 (80.1)
Age, years (range)	56.4 ±14.4 (14–83)
Hypertension (%)	74 (49)
Coronary artery disease (%)	25 (16.6)
Renal insufficiency (%)	5 (3.3)
Marfan syndrome (%)	21 (13.9)
Bicuspid aortic valve (%)	13 (8.6)
Acute type A dissection (%)	7 (4.6)
Reoperation (%)	3 (2)
NYHA (%)	
• I	48 (31.8)
• II	60 (39.7)
• III	37 (24.5)
• IV	6 (4)

NYHA = New York Heart Association.

The Valsalva Graft

The peculiarity of the Valsalva graft is the possibility of reconstructing the sinuses of Valsalva upon graft implantation and pressurization. The graft design has been described in detail elsewhere [6]. Briefly, it is a standard Dacron conduit that incorporates a short segment of the same material with corrugation at a 90-degree angle with respect to the rest of the graft. This segment, called the skirt, has a length equal to the graft diameter, and it is resilient in the horizontal plane so that upon implantation and pressurization, it will generate pseudosinuses of Valsalva. The suture joining these two sections of Dacron acts as a new sinotubular junction.

Operative Procedures

Cardiopulmonary bypass was instituted through cannulation of the right atrium and the ascending aorta. The systemic temperature was lowered to 32°C. In patients who had an aneurysm of the aortic arch or acute type A dissection, a peripheral cannulation, right femoral or axillary artery was preferred. In these cases, a systemic body temperature of 26°C was used, and antegrade selective cerebral perfusion was utilized during the period of circulatory arrest. Myocardial protection was achieved by antegrade infusion of cold (5°C to 10°C) crystalloid HTK solution (Custodiol; Koehler Chemie, Alsbach-

Haenlein, Germany) or by intermittent blood antegrade cardioplegia depending on the surgeon preferences. The left ventricle was vented by inserting a cannula through the superior right pulmonary vein.

The surgical procedure followed the steps described by David and Feindel [11] in their original article. After the aortic wall is excised, U stitches of Ethibond 3-0 (Ethicon Inc, Johnson and Johnson Co, Somerville, NJ) are passed below the aortic valve, at the level of the ventriculoarterial junction, in a circular fashion. The aortic annulus is then measured with a standard valve sizer, and a 5-mm larger prosthetic tube is chosen (ie, if the aortic annulus measures 25 mm, a 30-mm Valsalva conduit is used). In case of dilated annulus, the sinotubular junction is sized instead. In detail, once a proper leaflet coaptation is obtained by pulling and aligning on the three commissures, the sinotubular junction can be easily measured and the proper size (+5 mm) of the Valsalva graft can be chosen. In case of an overdilated annulus, a subcommissural annuloplasty is performed using pledgeted Ethibond 2-0 at the level of the interleaflet triangles.

Once the Valsalva graft size has been selected, one important step is to adapt the height of the skirt to the height of the patients commissures (Fig 1). The key point of the surgical technique when using a Valsalva conduit is the correct placement of the top of the commissures at the level of the union of the skirted section and the standard graft, which represents the new ST junction. This is achieved by sizing the height of the commissures from the annulus to the top of the commissure. The three commissures are usually of different heights, and the one in between the right and the left cusp is shorter. Therefore, the base of the skirt can be scalloped accordingly to compensate for this length difference. This can also prevent the impingement of the "annular to sinus junction."

After the annular stitches have been passed through the graft and tied, the commissures are retrieved from inside and are pulled at the level of the neo-sinotubular junction. Next, the valve remnants are secured to the Dacron wall and the coronary buttons reattached to the corresponding sinus.

Sixteen patients (10.6%) had associated cusp repair consisting of one or more of the following procedures: shortening of the free margin either by central plication or by weaving a double layer of 6-0 polytetrafluoroethylene suture in 11 patients; raphe resection with annular plication in 7 patients (in 2 of these, shortening of the free margin by a double layer suture was also performed, and in another 1, an autologous pericardium patch was utilized to reconstruct the leaflet where the raphe was present); suturing of a cusp fenestration with 6-0 polypropylene suture in 3 patients.

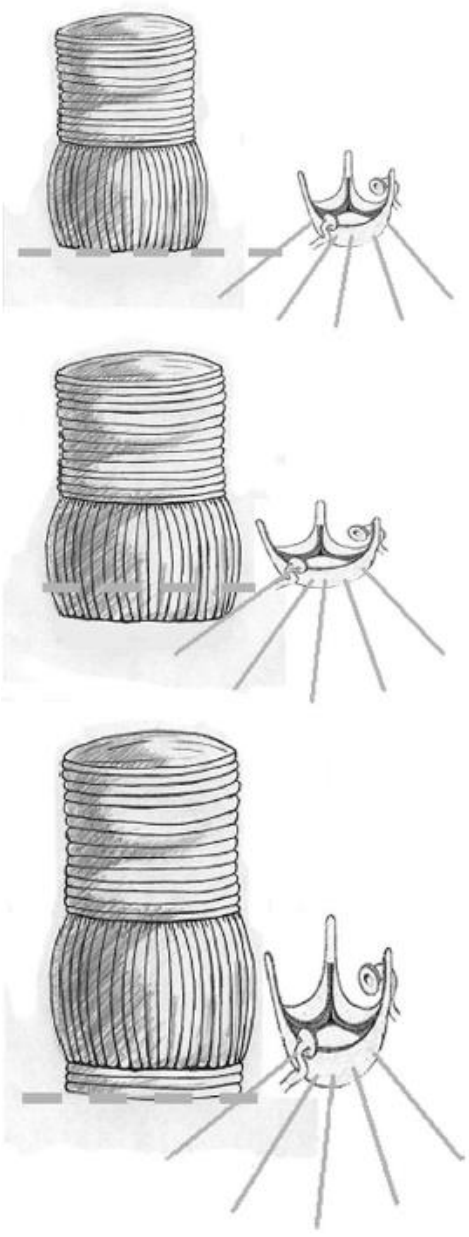

Fig 1. Techniques description: adjustment of the Valsalva graft to the patient's valve remnants to obtain the correct placement of the commissures at the level of the prosthesis sinotubular junction. See text for details.

Aortic arch or hemiarch replacement was performed in 14 patients (9.3%), and in 1 case, an elephant trunk technique was utilized. Antegrade selective cerebral perfusion was used for cerebral protection in all cases. Twenty-one patients (13.9%) underwent coronary artery bypass, 10 patients (6.6%) underwent mitral valve repair or replacement, 3 patients had atrial septal defect repair, and 4 patients underwent radiofrequency ablation for atrial fibrillation. Table 2 summarizes the operative data.

Table 2: Operative Data

Characteristic	Value
Cusp repair (%)	16 (10.6)
Aortic arch replacement (%)	14 (9.3)
• Hemiarch	9 (6)
• Total arch	3 (2.6)
• Elephant trunk	1 (0.7)
CABG (%)	21 (13.9)
MVR/MVP (%)	10 (6.6)
ASD repair	3 (2)
Radiofrequency ablation	4 (2.6)
CPB time, minutes (range)	143 ± 35.4 (99–373)
CC time, minutes (range)	119 ± 24.1 (67–229)

ASD = atrial septal defect; CABG _ coronary artery bypass graft; CC = cross clamp; CPB _ cardiopulmonary bypass; MVP = mitral valve plasty; MVR = mitral valve replacement.

Follow-Up

All hospital survivors were available for follow-up at intervals ranging from 1 to 60 months (mean, 18). Follow- up information was obtained by direct examination or by correspondence with the patient. The date of the last inquiry was between May and August 2005. Every patient had an echocardiogram at 3 and 9 months after the operation and then every year. The degree of residual valve regurgitation was assessed semiquantitatively as follows: 0, none; 1, minimal; 2, mild; 3, moderate; 4, severe. In case of valve insufficiency of grade 3 or greater, echocardiography was repeated at shorter intervals. Echocardiographic data are summarized in Table 3.

Table 3: Echocardiographic Data

	Early Postoperative	Last Visit[a]
Grade of aortic regurgitation (%)		
• 0-1+	104 (71.2)	95 (69.8)
• 2+	35 (24)	39 (28.7)
• 3+	5 (3.4)	2 (1.5)
• 4+	2 (1.4)	0

[a] Eight patients reoperated on during follow-up were excluded; 2 patients died during follow-up and were excluded.

Statistical Analysis

Statistical analysis was performed with SPSS 11.0 statistical software (SPSS, Chicago, Illinois). Continuous variable were expressed as the mean ± SD and were compared with an unpaired two-tailed *t* test. Categorical variables were analyzed with a X^2 test or Fisher's exact test where appropriate. Survival analyses were calculated using the Kaplan-Meier actuarial technique; in addition, freedom from grade 3 or 4 aortic insufficiency and freedom from aortic valve replacement were calculated. Subgroup comparisons were made by means of the log-rank test.

Results

Early Outcomes

There were 5 in-hospital deaths (3.3%): 2 due to multiple organ failure, 2 due to low cardiac output, and 1 due to intestinal ischemia. Three of these patients were operated on because of acute type A aortic dissection and 2 because of annuloaortic ectasia. In-hospital mortality was significantly higher among patients operated on for acute dissection (42.9% versus 1.4%; p = 0.001) and among symptomatic patients (New York Heart Association class III to IV; 9.5% versus 0.9%; p = 0.021). One patient operated on for acute dissection had an acute severe aortic insufficiency on the second postoperative day. At reoperation, a commissural detachment causing prolapse of the left and the noncoronary cusps was found. The patient underwent aortic valve replacement with a

mechanical valve, leaving the reimplanted aortic tissue inside the graft. Three days later, a transesophageal echocardiogram showed a malfunction of the valve due to a mechanical leaflet blockage. This had been caused by some aortic wall tissue becoming detached from the graft. The patient underwent a third operation for total root replacement with a composite valved graft. Weaning from cardiopulmonary bypass was impossible, and a biventricular assist device was implanted. The patient died 2 days later. Two other deaths occurred in patients operated on for acute dissection with peripheral malperfusion and tamponade. They died of multiple organ failure during the postoperative period. The fourth patient was operated on for annuloaortic ectasia, but the postoperative course was complicated by aortic dissection originating from the distal anastomosis; renal insufficiency developed and the patient died of multiple organ failure on the 12th postoperative day. The last patient underwent successful reimplantation procedure associated with CABG but died of intestinal ischemia after 12 days.

Four patients required rethoracotomy for bleeding. At discharge, 5 patients had grade 3 and 2 patients had grade 4 residual aortic regurgitation.

Late Outcomes

There were 2 late deaths (1.4%). The causes of death were gastric hemorrhage and multiple organ failure. Both patients had only trivial aortic regurgitation. The 5-year survival for all patients was 91.2% ± 3.4% (Fig 2). Eight patients were reoperated on during follow-up and required aortic valve replacement because of residual aortic regurgitation. Five of these patients had already a significant valve regurgitation at the time of discharge and were reoperated on within a period between 1 month and 20 months. Two patients had a rapid appearance of aortic valve regurgitation because of endocarditis in 1 case and leaflet elongation (probably due to extreme growth spur in a Marfan child) in another case. The last patient (who had a grade 2 residual valve regurgitation at the time of discharge because of untreated leaflet prolapse) had a progressive worsening of valve regurgitation with initial ventricular enlargement. Two patients with grade 3 residual aortic regurgitation since hospital discharge are asymptomatic with normal left ventricular size and function and are being followed closely by serial echocardiograms. The incidence of reoperation was significantly higher among patients who had undergone cusp valve repair (25% versus 3%; $p = 0.005$). In fact, 4 of the reoperated patients with grade 3 to 4 aortic insufficiency had a cusp repair

procedure.

At 5 years, freedom from late aortic valve replacement and freedom from combined grade 3/4 aortic insufficiency and aortic valve replacement was 90.8% ± 3.3% and 88.9% ± 3.3%, respectively (Fig 3A, B). The sinuses of Valsalva were well reproduced, as shown by echocardiography, in all patients (Fig 4). Some patients also underwent other imaging modality such as computed tomography scan, magnetic resonance imaging, or angiography that confirmed the echocardiographic findings (Figs 5, 6).

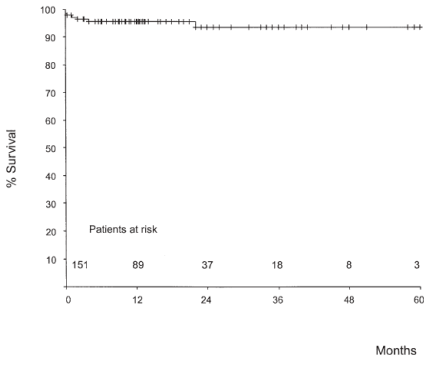

Fig 2: Overall actuarial survival for all patients. Survival was 93.5% at 1 year and 91.2% at 5 years.

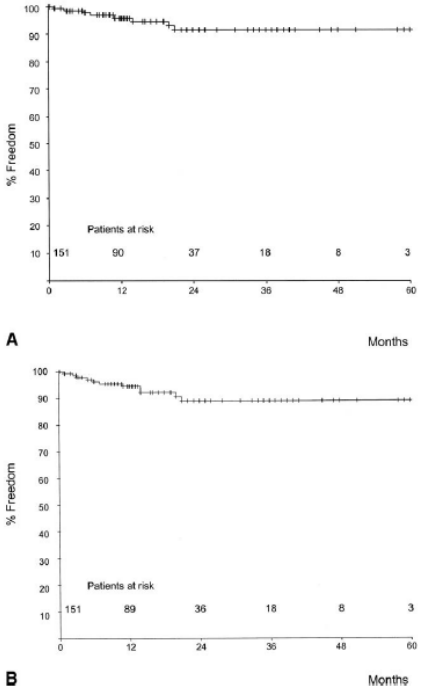

Fig 3: (A) Actuarial freedom from late aortic valve replacement. Freedom from aortic valve replacement was 95.7% at 1 year and 90.8% at 5 year.

(B) Actuarial freedom from residual grade 3-4 aortic regurgitation and aortic valve replacement. Freedom from combined residual grade 3-4 aortic regurgitation and aortic valve replacement was 94.7% at 1 year and 88.7% at 5 years.

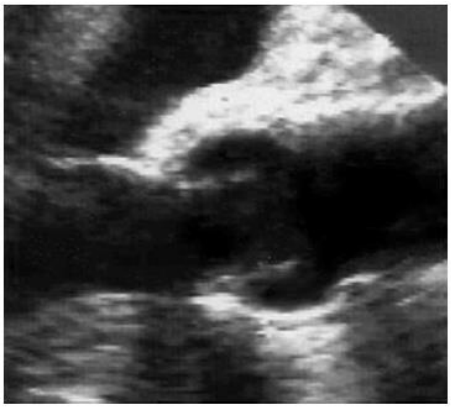

Fig 4: Postoperative echocardiographic aspect of the aortic root in a patient after a reimplantation procedure with the Valsalva graft.

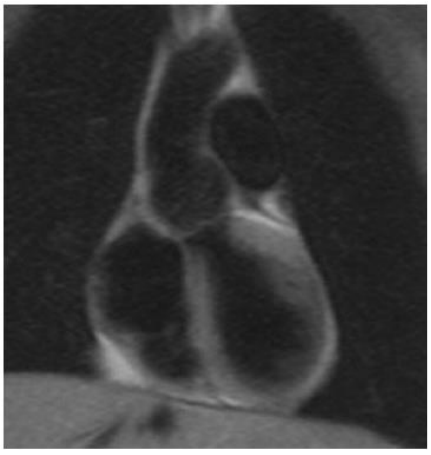

Fig 5: Postoperative magnetic resonance image of a Marfan syndrome patient 3 years after aortic reimplantation procedure with the Valsalva graft.

Fig 6: Postoperative multislice computed tomography scan reconstruction of the entire aorta after a reimplantation procedure with the Valsalva graft: the left and the noncoronary sinuses are clearly detectable.

Comment

Aortic valve-sparing procedures are particularly appealing for patients with aortic root dilatation because these procedures avoid the problems of prosthetic heart valves, but pose the problem of the long-term durability of the spared aortic valve. Residual aortic valve regurgitation is the Achille's heel of this type of surgical procedure. Among the two major techniques of valve-sparing procedures, remodeling [12] or reimplantation [11], the latest has gained popularity in the past years because it provides a better annulus stabilization, which has been shown as an important variable in the long-term durability of the result. The drawbacks of the reimplantation technique is that it completely abolishes the sinuses of Valsalva that have been demonstrated of paramount importance in assuring a physiologic movement of the aortic leaflets and at the same time reducing leaflet stress. For these reasons, several variations in the original David I technique have been introduced by various authors [4, 5, 13]. Nonetheless, the classic David I technique has demonstrated encouraging medium-term results in an adult [14, 15] as well as in a Marfan [16, 17] population in various reports. Our preference goes to the use of the Valsalva graft (Gelweave Valsalva) because it has all the advantages of the reimplantation procedure while allowing a proper reconstruction of the sinuses without significant modification in the surgical technique. It is hoped that the anatomical reconstruction that is possible using the Valsalva graft could contribute to a better and longer preservation of valve integrity. It has been proved that the absence of sinuses, among other factors, causes an alteration in the opening and closing characteristics of the valve leaflets that could induce, with time, thickening and rolling of the cusps' free margins [1, 2].

It goes without saying that a perfect postoperative result with absence of residual aortic regurgitation is required if we want to compare, in terms of long-term benefit, the positive effect of the presence of sinuses of Valsalva. Presence of more than trivial residual valve regurgitation is the sign of cusp malalignment, torsion, altered coaptation, and cusp prolapse among others; all these different anatomical factors will invariably tend to a progressive worsening with time, with the consequent increase of valve insufficiency.

Imperfect results, independently from the technical or anatomical reasons that have caused them, should not be considered if the scope of the study is to ascertain whether the presence of physiologic eddy currents inside the reconstructed sinuses are important in preserving valve integrity in the long term. In any case, imperfect results

with more than trivial residual valve regurgitation should not be accepted because the patient will face a second operation within a short time.

The initial results of this multicenter study clearly show that an imperfect result in the immediate postoperative period should be strongly avoided. In fact, excluding one case of endocarditis and a pediatric case with a significant growth spur, all reoperated patients had already evidence of grade 2 or higher aortic regurgitation at time of discharge. Furthermore, all patients were reoperated on in a period ranging from 1 to 20 months. This clearly indicates that residual aortic valve regurgitation has a tendency to worsen at a rapid pace. If the postoperative transesophageal echocardiogram shows a more than trivial valve regurgitation, it is advisable reopen the graft and either fix the problem if possible or, better, immediately proceed for valve replacement. Most of the failures reported are obviously the consequence of our learning curve. All centers did not have a previous direct experience with the reimplantation type of valve-sparing procedure, which started only after the Valsalva graft became available. Therefore, we must consider not only a learning curve for the correct use of the graft but also for the surgical procedure itself.

If other procedures are added on the valve cusps, such as triangular resection or plication, free-edge reinforcement to correct an intrinsic leaflet prolapse, or a cusp prolapse that has been induced by a suboptimal orientation of the valve, the chances of ending up with an imperfect result are much higher. As a matter of fact, among all patients who required an aortic valve replacement, half of them had received some sort of cusp plasty.

On the other hand, it appears evident from this initial experience that a proper root and sinuses reconstruction remains stable at least for the time considered. It is therefore evident that only these patients should be considered in a long-term evaluation to ascertain whether the use of the Valsalva graft, with optimal sinuses reconstruction, is superior for preserving valve integrity.

In conclusion, this initial experience from three different centers has shown satisfactory midterm results. Proper patient selection and correct surgical technique will contribute to better root reconstruction. Patients with satisfactory reconstruction show, for the time being, stable results over time.

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CHAPTER 4

Reimplantation valve-sparing aortic root replacement with the Valsalva graft: what have we learnt after 100 cases?

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Abstract

Objectives: Reimplantation valve-sparing aortic root replacement has been increasingly performed with improving perioperative and midterm results. The success of this operation primarily depends on preserving the highly sophisticated dynamic function of the aortic valve by recreating an anatomical three-dimensional configuration similar to the normal aortic root, thus minimizing the mechanical stress and strain on the cusps. Over the years several techniques have been proposed to reproduce the sinuses of Valsalva. We reviewed our experience with aortic valve reimplantation by means of a modified Dacron graft that incorporates sinuses of Valsalva, in a series of 100 consecutive patients.

Methods: During a 60-month period, 100 patients with aortic root aneurysm underwent aortic valve reimplantation using the Gelweave Valsalva™ prosthesis. There were 74 males and the mean age was 60±12 years (range 28–83 years). Five patients had the Marfan's syndrome, 15 had a bicuspid aortic valve. Cusp repair was performed in five patients. The mean follow-up time was 28.6 months (range 1–60). Transesophageal echocardiogram was performed at the end of each procedure to assess the aortic valve in terms of competence, dynamic motion and level of coaptation within the graft.

Results: There was one hospital death and two late deaths. Overall survival at 60 months was 91.7±5.1%. Five patients developed severe aortic incompetence (AI) during follow-up requiring aortic valve replacement (AVR). The 60 months freedom from re-operation due to AI was 90.9±4.4%. One patient had moderate AI at latest echocardiographic study. The 60 months freedom from AI>2+ was 91.6±7.9%. Cox regression identified cusp's repair as independent risk factor (P=0.001) for late reimplantation failure (AVR or AI>2+). There were no episodes of endocarditis and the majority of the patients (88%) were in New York Heart Association functional class I.

Conclusions: The aortic valve reimplantation with the Gelweave Valsalva™ prosthesis provided satisfactory mid-term results. An accurate assessment of the level of coaptation of the aortic cusps in respect to the lower rim of the Dacron graft by means of intraoperative transesophageal echocardiogram at the end of each procedure is mandatory in order to avoid early reimplantation failure. Cusp's repair may play an important role in the development of late AI. However, long-term results are needed in order to define the durability of this technique.

Introduction

Aortic valve reimplantation procedure introduced by David in 1995 [1], is now considered a safe operation with satisfactory mid- and long-term results. To overcome the main limit of this technique, the lack of the sinuses of Valsalva, in 2000 De Paulis introduced the Valsalva graft [2], a modified Dacron conduit that on implantation recreates the sinuses of Valsalva of normal shape and dimension [3]. Since then, an increasing number of surgeons have been using this prosthesis. The aim of this retrospective single institution study is to review our experience with aortic valve reimplantation using the Valsalva graft, in a series of 100 consecutive patients during a 5-year period.

Materials and methods

From October 2002 to November 2007, 100 consecutive patients underwent aortic root reimplantation using the Valsalva graft. Patients' demographic profile is reported in Table 1. Our technique has been previously described in detail [4]. The Maselli technique to reposition the 'Valsalva graft sinotubular junction' [5] was used in three cases. The graft sizes used were 28 mm in two patients, 30 mm in 28 patients and 32 mm in 70 patients.

The mean cardiopulmonary bypass (CPB) time was 125± 22 min (range 90–201) with a mean aortic cross-clamp time of 107±17 min (range 67–170). Hemiarch reconstruction using moderate hypothermic circulatory arrest (24 °C nasopharyngeal) and antegrade selective cerebral perfusion (ASPC) was performed in the only patient operated on for acute type A aortic dissection, with ASCP time of 27 min and HCA time of 29 min.

Cusp's repair was performed in five patients and all of them had a bicuspid aortic valve. Repair consisted of free margin shortening in two cases and triangular resection in three.

Concomitant procedures included mitral valve repair in nine patients (9%), scheduled coronary artery bypass in 12 patients (12%), non-scheduled coronary artery bypass in two patients (2%), atrial septal defect repair in one patient (1%), and radio frequency ablation for atrial fibrillation in two patients (2%).

Transesophageal echocardiogram was performed at the end of each procedure to assess the reimplanted valve's dynamic motion and incompetence grade. In all patients, the reconstruction of the 'pseudo-sinuses' assured a sufficient gap to avoid any contact

between the open leaflet and the Dacron wall. None of the patients left the operating room with an AI greater than mild. From 2004 onwards, the level of coaptation of the aortic cusps within the Dacron graft was also evaluated. Since then, a level of coaptation >2 mm below the lower border of the Dacron graft was not considered acceptable. All the patients underwent a further transthoracic echocardiogram before discharge.

Table 1: Patient demographic profile

Characteristic	**n=100**
Age (years)	60±12
NYHA functional class	
• I	41
• II	35
• III	22
• IV	2
Pathology	
• Aortic root aneurysm	94
• Chronic dissection	5
• Acute type A dissection	1
Left ventricular ejection fraction	
1. >60%	68
2. 40-59%	27
3. <39%	5
Aortic incompetence	
• None/trivial	19
• Mild	17
• Moderate	27
• Severe	37
Marfan syndrome	5
Bicuspid aortic valve	15
Coronary disease	14
Mitral regurgitation greater than mild	8
Diameter of aneurysm (mm)	
• Annulus	26.9±6.3
• Sinus segment	48±8.8
• Ascending aorta	51.2±9.1

Values are mean±1 S.D.

Follow-up

Follow-up was conducted by one investigator in December 2007 and was 100% complete. Transthoracic echocardiogram was used for AI evaluation. AI was scored as none, trivial, mild, moderate, or severe (0–4+). The mean follow-up time was 28.6 months, ranging from 1 to 60 months.

Statistical analysis

Continuous variables were expressed as the mean±S.D. and were analyzed by using the unpaired two-tailed t-test. Categorical variables were presented as percentage and were analyzed with the χ^2-test or Fisher exact test when appropriate. All preoperative, intraoperative and postoperative variables were first analyzed by using univariate analysis to determine whether any single factor influenced AI during follow-up. Variables that achieved a P-value of <0.2 in the univariate analysis were examined by using multivariate analysis with forward stepwise logistic regression to evaluate independent risk factors for the AI during follow-up. Estimates for long-term survival and freedom from morbid events were made by the Kaplan–Meier method. Differences between survival curves were evaluated with the log-rank statistic.

Results

There was one hospital death and two late deaths. The cause of the hospital death was sepsis at four months after reimplantation in a patient that had a cardiac arrest on postoperative day 4. Although resuscitation was successful, the patient had a devastating neurological injury due to anoxia. Coronary angiography demonstrated no evidence of coronary button occlusion, and the cause of the cardiac arrest remains unclear. The causes of late death were cardiac (sudden death) in one patient at 37 months and non-cardiac (hepatocellular carcinoma) in the other patient at 48 months. At the time of surgery, there was no evidence of hepatic neoplasm. Liver function test, hepatitis B and C markers were negative. Both patients had trivial AI at latest follow-up. Overall survival at 60 months was 91.7±5.1% (Fig. 1).

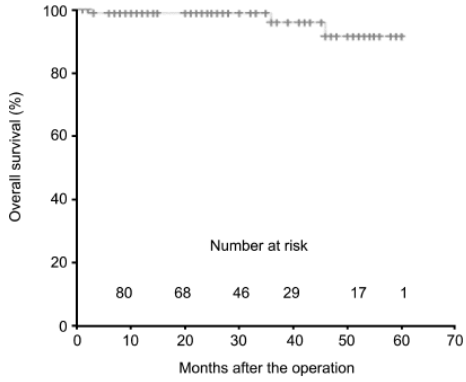

Fig 1: overall survival

Eight patients required early re-exploration (<24 h) for bleeding and tamponade. Three patients developed postoperative myocardial infarction (creatinine phosphokinase >300 IU/myocardial band >5%) without hemodynamic deterioration and with no significant ejection fraction reduction. Intubation time longer than 48 h occurred in four cases. Postoperative renal failure requiring dialysis occurred in one patient. Two patients developed bacterial mediastinitis and were treated successfully with the vacuum-assisted closure device (VAC). Two patients underwent pacemaker implantation because of permanent atrio-ventricular block.

Re-operations and aortic valve function

During follow-up five patients developed significant AI requiring aortic valve replacement (AVR), respectively 1, 7, 8, 33, 42 months after the first procedure. Re-operated patients' details are shown in Table 2. The 60 months freedom from re-operation due to AI was 90.9±4.4% (Fig. 2).

At the closure of the study, the grade of AI among the 92 survived, non-re operated patients was as follows: none or trivial (0–1+) 47 patients, mild (2+) 44 patients, moderate (3+) 1 patient, severe (4+) none.

The 60 months freedom from AI greater than mild was 91.6±7.9%. Cusp's repair turned out to be a significant risk factor for reimplantation failure (AVR or AI>2+) both to univariate analysis (P=0.002) and Cox regression (P=0.001).

Table 2: Re-operated patient characteristics

	Age (years)	Valve morphology	Cusp's repair	Level of cusps coaptation>2mm below the graft	Aortic incompetence at discharge	Months between first procedure and re-operation
Patient 1	28	Tricuspid	No	Yes	Moderate	1
Patient 2	33	Bicuspid	Free margin shortening	No	Mild	7
Patient 3	36	Bicuspid	Triangular resection	No	Mild	8
Patient 4	51	Tricuspid	No	No	Mild	33
Patient 5	65	Tricuspid	NO	No	No incompetence	42

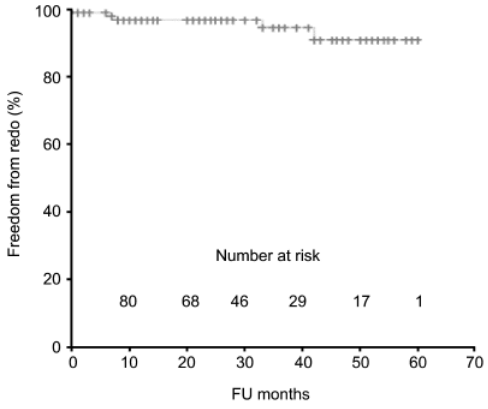

Fig. 2. Freedom from re-operation.

Discussion

Since its introduction in 1995, the original aortic valve reimplantation technique underwent several modifications, mostly devised to reproduce the sinuses of Valsalva [6–8]. When we began our experience with this procedure in October 2002, we chose the Valsalva graft for two main reasons. Firstly, we thought it was based on a very simple and effective idea to reproduce an anatomical configuration very similar to the normal aortic root. Furthermore, over the years this graft has proven to be reliable and has shown encouraging mid-term results [9]. Although the radial compliance of this graft at the skirt (the prosthetic aortic root) has not been shown to be maintained over the years, its curvature is supposed to reduce the stress and strain of the aortic cusps

during systole and diastole, perhaps providing a long durability of the native valve [10]. The second reason that led us to adopt the Valsalva graft is the simplicity of the implantation technique, as it is the same as the original one described by David [11] except for the need to measure the heights of the interleaflet triangles, tailoring the graft according to it. Indeed, the precise placement of the top of the commissures at the junction between the skirt and the tubular part of the graft (the prosthetic sinotubular junction) is crucial to obtain good cusps' coaptation. Because the heights of the three commissures are often unequal (the height of the interleaflet triangle between the non-coronary and the left coronary cusps is usually shorter than the other two), heights of all three interleaflet triangles are carefully measured. According to it, the Maselli modification [12] may be useful when an imperfect alignment between the prosthetic STJ and the top of the commissures is noted. We actually used this tip in three patients with good results in terms of cusps' coaptation.

