Aortic root replacement with a pulmonary autograft

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Aortawortel vervanging met een pulmonale autograft

Proefschrift

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Voor Irene

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Chapter 1

Introduction

Background

Aortic valve disease in the pediatric age group is usually a consequence of congenital aortic stenosis, which may be isolated or may be a part of an anomaly of the left ventricular outflow tract or the aortic root.[1-4] Management of these patients is difficult. Neonates and infants with severe congenital aortic stenosis may suffer from congestive heart failure and are critically ill. Older children usually have less severe clinical symptoms, if it all. Invasive treatment is indicated in the case of severe aortic stenosis.[1,5] For isolated congenital valvular stenosis, balloon valvuloplasty is the current therapy and is technically feasible in most patients.[6-8] Therefore, surgical valvulotomy is no longer the first therapeutical option in managing aortic valve stenosis in neonates and in older children.

Experience indicates that the outcome of both balloon valvuloplasty and surgical valvulotomy in patients with a non-tricuspid valve and the presence of aortic regurgitation is unfavourable.[9] Both procedures can, to a certain extent, be regarded as palliative and may result in aortic valve regurgitation,[1] usually when children are managed early in life.[7,10] Rheumatoid diseases[11] and endocarditis[12] rarely cause aortic valve dysfunction (mostly aortic regurgitation) in this population. If invasive treatment is indicated and valvulotomy or valvuloplasty cannot be applied because of coexisting regurgitation or morphologic aspects, the aortic valve must be replaced. Aortic root replacement using the pulmonary autograft is a possible treatment modality in this respect. The discussion on when and how children must be managed will not be dealt with in the following chapters. This thesis presents aspects and results of the pulmonary autograft procedure in pediatric and adult patients.

Aortic root replacement with a pulmonary autograft

Aortic valve replacement in the pediatric population faces serious dilemmas and is a challenge for the cardiac surgeon.[2,13] Children are small, they grow and have a lifestyle in which anticoagulant therapy is better avoided. Bioprosthetic, mechanical and allograft valves do not grow and need to be replaced later in life when the child has outgrown the prosthesis. Moreover, bioprosthetic and allograft valves are, at present, prone to structural degeneration and anticoagulant therapy remains obligatory for the use of contemporary mechanical valves.

Consequently, the technique of aortic root replacement with a pulmonary autograft, as introduced by Ross in 1986, seems to offer an attractive alternative in the pediatric age group.[14] This operation was introduced at the University Hospital Rotterdam in 1987. The relative frequency in the pediatric age group of the different surgical techniques before and after the introduction of the pulmonary autograft in Rotterdam is shown in Figure 1.

A pulmonary autograft is not prone to structural degeneration and does not require anticoagulant therapy. It offers the advantage of growth potential, thus avoiding reoperation for an increasing pressure gradient across the valve in the growing child. In addition, the (extended) root replacement technique allows treatment of the entire stenotic area, thus being suitable for patients with concomitant subannular or supraannular stenosis.[15,16] Moreover, the increased incidence of (late) endocarditis related to the use of the pulmonary autograft with the subcoronary implantation technique is avoided.[17] However, concomitant replacement of the right ventricular outflow tract is necessary and the allograft valve, used for the operation, is prone to structural degeneration. The long-term function of allograft valves in this position has been proven to be good in older children and adults,[17-19] but the long-term results in younger children are not known. Therefore, reoperation for allograft replacement is to be expected in the long term.

The advantages of the use of a pulmonary autograft are not limited to children. Adults may also benefit from the absence of structural degeneration and the need for anticoagulant therapy. Therefore this operation was extended to adults. However, a pulmonary autograft diameter increase, being favourable in children, is not advantageous in adult patients and this subject needs further investigation, because diameter increase may lead to aortic regurgitation.[20,21] The selective introduction in adults is reflected in the relative frequency of the different surgical techniques for aortic valve surgery in adults before and after the introduction of the autograft procedure in 1987, as shown in Figure 2.

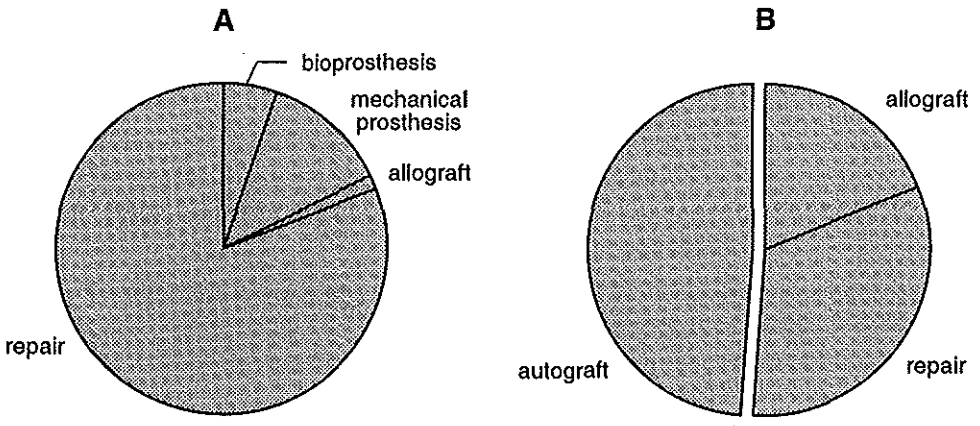

Figure 1. Aortic valve surgery in Rotterdam in children (<18 years), before (A) and after (B) the introduction of the pulmonary autograft in 1987. The first operation on the aortic valve in a child was in 1962 (valvulotomy); the first aortic valve replacement in this age group was performed in 1969.

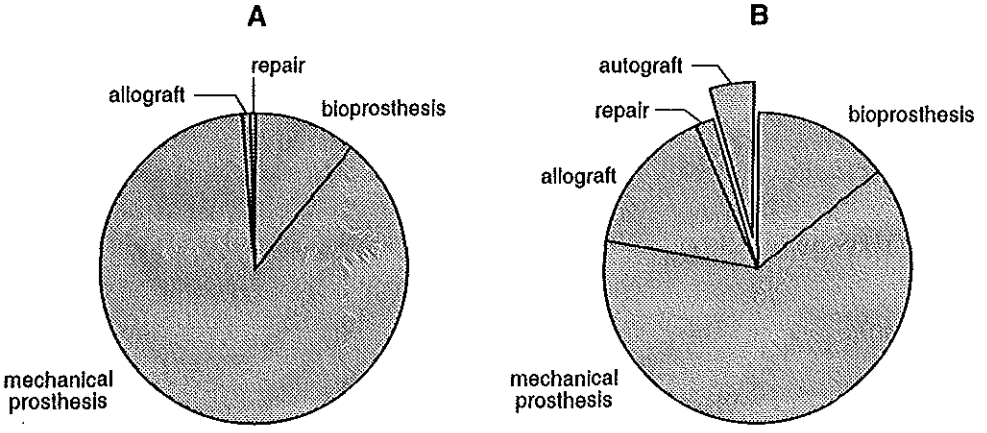

Figure 2. Aortic valve surgery in Rotterdam in adults (≥18 years), before (A) and after (B) the introduction of the pulmonary autograft in 1987. The first operation on the aortic valve in an adult was in 1963 (valvulotomy); the first aortic valve replacement in this age group was performed in 1967.

Aim of the study

The aim of the studies presented in this thesis is to investigate the suitability of the pulmonary autograft for aortic root replacement in children, avoiding aortic valve replacement due to growth of the child and taking into consideration the active lifestyle of the child. Subsequently the suitability of this technique in adult patients is investigated as well.

Knowledge of the morphology of the pulmonary and aortic roots, and the differences between them, is important when using the autograft for aortic root replacement, and the surgeon should bear in mind that the pulmonary autograft is subject to the high pressures of the systemic circulation. The clinical improvement of the patients after the pulmonary autograft procedure, the function of the pulmonary autograft and the allograft in the right ventricular outflow tract, and the fate of the pulmonary autograft diameters must be evaluated, in children and in adults. The autograft procedure was used in children because increasing pulmonary autograft diameters were expected, obviating future valve replacement. However, whether the increase of the pulmonary autograft diameter is caused by growth or dilatation is a matter of debate, and in adults this increase of diameter may not be advantageous. Registration of these diameters in adults is of utmost importance in relation to autograft function. Measurement of pulmonary autograft diameters can be performed with transthoracic and transesophageal echocardiography and with magnetic resonance imaging. We investigated the advantages and disadvantages of the latter technique in relation to the echocardiographic imaging modalities.

Outline of this thesis

Chapter 2 is a description of a microscopic study of the components of the pulmonary trunk and aortic root, their relations to each other and their insertion into the myocardium. The differences between the two arterial roots are identified and the suitability of the pulmonary root for transplantation to the aortic position is discussed, especially with regard to the surrounding supportive structures of the aortic annulus.

Chapter 3 presents a follow-up study of the children operated on until 1996, using the pulmonary autograft. The clinical outcome is evaluated and pulmonary autograft diameter and function in time are studied. Special attention is paid to left ventricular function during follow-up, measured with echocardiography.

Chapter 4 presents a follow-up study of all patients in our center who underwent aortic root replacement using the pulmonary autograft until May 1994. The medium-term clinical results are investigated, as well as pulmonary autograft and allograft function and autograft diameter in time. Contraindications for the use of a pulmonary autograft are

discussed.

Chapter 5 is a description of the echocardiographic follow-up of pulmonary autograft diameters of adult patients. Pulmonary autograft diameters in this patient population are measured with echocardiography before and at different times after the operation. The possible correlations between diameter increase on the one hand, and length of follow-up and severity of aortic regurgitation on the other, are studied.

Chapter 6 presents the magnetic resonance imaging studies on pulmonary autograft diameter measurements. An internal validation study is performed to clarify factors determining measurement variability. Different planes through the long-axis of the pulmonary autograft are used for measurements and correlated with the measurements in planes perpendicular to the long axis of the pulmonary autograft.

In **Chapter 7** we describe the results of a study in which the pulmonary autograft diameters were measured in adult patients, using transthoracic and transesophageal echocardiography and magnetic resonance imaging. The image quality of transthoracic echocardiography is not always adequate for aortic root diameter measurements. This is especially true for the distal part of the aortic root. Transesophageal echocardiography is a better technique in this regard but more difficult to use. Magnetic resonance imaging is a rather new technique in cardiac imaging and its possible additional value for pulmonary autograft measurements was investigated. The measurements obtained with the different imaging modalities are compared and the advantages and disadvantages of the different techniques are discussed.

Chapter 8 presents a comprehensive discussion about the results of the studies.

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Chapter 2

Morphology of the pulmonary and aortic roots with regard to the pulmonary autograft procedure

Raymond B. Hokken, Margot M. Bartelings, Ad J.J.C. Bogers, Adriana C. Gittenberger - de Groot.

J Thorac Cardiovasc Surg 1997; 113: 453-61.

Abstract

Aortic root replacement with the pulmonary autograft warrants a thorough histological comparison of the morphological characteristics of the pulmonary and aortic roots. For this purpose nine normal heart specimens (seven neonatal and two adult hearts) were studied. Histologic study confirmed the collagenous annulus in both roots to be a complex circular-shaped structure, intricately interposed between the elastic lamellae of the arterial wall and the ventricular structures of the heart. In the sinus the elastic lamellae of the arterial wall continue along the luminal side with collagen being situated at the outside. At the interleaflet triangle this relation is reversed. Surprisingly, islets of elastic fibres were found in the otherwise completely collagenous interleaflet triangles. The amount of elastic lamellae distal to the commissures was in both arteries higher than in the middle of the sinuses, with a preponderance in the aorta as compared with the pulmonary trunk. The pulmonary root annulus proximally inserts into the relatively thin right ventricular myocardium, whereas the aortic root annulus inserts into the thick left ventricular myocardium and several fibrous structures. The pulmonary root is hardly supported by the right ventricular myocardium, whereas the aortic root is supported by its wedged position between the left and right atrioventricular annuli and the bulging thick left ventricular myocardium. When the pulmonary autograft is used for aortic root replacement it should be inserted as proximally as possible to get the support of the fibrous structures of the left ventricular outflow tract and the surrounding ventricular and atrial myocardium.

Introduction

Morphologic descriptions of the aortic and pulmonary valve and root had already been published by the first half of this century.[1,2] More recent studies describe the morphology of the aortic valve and root in relation to function[3] and in relation to congenital malformations.[4,5] With the use of the pulmonary autograft for aortic root replacement, a method started by Ross in 1986,[6] the question with regard to the suitability of the pulmonary valve and root for use in the aortic position is relevant. The clinical results of the pulmonary autograft implanted in the aorta with the subcoronary technique[7] are good.[8] However, when the complete aortic root is replaced by the pulmonary root, not only the pulmonary valves but also the pulmonary wall is exposed to systemic pressures. Although the short-term results with this technique are satisfactory with regard to the clinical performance,[9-11] some surgeons advise wrapping the pulmonary autograft to avoid dilatation.[7,12] In this regard the pathophysiologic nature of native aortic regurgitation caused by aortic root dilatation[13,14] may also be applicable to the pulmonary autograft in the aortic position.

Therefore a microscopic morphologic study of the components of the pulmonary and aortic roots and their proximal insertion with a description of the surrounding structures seems appropriate and may give insight into the differences between the pulmonary and aortic roots in general and the consequences of implantation of the pulmonary autograft in the aortic position.

Material and methods

Material

Nine normal heart specimens were studied. Seven hearts of children who died perinatally at a mean gestational age of 38 weeks (range 34 to 40 weeks) were obtained from the Leiden Collection of heart-lung specimens. Two adult hearts (42 and 47 years old) from the Department of Pathology of the University Hospital Rotterdam were included to investigate possible age-related differences.

Methods

The specimens were cut in serial sections approximately perpendicular to the aortic axis with a thickness of 10 μm. Four consecutive sections of the entire specimen were put together on one slide. The slides were stained alternately with azan, resorcin-fuchsin, hematoxylin-eosin, and modified van Gieson's stains. Because the pulmonary axis is not parallel to the aortic axis, the plane of sectioning of the pulmonary trunk was not transverse. With use of these sections three-dimensional reconstructions were made to clarify and describe the relationships

between the elastic and collagenous components of the pulmonary and aortic roots and of their insertions in the myocardium.

Elastic lamellae in the wall of the pulmonary trunk and aorta were counted in each specimen at six different places: in the middle of each of the three sinus walls and 2 mm distal to each of the commissures.

Definitions

Pulmonary root: First part of the pulmonary trunk, from the insertion of the pulmonary annulus in the right ventricular myocardium, including the semilunar valve leaflets, the wall of the sinuses, the interleaflet triangles, the commissures, and the sinotubular junction.

Aortic root: First part of the aorta, from the insertion of the aortic annulus in the left ventricular myocardium and the continuation in proximal fibrous structures, including the semilunar valve leaflets, the wall of the sinuses of Valsalva (with the coronary orifices), the interleaflet triangles, the commissures, and the sinotubular junction.

Sinuses: Pockets or cavities of the pulmonary and aortic roots between the arterial wall and the arterial side of the semilunar valve leaflets. The sinuses of the aorta are named according to the coronary arteries with their ostia (left and right coronary sinuses), and the sinus without a coronary ostium is the noncoronary sinus. The pulmonary sinuses are named by their relationship to the aortic sinuses: left facing, right facing and nonfacing sinuses.[15]

Sinotubular junction: Borderline between the more distal arterial wall and the thinner arterial wall of the sinuses.

Commissures: Sites at the arterial wall where two valve leaflets meet.

Interleaflet triangle: Triangular part of the arterial wall in between two sinuses with its base on the ventricular myocardium and extending up to the commissures.[4,5]

Annulus: Fibrous structure in the arterial root to which the semilunar valve leaflets are attached.

Proximal fibrous structures: Fibrous structures proximal to the aortic annulus.

Surrounding structures: Peripheral structures that lie adjacent to the aortic or pulmonary root.

Statistical analysis

The mean values of the elastic lamellae counts at both levels in the pulmonary trunk and aorta were calculated. A *t* test was used to evaluate the differences between both levels of pulmonary trunk and aorta and between both arteries at the same level.

Results

Pulmonary root

The distal part of the pulmonary trunk consists largely of elastic lamellae arranged in a concentric fashion. Collagen and smooth muscle cells are visible between its layers. Going upstream the pulmonary wall shows three protrusions at the luminal side. Further toward the heart, collagenous condensations are found in the center of these protrusions, constituting the most distal extension of the commissures. Slightly more proximally, these collagenous condensations bulge into the arterial lumen, and here the valve leaflets originate (Figures 1 and 2).

The collagenous tissue of the commissures is continuous with the collagenous tissue of the interleaflet triangles, situated between the diverging valve leaflets. The apical one third of the triangle, like the commissures, consists of collagenous tissue on the inside and elastic lamellae on the outside. Going upstream, the thickness of the outer elastic wall gradually decreases until the entire thickness of the wall is formed by collagen (Figures 2 and 3). In the middle of the interleaflet triangle, an isolated condensation of elastic fibres is present at the luminal side, which, because it is more obvious in the aortic root, will be further described in that section.

Although it has the same components as the interleaflet triangles, the wall of the adjacent sinuses has a different design. The distal part of the sinus wall consists of concentric elastic lamellae, comparable to the more distal vessel wall. Going upstream, the number of elastic lamellae decreases and the amount of collagen between the elastic lamellae increases. In the proximal half of the sinus wall the layer of elastic lamellae is restricted to the luminal side. The outer side is formed by a collagenous layer, which is continuous with the interleaflet triangles (Figures 2 and 3). In contrast to the elastic component in the interleaflet triangle where it becomes more and more limited to the outer side of the wall, in the sinus wall the elastic component is restricted to the luminal side, until it disappears at the base of the sinus. Here collagenous tissue constitutes the entire thickness of the wall (Figures 2 and 3). At the base of the interleaflet triangles and the sinuses many fingerlike protrusions of the collagenous tissue extend into the underlying myocardium, providing an extensive anchorage of the base of the arterial root. The larger part of the pulmonary annulus inserts into the free wall of the right ventricular myocardium. The interleaflet triangle between the left and right pulmonary sinuses, with parts of the right and left pulmonary sinuses, inserts in the septal part of the right ventricular myocardium (Figure 4A).

The valve leaflets originate from the intricately shaped, circular, collagenous structure that extends from the commissures, where it is wedged into the elastic vessel wall, to the base of the sinuses and the interleaflet triangles. It should be noted, however, that the border of the underlying right ventricular myocardium is curved, thus the base of the interleaflet.

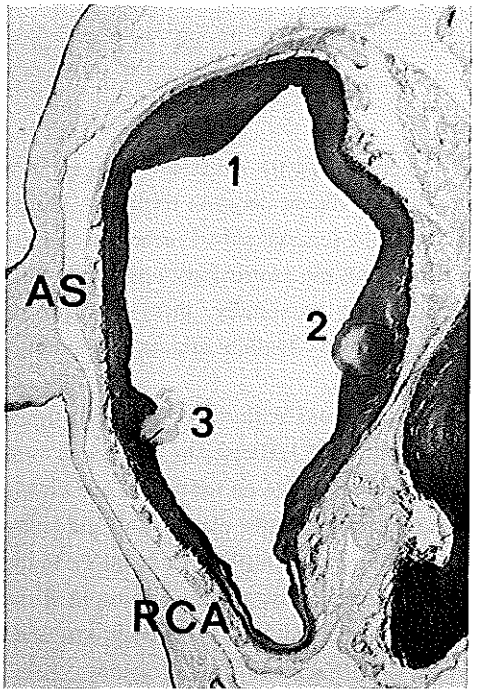


Figure 1.

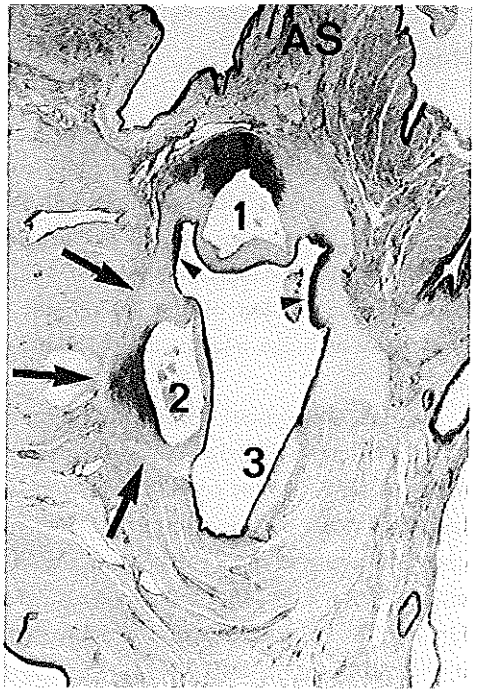


Figure 3.

Figure 1 Section of the distal part of the aortic root. 1: Protrusion of the elastic (darkly stained) vessel wall, slightly above a commissure. 2: Collagenous (lightly stained) area surrounded by elastic lamellae, constituting the most distal extension of the commissure. 3: The commissure itself, where the two valve leaflets meet. AS: atrial septum. RCA: right coronary artery.