The importance of intraoperative TEE at the end of each procedure in order to assess the competence and the dynamic motion of the valve is nowadays well known. Specifically, as previously suggested by the Hannover group [13], from 2004 onwards we pay particular attention to the level of coaptation of the cusps in respect to the lower rim of the graft. It has been shown that a level of coaptation within the tube graft is essential to achieve valve competence. Looking at it retrospectively, the intraoperative TEE of the patient re-operated on for severe AI one month after the first procedure (November 2002), showed a level of coaptation frankly below the lower rim of the Dacron graft. A second interesting element detected by TEE is the lack of contact between the open aortic leaflet and the Dacron wall that, as previously noted [3], could be an important characteristic for valve's durability in the long-term.

In our series, two out of five patients who underwent cusp's repair were re-operated on for severe AI with a strong statistical significance. It must be stressed that both had a bicuspid aortic valve with asymmetric cusps. The other three patients who underwent cusp's repair also had a bicuspid aortic valve but the asymmetry was less evident and required a less extensive cusp's repair. Therefore, according to our experience, we have recently adopted the policy to spare bicuspid aortic valves only in case of symmetric cusps with no need for extensive additional repair. However, other authors have described excellent results with bicuspid valve-sparing operations regardless of the valve's morphology. In particular, Aicher et al. in a clinical study comparing the results of valve-sparing root replacement in bicuspid and tricuspid aortic valve, failed to show any significant difference between the two groups in terms of valve durability [12]. Similarly,

El Khoury et al. described encouraging results after cusp's prolapse correction during valve-sparing operation [13].

The results of our study, in terms of freedom from aortic valve re-operation, are consistent with the outcomes of others. Pacini et al. [14], in a similar mid-term study on aortic valve-sparing reimplantation, including 57 patients treated with the Valsalva graft, reported a three-year freedom from AVR of 92%. Kallenbach et al. reported, in a large series of aortic valve-sparing operations using a tubular graft, an actuarial freedom from re-operation of 95%, 91% and 87%, respectively, at 3, 5 and 10 years [15].

During follow-up none of the patients developed endocarditis. This must be regarded as a considerable advantage of valve-sparing procedure over the Bentall operation that has invariably a certain incidence of valve related complications including endocarditis either with mechanical or tissue valve [16–18].

The main limitations of this study are to be retrospective and the length of follow-up (maximum 60 months), but to our knowledge is one of the largest single-center experience with a valve-sparing operation using the Valsalva graft.

In conclusion, the aortic valve reimplantation with the Gelweave Valsalva™ prosthesis provided satisfactory midterm results. An accurate assessment of the valve's dynamic motion and of the level of cusps' coaptation within the graft by means of TEE at the end of each procedure is mandatory in order to avoid early reimplantation failure. Cusp's repair may play an important role in the development of late AI and should be performed with caution in cases of asymmetric bicuspid aortic valve. The radial extension of the skirt portion of the Valsalva graft over the years has not yet been demonstrated and should be investigated. Long-term results are needed in order to define the durability of this technique.

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CHAPTER 5

Compliance of the Valsalva graft's pseudosinuses at midterm follow-up with cardiovascular magnetic resonance

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Abstract

Background. In previous studies, the Valsalva graft's compliance at the level of the Dacron pseudosinuses was found similar to that of normal sinuses shortly (2 ± 1 months) after the operation. We sought to investigate with cardiac magnetic resonance the compliance of the Valsalva graft pseudosinuses at midterm follow-up.

Methods. Seven patients (group A) and 7 age-matched controls (group B) were studied with steady-state free precession and phase-contrast cardiac magnetic resonance for aortic root and ascending aorta evaluation. Blood pressure was measured during phase-contrast acquisition to derive the following mechanical properties of the vascular prosthesis: pulsatility, compliance, distensibility, and elastic modulus.

Results. Mean postoperative follow-up was 55 ± 9.84 months. Mean age was 69.2 ± 4.98 years in group A, and 65.7 ± 7.16 years in group B. All the studied variables were coherent in showing a significant difference between the two groups, and between aortic root (skirt portion of the graft) and ascending aorta (tubular part of the graft) in group A. The presence of periaortic fibrosis did not show any correlation with the ascending aorta's mechanical properties.

Conclusions. At midterm follow-up, the pseudosinuses compliance of the Valsalva graft is still appreciable and significantly greater than the tubular portion.

The original technique of reimplantation of the aortic valve using a standard Dacron (C.R. Bard, Haverhill, PA) conduit, described by David and Feindel [1] in 1992, does not allow a proper reconstruction of the sinuses of Valsalva. To overcome this limit, in 2000, De Paulis and associates [2] introduced a new Dacron conduit, the Valsalva graft, that incorporates sinuses of Valsalva (the skirt portion of the graft), recreating sinuses of normal shape and dimensions (pseudosinuses). Reconstruction of the sinuses of Valsalva is aimed to assure a normal valve motion, decreasing mechanical stress and thereby increasing valve durability [3]. It has been shown that a loss of sinus compliance may play a role in both the natural process of aortic valve degeneration as it occurs in aortas stiffened by old age fibrosis or by atherosclerosis, as well as in the degeneration of aortic bioprostheses [4].

Previous studies demonstrated that the distensibility of the Valsalva graft at the level of the Dacron pseudosinuses in the very short term (2 ± 1 months after the operation) is similar to the sinuses distensibility of control healthy subjects [5]. However, it is unknown whether the compliance of the Valsalva graft at the pseudosinuses is maintained over the years. Because cardiac magnetic resonance (CMR) allows an accurate a reproducible assessment of great vessel anatomy and deformation over time, we sought to use this technology to investigate the Valsalva graft's skirt compliance at midterm follow-up.

Material and Methods

Patient Population

From October 2002, all patients admitted to our department with aortic root aneurysm and normal or nearly normal aortic cusps underwent aortic valve reimplantation using the Valsalva graft. Surgical technique has been previously reported in detail [6]. Among them, 7 nonselected patients with a similar follow-up duration agreed to undergo a CMR study aimed at aortic root compliance assessment, and were selected to form the study group (group A). Patients with atrial fibrillation, potentially hampering an accurate CMR evaluation of aortic distensibility, were excluded from the study. Seven agematched subjects without any evidence of heart disease and with normal aortic root anatomy, after a CMR study performed for various clinical reasons,, underwent an aortic root and ascending aorta assessment, and served as a control group (group B). Our Institutional

Review Board approved the study. All subjects gave written informed consent. Patient characteristics are reported in Table 1.

Table 1. Patient Characteristics

Characteristic	Surgical Group	Control Group	*p* Value
Male/Female	6/1	7/0	
Age at surgery, years	64.5 ± 5.1	–	
Age at follow-up, years	69.2 ± 4.9	65.7 ± 7.1	0.07
Follow-up after surgery, months	55.2 ± 9.8	–	
Weight, kg	79 ± 15.25	82 ± 9.72	0.715
Height, cm	170 ± 7.48	177.5 ± 4.76	0.095
SBP, mm Hg	127.85 ± 9.94	126.14 ± 9.55	0.817
DBP, mm Hg	76.42 ± 4.75	75.86 ± 6.09	0.982
Pulse pressure, mm Hg	51.42 ± 10.69	50.29 ± 10.50	0.933

Data are expressed as mean ±SD.
DBP = diastolic blood pressure; SBP = systolic blood pressure.

Magnetic Resonance Study and Measurements

All studies were performed on a 1.5-T magnetic resonance imaging system (Philips Achieva, release 1.6; Philips Medical Systems, Best, Netherlands) equipped with a five-elements phased array surface coil. Vectorcardiographic gating was used, with images acquired during midexpiratory breath-holds. After acquisition of standard cardiac planes according to the Society of Cardiovascular Magnetic Resonance recommendations [7], an additional steady-state free precession (SSFP) plane, perpendicular to the left ventricular outflow tract, was prescribed to depict two orthogonal planes dissecting the aortic root (Fig 1).

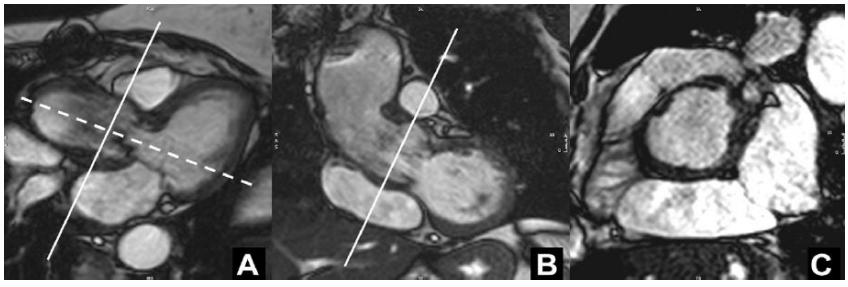

Fig 1. (A) Original horizontal long-axis three-chamber view image. (B) Derived three-chamber image. Scan plane perpendicular to the dash line in (A). (C) Derived image on aortic root. Scan plane indicated by solid line in (A) and (B).

Thereafter, an SSFP image (slice thickness 5 mm, temporal resolution 30 ms or less) was acquired at the aortic root level. This latter was then repeated on the ascending aorta, 3 cm above the aortic valve plane, perpendicular to the vessel. Finally, for the quantitative flow measurements, a retrospectively gated phase-contrast sequence was used during expiratory breath-holds, velocity encoded through-plane in the slice select gradient direction. The following imaging parameters were used: 40 frames per heartbeat; field of view 320 mm; repetition time 7 ms; echo time 3.5 ms; flip angle (α) 15 degrees; matrix 256 × 128.

Typically, the velocity encoding range was set at 135 cm/s. Flow images were reacquired with a higher velocity encoding range if velocity aliasing occurred. During the acquisition of velocity encoded data, noninvasive blood pressure was measured with a MR-safe monitor (Veris MR Vital Signs Monitor; Medrad, Indianola, PA). For the quantitative flow measurements and contour tracing of the vessels, data were transmitted to offline image analysis software (CMR42; Circle Cardiovascular Imaging Inc, Calgary, AB, Canada).

The contours of the aortic root and ascending aorta cross sections were traced in each phase, and the maximal and minimal areas were recorded. Tracings were performed on the magnitude images, using the velocity images as reference. Moreover, we measured the area of periaortic fibrosis from a still frame of SSFP images, both at root and ascending aorta level. Various indexes descriptive of the mechanical stiffness of the vessel were calculated from CMR and noninvasive blood pressure measurement, as shown in Table 2.

Table 2. Indexes of Aortic Stiffness

Variable	Units	Formula	Definition
Pulsatility	%	maxA − minA / minA × 100	Relative change in lumen area during the cardiac cycle
Compliance	mm^2/mm Hg	[(maxA − minA) / PP]	Absolute change in lumen area for a given change in pressure
Distensibility	%/mm Hg	[(maxA − minA) / PP × minA] × 100	Pressure change driving a relative increase in lumen area
Elastic modulus	mm Hg	PP × minA / (maxA − minA)	Pressure change driving a relative increase in lumen area

maxA = maximal area; minA = minimal area; PP = pulse pressure.

Statistical Analysis

Data are expressed as number or percentage, or median and range, where appropriate. Differences between groups were evaluated with Mann-Whitney U test for discrete and continuous variables. A p value less than 0.05 was considered as significant. All the analyses were performed using Stata version 10 software (StataCorps, College Station, TX).

Results

Mean follow-up after surgery was 55.2 ± 9.8 months. The systolic blood pressure was similar between patients of the same group, reducing the possible effect of blood pressure on the observed vessel's area changes.

The main results are listed in Table 3. In normal control subjects, we observed no substantial difference between aortic root and ascending aorta mechanical properties: vessel mechanical properties were very similar at the two observed levels, with a constant nonsignificant difference between aortic root and ascending aorta, the latter showing greater stiffness, with reduced pulsatility, distensibility, and compliance, and a higher elastic modulus. When compared with normal control subjects, patients with the Valsalva graft showed a clear and constant reduction in aortic root elastic properties, but a near total loss of the elastic properties of the ascending aorta. However, while distensibility and pulsatility at the level of the tubular portion of the graft were virtually absent, at the level of pseudosinuses they were only about half of the normal values as measured in the control group. In fact, a significant difference in all measured variables was evident between the pseudosinuses and the tubular portion of the graft. Furthermore, we sought to measure the amount of periaortic fibrosis, nearly always present in variable fashion among operated patients, to assess the possible relationship with the ascending aorta stiffness. The amount of periaortic fibrosis showed high variability: mean observed value at aortic root level was 9.35 ± 5.63 cm2 (range, 4 to 19 cm^2; median value 8 cm^2). The amount of fibrosis, however, did not show any relationship with the mechanical properties of the vessel (Fig 2).

Table 3. Mechanical Proprieties of Native Aorta (Control Group) and Valsalva Prosthesis (Surgical Group)

	Surgical Group n=7	Control Group n=7	*p* value
Pulsatility, %			
• Aortic root	10.42 ± 4.51[a]	23.55 ± 8.94	0.007
• Ascending aorta	3.54 ± 3.17[b]	21.14 ± 8.55	0.001
• *p* value	0.002	0.916	
Compliance, mm2/mm Hg			
1. Aortic root	1.81 ± 0.69[a]	4.06 ± 2.23	0.003
2. Ascending aorta	0.68 ± 0.83[b]	2.85 ± 1.10	0.001
3. *p* value	0.001	0.254	
Distensibility, %/mm Hg			
1. Aortic root	17.41 ± 9.98[a]	36.88 ± 27.02	0.037
2. Ascending aorta	6.33 ± 8.00[b]	19.49 ± 7.35	0.005
3. *p* value	0.002	0.118	
Elastic modulus, mm Hg			
• Aortic root	6.03 ± 3.47[a]	2.42 ± 0.74	0.015
• Ascending aorta	31.859 ± 31.129[b]	3.02 ± 1.87	0.02
• *p* value	0.039	0.7	

[a] Skirt portion of the prosthesis.
[b] Tubular portion of the prosthesis.

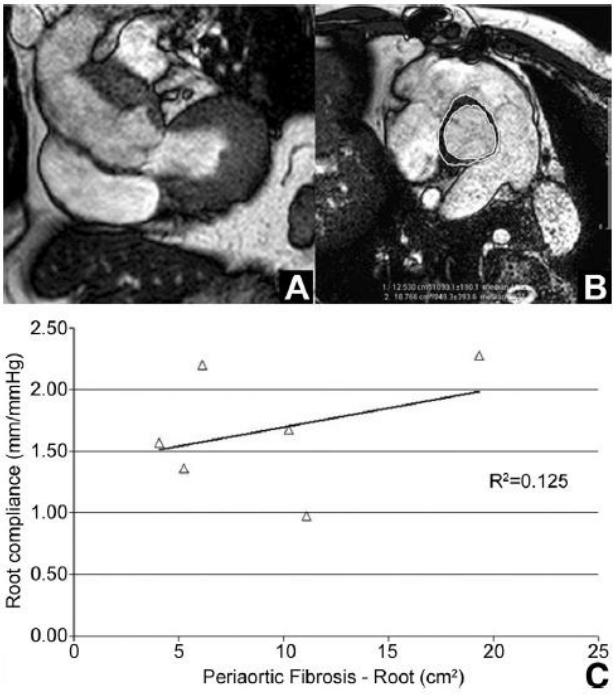

Fig 2. (A, B) The amount of periaortic fibrosis showed high variability among patients: mean observed value at aortic root level was 9.35± 5.63 cm^2 (range, 4 to 19; median value 8). The amount of fibrosis, however, did not show any relationship with the mechanical properties of the vessel, as shown in (C).

Comment

Aortic root dynamics are functional to optimized transvalvular hemodynamics and to minimized cusp stress and strain by creating optimal cusp loading conditions and by lowering transvalvular turbulence; hence, cusp fatigue throughout the complex opening and closing mechanics of the cusps 30 to 40 million times a year [8] (and the likelihood of structural valve deterioration), may be minimized by the dynamics of the aortic root. The importance of the sinuses of Valsalva, firstly investigated by Leonardo da Vinci about 4 centuries ago, has been confirmed by recent observations. Robicsek and Thubrikar [5] have demonstrated that in vitro under normal hemodynamic conditions, although stiffening of the exterior of the aortic root does not change pressure flow relations, it does lead to severe dysfunction and increased stress loading of the aortic valve cusps. Based on this concept, several authors have introduced in recent years some changes in aortic valve-sparing surgery to make this operation more physiologic [9, 10].

In 2002, De Paulis and colleagues [5] published an echocardiographic analysis of valve motion after aortic valve reimplantation with the Valsalva graft and found that shortly after the operation (mean follow-up was 2 months), the anatomic reconstruction of the aortic root allowed leaflet motion similar to that of normal subjects. In particular, graft distensibility was found to be maintained at the pseudosinuses, whereas it was reduced both at the annulus and at the sinotubular junction [5].

Schoenhoff and colleagues [11], by means of CMR, have recently confirmed the compliance of the Valsalva graft's skirt during the postoperative course. Nevertheless, they utilized the peak velocity above the aortic valve as an indirect marker of compliance [11].

According to our knowledge, until now, no data were available in literature about the mechanical proprieties of this graft in the midterm follow-up. Our results show that the mechanical proprieties of the aorta are significantly different between the surgical group and the control group. In details, the aortic root of the surgical patients (the skirt portion of the graft) seems to have distensibility, pulsatility, and compliance approximately halved compared with controls. However, surprisingly enough, our data show that the elastic proprieties of the pseudosinuses are still appreciable over the years. Indeed, the pulsatility, compliance, distensibility, and elastic modulus of the skirt are significantly different than those of the tubular portion of the prosthesis. This finding seems to confirm that, over the years, the Valsalva graft continues to behave like the

native aortic root not only from a static point of view (curvature of the sinuses) but also from a dynamic point of view, somehow responding to the systodiastolic changes in pressure. Moreover, it is not surprising that in the surgical group, contrary to the control group, elastic changes in the tubular portion of the graft are minimal. In fact, the tubular portion of the graft behaves like a conventional vascular Dacron prosthesis, which, as is known, is not able to guarantee the Windkessel effect [12].

A further interesting point is the lack of relationship between the periaortic fibrosis and the mechanical proprieties of the prosthesis, indicating that the inflammatory postoperative reaction generated by the graft does not affect in any way its dynamic function. Based on these results, it is therefore reasonable to assume that the root portion of the prosthesis maintains its compliance even in the long term.

In conclusion, our study shows that the mechanical proprieties of the Valsalva graft are, to a certain extent, maintained during the midterm follow-up. That could play an important role in the durability of the native aortic valve by reducing the stress and strain on the cusps. Nevertheless, long-term results are still needed to draw definitive conclusions.

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INVITED COMMENTARY

Replacing any part of the human aorta by a standard vascular graft results in an increase of characteristic impedance leading to decreased compliance and a decreased ability to maintain the "Windkessel" function of the aorta. These effects may be most pronounced, if the sinus of Valsalva is to be replaced, because the dynamic characteristics in this part—aiming at reducing stress to the cusps of the aortic valve and optimizing ventriculoarterial coupling— are crucial to maintain physiologic flow in the coronary arteries and physiologic instantaneous movement patterns of the valve leaflets and the aortic wall.

Especially the latter subject attracted clinical notice when the original Bentall operation for repair of aortic root pathologies was more and more replaced by valvesparing techniques during the last 15 years. The remodelling procedure was considered to maintain the function of the sinus, but redilatation of the aortic root frequently occurred. This problem was avoided by the reimplantation technique, which, however, completely abolished the function of the sinus of Valsalva, with the risk of increased stress on the native valve leaflets probably resulting in poor durability of the repair.

Although the controversies concerning the pros and cons of these techniques were going on and technical refinements of both procedures were proposed, the Valsalva graft with a distensible proximal part (the "skirt") was introduced into clinical practice. Initial short-term results were encouraging, but scepticism widely persisted concerning the maintenance of the elastic properties over time. The formation of adhesions and pseudoneointimal ingrowth was considered to diminish these favorable effects in the long run.

The article presented here [1] addresses this crucial question. Even if the cohort of patients was small, this nicely performed magnetic resonance imaging study demonstrated that there still was compliance of the "skirt" of the graft compared with the tubular part after a follow-up of roughly 5 years. Even if the distensibility was lower compared with the native aorta of control subjects, these findings give hope that the best of the two worlds of valve-sparing surgery of the aortic root may be combined by the use

of this graft. Larger, comparative studies are now warranted to demonstrate the superiority and clinical benefit of the Valsalva graft over a simple tubular prosthesis.

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PART 2

THE VALVE-SPARING AORTIC ROOT REPLACEMENT IN DIFFERENT SETTINGS: MARFAN SYNDROME, BICUSPID AORTIC VALVE AND OLDER PATIENTS

CHAPTER 6

Reimplantation valve-sparing aortic root replacement in Marfan syndrome using the Valsalva conduit: an intercontinental multicenter study

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Abstract

Background. Introduced by DePaulis in 2000, the Gelweave Valsalva graft (Sulzer Vascutek, Refrewshire, Scotland) is a modified Dacron conduit (DuPont, Wilmington, DE), with prefashioned sinuses of Valsalva. The aim of this study was to evaluate the mid-term results of the reimplantation valve-sparing aortic root replacement using the Gelweave Valsalva prosthesis in Marfan syndrome patients.

Methods. A retrospective review was performed of 35 patients with Marfan syndrome in four centers who underwent the reimplantation valve-sparing aortic root replacement using the Gelweave Valsalva prosthesis.

Results. The patients were predominantly men, with a mean age of 36.5 ± 12.6 years (range, 14 to 62 years). Two patients presented with acute type A dissections and underwent emergent operations. Elective hemiarch reconstruction using hypothermic circulatory arrest was required in 11 patients. Aortic valve cusp repair was performed in 2 patients. There were no operative or hospital deaths, and no patients died during follow-up. The mean follow-up was 19 months (range, 1 to 60 months). Significant (>2+) aortic insufficiency (AI), requiring aortic valve replacement, developed in 3 patients during follow-up that requiring aortic valve replacement. The 5-year freedom from reoperation owing to structural valve deterioration was 88.9% ± 8.1%. There were no episodes of clinically significant thromboembolism.

Conclusions. Reimplantation valve-sparing aortic root replacement with the Gelweave Valsalva prosthesis in Marfan patients provides satisfactory mid-term results, thus encouraging further use of this type of repair. However, long-term results are needed in order to define the durability of this technique.

Marfan syndrome is an autosomal-dominant connective tissue disorder characterized by manifestation in different organ systems involving the ocular, skeletal, and cardiovascular system [1]. Cardiovascular complications such as rupture of aortic root aneurysm and aortic dissection are the primary causes of premature death [2]. Until recently, the standard treatment of aortic root aneurysms in patients with Marfan syndrome has been replacement of the aortic root and ascending aorta [3]. Although the results of this technique have been satisfactory, the patients must undergo the placement of mechanical valve prostheses and anticoagulation-related complications may occur [4].

Despite the presence of aortic insufficiency (AI) with aortic root and ascending aortic aneurysm, the aortic valve leaflets are often normal in Marfan patients. Valve-sparing aortic root replacement, first described by Yacoub and colleagues (remodelling) [5] and David and Feindel (reimplantation) [6] in the early 1990s, is increasingly gaining acceptance, particularly for patients with Marfan syndrome [7–9]. Although the remodelling technique achieves reconstruction of the sinuses, recent data suggest that its failure to stabilize the annulus has resulted in higher incidence of recurrent AI [8, 10]. Conversely, the standard reimplantation technique has been criticized for the absence of sinuses of Valsalva, and thus, a potential deleterious effect on leaflet stress and questionable durability. This has led to multiple modifications of the standard reimplantation technique to incorporate sinuses of Valsalva [10 –12]. In 2000, De Paulis and colleagues [13] introduced a Dacron (DuPont, Wilmington, DE) conduit (Gelweave Valsalva, Sulzer Vascutek, Renfrewshire, Scotland) modified with prefashioned sinuses of Valsalva.

Reimplantation valve-sparing root replacement using this Valsalva graft has demonstrated satisfactory short-term results [13]. In this study, we have examined the mid-term results of reimplantation valve-sparing aortic root replacement in Marfan patients using the Valsalva graft in four cardiac surgical facilities.

Material and Methods

From October 2000 to February 2006, 35 patients diagnosed with Marfan syndrome according to the Gent criteria [14] underwent reimplantation valve-sparing aortic root replacement using the Gelweave Valsalva prosthesis at the Istituto Clinico Humanitas (Rozzano, Italy), at the Sant Orsola Hospital (University of Bologna, Italy), at the Tor

Vergata University Hospital (Rome, Italy), and at the University of Pennsylvania Medical Center (Philadelphia, PA). A retrospective review was performed. The study and all research protocols were conducted in compliance with the Institutional Review Boards at their respective institutions.

Operative Techniques

Median sternotomy was performed and cardiopulmonary bypass was instituted with arterial cannulation through the ascending aorta or femoral artery and venous cannulation through bicaval or right atrial cannulation. In patients for elective hemiarch reconstruction, deep hypothermic circulatory arrest and retrograde cerebral perfusion were used during the open distal anastomosis [15]. In patients with acute type A dissection, a systemic body temperature of 26°C was applied, and antegrade selective cerebral perfusion was used during the period of circulatory arrest. Depending on the surgeon's preferences, myocardial protection was achieved by combination of antegrade and retrograde Custodiol (Kohler Chemie, Alsbach-Haenlein, Germany) cardioplegic solution and topical cooling with 4°C saline solution or by intermittent antegrade and retrograde blood perfusion.

All patients underwent the reimplantation valve-sparing aortic root replacement according to the technique described by David and colleagues [16]. At the beginning of our experience, the diameter of the prosthesis was calculated from the average height of the three aortic cusps using David's original formula [16]. More recently, some surgeons have modified their calculation of the size of the prosthesis based on direct measurement of the aortic annulus with a standard valve sizer and adding 5 mm to the calculation. In cases of dilated annulus (>28 mm), some surgeons prefer sizing the prosthesis based on the sinotubular junction measurement, once proper leaflet coaptation is obtained by pulling and aligning the three commissures.

To reconstruct the commissures precisely at the level of the "neo-sinotubular junction" of the graft, which is the connection between the skirt and the standard tubular section, the length of the commissural posts are matched against the length of the skirted section of the graft. The annular collar is then trimmed to customize the prosthesis to the patient's anatomy. Because of the right ventricular outflow tract, the base of the skirt at the commissure between the right and left coronary sinuses needs to be fashioned to facilitate reimplantation of the conduit at the subannular level. When relative prolapse

owing to unequal cusp length was noted (2 cases), plication of the free margin with a 6-0 Gore-Tex (W.L. Gore & Assoc, Flagstaff, AZ) running suture was performed.
Concomitant procedures included mitral valve repair in 3 patients and patent foramen ovale closure in 3 others. The distribution of graft sizes chosen is illustrated in Figure 1.

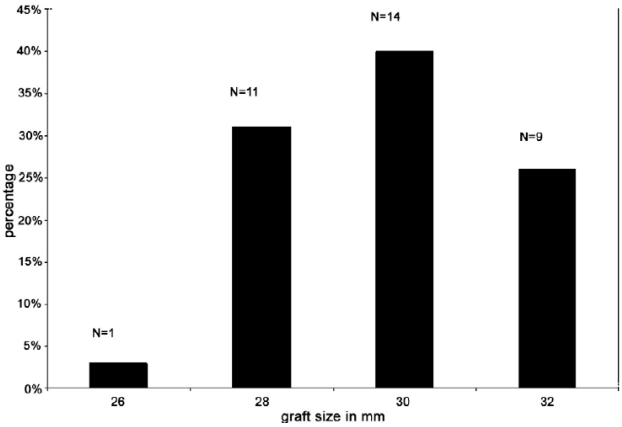

Figure 1: Graft size distribution. Numbers over the column indicate the number of patients for each group.

Echocardiography

Intraoperative transesophageal echocardiogram (TEE) was performed in all patients to assess the degree of AI preoperatively and post reimplantation. Transthoracic echocardiogram (TTE) was used in follow-up evaluation of AI. AI was scored as none, trivial, mild, moderate, or severe (0 to 4+).

Statistical Analysis

All data are reported as the mean ± SD unless otherwise specified. Actuarial freedom from adverse late events was plotted using the Kaplan-Meier method.

Results

Patient Demographics

Preoperative demographic data are listed in Table 1.

Table 1: Preoperative Patient Characteristics

Characteristic[a]	**No. Patients (%) (n = 35)**
Age (years)	36 ±13
Sex (male)	23 (66)
NYHA functional class	
• I	21 (60)
• II	7 (20)
• III	7 (20)
• IV	–
Left ventricular ejection fraction	
• >0.60	24 (69)
• 0.40–0.59	10 (28)
• <0.39	1 (3)
Aortic incompetence	
• None/trivial (0 to 1+)	11 (31)
• Mild (2+)	9 (26)
• Moderate (3+)	8 (23)
• Severe (4+)	7 (20)
Bicuspid aortic valve	3 (9)
Acute A dissection	2 (6)
Mitral regurgitation	3 (9)
Diameter of aneurysm (mm)	
• Annulus	27.5 ±2.8
• Aortic root	52.4±5.7
• Ascending aorta	49.1 ±11.4

[a] Continuous variables are presented as mean _ 1 standard deviation; categoric variables are presented as n (%).

NYHA = New York Heart Association.

Patients were predominantly male, and the mean age was 36.5 ± 12.6 years (range, 14 to 62 years). Most patients had normal left ventricular function. Preoperatively, absent-to-mild AI was seen in 20 of the 35 patients, and moderate-to-severe AI was present in 15.

A bicuspid aortic valve was present in 2 patients. Elective reimplantation was performed in 33 patients, and 2 underwent emergent operation for acute type A dissections. Aortic valve cusp repair was performed in 2 patients. The mean follow-up was 19 months (range, 1 to 60 months) and was 100% complete.

Operative Outcome

The mean CPB time was 186 ± 72 minutes, with a mean aortic cross-clamp time of 157 ± 64 minutes. Elective hemiarch reconstruction using hypothermic circulatory arrest was required in 11 patients, with a mean circulatory arrest time of 19 ± 4 minutes. There were no operative or hospital deaths, and no patients died during follow-up.

Four patients required early reoperation (<24 hours) for bleeding. None had evidence of acute aortic dissection at reoperation. Temporary right ventricle dysfunction with tricuspid regurgitation developed postoperatively in 1 patient. Right ventricular function fully recovered with perioperative medical management, and echocardiography at the time of discharge from the hospital demonstrated no further evidence of tricuspid regurgitation. A late pericardial effusion occurred in 1 patient, and a pleuropericardial window was required.

Aortic Valve Function

No patient left the operating room with greater than mild AI. Significant AI (>2+) developed in 3 patients during follow-up, and they required aortic valve replacement with mechanical prosthesis. In the first patient, postoperative TEE at the completion of surgery demonstrated mild AI. At the time of discharge from the hospital, the AI had progressed to moderate (3+). This patient required a reoperation 1 month after the first procedure because of rapid increase in left ventricle volumes.

In the second patient, the underlying cause was bacterial endocarditis. Discharged home after the first operation with trivial AI, the patient was readmitted 6 months later with complains of high fever and general fatigue. Echocardiography demonstrated severe AI and leaflet vegetations. Methicillin resistant Staphylococcus aureus was isolated from blood cultures. At reoperation, the valve was completely detached from the Dacron prosthesis, and friable vegetations were attached to the three leaflets.