Figure 3 Section through the aortic root at a more proximal level as compared to Figure 1. The *arrows* indicate part of the borderline between the lightly stained collagen and the slightly darker stained myocardium. The elastic lamellae are darkly stained. 1: Noncoronary sinus with elastic lamellae making up the entire thickness of the sinus wall. 2: Slightly more proximal, the right coronary sinus shows elastic lamellae on the luminal side and collagenous tissue inserting into the myocardium on the outer side. 3: More proximal, at the base of the left coronary sinus, there is only collagenous tissue. The *arrowheads* indicate the elastic fibres at the luminal side of the interleaflet triangles. AS: atrial septum.

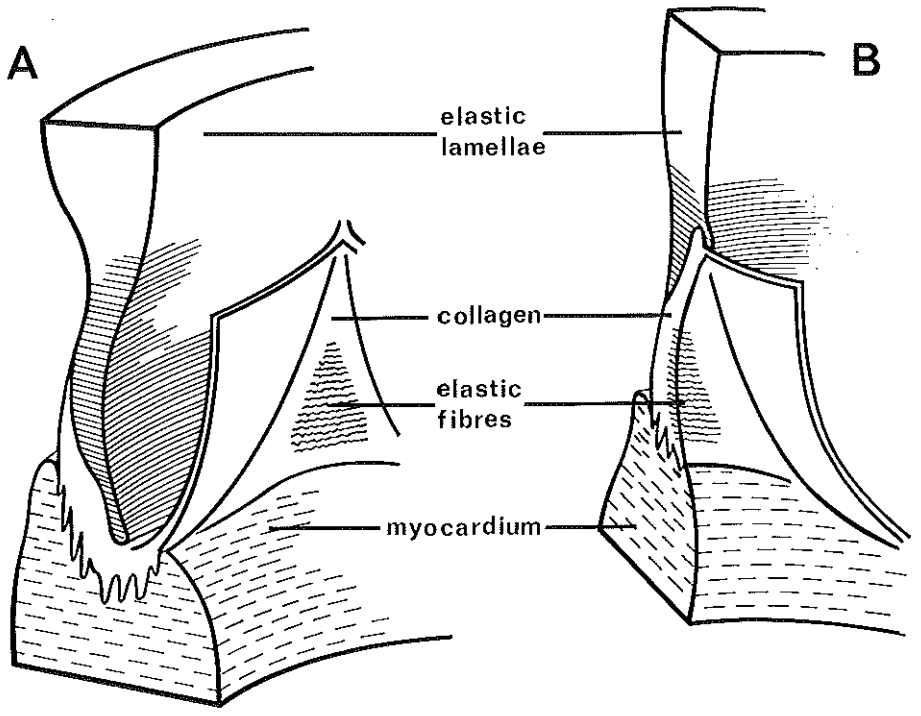


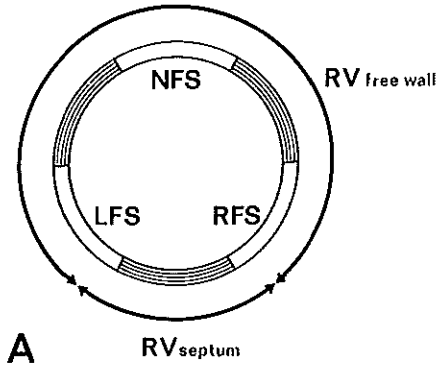
Figure 2 Schematic drawings of the arterial root after three-dimensional reconstruction showing longitudinal sections through (A) the middle of a sinus wall and (B) the middle of a commissure and interleaflet triangle.

triangles is situated more cranially than the base of the sinuses.

The pulmonary root has no surrounding structures except for the adjacent aorta. In some cases (n=2) a collagenous connection was present between aortic and pulmonary roots. This collagenous connection extended from the interleaflet triangle between the right and left pulmonary sinuses to the interleaflet triangle between the right and left coronary sinuses of the aortic root (Figure 5). The right ventricular myocardium, the septal part more than the thin free wall, slightly bulges on the outside. Loose connective tissue is situated in between the pulmonary root and the myocardium.

Aortic root

Although the general principle of a collagenous structure that is intricately interposed between a largely elastic vessel wall and ventricular structures, as described in the section on the pulmonary root, is also applicable to the aortic root, there are major and minor differences



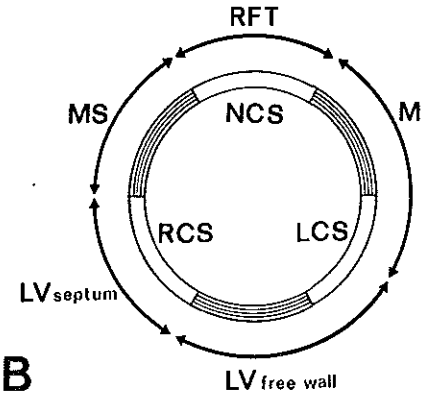


Figure 4.

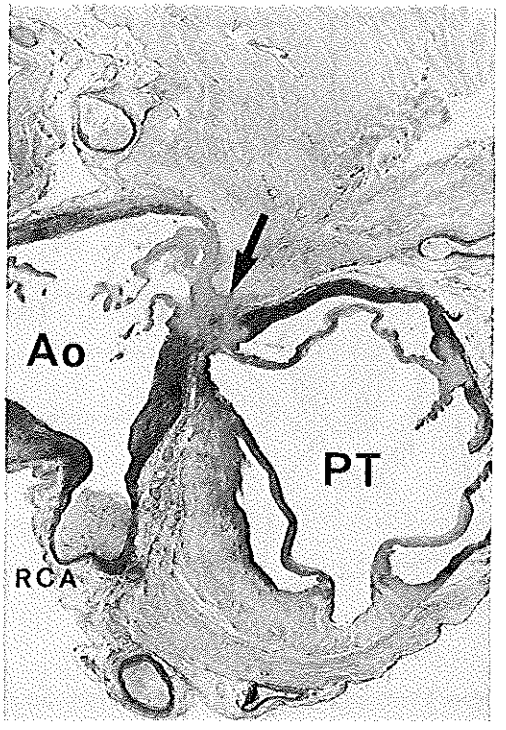


Figure 5.

Figure 4A Schematic representation of the pulmonary root related to the site of insertion into the myocardium. RV: right ventricle. RFS: right facing sinus. LFS: left facing sinus. NFS: nonfacing sinus.

Figure 4B Schematic representation of the aortic root related to the site of insertion into the myocardium and fibrous structures. LV: left ventricle. The left fibrous trigone is situated between the anterior mitral valve leaflet and the left ventricular free wall. RCS: right coronary sinus. LCS: left coronary sinus. NCS: noncoronary sinus. MS: membranous septum. RFT: right fibrous trigone. M: anterior mitral valve leaflet.

Figure 5 Section of the pulmonary and aortic roots. The *arrow* indicates the conus tendon between both roots. Ao: aorta. PT: pulmonary trunk. RCA: right coronary artery.

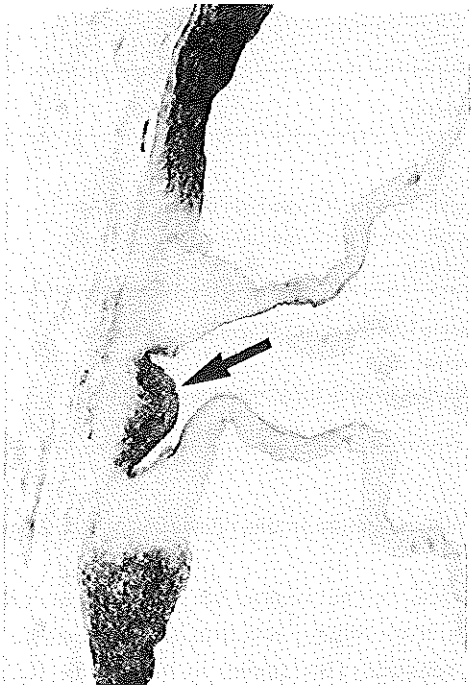


Figure 6.

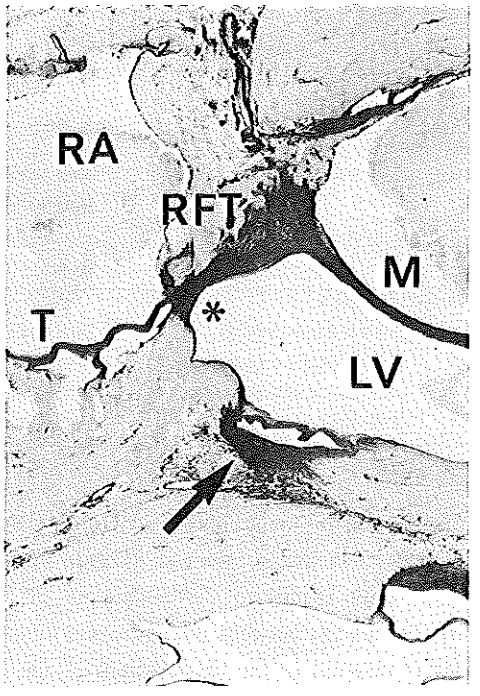


Figure 7.

Figure 6 Detail showing part of the isolated condensation of elastic fibres (*arrow*) in the interleaflet triangle, reconstructed in Figure 2.

Figure 7 Section of the proximal part of the aortic root. The collagen is darkly stained. The *arrow* indicates the 'third body', situated at the proximal part of the right coronary sinus. *: membranous septum. RFT: right fibrous trigone. RA: right atrium. M: anterior mitral valve leaflet. LV: left ventricle. T: tricuspid valve leaflet.

between the roots. One of the minor differences is that the sinus walls and the interleaflet triangles of the aorta appear to be thicker. As mentioned previously, the isolated condensations of elastic fibres in the collagenous interleaflet triangles are more pronounced. These elastic islets are not continuous with the elastic lamellae of the arterial wall and they are situated at the luminal side of the triangle (Figures 3 and 6). With the decreasing thickness of the interleaflet triangle, toward the heart, the number of elastic fibers decreases until they are absent at the base of the triangle. The proximal part of the right coronary sinus was continuous with a discrete accumulation of collagen in three specimens; this accumulation of

Table 1 Proximal structures of the aortic root.

Proximal structures	Aortic circumference
Myocardium	
Left ventricular myocardium	Half left sinus
	Interleaflet triangle between left and right coronary sinuses
Septal myocardium	Interleaflet triangle between left and right coronary sinuses
	Right coronary sinus
Fibrous structures	
Membranous septum	Interleaflet triangle between right and noncoronary sinuses
Right fibrous trigone	Noncoronary sinus
Anterior mitral valve leaflet	Interleaflet triangle between left and noncoronary sinuses
Left fibrous trigone	Left sinus

collagen was in direct continuity with the membranous septum in one specimen, whereas in the others this was not the case (Figure 7).

With regard to the anchorage of the roots in the ventricular structures major differences exist between the aortic and pulmonary roots. Slightly less than half of the aortic root is inserted in the myocardium of the left ventricle. This applies to half of the left coronary sinus wall, the interleaflet triangle between left and right coronary sinuses and the right coronary sinus wall (Figure 4B, Table 1). Similar to the pulmonary root, the base of the collagenous part of the aortic root in this area has fingerlike protrusions that extend into the underlying myocardium. This myocardium is, however, much thicker than that of the right ventricle, which provides a broad area of connection between the collagenous protrusions and the myocardium.

More than half of the aortic root circumference does not insert in myocardium but continues in proximal fibrous structures (Figure 4B, Table 1). The interleaflet triangle between the right coronary and noncoronary sinuses proximally continues in the membranous septum, which separates the left ventricle from the right ventricle and right atrium (Figure 7). Proximally, the right atrial part of this membranous septum inserts into the atrioventricular (muscular) septum, separating the right atrium and left ventricle. This part contains the atrioventricular node. The right ventricular part of the membranous septum inserts proximally into the ventricular septum myocardium, which contains conducting tissue (bundle of His). The left fibrous trigone is situated at the proximal part of the left sinus. At one side it is continuous with the interleaflet triangle between the left and noncoronary sinuses, which proximally continues in the anterior mitral valve leaflet. The other side inserts into the left ventricular myocardium (Figure 4B, Table 1). The right fibrous trigone, presenting as a huge accumulation of collagen, is located adjacent to the base of the noncoronary sinus (Figure 7). Both the anterior mitral valve leaflet (with the left fibrous trigone) and the membranous

Table 2 Elastic lamellae count in nine heart specimens.

Level		No.	
		Pulmonary trunk	Aorta
Sinuses			
	Children	39 (range 30 - 46)	39 (range 34 - 45)
	Adults	38 (37 and 39)	42 (40 and 44)
Distal			
	Children	50 (range 42 - 65)	63 (range 56 - 69)
	Adults	59 (55 and 62)	78 (76 and 79)

septum are continuous with this structure (Figure 4B). Proximally the right fibrous trigone inserts into the left ventricular myocardium.

The aortic root has more surrounding structures than the pulmonary root. The thick left ventricular myocardium and septal myocardium bulge on the outside, forming a collar around the proximal part of the aortic root. Loose connective tissue is situated between the myocardium and the aortic root. The annuli of right and left atrioventricular valves are continuous with the membranous septum and left fibrous trigone respectively and both are continuous with the dorsal side of the right fibrous trigone. The aorta apparently is in a wedged position between the right and left atrioventricular annuli. The right fibrous trigone is also connected to the atrial myocardium but fingerlike protrusions of collagen are not present. In three specimens the noncoronary sinus distal to the right fibrous trigone was closely related to atrial muscle fibre. In the others loose connective tissue was present between these structures.

Elastic lamellae count

The site 2 mm distal to the commissures appeared to be representative for the distal part of the pulmonary trunk and aorta. The numbers of elastic lamellae at this level and in the middle of the sinus walls are presented in Table 2. The difference between pulmonary trunk and aorta at the distal level was evident: there were more elastic lamellae in the aortic wall compared with the pulmonary wall (66 versus 52; p=0.0008). There was no statistically significant difference in the middle of the sinuses between the two arteries (40 and 39 respectively; p=0.46). Thus the difference within the aorta at the two levels (p=0.000004) was larger than the difference within the pulmonary trunk (p=0.004). In the nine specimens studied, the two adult hearts exhibited more elastic lamellae at the distal level of the two arteries than the other specimens. In the middle of the aortic and pulmonary sinus walls there were no differences.

Discussion

As recognized by several authors the components of the arterial roots comprise the vessel wall, characterized by concentric lamellae, ventricular structures (myocardial or collagenous), and a collagenous structure that is interposed between the vessel wall and the ventricular structures.[1,2] It is this interposed collagenous structure, to which the valve leaflets are attached, that we consider to represent the annulus. Zimmerman in 1969 described this structure as 'a crownlike formation of collagenous tissue'.[16] By 1923, Lewis and Grant had observed that the annulus 'is not a simple ring'.[1] Anderson and associates in 1991 opposed to the term *aortic annulus* on the grounds that 'the attachments of the leaflets are not arranged in a ringlike fashion'.[5] Indeed, the leaflets follow a semilunar pattern. It is, however, not the attachment of the leaflets that we consider to represent the annulus, but the entire collagenous structure to which they are attached. This collagenous structure is basically a circular band that has its distal edge formed like a three peaked crown, whereas its proximal border is characterized by three fimbriated, less pronounced curves. Its connection to the adjacent vessel wall distally and the ventricular structures proximally is very intricate. Notwithstanding the fact that in the case of the aorta a distinctive borderline cannot be seen between part of its annulus and the proximal fibrous structures, we consider the term *annulus* applicable.

The reversed relation of the elastic vessel wall and the collagenous annulus in the sinus wall (elastic layer inside) and in the interleaflet triangle (elastic layer outside) as found by us in both the pulmonary and aortic root, had already been recognized in the aortic root by Lewis and Grant.[1] The isolated condensations of elastic fibres in the interleaflet triangles of the aortic (more pronounced) and the pulmonary (less conspicuous) roots have, as far as we are aware, not been described before. They might be indicative of elastic properties to pass on end-diastolic left ventricular pressure, which is useful in the opening mechanism of the semilunar valves, as described for the aortic valve by Thubrikar and associates.[17] A collagenous tendon between two opposing interleaflet triangles of the pulmonary and aortic root was found in two of the nine specimens. This structure is known as the conus tendon.[18,19] The prevalence of this tendon is not known. Kerr and Goss, having studied the relation between the pulmonary and aortic valves in 200 hearts did not mention this tendon.[20] The collagenous condensation at the proximal part of the right coronary sinus wall, as present in three of nine specimens has been described before by Zimmerman, who assigned the term *third body* to it.[16,21] He described it as being continuous with the anterior part of the membranous septum. This *third body* was, however, continuous with the membranous septum in only one of our specimens, whereas in the other two specimens the third body and the membranous septum were separated by muscular ventricular septum.

With respect to the differences between the pulmonary and aortic roots it appears that these are both major and minor. The annulus of the pulmonary root is anchored in

myocardium over its entire circumference, whereas this applies to only half of the aortic circumference. The right ventricular myocardium is thin, thus providing a more delicate attachment of the pulmonary annulus. This contrasts with the thick left ventricular myocardium and the proximal continuation of more than half of the aortic annulus in fibrous structures such as the membranous septum, the right fibrous trigone, the anterior leaflet of the mitral valve and the left fibrous trigone. The sinus walls and the interleaflet triangles of the aorta appear to be thicker. Surprisingly, we found no significant differences between the elastic lamellae count in the pulmonary and aortic sinuses, nor was there a significant difference at this level between the counts in children and adults. Although the number of studied specimens was small, it appears that the number of lamellae in the sinuses is fixed. The difference in thickness of the sinus walls might be the result of a difference in the amount of collagen, smooth muscle cells or ground substance and/or in the thickness of the elastic lamellae themselves. At the level distal to the commissures, the number of elastic lamellae in both arteries was higher than that in the sinus walls. In contrast to the situation in the sinus walls, at the distal level, this number is not fixed. In agreement with the findings of others,[22,23] the adult specimens showed a higher count. The aorta has more elastic lamellae than the pulmonary trunk and this difference was even more pronounced in the adult heart specimens. With regard to a possible growth potential of these lamellae no conclusions can be drawn, because the thickness of the lamellae, their organization and other components of the medial layer of the vessel wall have to be taken into acount.[24,25]

With regard to the surrounding structures the aorta is better encased. In addition to the thick left ventricular myocardium, that bulges and forms a collar around the proximal part of the aortic root, the aortic root is wedged between the right and left atrioventricular annuli and atrial myocardium. The pulmonary root is only slightly supported by the thin right ventricular myocardium and the adjacent aorta.

When the pulmonary autograft is used for aortic root replacement the following aspects are relevant. It should be appreciated that the structures of the semilunar valve leaflets[2] and the walls of the sinuses in both roots are not essentially different. The pulmonary autograft, however, has thinner interleaflet triangles, the proximal border consists of a ridge of relatively thin right ventricular myocardium and it does not contain the proximal fibrous structures of the left ventricular outflow tract. For this reason the pulmonary autograft should be trimmed to leave only a few millimeters of right ventricular myocardium as suture area, followed by implantation at the level of the annulus[9] to obtain maximal support of the fibrous structures of the left ventricular outflow tract and the surrounding ventricular and atrial myocardium. In contrast, in an extended autograft procedure this support is not optimal because these fibrous structures are not left intact as a result of the procedure.

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Chapter 3

Clinical outcome and left ventricular function after pulmonary autograft implantation in children

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Abstract

Aortic root replacement with a pulmonary autograft is an alternative treatment for children with aortic valve or root disease, or both. Twenty-six patients (18 boys and eight girls) with a mean age of 10.9 years (range 0.3 to 16.9 years) underwent this procedure in a 7-year period. The mean follow-up period was 3.2 years (range 0.2 to 7.5 years). During follow-up three patients died and one autograft was replaced with a mechanical valve. The actuarial survival and actuarial event-free survival rates were 87 and 79%, respectively, at both 5 and 7 years. None of the surviving patients had complaints, and all have done well and are living normal lives. Electrocardiographic signs of myocardial ischemia and left ventricular hypertrophy were not present. Echocardiography showed autograft valve regurgitation to be absent or trivial (n=17) or mild (n=5). Stenosis was not present. Increasing autograft annulus diameters were noted during follow-up, but this was not related to the severity of autograft regurgitation. Left ventricular dimensions and function were within normal limits later than 1 year after the operation. Only two patients had a moderate pulmonary stenosis without right ventricular hypertrophy.

Conclusion. The surgical results, clinical outcome, valve function, and left ventricular function in our patients have been good. This procedure is recommended as a method of aortic valve replacement in children.

Introduction

The use of the pulmonary autograft for aortic root replacement has become a well-established treatment for aortic valve and root disorders in children.[1-3] The advantages of this technique are obvious: there is no risk of thromboembolism, no need for anticoagulants, and no immunologic degeneration of the autograft; perhaps most importantly, the autograft has growth potential,[1,4] thereby avoiding the need for reoperation in the growing child. Furthermore, the root replacement technique is a technically less demanding technique than the implantation of a pulmonary autograft within the aortic root (intraaortic cylinder or subcoronary implantation).[5] We reported our initial experience with this aortic root replacement technique in children in 1992.[3] The present study incorporates a larger follow-up period and thus an improved view of the medium-term results with regard to clinical outcome, left-sided pulmonary autograft and right-sided pulmonary allograft function, and the increase in the diameter of the pulmonary autograft. A further goal of this study was to evaluate the results of the pulmonary autograft procedure with regard to clinical outcome and left ventricular function.

Patients and methods

Patients

From November 1988 to September 1995, 26 children (18 boys and eight girls) underwent aortic root replacement in which a pulmonary autograft was used. The mean age of the children was 10.9 years (range 0.3 to 16.9 years). The aortic valve lesion was congenital in origin in 23 patients; 21 of them had bicuspid valves, and two also had subaortic stenosis. The cause of the lesion in the remaining 3 patients was endocarditis (one patient), juvenile rheumatoid arthritis (one patient), and rheumatic fever (one patient). Previous cardiac operations and procedures performed in the patients are listed in Table 1; surgical valvotomy and balloon valvuloplasty were the most frequent procedures. The actual indication for aortic valve replacement was aortic stenosis (five patients), aortic regurgitation (nine patients), and both (12 patients). Altered left ventricular morphology, increased left ventricular wall thickness, or left ventricular dilatation, or a combination of these, was present in all patients, depending on the cause of the valve lesion.

Table 1 Previous cardiac procedures in the 26 patients operated on with the pulmonary autograft procedure.*

Procedure	N	Percentage
Valvotomy	13	50
Balloon valvuloplasty	13	50
Valvuloplasty	2	8
Enucleation of subvalvular membrane	4	15
Resection of aortic coarctation	2	8
Dilatation of ascending aorta	2	8
Closure of ventricular septal defect	1	4
No procedures	7	27

*: Thirty seven procedures in 19 patients.

Operation

Standard cardiopulmonary bypass techniques were used. The mean aortic clamp time was 136 minutes (range 97 to 203 minutes), and the mean perfusion time was 204 minutes (range 153 to 465 minutes). The aortic root was excised, leaving the coronary arteries in situ with a button of aortic wall. The pulmonary trunk was then excised with a small ridge of right ventricular musculature. This pulmonary autograft was placed on the left ventricular outflow tract with three running sutures. No attempt was made to wrap the autograft. The coronary arteries were inserted in the sinuses of autograft. One aortic and 25 pulmonary allografts were implanted between the right ventricle and pulmonary bifurcation; these comprised 24 cryopreserved allografts from the Rotterdam Heart Valve Bank[6] and two antibiotic-preserved allografts the Heart Valve Bank of the London National Heart Hospital. An extended description of our operative procedure has been published elsewhere.[5] Blood group compatibility was not taken into account in selecting the allografts. Concomitant procedures were enucleation of a subvalvular stenosis (two patients), closure of a patent arterial duct (one patient), and enlargement of the ascending aorta (one patient).

Follow-up

Our follow-up protocol consisted of a yearly physical examination performed in the outpatient clinic. The clinical condition of adolescents and adults was scored using the New York Heart Association classification for dyspnea. A comparable classification was used for children. Height, weight and blood pressure were noted. Auscultation was performed to detect important valvular stenoses or regurgitation. Electrocardiography was performed to evaluate the cardiac rhythm and determine whether there was left ventricular hypertrophy.[7] Thirteen

patients underwent bicycle exercise testing, and the results were described as the percentage of the mean values in a normal population of the same age using the protocol of Godfrey and associates.[8] Endocarditis, thromboembolism, structural deterioration, and nonstructural dysfunction were defined as valve-related events, according to the criteria of Edmunds.[9] Total heart block was included as a cardiac event.

Echocardiography

Echocardiography was performed regularly postoperatively. Precordial two-dimensional color Doppler echocardiography was used to semiquantitatively classify aortic and pulmonary regurgitation by the length and width of the regurgitation jet in the parasternal long-axis view. Aortic regurgitation was graded as none if there was no regurgitation jet; trivial if a short, narrow jet was present just beneath the aortic valve; mild if the jet was limited to the left ventricular outflow tract; moderate if the jet reached halfway to the ventricle; and severe if the jet reached more than halfway to the ventricle and there was also left ventricular dilatation and considerable diastolic back flow in the aortic arch. Pulmonary regurgitation was graded as none if there was no regurgitation; trivial if a short, narrow jet was present just beneath the pulmonary valve; mild if a narrow regurgitation jet was visible in the right ventricular outflow tract; moderate if a broad regurgitation jet was seen extending into the right ventricular outflow tract; and severe if the retrograde flow started within the right and left pulmonary arteries and there was also considerable right ventricular dilatation. Continuous-wave Doppler echocardiography was used to detect aortic and pulmonary stenosis by measuring the maximal blood flow velocity. Stenosis was graded as none, trivial, moderate, or severe.

Two-dimensional echocardiography was used to measure the diameters of the pulmonary autograft annulus. The inner diameter of the autograft annulus was measured at the hinge points of the valve leaflets in an early systolic, parasternal, long-axis view of every initial postoperative precordial two-dimensional echocardiogram (less than 10 days postoperatively) and one or two subsequent echocardiograms obtained during follow-up. Only those subsequent echocardiograms obtained from patients more than 1 year after the autograft procedure were measured. To compare the autograft annulus diameters with normal ones we used the results of Snider and colleagues,[10] who used two-dimensional echocardiography to measure pulmonary trunk diameters in 110 normal subjects, aged 1 day to 18 years.

The dimensions of the left ventricle during systole and diastole were determined, and the fractional shortening was calculated from these. The septal and posterior wall thicknesses at end-diastole were also measured, but only in echocardiograms obtained from patients more than 1 year after the autograft procedure. Measurements were compared with those noted for normal Dutch children.[11] The relative end-diastolic wall thickness was expressed as the ratio of end-diastolic posterior wall thickness to the diameter of the left ventricle.[12]

Echocardiography in two children was performed at another hospital using the same protocol.

Statistical analysis

Estimated survival and event-free survival curves were made using the Kaplan-Meier method[13] with 70% confidence limits (CL).

Results

There were no early deaths. Early morbidity occurred in one patient, who suffered from a complete atrioventricular block after extensive resection of a subvalvular stenosis; a pacemaker was implanted in this patient. The mean follow-up time was 3.2 years and ranged from 0.2 to 7.5 years. Except for the patient followed up for 0.2 year, follow-up in all patients was longer than 1 year.

Three patients died during follow-up. Two patients died of heart failure caused by restrictive cardiomyopathy with pulmonary hypertension, which was documented by cardiac catheterization. A severe *Candida* sepsis was present in one; she died 2 months postoperatively. The second patient died after 22 months. The third patient died 6 months postoperatively as the result of relapse of chronic juvenile rheumatoid arthritis, resulting in autograft and mitral valve destruction.[14] One patient was reoperated on 22 months postoperatively because of relapse of acute rheumatic fever that led to the destruction of the pulmonary autograft.[15] There were no reoperations necessitated by technical reasons or structural degeneration. Endocarditis did not occur. Thromboembolic complications were not observed. The survival and reoperation-free survival curves are shown in Figure 1. The estimated 5- and 7-year survival rate was 87% (70% CL at 5 years: 75% to 99%), and the event-free survival rate was 79% (70% CL at 5 years: 66% to 92%). The patient with the postoperative complete atrioventricular block was reoperated on for mitral and tricuspid regurgitation 6.5 years after the pulmonary autograft procedure. The mitral valve was replaced with a mechanical valve and vavuloplasty was performed on the tricuspid valve. Concomitantly his endocardial pacemaker was replaced with an epicardial pacemaker.

The clinical condition of the survivors at last follow-up was good. All adolescents and adults were in New York Heart Association functional class I, and the younger children were also doing well and comparable with siblings or children of the same age group. Medication was not being used, except in the patient reoperated on for tricuspid and mitral regurgitation who was being treated with diuretics and an angiotensin-converting enzyme inhibitor. Growth curves were normal, with height and weight between the 5th and 95th percentile compared with the normal Dutch population[11] Electrocardiography did not show myocardial ischemia or signs of left ventricular hypertrophy. Ergometry revealed an exercise capability of between

Table 2 Pulmonary autograft and allograft function after the pulmonary autograft procedure.*

	Aortic Stenosis	Aortic Regurgitation	Pulmonary Stenosis	Pulmonary Regurgitation
None, trivial	22	17	18	21
Mild	-	5	2	1
Moderate	-	-	2	-
Severe	-	-	-	-

*: This was determined from the last precordial echocardiogram obtained in patients with a pulmonary autograft in situ (22 of 26 patients).

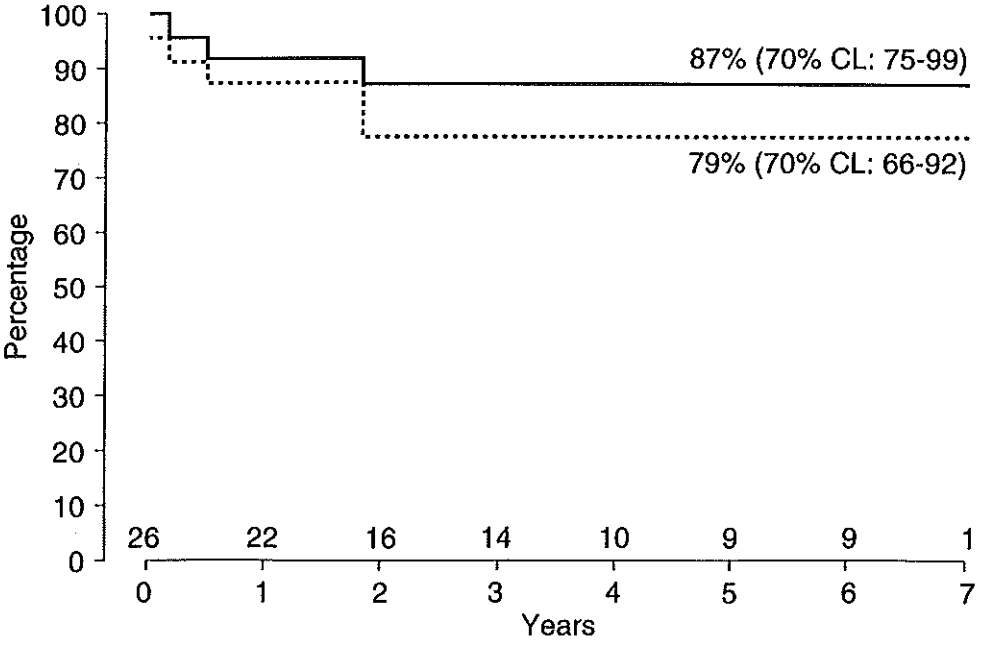

Figure 1 Kaplan-Meier curves of survival (solid line) and reoperation-free survival (dotted line) for children after the pulmonary autograft procedure (numbers are equal for both curves). (CL: confidence limits.)

Table 3 Variables of left ventricular function after the pulmonary autograft procedure in the 19 patients beyond the first postoperative year.

Variable	Range	Range Percentile
Left ventricle dimension in systole (mm)	20 - 41	5 - 95
Left ventricle dimension in diastole (mm)	34 - 61	5 - 95
Thickness of interventricular septum in diastole (mm)	5 - 13	5 - 95
Thickness of posterior wall in diastole (mm)	5 - 14	5 - 90
Shortening fraction	0.23 - 0.48	--
Relative wall thickness	0.12 - 0.27	--

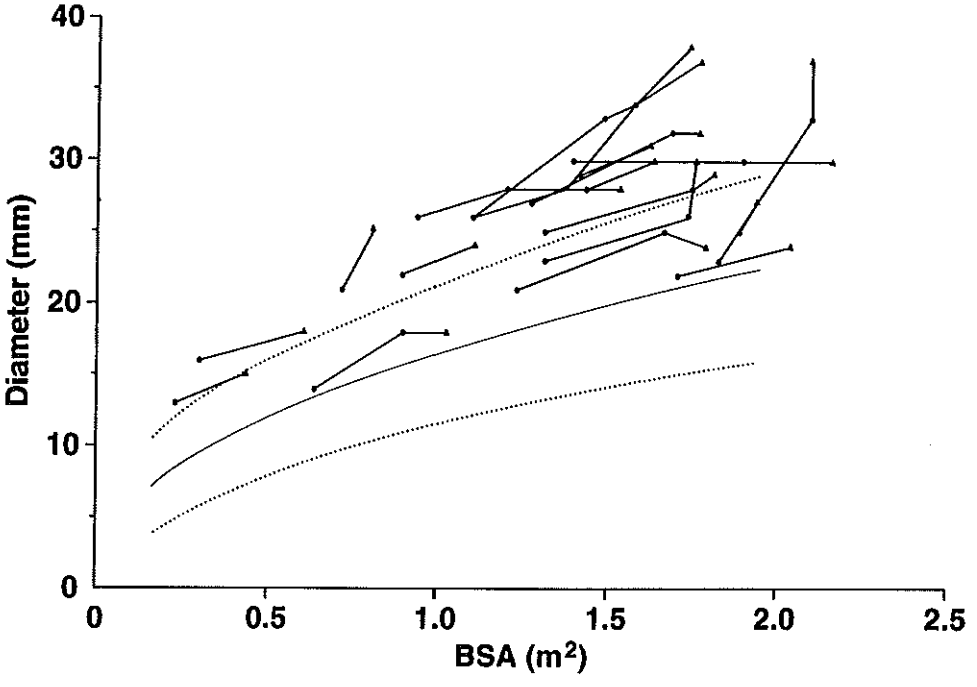

Figure 2 Diameters of the pulmonary autograft annulus during follow-up in 19 children who had undergone the pulmonary autograft procedure. The dotted lines represent the 80% prediction interval of normal pulmonary trunk diameters measured by Snider and associates[10] in 110 normal children (aged 1 day to 18 years) using two-dimensional echocardiography. (BSA: body surface area).

80 and 120% compared with a normal population.[8] Rhythm disturbances were not seen, and heart rate and blood pressure were within normal limits.

Echocardiography

Aortic and pulmonary valve function were described semiquantitatively at the last follow-up (Table 2). Moderate or severe aortic regurgitation or stenosis was not seen. The five patients with mild aortic regurgitation had been found to have trivial aortic regurgitation early after operation. These regurgitation jets had become mild by 3 to 5 years after operation. However, the clinical status of these patients was good. Moderate or severe pulmonary regurgitation was also not found. Moderate pulmonary allograft stenosis was noted in two patients, with blood flow velocities of between 3.5 and 4.0 m/s along the right ventricular outflow tract. It occurred in two patients with cryopreserved pulmonary allografts inserted at 5 and 16 years of age; the gradients became mild 3 and 4 years postoperatively. The clinical status of these patients was good.

It was possible to measure the diameters of the pulmonary autograft annuli relative to the body surface area in 19 patients at different time points during follow-up. The results are presented in Figure 2. Most diameters were larger than the mean pulmonary annulus diameters measured by Snider and associates.[10] The three patients with the largest increase (more than 10 mm) showed mild (two patients) and trivial (one patient) aortic regurgitation. When patients were grouped according to severity of their aortic regurgitation (none, trivial, mild), however, no relationship with an increase in the autograft annulus diameter was found.

The diameters of the left ventricles and the thicknesses of the posterior and interventricular walls varied within normal limits according to patient weight (Table 3). The shortening fraction of the left ventricular wall was normal in all but one patient. The relative end-diastolic wall thickness varied between 0.12 and 0.27. The patient reoperated on for mitral and tricuspid regurgitation showed the lowest of the latter two measurements (7 months after reoperation). The measurements in the other patients were comparable to those in normal children.[12]

Discussion

The use of the pulmonary autograft for aortic valve replacement is a good option for treating aortic valve disorders in children. Balloon valvuloplasty is the preferred treatment for valvular aortic stenosis.[16] Aortic valve replacement is indicated if a considerable gradient recurs or if aortic regurgitation is the predominant feature, regardless of whether it is due to balloon valvuloplasty. There are important disadvantages to the use of mechanical, bioprosthetic and allograft valves, however. For example, reoperation in the growing child may be necessary.

In addition, structural degeneration of the bioprosthetic valves and allografts will occur, and mechanical valves are associated with thromboembolic complications and bleeding disorders in patients treated with anticoagulants. These problems are avoided if a pulmonary autograft is used for the left side of the heart, though the operation time is longer (in this series the mean aortic clamp time was 136 minutes), and an allograft valve, which is prone to degeneration, is inserted on the right side of the heart. We have been performing this procedure since 1988 and now exclusively use the pulmonary autograft as a freestanding aortic root, thereby avoiding the distortion of the autograft that occurs when subcoronary and intraaortic cylinder techniques are used in a patient with an often smaller aorta.

There were no early deaths in this group of patients with complex abnormalities. Two patients died during follow-up for reasons not related to the autograft procedure. Another patient died as the result of recurrent chronic juvenile rheumatoid arthritis that destroyed the autograft.[14] Reoperation was necessary in a patient with recurrent acute rheumatic fever that destroyed the autograft.[15] Chronic juvenile rheumatoid arthritis is regarded as a contraindication to the pulmonary autograft procedure, and acute rheumatic fever is regarded as a relative contraindication, depending on the adequacy of antibiotic profylaxis for the disease.

The clinical outcome of the remaining patients in this series was good. They are doing well and showing normal growth patterns. Only one patient is taking medication. Other studies have also shown improvement in the functional class in patients who receive pulmonary autografts,[1,2] but the assessment in these studies did not include exercise capability testing. The children undergoing this exercise testing in our study performed excellently, with capabilities in accordance with those of age-matched normal children. Electrocardiographic signs of left ventricular hypertrophy or myocardial damage were not found in our patients after 1 year of follow-up, contrasting with the electrocardiographic changes found in 20 adult patients, three of whom had a right bundle branch block and two of whom had signs of severe ischemia.[17] Pulmonary autograft valve stenosis was not found, and any regurgitation was trivial or mild. This good valve function in the medium-term has been reported by others as well.[1] Oury and Mackey, in their report ragarding the Ross Procedure Registry, also noted good valve function in most of the patients, both children and adults, in the root replacement group.[18]

The allograft implanted in the right ventricular outflow tract may be of more concern. The pulmonary regurgitation in such patients has not been found to be important, but two of the patients in our series have important gradients across the allograft in this location. Although right ventricular hypertrophy has not been found and clinical function is good in these patients, it may be that structural degeneration will occur in these right sided pulmonary allografts and necessitate reoperation in the future. In this regard, however, the long-term functional results of right sided pulmonary allografts must be distinguished from the function

of allografts used for congenital right heart defects.[19]

As has been reported before, the greatest advantage to the use of a pulmonary autograft is its ability to increase in diameter over time.[1] Our study confirmed the increasing diameter of the pulmonary autograft in the patients who had undergone their operation more than a year before. As compared with the 80% prediction interval cited by Snider and colleagues,[10] however, most of the diameters are above this interval, indicating that the measurements of native pulmonary annuli are questionable as reference values. Although in most patients this increase was less than 20%, there were three patients with an increase of more than 50% (more than 10 mm). Elkins and associates[1] reported a greater increase in the diameter of freestanding pulmonary autografts than in the diameter of autografts placed using the intraaortic cylinder technique, and they attributed this 'extra' increase to dilatation of the graft. Long-term follow-up is therefore necessary to come to any conclusions about the behavior of the pulmonary autograft diameter. Its relationship to aortic regurgitation especially warrants an in-depth follow-up. In our series in which the mean follow-up was 3.2 years and the longest follow-up was 7.5 years, only limited aortic regurgitation of some autografts and no important gradient across the autograft valve were noted. Correlations between an increase in the autograft annulus diameter and the severity of aortic regurgitation could not be found.

Functional status and survival rates are not only improved in adult patients who undergo aortic valve replacement,[20] there is also a regression in the myocardial mass and an improvement in systolic and diastolic left ventricular function in such patients.[21-23] In children, left ventricular dimensions often remain impaired after aortic valve procedures for congenital stenosis, probably related to the remaining gradient across the valve.[24,25] All variables related to left ventricular size and function were within normal limits in all our patients except one, contrasting with the abnormal situation before operation. This is in agreement with the results noted by others, who also found an improvement in the left ventricular dimensions in children, indicating the lack of sequelae from this operation.[26,27] A limitation to our study, however, is that adequate echocardiographic measurements of the left ventricle could not be obtained in all patients.

We conclude that the surgical results, clinical outcome, valve function and left ventricular function are good after aortic root replacement with a pulmonary autograft and recommend this procedure for aortic valve replacement in children.