The third patient requiring a reoperation was a 14-year-old boy who had an extreme growth spurt within a 22-month period. The discharge echocardiogram after reimplantation had demonstrated trivial AI. The follow-up echocardiogram at 22 months demonstrated severe AI. At the time of reoperation, all three leaflets were found to have extremely elongated free margins (>45 mm).

The overall 5-year freedom from reoperation and significant AI (>2+) was 83.5% ± 8.6% (Fig 2). The 5-year freedom from reoperation owing to structural valve deterioration and significant AI (2+) (thus excluding the patient with endocarditis) was 88.9% ± 8.1%. At the close of the study, the severity and number of patients with AI were 13 with 0 AI, 15 with 1+ AI, 4 with 2+ AI, and 0 with >2+ AI (Fig 3). There were no episodes of clinically significant thromboembolism.

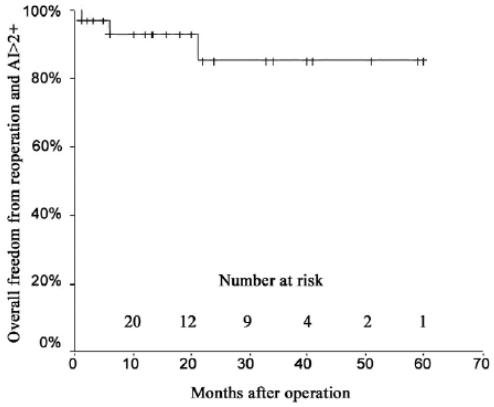

Fig 2. Overall freedom from reoperation and aortic insufficiency (AI) exceeding 2+.

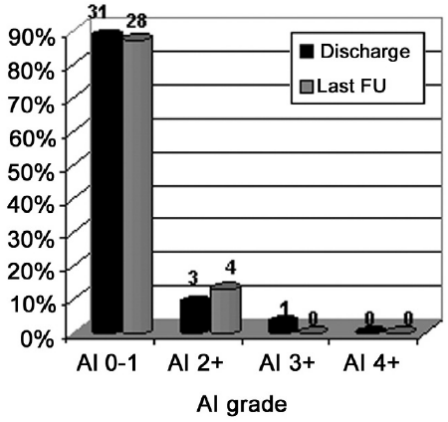

Fig 3. Comparison between aortic insufficiency (AI) at time of discharge (solid columns) and last follow-up AI (gray columns). Numbers over the columns indicate the number of patients for each group.

Comment

Since its first description in the early 1990s, valve-sparing aortic root replacement has gained acceptance, particularly in Marfan patients who have isolated root pathology with functionally normal valve leaflets. The native valves are preserved, and the disadvantages of a mechanical prosthesis and the complication of life-long anticoagulation are avoided.

The two basic techniques are reimplantation (David) and remodelling (Yacoub). The principal advantage of the reimplantation technique [6], compared with the remodelling technique [5], is the stabilization of the annulus. This is particularly important for patients with connective tissue disorders such as Marfan syndrome, where the annulus may dilate over time. The advantage of the remodelling technique, in contrast with the original reimplantation technique, is the creation of sinuses of Valsalva and thus an anatomic reconstruction of the aortic root and normal leaflet motion and stresses. However, recent reports have suggested higher incidence of late AI compared with the reimplantation technique, most likely secondary to the lack of annular fixation [10, 12].

The higher incidence of late AI in the remodelling group has convinced most surgeons to choose the reimplantation technique as the preferred technique. However, the major criticism of the standard reimplantation technique has been the absence of sinuses of Valsalva. Several studies [17–21], including finite element analysis [22] and a threedimensional phase-contrast magnetic resonance imaging study [23], have demonstrated the anatomic importance of the sinuses. These findings have led to modifications to the reimplantation technique [10–12, 24].

Short-term data on the modification of the reimplantation technique using the Valsalva conduit have previously been reported with satisfactory results [25]. This current multicenter study has examined the mid-term results of the reimplantation technique using the Valsalva conduit in Marfan patients.

Three patients required aortic valve replacement during follow-up secondary to the development of significant AI. Postoperative TEE at the completion of the operation demonstrated mild AI in the first patient; but at the time of discharge, AI had progressed significantly (3+). This was the first valve-sparing aortic root replacement performed at the institution. An incorrectly undersized prosthesis was the most likely cause of the early failure. Although it is difficult to draw definitive conclusions from a single patient's experience, we would not recommend leaving the operating room if the postoperative TEE shows mild or greater AI.

Two other patients had rapid development of significant AI, and both demonstrated trivial AI on echocardiography at the last follow-up before readmission. Endocarditis secondary to methicillin resistant Staphylococcus aureus developed in 1 patient. No aortic valve cusp repair was performed during the first operation. Severe AI was found to have developed at the 22-month follow-up in the other patient, a 14-year-old boy. During reoperation, the free margins of all three leaflets were noted to be in excess of 45 mm. In retrospect, this patient was probably not a candidate for the reimplantation technique owing to his abnormally stretched leaflets.

According to the guideline of Edmunds and colleagues [26], the 5-year freedom from reoperation in our series owing to structural valve deterioration (thus excluding the patient with endocarditis) and significant AI (>2+) was 88.9% ± 8.1%. Our data are consistent with other reported series [9, 10]. Recently, David and colleagues reported 8-year freedom from moderate-to-severe AI of 90% ± 6% with the reimplantation technique. A modification involving the creation of neo-sinuses was implemented during the last 2 years of the David group's experience.

In a smaller series from the same center consisting of Marfan syndrome patients exclusively, De Oliveira and colleagues [8] reported a 10-year freedom from reoperation of 100%. However, the actual freedom from AI exceeding 2+ was 75% ± 13% at 10 years. Further subgroup analysis demonstrated that freedom from AI exceeding 2+at 8 years was 71% ± 21% in the remodelling group and 96% ± 4% in the reimplantation group [27].

Others [12] have echoed our preference for the Valsalva conduit. Clinical analyses have suggested that leaflet motion after the reimplantation technique with the Valsalva graft is similar to that of normal subjects [25]; however, longer follow-up is needed to draw definitive conclusions. The Valsalva conduit combines the advantages of annular fixation—a feature of the standard reimplantation—with the creation of sinuses in the remodelling technique, without adding to the technical complexity of the operation (ie, creating sinuses from a standard graft). Furthermore, using preconstructed sinuses of Valsalva potentially allows for more reproducibility and uniformity.

Criticism of the Valsalva conduit has centered on the predetermined height of the sinus segment and the fixed diameters of the conduit [11]. In patients with Marfan syndrome, the commissural heights may not match the predetermined dimensions of the sinus segment chosen from the corresponding annular diameter. Suboptimal re-creation of leaflet coaptation may result in early failure of the repair. We argue that the Valsalva conduit can be adjusted to the patient's specific dimensions because the collar and the

skirt can be fashioned to adapt to the patient's anatomy. Moreover, techniques to adjust and reposition the height of the new sinotubular junction when the commissural heights are shorter than the height of the skirt have been described [28, 29].

Our study is limited by its retrospective nature and its size of 35 patients. However, the mid-term results in this multicenter study examining reimplantation valvesparing root replacement in Marfan patients with the Gelweave Valsalva prosthesis are satisfactory, and thus encourage further use of this type of repair. Nevertheless, at mean follow-up of 19 months, 4 patients had 2+ AI, suggesting that long-term results are needed to further define the durability of this technique.

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CHAPTER **7**

Reimplantation valve-sparing aortic root replacement for aortic root aneurysm in the elderly: are we pushing the limits?

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Abstract

Objectives: Reimplantation valve-sparing aortic root replacement has been increasingly performed with improving perioperative and midterm results. However, extending the age criterion in patient selection remains a debate. This study reviews the results of reimplantation valve-sparing aortic replacement in patients greater than 60 years of age.

Methods: During a 51-month period, 63 patients with aortic root aneurysms underwent reimplantation valve-sparing aortic root replacement. The Gelweave Valsalva™ prosthesis (TERUMO CardioVascular Systems Corp., Ann Arbor, MI, USA) was used in all but one case. The patients were predominantly male, and the mean age was 67 years (range, 61–83 years). Four patients had congenital bicuspid aortic valves, and cusp repair was required in one patient. The mean follow-up was 25 months (range, 1–51 months).

Results: There were one hospital and two late deaths. Overall survival at 51 months was 84 ± 9.9%. During follow-up, one patient developed severe aortic incompetence (AI) requiring an aortic valve replacement (AVR). Freedom from reoperation at 51 months was 92.8 ± 6.8%. Moderate AI was present at latest echocardiogram in one patient. Freedom from moderate or severe AI at 51 months was 90 ± 9.4%. There was no episode of endocarditis on follow-up. Univariate analysis demonstrated that no preoperative or intraoperative factor was a predictor for late reimplantation failure.

Conclusions: Reimplantation valve-sparing aortic root replacement in patients greater than 60 years old can be performed with satisfactory perioperative and midterm results. Long-term results are needed to define the durability of this technique and its role in this subset of patients.

Since its first description by David, the criteria in patient selection for reimplantation valve-sparing aortic root replacement have evolved. Initially, the technique was reserved for patients with normal, tricuspid aortic valve morphology [1,2]. As clinical experience and surgical confidence grew, the indications were extended to patients with leaflet abnormality such as cusp prolapse, Marfan's syndrome, acute aortic dissections, and bicuspid aortic valves. Multiple studies have demonstrated satisfactory results in these subsets of patients [3-7].

However, many surgeons remain reluctant in performing valve-sparing aortic root replacement in older patients even if appropriate anatomical criteria are met. Subgroup analysis in previous studies has suggested increased morbidity and mortality in older patients [8,9]. Furthermore, others argue that in the older patients, bioprosthesis aortic root replacement can be performed with less technical demand, presumed lower morbidity and mortality, and satisfactory durability.

Current population study has demonstrated a consistent increase in life expectancy compared to previous decades. According to the current U.S. population study, patients age 60 and 65 years old have a life expectancy of 22 and 18 years, respectively [10]. With this increasing life expectancy in the elderly, reoperation in octogenerians with previous aortic root replacement may become more common. Alternatively, mechanical prosthesis is not an ideal option, as anticoagulation in this aging population is not without complications. Preservation of the native aortic valve remains the ideal solution. The aim of this study was to review the results of reimplantation valve-sparing aortic replacement, performed in two different cardiac centers, in patients greater than 60 years of age.

Material and Methods

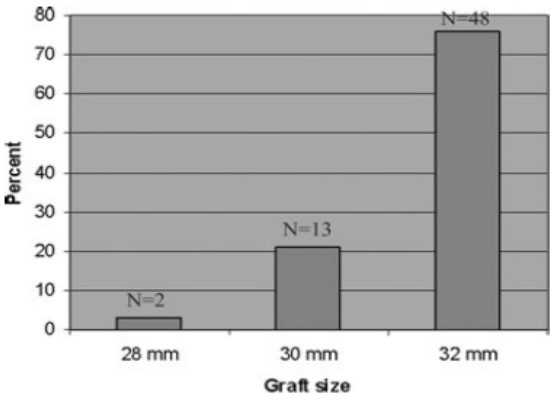
From January 2003 to April 2007, a total of 127 patients underwent reimplantation valve sparing aortic root replacement at the Istituto Clinico Humanitas (Rozzano, Italy) and at the University of Pennsylvania Medical Center (Philadelphia, PA, USA). Sixty-three (49%) patients were greater than 60 years old. All 63 cases were elective, as no reimplantation was performed emergently in this group of patients. A retrospective review of this subgroup of patients was performed.

The operative technique has been previously described [4]. Briefly, median sternotomy was performed and cardiopulmonary bypass was instituted with arterial cannulation via

the ascending aorta or femoral artery and venous cannulation via bicaval or right atrial cannulation. In patients undergoing elective hemiarch reconstruction, deep hypothermic circulatory arrest and retrograde cerebral perfusion (DHCA/RCP) were employed during the open distal anastomosis. Depending on the surgeon's preference, myocardial protection was achieved by combination of antegrade and retrograde Custodiol ® cardioplegic solution (Dr. F. Köhler Chemie, Alsbach, Germany) and topical cooling with 4 °C saline solution or by intermittent antegrade and retrograde cold blood perfusion.

All patients underwent the reimplantation valvesparing aortic root replacement according to the technique described by David [1]. The Gelweave ValsalvaTM prosthesis (TERUMO CardioVascular Systems Corp., Ann Arbor, MI, USA) was used in all cases but one. The graft sizes used are summarized in Figure 1. Four patients had bicuspid aortic valves. In one patient, the right and left coronary cusps were fused with a median raphe that was neither thickened nor fibrosed. The free margin was significantly longer than the free margin of the noncoronary cusp, resulting in prolapse of the fused right and left coronary cusps. The fused cusp was pliable and simple plication of the free margin with 6-0 Gore-Tex suture (W.L. Gore & Associates, Flagstaff, AZ, USA) was performed. The three other bicuspid aortic valves had nearly symmetrical cuspswith no evidence of prolapse; no leaflet repair was required. Hemiarch reconstruction was performed utilizing DHCA/RCP in all four patients. Concomitant procedures included mitral valve repair in seven patients (11%), coronary artery bypass in 10 patients (16%), atrial septal defect repair in one patient (2%), and radiofrequency ablation for atrial fibrillation in two patients (3%).

Fig 1. Graft size distribution



Echocardiography

Intraoperative transesophageal echocardiogram (TEE) was performed in all cases to assess the degree of aortic incompetence (AI) preoperatively and post reimplantation. Transthoracic echocardiogram (TTE) was used in follow-up for the evaluation of AI. Aortic insufficiency was scored as none, trivial, mild, moderate, or severe.

Statistical analysis

Continuous variables were expressed as the mean ± SD and were analyzed using the unpaired 2-tailed t - test. Categorical variables were presented as a percentage and were analyzed with the chi-square test or Fischer's exact test when appropriate. Univariate analysis was performed to identify risk factors for late reimplantation failure as demonstrated by either the presence of moderate or severe AI or the requirement of aortic valve replacement (AVR). Preoperative factors examined were renal failure, New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF), severity of preoperative AI, presence of bicuspid aortic valve, diameter of the annulus, sinus segment, and ascending aorta. Intraoperative factors examined were cardiopulmonary bypass (CPB) and aortic cross clamp time, the graft size used for reconstruction, and concomitant cusp repair, mitral valve repair, coronary artery bypass graft, and hemiarch reconstruction. Actuarial survival, freedom from reoperation, and freedom from moderate or severe AI were plotted using the Kaplan-Meier method.

Results

Patient demographics

Preoperative demographic data are listed in Table 1. Patients were predominantly male, and the mean age was 67.1 years old (range, 61–83 years old). The majority of patients were NYHA class I or II with normal left ventricular ejection fraction. Moderate or severe AI was present in 62% of the patients preoperatively. All patients underwent elective operation for aortic root aneurysms.

Table 1: Clinical Profile of Patients

Characteristic	**n = 63**
Age (years)	67.1±5.3
Sex (male)	45 (71)
NYHA functional class	
1. I	19 (30)
2. II	27 (43)
3. III	15 (24)
4. IV	2 (3)
Left ventricular ejection fraction	
1. > 60%	44 (70)
2. 40–59%	16 (25)
3. < 39%	3 (5)
Aortic incompetence	
1. None/trivial	13 (21)
2. Mild	11 (17)
3. Moderate	23 (37)
4. Severe	16 (25)
Bicuspid aortic valve	4 (6)
Mitral regurgitation grater than mild	7 (11)
Diameter of aneurysm (mm)	
1. Annulus	25 ± 0.5
2. Sinus segment	50 ± 0.6
3. Ascending aorta	52 ± 0.7

Values are mean ± 1 SD.
Numbers in parenthesis are percent.

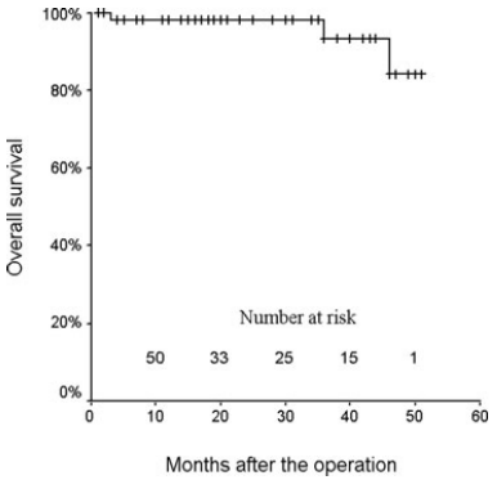
Operative outcome

The mean CPB time was 134 ± 46 minutes with a mean aortic cross clamp time of 116 ± 39 minutes. Elective hemiarch reconstruction using hypothermic circulatory arrest was required in four patients, with a mean DHCA/RCP time of 18 ± 3 minutes.

There was one hospital death and two late deaths. The cause of the hospital death was sepsis at four months after reimplantation in a patient who had a cardiac arrest on postoperative day 4. Resuscitation was successful; however, the patient suffered a

devastating neurologic injury due to anoxia. The patient had previously been discharged from the intensive care unit on postoperative day 1. Coronary angiography demonstrated no evidence of coronary button occlusion, and the cause of the cardiac arrest remains unclear. The causes of late death were cardiac (sudden death) in one patient at 37 months and noncardiac (hepatocellular carcinoma) in the other patient at 48 months. At the time of surgery, there was no evidence of hepatic neoplasm. Liver function test and hepatitis B and C markers were negative. Both patients had trivial AI at latest follow-up. Overall survival at 51 months was 84 ± 9.9% (Figure 2). Eight patients required re-exploration (< 24 hours) for bleeding and tamponade. One patient sustained a transient stroke but demonstrated complete neurologic recovery on follow-up. No thromboembolic events or endocarditis occurred during the follow-up period. Six patients (9%) are currently receiving oral anticoagulation therapy for atrial fibrillation.
At the closure of the study, 48 (80%) of the remaining 60 patients were in NYHA class I, nine (15%) in class II, and three (5%) in class III. The mean follow-up was 25 months (range, 1–51 months) and was 100% complete.

Fig 1. Overall survival at 51 months.



Aortic valve function

No patient left the operating room with greater than mild AI. One patient developed severe AI during followup and required aortic valve replacement with a bioprosthesis 42 months after the first operation. At the time of discharge from the hospital after the initial reimplantation procedure, the patient had no AI on echocardiography. The first follow-up echocardiogram at 15 months demonstrated mild AI, with progression to severe AI at 42 months follow-up. Due to the presence of symptoms and increasing left ventricular dimensions on echocardiography, the patient underwent AVR.

At reoperation, the Valsalva graft was opened and the native valve inspected. A prolapse of the noncoronary cusp was identified as the probable cause of the severe AI. The three cusps were removed and a bioprosthetic aortic valve was implanted within the Valsalva graft with a standard AVR technique. In retrospect, a shortening or a plication of the free margin of noncoronary cusp at the time of the first operation could have avoided the AI recurrence.

Two other patients developed moderate AI during follow-up. The first patient had been discharged from the hospital with mild AI. Aortic insufficiency continued to be stable at 24 and 36 months follow-up. However, at 46 months follow-up, progression to moderate AI was demonstrated by echocardiography. The first patient, discharged from the hospital with mild AI, was found to have, at 46 months of follow-up, moderate AI. Nevertheless, the patient has remained stable in NYHA class I with a left ventricular ejection fraction of > 60% and no increase in left ventricle dimensions. The second patient also had been discharged from the hospitalwithmild AI. Echocardiography performed during the first follow-up at 14 months demonstrated the presence of moderate AI. At 26 months follow-up, AI had regressed to mild AI. The two studies had been performed by the same echocardiographer. A subsequent third study performed by a second echocardiographer confirmed only mild AI. On retrospective review, the two echocardiographers agreed that there was an overvaluation of the AI grade at the second follow-up echocardiogram. At the closure of the study, the severity and number of patients with AI were the following: no AI, n = 14; trivial AI, n = 15; mild AI, n = 29; moderate or severe AI, n = 1. Table 2 shows a comparison between preoperative and latest follow-up degree of AI. The 51-month freedom from moderate or severe AI was 90 ± 9.4%. The overall 51-month freedom from reoperation was 92.8 ± 6.8% (Figure 3). Univariate analysis demonstrated that no preoperative or intraoperative factor was a

predictor for late reimplantation failure as demonstrated by moderate or severe AI or the requirement of AVR.

Table 2: Preoperative and Latest Follow-Up AI

	Preoperative AI	Latest Follow-Up AI
None	2 (3)	14 (24)
Trivial	11 (17)	15 (25)
Mild	11 (17)	29 (47)
Moderate	23 (37)	1 (2)
Severe	16 (26)	1*(2)

AI = aortic incompetence. Numbers in parenthesis are percent.
*The only patient reoperated for severe AI.

Conclusions

Age as a selection criterion remains unclear in patients undergoing reimplantation valve-sparing aortic root replacement. The operation is technically demanding, and concerns regarding increased morbidity and mortality in the elderly patients remain. Furthermore, technologic advancement has resulted in the improvement of bioprosthesis durability. This leads to the fundamental question of whether there is an advantage with valve-sparing aortic root replacement when compared to bioprosthesis aortic root reconstruction in older patients.

Our study demonstrates that reimplantation valve-sparing aortic root replacement can be performed with low perioperative morbidity and mortality in patients age greater than 60 years. The hospital mortality was 1.5% (1/63 patients) with a late mortality rate of 3% (2/63 patients). Although other valve-sparing aortic root replacement series have similar outcome, subgroup analysis within these studies has suggested that increasing age is associated with poor outcome. David et al. recently reviewed the Toronto experience of 220 valve-sparing aortic root replacement and identified age over 65 years, LVEF < 40%, and advanced NYHA class as predictors of poor outcome [9]. Kallenbach et al. recently reported the Hanover experience and identified that age greater than 70 years influenced survival negatively [8]. However, both of these studies were total reviews of their respective institutional experiences with a heterogeneous population of patients. Indications included aneurysms, aortic dissection, and patients

with Marfan's syndrome. Moreover, between 13% and 19% of cases were emergent surgical interventions. On the contrary, our series did not include patients with aortic dissections or emergent indications. The majority of the patients were in NYHA class I or II (73%) with LVEF greater than 60% (70%). The data suggest that in appropriately selected patients, age as a sole criterion for patient selection is perhaps less critical.

In our series, the reoperative rate for bleeding was 13%. Possible explanations may be that our series involve an older population (mean age 67 years) and perhaps a high rate of concomitant procedures (> 30%). Our midterm results also suggest that the durability of reimplantation valve-sparing aortic root replacement is acceptable in patients over 60 years old. Freedom from reoperation and freedom from moderate or severe AI at 51 months were 92.8 ± 6.8% and 90 ± 9.4%, respectively. Although the mean follow-up was 25 months, our data are similar to other early and midterm series [4,11,12]. Follow-up was also encouraging with an overall survival of 84 ± 9.9% at 51 months.

Even though our series have demonstrated low perioperative morbidity and mortality with good midterm results, many surgeons may continue to advocate bioprosthesis aortic root replacement (because of its presumed lower morbidity and mortality) in favor of reimplantation. Careful review demonstrates that our results are comparable to other contemporary bioprosthesis aortic root replacement series, and the presumed differences in morbidity and mortality is not clear. Gleason et al. recently reported a series of 176 patients undergoing aortic root replacement with the St. Jude Medical (St. Paul, MN, USA) full porcine root bioprosthesis [13]. The operative mortality was 3.9%. The perioperative stroke rate was 1.1% and endocarditis rate was 1.1%. Etz et al. recently reviewed the Mount Sinai experience with aortic root reconstruction using a bioprosthetic valved conduit in 275 consecutive patients. Hospital mortality was 6.2% with four patients (1.5%) having sustained permanent strokes [14]. Earlier in 2001, the Mount Sinai group had reported its subgroup analysis of patients greater than 65 years undergoing bioprosthesis aortic root replacement with a similar technique. In a series of 84 patients, the operative mortality was 8.3% with an overall rate of valve-related complications (endocarditis or thromboembolism) of 7.1% after discharge.

Although no randomized study comparing the durability of valve sparing procedures and Bentall operation in the elderly has been performed, with the current third generation bioprosthesis and their improved durability (10 years freedom from reoperation ranging from 87% to 99%), [14,15,16] many question the need to subject older patients to a longer and more technically demanding reconstruction with valve-sparing aortic root replacement. The debate focuses on the expected survival of elderly

patients versus the long-term durability of the current bioprosthesis. Current population study has demonstrated a consistent increase in life expectancy in recent decades, with patients aged 60 and 65 years old having a life expectancy of 22 and 18 years, respectively [10]. Although long-term studies of bioprosthesis aortic root replacement have been reported, [16,17] series with 20-year follow-up have been limited. Furthermore, reoperative aortic root replacement is technically demanding, with evidence suggesting that older age is a negative predictor of outcome [18]. Alternatively, mechanical prosthesis is not an ideal option, since anticoagulation in this aging population is not without complications.

In addition to age criterion, our study confirms with others that extending the indication for valve-sparing aortic root replacement to patients with bicuspid aortic valves is appropriate. In our series, four patients with bicuspid aortic valve underwent the valve-sparing procedure with satisfactory result. Also similar to other studies, preoperative severity of AI and aneurysm size were not predictors of late reimplantation failure. Sixty-two percent of the patients in our series had moderate or severe AI preoperatively, compared to 2% after the reimplantation procedure. No other preoperative or intraoperative factor was found to be a predictor of late reimplantation failure. The fundamental concept in achieving satisfactory repair is the precise geometric reconstruction of the aortic root apparatus and leaflet coaptation.

We firmly believe that preservation of the native valve is the most ideal option in aortic root reconstruction. The performance and the durability of native aortic leaflets are unmatched by any valvular prosthesis. Clinical analysis has also demonstrated that leaflet motion after reimplantation with the Gelweave ValsalvaTM prosthesis is similar to that of normal patients [19]. Freedom from anticoagulation and the low rate of thromboembolic events and endocarditis are extremely appealing for older patients [20]. Following the paradigm of mitral valve repair a few decades ago, increase in surgical experience has resulted in extending the age criterion for valve-sparing aortic procedure. We believe that increasing age is not a contraindication for valve-sparing aortic root replacement, and that the procedure does offer an advantage over bioprosthesis in properly selected patients greater than 60 years of age. Our experience demonstrated that good surgical outcome can be accomplished and should be expected in this subset population of patients if appropriately selected. Nonetheless, age should never be the sole criterion in patient selection, but must include a comprehensive evaluation of the comorbidities of the patient.

Limitations of this study are the relatively small sample size and the length of the mean follow-up. However, our results demonstrated that reimplantation valve-sparing aortic root replacement can be performed successfully in the elderly patients with very low hospital mortality. Moreover, our series demonstrated excellent midterm survival and freedom from reoperation and freedom from significant AI.

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CHAPTER 8

Bicuspidity does not affect reoperation risk following aortic valve reimplantation

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Abstract

Aortic valve reimplantation has been shown to be a safe procedure. However, evidences of durability in bicuspid aortic valves (BAVs) are limited in the literature. Between 2002 and 2011, 132 patients (mean age 61 ± 12 years) underwent aortic valve reimplantation. In 24 patients (18%), aortic valve was bicuspid. Mean follow-up was 50 ± 26 months (range 1–102 months) and was 99% complete. In-hospital mortality was 0.8% (1 patient). Survival at 1 and 5 years was 99 and 94%, respectively. Overall freedom from aortic valve reoperation at 1 and 5 years was 96 and 90%, respectively, without significant difference between patients with bicuspid and tricuspid aortic valve. Freedom from aortic valve regurgitation >2+/4+, excluding patients reoperated, was at 1 and 5 years of 100 and 99%, respectively. Patients with valve cusp repair showed a higher rate of aortic valve reoperation; however, only postoperative aortic regurgitation >2+/4+ was significant risk factor for redo procedure at multivariate analysis. Aortic valve reimplantation in BAV without cusp repair provides excellent mid-term results. Further observations and longer follow-up are necessary to determine if BAV sparing, even in the presence of cusps alterations, could allow satisfying durability.

Introduction

Aortic valve-sparing operation with valve reimplantation was introduced to treat patients with aortic root aneurysm associated with normal or minimally abnormal aortic cusps [1]. Nowadays, this procedure is considered safe and has a proved durability at long-term follow-up [2], so that indications were extended to patients with severe aortic regurgitation, bicuspid aortic valve (BAV) and aortic cusp prolapse or abnormalities. Cusp repair is performed with great variability among published surgical experiences in up to 55% of the cases [2–4], on the contrary evidences of durability of BAV reimplantation are limited [2, 5, 6].

The aim of this study was to examine our experience with reimplantation valve-sparing operation focusing on influence of preoperative valve characteristics in determining need for reoperation.

Material and methods

Between 2002 and 2011, 132 consecutive patients underwent aortic valve-sparing operation with valve reimplantation. The indication for operation was the presence of aortic root aneurysm. The Ethics Committee approved the study and waived the need for patient consent. The patients' characteristics are shown in Table 1.

Our surgical technique has been previously described in detail [7]. A Gelweave Valsalva™ graft was implanted in all the patients; the graft sizes used were: 26 mm in 2 patients, 28 mm in 13, 30 mm in 42 and 32 mm in 75.

In 13 cases, anatomical or cusp motion abnormalities concurred in determining aortic regurgitation and needed an adjunctive cusp repair. This finding was more frequent in patients with BAV (10/24 patients, 42%) than in tricuspid aortic valve (TAV) (3/108 patients, 3%). Cusp prolapse was found in seven patients with BAV and was corrected with free margin shortening (four patients), central cusp plication along the nodule of Arantius (one case) or cusp triangular resection (two patients). In the remaining three cases, stress fenestration repair with pericardial patch (one patient) and shaving of a calcified raphe (two patients) were performed. Cusp prolapse correction (central plication of right coronary cusp in one case, free margin shortening of right coronary and non-coronary cusps in one case) was necessary in two patients with TAV; in the remaining case, stress fenestration repair with pericardial patch was performed.

Table 1: Patient characteristics

Variable	No. of patients (%) or mean ± SD
Gender	
Male	96
Female	36
Age (years)	61 ± 12
LVEF > 45%	116 (88%)
Aortic regurgitation degree >2+/4+	88 (67%)
BAV	9/24 (38%)
TAV	79/108 (73%)
NYHA class III–IV	25 (19%)
Emergent operation	2 (1.5%)
CAD	17 (13%)
COPD	24 (18%)
CRF (creatinine > 200 μmol/l) or preoperative HD	6 (4.5%)
Marfan syndrome	5 (3.8%)
Bicuspid aortic valve	24 (18%)
AAD	1 (0.8%)
Chronic aortic dissection	5 (4%)
Diameter (mm)	
Aortic root	48 ± 9
Ascending aorta	51 ± 9

AAD: acute aortic dissection; BAV: bicuspid aortic valve; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; HD: haemodialysis; LVEF: left ventricular ejection fraction; TAV: tricuspid aortic valve.

Concomitant procedures were mitral valve repair (10 patients, 7.5%), scheduled coronary artery bypass (12 patients, 9%), atrial septal defect repair (3 patients, 2%) and radio frequency ablation for atrial fibrillation (2 patients, 1.5%).