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Chapter 4

Aortic root replacement with a pulmonary autograft

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Abstract

A series of 42 consecutive patients with exclusively aortic root replacement using the pulmonary autograft is presented. The mean age at operation was 19.3 years (range 0.3 to 41.4 years). Two patients died in hospital (4.8%; 70% CL: 0.0% to 8.2%). This mortality was not related to the autograft procedure. The mean follow-up time was 30 months (range 3 to 70 months; SD: 20 months). Late mortality consisted of two patients; in one of these severe autograft failure occurred due to chronic juvenile rheumatoid arthritis. The estimated survival rate at 4 years was 88.8% (70% CL: 83.3% to 94.5%). Morbidity involved three patients. One had a total heart block after operation, requiring pacemaker implantation and two patients were reoperated: one patient for severe autograft failure due to recurrent acute rheumatic fever and the other patient for severe stenosis at the distal anastomosis of the pulmonary allograft. Thromboembolic complications and endocarditis were not registered. Reoperations for technical or degenerative reasons were not necessary. The estimated event-free survival rate at 4 years was 78.7% (70% CL: 71.0% to 86.4%). Serial echocardiography (n=28) showed a significant increase of the autograft annulus diameter of 2.9 mm (SD: 2.7 mm). Thirty-five of the 37 patients with an autograft in situ were in NYHA class I and two in class II. At last follow-up precordial color Doppler echocardiography showed moderate aortic regurgitation in one patient and no, trivial or mild aortic regurgitation in 36 patients. Stenosis of the autograft was not observed.

Conclusion: These medium-term results are promising with respect to mortality, morbidity and functional results. The autograft procedure may be contraindicated in patients with chronic juvenile rheumatoid arthritis and relatively contraindicated in patients with a history of acute rheumatic fever. Extended follow-up is warranted to observe progression of autograft annular dilatation and its clinical consequences.

Introduction

After having described the pulmonary autograft replacement of the aortic valve using the subcoronary technique in 1967[1] and the intraaortic cylinder technique in 1982, Ross introduced aortic root replacement using a pulmonary autograft in 1986.[2] For all these techniques the aim was to have a viable and permanent aortic valve substitute without the problem of degeneration present in bioprosthetic and allograft valves. For these techniques the anticoagulation therapy is not needed, which is regarded as a major advantage compared to the mechanical valves. The use of the pulmonary autograft to replace the aortic root offers advantages over the subcoronary technique, because replacement of the pulmonary valve in its own functional unit avoids malpositioning of the valve and allows growth, which may be favourable in children. In addition, pathology of the aortic root can be treated adequately.

We started with autograft aortic root replacement to treat aortic valve and aortic root pathology in children in 1988.[3] With increasing experience this autograft root replacement technique was extended to adolescent and adult patients. Although the growth potential of the pulmonary autograft is not of importance in grown-up patients, the expectation of having a valve substitute without degeneration is regarded as an attractive option in these patients as well. In this regard it is important to know how the pulmonary autograft holds in the systemic circulation. Biomechanical testing proved that pulmonary valves could stand systemic pressures.[4] The functioning of the autograft root, however, is unknown.

The acceptable results of cryopreserved pulmonary allografts in the right ventricular outflow tract[5,6] and the possibility of storage of allografts with this preservation technique offered a solution to the problem of replacing the right ventricular outflow tract.

In this paper we present our experience with a series using exclusively the aortic root replacement technique with a pulmonary autograft, in patients ranging from 3 months to 41 years of age. Fourteen children have been described earlier.[7]

Patients and methods

Patients

From november 1988 till March 1994, 42 patients received pulmonary autografts. There were 24 males and 18 females with a mean age of 19.3 years (range 0.3 to 41.3 years); 19 were children (younger than 18 years) and 23 adults (18 years or older). Thirteen patients were operated for aortic stenosis, 14 patients for aortic regurgitation and 15 patients had both stenosis and regurgitation. According to the New York Heart Association (NYHA) 14 patients were in functional class I, 14 in class II, nine in class III, four in class IV, while one patient was in cardiogenic shock (class V). Of the 14 patients in class I, deterioration of left

Table 1 Previous operations and procedures in 26 patients of 42 patients operated on with the pulmonary autograft procedure.

Operation or procedure	N
Aortic valvulotomy	16
Aortic valve replacement	5
Enucleation subvalvular obstruction	5
Repair aortic coarctation	6
Closure ventricular septal defect	3
Enlargement ascending aorta	2
Closure patent arterial duct	2
Aortic valve repair	1
Closure fistula aorta - left ventricle	1
Aortic balloon valvuloplasty	11
No procedures	16

ventricular parameters in 11 patients (progressive dilatation in seven patients, progressive hypertrophy in four patients), repolarization disorders on the electrocardiogram during exercise in one patient and collapse in two patients were the indication for operation. In two patients collapse was the reason for operation. Twenty-three patients had previously been operated via a median sternotomy (17 patients once, six patients twice). Previous operations and procedures are listed in Table 1.

The original etiology of the aortic valve lesions is described in Table 2. In five patients the aortic valve had previously been replaced by a bioprosthetic valve (n=3), a mechanical prosthesis (n=1), or an allograft valve (n=1). In one patient an aortic valve repair was performed. Important dysfunction of these valves was the indication for valve replacement. Prior to the operation, precordial two-dimensional (2D) color Doppler echocardiography, and angiography if available, were used to assess the pulmonary valve function. Patients with abnormal pulmonary valve function were excluded from the use of a pulmonary autograft for aortic root replacement.

Operative technique

All patients were operated through a median sternotomy. The pulmonary valve was again evaluated intraoperatively with epicardial echocardiography before extracorporeal circulation was instituted. Aprotinin was included in the priming. The superior and inferior caval veins (n=32) or the right atrium (n=10) and aorta were cannulated after heparinization. The left atrium or left ventricle was drained by cannulating the upper right pulmonary vein. Moderate hypothermia (25° C) was used and topical cooling of the heart was carried out with a

Table 2 Original etiology of aortic valve lesion.

Etiology	N
Congenital (bicuspid valve)	16[a]
Degenerative	4
Endocarditis (cured)	3[b]
Aneurysm ascending aorta	1
Chronic juvenile rheumatoid arthritis	1
Acute rheumatic fever	1
Total	42

a: Including seven patients with a subvalvular aortic stenosis and one patient with a supravalvular aortic stenosis.
b: Including two patients with endocarditis on a bicuspid aortic valve.

physiologic saline solution and crushed ice. Deep hypothermia with circulatory arrest was necessary in two patients: in one for repair of a perforation of the ascending aorta during a resternotomy and in the other for patch enlargement of the ascending aorta. After aortic cross-clamping and aortotomy, cristalloid cardioplegia was given intracoronarily and repeated after 1 h. The left ventricular outflow tract was inspected. The aortic and pulmonary roots were than separated as far as possible. The coronary orifices were excised including a button of aortic wall. The remaining part of the aortic root was resected. The pulmonary root was transected just proximal to the pulmonary bifurcation and cut at the proximal site with a ridge of right ventricular muscle, taking care to avoid the left coronary artery and the first septal branch. The autograft was placed on the left ventricular outflow tract with three running sutures polypropylene 4.0 or 5.0 (polydioxanone suture 7.0 in two patients). The right and left sinuses of Valsalva of the autograft were incised longitudinally and the coronary arteries were implanted with polypropylene 6.0 (7.0 in two patients). Three aortic and 39 pulmonary allografts with a mean diameter of 25 mm (range 13 to 31 mm) were inserted as pulmonary roots. The distal anastomosis was made with polypropylene 5.0 (7.0 in one patient) and the proximal anastomosis with polypropylene 4.0 or 5.0. Finally the autograft was anastomosed to the ascending aorta with polypropylene 5.0 (6.0 in two patients). All suture lines were sealed with fibrin glue. Seven concomitant procedures were performed in five patients: in one patient a patent arterial duct was closed, while a subvalvular obstruction was enucleated in four patients; in one of these a venous graft was used to connect the right coronary artery (coming from an excentric ostium) to the pulmonary autograft, and in another patient patch enlargement of the ascending aorta, just proximal of the brachiocephalic artery was necessary. After rewarming, decannulating and hemostasis, the result was evaluated with epicardial echo.

Finally the sternotomy was closed.

Follow-up

No patient was put on anticoagulation therapy. The first postoperative echocardiogram was made while the patient was still in hospital. Our follow-up protocol consists of regular physical examination at the out-patient clinic. Postoperative echocardiographic evaluation is scheduled every year. Aortic and pulmonary regurgitation were semiquantitatively classified on precordial 2D color Doppler echocardiography by the length and width of the regurgitation jet in the parasternal long-axis view. Aortic regurgitation was scored as none if there was no regurgitation jet, trivial if a short, narrow jet was present just beneath the aortic valve, mild if the jet was limited to the left ventricular outflow tract, moderate if the jet reached halfway in the ventricle and severe if the jet reached more than halfway in the ventricle. Pulmonary regurgitation was scored as none if there was no regurgitation, trivial if a short, narrow jet was present just beneath the pulmonary valve, mild if a narrow regurgitation jet was visible in the right ventricular outflow tract, moderate if a broad regurgitation jet was visible extending into the right ventricular outflow tract and severe if the retrograde flow already started within the pulmonary branch arteries. Aortic and pulmonary stenoses were measured by continuous wave Doppler echocardiography and graded as none if there was no gradient, trivial if the peak gradient was less than 16 mm Hg, mild if this gradient was between 16 and 35 mm Hg, moderate if it was between 35 and 60 mm Hg and severe if it was more than 60 mm Hg.

Diameters of the autograft annulus were measured on 2D echocardiography. The inner diameter of the autograft annulus was measured at the hinge points of the valve leaflets in an end-diastolic parasternal long-axis view, in every first (less than 10 days postoperatively) and on the latest postoperative precordial 2D echocardiogram. For comparison of the autograft annulus diameters we used the results of Snider et al.[8] who measured pulmonary trunk diameters in 110 normal subjects, aged 1 day to 18 years, with 2D echocardiography.

Endocarditis, thromboembolism, structural deterioration and nonstructural dysfunction were defined as valve-related events according to Edmunds.[9] Total heart block was included as an event.

Statistical analysis

A Student *t* test with equal variances was used to analyze continuous variables. Significance was assumed if the *p*-value was <0.05. Mean values were given with range and standard deviation (SD) where applicable. Estimated survival and event-free survival curves were made with the Kaplan-Meier method[10] with 70% confidence limits (CL). All analyses were performed on a personal computer using SPSS version 6.0 as the statistical package.

Results

Operation

Mean aortic clamp time was 145 min (range 97 to 233 min). Adults (18 years or older) needed longer clamping times, 154 min (range 118 to 233 min) against 136 min (range 97 to 203 min) in children ($p<0.05$). The mean perfusion time was 214 min (range 153 to 465 min) and did not differ between adults and children.

Hospital mortality and morbidity

Two (adult) patients died in hospital (4.8%). One patient, with Marfan's syndrome, was preoperatively in cardiogenic shock (NYHA class V) due to severe aortic regurgitation. He was operated on an emergency basis and died 4 h after operation. Autopsy showed massive pulmonary thromboembolism originating from a venous thrombosis in the prostatic plexus. The second patient needed resternotomy 13 days after operation for aortic arch bleeding due to mediastinitis (and sepsis). After replacement of a fragile part of the aorta, the patient could not be weaned from extracorporeal circulation. Autopsy showed endocardial fibroelastosis of the left ventricle and large non-vital parts in the aortic media of the resected aorta. Resternotomy for bleeding or tamponade early postoperatively was necessary in nine adult patients (21%). These were not related to the autograft or allograft anastomoses. Five of these nine patients had a history of previous cardiac surgery. One child, after extensive resection of a subvalvular stenosis needed implantation of a pacemaker for a total heart block. The mean hospital stay of the survivors was 13 days (range 8 to 42 days).

Follow-up

The mean follow-up period of the hospital survivors ($n=40$) was 30 months (range 3 to 70 months; SD: 20 months). Two children died during this period. The youngest, operated upon at the age of 3 months, after cured endocarditis on a balloon dilated valve, died 22 months after surgery because of left heart failure due to restrictive cardiomyopathy in the presence of severe allograft failure, without autograft regurgitation. Autopsy was not obtained, but echocardiography had shown endocardial fibroelastosis. The other patient had been operated on for chronic juvenile rheumatoid arthritis with aortic regurgitation and died 6 months postoperatively because of right and left heart failure due to severe mitral and aortic regurgitation. The allograft functioned well. At autopsy myocarditis and pericarditis were found and the architecture of the autograft was completely destroyed showing fibrinoid necrosis and inflammation, suggestive of a relapse of the rheumatoid disease.[11] The allograft was not affected.

Two patients were reoperated. One patient had a relapse of acute rheumatic fever after termination of antibiotic prophylaxis. The pulmonary autograft showed massive regurgitation;

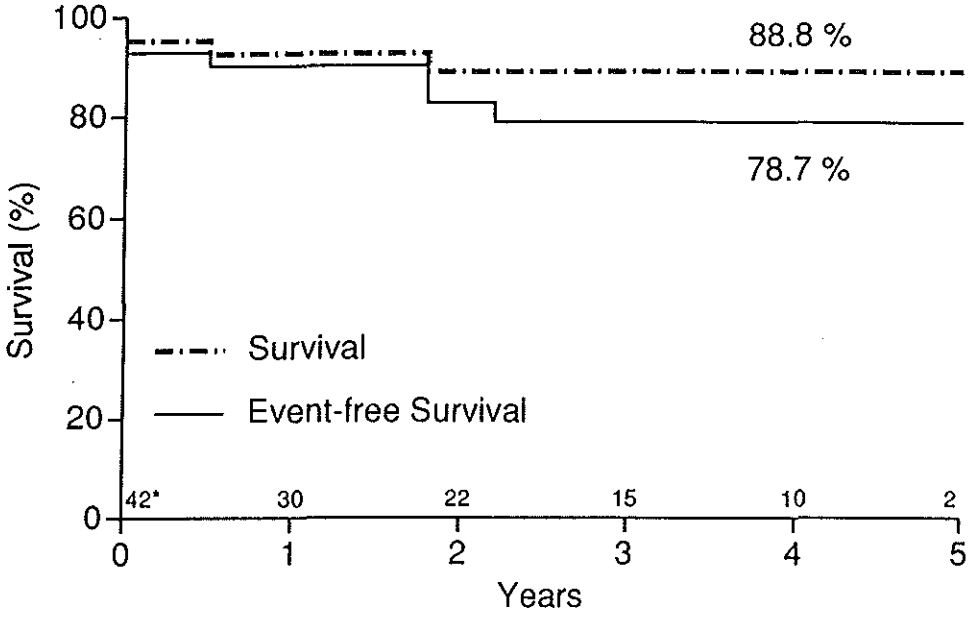

Figure 1 Survival and event-free survival curves. *: patients at risk (numbers are equal for both curves during follow-up).

the allograft function was normal. He was reoperated 22 months after autograft implantation and a mechanical prosthesis was implanted.[12] The second patient presented with stenosis at the distal anastomosis of the allograft (echocardiographic peak gradient 77 mm Hg) and had been dyspneic (NYHA class II) since operation. Twenty-four months postoperatively the distal anastomosis of the pulmonary allograft was enlarged with an allograft patch. Thirty-five patients with an autograft in situ were in NYHA class I and two patients were in class II at last follow-up. There were no reoperations for either technical reasons or autograft degeneration. Endocarditis did not occur. Thromboembolic complications were not observed. Infarctions or ischemic electrocardiographic changes were not present. The survival and event-free survival curves are shown in Figure 1. The estimated 4-years survival rate was 88.8% (70% CL: 83.3 to 94.5) and the event-free survival rate was 78.7% (70% CL: 71.0 to 86.4).

Echocardiographic follow-up

Aortic and pulmonary valve function and autograft annulus diameters were studied in all hospital survivors (n=40) with precordial 2D color Doppler echocardiography. The function of the valves at the latest echocardiogram or the last echocardiogram before an event are presented in Table 3. In 12 of these only one postoperative echocardiogram was available, while in 28 patients two or more postoperative 2D echocardiograms were available. There was

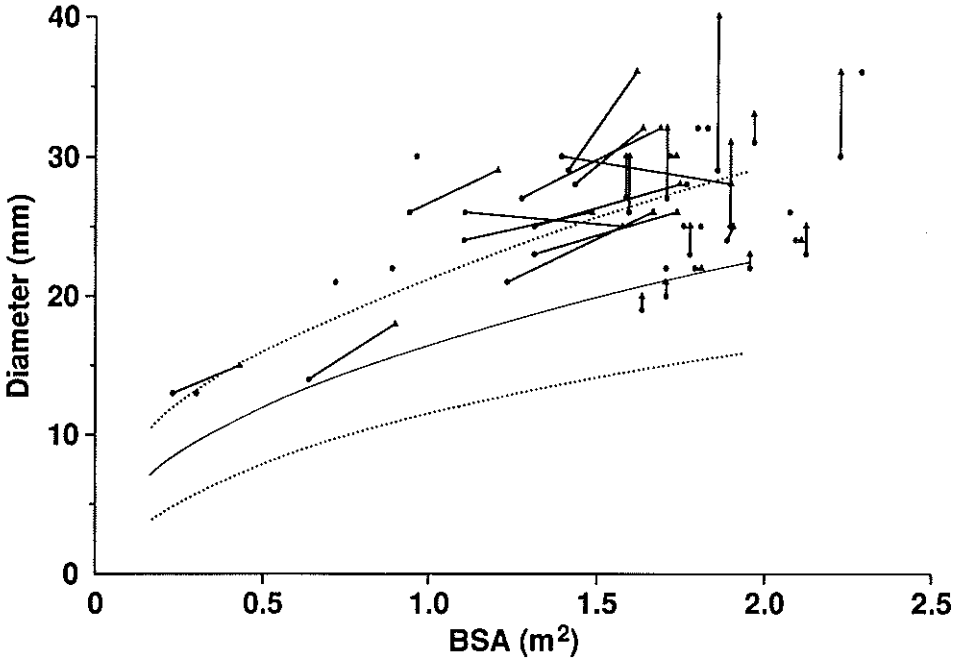

Figure 2 Autograft annulus diameters (hospital survivors, n=40). The dotted lines represent the 80% prediction interval of normal pulmonary trunk diameters measured by Snider et al. on 2D echocardiography in 110 normal children, aged 1 day to 18 years.[8] The dots and triangles represent the first and last postoperative measurements respectively. BSA: body surface area.

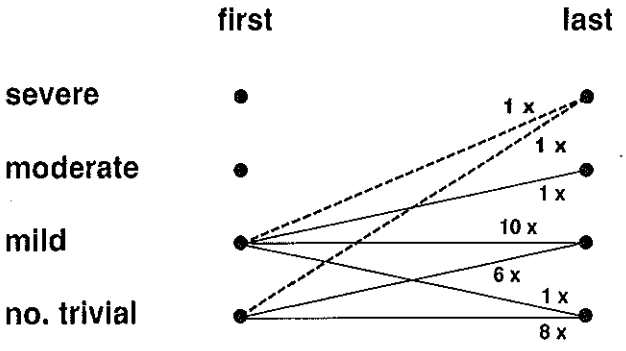

Figure 3 Aortic regurgitation at first and last postoperative echocardiograms (n=28). The dotted lines represent patients with an event.

Table 3 Autograft and allograft valve function at last echocardiogram or at last echocardiogram before an event (hospital survivors, n=40).

	Aortic stenosis	Aortic regurgitation	Pulmonary stenosis	Pulmonary regurgitation
None, trivial	40	19	31	24
Mild	-	18	8	15
Moderate	-	1	-	-
Severe	-	2	1	1

Table 4 Mean echocardiographic autograft annulus diameter.

	Children (n=13)	Adults (n=15)	All (n=28)
Annulus (mm) *first echo*	23.9 (range 13-28)[a]	25.2 (rage 19-30)[b]	24.6 (range 13-30)[c]
Annulus (mm) *last echo*	26.6 (range 15-32)[a]	28.1 (rage 20-40)[b]	27.4 (range 15-40)[c]

a,b: No significant difference between diameter at the first postoperative, compared to the last postoperative, echocardiogram. c: Significant difference (p<0.05) between diameter at the first postoperative, compared to the last postoperative, echocardiogram.

no aortic stenosis. In two patients severe aortic regurgitation was documented before an event (reoperation or death). One patient showed moderate aortic regurgitation at last follow-up and was in NYHA class I. The patient with severe pulmonary stenosis was reoperated and the patient with severe pulmonary regurgitation died. Autograft annulus diameters of the hospital survivors (n=40) are shown in Figure 2. The mean autograft annulus diameters in the first and last postoperative echocardiograms (n=28) are shown in Table 4. The mean diameter measured at the last postoperative echocardiogram was significantly larger (2.9 mm; SD: 2.7 mm) compared to the first postoperative echocardiogram for the whole group. When patients were grouped by children and adults, the autograft annulus measurements were not significantly different (Table 4). In this group of 28 patients, with two or more postoperative echocardiograms, specific attention was paid to aortic regurgitation during follow-up. Figure 3 shows the aortic regurgitation at the first and last postoperative echocardiograms. Most patients showed only mild aortic regurgitation at the last postoperative echocardiogram as opposed to no, trivial or mild aortic regurgitation at the first one.

Discussion

Since the introduction of the pulmonary autograft by Ross, with the subcoronary (1967), intraaortic cylinder (1982) or root replacement technique (1986),[1,2] we have started to use the latter technique to treat aortic valve and aortic root pathology in children. Although the long-term results of Ross with subcoronary implantation are good,[13,14] we avoided the technically demanding subcoronary or intraaortic cylinder technique with the risk of paravalvular leakage and anatomic malpositioning of the valves.[14-16] Replacement of the pulmonary valve within its own functional unit may prevent these problems. Indeed, technical errors requiring replacement of the autograft did not occur in our series. In another series reoperation for technical reasons was reported (false aneurysm at the proximal sutureline, perforation of a cusp).[17] Another advantage of aortic root replacement with the pulmonary autograft is that the diameter of the autograft is less critical since the entire root is replaced.

In our series of exclusive autograft root replacement, the hospital mortality was low (4.8%; 70% CL: 0.0 to 8.2) and could not be attributed to the autograft procedure. We do, however, doubt whether Marfan's syndrome is a suitable condition for aortic root replacement using a pulmonary autograft because the disease may affect the pulmonary artery as well.[18] As described previously, we regard chronic juvenile rheumatoid arthritis to be a contraindication for the use of an autograft[11] and acute rheumatic fever to be a relative contraindication.[12] This corresponds with the concern of Kumar et al. who operated on 48 patients with rheumatic fever.[17] After initially good results,[19] three patients had to be reoperated (one with recurrent rheumatic activity) despite continuous use of antibiotic prophylaxis. Thromboembolic complications were not registered in the absence of anticoagulation therapy. Reoperations for degenerative valve failure were not necessary. This had already been shown for the subcoronary implanted pulmonary autograft by Ross et al.[13,14] This lack of degenerative changes is the justification for more liberal application of the technique in adults.

Root replacement keeps the pulmonary valve in its own structure, which, at least in children, may be favourable for enlargement because there is no restraint on surrounding tissue.[20] Elkins and colleages showed this enlargement of the pulmonary autograft in both the intraaortic and the root replacement techniques in patients ranging from 1.8 to 21.0 years of age.[15,21,22] In his series with root replacement, serial echographic measurements were available. When indexed to body surface area, the annulus of the intraaortic replacements remained appropriate over time. For the root replacement group, however, it was associated with dilatation.[22] However, no enlargement was found in the series with root replacements by Kouchoukos et al.[23] who measured autograft diameters on 2D echocardiography and Sievers et al.,[7] who measured annulus diameter by M-mode echocardiography at the commissural level. These series concerned mainly adult patients. The 28 patients in our series with two or

more postoperative echocardiograms also showed autograft enlargement. When these measurements are compared to the normal pulmonary trunk diameters of Snider et al.[8] it is evident that many pulmonary autograft annulus diameters are not within the normal range (Figure 2). Snider et al. measured diameters in normal subjects aged 1 day to 18 years. One explanation may be that, in adults, aging and sex may be important factors with regard to diameter measurements.[24,25] Apart from the relation of autograft annulus diameters to normal values, most of the pulmonary autografts are observed to show enlargement in time. Whether this enlargement is due to growth (proliferation of cells) remains to be seen. Mechanical stretching of the pulmonary autograft and adaptation of the collagen and elastic fibers may play a significant role.[4,26] Kadoba and colleagues are concerned about aneurysmal dilatation of the pulmonary autograft at systemic pressures;[27] enlargement was a reason for Moritz et al.[28] and Pacifico et al.[29] to wrap the autograft. Whatever the cause for this enlargement, as confirmed in our series, it did not result in major aortic valve regurgitation[14,15,22,30] and may be of advantage in children in whom reoperation can be avoided. More extended follow-up is required to evaluate autograft enlargement and its relation to aortic regurgitation. This applies especially to adult patients because enlargement in these patients is not likely to be favourable.

Implantation of an autograft valve in the aortic position makes it necessary to operate on a second valve. The previously well functioning pulmonary root must be replaced at its right ventricular outflow tract and, having found a lifelong substitute for the aortic valve, it may be the degeneration of the right-sided valve that requires reoperation. Fortunately the results of allografts in the pulmonary position are satisfactory,[6,31] the conduit of choice being a cryopreserved pulmonary allograft.[5] Important pulmonary regurgitation was not present except in one child in whom left ventricular failure was regarded to be the primary cause of death. In one child peripheral pulmonary stenosis developed at the distal anastomosis and was successfully enlarged with a patch. Pulmonary stenosis occurred in other series as well[15,23,29] and must be regarded as a possible complication.

It is concluded that replacement of the aortic root by an autograft is a satisfactory procedure with low hospital mortality and good functional medium-term results. It can be used at a young age and there are no contraindications for its use in adult patients. In our series it became evident that chronic juvenile rheumatoid arthritis is a contraindication for the use of an autograft and that a history of rheumatic fever is a relative contraindication. Extended follow-up is needed to evaluate the autograft annulus enlargement and its clinical consequences.

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Chapter 5

Does the pulmonary autograft in the aortic position in adults increase in diameter? An echocardiographic study

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Abstract

The objective of this study was to discern the fate of the pulmonary autograft diameter over time in adults and its relation to aortic regurgitation in the setting of aortic root replacement. From January 1989 to May 1995, 36 consecutive adult patients underwent aortic root replacement with a pulmonary autograft for aortic valve disease. The mean age of 20 male and 16 female patients was 29.1 years (range 19.3 to 52.1 years). The mean follow-up was 2.3 years (range 0.3 to 6.0 years). Two patients died in hospital. One other patient had a second operation for stenosis at the distal suture line of the allograft in the pulmonary position. Pulmonary autograft annulus and sinus diameters were measured with epicardial echocardiography before (only annulus) and after cardiopulmonary bypass, with transthoracic echocardiography at hospital discharge, and with transesophageal echocardiography during follow-up. The mean autograft annulus diameter did not increase immediately after cardiopulmonary bypass (mean diameter 26.2 mm before and 26.4 mm after cardiopulmonary bypass). The mean autograft sinus diameter after cardiopulmonary bypass was 36.5 mm. The mean autograft annulus diameter increased to 31.5 mm at follow-up, an increase of 5.1 mm (19%). The mean autograft sinus diameter increased to 43.9 mm at follow-up, an increase of 7.4 mm (20%). Fifty-nine percent of the annulus diameter increase and 40% of the sinus diameter increase was already reached at hospital discharge (7 to 10 days after the operation); the other part of the increase occurred during follow-up. Diameter increase was associated with neither the length of follow-up (follow-up less than 1 year compared with a longer follow-up) or severity of aortic regurgitation.

Conclusion. Pulmonary autograft annulus and sinus diameters increase the first year after aortic root replacement with a pulmonary autograft. This occurs rapidly within 10 days after the operation, with a further increase during follow-up, without causing significant aortic regurgitation at medium-term follow-up.

Introduction

The pulmonary autograft procedure is a surgical technique for treatment of aortic valve or root disease. Although the initially reported series mainly comprised of children, the autograft is nowadays more often used in older patients as well.[1-4] The expected lifelong durability without degeneration and the absence of the need for anticoagulants offer considerable advantages for adult patients. In contrast to the subcoronary or intraaortic cylinder implantation techniques, the root replacement technique is advantageous because it is technically less demanding.[2,5] The autograft is exposed to higher pressures, which may result in an increase of its diameter. An increase in autograft diameter has been reported in children, being explained as growth.[6-8] In adults an increase in diameter has not been reported so far.[2,4] The purpose of this study is to present serial measurements of the pulmonary autograft annulus and sinus diameters and their relation to aortic regurgitation in an adult patient group.

Patients and methods

Patients

We initially performed the pulmonary autograft procedure in November 1988 in a child. However, children (age < 17 years) were not incorporated in the present study. From January 1989 until May 1995, 36 consecutive adults (20 male and 16 female patients with a mean age of 28.7 years, ranging from 19.0 to 52.0 years) underwent aortic root replacement with a pulmonary autograft for aortic valve disease. The nature of the original aortic valve disease was either congenital (n=27), degenerative (n=5), cured endocarditis (n=3), or annuloaortic ectasia (n=1). The hemodynamic diagnosis was aortic stenosis in 13 patients, regurgitation in 16 and both stenosis and regurgitation in seven patients. A discrete subaortic stenosis was present in two patients in addition to valvular stenosis. Standard procedures were applied with regard to cardiopulmonary bypass techniques, using moderate hypothermia and crystalloid cardioplegic arrest.[3] The autograft was placed on the left ventricular outflow tract and annulus with a short rim of right ventricular muscle. No attempts were made to wrap the autograft or to reinforce the base of the autograft. Extended Ross procedures were not used and annular enlargement was not perfomed. For replacement of the pulmonary root a cryopreserved pulmonary allograft was used in 35 patients and an aortic allograft in one patient.

Echocardiography

Epicardial echocardiography was routinely used after sternotomy to evaluate aortic valve disease and pulmonary valve function at the onset of the procedure. The autograft and allograft function were studied immediately after cardiopulmonary bypass. Seven to 10 days

after the operation a transthoracic echocardiogram was performed. After discharge all patients visited the outpatient clinic at 3 and 6 months postoperatively and yearly thereafter. Twenty-eight patients consented to transesophageal echocardiography during the past year (six patients refused). The interval between the operation and transesophageal echocardiography therefore varies according to the length of follow-up of each patient. All echocardiograms were made on a Toshiba echocardiographic machine (SSH 140, Toshiba Corp., Tokyo, Japan) and taped on VHS videotape. Multiplane transesophageal echocardiography was performed with a 5 MHz probe (Oldelft Instruments, Delft, The Netherlands). Measurements were made off-line, using a two-dimensional contour acquisition program on a personal computer with electronic callipers.

Autograft diameters were measured at two different levels: the annulus at the level of the autograft leaflet hinges and the sinus of Valsalva at the largest anteroposterior diameter. This was done in the long-axis plane from a two-dimensional image (with the largest diameters of the proximal autograft visible) using the inner wall distance, during systole with maximal opening of the valve leaflets. At each level, five cardiac cycles with the best quality were used for measurements. At transesophageal echocardiography, aortic regurgitation was measured semiquantitatively. For interobserver variability, 25 diameter measurements (at discharge and at follow-up) were analyzed by a second observer. Aortic regurgitation was scored as none if there was no regurgitation jet, trivial if a short, narrow jet was present just beneath the aortic valve, mild if the jet was limited to the left ventricular outflow tract, moderate if a broad jet reached halfway across the ventricle, and severe if a broad jet reached more than halfway across the ventricle.

Statistical analysis

A correlation coefficient was calculated for the annulus diameters measured with epicardial echocardiography before and after the autograft procedure. A paired *t* test was used for analysis of the difference of the diameter between two time points.

For graphic representation of the mean autograft annulus and sinus diameters at follow-up, a 'moving band' method was used.[9] This method was chosen because of the variable follow-up period. With this method the mean follow-up time and the mean diameter were calculated for the five patients with the shortest follow-up period. Then the 'band' moved in time, incorporating the sixth patient and excluding the first patient. For these patients a mean follow-up period and a mean diameter were calculated again. This was repeated until the five patients with the longest follow-up period were included. The width of the 'band' thus consisted of five patients and varied with time. So that the individual behaviour of the autograft annulus and sinus diameters could be clarified, the diameter increase was shown for each patient with at least two measurements.

For comparison and the relative increase of pulmonary autograft annulus and sinus diameters after the operation, only patients with all measurements available were analyzed.

For two patients without an epicardial echocardiogram after cardiopulmonary bypass, the annulus measurements before cardiopulmonary bypass were used. A *t* test with paired variables was used for the difference of the mean at different time points. Beside this test we perfomed a repeated-measurements analysis, with four measurements of the autograft annulus diameter and three measurements of the autograft sinus diameter. This analysis was performed with multivariate analysis of variance (MANOVA) in SPSS for windows (SPSS, Inc., Chicago, Ill).

The relation of the increase in autograft annulus and sinus diameter to the length of follow-up was tested with a *t* test, dividing the patients into two groups: one group with a transesophageal echocardiogram less than 1 year after the operation and another group with a transesophageal echocardiogram longer than 1 year after the operation. The relation of the increase in autograft annulus and sinus diameter to the severity of aortic regurgitation was tested with a *t* test, dividing the patients into two groups according to the semiquantitative measurement of aortic regurgitation (none and trivial vs. mild and moderate).

The intratechnique variability consisted of the variability within one observer, using five different images for measurements. The standard deviation of these measurements was calculated. The mean of these standard deviations for each level at each time point was determined and regarded as characteristic for the intratechnique variability. The interobserver variability was determined by the mean difference between two observers and the standard deviation of this difference. Statistical significance for all analyses was assumed if the *p*-value was less than 0.05.

Results

Patients

Two patients died in hospital (5.6%). One patient, preoperatively in cardiogenic shock, died 4 hours after the operation of a pulmonary embolus originating from the prostatic plexus. The other patient died 2 weeks after surgery of low output; this patient had required a second operation for aortic arch bleeding resulting from to mediastinitis and sepsis and could not be weaned from cardiopulmonary bypass. The mean follow-up of the 34 surviving patients was 2.3 years (range 0.3 to 6.0 years). There were no reoperations for autograft failure, thromboembolic complications, or instances of endocarditis during follow-up. One patient was reoperated on 2 years after the initial operation for significant pulmonary stenosis at the distal suture line of the pulmonary allograft with secondary tricuspid regurgitation. One patient was in New York Heart Association class II at most recent follow-up; the remaining patients were all in class I.

Diameters

Twenty-eight epicardial echocardiograms before cardiopulmonary bypass were of sufficient quality for pulmonary annulus measurement. The image quality distal to this level was poor and measurements were not reliable. Epicardial echocardiograms after cardiopulmonary bypass were available in 32 patients. Annulus measurements before and after cardiopulmonary bypass were available in 25 patients. At discharge the quality of the transthoracic echocardiogram was poor in two patients. In the remaining 32 patients, autograft annulus and sinus diameters could be measured. Transesophageal echocardiography was performed in 26 patients with a mean follow-up time of 1.9 years (range 0.3 to 5.2 years). The mean autograft annulus and sinus diameters could be measured in all patients. The mean values of all available autograft annulus and sinus measurements before and at different timepoints after the operation are shown in Figures 1 and 2 respectively. The individual increase of autograft annulus and sinus diameters of patients with two or more measurements available are presented in Figures 3 and 4 respectively.

All postoperative autograft annulus measurements were available in 22 patients and all postoperative autograft sinus measurements were available in 17 patients. In these patients the diameter increase was determined (Table 1). There was no statistically significant difference between the mean autograft annulus diameter before and directly after cardiopulmonary bypass (26.2 mm and 26.4 mm respectively). The mean autograft sinus diameter directly after cardiopulmonary bypass was 36.5 mm. The mean autograft annulus and sinus diameters were larger at hospital discharge (29.5 and 39.6 mm respectively). At follow-up the mean autograft annulus and sinus diameters were again larger when compared with the findings on the echocardiograms at discharge (31.5 mm and 43.9 mm respectively). The repeated-measurements analysis (MANOVA) indicated that both the autograft annulus and sinus diameters increased to a statistically significant degree during follow-up ($p<0.01$ for both analyses). A small, statistically nonsignificant increase was noted for the autograft annulus diameter before and after cardiopulmonary bypass ($p=0.6$). Measurements thereafter were significantly larger than the initial measurements ($p<0.01$ for both analyses).

The mean increases in autograft annulus and sinus diameters at follow-up relative to the diameters after cardiopulmonary bypass was 5.1 and 7.4 mm, respectively (Table 1). The mean relative increases were 19% and 21% respectively. Almost half of the increases in autograft annulus and sinus diameters (59% and 40% respectively) were noted at hospital discharge; the other part occurred after discharge.

When the patients were grouped according to a follow-up time less than 1 year ($n=14$) and more than 1 year ($n=13$), there were no statistically significant differences with regard to absolute or relative increases of the autograft annulus and sinus diameters ($p>0.4$).

Autograft regurgitation, measured at follow-up with transesophageal echocardiography, was absent in seven, trivial in six, and mild in 13 patients; one patient had moderate aortic regurgitation. When the patients were grouped according to the severity of

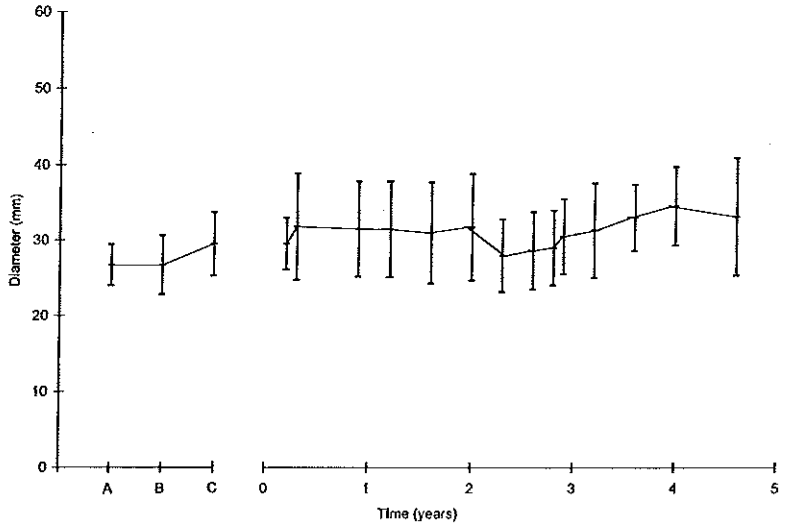

Figure 1 Mean autograft annulus diameter, using all available measurements of 34 patients, before cardiopulmonary bypass (A), after cardiopulmonary bypass (B), at discharge (C) and at follow-up. For the transesophageal echocardiographic measurements at follow-up a 'moving band' method was used. The mean annulus diameter is given with a 70% confidence interval.

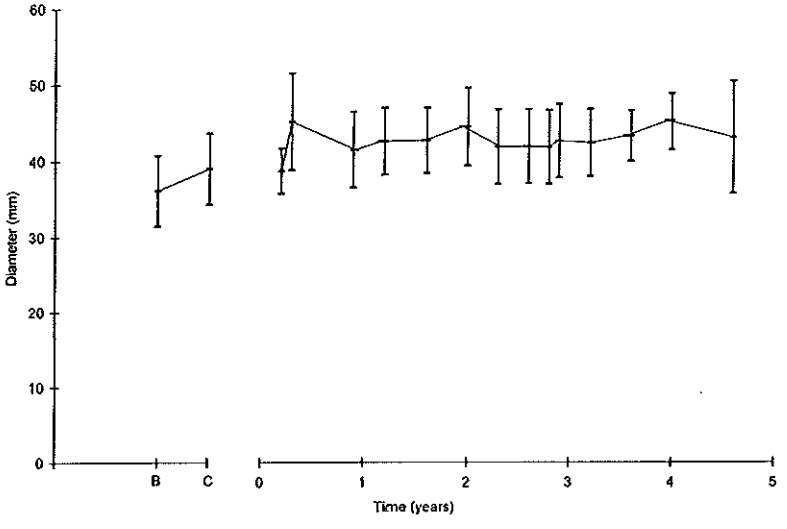

Figure 2 Mean autograft sinus diameter, using all available measurements of 34 patients, after cardiopulmonary bypass (B), at discharge (C) and at follow-up. For the transesophageal echocardiographic measurements at follow-up a 'moving band' method was used. The mean sinus diameter is given with a 70% confidence interval.

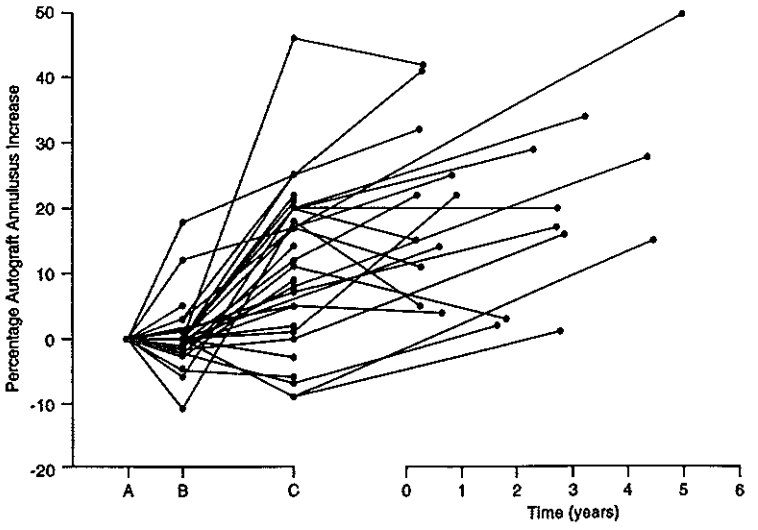

Figure 3 The individual increase of the autograft annulus diameter of patients with two or more measurements available, before cardiopulmonary bypass (A), after cardiopulmonary bypass (B), at discharge (C) and at follow-up.