Mean cardiopulmonary bypass time was 134 ± 30 min (range 90–279 min) and the mean duration of aortic cross-clamping time was 114 ± 23 min (range 67–204 min).

Aortic regurgitation was graded as none, trace (1+/4+), mild (2+/4+), moderate (3+/4+) or severe (4+/4+). A transoesophageal echocardiogram (TEE) was carried out intraoperatively in all the patients after weaning from cardiopulmonary bypass in order to evaluate residual aortic valve regurgitation and to characterize cusps' level of

coaptation. Transthoracic echocardiography was performed before discharge and at 6 and 12 months and every year thereafter.
Follow-up ranged from 1 to 102 months (mean 50 ± 26 months) and was available in 130 of 131 patients (99% complete).

Statistical analysis

Continuous variables were expressed as the mean ± SD. Categorical variables were compared with the Chi-square or Fisher exact test when appropriate. Six variables (Marfan syndrome, BAV, preoperative cusp prolapse, valve cusp repair, preoperative aortic regurgitation degree>2+/4+, postoperative residual aortic regurgitation degree>2+/4+) were entered into a univariate analysis to determine whether any single variable influenced the risk for reoperation and into a model of Cox regression analysis to study its independent predictability.
Survival rates and freedom from reoperation were calculated using the Kaplan–Meyer method. Univariate comparisons for failure time data were performed using the Wilcoxon test. Statistical analyses were performed using the Stat-View Statistical Software Package 5.0 (SAS Institute, Inc., Cary, NC, USA), NCSS 2001 (Number Chruncher Statistical System, Kaysville, UT, USA).

Results

In-hospital outcome

There were no intra-operative deaths. The mortality predischarge was 0.8% (one patient). Early reoperation for excessive bleeding or tamponade was necessary in 15 patients (11%) and in 3 cases (2.2%) for sternal dehiscence/mediastinitis. Perioperative myocardial infarction occurred in two patients (1.6%). Cerebrovascular accidents were registered in three patients (2.2%); stroke in one and transient ischaemic attack in two. A permanent pacemaker implantation was necessary in three patients (2.2%) for complete AV block.

Seven patients were discharged with a residual aortic regurgitation degree >2+/4+; nevertheless in last 4 years, all patients were discharged with residual aortic regurgitation degree <2+/4+.

Survival

There were eight late deaths during follow-up; in three cases because of cancer, one had acute bowel ischaemia after descending thoracic aorta endovascular procedure, two patients had worsening heart failure and in two cases sudden death occurred. The cumulative 1-year and 5-year survival rates (excluding hospital mortality) were 99 and 94%, respectively.

Freedom from aortic valve endocarditis was 100 and 99% at 1 and 5 years. Thromboembolic events occurred in two patients during follow-up with a rate of freedom from cerebrovascular ischaemic events at 1 and 5 years of 99 and 97%, respectively.

Reoperation

Eleven patients underwent aortic valve reoperation during follow-up for recurrent aortic insufficiency, in one case because of aortic valve endocarditis. All the patients underwent successful aortic valve replacement and the survival rate was 100% at 38 ± 27 months. Table 2 reports data about reoperation. At univariate analysis, preoperative cusp prolapse ($P = 0.013$), valve cusp repair ($P = 0.023$) and postoperative aortic regurgitation >2+/4+ ($P < 0.001$) were significant risk factors for aortic valve reoperation. Preoperative aortic regurgitation degree >2+/4+ ($P = 0.08$), Marfan syndrome ($P = 0.06$) and bicuspidy ($P = 0.32$) showed no significance. At the multivariate analysis, postoperative aortic regurgitation degree >2+/4+ ($P = 0.032$) was the only significant independent risk factor for aortic valve reoperation.

Overall freedom from reoperation for aortic valve regurgitation was 96% at 1 year and 90% at 5 years.

Cumulative freedom from aortic valve reoperation and from residual aortic regurgitation degree >2+/4+ was 96 and 89% at 1- and 5-year follow-up, respectively.

Patients with preoperative none or trace aortic regurgitation (AR) had a freedom from reoperation at 1 and 5 years of 98%; in patients with AR degree >2+/4+, freedom from

aortic valve redo was at 1 and 5 years of 95 and 87%, respectively (AR ≤ 2+/4+ vs. AR > 2: P = 0.11).

Table 2: Aortic valve characteristics and mechanisms of recurrent aortic regurgitation in patients who underwent aortic valve reoperation

Patient	AV	Preop AVR	AV repair	Reason for recurrent AVR	Interval time (months)
1	TAV	Trivial		Three cusps prolapse, technical problem	1
4	TAV	Severe		RC and LC retraction, normal annulus	79
7	BAV	Severe	Free margin shortening NC-RC cusp	NC-RC cusp retraction	7
23	TAV	Severe		NC cusp prolapse, no cusps abnormalities	34
30	TAV	Severe		NC cusp prolapse, no cusps abnormalities	15
45	TAV	Moderate		Not well defined	34
54	TAV	Severe		LC cusp prolapse, no cusps abnormalities	31
67	TAV	Moderate		Endocarditis	48
72	BAV	Severe	NC cusp triangular resection and central plication	NC cusp prolapse	9
91	TAV	Moderate	Fenestration repair	Not well defined	4
105	BAV	Moderate	NC cusp triangular resection and central plication	NC cusp tear (suture dehiscence?)	6

BAV: bicuspid aortic valve; LC: left coronary; NC: non-coronary; RC: right coronary; TAV: tricuspid aortic valve.

Patients with BAV showed freedom from aortic valve reoperation of 86% after 1 year with stable results in the first 5 years. There was no difference comparing the durability between TAV (freedom from reoperation of 98 and 92% at 1 and 5 years, respectively) and BAV (P = 0.26) (Fig. 1).

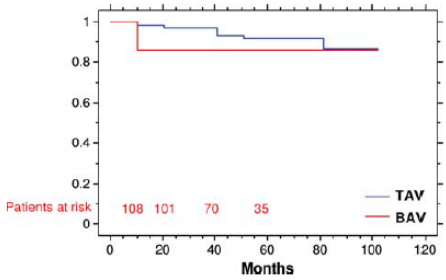

Fig 1. Freedom from aortic valve reoperation in patients with tricuspid and BAV (P = 0.26).

Overall freedom from reoperation in patients with preoperative normal or minimally abnormal aortic valve cusps was 99 and 93% at 1 and 5 years, respectively (Fig. 2). Patients needing cusp repair showed freedom from aortic valve redo of 69% at 5 years (P < 0.001). No difference between BAV and TAV was found in durability after stratification for adjunctive cusp repair (Fig. 3).

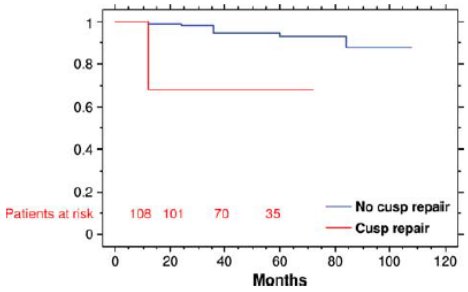

Fig 2. Freedom from aortic valve reoperation according to the adjunct of cusp repair (P <0.001).

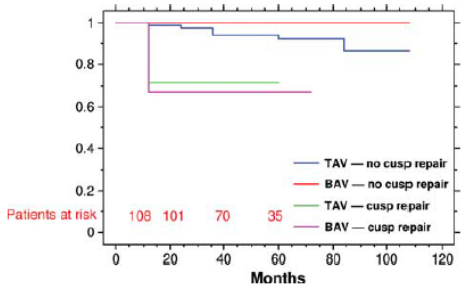

Fig 3. Freedom from aortic valve reoperation in patients with tricuspid or BAV associated or not with valve cusp repair.

BAV and TAV reimplantation without cusp repair provided a freedom from aortic valve reoperation at 1 year of 100 and 99%, respectively, at 5 years of 100 and 93%, respectively. Freedom from reoperation at 5 years in patients who underwent associated cusps repair was 72% in TAV and 67% in BAV.

Discussion

The BAV annular asymmetry is considered to be better preserved with root remodelling [6, 8]. Previous experiences [3, 8] showed no differences in durability between preserved BAV and TAV. These results were supported by a recent work by Schäfers et al. [9] with excellent results and freedom from aortic valve reoperation of 97% at 10 years.

Annular dilatation, together with cusp injuries or retraction, stress tears and fenestration, developing fibrosis and, of course, failure of suboptimal surgical correction [8, 10–12], are possible mechanisms leading to aortic regurgitation recurrence [10, 13, 14]. Valve-sparing reimplantation is the only operative approach able to stabilize the size of a dilated aortoventricular junction thus preventing future dilatation [2, 14]. This characteristic could be more effective in preventing recurrence of valve regurgitation in BAV. However, despite the widespread of this technique, few reports focused on BAV [5, 12]; even in experiences with large population, the number of BAV patients is limited [2, 4, 15] or the results not discussed [13].

In our experience, a favourable anatomical and functional cusp condition allowed satisfying mid-term durability with a global freedom from reoperation of 94% at 5 years; in particular, excellent results were registered in the BAV subgroup. However, especially in BAV, cusp abnormalities are not uncommonly associated [12]. We were led to add valve cusp repair in only 10% of the cases, but this rate is lower than in several other experiences reporting cusp repair incidences ranging from 20 to 60% [2, 3, 10, 12, 15]. Even if bicuspidy did not emerge as a risk factor for aortic valve reoperation [2–6, 12, 15], there is no general agreement about the durability of BAV sparing with adjunctive cusp repair [2, 3, 10, 12] and our data are supportive for a less satisfying durability in this subgroup of patients. However, a very recent paper from de Kerchove et al. [14], focusing on patients with BAV reimplantation with adjunctive cusp repair in 93% of the cases, has reported a superb freedom from reoperation: 100% at 6 years.

We found a tendency in early failure (less than 1 year from valve-sparing procedure) in patients with BAV who needed valve cusp repair (Figs 2 and 3). Interestingly, similar results were reported in literatures with most of the reoperations (up to 80%) performed during the first year of the follow-up [3, 8, 11, 12, 15]. Cusp lesions and technical failure were reported as the main cause for reoperation in these cases. Furthermore, many of these patients were discharged with a residual mild insufficiency degree that abruptly hesitated in moderate or severe regurgitation. Postoperative degree of aortic regurgitation is recognized to be an independent risk factor for recurrent aortic regurgitation [3] and our data confirm this finding. In the early phase of our experience, seven patients were discharged with a suboptimal result and four of these underwent aortic valve reoperation during the first year after the valve-sparing repair. Concerning intraoperative TEE, a residual aortic regurgitation ≥2+/4+ and a level of coaptation> 2 mm below the lower border of the Dacron graft is considered inacceptable nowadays. Our policy allowed us to register no early failure in last 3 years and will probably provide an even better mid- and long-term outcome in the future.

Limitations

The main limitation of the study was the small number of patients with BAV; however, the presented subgroup is one of the most representative single-centre series in the literature. This is a retrospective analysis even if performed on a prospectively collected database. Data about residual aortic regurgitation or development of significant aortic insufficiency were extrapolated in up to 20% of the cases from echocardiography evaluation performed in peripheral centres.

Conclusion

If a BAV does not present cusp calcification or some stenosis degree, for which the indication for valve replacement is clear, a valve-sparing procedure should be considered as a primary approach. We are familiar with the reimplantation technique since 2002 and we agree with the potential role in annular stabilization provided by valve reimplantation.

Preoperative aortic regurgitation degree is not an independent risk factor for recurrent aortic insufficiency in BAV sparing.

Although bicuspidy could present as a complex disease causing aortic regurgitation, it did not emerge as a risk factor for reoperation after valve-sparing procedures. Several pathogenetic mechanisms could lead to recurrent aortic regurgitation along annular or root dilatation and therefore to the need for further procedures. BAV preservation is particularly interesting in patients developing aortic regurgitation or undergoing aortic root surgery who deny mechanical prostheses and could suffer from suboptimal durability of biologic prostheses. Sparing BAVs with minimal cusp alterations provide excellent mid-term results. A proper intraoperative assessment, a close postoperative follow-up and the limited risk during redo procedure in these young patients could allow experienced surgeons to make efforts in sparing BAV even in the presence of cusp abnormalities. However, further evidences and longer follow-up are required to state if this particular subgroup of patients could benefit from a satisfying durability.

Conflict of interest: none declared.

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PART 3

THE ADDITIONAL CUSP REPAIR TO THE PROCEDURE OF VALVE-SPARING AORTIC ROOT REPLACEMENT IN BICUSPID AND TRICUSPID AORTIC VALVE AND ITS IMPACT ON RESULTS

CHAPTER **9**

Cusp repair during aortic valve-sparing operation: technical aspects and impact on results

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Abstract

Aim. Aortic valve-sparing operations are nowadays considered safe and reliable procedures in terms of mid-term and long-term results. Although surgical techniques regarding the modality of grafts' implantation have been properly addressed, the modality of cusp repair, when needed, is still open to debate. We sought to review the literature to try to shed light on when the cusp repair is required and how it should be performed.

Methods. We searched the *PubMed* database using the keywords aortic valve-sparing operation, aortic valve-sparing reimplantation, valve-sparing aortic root replacement, aortic valve repair, and aortic cusp repair. Only studies that included and described in detail the technique of cusp repairs in adjunct to aortic valve-sparing operation were considered.

Results. Bicuspid aortic valve more often requires correction when compared with tricuspid valve. The range of the techniques varies from the 'simple' free margin plication to the more complex triangular resection with patch repair. Results in the literature seem to be encouraging, showing that, in most of the cases, cusp repair does not affect valve competence in the mid-term and long-term.

Conclusion. Correction of the cusp is a delicate balance between undercorrection that could lead to residual prolapse and overcorrection that could lead to cusp restriction. Although complex repair of the aortic valve in addition to root replacement provided satisfactory results, it should be reserved for experienced centers with a large volume of patients.

Introduction

Since their introduction between the late 1980s and the early 1990s, valve-sparing operations have progressively spread. Basically, there are two main types of aortic valve-sparing operations: reimplantation of the aortic valve and remodeling of the aortic root [1,2]. More recently, a third technique, the so-called 'Florida sleeve', has been proposed [3]. Although these procedures were initially reserved for younger patients with normal or nearly normal aortic valve, the encouraging mid-term and long-term results in terms of mortality, morbidity, and valve durability [4–7] have convinced many surgeons to expand the indication to older individuals with more compromised aortic valve [8–10]. This evolution has resulted in the need to develop a technique that, in addition to the root graft implantation, could correct residual aortic insufficiency due to abnormalities of the aortic valve. These abnormalities may be either a consequence of the increased mechanical stress and strain on the aortic cusps generated by the root aneurysm itself or intrinsic alterations of the valve [11]. If at the beginning of the experience, the cusp repair was limited to tricuspid aortic valves, over time even the most challenging bicuspid valves have begun to be treated [12,13]. Nowadays, surgeons have a wide range of techniques to reduce the cusps' prolapse, restore the cusps' motion, and to increase the coaptation surface of the free margin [14–16]. Our aim is to review the literature to clarify when cusp repair is required and how it should be performed.

Methods

For this review, we searched the *PubMed* database using the keywords aortic valve-sparing operation, aortic valvesparing reimplantation, valve-sparing aortic root replacement, aortic valve repair, and aortic cusp repair. Only studies that included and described in detail the technique of cusp repairs in adjunct to aortic valve-sparing operation were considered.

Results

Mechanisms of aortic regurgitation in root dilatation and anatomical bases of residual aortic insufficiency

Enlargement of the aortic root may functionally cause aortic regurgitation even in the presence of normal aortic valve cusps (type I lesion according to the functional classification of the aortic valve regurgitation) [17]. Moreover, dilatation of the aortic root may increase the stress on specific areas of the cusps. By means of a finite element model, Grande *et al.* [11] demonstrated that when the aortic root dilatation exceeds 50%, an increase of strain on the cusps occurs (ranging from 39 to 189%) and it is disproportionately higher at the attachment edge and coaptation area. This can lead to the elongation of the free margin of the cusp and to fenestration at the commissure sites, creating the bases of residual aortic regurgitation after a valve-sparing procedure. In this setting, repair of the prolapsed cusp (type II lesion, most commonly due to cusp free margin elongation) is required. Furthermore, primary cusp abnormalities, such as the presence of a fibrotic/calcified cusp raphe, can lead to limited cusp motion (type III lesion), affecting early results and durability of the valve-sparing procedure.

As the aortic valve becomes fully assessable only after restoring the aortic sinuses' three-dimensional geometry altered by the dilatation of the aortic root, aortic cusp repair should be performed (in the case of tricuspid aortic valve), or at least thoroughly checked [in the case of bicuspid aortic valve (BAV)], after the reconstruction of the aortic root by means of the graft [18]. It is of crucial importance to make sure that the cusps are coapting at the same level and well above the nadir of the aortic annulus (8–11mm) and the cusps have no 'restricted' motion. It has been demonstrated that, although suboptimal cusp coaptation can exist without aortic incompetence in the short-term, normal coaptation is associated with optimal long-term function of the valve [19].

The most frequently used cups repair techniques are reported in Table 1.

In an attempt to evaluate the stress to which the cusps are exposed after surgical repair, Labrosse *et al*. [20], in a finite element study simulating leaflet correction, demonstrated that different techniques have different impacts. In particular, free margin shortening did not induce significant increase in cusp stress with respect to the reference value. On the contrary, the central cusp plication and the commissural plication did, with increases in excess of 36 and 45%, respectively.

Table 1. Most frequent cusp repair techniques

Valve	Cusp repair techniques
TAV/BAV	Free margin shortening/resuspension
TAV/BAV	Nodule of Arantius plication
TAV/BAV	Triangular resection
BAV	Raphe shaving
BAV	Raphe resection and closure
BAV	Raphe resection and patch repair

BAV, bicuspid aortic valve; TAV, tricuspid aortic valve.

Cusp repair during valve-sparing operation in tricuspid aortic valve

In a recent publication, David and Armstrong [16] presented their long-term results with valve repair during valve-sparing operations, when alterations secondary to aortic root aneurysm occur. It is emphasized that if the free margin of a cusp is elongated, it will prolapse after correction of the dilatation of the sinotubular junction and, in addition, cusps with stress fenestration, usually located at the commissures that are considered the 'hinge point', may rupture after reconstruction of the aortic root. They suggest correcting the cusp prolapse by plication of its central portion along the nodule of Arantius (Fig. 1b) or by weaving a double layer of a fine polytetrafluoroethylene (PTFE) suture (Gore-Tex) along the free margin and shortening the free margin; the suture has to be secured outside the graft used for the reconstruction of the aortic root (Fig. 1a). They recommend, furthermore, using the two techniques in combination when cusp prolapse is associated with stress fenestration in the commissural area. In their large series including 267 patients treated with aortic-valve-sparing operations, cusp repair was performed with these techniques in 24% of the cases (58 patients during aortic valve reimplantation and six during aortic root remodeling). The results are outstanding: only one patient underwent reoperation for severe aortic incompetence 12 years after the procedure. They concluded that cusp repair by plication of the central portion alone, PTFE suture alone, or a combination of the two techniques had no negative effect on the durability of aortic valve-sparing operations.

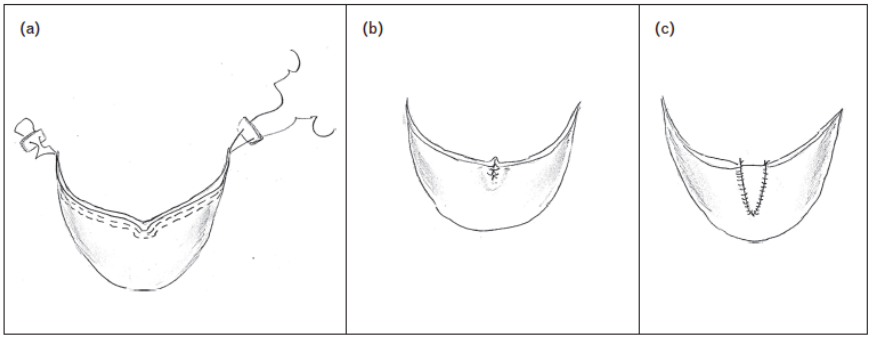

Figure 1. (a) Correction of the cusp prolapse by weaving a double layer of a fine polytetrafluoroethylene suture (Gore-Tex) along the free margin and shortening the free margin; the suture has to be secured outside the graft used for the reconstruction of the aortic root. (b) Correction of the cusp prolapse by plication of its central portion along the nodule of Arantius. (c) Correction of the cusp prolapse by triangular resection and reconstruction with autologous pericardium patch.

A very similar approach is reported by El Khoury *et al.* [18]. The residual or new aortic valve prolapse is corrected, after having fixed the root by means of the graft, by free edge plication with one or two simple sutures placed from one side of the nodule of Arantius to the other side and tied, or by shortening the free margin with a running Gore-Tex suture to adjust the coaptation height (they define the latter technique 'free margin resuspension'). In a series including 376 patients with tricuspid aortic valve who underwent cusp repair with these techniques, 39 had contextually a root replacement (36 reimplantation and three remodeling) [14]. Among them, the residual or new prolapse was corrected with free margin resuspension in 14 cases, free edge plication in 18, and plication along with resuspension in six. Reoperation for significant aortic insufficiency was necessary in two patients. In one, recurrent aortic insufficiency 3+ developed 29 months after root remodeling with resuspension of the three cusps. At reoperation, valve analysis detected a slightly restrictive left coronary cusp and recurrent prolapse of the two other cusps. The other patient, who initially had root reimplantation with cusps thinning and plication along with resuspension on two cusps, developed 30 months later aortic insufficiency 3+ and aortic valve stenosis. At reoperation, low coaptation and cusp calcification were found. As the median follow-up of this series is about 4 years, no long-term conclusion can be drawn. According to the authors, free margin plication is their technique of choice to treat residual tricuspid valve prolapse, whereas they use the resuspension technique to close stress fenestration.

Aicher *et al*. [21] described a more 'aggressive' approach for correction of residual prolapse. Although they perform, as the preferred technique, plication of the central portion of the cusp (one to five plication 5–0 or 6–0 polypropylene stitches placed in a stepwise fashion), in the presence of marked tissue redundancy (> 10mm), a triangular resection is carried out. If the gap between the two portions of the cusp is limited, it is reconstructed by interrupted stitches (6–0 polypropylene); otherwise, a patch of fixed autologous pericardium is inserted (Fig. 1c). Autologous pericardium is also used in the presence of cusp fenestration. Regardless of the type of repair performed, their aim is to achieve an identical height of the free margin and an effective height of 7–8mm (the height difference between aortic insertion and free margin of the cusps). In their large series of 274 patients who underwent aortic root remodeling, 193 had a tricuspid aortic valve. In this subgroup, the cusp prolapse correction was necessary in 103 patients involving one cusp in 53 cases, two cusps in 29 cases, and three cusps in 21 cases. The prolapse correction consisted of plication of the central portion of the cusp (*n*= 102), triangular resection (*n*= 2), and pericardial patch repair (*n*=4). Reoperation for significant aortic regurgitation was required in seven (out of 193) patients and symmetric cusp prolapse was found in the majority of the patients, but no indication whether they underwent cusp repair during the first procedure is provided.

Oka *et al*. [22] reported 101 cases of patients with aortic valve reimplantation. Among them, 51 had adjunctive cusp repair. The majority of the patients (88%) had a tricuspid aortic valve. Various cusp repair techniques were attempted, including central plication at the nodules of Arantius by means of 5–0 or 6–0 polypropylene (32 patients), reinforcement of the free margin using Gore-Tex CV7 sutures (15 patients), cusp perforation closure using autologous pericardial patches (eight patients), and plication of the free margin at the commissures (two patients). In this subgroup of 51 patients, four had early failure (one had BAV) and six late failure (including two BAV). Two out of four patients with early failure received free margin cusp plication at the commissures. According to the authors, the latter technique has been abandoned because of disappointing results in the short-term. Considering that about one-fifth of patients who underwent cusp repair had a failure, it is no wonder that repaired 'thin' cusps turned out to be an independent risk factor for recurrent aortic insufficiency. Characteristics and results of cusp repair during valvesparing operation in tricuspid aortic valve are summarized in Table 2.

Table 2. Characteristics and results of cusp repair during valve-sparing operation in tricuspid aortic valve.

	David and Armstrong [16]	de Kerchove *et al.* [14]	Aicher *et al.* [21]	Oka *et al.* [22]
Sparing operation	267	39	193	101
Tricuspid aortic valve/bicuspid aortic valve	TAV	TAV	TAV	TAV/BAV
Valve repair	64 (24%)	39	103 (53%)	51 (50%)
Reimplantation	58 (90.7%)	(100%)	0	51 (100%)
Remodeling	6 (9.3)	36	103(100%)	0
		(92.3%)		
		3 (7.6%)		
Free margin shortening/resuspension	4 (6.25%)	14	0	15 (29.4%)
		(35.8%)		
Plication of Arantius nodule	0	18	102 (99%)	32 (62.7%)
		(46.1%)		
Plication at the commissures	0	0	0	2 (2.9%)
Free margin shortening/resuspension+plication of Arantius nodule	60 (93.7%)	6 (15.3%)	0	0
Triangular resection	0	0	2 (1.9%)	0
Pericardial patch	0	0	4 (3.8%)	8 (15.6%)
Reoperation for valve failure	1/64	2/39	n.a.	7/51(13.7%)
	(1.5%)	(5.1%)		(5 TAV+2 BAV)

BAV, bicuspid aortic valve; TAV, tricuspid aortic valve.

Cusp repair during valve-sparing operation in bicuspid aortic valve

A few considerations must be taken into account when the decision to spare a BAV is to be made in the setting of an aortic root replacement.

The morphology of the BAV is variable. The cusps may be nearly equal in size (symmetric bicuspid valve), or more often, one cusp may be larger than the other (asymmetric bicuspid valve). The larger cusp very frequently has a raphe in the middle, marking the place where the leaflet should have divided during development. It must be noted that the triangle lying beneath the raphe is reduced in height considerably,

contributing to restricting cusp mobility [23,24]. Orientation of the cusps is also variable: antero-posterior is more common, occurring in almost 80% of the cases, and both coronary arteries take origin from the anterior sinus. Usually, the raphe is located in the anterior cusp. In the left–right arrangement, a coronary ostium can be found in each sinus with the raphe invariably in the right cusp.

The BAV requires compensatory mechanisms to be able to function appropriately [25]. The anatomical length of the cusp free margin is constant, but their 'functional' length must change. To compensate for free margin discrepancy, in order to match the geometry of full closure and opening, the cusps' gradual folding and unfolding seems to be necessary. An alternative way to compensate is to extend the coaptation area and this is achieved by an increased bulge (doming) of the 'cusp bellies', which allows the cusp free margin to either fold or travel in upward convex arch, or both.

Patients with BAV undergoing valve-sparing operations more often require additional correction of cusp pathologic conditions when compared with patients with tricuspid aortic valve [21].

In the setting of valve-sparing operations, prolapse is the most frequent mechanism of bicuspid valve leading to residual incompetence after valve reimplantation within the graft. It more commonly involves the congenitally fused cusp, but may also be present in the normal non-fused cusp [26].

As described by the Homburg group in 2000, the geometry of the BAV needs to be inspected once the sinuses of Valsalva have been excised (and before reconstruction of the aortic root) by applying radial tension on the two commissures. This maneuver allows comparing the length of the two cusps [27]. In 2007, Schäfers *et al.* [13] reported the results of a series of 173 patients with repaired incompetent BAV. Among them, 78 patients, because of root dilatation, underwent root remodeling. In this subgroup, the aortic valve was repaired by means of plication of the free margin in 56 cases, triangular resection in 33, and cusp replacement with pericardium reconstruction in one. The choice of repair technique was based on the cusp's aspect: if limited tissue redundancy was noted, central plication sutures were placed on the free margin until both free margins were at identical height. If extensive tissue redundancy or limited fibrosis was encountered, triangular excision of cusp tissue with direct approximation of cusp tissue was chosen. In the presence of more extensive disorder (i.e., calcification in the raphe), the pathological tissue was excised and the cusp was reconstructed by implantation of an autologous pericardial patch (preserved in 1.5% glutaraldehyde for 3 min and rinsed

for 2 min). Freedom from aortic regurgitation II or greater at 5 years was 95.5% and freedom from reoperation at 5 years was 97%.

In a series of 161 consecutive patients who underwent BAV repair, de Kerchove *et al.* [28] created two matched subgroups of 53 patients each. One, consisting of patients in whom the root was not treated (this subgroup analysis is outside the purpose of this review) and the other consisting of patients who underwent aortic valve reimplantation. In this latter subgroup, aortic cusp repair was needed in the majority of patients (93%, *n.*=49). Several different techniques were used: raphe shaving (23%), raphe resection and primary closure (38%), raphe resection and patch repair (11%), cusp prolapse repair (77%), patch repair for cusp perforation (6%), and any patch repair (17%). Excellent results were obtained at a 52-month follow-up: none of the patients were reoperated on for severe aortic incompetence and all of the patients had residual aortic incompetence grade of 2 or less.

Kari *et al.* [29] from Stanford University reported mid-term results in 75 patients with BAV who underwent aortic valve reimplantation. In 50 cases, cusp free margin repair (≥ one cusp free margin shortening stitch) was added and it was associated to triangular raphe resection in seven patients and commissural suspensory neochord creation in three cases. This latter technique was associated to significant aortic regurgitation progression and was abandoned. At the mean follow-up of 2.8 years, overall freedom from reoperation was 90%, a log-rank test did not show difference in terms of durability between patients who had free margin shortening with those who did not (P=0.8), and similarly no difference was found according to BAV configuration type. At the time of latest transthoracic echocardiogram assessment (median follow-up time of 2.4 years), the median aortic regurgitation degree was 0 (interquartile range 0–1) and unchanged when compared with the early postoperative echocardiography examination. Again cusp repair, number of free margin sutures placed, and BAV type did not have a significant impact on aortic regurgitation progression over time.

Characteristics and results of cusp repair during valvesparing operation in BAV are summarized in Table 3.

Table 3. Characteristics and results of cusp repair during valve-sparing operation in bicuspid aortic valve.

	de Kerchove *et al.* [28]	Schäfers *et al.* [13]	Kari *et al.* [29]
Sparing operation	58	78	75
Valve repair	49 (93%)	78 (100%)	50 (67%)
Reimplantation	49 (100%)	0	50 (100%)
Remodeling	0	78 (100%)	0
Plication free margin	0	56 (71%)	0
Triangular resection	0	33 (42%)	7 (9%)
Free margin shortening	0	0	50 (67%)
Commissural neochord	0	0	3 (4%)
Raphe shaving			
Raphe resection and closure	12 (23%)	0	0
Raphe resection and patch repair	20 (38%)	0	0
Cusp prolapse repair	41 (77%)	0	0
Pericardial patch repair for perforation	3 (6%)	0	0
Patch repair	9 (17%)	1 (1.2%)	0
Reoperation for valve failure	0	n.a.	1/50 (2%)

Cusp repair during valve-sparing operation in children

Valve-sparing root replacement is an attractive option for children with aortic root aneurysms when the aortic valve is functionally normal or repairable. The two most common scenarios for this procedure are connective tissue disorders and BAV. The approach of the Johns Hopkins Hospital group to correct a possible leaflet prolapse does not differ substantially from that used in adults and consists of midleaflet plication or free edge suspension with a fine Gore-Tex suture. The former is preferred in young patients with connective tissue disorders [30]. In a series of 56 children who underwent valve-sparing root replacement (78% reimplantation and 22% remodeling, respectively), only two (3.6%) had concomitant aortic valve repair. Regarding a possible cusp repair, it must be underlined that their relative contraindications for valve-sparing operation include marked leaflet fenestration and asymmetry; giant root with marked leaflet irregularities; or bicuspid valves with extensive calcification, severe prolapse

and/or marked fenestrations. Four patients were reoperated during follow-up for recurrent aortic insufficiency (all from the remodeling group), but unfortunately no indication whether they had concomitant valve repair during the first operation is given [31]. To our knowledge, no other experiences of aortic valve-sparing procedures and concomitant cusp repair in children have, so far, been published.