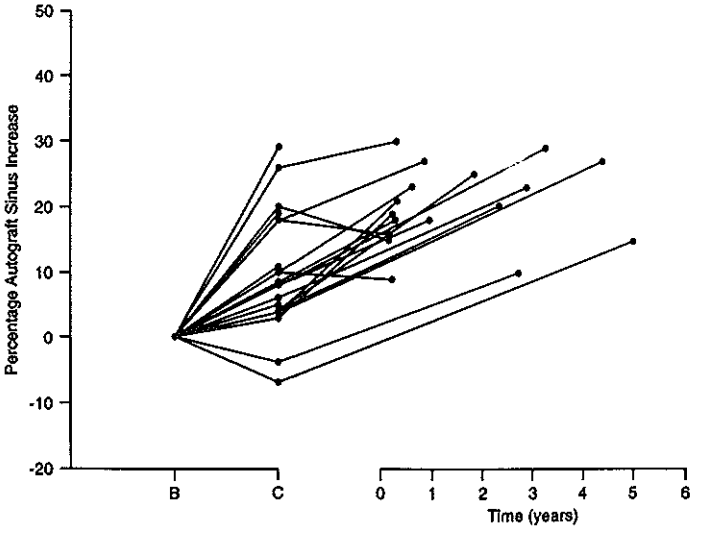

Figure 4 The individual increase of the autograft sinus diameter of patients with two or more measurements available, after cardiopulmonary bypass (B), at discharge (C) and at follow-up.

Table 1 Autograft annulus and sinus diameter measurements (mm) at different times.*

	Annulus (SD; range)	P-value	Sinus (SD; range)	P-value
Before bypass	26.2 (2.8; 21-31)		--	
		NS [a]		--
After bypass	26.4 (3.9; 18-34)		36.5 (4.6; 30-46)	
		<0.001 [b]		<0.001 [b]
Discharge	29.5 (4.0; 24-36)		39.6 (4.8; 26-48)	
		<0.01 [c]		< 0.001 [c]
Follow-up	31.5 (4.2; 22-42)		43.9 (5.1; 35-55)	
Increase [d]	5.1 (2.8; 0-10)	<0.001	7.4 (2.1; 3-10)	<0.001
% increase	19%		21%	

*: Only patients with all measurements available were included. For the autograft annulus and sinus diameter measurements these were 22 and 17 patients respectively. SD: standard deviation. ns: not statistical significant. a, b, c : P-values for differences between measurements before and after cardiopulmonary bypass (a), between measurements after cardiopulmonary bypass and at discharge (b) and between measurements at discharge and at follow-up (c). d: Increase of diameter between measurements directly after cardiopulmonary bypass and at follow-up.

Table 2 Increase in autograft annulus and sinus diameter related to semiquantitatively measured aortic regurgitation at follow-up (22 and 17 patients respectively).

	Aortic regurgitation		
	None, trivial	Mild	P-value
Annulus (mm)	3.3 (23%)	2.7 (19%)	NS
Sinus (mm)	6.8 (19%)	7.8 (21%)	NS

NS: not statistical significant

aortic regurgitation (none or trivial versus mild and moderate), there was no statistically significant difference with regard to absolute or relative increase of the autograft annulus and sinus diameters (Table 2). The three patients with an increase in annulus diameter of more than 30% (Figure 1) had trivial (n=2) and mild (n=1) aortic regurgitation.

Variability

With regard to the intratechnique variability, the standard deviations for autograft annulus measurements before and after cardiopulmonary bypass, at discharge and at follow-up were 0.8, 0.6, 1.0, and 0.9 mm, respectively. For the autograft sinus diameters after cardiopulmonary bypass, at discharge and at follow-up the standard deviations were 1.0, 1.0, and 0.6 mm, respectively. The standard deviation of the measurements of the second observer for autograft annulus at discharge and at follow-up were 1.2 and 1.0 mm, respectively. For the sinus measurements these were 1.3 and 0.9 mm, respectively. The difference between the first and second observer for echocardiograms at discharge and at follow-up was 0.3 mm (SD: 0.2 mm) for the autograft annulus measurements and 0.2 mm (SD: 0.1 mm) for the autograft sinus measurements.

Discussion

The pulmonary autograft procedure for aortic root replacement is a well-established operation technique. It seems to be a highly adequate treatment modality for children with congenital aortic valve disease. Stimulated by the good results in children,[3,10] others have used the procedure in older patients, and short-term results in this age group are promising as well.[2-4] This is confirmed in our series, without reoperations for autograft failure, thromboembolic complications, and endocarditis. Moderate autograft dysfunction occurred in one patient only, and all patients were in New York Heart Association class I at their most recent follow-up examination, except for one patient in class II. Nevertheless, increasing autograft diameter remains a concern in adults with regard to the long-term results.[2,3] Both the strength and durability of the pulmonary valve under systemic pressures, whether implanted in the subcoronary position or as intraaortic cylinder, have been found adequate in the experimental as well as in the clinical situation.[11,12] When the pulmonary autograft is used as a root, the thinner pulmonary wall may be subject to an increase in diameter.[2,13-17] An increase in diameter has been noticed in children and is regarded as concordant with growth, although some children showed a greater increase than appropriate for body surface area.[6,8,10] Studies with adult patients did not show autograft diameter increase, but diameters were studied with the first measurement being at discharge.[2,4] In our study, increasing diameters of the autograft were noted. This could be expected from the work of Weerasena and associates,[18] who showed dilatation of the pulmonary root (more than an aortic root) with increasing pressure

and consider this a physiologic mechanism to decrease the pressure drop across the valve leaflets.

Increase of autograft annulus and sinus diameter was present between the measurements after cardiopulmonary bypass and at follow-up, in absolute (5.1 and 7.4 mm respectively) and in relative terms (19% and 20% respectively). Fifty-nine percent of the annulus increase and 40% of the sinus increase was achieved at 7 to 10 days after the operation. This is congruent with the experiments of Kadoba and colleagues,[20] who implanted a cryopreserved pulmonary allograft in the descending aorta in sheep; 60% of the dilatation occurred in the first week and the remaining 40% in the following year.

Our observations during surgery and those of others[4] show that immediately after disconnection of cardiopulmonary bypass the autograft diameter increases as the consequence of the high aortic pressures. In this study, however, we found that the diameter of the pulmonary autograft annulus did not increase immediately after cardiopulmonary bypass. This may be due to the relatively low aortic pressures (systolic 70 to 80 mm Hg) and to the structure of the pulmonary annulus. The observation of the increasing diameter may account for the distal part of the autograft, which has a thinner wall than the aorta.[13,14]

Because the increases in autograft diameters were the same for patients with a follow-up less and more than 1 year, we conclude that the increase of autograft diameters is most prominent in the first year after the operation. Dilatation was the reason for Ross to stress the importance of autograft implantation within the aortic annulus, which is supported by the left ventricular musculature.[1] For others, the possibility of dilatation was a reason to wrap the autograft root.[15] Wrapping may prevent the increase in autograft diameter found in this study, but makes the operation more complicated, necessitating longer aortic clamp times. The necessity for wrapping is mostly dependent on the relation between the increasing autograft diameter and valvular function.

Aortic regurgitation

Experimental findings and clinical experience with patients with Marfan's syndrome and idiopathic annuloaortic ectasia show a correlation between increase in aortic diameter and aortic regurgitation.[20-22] Hourihan and colleagues[23] reported a series of arterial switch operations for transposition of the great arteries and showed aortic regurgitation to be related to neoaortic (pulmonary artery) root diameters. In our series, with limited follow-up, no association was found between increasing autograft diameter (absolute and relative) and severity of aortic regurgitation.

Limitations to the study

The different echocardiographic techniques may account for confounding effects on the measurements. The epicardial echocardiograms were retrospectively analyzed. It was remarkable, however, that the autograft annulus measurements before and after

cardiopulmonary bypass were not significantly different. Although standard deviations were acceptable with regard to intratechnique and interobserver variability, image acquisition and analyzing methods are vulnerable to imprecise calculations. We are well aware that the number of patients studied is small and the follow-up period relatively short. A longer follow-up period with more patients would possibly strengthen the value of our study.

Conclusion

We conclude that the autograft procedure is an attractive treatment modality for adult patients with aortic valve or root disease. The results are good with regard to hospital mortality, valve related events, symptoms, and valve function. Autograft annulus and sinus diameters increase by 20% within the first year, especially in the first 10 days after the operation. This increase was not associated with aortic regurgitation.

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Chapter 6

Gradient echo MRI for measurement of the pulmonary autograft diameter after aortic root replacement. A validation study

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Submitted for publication.

Abstract

The purpose of this study was the evaluation of pulmonary autograft diameters after transplantation to the aortic root in adults. An MRI protocol using gradient echo cine sequences was developed for measuring pulmonary autograft diameters in 27 adults, 2.3 years (range 0.3 to 6.2 years) postoperative (mean age at operation: 29 years; range 19 to 54 years). Systolic and diastolic diameters were measured on the long-axis view at 5 levels: the subannular region (1), annulus at the hinge points (2), sinus (3), sinotubular junction (4) and 10 mm distal to the sinotubular junction (5). For validation diastolic short-axis views of the sinus level were used. The long axis mean systolic diameters in 25 patients were 36.4, 32.5, 45.2, 36.7 and 37.0 mm for level one to five respectively, and the mean diastolic diameters were 33.9, 31.1, 44.1, 36.3 and 36.3 mm respectively. The correlation coefficient (r^2) between long and short-axis measurements for corresponding sinuses was 0.97. The mean difference (long-axis minus short-axis) was 0.3 mm (SD 1.3 mm).

Conclusion. The MRI protocol selected proved to be eligible for measuring pulmonary autograft diameters. Agreement between long and short-axis measurements for sinus level values was very good. Cine gradient echo MRI is an appropriate technique to evaluate pulmonary autograft diameters during follow-up.

Introduction

Aortic root replacement with a pulmonary autograft is a well established technique to treat aortic valve or root disease.[1-3] Although initially reported series mainly consisted of children, the pulmonary autograft is increasingly used in older patients as well.[1,3-5] The expected long-term durability without degeneration and the absence of the need for anticoagulants are considered to be advantageous in all age groups. However, the pulmonary autograft will be exposed to aortic pressures, which may lead to a diameter increase. This was reported in several series concerning children and interpreted as growth.[2,6,7] In adults, however, studies on the pulmonary autograft diameter are scarce.[3-5] Therefore, follow-up studies with good imaging of the entire pulmonary autograft are necessary.

In literature reported pulmonary autograft studies were performed with transthoracic echocardiography.[2,4,5] The window obtained with transthoracic echocardiography, however, is not always sufficient to visualize the entire pulmonary autograft, especially its distal part. Transesophageal echocardiography has better access to the distal part but is a semi-invasive investigation modality. For these reasons and because of the increasing experience with (gradient echo) magnetic resonance imaging (MRI) in aortic diseases,[8-11] a protocol was designed and applied to measure the pulmonary autograft diameter in systole and diastole. This study reports our initial experience with this protocol in 25 adult patients.

Patients and methods

Patients

From January 1989 until May 1995 38 adult patients underwent aortic root replacement with a pulmonary autograft. The series comprised 21 male and 17 female patients with a mean age of 28.7 years (range 19.0 to 52.0 years). The original disease of the aortic valve or root in these patients was either congenital (n=28), degenerative (n=6), cured endocarditis (n=3), or annuloaortic ectasia (n=1). The patients were operated with standard cardiopulmonary bypass techniques, using moderate hypothermia and cardioplegia. During operation the complete aortic root was excised and the coronary arteries were left in situ with a button of aortic wall tissue. The pulmonary trunk was excised with a proximal ridge of right ventricular tissue. This pulmonary autograft was implanted in the left ventricular outflow tract and the coronary arteries were reimplanted. The right ventricular outflow tract was replaced by a cryopreserved pulmonary allograft. The technique of this operation is shown in Figure 1. Early (hospital) mortality concerned two patients (5.3%). The mean follow-up period of the surviving 36 patients was 2.8 years (range 0.8 to 6.7 years). No patient died during follow-up. Thirty-three patients consented to MRI investigation, which was performed once in each patient.

Technique

MRI examinations were performed on a 1.5T Siemens Magnetom Vision system (Siemens, Erlangen, Germany). The body coil was used for excitation and a quadrature phased array body coil was used for signal reception to obtain a high signal to noise ratio. Patients were positioned supine and ECG electrodes were attached to trigger this data collection.

A three-plane scout was performed. Than a spin echo (SE) sequence (TE=30 ms, motion compensated along the frequency encoding direction and dephased along the slice select direction) was chosen to obtain a good anatomical view of the complete heart with 'black' blood. Transverse slices were acquired with a slice thickness of 8 mm and a 20% interslice gap. Additionally, oblique sections were selected, using the transverse sections as scout, with a slice thickness of 4 mm without a gap. The field of view (FOV) selected ranged from 300 to 380 mm using a 256 matrix. Three excitations were averaged. Data collection was set to approximately 85% of the patients' RR interval, starting the acquisition at the QRS complex. No respiratory compensation was used; patients were asked to breathe superficially.

A velocity compensated gradient echo cine sequence (FISP2D) was selected for multiphasic imaging of the pulmonary autograft. Retrospective ECG gating was used to obtain images during the entire cardiac cycle. Three levels could be encoded with a time resolution of 40 msec using TR=7 ms and a flip angle of 40°. Slice thickness varied between 7 to 9 mm. A matrix of 256 was selected with a FOV of 350 mm. Three excitations were averaged, leading to an acquisition time of approximately 4 to 5 minutes. Alternatively, a breathheld segmented k-space cine sequence (seven lines per segmented phase, 80 ms time resolution) was evaluated with TE=6.1 ms and a flip angle of 25°. Twenty-four heartbeats were used to encode a 256 matrix (breathhold time approximately 15-20 seconds with RR interval of 750 to 1000 ms) using the same FOV and section thickness as above. A single level was evaluated.

Imaging plane selection protocol

SE multislice studies were performed in the transversal plane through the heart and ascending aorta. Depending upon the heart rate (and thus TR), up to 16 sections were obtained. The section through the aortic valve was used as the scout image for a set of oblique images through the pulmonary autograft root, oriented along the long axis of the left ventricular outflow tract and pulmonary autograft. This selection thus entirely depends on the position of the pulmonary autograft in the human body and may vary for each patient. This is also true for the following cine sequence selections. Perpendicular to the oblique SE images a cine sequence along the flow direction through the pulmonary autograft root then was obtained. When images of the SE detail sequence or cine sequence in this direction were not satisfactory, another set of oblique cine slices was oriented through the pulmonary autograft with the previous sequence as scout image. Using any of the obtained (long-axis) oblique cine

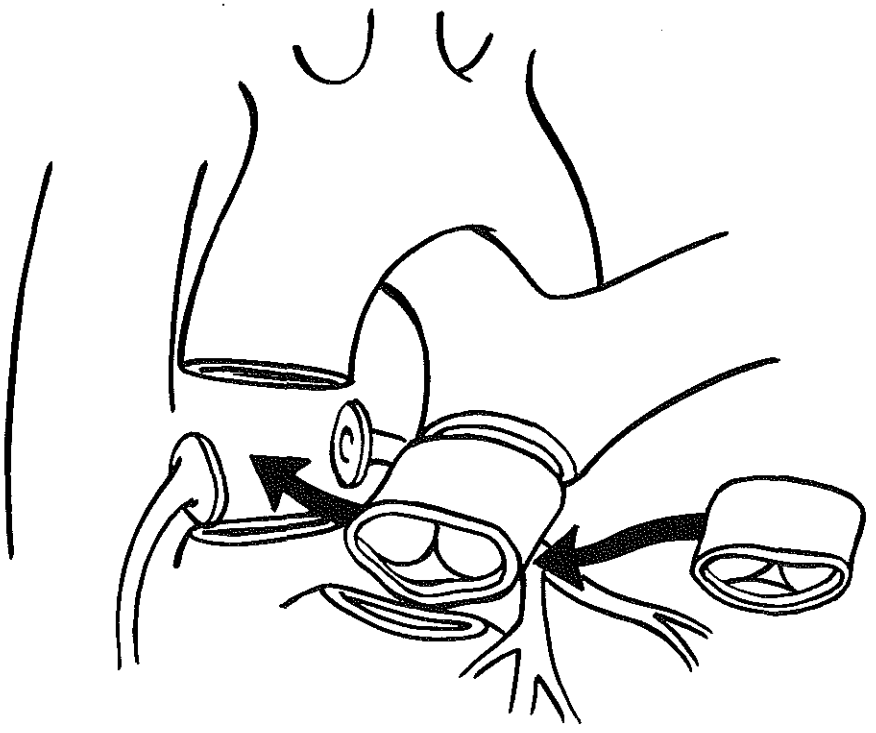

Figure 1 Aortic root replacement with a pulmonary autograft. The aortic root is excised and the coronary arteries are left in situ with a button of aortic wall. The pulmonary trunk is transplanted to the aortic root and the coronary arteries are reimplanted. A cryopreserved pulmonary allograft is inserted in the right ventricular outflow tract.

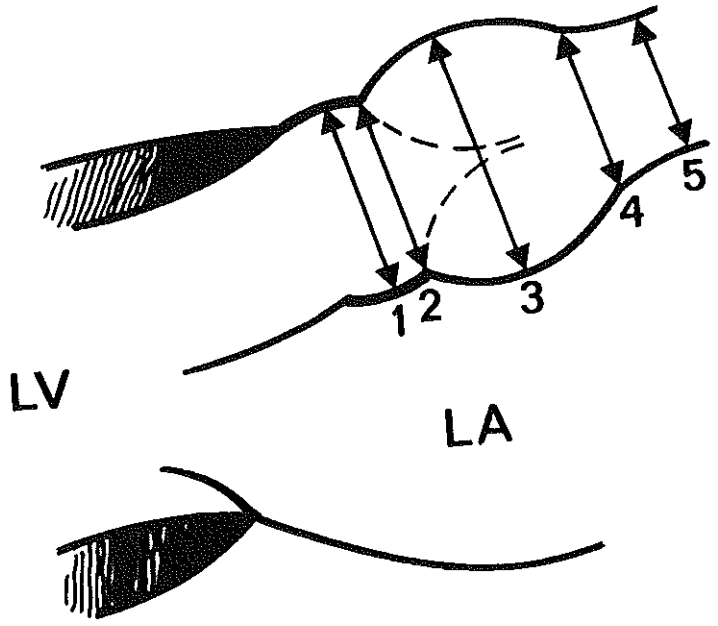

Figure 2 Measurements of the pulmonary autograft diameter at different levels on the long axis. The subannular region (1), the annulus at the hinge points (2), the widest part of the sinuses (3), the sinotubular junction (4) and 10 mm distal to the sinotubular junction (5).

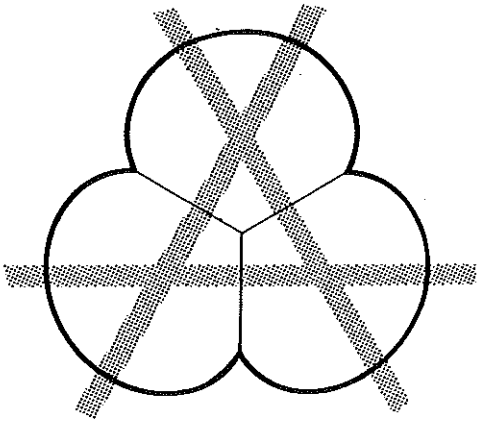

Figure 3 The epitrochoid shape of the aortic and pulmonary sinuses in diastole. Measurements were performed at the largest diameter between two sinuses (dotted areas). Note that when the direction of the dotted lines is slightly changed it has only little effect on the diameter.

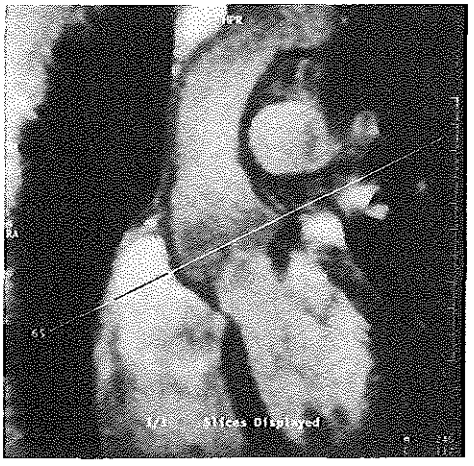

Figure 4A

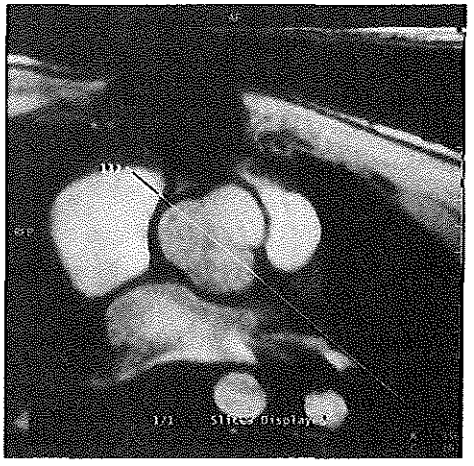

Figure 4B

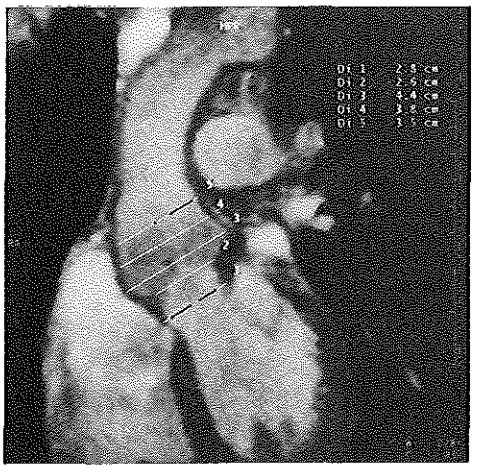

Figure 4C

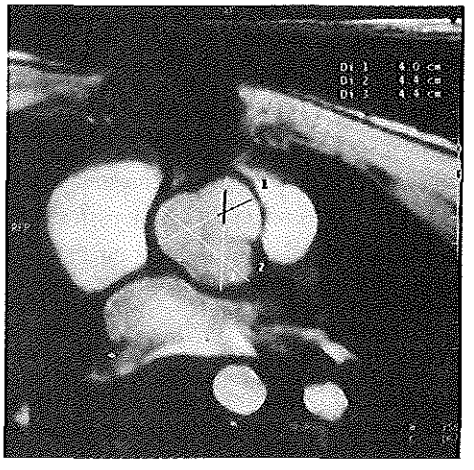

Figure 4D

Figure 4 Long and short-axis images of the autograft sinuses in diastole. A: Long-axis view with the level of the short axis image projected in the sinus. B: Short-axis view with the level of generation of the long-axis view projected in the sinus. C: Long-axis view with the levels of measurement: the subannular region (1), the annulus at the hinge points (2), the widest part of the sinuses (3), the sinotubular junction (4) and 10 mm distal to the sinotubular junction (5). D: Short-axis view with three lines of measurement between two sinuses (1: noncoronary and right coronary sinuses; 2: noncoronary and left coronary sinuses; 3: right and left coronary sinuses).

images as a scout, two (short-axis) cine slices of 5 to 7 mm were obtained perpendicular to the long-axis at the level of the annulus (hinge points) and at the widest diameter of the sinuses respectively (Figures 2 an 4).

Measurements

Pulmonary autograft diameters were measured off-line in systole and diastole at five different levels on the long-axis view (Figures 2 and 4): the subannular region (level 1), the annulus at the hinge points (level 2), the widest part of the sinuses (level 3), the sinotubular junction (level 4) and 10 mm distal from the sinotubular junction (level 5). The three best images in systole and diastole were selected and two observers performed one measurement on each image, based on agreement.

On the diastolic short-axis views at the sinus level views the sinuses could be identified as the right, left or noncoronary sinuses. Three possible sinus diameter combinations were measured (Figures 3 and 4; diameters between right and left coronary sinuses, right and noncoronary sinuses and left and noncoronary sinuses. The planes of the long-axis views were projected on the short-axis view to identify the corresponding short-axis sinus diameter combination.

Statistical analysis

Measurements were performed on three consecutive long-axis views for each level in systole and diastole. The mean systolic and diastolic diameter of each patient at each level was calculated and from these the mean diameter for the entire study population with its standard deviation. The standard deviations for the three measurements at each level at systole and diastole were calculated and from these the mean standard deviations for the entire study population. This was regarded to represent the intramethod variability.

Validation was perfomed by comparison of long-axis and short-axis views of the sinus level (level 3) in diastole. The long-axis measurements were correlated with the corresponding sinuses of the short-axis measurements and with the mean of all three sinus combinations (Figures 3 and 4). For assessing the agreement between long and short-axis measurements the method of Bland and Altman was used.[12]

For the difference between systolic and diastolic measurements at each level a paired *t* test was used to test significance. Significance was assumed if a *p*-value was less than 0.05.

Results

Two patients of the 33 patients who consented to MRI investigation were rejected: one patient for the presence of a pacemaker and another patient for claustrophobic anxiety. In one patient

Table 1 Autograft measurements (mm) at systole and diastole at different localizations in 24 patients after aortic root replacement with a pulmonary autograft.

	Systole				Diastole				Diff
Level	N	D	SD[a]	SD[b]	N	D	SD[a]	SD[b]	P
Subannular region	28	36.4	0.9	7.5	28	33.9	1.9	6.2	0.01
Annulus	29	32.5	1.0	6.7	30	31.1	1.1	5.9	0.06
Sinus	29	45.2	0.9	6.2	30	44.4	0.6	5.8	0.06
Sinotubular junction	28	36.7	1.3	4.7	29	36.3	0.9	4.6	0.5
Distal part	27	37.0	1.4	5.8	28	36.3	0.8	5.6	0.2

D: diameter. SD: standard deviation. Diff: difference. a: Mean standard deviation of each diameter. b: Standard deviation of the mean diameter. P: p-value for paired t test for the difference between systolic and diastolic diameters.

the image quality was inadequate due to respiratory artefacts. The mean systolic and diastolic pulmonary autograft diameters of the remaining 30 patients at different levels are listed in Table 1. In these patients some levels could not be measured due to motion artefacts or artefacts caused by metal sternal wires, this accounts for $n<30$ at some levels in Table 1.

Intramethod variability

The standard deviation of the systolic diameters ranged from 0.9 to 1.4 mm for the different levels. The diastolic measurements were slightly less variable, ranging from 0.6 to 1.1 mm (Table 1). This is near the pixel size of the reconstruction (1.4 mm). The sinus level showed the lowest variability, in systole as well as in diastole. The difference between the systolic and diastolic measurements was significant for the subannular region ($p<0.05$) and borderline significant for annulus and sinus ($p=0.06$). The two distal levels of the pulmonary autograft showed no significant differences (Table 1).

Validation

In 18 patients comparison of long-axis measurements with short-axis measurements was possible; in five patients two comparisons were available, resulting in 23 data pairs. The correlation coefficient between the long and corresponding short-axis measurements was 0.97 (Figure 5A). The mean difference was 0.3 mm with a standard deviation of 1.3 mm (Figure 6A). When the long-axis measurements were compared with the mean of all three sinus combinations (Figure 3) the correlation coefficient was 0.85 (Figure 5B). The mean difference then was 1.5 mm with a standard deviation of 3.2 mm (Figure 6B).

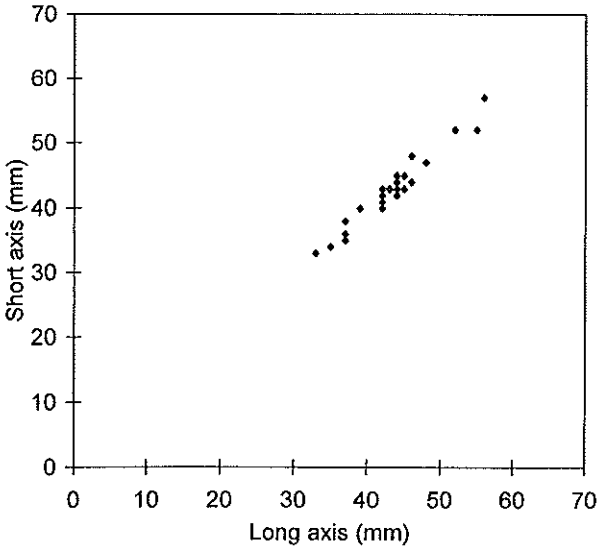

Figure 5A Correlation between long axis diameters at the sinus level in diastole and the corresponding sinuses at the short axis.

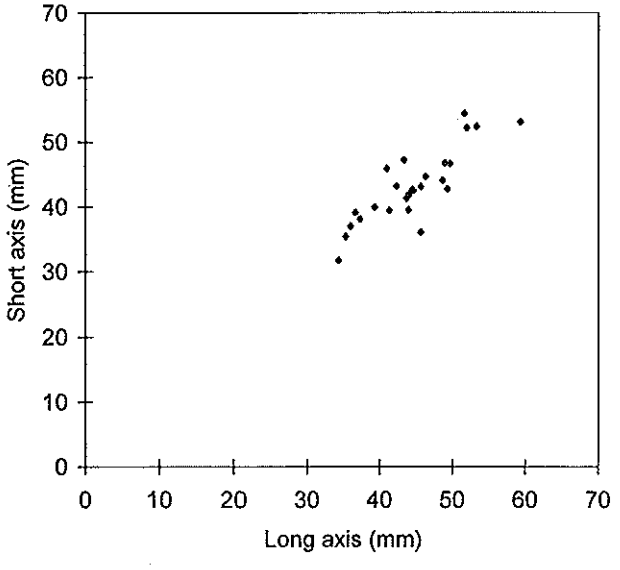

Figure 5B Correlation between long axis diameters at the sinus level in diastole and the average of three sinus measurements at the short axis.

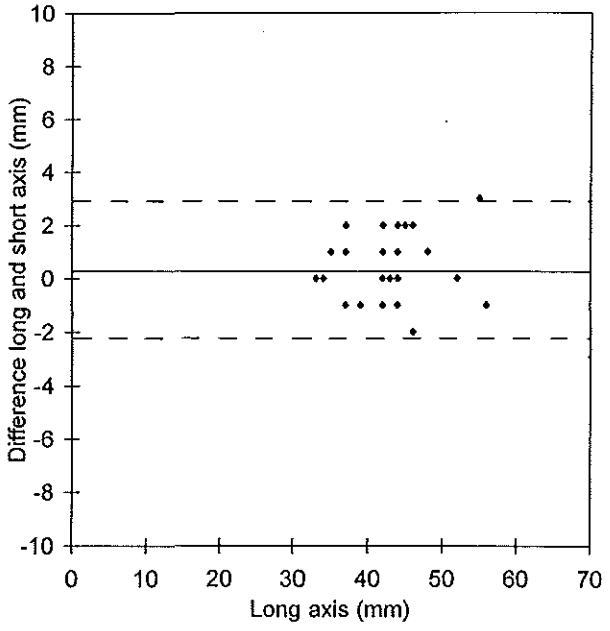

Figure 6A Difference between long axis diameters at the sinus level in diastole and the corresponding sinuses at the short axis. The mean difference (0.03 mm) with two standard deviations are given.

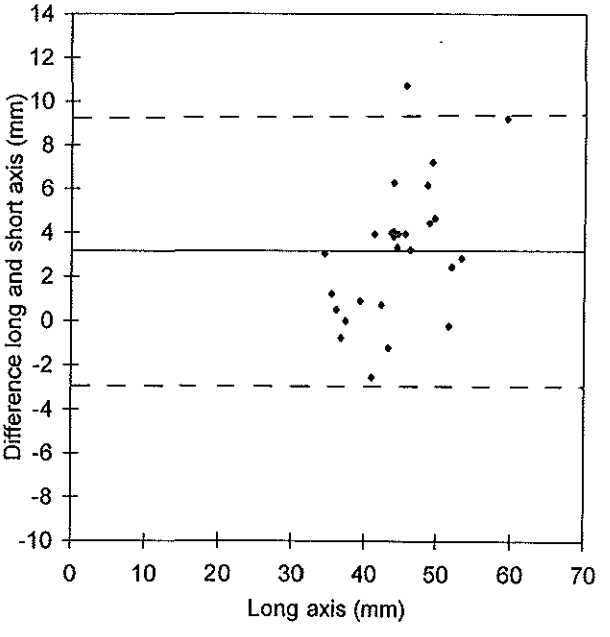

Figure 6B Difference between long axis diameters at the sinus level in diastole and the average of three sinus measurements at the short axis. The mean difference (1.5 mm) with two standard deviations are given.

Discussion

MRI has proven its value in various cardiac diseases[9,13-15] and aortic disease.[9,16-19] Aortic and pulmonary diameter measurements distal to the root have been performed,[8,13,20] but studies with MRI on the different parts of the aortic (or pulmonary) root are limited.[21] We developed a protocol to measure the aortic root at different levels using gradient echo images, because of its ability to cover the entire cardiac cycle.[9,10] With this protocol adequate images could be obtained of the pulmonary autograft after transplantation to the aortic root.

We used long axis images for diameter measurements because these are used in echocardiography.[22,23] The intramethod variability of the diameter measurements was regarded acceptable and it was comparable to echocardiographic measurements.[22,24] The slightly lower intramethod variability of the diastolic measurements suggests a better quality of the images in diastole. This corresponds to our subjective observations and may be due to less turbulent flow and movement of the heart during diastole.

We tested the validity of MRI measurements by comparing long-axis and short-axis measurements of the sinus level in diastole. In our protocol short-axis sections were made at the annulus and sinus level. The annulus level was not appropriate for comparison because it is proximally and distally bound by the wider subannular region and sinus respectively (Figure 2). The thickness of the short-axis slices was 10 mm and the annulus, the narrowest part within this slice cannot be identified. Apart from this, a small deviation of the direction of the short axis leads to inadequate sectioning through the annulus. The sinus level is better for comparison. At this level the maximal diameter was sought (Figure 3). With the use of 10 mm slices the short axis plane mostly incorporated these maximal diameters. Because of the epitrochoid form of the sinuses the direction of the plane is of lesser importance.[25]

When the corresponding sinuses on long and short axis were compared, the correlation and agreement were very good. When all three possible sinus diameter combinations on the short axis were averaged, correlation and agreement decreased, indicating that the sinuses have different sizes.

Diameter changes during the cardiac cycle have been reported.[22,24,26] In our study the differences were of lesser significance when the level of interest was further away from the heart, suggesting lesser elastic properties at the distal part of the autograft compared to the subannular, annulus and sinus levels. The subannular region consists of the thin right ventricular muscular cuff of the autograft which is a flexible structure, thus causing significant differences between systolic and diastolic diameter measurements.

Two patients were rejected from the study: one patient with a pacemaker and another patient for claustrophobic anxiety. In one patient no diameters could be measured because of respiratory artefacts. These rejections are specifically related to the MRI technique. Another disadvantage was the rather long acquisition time necessary to finish the protocol; at least 40

minutes were necessary for each patient. Further development of MRI, in particular the development of T2 weighted 3D volume breathhold techniques,[27,28] may reduce these acquisition times. Artefacts of the metal sternal wires were always present. When present in the field of interest, another set of slices with a different angle was required to get a clear image of the pulmonary autograft. In all patients these artefacts could thus be restricted to non important areas.

Aortic root replacement with a pulmonary autograft needs a scrupulous follow-up with regard to the pulmonary autograft diameter.[2-4] The pulmonary autograft annulus diameters obtained with MRI in this study (a mean of 32.5 mm and 31.1 mm for systolic and diastolic measurements respectively) are larger than aorta or pulmonary artery annulus at post-mortem studies, with mean aortic annulus diameters below 25 mm and mean pulmonary diameters around 25 mm.[29-31] When compared to echocardiographic studies with normal aortic dimensions, the pulmonary autograft annulus, sinuses, ridge and proximal aorta diameters were larger as well.[22,23,32] The same is true when the pulmonary autograft annulus diameters were compared with normal pulmonary annulus measurements.[26] It is obvious that native aortic or pulmonary root diameter measurements are not eligible as reference values for the pulmonary autograft in the aortic position. Another explanation may be that MRI is not eligible for comparison with post-mortem or echocardiographic studies. For this reason a study is going on, comparing the MRI measurements with echocardiographic measurements.

The pulmonary autograft diameter measurements obtained in this study with MRI can be repeated during follow-up. The same individual parameters can be used to perform the same measurements. This may be an appropriate method to evaluate the fate of the pulmonary autograft diameter in time.

In conclusion, we developed an MRI protocol for measuring pulmonary autograft diameters, at different levels in systole and diastole. The agreement between long and short axis measurements at the sinus level was very good. MRI may be useful to evaluate pulmonary autograft diameters during follow-up in a noninvasive manner. Further development of MRI may reduce aquisition times in the near future.

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Chapter 7

A comparison of adult pulmonary autograft diameter measurements with echocardiography and magnetic resonance imaging

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Abstract

Thirty-eight consecutive patients underwent aortic root replacement using the pulmonary autograft. Investigation was performed with transthoracic echocardiography (TTE), transesophageal echocardiography (TEE) and magnetic resonance imaging (MRI) in 31, 27 and 27 patients respectively. The mean age at operation was 28.7 years (range 19.0 to 52.0 years) and the follow-up period was 2.8 years (range 0.8 to 6.7 years). The pulmonary autograft diameter was measured at the subannular region (1), annulus at the hinge points of the valve leaflets (2), sinus (3), sinotubular junction (4) and at the distal part of the autograft (5). With TEE the mean systolic measurements at levels 1 to 5 were 32, 31, 42, 35 and 34 mm respectively. The corresponding diastolic measurements were smaller: 25, 28, 42, 35 and 34 mm respectively. There was no significant difference between TTE and TEE measurements of the proximal autograft (levels 1 to 3). Diameters obtained with MRI were 1 to 3 mm larger than those obtained with TTE and TEE ($p<0.05$), except the annulus at systole ($p>0.3$).

Conclusion. The mean pulmonary autograft diameters with TTE, TEE and MRI were larger than native aortic and pulmonary diameters of a normal population in the same age group. Diameters of the distal two levels could not be imaged reliably with TTE. MRI diameter measurements were in general larger than with echocardiography.

Introduction

Aortic root replacement with a pulmonary autograft is a relatively new but established surgical technique to treat aortic valve or root pathology. Although initial series mainly reported on children, the pulmonary autograft is nowadays also used in older patients.[1-4] The expected long-term durability and the absence of the need for anticoagulants are advantageous for all age groups. Initially the pulmonary autograft was implanted 'freehand' inside the native aorta.[1,5] Currently many surgeons prefer aortic root replacement, using the pulmonary valve and trunk as a functional unit.[1] However, the pulmonary autograft is exposed to systemic pressures, which may lead to an increase in pulmonary autograft diameter.[6,7] An increase of the pulmonary autograft annulus diameter was reported in several pediatric series and interpreted as growth.[8-10] In adults, however, studies on the postoperative pulmonary autograft diameter are scarse.[2,11] Beside pulmonary autograft annulus measurements, it may be important to measure diameters of the distal part of the pulmonary autograft. Bellhouse in 1973 already stressed the importance of a normal geometry of the sinotubular junction to prevent aortic regurgitation[12] and redressing this geometry was successful in dissolving aortic regurgitation.[13]

In our experience the distal part of the aortic root, and thus the pulmonary autograft in the aortic position, cannot be viewed with the available TTE window. In order to validate the TTE measurements of the proximal part of the pulmonary autograft and to find better imaging methods for the entire pulmonary autograft, comparison was made with transesophageal echocardiography (TEE) and magnetic resonance imaging (MRI). TTE and TEE are well established techniques for cardiac and aortic imaging but few data have been reported on the relative value of these methods for aortic root diameter measurement.[13] MRI is a fast developing imaging method and is increasingly used in cardiologic practice in the last decade.[14] Its value is reported for various diseases and abnormalities of the heart, aorta and pulmonary artery.[15-19] However, diameter measurements of the aortic root with MRI have only rarely been reported.[20]

The purpose of this study was to compare measurements of pulmonary autograft diameters in systole and diastole at different levels in adults with TTE, TEE and MRI.

Patients and methods

Patients

From January 1989 until May 1995 38 consecutive adult patients underwent aortic root replacement with a pulmonary autograft. There were 21 males and 17 females with a mean age of 28.7 years (range 19.0 to 52.0 years). The original cardiac pathology of the patients was either congenital (n=28), degenerative (n=6), cured endocarditis (n=3) or annuloaortic ectasia (n=1). A discrete subaortic stenosis was present in two patients in addition to valvular stenosis. The patients were operated upon with standard cardiopulmonary bypass techniques, including moderate hypothermia and cardioplegia. During operation the complete aortic root was excised and the coronary arteries were left on a button of aortic wall tissue. The pulmonary trunk, including the sinotubular ridge, was excised with a proximal ridge of right ventricular tissue. The pulmonary autograft was transplanted to the left ventricular outflow tract and the coronary arteries were reimplanted. No attempt was made to wrap the base of the autograft. The pulmonary trunk was replaced by a cryopreserved pulmonary allograft in 37 patients and an aortic allograft in one patient.

Hospital mortality concerned two patients (5.3%). The mean follow-up period of the surviving 36 patients was 2.8 years (range 0.8 to 6.7 years). No patient died during follow-up. One patient was reoperated two years after the pulmonary autograft procedure for significant peripheral pulmonary stenosis at the distal sutureline of the pulmonary allograft (peak gradient: 77 mm Hg), resulting in severe tricuspid regurgitation. Autograft failure, thrombo-embolic complications or endocarditis did not occur during the follow-up period.

Measurements

Follow-up for patients after the pulmonary autograft procedure consists of a yearly visit to the outpatient clinic with clinical examination and TTE. All patients were requested to undergo TEE and MRI investigation. The (postoperative) follow-up period of the patients varied as mentioned above. The time interval between the three investigations was as short as possible, with a maximum of 3 months.