Discussion

The expanding indications of aortic valve-sparing operations to more complicated cases have recently generated a growing interest in cusp repair. Repairing the valve is not only needed when clear alterations of the cusp are detected, but also in apparently 'normal valve' to increase the coaptation length to ensure long-term durability. The techniques described in the literature are basically intended to correct the possible residual incompetence and achieve adequate coaptation height.

Correction of the possible residual incompetence

TRICUSPID AORTIC VALVE

The main techniques to achieve the correction of residual aortic incompetence are as follows:

(1) Central cusp plication along the nodule of Arantius.
(2) Shortening of the free margin.
(3) Combination of the two techniques.

It makes intuitive sense that central plication is easy and fast, the nodules of Arantius are thick enough to hold a 6–0 suture, and reduction of the free margin length can be obtained millimeter by millimeter. Nevertheless, according to Labrosse *et al.* [20], it considerably increases the stress and strain on the cusp and larger stresses are expected, in theory, to promote tears and local calcification. In addition, central plication restores smaller coaptation areas than leaflet resuspension. It, therefore, stands to reason that free margin shortening would be the best technique for individual cusp correction, although it is more technically demanding and more 'invasive', considering

that the cusp free margin, except for its central portion, is usually thin. According to this, central plication should play a role mainly in the presence of very limited tissue redundancy conditioning mild prolapse. It should be emphasized that the results obtained by David and Armstrong [16] with these two techniques are outstanding: among 64 patients treated, only one needed reoperation in the long-term. Nevertheless, as the three-dimensional geometry of tricuspid aortic valve is complex, they recommend using caution when more than one cusp needs repair. According to this, it should be noted that in the Brussels' series, both patients who needed reoperation for severe aortic insufficiency had, during the first procedure, more than one cusp repaired [18]. We do believe that in presence of more than one cusp requiring complex repair, the Bentall procedure, which has been demonstrated to be safe and durable, should be seriously considered even in young patients.

Triangular resection in tricuspid valve is a more 'invasive' and technically demanding technique. According to the recommendation by Schäfers *et al.,* it is indicated only in the presence of marked tissue redundancy (> 10 mm), which is an unusual presentation. However, cusps with strongly elongated free margin are frequently thin and the risk of distortion and/or tear during or after the reconstruction (either with direct suture or with patch insertion) should not be underestimated. A second consideration regards the durability of the pericardial patch in the mid-term and long-term. As calcification is known to develop more frequently in xenograft patches, immunological factors are considered to be important items. Fixation of autologous pericardium in glutaraldehyde solution reduces tissue retraction and promises good long-term results. Chauvaud *et al.* [32] reported that 15 min fixation in 0.625% glutaraldehyde solution reduces the immunologic reaction because of the stabilizing effect induced by the cross-linkage of collagen materials. According to this, the use of fixed autologous pericardium should be considered superior to that of bovine pericardium, although good preliminary results were reported with photo-oxidized bovine pericadium [33] and, in limited series, with decellularized porcine intestinal submucosal extracellular matrix [34]. PTFE has also been proposed for cusp extension during aortic valve repair and initial experience in limited series showed promising results [35]. PTFE has been quite commonly used for leaflet repair in atrioventricular valves or as a leaflet or chordate substitute and has shown the ability to withstand prolonged mechanical stress [36]. However, long-term function of PTFE as a valve patch is still unclear. On the contrary, the use of PTFE suture along the free margin of the aortic cusp has shown excellent long-term results [16]. However, it must be highlighted that, in the large Homburg series, the majority of

patients underwent, to get a proper coaptation, a 'simple' plication of the central portion of the cusp, whereas triangular resection and pericardial patch repair were rarely used [21]. These data suggest that, to achieve satisfactory cusp coaptation in tricuspid aortic valve, in most cases, only the central plication (that is considered the less technically demanding and time-consuming technique) is needed.

Commissural free margin plication is a much less used technique and the lack of data does not permit one to draw any definitive conclusion, although a recent finite element study has shown an increase in the cusp stress associated with the use of the latter technique [20]. Very limited clinical data also seem to lean toward a greater incidence of early failure [22].

Considering the technical difficulty of the tricuspid valve complex repair, in relation particularly to the threedimensional geometry of the valve and to the 'fragility' of the free margin of the cusps, we recommend using the central plication whenever possible, as it is the easier and most reproducible technique. It must be also stressed that if the immediate result is not satisfactory, the plication can be easily removed or slightly addressed. When more than one cusp need to be repaired, the safe and durable alternative offered by a valve conduit, although less appealing, should not be forgotten.

BICUSPID AORTIC VALVE

Apart from the free margin plication, techniques are mainly aimed at the raphe assessment and precisely at the following assessments:

(1) Raphe shaving.
(2) Raphe resection and primary closure.
(3) Raphe resection and patch repair.

Observations by Robicsek *et al.* [25] indicate that the fused cusp is exposed to abnormally high stress in both diastole and systole. This could be the pathogenetic mechanism underlying the unfavorable evolution of this cusp toward the free margin elongation or calcification conditioning restricted motion. This finding suggests to shave or to remove the raphe if it causes an alteration of the normal opening and closing mechanism of the cusp. According to Schäfers *et al* . [13], who described precisely the indications to use one or the other technique, the choice of repair type is based on cusp's aspect; they suggested central plication for limited tissue redundancy, triangular excision of cusp tissue with direct approximation for extensive tissue redundancy or

limited fibrosis, pathological tissue excision and cusp reconstruction bymeans of autologous pericardial patch for calcification in the raphe. Following this systematic approach, they obtained excellent freedom from reoperation at follow-up [27]. de Kerchove *et al.* [28] showed excellent results with several different techniques including raphe shaving, raphe resection and primary closure, raphe resection and patch repair, cusp prolapse repair, patch repair for cusp perforation, and any patch repair. The analysis of the data coming from the two more experienced centers in BAV repair [13,28] indicates that, to achieve durable competence of BAV, in a large number of cases, raphe resection is required. Among the patients who needed cusp repair in the Homburg series, about one-half were treated with triangular resection as well as in the Brussels' series, raphe resection was utilized in a little more than half of the cases. Although the excellent results of these two series could lead to a broad use of these techniques, we strongly believe that BAV reconstruction by means of raphe resection with or without patch should be reserved for centers with extensive experience in valvesparing surgery and valve repair.

Achieving an identical height of cusp free margin and an effective height of 7–8mm

That suboptimal cusps' coaptation is a risk factor for recurrent aortic insufficiency is nowadays a well established concept. The height of coaptation seems to be crucial in maintaining valve stability during the first year of follow-up. The functional aortic valve failure following valve-sparing operations, was first described by Bassano *et al.* [37]. Similarly, Pethig *et al.* [38] in a series of 75 patients with aortic valve reimplantation and echocardiography follow-up identified coaptation cusp level below the inferior rim of the prosthesis as an independent risk factor for early procedure failure. It seems, therefore, crucial to recreate an anatomical aspect of the valve within the prosthesis as similar as possible to healthy individual's aortic root, in which the height difference between aortic insertion and free margin of the cusps (effective height) ranges between 8 and 11mm [39]. In our opinion, this concept involves the absolute need for an exhaustive and thorough intraoperative transesophageal echocardiogram, aimed not only at evaluating the valve competence, but also its three-dimensional morphology within the root graft. The surgeon must be aware that inadequate coaptation reserve increases, even in the presence of perfect competence, the risk of procedure failure.

In conclusion, it seems that BAV more often requires correction when compared with tricuspid valve. Range of the techniques varies from the 'simple' free margin plication (used in most of tricuspid aortic valve) to the more complex triangular resection with patch repair. Results in the literature seem to be encouraging showing that, in most cases, cusp repair does not affect valve competence in the mid-term and long-term. However, we should not forget that correction of the cusp is a delicate balance between undercorrection that could lead to residual prolapse and overcorrection that could lead to cusp restriction. Complex repair of the aortic valve in addition to root replacement should be reserved for experienced centers with a large volume of patients.

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CHAPTER **10**

Impact of cusp repair on reoperation risk after the David procedure

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Abstract

Background. We assessed whether additional cusp repair during valve-sparing aortic root replacement affects the echocardiographic mid-term results; a subgroup analysis among patients with bicuspid aortic valve (BAV) and tricuspid aortic valve (TAV) was performed.

Methods. Between June 2002 and May 2015, 157 consecutive patients underwent valve-sparing aortic root replacement with the David technique. Thirty patients (19%) had BAV. In 19 patients (12%), cusp motion or anatomic abnormalities contributed in determining aortic regurgitation requiring an additional cusp repair. Mean follow-up was 7 ± 3.4 years.

Results. The cumulative 1-, 5-, and 12-year survival rates were 98%, 94%, and 90%, respectively. Fourteen patients (9%) required aortic valve replacement during follow-up. In 2 patients the underlying cause was bacterial endocarditis. Freedom from aortic valve reoperation was 96% at 1 year, 92% at 5 years, and 89% at 12 years. Reoperation rate was significantly higher ($p < 0.001$) in patients who received leaflet repair compared with patients who did not, with a freedom from reoperation at 8 years of 58% versus 94%. Among patients with BAV, those who did not require cusp repair had a freedom from reoperation at 8 years of 94%, with a significant difference compared with patients who received cusp repair ($p = 0.04$). Cusp repair did not affect reoperation risk in patients with tricuspid aortic valve.

Conclusions. Adjunctive cusp repair seems to affect the mid-term reoperation risk in patients with BAV and not in patients with tricuspid aortic valve. We recommend caution in using this technique in case of asymmetric BAV requiring cusp repair.

The valve-sparing aortic root replacement (V-SARR) is currently considered a safe and reliable procedure with encouraging mid-term and long-term results [1, 2]. Initially designed for a valve with preserved cusp morphology, over the years the technique has been extended also to valves with anatomic abnormalities requiring an additional cusp repair [3, 4]. However, evidence of durability after correcting cusp abnormalities is limited in literature.

Materials and Methods

A total of 157 patients underwent V-SARR with the David technique at the Humanitas Research Hospital from June 2002 to May 2015. The local ethics committee approved the study and waived the need for patient consent.

Indication for Surgery

Indication for surgery was proximal aortic dilatation with or without aortic incompetence (AI) and lack of significant aortic cusp calcification. Age older than 60 years [5], BAV [6], cusp prolapse, high grade of AI (≥3+), large-sized aortic root aneurysm (≥60 mm), and left ventricular ejection fraction of 0.40 or less were not considered contraindications. The procedure was performed in the setting of acute aortic dissection in only 1 patient.

The operative technique has been previously reported in detail [7]. Based on surgeon preference, the technique proposed by Cameron and Vricella in 2005 [8], consisting of anchoring the polyethylene terephthalate fiber (Dacron) graft (CarboMedics, Austin, TX) by means of a single horizontal mattress suture at the nadir of each cusp, was used in 18 patients (11%). In all the other patients, the graft was anchored by means of a continuous horizontal row of mattress sutures at the level of the ventriculoaortic junction. The Gelwave Valsalva graft was invariably used.

Additional cusp repair was required in 19 patients (7 with TAV and 12 with BAV; $p < 0.01$), of whom 12 underwent single cusp repair and 7 had multiple cusp repairs. Preoperative and intraoperative data, according to the need for cusp repair, are listed in Tables 1 and 2, respectively. Cusp repair procedures were performed according to standard techniques [9] either after reconstruction of the aortic root (when the three-

dimensional geometry was restored), in case of TAV, or before root reconstruction (soon after excision of the sinuses of Valsalva) in case of BAV. Details of cusp repair, according to the valve anatomy, are reported in Table 3. There were no intraoperative conversions to Bentall procedure. None of the patients required a second cardiopulmonary bypass run to revise the valve after intraoperative evaluation by transesophageal echocardiography.

Table 1. Preoperative Data[a]

Variables	All (n = 157)	Cusp Repair (n = 19)	No Cusp Repair(n = 138)
Age, y	61 ± 12	52 ± 14	62 ± 11
Sex, male	118 (75%)	17 (90%)	101 (73%)
Hypertension	99 (63%)	9 (47%)	90 (65%)
Diabetes	9 (6%)	1 (5%)	8 (6%)
Smoke	64 (41%)	7 (37%)	57 (41%)
COPD	27 (17%)	2 (10%)	25 (18%)
Renal failure	8 (5%)	–	8 (6%)
NYHA class			
I	79 (51%)	15 (79%)	64 (46%)
II	47 (29%)	1 (5%)	46 (33%)
III	29 (18%)	3 (16%)	26 (20%)
IV	2 (1%)	–	2 (1%)
Marfan syndrome	6 (4%)	1 (5%)	5 (4%)
LVEF			
≤0.40	12 (8%)	1 (5%)	11 (8%)
0.41–0.49	9 (6%)	–	9 (7%)
≥0.50	136 (86%)	18 (95%)	118 (85%)
Preoperative AI grade			
None/Trace	35 (22%)	2 (10%)	33 (24%)
Mild	25 (16%)	3 (16%)	22 (16%)
Moderate	50 (32%)	5 (26%)	45 (33%)
Severe	47 (30%)	9 (48%)	38 (27%)
Aortic valve anatomy			
Tricuspid	127 (81%)	7 (37%)	120 (87%)
Bicuspid	30 (19%)	12 (63%)	18 (13%)
Aortic root diameter			
<60 mm	141 (90%)	17 (90%)	124 (90%)
≥60 mm	16 (10%)	2 (10%)	14 (10%)
Elective surgery	156 (99%)	19 (100%)	137 (99%)
Type A aortic dissection			
Acute	1 (0.6%)	–	1 (0.7%)
Chronic	5 (3%)	–	5 (4%)
Mitral incompetence (>2+)	31 (20%)	4 (21%)	27 (19%)
Coronary artery disease	19 (12%)	1 (5%)	18 (13%)

[a] Results are expressed as number (%) or mean±SD. AI = aortic incompetence; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; NYHA.=New York Heart Association.

Table 2. Intraoperative Data[a]

Variables	All (n= 157)	Cusp Repair (n = 19)	No Cusp Repair (n = 138)
CPB time (min)	138 ± 32	152 ± 32	136 ± 31
Aortic cross-clamp time (min)	118 ± 25	125 ± 23	117 ± 25
Graft size (mm)			
26	2 (1%)	–	2 (1%)
28	20 (13%)	5 (26%)	15 (11%)
30	52 (33%)	7 (37%)	45 (33%)
32	83 (53%)	7 (37%)	76 (55%)
Aortic arch replacement	1 (0.6%)	–	1 (0.7%)
Mitral valve repair	11 (7%)	–	11 (8%)
Coronary artery bypass graft	17 (11%)	–	17 (12%)
Radiofrequency ablation for atrial fibrillation	2 (1%)	1	1 (0.7%)
Atrial septal defect closure	3 (2%)	–	3 (2%)

[a] Results are expressed as number (%) or mean ±SD. CPB = cardiopulmonary bypass.

Table 3. Cusp Repair Techniques in Tricuspid and Bicuspid Aortic Valves

Technique	BAV	TAV
Free-margin shortening with running suture	–	1
Nodule of Arantius plication	4	5
Debridement of cusp calcification	1	–
Repair of stress fenestration	2	1
Raphe resection and primary closure	N/A	5
Raphe shaving	N/A	5

BAV= bicuspid aortic valve; N/A= not applicable; TAV= tricuspid aortic valve.

Echocardiographic and Clinical Follow-Up

Intraoperative transesophageal echocardiography was performed after weaning from cardiopulmonary bypass and achieving hemodynamic stability to evaluate the dynamic motion and residual AI grade of the reimplanted valve. None of the patients left the operating room with an AI grade greater than mild. Postoperatively, transthoracic echocardiography was performed at 1 week, 6 and 12 months, and every year thereafter.

Patients were treated with warfarin sodium for anticoagulation only if a concomitant procedure required it; otherwise they were prescribed only aspirin.
Clinical follow-up, performed by means of office visit or phone call, ranged from 1 to 12 years (mean, 7 ± 3.4 years) and was 99% complete with a total of 2 patients lost to follow-up.

Statistical Analysis

Continuous variables were expressed as the mean ± SD and were analyzed by using the unpaired two-tailed Student's t test. Categorical variables were presented as percentage and were analyzed with the X^2 test or Fisher's exact test when appropriate. Estimates for longterm survival and freedom from morbid events were made by the Kaplan-Meier method. Differences between survival curves were evaluated with the log-rank statistic.

Results

Early Results

There were no intraoperative deaths. Hospital mortality was 1.2% (2 patients). In one case hospital death was attributable to sepsis at 4 months after reimplantation in a patient who had a cardiac arrest on postoperative day 4. Although resuscitation was successful, the patient had a devastating neurologic injury as a result of anoxia. Coronary angiography demonstrated no evidence of coronary button occlusion, and the cause of the cardiac arrest remains unclear. Another patient died of sudden cardiac arrest on postoperative day 6 during the rehabilitation program; post-mortem examination failed to identify the cause of death.
Permanent neurologic deficit was observed in 2 patients.
Another 2 patients had transient neurologic deficit. Four patients had a perioperative myocardial infarction, 3 patients had implantation of permanent transvenous pacemaker, and 4 patients experienced renal failure. Reexploration for bleeding was necessary in 16 patients. Sternal dehiscence or mediastinitis was observed in 3 patients. Assisted ventilation for more than 48 hours was needed in 5 patients.

Late Results

The cumulative 1-, 5-, and 12-year survival rates were 98%, 94%, and 90%, respectively (Fig 1A). The 10-year survival rate of patients who underwent cusp repair and patients with no need of cusp repair was 95% and 89%, respectively, with no significant difference (p = 0.8; Fig 1B). Eight patients died during follow-up. Causes of deaths were cardiac related in 4 patients (2 sudden deaths and 2 heart failures). Two patients experienced stroke during follow-up, 4 months and 2 years after the operation. Aortic valve infective endocarditis developed in 2 patients, 2 and 4 years after the operation.

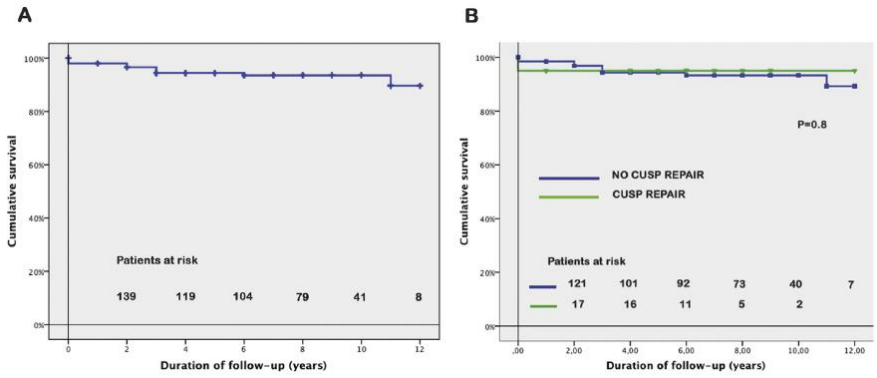

Figure 1: (A) Overall cumulative survival. (B) Cumulative survival according to need for cusp repair (green line) or not (blue line).

Reoperation

OVERALL. Thirteen patients experienced significant (>2+) AI and 1 patient had severe aortic stenosis (AS) during follow-up and required aortic valve replacement. The overall freedom from reoperation as a result of significant AI or severe AS was 96% at 1 year, 92% at 5 years, and 89% at 12 years (Fig 2). The overall freedom from aortic valve reoperation and moderate or severe residual AI was 96% at 1 year, 92% at 5 years, and 78% at 12 years (Fig 3). Aortic valve characteristics and mechanisms of recurrent AI or AS in patients who underwent aortic valve replacement are reported in Table 4. In 2 patients, the underlying cause was bacterial endocarditis; the infection affected 1 patient with BAV and 1 with TAV. Neither of the valves in these 2 patients required an

adjunctive cusp repair during the first procedure; at latest follow-up before the event, 1 patient had no residual AI and the other had mild residual AI.

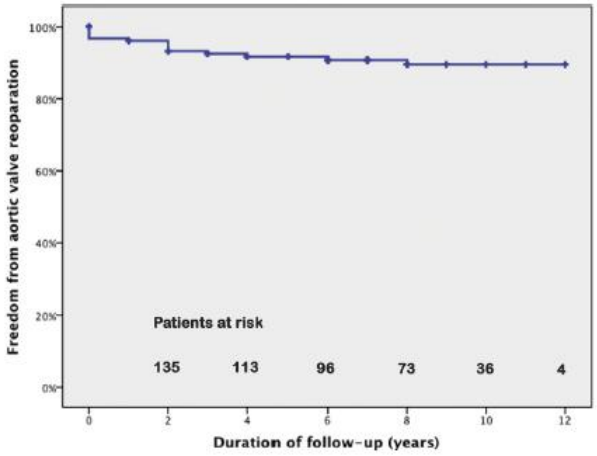

Figure 2: Overall freedom from aortic valve reoperation.

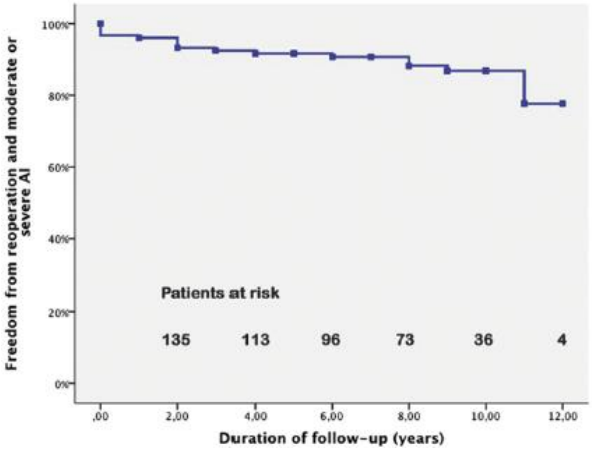

Figure 3: Freedom from aortic valve reoperation and moderate or severe aortic incompetence (AI).

Table 4. Aortic Valve Characteristics and Mechanisms of Recurrent Aortic Incompetence in Patients Who Underwent Aortic Valve Replacement

Patient	Age (y)	Valve Anatomy	Grade of Preoperative AI	Cusp Repair Technique	AI at Discharge	Cause of Recurrent AI	Interval Time (mo)
1	28	TAV	None	None	Modearte	Three cusps prolapse, technical problem	1
4	65	TAV	Severe	None	Mild	NC cusp prolapse	80
7	33	BAV	Severe	NC-RC cusp free-margin shortening (running suture)	Moderate	NC-RC cusp retraction	7
8	65	TAV	Severe	None	None	NC cusp prolapse	42
23	51	TAV	Severe	None	Mild	NC cusp prolapse	33
30	45	TAV	Severe	None	Mild	NC cusp prolapse	14
45	67	TAV	Moderate	None	Mild	Unknown	33
54	33	TAV	Severe	None	Mild	LC cusp prolapse	30
67	71	TAV	Moderate	None	Mild	Endocarditis	48
72	36	BAV	Severe	NC cusp triangular resection	Moderate	NC cusp prolapse	8
76	33	BAV	Moderate	LC-RC cusp raphe shaving and nodule of Arantius plication	None	Aortic stenosis owing to cusps fibrosis and posterior commissure calcification	96
91	37	TAV	Moderate	LC cusp fenestration repair with pericardial patch	Moderate	Three cusp prolapse	4
105	63	BAV	Moderate	LC-RC cusp raphe resection and primary closure and NC cusp nodule of Arantius plication	Trivial	Commissure detachment (suture dehiscence)	5
166	52	TAV	Trivial	None	None	Endocarditis	29

AI = aortic incompetence; BAV=. bicuspid aortic valve; LC = left coronary cusp; NC = noncoronary cusp; RC = right coronary cusp; TAV = tricuspid aortic valve.

A 33-year-old patient with BAV exhibited AS and underwent valve replacement at 8 years; during the first procedure, a valve repair consisting of left coronaryright coronary cusp raphe shaving and nodule of Arantius plication was performed. Predischarge and 3 and 36 months' echocardiography showed no residual AI and no transaortic pressure gradient. At 70 months, moderate AI and mild-to moderate AS was documented. Two years later, despite a stable moderate AI, severe AS was diagnosed. On reoperation, strongly fibrotic cusps and calcification of the posterior commissure were found.

IMPACT OF THE LEARNING CURVE AND SURGICAL TECHNIQUE. To evaluate the impact of the learning curve on the reoperation rate we compared the results of the patients who had undergone surgery in the first 3 years of experience with those treated in the subsequent years. Freedom from reoperation at 8 years was 85% versus 91% (p= 0.17), respectively.

We also compared the freedom from reoperation of patients in whom the Valsalva graft was anchored to the ventriculoaortic junction by means of a single suture (Cameron-Vricella technique) with those treated with the standard technique. Freedom from reoperation at 5 years was 90% versus 92% (p= 0.89), respectively.

SUBGROUP ANALYSIS. Freedom from reoperation was 93% at 5 years and 91% at 10 years for TAV and 86% at 5 years and 78% at 10 years for BAV (p= 0.07; Fig 4A). Freedom from aortic valve reoperation and moderate or severe residual AI was 93% at 5 years and 89% at 10 years for TAV and 86% at 5 years and 78% at 10 years for BAV (p= 0.1; Fig 4B). The rate of aortic valve reoperation was significantly higher ($p < 0.001$) in patients who received cusp repair compared with patients who did not, with a freedom from reoperation of 78% versus 98% at 1 year and of 58% versus 92% at 8 years, respectively (Fig 5).

Among patients with TAV, the additional cusp repair did not significantly affect the freedom from reoperation (83% versus 92% at 8 years; p= 0.26; Fig 6A). Conversely, among patients with BAV, those who required an additional cusp repair had a significantly lower freedom from reoperation (50% versus 94% at 8 years; p= 0.04; Fig 6B). Excluding the two cases of endocarditis, the results did not change significantly (p= 0.2 for TAV and p= 0.01 for BAV), but of note, the freedom from reoperation for BAV with no need for cusp repair was 100% at 10 years.

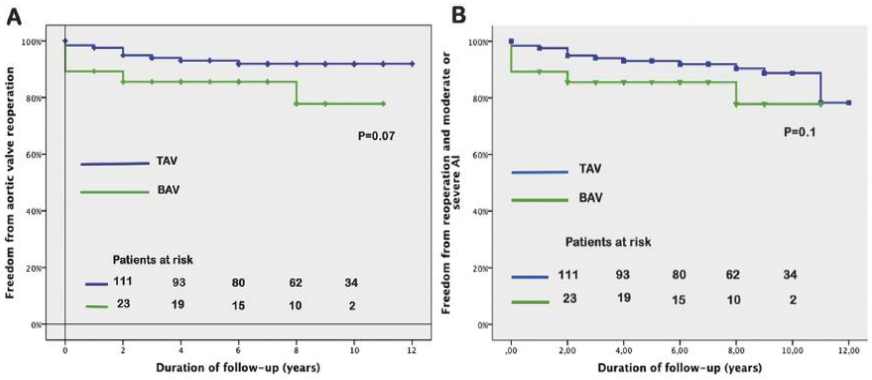

Figure 4: (A) Freedom from aortic valve reoperation according to the valve anatomy. Bicuspid aortic valve (BAV; green lines) and tricuspid aortic valve (TAV; blue lines) are shown. (B) Freedom from aortic valve reoperation and moderate or severe aortic incompetence (AI) according to the valve anatomy. Bicuspid aortic valve (BAV; green lines) and tricuspid aortic valve (TAV; blue lines) are shown.

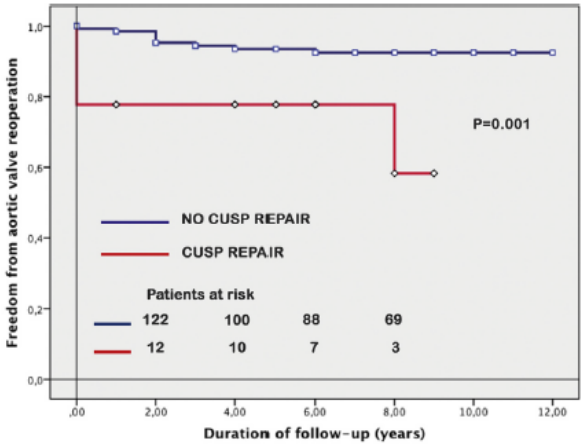

Figure 5: Freedom from aortic valve reoperation according to the need for cusp repair (red line) or not (blue line).

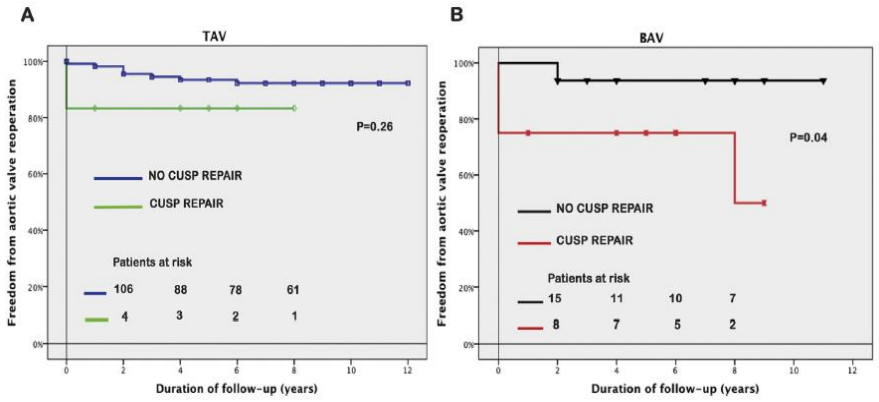

Figure 6: (A) Freedom from aortic valve reoperation in tricuspid aortic valve (TAV) according to the need of cusp repair (green line) or not (blue line). (B) Freedom from aortic valve reoperation in bicuspid aortic valve (BAV) according to the need of cusp repair (red line) or not (black line).

Comment

We started our experience with the V-SARR in October 2002; since then we have not applied any restrictions in surgical indication in terms of patient age, valve anatomy, grade of AI, aortic root aneurysm size, and left ventricle function. Instead, despite the encouraging results reported in the literature, we are reluctant to use this technique in urgent or emergency cases. Indeed the large majority of our patients were operated on electively [10, 11].

In our series, we have invariably used the Valsalva graft, which, once pressurized, generates bulging pseudosinuses without the need for any substantial variation in the original reimplantation technique [12]. The particular design of the graft makes it possible to adapt to each individual anatomy, re-creating the original root geometry even in the most challenging asymmetric BAV. We previously demonstrated that the compliance of pseudosinuses of the Valsalva graft is maintained over the years [13].

To evaluate the impact of the learning curve on the reoperation rate, we compared the results of patients who had undergone surgery in the first 3 years of experience with those treated in the following years. The freedom from reoperation at 8 years was not significantly different in the two subgroups (85% versus 91%; $p = 0.17$); apparently, the first years of our experience did not affect the overall reoperation rate.

In considering the prospect of an aortic valve-sparing procedure, a deep knowledge of the surgical anatomy of the aortic root is mandatory. The aortic valve needs to be considered a functional unit composed of three structures: (1) the functional aortic annulus, comprising the ventriculoaortic junction and the sinotubular junction, (2) the aortic cusps, and (3) the three sinuses of Valsalva. Although the anatomic ventriculoaortic junction seems to be placed at approximately one third of the height of the aortic root, the surgical intraluminal ventriculoaortic junction is a virtual ring formed by joining the basal attachment of the aortic cusps [14, 15]. On the extraluminal side of the aortic root, the limit of the surgical dissection during V-SARR corresponds to the roof of the left atrium on the side of the noncoronary and left coronary sinus and to the myocardium coming from the ventricular septum and continuing laterally to the right ventricular outflow tract on the side of right coronary sinus [16]. Since 2008, based on surgeon preference, the Cameron-Vricella technique [8], consisting of placing a single mattress suture at the level of each cusp nadir, was used in a minority of cases (11%), apparently with no impact on results at 5 years ($p = 0.89$). We believe that what matters is not the number of mattress sutures that are placed to anchor the Dacron graft, but rather how deep into the ventriculoaortic junction the graft is lowered. To achieve a proper positioning of the graft, the dissection outside the aorta must be to the level described above, so that the prosthesis can incorporate the entire functional aortic annulus, thus preventing the aortic root from further dilatation.

Valve-related complications such as thromboembolism and infective endocarditis were relatively rare in our series (1.2% in both cases); if the rate of thromboembolic event in the literature is certainly lower after V-SARR than after the Bentall procedure, the incidence of endocarditis seems to be comparable, at least in the younger population [17, 18]. In this sense, the lack of a prosthetic valve does not seem to protect patients from bacterial infection. However, because endocarditis is an unpredictable event that is probably not related to the surgical technique, we thought it best in our analysis to perform the survival curves also excluding the patients who had endocarditis to assess the freedom from reoperation without this potential bias; nevertheless, the outcomes did not change significantly.

In our experience, valve anatomy per se (BAV or TAV) had no significant impact on the freedom from reoperation, and these data are consistent with the literature [3, 19]. Going deeper into the analysis, we found that the additional cusp repair significantly affected the reoperation risk. This finding does not appear to be in line with the largest published series [4, 9]. The relatively small number of patients who underwent cusp

repair may have affected the outcome. However, we find it necessary to make the following observations: first, the term “additional cusp repair” is too generic as it includes a wide variety of techniques ranging from a “simple” freemargin plication (mostly used in TAV) to the more complex triangular resection with patch repair; and second, the BAV more frequently requires cusp correction in comparison with TAV, and the type of repair needed is usually more complex. In this sense, a subgroup analysis of patients with the two types of valve seems to be necessary. With regard to patients with BAV, based on the analysis of our results, since 2011 we began to be more careful to treat the asymmetric valves requiring complex adjunctive cusp repair by means of V-SARR [6]. However, at that time the mean follow-up of approximately 4 years was not long enough to draw conclusions. The current investigation, with a longer follow-up time, shows more clearly that BAV requiring cusp repair (12 of 30 patients; 40%) is affected by a significantly higher reoperation rate. Conversely, BAV with minimal cusp abnormalities and no need for cusp repair provided excellent 10-year results. This latter type of BAV (type 0, according to the classification by Sievers and Schmidtke [20]) has usually symmetric cusps with the two commissures facing each other at 180 degrees and a lack of raphe or minimally represented raphe. As the V-SARR basically consists of a three-dimensional reconstruction of the aortic valve within a Dacron neoroot, in our opinion this configuration is even easier to treat than TAV, with only two reference points to realign symmetrically at the level of the sinotubular junction of the neoroot. Recently, Bavaria and colleagues [21] showed an interesting approach to V-SARR in asymmetric raphed BAV (type 1 Sievers). They advocate, during root reconstruction, respect for the native commissures orientation, and discourage the forcing of a 150- to 210-degree geometry into a 180- to180-degree configuration. However, it must be noted that in this scenario, frequently a complex cusp repair including free-margin equalization, optimization of coaptation zone, raphe release or resection, and debridement of any cusp calcification is required. This means that several variables are added to the procedure, potentially affecting the result in terms of valve durability. Midterm and long-term outcomes of this subset of patients will need to be analyzed to validate this approach. In our series, the number of patients with BAV with cusp repair is not large enough to allow a further analysis of the result based on the type of repair performed in this subset of patients. Conversely, among patients with TAV, the cusp repair did not seem to affect the freedom from reoperation, even at 8 years. In this regard, we note that among the patients with TAV treated with additional cusp repair, only 1 underwent reoperation. We believe that the less technically demanding type of

valve repair needed in case of TAV could explain this finding. On the contrary, among patients with TAV who underwent reoperation, 8 of 9 did not undergo cusp repair during the first procedure and the large majority of them had cusp prolapse on reoperation. These data suggest a more aggressive approach to the TAV during reimplantation, in terms of cusp repair, to reduce even the smallest differences in length of the free margins to achieve the maximal coaptation depth.

Finally, in a young patient with raphed BAV, the cause of valve replacement was a severe AS that occurred at 96 months. The "natural history" of the reimplanted BAV (which is not supposed to be stenotic at the time of surgery) after V-SARR is mostly unknown; however, its evolution toward stenosis seems to be extremely rare [22]. A possible explanation of this low incidence can be provided by recent studies that show that BAV stenosis with aortic dilatation and BAV insufficiency with root dilatation represent two different phenotypes [23, 24]. In conclusion, our 12 years' experience with V-SARR provided satisfactory results in terms of survival and aortic valve function. The anatomy of the valve per se had no impact on the outcomes. Additional cusp repair seems to affect the mid-term reoperation risk in patients with BAV and not in patients with TAV. Probably the complexity of cusp repair required by the BAV with cusp abnormality could have had a significant impact on valve function during follow-up. Correction of even minimal and apparently irrelevant cusp prolapse in TAV could possibly reduce the reoperation risk in this subset of patients. We recommend caution in performing V-SARR in patients with asymmetric BAV requiring a complex cusp repair.

The major limitation of the current investigation is the retrospective approach of the analysis. Another limitation is the small number of patients who underwent additional cusp repair, particularly in the BAV subgroup, and this may have affected the outcomes. Finally, not all of the follow-up echocardiographic studies were performed at our institution, so that some important quantitative and qualitative factors were, in some cases, missing.

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PART 4

BENTALL PROCEDURE FOR AORTIC ROOT REPLACEMENT

CHAPTER **11**

Aortic root replacement with the Carboseal composite valve graft: analysis of risk factors

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Abstract

This retrospective analysis of a selected series of Bentall-De Bono procedures was carried out in order to evaluate the performance of the Carboseal composite valve graft (Sulzer Carbomedics Inc, Austin, TX, USA). Between October 1997 and April 2004, 120 patients underwent aortic root replacement with the Carboseal Composite Valve Graft. The mean age of patients was 59.7±13.4 years (range, 21– 83 years); 96 patients (80%) were male. Eighty- nine patients (74.2%) had annulaortic ectasia, 10 patients (8.3%) post-stenotic dilatation, 3 (2.5%) post dissection aneurysm, 2 (1.7%) acute type A dissection and 1 (0.8%) endocarditis. The average follow-up duration was 29.2 months (range 2–82 months). Hospital mortality was 1.7% (2 of 120 patients). The actuarial survival rate (including hospital mortality) was 97.2±1.5% at 1 year, 91.6±3.5% at 3 years and 84.0±8.0% at 5 years. Chronic renal failure was an independent risk factor for late mortality (P=0.02). The actuarial freedom from pseudoaneurysms at 3 years was higher among patients without Marfan syndrome (94.7±3.2% vs. 75.0±21.6% at 3 years, P<0.003). In our recent series, the Bentall-De Bono operation provided good results with low incidence of prosthetic related complications. Pseudoaneurysms requiring re-operation have a higher incidence among patients with Marfan syndrome.

1. Introduction

In order to assess the performance of the Carboseal composite valve graft (Sulzer Carbomedics Inc, Austin, TX, USA) we retrospectively analysed a selected series of Bentall-De Bono procedures.

2. Materials and methods

2.1. Patients

Between October 1997 and April 2004, 120 patients underwent aortic root replacement with the Carboseal composite valve graft. Until November 2003 we have exclusively used this conduit regardless of patient's age. After this date we also started implanting 'home made' biological conduits (pericardial valve, Mosaic® Medtronic Inc., Minneapolis, MN, USA and a tubular graft, Sulzer Vascutek, Renfrewshire, Scotland, UK) in patients aged >65 years. So far our experience with biological conduits is limited to 12 cases. Patients preoperative characteristics are listed in Table 1.

2.2. Operative technique

A median sternotomy was performed and hypothermic cardiopulmonary bypass (32 °C) was instituted with cannulation of the ascending aorta, aortic arch or femoral artery and right atrium. Myocardial protection was achieved with a combination of antegrade and retrograde cardioplegic solution and topical cooling with 4 °C saline solution. The 'button technique' [1] was used in all cases and all patients received the Carboseal composite valve graft. If aortic dissection was present, continuity between the separated layers of the aorta was restored using gelatin-resorcinol formaldehyde biologic glue (GFR; F.I.I, Saint-Just Malmont, France) [2] and the distal anastomosis was further reinforced with an inner and outer Teflon felt strip. Concomitant procedures included planned coronary artery bypass grafting in 18 patients (15%), coronary artery bypass grafting due to perioperative technical problems in 4 patients (3%), mitral valve replacement in 4 patients (3%), mitral valve repair in 3 patients (2%) and left atrial ablation for atrial fibrillation in 3 patients (2%). The mean cardiopulmonary bypass

time was 99±30 min (range 61–213 min) and the mean aortic cross-clamp time was 82±21 min (range 52–159 min).

Table 1. Preoperative patients characteristics

Characteristic	**N=120**
Age (years)	59.7±13.4
Sex (male)	96 (80)
NYHA functional class	
I	24 (20)
II	57 (48)
III	39 (32)
IV	–
Left ventricular ejection fraction	
>60%	66 (55)
40–59%	44 (37)
<39	10 (8)
Marfan syndrome	4 (3)
Indications for operation	
Primary operation	105 (87)
Anuloaortic ectasia	89
Poststenotic dilatation	10
Acute aortic dissection	2
Chronic aortic dissection	3
Endocarditis	1
Reoperation	15 (13)
Aortic valve prosthesis	1
Valsalva sinus aneurysm after AVR or AAR	11
Valsalva sinus aneurysm after CABG	3

Values are mean±1 SD. Numbers in parentheses are percent. NYHA=New York Heart Association. AAR=ascending aorta replacement. AVR=aortic valve replacement.

2.3. Follow-up

Follow up was conducted between March and April 2004 and was 96% complete. The 5 patients, whose follow-up was incomplete, were censored at the time of their last follow-up. The average follow-up duration was 29.2 months (range 2–82 months).

2.4. Statistical analysis

Univariate and multivariate analysis to determine whether any single factor influenced hospital mortality was not carried out due to the low incidence (2 cases). Preoperative, intraoperative and postoperative variables were analysed for their influence on mortality during follow-up. Variables considered were: sex, age, NYHA class, chronic renal insufficiency (creatinine levels greater than or less than 1.9 mg/dl), left ventricle ejection fraction (<40% or >40%), coronary artery disease, Marfan syndrome, bicuspid aortic valve, indication for operation (anuloaortic ectasia, post-stenotic dilatation, dissection, endocarditis) previous aortic valve or aortic operation, cross clamping time, cardiopumonary bypass time, concomitant procedures and postoperative complications (myocardial infarction, respiratory insufficiency, bleeding, neurologic deficit, hemodialysis). Variables achieving a *P*-value of less than 0.2 in the univariate analysis were examined using Cox proportional hazard regression. Estimates for long term survival and freedom from morbid events were made with the Kaplan– Meier method. Differences between survival curves were evaluated with the log-rank statistic.

3. Results

3.1. Early mortality

Hospital mortality rate, defined as all patients who died within 30 days after the operation or during initial hospitalisation was 1.7% (2 of 120 patients). Cause of death was acute prosthetic endocarditis complicated by acute myocardial infarction and sepsis in one patient and multiple organ failure (MOF) in the other patient. Because of the small number of the events (2 cases), unvariate and multivariate analysis was not carried out.

3.2. Early morbidity

Early (<24 h) re-intervention for excessive bleeding was necessary in 11 patients (9.2%). Perioperative myocardial damage (serum creatinine kinase level 300 IU/l, with a creatinine kinase MB isoenzyme fraction 3%) occurred in 4 patients (3.3%). Haemodialysis for renal insufficiency was necessary in 3 patients (2.5%). Permanent neurological deficits developed in 2 patients (1.7%). Transient neurological deficits

involving left or right side weakness were observed in 2 patients (1.7%) and in both cases the deficit was fully recovered. One patient (0.8%) developed prosthetic endocarditis and died from sepsis 15 days after the operation.

3.3. Late mortality

There were 7 (6.4%) late deaths. Causes of death were cerebral haemorrage in 3 patients, ischemic heart disease in 1 patient, uncontrollable bleeding during reoperation in 2 patients and cholecystic cancer in 1 patient. Overall actuarial survival is shown in Fig. 1. The survival rate was 97.2±1.5% at 1 year, 91.6±3.5% at 3 years and 84.0±8.0% at 5 years. The difference in survival between Marfan and non-Marfan patients was not significant (*P*=0.584). Univariate analysis showed a significant association between late death chronic renal insufficiency (P<0.001), left ventricle ejection fraction (LVEF) <40% (*P*=0.04) and re-operation on the aortic root (*P*=0.04). In the Cox multivariate analysis chronic renal insufficiency (creatinine levels greater than 1.9 mg/dl) was found to be the only independent risk factor for late mortality (*P*=0.02; OR=11.5). The results of univariate and multivariate analysis are reported in Table 2.

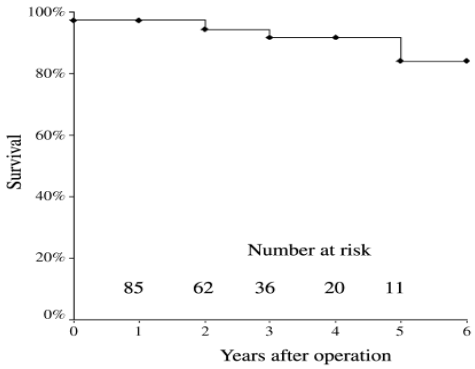

Figure 1: Overall actuarial survival.

Table 2. Univariate and multivariate analysis of late mortality

Variable	Univariate *P* value	Odds ratio	Multivariate 95% Confidence interval	P value
Chronic renal insufficiency	<0.001	11.5	1.29–103.70	0.02
LVEF <40%	0.04			
Redo on the aortic root	0.04			

LVEF=left ventricle ejection fraction.

3.4. Re-operations

Re-operation as a result of complications in the composite valve graft procedure was necessary in 6 (5.5%) patients, 3 to 65 months after primary operation.

Pseudoaneurysm at the aortic or coronary ostial suture lines occurred in 4 (3.5%) patients, 2 of which had Marfan syndrome. All patients with pseudoaneurysm except one were re-operated at our institute and survived the operation. The other patient underwent re-operation in another hospital and died from uncontrollable bleeding during the procedure.

Two more patients required re-operation for prosthetic valve endocarditis, where the composite valve graft was replaced with an aortic homograft root. One of them died during the operation from uncontrollable bleeding. Freedom from re-operation due to complications of the composite valve graft procedure was 97.9±1.4% at 1 year, 93.8±3.2% at 3 years and 78.1±10.4% at 5 years (Fig. 2). The rate of freedom from re-operation for patients with Marfan syndrome was lower than that of the remaining patients (75.0±21.6% vs. 94.7±3.2% at 3 years), and the difference was significant (*P*=0.003).

3.5. Operations on the remaining aorta

Three patients (2.7%) underwent subsequent operations for aneurismal disease of the abdominal aorta respectively 3, 7 and 15 months after the initial operations. None of them had Marfan syndrome. The freedom from operation on the remaining aorta was 98.5±1.4% at 2 years, 95.9±2.9% at 3 years and 91.5±5.1% at 5 years.

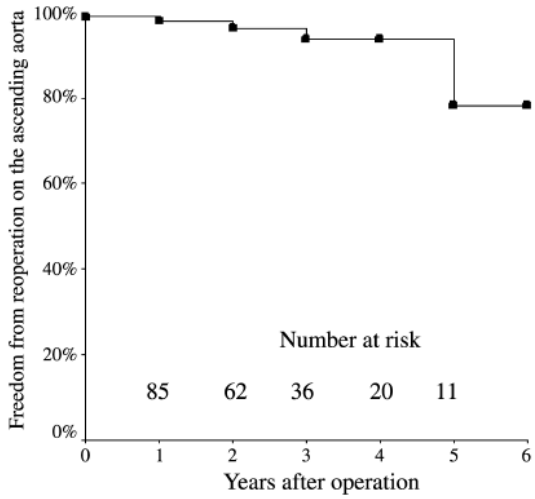

Figure 2: Freedom from re-operation due to complications of the composite valve graft procedure.

3.6. Prosthetic endocarditis

Two patients (1.8%) developed prosthetic valve endocarditis respectively 3 and 19 months after the operation. The infected valve conduit was replaced in both cases by a homograft aortic root. The first patient, as previously mentioned, died during the re-operation from uncontrollable bleeding; the second made a complete recovery and, at the time of the last follow-up, was in NYHA class I. The freedom from prosthetic endocarditis was 99.1±0.8% at 1 year, and 90±7.9% at 5 years.

3.7. Thromboembolism

Thromboembolic events occurred in 2 patients (1.8%). Both of them had a stroke and survived the event, but with a permanent neurological deficit. The freedom from thromboembolism at 5 years was 98±1.4%.

3.8. Anticoagulant-related complications

Three patients (2.7%) suffered cerebral haemorrhage respectively 31, 35 and 37 months after the initial operation. All of them died. The freedom from anticoagulantrelated complications was 97±2.0% after 2 years, and 94.4±3.2% after 5 years.

When including death, re-operation, endocarditis, thromboembolism and anticoagulant-related complications as events, the event free survival was 95.3±2.0% at 1 year, 79.5±5.5% at 3 years and 61.8±10.3% at 5 years (Fig. 3).

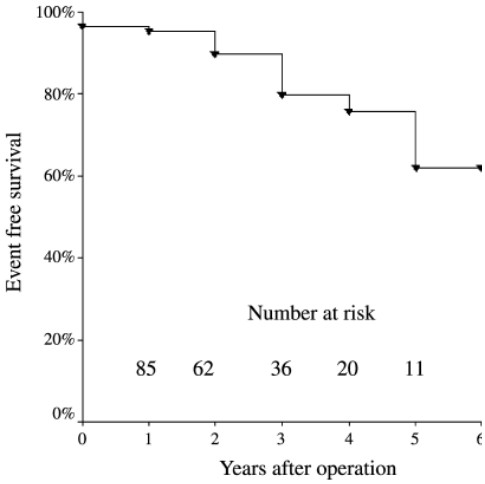

Figure 3: Event free survival.

4. Discussion

Composite valve graft replacement is the most radical mode of treating the combined disease of the aortic valve and aortic root. Although our experience began in 1997, from October 2002 onwards we have only used this approach in cases of gross structural defects of the aortic valve, preferring the aortic valve sparing operations [3] when the anatomy is suitable for repair.

Four patients underwent unscheduled bypass grafting because of electrocardiogram's ischemia soon after the weaning from CPB. Intra-operative transesophageal echocardiogram documented a hypokinetic left ventricular anterior wall in two cases and hypokinetic left ventricular posterior wall in the other two. The treatment consisted

of safenous vein grafting of either left anterior descending artery or right coronary artery, depending on the area involved. A kinking at the coronary ostium site was supposed to be the cause in all four cases.

Two patients (1.8%) experienced an early stroke. Both of them had risk factors for adverse cerebral outcome. The first was an 80-year-old patient with previous cerebral events; the second, because of ischemia after the weaning from the cardiopulmonary bypass (CPB) requiring a venous graft on the right coronary, had a long cross-clamping time (158 min) and CPB time (187 min).

The most frightening late complication within our group of patients was the anticoagulant-related cerebral haemorrhage that occurred in 3 cases and caused death in all of them. The reasons were patient related: the uncontrolled usage of anticoagulation and postponement of routine controls. It is well known that antithrombotic therapy with coumarin derivates carries a substantial risk of bleeding that varies with the drug used, the intensity of the anticoagulant effect and the clinical circumstances of individual patients. Abe and associates [6] showed, in patients with a CarboMedics biliflet valve in the aortic position, approximately 1.1%/yr thromboemboli or thrombosis with an international normalised ratio (INR) of 2.0 to 3.5. Wang and associates [7] with the same valves, used a target INR of 1.5 and observed thromboemboli in 2.7%/yr. For this reason, we recommend to our patients a target INR of 2.5 (range 2–3) [8].

Although our cut-off for the use of biological prosthesis is aged >65 years, 35% of our patients, though 'elderly', received a mechanical conduit. At the beginning of our experience we considered not reliable 'home made' biological conduits and we used to perform the Bentall-De Bono operation exclusively with mechanical conduits. More recently, on the basis of other authors experience [15] we started using, in patients aged >65 years, a 'home made' conduit. This consisted of a pericardial valve (Mosaic® Medtronic Inc., Minneapolis, MN, USA) and a tubular graft (Sulzer Vascutek, Renfrewshire, Scotland, UK), preserving mechanical prosthesis only to patients having thromboembolic problems.

Pseudoaneurysms occurred in 4 patients; the leak was localised at the proximal suture line in 2 cases and at the coronary ostial suture line in the other 2 cases. Hilgenberg and associates [9] reported no re-operation for coronary ostial pseudoaneurysm. However, the incidence of this complication with the button technique in other series varies from 3.1% to 9% [1,4,10]. Miller and Mitchell [11] describe the use of a 'life saver' or doughnut of Teflon felt or autologus pericardium (tanned in 0.625% glutaraldehyde

solution for 10 to 15 min) placed around the coronary ostium on the adventitional aspect to prevent tearing of tissues. We did not use any reinforcement of the coronary ostial suture lines in any of the patients. It must be said that both patients with pseudoaneurysms at the coronary ostial suture line had Marfan syndrome, which is well known to be associated with severe medial cystic necrosis of the ascending aorta (grade 4). In consistence with other experiences [4,5], our study suggests that suture line reinforcement in patients with connective disorders must probably be taken into consideration.

The GFR glue was used in case of acute aortic dissection (2 patients) to obliterate the false lumen and reinforce the aortic layers. The use of tissue glue in the treatment of this pathology has been reported to reduce significantly the mortality [12]. Nevertheless, recent reports [13,14] have documented the necrosis of the arterial wall after application of glue and this is supposed to be one of the causes of subsequent formation of pseudoaneurysms. Considering that we still do not have a perfect glue, we think we may pay the small price of occasional pseudoaneurysm formation for the greater benefit of improving survival in acute type A dissection.

In conclusion we assume that composite graft aortic root replacement is the treatment of choice in many pathologic conditions affecting the aortic root and the aortic valve. In our recent series (mean follow-up time is 29.2 months), the Bentall-De Bono operation provided good results with low incidence of prosthetic related complications. Given that longer follow up is needed to draw definitive conclutions, we thus believe that aggressive use of the Bentall- De Bono operation is appropriate if aortic valve surgery is necessary in patients with even moderate ascending aorta dilatation.

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CHAPTER **12**

Aortic root replacement with composite valve graft

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Abstract

Background. Composite valve graft replacement is currently the treatment of choice for a wide variety of lesions of the aortic root and the ascending aorta. In this study we report our experience with aortic root replacement using a composite graft.

Methods. Between October 1978 and May 2001, 274 patients (79.6% male and 20.4% female) with a mean age of 53.5 years underwent composite graft replacement of the aortic root. One hundred sixty-one patients (70.8%) had annuloaortic ectasia and 46 (16.8%) aortic dissection. The classic Bentall technique was used in 94 patients (34.3%), the "button technique" in 172 patients (62.8%), and the Cabrol technique in 8 patients (2.9%).

Results. The early mortality rate was 6.9% (19 of 274 patients). Cardiopulmonary bypass time longer than 180 minutes and associated coronary artery bypass grafting were found to be independent risk factors of early mortality. The actuarial survival rate was 77.7% at 5 years and 63% at 10 years. The independent risk factors for late mortality were coronary artery disease, chronic renal failure, and postoperative dialysis. The actuarial freedom from reoperation on the remaining aorta was higher among patients without Marfan syndrome (94.6% versus 79.6% at 10 years, $p = 0.008$).

Conclusions. Composite valve graft replacement can be performed with low hospital mortality and morbidity. The button technique offers some advantages and should be used whenever possible. In case of acute aortic dissection root replacement is usually not necessary. Marfan patients should be treated with early root replacement before dissection occurs.

Composite valve graft implantation described first in 1968 by Bentall and De Bono [1] is a well-documented technique of aortic root replacement used for a large spectrum of pathologic conditions involving the aortic valve and the ascending aorta [2– 4]. In the present study we have evaluated the results of our 23-year experience with aortic root replacement (ARR) using a composite valve graft in 274 patients.

Material and Methods

Patients

From October 1978 to May 2001, 274 patients underwent ARR using composite valve graft. Two hundred eighteen patients (79.6%) were male and 56 were female (20.4%). The mean age (± one standard deviation) was 53.5 ± 14.5 years (range, 13 to 80). Thirty-five patients (12.8%) had Marfan syndrome, 2 had Behçet's disease, and 1 had Turner syndrome. Twenty patients (7.3%) were in New York Heart Association (NYHA) functional class I, 84 (30.7%) in functional class II, 113 (41.2%) in functional class III, and 57 (20.8%) in functional class IV.

The most common indication for operation was annuloaortic ectasia (161 patients, 58.8%). Thirty-nine patients (14.2%) had previously undergone surgical intervention on the aortic valve or ascending aorta or both. They required reoperation because of progressive dilatation of the Valsalva sinuses in 34, prosthetic aortic valve endocarditis in 4, and acute aortic dissection in 1. The patients' profiles are reported in Table 1.

Operative Techniques

A standard median sternotomy was performed. Cardiopulmonary bypass (CPB) was instituted by cannulation of the ascending aorta, aortic arch, or femoral artery (depending on the extension of the aneurysm and the presence of dissection) and the right atrium or the superior and inferior vena cavae. Myocardial protection was obtained by antegrade administration of cold hyperkalemic crystalloid cardioplegia and topical cooling with 4°C saline solution.

Table 1. Patient Characteristics

Characteristic	No. (%)
Number of patients	274
Sex	
Male	218 (79.6)
Female	56 (20.4)
Age (years)	
Mean ± SD	53.5 ± 14.5
Range	13-80
NYHA class	
I	20 (7.3)
II	84 (30.7)
III	113 (41.2)
IV	57 (20.8)
Marfan syndrome	35 (12.8)
Behçet disease	2 (0.7)
Indications for operation	
Primary operation	235 (85.8)
Anuloaortic ectasia	161 (68.5)
Aortic dissection	46 (19.6)
Acute	18
Chronic	28
Poststenotic dilatation	25 (10.6)
Endocarditis	3 (1.3)
Reoperation	39 (14.2)
Aortic valve prosthesis endocarditis	4 (10.3)
Valsalva sinus aneurysm after AVR or AAR	34 (87.1)
Acute aortic dissection	1 (2.6)

AAR = ascending aorta replacement or repair; AVR = aortic valvevreplacement; NYHA = New York Heart Association.

For the first 94 patients (34.3%) the classic Bentall operation [1] with inclusion and wrapping technique was used. In 1994 the Bentall procedure was abandoned in favor of the "button technique" [2– 4]. Since then it has been used in 172 patients (62.8%). The coronary reimplantation suture lines were rarely reinforced externally with a Teflon strip. The Cabrol technique [5, 6] was used in 8 patients (2.9%). This method of

coronary reimplantation was utilized only in case of extreme aortic dilatation or reoperation because of difficult mobilization and approximation of coronary arteries to the aortic graft.

In case of acute aortic dissection a hemiarch replacement was usually performed using the open technique. Nevertheless 3 patients required a total arch replacement. In 4 patients the dissection was limitated to the ascending aorta and a closed distal anastomosis was performed. The continuity between the separated layers of the aorta was restored using gelatin-resorcineformaldehyde glue (GRF) and the distal anastomosis was furtherly reinforced with an inner and outer felt strip of Teflon.

Concomitant procedures included coronary artery bypass grafting in 23 patients (8.4%), mitral valve replacement in 5 (1.8%), extra-anatomic aorto-aortic bypass in 2, and atrial septal defect repair in 1. Thirty-one patients (11.3%) had associated aortic arch replacement.

Cerebral protection was obtained with deep hypothermia with circulatory arrest (DHCA) in 15 patients, DHCA and retrograde cerebral perfusion in 1, and antegrade selective cerebral perfusion with moderate systemic hypothermia in 26 [7]. Mean duration of cardiopulmonary bypass (CPB) was 153 ± 49.1 minutes (range, 92 to 425), and mean aortic cross-clamp time was 106.6 ± 32.4 minutes (range, 55 to 305).

A Björk-Shiley composite graft prosthesis (Shiley Inc., Irvine, CA) was used in 80 patients (29.2%); a Sorin composite graft (Sorin Biomedica S.P.A., Saluggia, Italy) in 56 (20.4%); a St. Jude composite graft (St. Jude Medical Inc., St. Paul, MN) in 35 (12.8%); a Carbomedics composite graft (Carbomedics Inc., Austin, TX) in 70 (25.6%); and an ATS (ATS Medical Inc., Minneapolis, MN) in 33 (12%).

Follow-Up

Of all hospital survivors, 239 (93.7%) were available for follow-up in intervals ranging from 3 months to 265 months (mean, 62.7) with a total of 1,431 patients-years. Follow-up information was obtained by our direct examination or by correspondence with the patient. The date of last inquiry was between May and October 2001. Postoperative complications were analyzed according to the “Guidelines for reporting morbidity and mortality after cardiac valvular operations” [8].

Statistical Analysis

Statistical analysis was performed with SPSS 8.0 Statistical software (SPSS, Chicago, IL). Continuous variables were expressed as the mean ± SD and were compared with unpaired two-tailed *t* test. Categorical variables were analyzed with a X^2 test or Fisher's exact test where appropriate. All variables that achieved *p* less than 0.2 in the univariate analysis were included in a multivariate model and examined by stepwise logistic regression for early mortality, and Cox multivariate analysis for late mortality. All variables analyzed are shown in Table 2. Survival and event-free data were analyzed with Kaplan- Meier actuarial techniques for estimation of survival probabilities and compared with log-rank tests.

Table 2. All Variables Analyzed by Univariate Analysis With Respect to Early and Late Mortality

Sex
Age (13–40; 41–60; 61–70; 71–80 years)
New York Heart Association class (I, II, III, IV)
Marfan syndrome
Annuloaortic ectasia
Aortic dissection (acute, chronic)
Aortic dissection (acute, chronic)
Associated coronary artery disease
Chronic renal failure
Reoperation
Cardiopulmonary bypass time (≤180, >181 minutes)
Clamping time (≤120, >121 minutes)
Emergency operation
Aortic arch replacement
Coronary artery bypass grafting
Postoperative dialysis
Cardiac complications
Postoperative pulmonary insufficiency
Postoperative sepsis
Postoperative bleeding

Results

Early Mortality

The overall early mortality rate (defined as death within 30 days or during initial hospitalization) was 6.9% (19 of 274 patients). Cause of death was operative myocardial infarction in 5 patients, cardiac arrest in 4, uncontrollable bleeding in 3, multiple organ failure in 2, myocardial failure with impossible weaning from CPB in 2, severe neurologic damage in 1, respiratory insufficiency in 1, and pulmonary thromboembolism in 1. In the univariate analysis (Table 3), coronary artery disease (p = 0.009), CPB time ($p < 0.001$), aortic cross-clamp time (p = 0.025), associated coronary artery bypass graft surgery ([CABG] p = 0.013), cardiac complications (p = 0.003), postoperative dialysis (p = 0.002), and sepsis (p = 0.014) were risk factors for early death. Multivariate analysis indicated CPB time longer than 180 minutes ($p < 0.001$; odds ratio [OR] = 12.5) and CABG (p = 0.025; OR = 4.6) as independent risk factors for early mortality (Table 3).

Early Morbidity

Cardiac complications occurred in 33 patients (12%) and were associated with an increased risk of early death on univariate analysis. The patients operated on using the Cabrol technique had an high incidence of these complications (3 of 8 [37.5%] versus 30 of 266 [11.3%]). All 3 patients sustained myocardial infarction and 2 of them died. Thirteen patients had persistent or recurrent atrial fibrillation, 8 from complete heart block requiring pacemaker implantation, 3 from ventricular tachycardia/ fibrillation; 1 from myocardial infarction, 1 from endocarditis, 1 from cardiac tamponade, and 1 from left ventricular failure.

Fifteen patients (5.5%) sustained respiratory insufficiency requiring prolonged mechanical ventilation (more than 48 hours). Sepsis occurred in 15 patients (5.5%) and was associated with an increased risk of early mortality (p = 0.014). Renal insufficiency requiring dialysis observed in 9 patients (3.3%) was associated with a higher mortality rate (44.4% compared with 5,7%; p = 0.002). Nine patients (3.3%) required rethoracotomy for bleeding: 6 (5.9%) underwent the classic Bentall or Cabrol procedure

and 3 (1.7%), the button technique. Permanent neurologic deficits developed in 4 patients (1.5%).

Table 3. Univariate and Multivariate Analysis for Early Mortality

						Multivariate		
Variables	**Patients No.**	**Patients %**	**Death No.**	**Death %**	**Univariate *p* Value**	**Odds Ratio**	**95% Confidence Interval**	***p* Value**
Endocarditis								
No	267	97.4	17	6.4	0.078			
Yes	7	2.6	2	28.6				
Associated CAD								
No								
Yes	245	89.4	13	5.3	0.009			
	29	10.6	6	20.7				
Chronic renal failure								
No								
Yes	267	97.4	17	6.4	0.078			
	7	2.6	2	28.6				
CPB time (minutes)								
≤180								
>181	224	81.8	8	3.6	<0.0001	12.5	3.9–40.3	<0.001
	50	18.2	11	22				
Clamping time (minutes)								
≤120	207	75.5	10	4.8	0.025			
>121	67	24.5	9	13.4				
Emergency operation								
No	249	90.9	15	6.0	0.061			
Yes	25	9.1	4	16.0				
CABG								
No	242	91.6	14	6.6	0.013	4.6	1.2–17.7	0.025
Yes	23	8.4	5	14.3				
Postoperative dialysis								
No	265	96.7	15	5.7	0.002			
Yes	9	3.3	4	44.4				
Cardiac complication								
No								
Yes	241	88	12	5.0	0.003			
	33	12	7	21.2				
Pulmonary insufficiency								
No	259	94.5	16	6.2	0.076			
Yes	15	5.5	3	20				
Sepsis								
No	259	94.5	15	5.8	0.014			
Yes	15	5.5	4	26.7				

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CPB = cardiopulmonary bypass

Late Mortality

There have been 57 late deaths (22.3%). The main cause of death was chronic heart failure. The other causes of late death are listed in Table 4. Overall actuarial survival of the 274 patients is shown in Figure 1. The survival rate was 77.7% at 5 years, 63% at 10 years, and 33.4% at 20 years. The survival rate of the patients with Marfan syndrome was lower than that for the remaining patients (61.9% versus 58.8% and 57.7% versus 29.4% at 10 and 15 years respectively) but the difference was not significant (p = 0.785; Fig 2A). Moreover Marfan patients with dissection demonstrated a 10-year survival of only 42.2% ± 13.4% whereas no-dissection Marfan patients demonstrated a long-term survival of 64% ± 26.3%.

Patients operated on for aortic dissection had a lower long-term survival rate compared with the remaining patients (65% and 58.7% versus 53.6% and 38.1% at 10 and 15 years respectively; Fig 2B).

Univariate analysis (Table 5) showed a significant association between late death and NYHA III-IV (p = 0.004) associated coronary artery disease (p = 0.05), endocarditis (p = 0.031), chronic renal insufficiency (p = 0.032), and postoperative dialysis (p = 0.028).

In the Cox multivariate analysis, associated CAD (p = 0.028; OR = 2.3), chronic renal failure (p = 0.012, OR = 4.0), and postoperative dialysis (p = 0.039; OR = 2.9) were independent risk factors for late mortality (Table 5).

Table 4. Causes of Late Deaths

Cause	Number
Congestive heart failure	13
Stroke	6
Prosthetic endocarditis	4
Myocardial infarction	5
Sudden death	11
Rupture of thoracic aorta	4
Cardiac arrest[a]	1
Suicide	1
Unknown	12
Total	57

[a] The patient died during operation for abdominal aortic aneurysms.

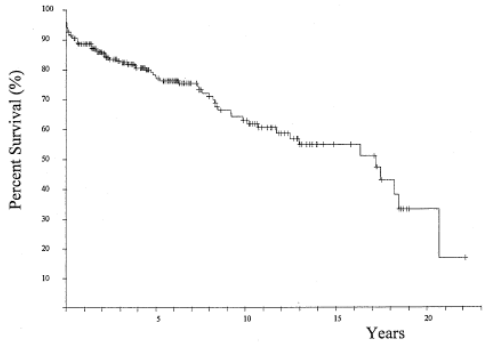

Figure 1: Actuarial survival rates (including hospital mortality) of the 274 patients. Percent survival ± SE is 88.6 ± 1.9 at 1 year, 77.7 ± 2.9 at 5 years, 63.0 ± 4.3 at 10 years, 54.7 ± 5.1 at 15 years, and 33.4 ± 8.2 at 20 years. Number of patients at risk at yearly intervals for years 0 through 20,

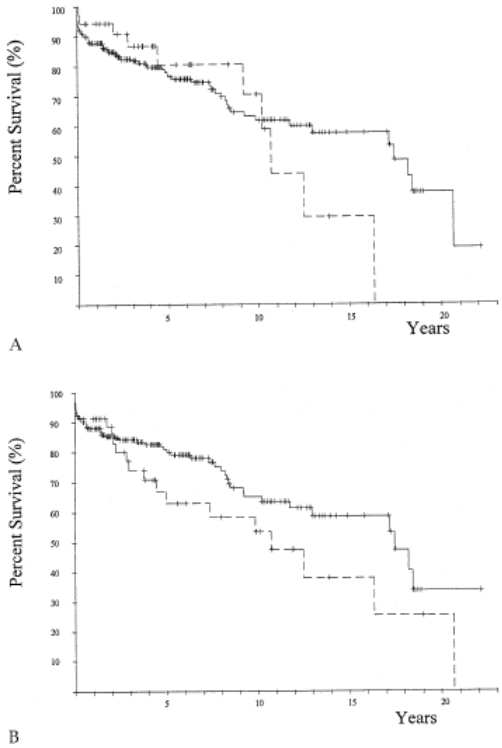

Figure 2: (A) Actuarial survival rates of the patients with Marfan syndrome(dashed lines) and without Marfan syndrome (solid lines); the difference between the two groups was not significant (p = 0.785). Percent survival ± SE for patients with Marfan syndrome is 94.3 ± 3.9 at 1 year, 80.6 ± 8.3 at 5 years, 70.6 ± 11.9 at 10 years, 29.4 ± 16.4 at 15 years, and 0 at 20 years; number of patients at risk yearly for years 0 through 16, respectively, is 35, 30, 26, 22, 17, 13, 12, 9, 9, 8, 6, 3, 3, 2, 1, 1, and 1. Percent survival for no Marfan syndrome is 87.8 ± 2.1 at 1 year, 77.3 ± 3.1 at 5 years, 62.0 ± 4.6 at 10 years, 57.7 ± 5.2 at 15 years, and 37.6 ± 8.9 at 20 years; number of patients at risk yearly for years 0 through 20, respectively, is 239, 198, 156, 126, 110, 92, 79, 64, 56, 49, 47, 37, 30, 24, 17, 15, 14, 14, 9, 2, and 2.

(B) Comparison of actuarial survival of patients with aortic dissection (dashed lines) and without aortic dissection (solid lines; p = 0.106). Percent survival with aortic dissection is 91.3 ± 4.2 at 1 year, 63.0 ± 8.5 at 5 years, 53.6 ± 9.5 at 10 years, 38.1 ± 11.8 at 15 years, and 25.4 ± 13.0 at 20 years; number of patients at risk yearly for years 0 through 20, respectively, is 46, 40, 32, 24, 21, 16, 15, 14, 12, 12, 10, 6, 5, 4, 3, 3, 2, 2, 2, 1, and 1. Percent survival for all other patients is 88.1 ± 2.2 at 1 year, 80.1 ± 3.0 at 5 years, 65.0 ± 4.8 at 15 years, 58.7 ± 5.6 at 15 years, and 33.8 ± 10.1 at 20 years; number of patients at risk yearly for years 0 through 20, respectively, is 288, 188, 150, 124, 106, 88, 76, 59, 52, 45, 43, 33, 28, 22, 15, 13, 12, 12, 7, 1, and 1

Table 5. Univariate and Multivariate Analysis of Late Mortality

		Multivariate		
Variables	**Univariate p Value**	**Odds Ratio**	**95% Confidence Interval**	***p* Value**
Preoperative NYHA III/IV	0.004			
Associated CAD	0.055	2.3	1.08–4.78	0.028
Aortic dissection	0.067			
Endocarditis	0.031			
Chronic renal failure	0.032	4.0	1.35–12.01	0.012
Postoperative dialysis	0.028	2.9	1.05–8.28	0.039

CAD = coronary artery disease; NYHA = New York Heart Association.

Late Morbidity

Thromboembolic events (TE) occurred in 9 patients (3.3%) and all of them had a stroke. Two patients died. The linearized rate of TE was 0.63/100 patient-years. Figure 3A shows the actuarial freedom from TE. At 15 years the actuarial freedom from TE was 90.9% ± 3.1%.

Thirteen patients (4.7%) had anticoagulant-related bleeding events necessitating hospital admission or blood transfusion or resulting in death. Five patients had cerebral hemorrhage and 4 of them died. Eight patients had gastrointestinal bleeding or retroperitoneal hematoma or both. The linearized risk of anticoagulant-related hemorrhage was 0.91/100 patient-years. Estimates for freedom from bleeding complications are shown in Figure 3B.

In 5 patients (1.8%) prosthetic valve endocarditis developed (1 early and 4 late). Two patients underwent reoperation (1 died) and 3 were treated with medical therapy (1 survivor). The linearized risk per 100 patient-years of prosthetic valve endocarditis (early and late) was 0.35. The actuarial freedom from endocarditis is shown in Figure 4A.

Four patients underwent reoperation for pseudoaneurysm of the coronary ostial suture line. In 2 of them the classic Bentall operation was used (2.1%) and in the other 2 (1 with Behçet's disease) the button technique was used (1.2%). The linearized rate of reoperation for pseudoaneurysm was 0.28/100 patient-years. Freedom from reoperation due to pseudoaneurysm for the classic Bentall and for the button technique was, respectively, 98.8% and 98.8% at 5 years, 98.8% and 95.5% at 10 years (Fig 4B). The difference between the two groups was not significant ($p = 0.776$).

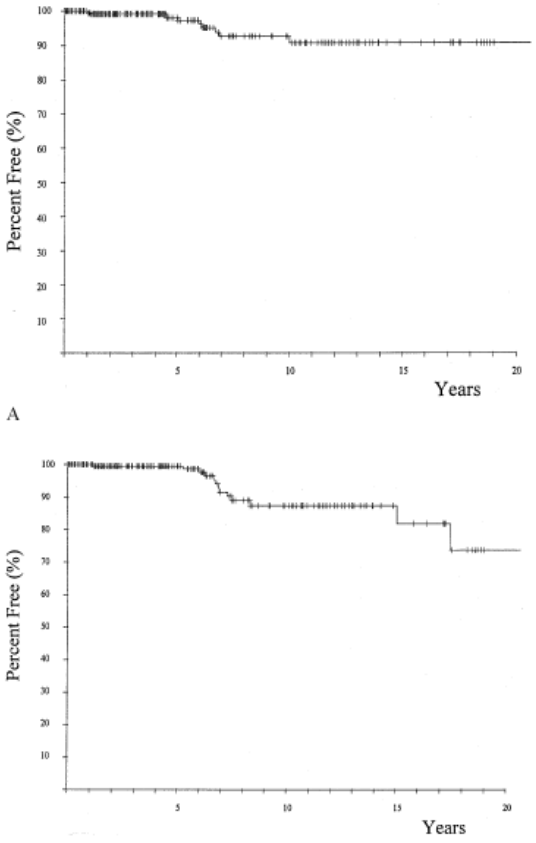

Figure 3: (A) Actuarial freedom from thromboembolism. Percent of patients free of thromboembolism ± SE is 99.6 ± 0.4 at 1 year, 98.2 ± 1.1 at 5 years, 90.9 ± 3.1 at 10 years, 90.0 ± 3.1 at 15 years, and 90.0 ± 3.1 at 20 years. Number of patients at risk yearly for years 0 through 20, respectively, is 274, 228, 182, 147, 126, 103, 89, 73, 65, 57, 52, 39, 32, 25, 17, 15, 14, 13, 8, 1, and 1.

(B) Actuarial freedom from anticoagulant-related hemorrhage. Percent of patients free of hemorrhage is 100 at 1 year, 99.6 ± 0.5 at 5 years, 87.4 ± 3.7 at 10 years, 81.9 ± 6.3 at 15 years, and 73.7 ± 9.6 at 20 years. Number of patients at risk yearly for years 0 through 20, respectively, is 274, 228, 183, 148, 127, 105, 91, 72, 63, 55, 51, 40, 33, 26, 18, 15, 14, 13, 8, 2, and 2.

Thromboemboic events, anticoagulant-related hemorrhage, prosthetic valve endocarditis, and reoperations for pseudoaneurysms were reviewed to evaluate overall valve graft-related morbidity. The actuarial estimate of percentage of patients free of any valve graft-related complications is shown in Figure 5.

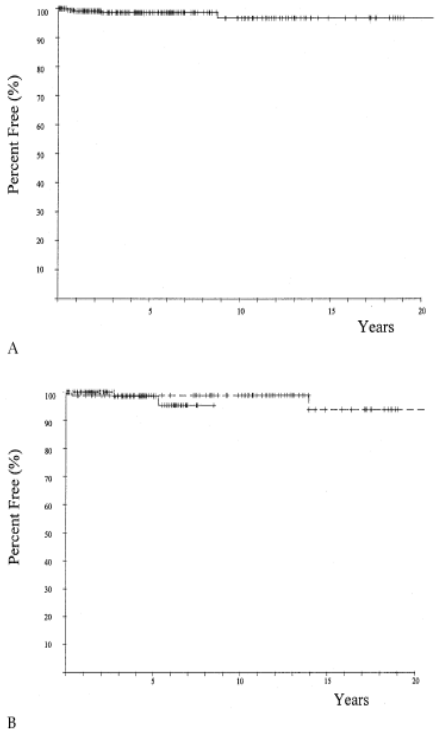

Figure 4: (A) Actuarial freedom from prosthetic endocarditis. Percent of patients free of prosthetic endocarditis ± SE is 98.8 ± 0.7 at 1 year, 98.2 ± 0.9 at 5 years, 96.4 ± 2.0 at 10 years, 96.8 ± 2.0 at 15 years, and 96.8 ± 2.0 at 20 years. Number of patients at risk yearly for years 0 through 20, respectively, is 274, 225, 181, 146, 125, 102, 88, 71, 62, 53, 42, 39, 32, 25, 17, 14, 13, 12, 7, 1, and 1.

(B) Actuarial freedom from reoperation for pseudoaneurysms according to the operative technique: classic Bentall technique (dashed lines) and "button" technique (solid lines; p = 0.776). Percent of Bentall patients free of pseudoaneurysms is 98.8 ± 1.2 at 1 year, 98.8 ± 1.2 at 5 years, 98.8 ± 1.2 at 10 years, 93.9 ± 4.9 at 15 years, and 93.9 ± 4.9 at 20 years; number of patients at risk yearly for years 0 through 20, respectively, is 94, 83, 77, 75, 73, 70, 68, 68, 63, 56, 53, 40, 33, 26, 18, 16, 15, 14, 9, 2, and 2. Percent of button technique patients free of pseudoaneurysms is 100 at 1 year, 98.8 ± 1.2 at 5 years, and 95.5 ± 3.5 at 10 years; number of patients at risk at yearly intervals for years 0 through 8, respectively, is 172, 140, 101, 70, 51, 31, 21, 4, and 1.

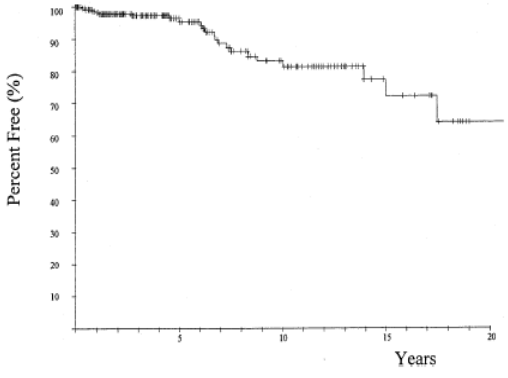

Figure 5: Actuarial freedom from valve graft related complications. Percent of patients free of complications ± SE is 97.9 ± 0.9 at 1 year, 96.0 ± 1.5 at 5 years, 81.0 ± 4.3 at 10 years, 71.6 ± 7.3 at 15 years, and 63.6 ± 10.0 at 20 years. Number of patients at risk yearly for years 0 through 20, respectively, is 274, 226, 182, 147, 126, 103, 89, 72, 63, 54, 49, 39, 32, 25, 17, 14, 13, 12, 7, 1, and 1.

Eleven patients have required one or more subsequent interventions for aneurysm or dissection of the remaining aorta; 4 were Marfan patients and all of them had aortic dissection. The rate of freedom from aortic reoperation of the patients with Marfan syndrome was lower than that for the remaining patients at 10 years (79.6% ± 13.6% versus 94.6% ± 2.6%) and the difference was significant (p = 0.008; Fig 6).

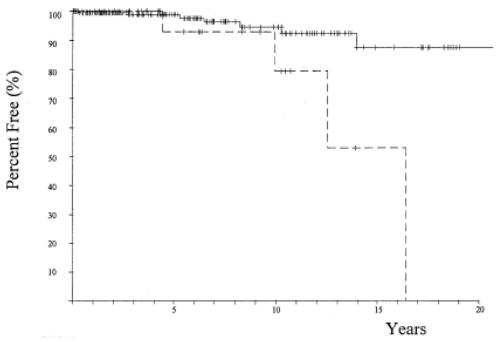

Figure 6 : Actuarial freedom from reoperation on the thoracic or abdominal aorta or both in patients with Marfan syndrome (dashed lines) and without Marfan syndrome (solid lines); the difference between the two groups was statistically significant (p = 0.008). Percent of Marfan patients free of reoperation ± SE is 100 at 1 year, 92.9 ± 6.9 at 5 years, 79.6 ± 13.6 at 10 years, 53.1 ± 23.5 at 15 years, and 0 at 20 years; number of patients at risk yearly for years 0 through 16, respectively, is 35, 30, 26, 22, 17, 13, 12, 9, 9, 7, 6, 3, 3, 2, 1, 1, and 1. Percent of non-Marfan patients free of reoperation is 99.5 ± 0.4 at 1 year, 98.8 ± 0.9 at 5 years, 94.6 ± 2.6 at 10 years, 87.6 ± 5.7 at 15 years, and 87.6 ± 5.7 at 20 years; number of patients at risk yearly for years 0 through 20,

Comment

Since its introduction in 1968 by Bentall and De Bono [1] the aortic valve and ascending aorta replacement with composite graft has led to a significant prolongation of life expectancy for patients affected by a variety of pathologic conditions involving the ascending aorta and aortic valve such as annuloaortic ectasia, cystic medial necrosis with or without Marfan syndrome, and type A aortic dissection [3, 4, 9–17].

Our retrospective analysis confirms, in agreement with other recent reports [14–17], that this surgical procedure presents a low operative risk. We found CPB time longer than 180 minutes and associated CABG to be independent risk factors of early mortality. In 1994 we abandoned the original Bentall operation with the inclusion technique and introduced the button technique [2–4] with several features that may reduce the incidence of early and late complications. Hemostasis may be improved by avoiding aortic wall wrapping. Since this modification repeat thoracotomy for bleeding has been reduced from 5.9% to 1.7%. Other factors such as the use of preclotting woven aortic

graft, improved surgeon experience, and more accurate use of eparine and protamine may have contributed to the reduction of intraoperative bleeding.

The button technique without complete aortic wall wrapping may prevent late pseudoaneurysm formation [2–4] secondary to dehiscence of the suture line of the aortic annulus, distal graft anastomosis, or mainly at the coronary ostial anastomosis particularly at the left coronary ostium in patients with Marfan syndrome or with aortic dissection [12, 18]. Kouchoucos and associates [3] have suggested that blood accumulation within the wrapped perigraft space results in increased tension on the anastomosis when the inclusion and wrap technique is used. We also believe that the circumferential resection of the distal part of the ascending aorta reinforced with two Teflon strips can reduce the stress along the suture line between composite prosthesis and aorta.

We rarely performed coronary reimplantation according to the Cabrol technique [5, 6]; it was used for patients who had undergone reoperation or for cases of extreme aortic dilatation because of difficult mobilization and approximation of the coronary arteries to the aortic graft. One of the greatest technical difficulties with this technique is the sizing and orienting of the graft between the right and left main coronary arteries to prevent kinking and subsequent myocardial ischemia or infarction. In our experience it was associated with a high early mortality rate (3 of 8, 37.5%) and a high incidence of perioperative myocardial infarction. Therefore since 1994 we have not used the Cabrol technique, and detachment and mobilization of the coronary arteries could be easily performed using the button technique.

As cardiovascular manifestations are the most important causes of death among Marfan patients, the survival of these patients depends on the prevention and control of these complications. A recent study [19] showed life expectancy improvement among patients with Marfan syndrome who had undergone surgical repair for aortic aneurysms. Now the median cumulative probability of survival is 61 years whereas 30 years ago, it was 47 years.

In our series the survival rate including 30-day mortality of the Marfan patients was slightly lower than that of the remaining patients (at 10 years 58.8% ± 14.6% versus 61.9% ± 4.6%) without statistical difference ($p = 0.785$). A factor that influenced the late survival of the Marfan patients was the presence of aortic dissection: at 10 years the survival rate of the Marfan patients with aortic dissection was 42.2% whereas that for the Marfan patients without dissection was 64%. Late mortality was associated with associated CAD, chronic renal failure, and postoperative dialysis.

Although some researchers have found long-term survival to be statistically less favorable among patients with aortic dissection at the time of root replacement [16] it was not a predictor of late mortality in our series. That may be due to a low rate of patients with Marfan syndrome in our series (12.8%) compared with that reported in the literature (69.3%) [16]. Crawford [2] underlined in a large series of patients with dissection or aneurysm of the ascending aorta or aortic arch that diseases of the aorta are often part of a more diffuse degenerative process. The same author [20] reported an elevated incidence of operation on the remaining aorta among patients with Marfan syndrome who underwent composite graft or aortic valve replacement. A recent paper [21] confirmed a significant progression of the disease in the remaining aorta in Marfan patients who had previously undergone composite graft replacement. Seventeen of the 48 patients studied by magnetic resonance imaging had a significant increase in diameter of the aorta with a mean rate of dilation of 2.3 ± 3.3 mm per year. Surgical intervention was necessary in 14 of them.

In our study the rate of freedom from reoperation on the remaining aorta of the patients with Marfan syndrome was lower than of the other patients at 10 years (79.6% ± 13.6% versus 94.6% ± 2.6%) and the difference was significant (p = 0.008). Moreover all Marfan patients reoperated on during follow-up had aortic dissection. According to this, all patients who have undergone aortic root replacement should be periodically evaluated by computed tomography scan, magnetic resonance imaging, or transesophageal echocardiography to detect the development of false aneurysms or the progression of the disease in the remaining aorta, particularly in patients with Marfan syndrome or with aortic dissection.

Despite refinements in the design of cardiac prostheses and in anticoagulation management, mechanical valve replacement is still associated with a variety of valve-related complications often leading to serious disability or death. In our series the rate of valve-related complications was low. Anticoagulant-related hemorrhage was the most common late complication with a rate of 0.91 events per 100 patient-years, followed by thromboembolisms (0.63/100 patient-years). Endocarditis was a serious complication with a high mortality rate (60%). It is our standard policy to replace the infected composite graft or prosthesis with a cryopreserved homograft root. Conservative treatment failed to eradicate infection in all patients treated except for 1 patient. Appropriate antibiotic prophylaxis remains the main preventative measure.

To avoid the disadvantages of prosthetic heart valves the valve-sparing procedure has been introduced [22]. Patients with aortic root aneurysm often have normal or

minimally diseased aortic cusps that can be preserved. Actually the valve-sparing operation has become our treatment of choice for aortic root aneurysm with normal aortic valve and in the past 24 months we have performed 24 procedures. However the current series does not include these patients and it reports only our experience with composite valve graft replacement.

Four patients (1.5%) required reoperation for pseudoaneurysm formation at the coronary suture lines: in 2 patients the original Bentall operation was used (2.1%) and in the other 2—1 of them with Behçet's disease—the button technique was used (1.2%). All patients underwent successful reoperation. Techniques used for reattachment of coronary arteries did not influence the incidence of reoperation for pseudoaneurysm during follow-up. Because not all patients were evaluated by diagnostic imaging studies such as magnetic resonance, computed tomography, or angiography the real incidence of pseudoaneurysm formation is unknown and may be higher.

When a pseudoaneurysm is detected it should be repaired before progressive dilation, adherence to the sternum, or rupture because all these situations, which require urgent or emergent operation, are associated with high operative risk [3]. Hahn and associates [23] reported no early deaths in a limited series of patients who had undergone aortic root reoperation for pseudoaneurysm or endocarditis but no operations were done emergently. In a study of 81 patients who had undergone reoperation on the aortic root or ascending aorta Kouchoukos and colleagues [24] presented an early mortality rate of 12.5% in 16 patients reoperated on for false aneurysm. In the same report reoperation for false aneurysm was a significant predictor of late mortality.

Eighteen of the 274 patients (66%) who underwent aortic root replacement had acute type A dissection. This number represents fewer than 10% of all patients operated on for acute type A dissection during the same period. We believe along with Elefteriades [25] that the vast majority of aortic dissections can be treated appropriately with a simple supracoronary hemiarch replacement and the aortic valve can be left alone or the commissures can be resuspended. Long-term survival after root replacement for acute aortic dissection was found to be statistically less favorable [10]. Composite graft replacement should be limitated to cases of frank annuloaortic ectasia, Marfan syndrome, and severe destruction of the proximal aorta.

Finally we should mention some limitations of the current investigation. First, this is a retrospective study over a long period of time in which many factors changed and could not be accounted for with the multivariate statistical techniques. Second, owing to incomplete data collection during the earlier years some important variables such as left

ventricular function and intraoperative myocardial protection were not included in the analysis. Therefore the influence of these variables on early and late mortality could not be studied.

In summary composite valve graft replacement can be performed with low rates of hospital mortality and morbidity. The button technique offers some advantages and should be used whenever possible. In case of acute aortic dissection root replacement is usually not necessary. Patients with Marfan syndrome should undergo early root replacement before aortic dissection occurs. Valve-related complications have a low incidence but often lead to disability or death. A careful follow-up is extremely important for evaluating the prosthetic aortic segment, the proximal and distal anastomosis, the morphology, and the diameter of the reimplantated coronary arteries and the remaining segments of the aorta.

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PART 5

ROSS OPERATION FOR AORTIC ROOT REPLACEMENT

CHAPTER **13**

The Ross operation: an evaluation of a single institution's experience

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Abstract

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

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 patient survival was 98.9 ± 1.0% 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 bicuspic 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 followup. 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.

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 minutes (range 133 to 287 minutes) and mean aortic cross-clamp time was 137.6 ± 26.5 minutes (range 98 to 232 minutes).

Table 1. Preoperative Patient Characteristics

Characteristic	Number = 103
Age (years)	35.2 ± 9.5
Sex (male)	71
NYHA functional class	
I	59 (57.3)
II	27 (26.2)
III	17 (16.5)
IV	–
Left ventricular ejection fraction	
> 50%	68 (66.0)
30-50%	31 (30.1)
< 30%	4 (3.9)
Predominant lesion	
Aortic stenosis	20 (19.4)
Aortic incompetence	51 (49.5)
Mixed aortic disease	32 (31.1)
Aortic valve morphology	
Bicuspid (congenital)	44 (42.7)
Tricuspid	59 (57.3)
Previous aortic valve surgery	
Valve replacement	2 (1.9)
Valvulotomy	5 (4.8)
Valvuloplasty	1 (0.9)
Enucleation of subvalvular membrane	2 (1.9)

Values are mean ± 1 standard deviation. Numbers in parenthesis are percent.

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 analyzed by using the unpaired two-tailed *t* test. Categorical variables were presented as percentage and were analyzed with the X^2 test or Fisher'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 analyzed 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 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 development 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 patient survival is shown with the Kaplan-Meier analysis in Figure 1, with 98.9 ± 1.0% at 1 year and 97.3 ± 1.9% at 10 years.

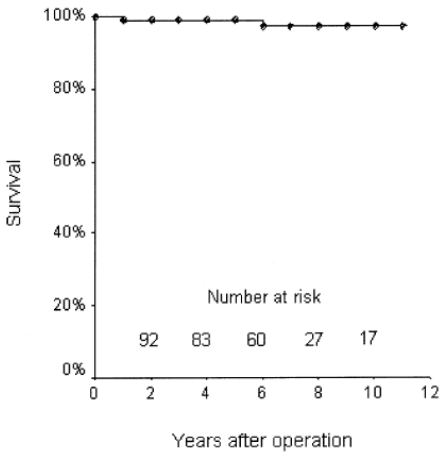

Figure 1: Overall patient survival.

Morbidity

Eleven patients (10.7%) required early reoperation (< 24 hours) for bleeding. Four patients (3.9%) developed myocardial infarction (creatinine 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 others 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.

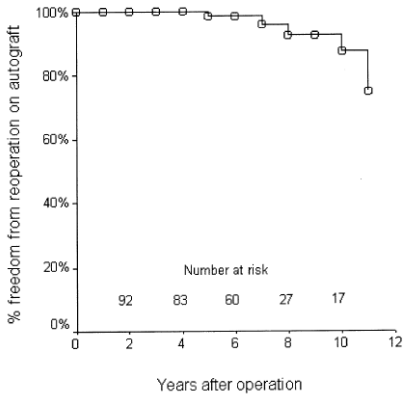

Figure 2: Actuarial freedom from reoperation on pulmonary autograft during follow-up.

Valvular Endocarditis

Endocarditis occurred in 2 patients. In the first patient the endocarditis was localized 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 localized on the pulmonary homograft and was fatal. Freedom from endocarditis is 98.3% ± 1.6% at 5 years and 95.7% ± 3% at 10 years.

Cerebrovascular Accident

Three patients had a 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 even- 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).

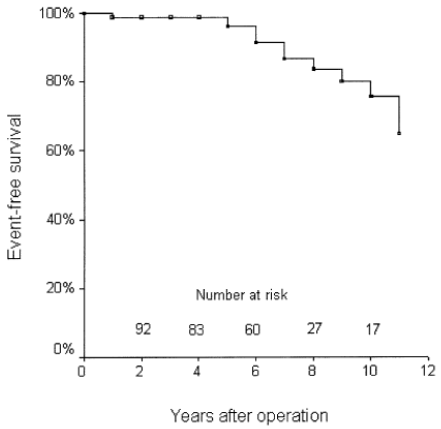

Figure 3: Event-free survival.

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 analyzed 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

Aortic Incompetence	Discharge to 3 Years	4 to 6 Years	7 to 9 Years	>10 Years
None	4	13	2	5
Trivial (grade I)	11	19	12	8
Mild (grade II)	2	8	2	4
Moderate (grade III)	1	2	1	
Severe (grade IV)	–	–	–	–

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).

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.

Table 3. Cox Proportional Hazards Regression for the Development of Pulmonary Homograft Stenosis

Characteristic	Range	Multivariate p Valuea	Multivariate Risk Ratio per Unit Increase (95% Confidence Limit)
Homograft diameter (increasing)	20–30 mm	0.001 (–)	0.6 (0.4, 0.8)
Donor age (increasing)	9–66 years old	0.002 (+)	1.05 (1.02, 1.09)

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

Comment

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 comorbiditiy 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 aortic bicuspid 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], de 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 aortic bicuspid 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 followup. 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 man 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 man 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.

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CHAPTER 14

GENERAL DISCUSSION

Since their introduction, the valve-sparing operations were faced with a tough challenge: to exceed the excellent results of the Bentall-De Bono procedure in the treatment of the aortic root pathology. As already happened many years before for the mitral valve repair, many surgeons were sceptical at the beginning, considering the procedure technically demanding, difficult to reproduce and possibly burdened with a high risk of reoperation. Satisfactory short and mid-term results, however, encouraged several aortic surgeons to embrace the technique so that, over the years, the valve-sparing operations have steadily expanded their indication to include patients with Marfan's syndrome, bicuspid aortic valve (BAV), acute type A aortic dissection, older age and additional cusp pathologies. Our data confirm that this procedure can be applied successfully in most of these pathologies without compromising the most important end-points such as mortality, freedom from recurrent aortic incompetence (AI) and freedom from reoperation.

The role of the sinuses of Valsalva

Since the beginning of the experience with the reimplantation technique, to reconstruct the aortic root we have been invariably using the Gelweave Valsalva graft for two main reasons: first, we are convinced that the Valsalva sinuses play an important role in the opening and closing mechanism of the aortic cusps during the cardiac cycle and, secondly, because there is no need for any substantial variation in the original reimplantation technique proposed by David (1,2). The role of the Valsalva sinuses has been largely investigated in literature. Interest in the aortic root blood flow date back to Leonardo da Vinci and was first investigated by Bellhouse and Bellhouse in 1968 (3). Modern studies, on the basis of mathematic models, have suggested that the flow patterns in the aortic root might affect the aortic valve function by allowing load and stress sharing between the valve cusps and the aortic wall (4). In this sense, each aortic cusp and the corresponding Valsalva sinus is to be considered, together with the sino-tubular junction, a *"functional unity"* that provides a smooth and rapid aortic valve closure minimizing the stress and strain on the valve cusps (5).

Chapter 2 presents single center preliminary results with the reimplantation technique using the Valsalva graft in a series including 32 patients. There were no intraoperative deaths, indicating that this operation can be performed safely at least in elective cases. Two patients developed significant recurrent AI requiring mechanical aortic valve replacement 4 and 6 weeks after the procedure, respectively. One was the very first case, a young man with the Marfan syndrome, in which was selected the wrong size of

the graft, probably too small that resulted in a prolapse of all 3 cusps. The other was a patient with a bicuspid aortic valve that during the first procedure underwent an additional cusp repair, consisting in a free margin shortening by running suture. Upon reoperation, we found a fibrotic retraction of the repaired cusp with a lack of coaptation. By these two cases two important lessons were learned: first, the aggressive downsizing of the graft is extremely counterproductive as it determines a distortion of the cusps leading to severe prolapse, particularly in patients with anulo-aortic ectasia. Second, the *free margin shortening with running suture* is probably a too aggressive method to reduce the free margin length of a prolapsing cusp, as a reactive fibrosis of the cusp needs to be expected. Since then, cusp repair has been abandoned in favour of the less invasive *plication of the nodule of Arantius*. Preliminary results of this study are consistent whit the experience of others both in term of mortality and reoperation rate (6,7).

In chapter 3, we show the short-term outcome of the same operation performed in 3 different Italian centers (Humanitas Research Hospital, Milan, S. Orsola Hospital, Bologna, Tor Vergata Hospital, Rome). This series of 151 patients included 7 cases (4.6%) operated on emergently for acute type A aortic dissection. In-hospital mortality was 3.3%, and it was significantly higher among patients operated on for acute dissection (42.9% vs. 1.4%; *p=0.001*). At 5 years, freedom from aortic valve replacement and freedom from AI grade 3 to 4 was 90.8% and 88.7%, respectively. Of note, the incidence of reoperation was significantly higher among patients who had undergone additional cusp repair when compared with patients who had not (25% vs. 3%; p= 0.005). Based on this finding, it was decided to abandon this technique for the treatment of acute aortic dissection and to be cautious with additional cusp repair. However, the number of cusp repair was not high enough to draw definitive conclusion also because the ideal cusp repair technique to use in this setting was not fully addressed. It must be emphasized that others reported encouraging results with the reimplantation of the aortic valve in acute aortic dissection (8,9).

In chapter 4, a single center experience of 100 cases of aortic valve reimplantation is described with a mean follow-up of 28 months (range 1 to 60 months). The series included 15 patients with bicuspid aortic valve. Two of them, with an evident asymmetry of the valve, required an additional cusp repair (free margin shortening by running suture and triangular cusp resection) and due to recurrent AI, underwent aortic valve replacement. Conversely, other 3 patients with a symmetric BAV (10) requiring a less extensive additional cusp repair, showed a stable function of the valve during

follow-up without significant AI. Therefore, in sight of this, the policy to spare the BAV only in case of symmetric cusps with no need of extensive additional cusp repair was adopted.

Chapter 5 focuses on the mechanical proprieties of the Valsalva graft, analysed by magnetic resonance, at mid-term follow-up. In previous studies, the Valsalva's graft compliance at the level of the Dacron *pseudo-sinuses* was found similar to that of normal sinus, shortly after the operation (2). By means of a case-control study, it was demonstrated that the compliance of the graft is maintained, although halved, during the mid-term follow-up. This finding shows that, over the years, the Valsalva graft continues to behave like the native aortic root not only from a static point of view (curvature of the sinuses) but also from a dynamic point of view and this is supposed to play an important role in the durability of the native valve by reducing the stress on the cups. To our knowledge, this is the first study investigating the mechanical proprieties of the Valsalva graft at mid-term follow-up. Nevertheless, the role of the Dacron neo-sinuses in the durability of the valve repair is still open to debate as emphasized by the recent editorial commentary published by Tirone David (11).

The valve-sparing aortic root replacement in different settings

In chapter 6, mid-term results of the aortic valve reimplantation in patients with the Marfan's syndrome were investigated by means of a retrospective multicenter study including four different centers (Humanitas Research Hospital, Milan, S. Orsola Hospital, Bologna, Tor Vergata Hospital, Rome, Hospital of the University of Pennsylvania, Philadelphia, USA). A pathological dilatation of the aortic root exists in about 75-85% of the patients with the Marfan's syndrome (12). Aortic root replacement using a mechanical valve conduit, also known as Bentall-De Bono procedure (13), has dramatically improved the survival of these patients and has long been considered the "gold standard" treatment, providing early and late excellent postoperative outcomes (14). In these individuals, the implantation of a mechanical valve is associated with low linearized rates of valve thrombosis, thromboembolism and haemorrhage (15). However, the majority of them are young and with a relatively high life expectancy that will lead to a considerable cumulative risk of valve-related morbidity. Moreover, very often, the aortic cusps are "functionally" normal (16). For these reasons, in the late '90s, the valve-sparing operations have emerged as an alternative to composite valve-graft to treat the aortic root pathology is this scenario.

The principal advantage of the reimplantation technique compared with the remodelling, is the stabilization of the annulus, which is of primary importance for patients with connective tissue disorders such as Marfan's syndrome, where the annulus may dilate over time. In this series, including 35 Marfan patients, three were reoperated for significant AI.

One patient was the very first case, already discussed in comment to chapter 2. Acute endocarditis was the cause of the reoperation in another patient, who had, at latest follow-up before readmission, trivial AI. No additional cusp repair was performed during the first procedure, so that we consider the event unpredictable and probably not related to the surgical technique. The third case, requiring reoperation at 22 months, was a 14-year-old boy with extremely elongated cusp free margins (>45 mm). In this case, we learned that patients with abnormally stretched leaflets are probably not suitable candidates for this technique. Five years results, with a survival rate of 100% and a freedom from reoperation due to structural valve deterioration and significant AI of 89%, are consistent with other reported series (17,18).

Although the ideal candidate for a valve sparing operation is a young patient with functionally normal or "nearly" normal aortic valve because of the long life expectancy and the disadvantages of a mechanical prosthesis in the long-term, in the elderly, the aortic valve reimplantation may be the ideal solution for two main reasons. First, with the increasing life expectancy in the older patients, reoperations in octogenarians with a previous aortic root replacement with a bio-prosthesis will become more common. Second, in this subset of patients, the alternative option of a mechanical valve may lead to a substantial risk of complications related to the anticoagulant therapy (19). In chapter 7, a series is described of 63 patients greater than 60 years of age, who underwent aortic valve reimplantation at two different centers (Humanitas Research Hospital, Milan, Italy, Hospital of the University of Pennsylvania, Philadelphia, USA). With an overall survival of 84% and a freedom from reoperation of 93% at 51 months it was found that in this subset of patients, the operation can be performed with encouraging results, both in terms of mortality and morbidity. However, age shouldn't be the sole criteria of patients' selection but should include an overall assessment of the comorbidities. It should be noted that in this study patients with aortic dissection and emergent indication were not included and the majority of the patients were in NYHA class I or II, with a LVEF grater than 60%. Others reported older age as predictor of poor outcome, however, the series of patients were heterogeneous including aneurysms, aortic dissection and Marfan's syndrome (20,21). Conversely, the study in Chapter 7

demonstrated that satisfactory outcome con be expected in this subset population if appropriately selected. To our knowledge, this is the first published report focusing selectively on the valve-sparing aortic root replacement in the elderly.

Bicuspid aortic valve is one of the main causes of AI, particularly in young subjects. As mentioned before for the Marfan patients, composite replacement with a mechanical prosthesis is a safe alternative but there is concern regarding the cumulative risk of the anticoagulant therapy. Moreover, anticoagulation may not be desired by young individuals who play sports. In chapter 8 we present a single center experience with aortic valve reimplantation focusing particularly on the impact of the bicuspid aortic valve on the reoperation risk at 5 years. The results showed that BAV, per se, had no impact on the reoperation risk. Indeed, overall freedom from aortic valve reoperation was 90% without significant difference between patients with bicuspid and tricuspid aortic valve. Moreover, no difference between bicuspid and tricuspid aortic valve was found in durability after stratification for adjunctive cusp repair. These results are consistent with the literature. Aicher et al., in a mid-term retrospective study comparing patients who underwent aortic root remodelling for tricuspid and bicuspid aortic valve, found no significant difference between the two groups in terms of valve stability (22). A few years later, Schäfers, from the same group, confirmed this result in a long-term study (23). Analysing the issue from a different point of view, de Kerchove et al, found that in patients with BAV requiring cusp repair, the aortic valve reimplantation stabilizes the functional aortic annulus, improves valve mobility (low gradient) and is associated in improved outcomes. Based on these data, aggressive root replacement is advocated with reimplantation technique even in patients with mild to moderate root dilatation (< 45 mm) (24). However, it should be noted that this " extreme" indication is not reported in the latest ESC guidelines on the treatment of the aortic disease (25). Given the favourable outcomes, as reported in this chapter and the results of other experienced aortic centers, the valve sparing aortic root replacement seems to be a reasonable approach in this subset of patients.

The impact of the additional cusp repair

The mechanisms that determine the AI in the setting of an aortic root aneurysm are basically two: the distortion of the root geometry with a lack of central cusp coaptation and consequent central regurgitant jet and/or the prolapse of one or more cusp that usually lead to an eccentric regurgitant jet. In addition, BAVs may have a restricted cusp motion due to presence of a raphe. The 3-D root geometry is restored by reimplantation

of the valve within the Dacron graft, while, the cusp prolapse need to be corrected by an additional cusp repair. Raphe shaving or resection may be required in BAVs. Nowadays, surgeons have a wide range of techniques to reduce the cusps' prolapse, restore the cusps motion and to increase the coaptation surface of the free margin (26-29). Nevertheless, the impact of the additional cusp repair on the valve durability is still open to debate, particularly in BAVs requiring complex repair. Chapter 9 is a review article entirely focused on this issue. According to the data of the major published series, BAV more frequently requires correction when compared with tricuspid aortic valve and, in most of the cases additional cusp repair does not affect valve competence in the mid and long-term. Nevertheless, we do believe that cusp repair is a too generic definition as it includes a wide variety of techniques ranging from a "simple" free margin plication to a more complex triangular resection with pericardial patch repair and, as emerged from our review, BAVs are more prone to complex repair. In line with this, a subgroup analysis, based on the impact of the cusp repair according to the valve anatomy seems necessary. In chapter 10, a single center long-term experience with the reimplantation technique is described, in which also a subgroup analysis of the impact of cusp repair on reoperation risk in bicuspid and tricuspid aortic valve is provided. The data confirm that even in the long-term the valve anatomy per se, being bicuspid or tricuspid, had not impact on the freedom from reoperation, whereas, the additional cusp repair continues to be a risk factor. If we look at the combination valve anatomy-cusp repair, BAVs requiring cusp repair are affected by a significant higher reoperation rate. Conversely, bicuspid with minimal cusp abnormalities and no need for cusp repair provided excellent 10-year results. Among patients with tricuspid aortic valve, additional cusp repair did not seem to affect the freedom from reoperation; indeed only one patient with tricuspid aortic valve and cusp repair was reoperated on. In contrast, 8 out of 9 of the patients with tricuspid aortic valve who underwent reoperation did not undergo cusp repair during the first procedure. By this long-term experience two important messages were obtained: first, the asymmetrical BAVs (type I Sievers) that frequently require complex repair didn't provide satisfactory results. Second, the cusp repair in tricuspid aortic valve, which frequently consists in a "simple" plication of the free margin, provided excellent results. The principal limitation of this study is that the number of patients with BAV that required additional cusp repair is not large enough to permit a further analysis based on the type of repair within this subgroup. Nevertheless, a policy that seems justified, is to be more aggressive with tricuspid aortic valves in terms of cusp repair, treating even valves with minimal prolapse so that to obtain a satisfactory

coaptation height and to be more cautious with Sievers type I BAV requiring extensive repair. A greater number of patients is needed to evaluate if BAV requiring simple repair (basically free margin plication) will provide favourable outcome.

Alternative techniques for aortic root replacement

The composite valve graft procedure, according to the modified Bentall technique is currently considered the gold standard for the treatment of the aortic root aneurysm or acute DeBakey type I dissection in the presence of an irreparable aortic valve. Nevertheless, despite its proven excellent long-term outcome, the procedure is not free from complications related to prosthetic valves such as life-long anticoagulation therapy for the mechanical prosthesis and structural valve deterioration for the biological prosthesis (19,30). In chapter 11, an analysis of risk factors related to this procedure is provided in a series of 120 patients treated exclusively with composite mechanical valve graft at Humanitas Research Hospital with a follow-up of 5 years. In-hospital mortality was 1.7% and overall survival was 84% at 5 years. Chronic renal failure, turned out to be the only independent risk factor for late mortality. Reoperation as the result of complications in the composite valve graft procedure was necessary in 5.5%. Endocarditis and anticoagulant- related complications occurred at a rate of 1.8% and 2.7%, respectively. These data confirm the reliability of this technique in terms of mortality. Although the vast majority of our patients were operated on electively, hospital mortality below 2% is to be considered an excellent outcome consistent with the largest published series (19,30). With regard to redo operation, that occurred in 6 patients, it must be noted that in 4 the cause was a false aneurysm with a leak localized at the proximal suture line in 2 cases and at the coronary ostial suture line in the other two. The incidence of coronary button dehiscence following the modified Bentall technique has been reported as high as 10% and connective tissue disorders, such as Marfan's syndrome, appear to play a significant role in the development of this complication (31). Of note, both of our patients that experienced coronary button dehiscence had the Marfan's syndrome, however, we did not use any reinforcement of the coronary ostial suture line. The role of Teflon felt or autologous pericardium placed around the coronary ostium to prevent tearing of tissue is still open to debate. If from one side it may prevent from bleeding and button detachment, from the other side it could make, in case of redo, difficult dissection of the ostia (30,32-38). Our study suggests that, suture line reinforcement in patients with connective tissue disorders should be taken into consideration. Regardless of the technique utilized to reinforce the

button's tissue, the reduction of the tension at the level of the anastomosis is of paramount importance. A recent fine element study, focusing on this issue, seems to indicate that the re-creation of a sinus-like graft expansion in the Bentall procedure reduces the stress at the coronary button anastomosis (39). The most serious late complication among our group of patients was the anticoagulant-related cerebral haemorrhage that occurred in 3 cases and caused death in all of them. The reasons were patients related: the uncontrolled usage of anticoagulant therapy and/or postponement of routine controls. Although the risk of complication related to anticoagulation depends on several factors including type of drug used, individual response and clinical circumstances, it seems that in patients with a CarboMedics bileaflet valve in aortic position an INR range between 2 and 3.5 is the ideal balance between the risk of thromboembolic events and bleeding (40,41). Based on this data, we recommend to our patients a target INR of 2.5.

Chapter 12 is, as well, a single center experience (S. Orsola Hospital, Bologna, Italy) focusing on aortic root replacement with composite valve graft. This study, with a mean follow-up of 62 months, includes patients treated both with mechanical and biological valves and emergency cases. The surgical technique has been changed over the years. Indeed, among the 274 patients included in the series, the first 94 (34%) underwent the classic Bentall operation, with inclusion and wrapping technique (13). In 1994 the classic Bentall technique was abandoned in favour of the "button technique" (42), so that this method has been used in 172 cases (63%). The Cabrol technique, consisting in suturing the coronary orifices to the tubular Dacron prosthesis by means of a second smaller Dacron tube, has been utilized in a minority of the cases (3%) in which, due to the extreme root dilatation or severe adherences, the approximation of the coronary arteries to the Dacron graft would have generated excessive tension (43). The overall early mortality rate was 6.9% and multivariate analysis indicated CPB time longer than 180 minutes and concomitant coronary artery bypass grafting as independent risk factors. Regarding the early morbidity, the patients who underwent the Cabrol technique had a higher incidence of cardiac complications (37% versus 11%) consisting in all of them in acute myocardial infarction. Correlation between the Cabrol method and myocardial ischemia, due to the thrombosis of the small Dacron connecting tube, has been reported in several series, so that it is nowadays utilized only when the button technique is not feasible (44-46). During follow-up, the incidence of false aneurism originating from the coronary ostia suture line was the same among patients treated with the classic Bentall technique and with the button technique (2 cases for each

group), but It must be noted that both of the two patients of the "button" group had a severe aortitis as the result of the Behçet's disease (47,48). However, our series failed to show the superiority of the button technique in terms of false aneurysm incidence's reduction. Probably, the small number of affected cases could have played an important role. Indeed, in a recent publication from the same center, updated with 1045 patients, the incidence of false aneurysm was significantly lower among patients treated with the button technique when compared with the classic Bentall (0.4% versus 2.1%).

The Ross operation, first described by Donald Ross in 1967 (49) and consisting of transplantation of the autologous pulmonary valve into aortic position, represents an alternative in the treatment of the aortic valve disease in selected young adults (50). Mechanical prostheses are durable but confer the risk of thromboembolism and bleeding as well as lifelong anticoagulation. Bio-prostheses, as an alternative has a considerable rate of failure, which is pronounced in young adults (51). Concerning the root aneurysm, the Ross operation has represented also an alternative treatment to the Bentall operation in young adults with aortic incompetence and aortic root aneurysm (52) but more recently, due to the spread of the successful valve-sparing operations, this indication is no longer considered. There is still a role for it in a subset of young adults and precisely those with non-reparable bicuspid aortic valve and aortic root aneurysm (53). In chapter 13, a single institution's evaluation of the Ross operation (St. Antonius Hospital, Nieuwegein, the Netherlands) in a population of 103 young adults with a mean follow-up 6 years, is provided. Outcome in terms of mortality was excellent: none of the patients died in hospital and there were two late deaths, one of which was non-cardiac related. This has been possible by careful patients selection: only young adults with few comorbidity were scheduled for the operation. The operative mortality associated with this procedure is quite variable among reports. A recent meta-analysis (that includes also our series) reported a pooled early mortality for adult series of 3.2% (range 1.4%-6.5%) (54). Although the Ross procedure is regarded as a complex procedure, its primary indication is the treatment of the aortic valve pathology in young adults so that, an early mortality far beyond 2%, is in our opinion not acceptable. Five patients required reoperation on the autograft valve for incompetence, with a freedom from reoperation on pulmonary autograft of 87.4% at 10 years. Cox regression failed to show any risk factor associated to the development of aortic incompetence during follow-up. Others, found a dilated aortic annuls (>28 mm) and preoperative aortic incompetence as independent predictors of late pulmonary autograft failure (55). As aortic insufficiency during follow-up is mainly caused by dilatation at the annular or sino-tubular level,

starting from 1997, we invariably used a reinforcement ring or a reduction annuloplaty if the aortic annular diameter exceeded the Z+2 value. As known, a second Achilles heel of the Ross operation is the pulmonary homograft, which may develop dysfunction during follow-up. In our series, 25% of the patients developed, at a mean follow-up of 6 years, pulmonary homograft stenosis and one of them underwent reoperation 1 year after the initial procedure. Cox regression identified smaller diameter of the homograft and older age of donor as independent risk factors for this complication. The fate of the pulmonary homograft varies among reports depending on how dysfunction is defined (56,57). David et al. recently reported a freedom form pulmonary reintervention of 92.7% at 20 years, but echocardiographic data showed a freedom pulmonary valve dysfunction, either incompetence or stenosis, of 53.8%. However, the reoperation rate due to this late complication is reasonably low and with the advent of catheter-based pulmonary valve implantation, the problem is further mitigated.

Conclusions

The valve-sparing aortic root replacement is now part of the surgical armamentarium to treat patients with aortic insufficiency and root aneurysm. Long-term results show that this technique is extremely reliable, at least in presence of normal or nearly normal aortic cusps. Concerns regarding the durability of the aortic valve remain for patients who require extensive cusp repair, particularly in case of bicuspid aortic valve.

The composite valve graft procedure, according to the modified Bentall technique, is currently considered the gold standard for the treatment of the aortic root aneurysm or acute type I dissection in the presence of a irreparable aortic valve.

The Ross operation represents an alternative treatment in young adults with non-reparable aortic valve with or without aortic root aneurysm, but due to the complexity of the procedure it should be reserved for centers of proven experience and with a high volume of patients.

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CHAPTER 15

SUMMARY

Chapter 2: single institution preliminary clinical and echocardiographic results of aortic valve reimplantation in 32 consecutive patients are provided. There were no deaths and the freedom form moderate to severe aortic incompetence at discharge was 94%.

Chapter 3: results during a 5-year period of valve-sparing reimplantation procedure are evaluated by a multicenter Italian study. In-hospital mortality was 3.3% and was significantly higher among patients operated on for acute dissection. Eight of 151 patients required late aortic replacement. Additional cusp repair turn out to be a significant risk factor for reoperation.

Chapter 4: single center experience with aortic valve reimplantation by means of a modified Dacron graft that incorporates sinuses of Valsalva, in a series of 100 consecutive patients. Overall survival and freedom from re-operation at 60 months were 91.7% and 90.9%, respectively. Cox regression identified cusp's repair as independent risk factor for late reimplantation failure.

Chapter 5: an assessment of the compliance of the Dacron pseudo-sinuses of the Valsalva graft at mid term follow-up was performed by means of magnetic resonance. At a mean follow-up of 55 months the compliance of the Dacron pseudo-sinuses is still appreciable and significantly greater than the tubular portion.

Chapter 6: a retrospective review was performed of 35 patients with the Marfan's syndrome who, in four different centers, underwent the reimplantation valve-sparing aortic root replacement using the Gelwave Valsalva prosthesis. There were no operative or hospital deaths and no patient died during follow-up. The 5-year freedom fro reoperation owing to structural valve deterioration was 88.9%.

Chapter 7: the results of reimplantation valve-sparing aortic root replacement, performed in two different cardiac centers, in patients grater than 60 years of age were evaluated. There were one hospital and two late deaths. Freedom from reoperation and freedom from moderate or severe residual aortic incompetence at 51 months were 92.8% and 90%, respectively. There was no episode of endocarditis on follow-up.

Chapter 8: a single institution experience with reimplantation valve sparing operation focusing on the influence of valve anatomy in determining the need for reoperation is provided. Overall freedom from aortic valve reoperation at 5 years was 90% without significant difference between patients with bicuspid and tricuspid aortic valve. Aortic valve reimplantation in patients with bicuspid aortic valve with no need of additional cusp repair provided excellent mid-term results.

Chapter 9: review of the literature to try to shed light on when, during aortic-valve sparing operation, the additional cusp repair is required and how it should be performed. Results in literature showed that, bicuspid aortic valve more often required correction in comparison with tricuspid aortic valve. According to the largest published series, cusp repair did not affect the valve competence even in the long-term.

Chapter 10: single center, retrospective experience with additional cusp repair during aortic valve reimplantation with a maximum follow-up of 12 years, is reported. Results indicated that adjunctive cusp repair affects the reoperation risk in patients with bicuspid aortic valve but not in patients with tricuspid aortic valve. Among patients with bicuspid aortic valve, those who did not require cusp repair showed a significantly higher freedom from reoperation compared with patients who received cusp repair.

Chapter 11: a retrospective single institution (Humanitas Research Hospital, Rozzano, Milan, Italy) analysis of a selected series of Bentall procedures was carried out in order to evaluate the performance of the Carboseal mechanical composite valve graft. The actuarial survival rate, including in-hospital mortality, was 84% at 5 years. Chronic renal failure was the only independent risk factor for late mortality. False aneurysm requiring re-operation had a higher incidence among patients with the Marfan's syndrome.

Chapter 12: a single center (S. Orsola-Malpighi Hospital, Bologna, Italy) experience with aortic root replacement using a composite graft in reported. The actuarial survival rate was 63% at 10 years. Risk factors for late mortality were coronary artery disease, chronic renal failure and postoperative dialysis. The freedom from reoperation on the remaining aorta was lower among patients with the Marfan's syndrome.

Chapter 13: risk factors for aortic valve incompetence and pulmonary homograft valve stenosis were identified in a single center series of young adults who underwent the Ross operation. There were no hospital deaths. Autograft function follow-up resulted in 5 of 103 patients requiring reoperation for severe aortic incompetence, whereas reoperation for homograft dysfunction occurred in 1 patient.

CHAPTER **16**

ACKNOWLEDGEMENTS
LIST OF PUBLICATIONS
CURRICULUM VITAE

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CURRICULUM VITAE

The author of this thesis, Fabrizio Settepani was born on July 31st, 1971 in Ravenna, Italy. He obtained his scientific high school certificate in 1990 at Liceo Scientifico "Sabin" in Bologna. He received his medical degree at the University of Bologna in 1997. In September 1996 he started his Internship as Medical Student at the Unit of Cardiac Surgery, University of Bologna and, after the completion of medical licence examination, he was admitted to the Cardiac Surgery residency program (chairman: Prof. A. Pierangeli). During the training, he spent 6 months (Sep 2000- Apr 2001) at the department of Cardio-Thoracic Surgery of the St. Antonius Hospital in Nieuwegein, the Netherlands as resident. He graduated Specialist Cardiac Surgeon at the University of Bologna in October 2002. Two months later on the same year, he moved back to Nieuwegein for a Cardio-Thoracic Surgery Fellowship at St Antonius Hospital until July 2003 under the supervision of Prof. W.J. Morshuis. During this period he had the opportunity to carry out, alongside the clinical activity, a research activity mainly focused on the aortic surgery. Later on the same year, he left the Netherlands and since September 2003 he is working as staff cardiac surgeon at the department of Cardiac Surgery of the Istituto Clinico Humanitas, Milan, Italy, where he is currently working. From December 2009 to March 2010 he worked as senior cardiac surgeon at the "Salam Centre for Cardiac Surgery", Khartoum, Sudan, Africa. From 2007 to 2014 he was Assistant Professor of Cardiac Surgery at the University of Milan, Italy and since July 2014 at the Humanitas University, Italy. At he Istituto Clinico Humanitas, he is continuing his research activity, focusing particularly on the aortic valve-sparing procedure, both as single and multicenter experience in scientific collaboration with reference centers for the aortic surgery in Italy and USA.