Echocardiography

Echocardiograms (TTE and TEE) were made with a Vingmed (Vingmed CFM 750, Horten, Norway) or with a Toshiba (Toshiba SSH 140-A, Otawara, Japan) echocardiographic system and recorded on VHS video-tape. For TTE a 3.5 MHz transducer was used. Multiplane TEE was performed with a 5 MHz probe (Oldelft Instruments, Delft, The Netherlands). Measurements were made off-line using a two-dimensional contour acquisition program on a personal computer with electronic calipers, which were calibrated against fixed calibration markers on the two-dimensional images. If possible, pulmonary autograft diameters were

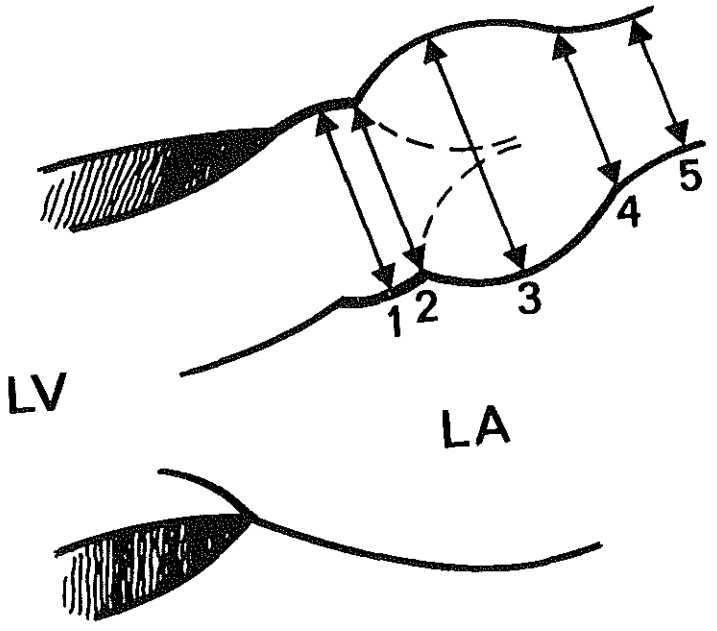

Figure 1 Levels of diameter measurements of the pulmonary autograft: subannular region (1), annulus at the hinge points of the pulmonary autograft leaflets (2), sinus at its largest diameter (3), sinotubular junction (4) and distal part of the pulmonary autograft (5).

measured at 5 levels (Figure 1): the subannular region (level 1), the annulus at the hinge points of the valve leaflets (level 2), the sinus at its largest diameter (level 3), the sinotubular junction (level 4) and 10 mm distal from the sinotubular junction (level 5). On TTE this was done in the parasternal long axis plane from a two-dimensional image, using the inner wall distance. TEE measurements were obtained from the mid esophagus, in a semi-longitudinal plane with a long-axis image, equivalent of TTE. For TTE as well as TEE the right coronary sinus, the right leaflet hinge point, the noncoronary sinus and the noncoronary leaflet hinge point were identified. For each level measurements were performed in systole and diastole. Systolic measurements were obtained at maximal opening of the autograft leaflets. Diastolic measurements were obtained from a frame with maximal opening of the mitral valve, subsequent to the systolic frame. Of each echocardiogram three systolic and three diastolic frames with the best image quality, were selected and two independent observers performed the measurements at each frame.

MRI

The magnetic resonance examinations were performed on a Vision MR system with a 1.5 T / 2.0 T Helicon superconductive magnet (Siemens, Erlangen, Germany). Imaging was carried out at 1.5 T. Spin Echo (SE) studies were performed with the optimized cardiac sequence provided by the manufacturer (T1 weighted with long echo times and additional dephasing). Repetition time (TR) was set to approximately 85% of the individual patient R-R interval, acquisition was synchronized to the heart cycle by prospective cardiac gating. No respiratory compensation was used. The first multislice studies were performed in the transverse plane through the heart and ascending aorta (slice thickness 8 mm). The section through the pulmonary autograft valve was used as the scout image for a set of oblique images (slice thickness 4 mm) oriented along the long-axis of the left ventricular outflow tract and pulmonary autograft.

Gradient echo cine sequences (FISP2D) were used for multiphasic imaging of the pulmonary autograft. TR and echotime (TE) were 40 ms and 7 ms respectively, flip angle was 40°. Slice thickness was 7 to 9 mm. Two or three slices were obtained in a sequence. Retrospective ECG gating was used to obtain images during the entire cardiac cycle, respiratory compensation was not used. Alternatively, a breath-held cine sequence (segmented FLASH) with TR=80 ms, TE=6.1 ms and a flip angle of 25°, was used with an acquisition time of 16 s (one level).

These cine sequences were oriented on the oblique SE images through the pulmonary autograft root. When images were not satisfactory, another set of oblique cine slices was oriented through the pulmonary autograft with the previous sequence as scout image.

Images were reconstructed on a 256 x 256 matrix to a pixel size of approximately 1.4 x 1.4 mm depending on the field of view. Three images in systole, with maximal opening of the autograft leaflets, were selected as well as three mid-diastolic images. At these images the pulmonary autograft diameter was measured at the same five levels as described for echocardiography, using the outer boundaries of the bloodflow.

Statistical analysis

For TTE and TEE two observers performed three measurements at each level in systole and diastole. For MRI, two observers judged each of three images images together and reached three consensus values. The observers were blinded for the information of other imaging modalities. For each imaging modality the mean systolic and diastolic diameters at each level were calculated for the entire study population. The mean difference between the imaging modalities was calculated only from the patients in whom TTE, TEE and MRI measurements were available; from these the mean difference for all patients with its standard deviation. A paired *t* test was used to test the significance of these differences. Note that the three *t* tests (TTE-TEE, TTE-MRI and TEE-MRI) are in fact multiple comparisons. The *p*-value should

hence be interpreted with some caution. Consequently, a $p<0.01$ is considered statistically significant instead of the standard level of 0.05. The differences between the imaging modalities were illustrated by the method of Bland and Altman.[22] The significance of the difference between systole and diastole was tested with a paired t test. Statistical significance in all analyses was assumed when $p<0.05$.

Variability

For each imaging modality, at each level in systole and diastole, the standard deviation was calculated from the three measurements of each observer for TTE and TEE measurements, and three consensus values for the MRI measurements. From these the mean standard deviation of the entire study population was calculated. This was regarded to represent the intramethod variability. Interobserver variability (TTE and TEE) was determined by the mean difference between the measurements of the two observers, with the standard deviation.

Results

TTE was available in 33 of the 36 surviving patients. In two of these patients the image quality was inadequate and no diameters could be measured. In the remaining 31 patients the sinotubular junction and the distal part of the pulmonary autograft were visible in 14 (45%) and five (16%) patients respectively.

TEE investigation was initiated in 28 patients. The probe could not be inserted in one patient. In the other 27 patients all measurements could be performed, except the sinotubular junction and the distal part of the pulmonary autograft in one and four patients respectively.

MRI investigation was approved by 33 patients. Two patients were rejected: one patient for the presence of a pacemaker and the other for claustrophobic anxiety. The time needed to finish the protocol varied between 40 and 50 minutes for each patient. In one patient the image quality was poor due to respiratory artefacts. In the remaining 30 patients some levels could not be measured due to motion artefacts or artefacts caused by metal sternal wires; for the levels 1 and 5 this concerned two patients and for level 4 this concerned one patient. In general, MRI was not possible to perform in as many patients as compared with TTE and TEE, 91% (30/33) versus 94% (31/33) and 96% (27/28) respectively.

The mean diameters of the pulmonary autograft at different levels in systole and diastole are shown in Table 1. The differences between the imaging modalities, of the patients with all three imaging modalities available are shown in Table 2 and the significance of the difference between the diameters in systole and diastole are shown in Table 3.

Table 1 Mean diameters of the pulmonary autograft and their standard deviations.

	TTE		TEE		MRI	
Level	D	(range)	D	(range)	D	(range)
Subannular region, systolic	31.9	(20.7 - 45.8)	31.7	(19.5 - 43.8)	36.4	(25.0 - 54.5)
Subannular region, diastolic	27.3	(15.0 - 39.1)	25.4	(15.0 - 34.0)	33.9	(23.3 - 44.7)
Annulus, systolic	31.9	(22.3 - 43.4)	30.7	(20.5 - 41.3)	32.5	(23.0 - 47.5)
Annulus, diastolic	29.1	(18.4 - 38.6)	27.5	(16.0 - 37.0)	31.1	(18.0 - 43.7)
Sinus, systolic	41.9	(28.7 - 53.2)	42.3	(31.5 - 55.0)	45.2	(34.7 - 57.5)
Sinus, diastolic	42.1	(31.6 - 52.5)	41.5	(29.7 - 54.5)	44.4	(34.3 - 59.3)
Sinotubular junction, systolic	38.7	(29.8 - 49.3)	34.8	(28.1 - 45.1)	36.7	(26.5 - 43.0)
Sinotubular junction, diastolic	37.8	(28.7 - 46.8)	34.5	(27.0 - 44.1)	36.3	(27.7 - 49.0)
Distal part autograft, systolic	--	--	34.2	(25.6 - 48.4)	37.0	(27.0 - 53.7)
Distal part autograft, diastolic	--	--	34.1	(25.5 - 46.4)	36.3	(30.3 - 48.0)

TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; MRI: magnetic resonance Imaging; D: mean diameter (mm).

Table 2 Comparison of pulmonary autograft diameters between different imaging modalities.*

	TEE-TTE			MRI -TTE			MRI-TEE		
Level	N	Diff	P	N	Diff	P	N	Diff	P
Subannular region systolic	26	0.8	0.2	27	3.6	<0.01	24	2.9	<0.01
Subannular region diastolic	25	-1.1	0.2	26	6.2	<0.01	24	8.2	<0.01
Annulus systolic	26	-0.6	0.3	28	0.1	0.9	25	0.6	0.4
Annulus diastolic	25	-0.7	0.4	28	1.8	0.04	26	2.8	0.01
Sinus systolic	26	0.6	0.3	28	2.9	<0.01	25	2.4	0.01
Sinus diastolic	26	-0.1	0.8	28	2.4	<0.01	26	2.5	<0.01
Sinotubular junction systolic	10	-4.0	<0.01	14	-2.9	0.01	23	2.2	<0.01
Sinotubular junction diastolic	11	-4.2	<0.01	15	-2.6	0.02	24	1.8	<0.01
Distal part autograft systolic		--	--		--	--	20	2.1	<0.01
Distal part autograft diastolic		--	--		--	--	20	1.2	0.04

*: The mean difference (mm) between TTE, TEE and MRI are given and the statistical significance of this difference; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography; MRI: magnetic resonance imaging; Diff: difference (mm); P: paired *t* test for the differences of the mean.

Table 3 Statistical significance of the differences between systolic and diastolic measurements of the pulmonary autograft diameters with TTE, TEE and MRI.*

	TTE	TEE	MRI
Level	P	P	P
Subannular region	<0.001	<0.001	0.01
Annulus	<0.001	<0.001	0.06
Sinus	0.05	<0.001	0.06
Sino-tubular junction	--	0.3	0.5
Distal part autograft	--	0.6	0.1

*: The mean systolic and diastolic pulmonary autograft diameters are given in Table 1.
TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; MRI: magnetic resonance imaging; P: paired *t* test for the difference of the mean between systolic and diastolic measurements.

Echocardiography

Systolic and diastolic diameter measurements with TTE and TEE were reasonably similar for the subannular region, annulus and sinus (Table 2, Figures 2A and 2B). On TTE the measurements of the sinotubular junction were statistically significant larger than on TEE. No differences were calculated for the distal part of the pulmonary autograft because TTE measurements at this level could only be performed in four patients (Table 2). Both TTE and TEE showed significant diameter differences between systole and diastole at the subannular region, annulus and sinus ($p<0.05$) (Table 3). The diameter at the sinotubular junction and the distal part of the pulmonary autograft did not show significant differences during the cardiac cycle at TEE (Table 3).

MRI

The MRI measurements were only congruent with echocardiography (TTE and TEE) for the autograft annulus diameter measurements in systole (Table 2, Figures 2C-2F). For the autograft annulus at diastole and for the other levels, MRI diameters were larger when compared with TEE: At the subannular region in diastole MRI measurements were 8.2 mm larger and the other diameters were 1.2 to 2.9 mm larger (Table 2). The difference between the diameters at systole and diastole showed the same pattern as echocardiography. Less extreme differences were noted at the annulus and sinus levels (Table 3).

Variability

The intramethod variability of TTE, TEE and MRI were represented by the standard deviations of the measurements of each observer. Variability of the TEE measurements was somewhat smaller than TTE measurements (Appendix, Table A). The subannular region in diastole had the highest standard deviation in both TTE and TEE, ranging from 1.5 to 1.9 mm. The standard deviation of the measurements at other levels varied between 0.6 and 1.6 mm (Appendix, Table A), with the smallest variability at the sinus level in diastole. The standard deviation of MRI overall was small, indicating that MRI measurements within one patient, within one session, were reproducible.

The interobserver variability (TTE and TEE) was represented by the mean difference between the observers and the standard deviation. The mean differences ranged from -0.6 to 1.2 mm with standard deviations between 0.5 and 1.5 mm (Appendix, Table B).

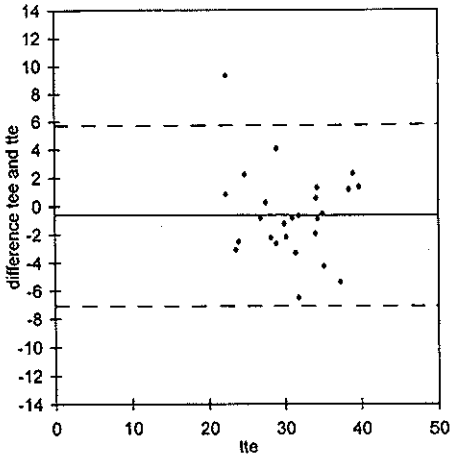

Figure 2A

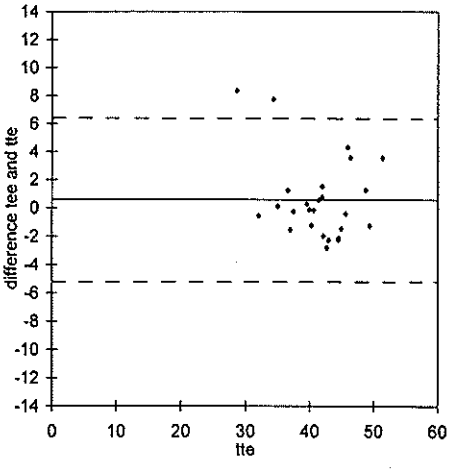

Figure 2B

Figure 2 Differences (in mm) between imaging modalities for the annulus and sinus diameter measurements of the pulmonary autograft in systole. The method of Bland and Altman was used.[22] The x-axis of all figures consists of the diameters measured with TTE. The y-axis of **Figures 2A and 2B** consists of the difference between TEE and TTE regarding the annulus and sinus respectively. The y-axis of Figures 2C and 2D consists of the difference between MRI and TTE. The y-axis of **Figures 2E and 2F** consists of the difference between MRI and TEE. The lines in all figures represent the mean difference with a 95% prediction interval.

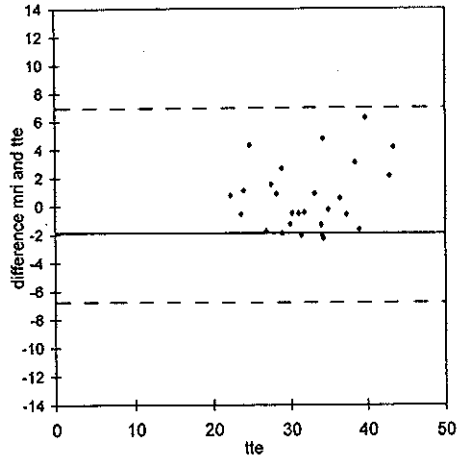

Figure 2C

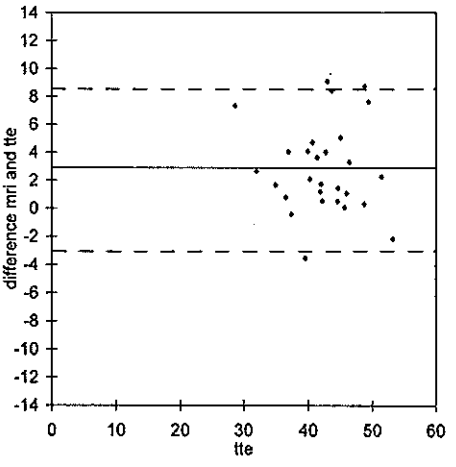

Figure 2D

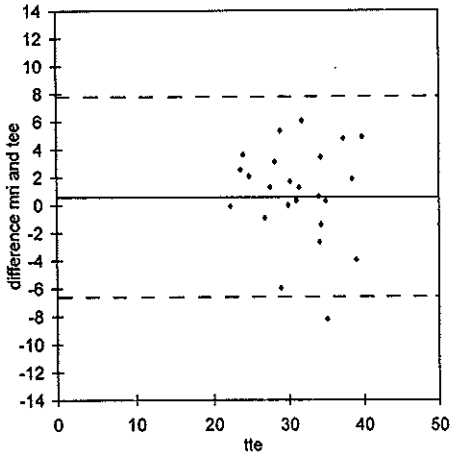

Figure 2E

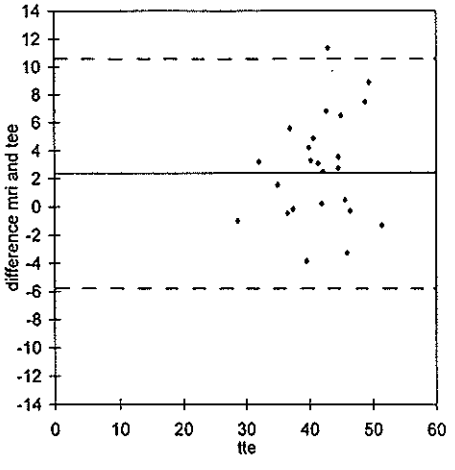

Figure 2F

Discussion

In this study the diameters of the pulmonary autograft in the aortic position were measured at different levels in systole and diastole. Three different imaging modalities were applied. Irrespective of the technique used, the pulmonary autograft diameters were large (Table 1). On echocardiography the mean diameter of the pulmonary autograft annulus (mean values at TTE and TEE higher than 30 mm) was larger when compared with the mean diameter of the native aortic annulus of a normal population in the same age group (mean value ca. 25 mm).[23-25] Roman et al. measured native aortic root diameters at the sinus, the sinotubular junction and the level distal to this junction on TTE. Also at these respective levels the autograft diameters were larger: 42 versus 32 mm, 35 versus 28 mm and 34 versus 29 mm respectively.[23] This mean pulmonary autograft annulus diameter was also larger when compared to the mean native pulmonary annulus diameter in this age group (ca. 25 mm).[26] The differences between mean pulmonary autograft annulus diameters and native aortic and pulmonary annulus diameters were even larger when post-mortem studies were used for comparison.[27-29]

Echocardiography

In this study TTE was not appropriate for visualizing the distal part of the pulmonary autograft. The sinotubular junction was measured in 14 patients, but the diameters were much larger than on TEE and MRI and were not congruent with the diameter differences at other levels. The most distal part of the pulmonary autograft was only visualized in four patients. The differences obtained at these levels are probably related to difficulty with imaging rather than a true difference. For the proximal three levels the diameters on TTE and TEE were not statistically different in systole nor in diastole. Agreement between TTE and TEE for aortic annulus measurements has been reported in one other series.[12] Beside the possibility for adequate visualization of the distal part of the pulmonary autograft, the image quality of TEE was superior to TTE. This was represented by the smaller variability of TEE than TTE.

Diameter changes during the cardiac cycle can be expected from two-dimensional echocardiographic studies of the aortic root.[14,25,26] In our study the proximal pulmonary autograft diameters were significantly larger in systole. The large difference in the subannular region may be due to the presence of the right ventricular muscular cuff at the proximal part of the pulmonary autograft between the native left ventricular outflow tract and the pulmonary autograft annulus. In systole this flexible structure is stretched and properly visualized in contrast to the diastolic images. In this respect the operative technique has been modified. Nowadays, a very small right ventricular cuff is used for proximal implantation of the pulmonary autograft. Others recommend to wrap the proximal part of the autograft to avoid dilatation at this site.[1,7] With TEE, cyclic diameter changes were absent at the sinotubular

junction and the distal part of the pulmonary autograft.

MRI

Although MRI has proven its value in aortic and pulmonary imaging[16-19,30] and diameter measurements distal to the aortic and pulmonary root,[20,31-33] few reports exist on the measurements of the aortic root.[21,34] One study compared aortic root measurements on MRI and echocardiography. The MRI protocol in our study, using gradient echo cine sequences, was adequate to visualize the entire pulmonary autograft in systole and diastole with good agreement of the measurements within patients. The annulus measurements at systole with MRI were not statistically different from the echocardiographic measurements. This may be related to the collagenous structure of the annulus, resulting in a fixed maximal diameter in systole. The other pulmonary autograft diameter measurements were larger on MRI than on echocardiography (TTE and TEE) ($p<0.05$). This is in contrast with the agreement of MRI and TTE measurements of the native pulmonary artery by Fogel et al.[20] Other studies also showed good correlations, but the mean differences between the imaging modalities were not reported.[19,32,33]

The differences between the three imaging modalities, as found in our study, may be explained fourfold. Firstly, the use of cine sequences with MRI in which the outer boundaries of the blood flow were measured, assuming that this represents the inner side of the aorta, rather than the inner side of the aortic wall as with two-dimensional echocardiography. The second explanation may be related to the construction of the MRI images as they consist of many cardiac cycles. Differences in duration of the cardiac cycles may have led to different extensions and/or positional differences of the autograft wall, resulting in larger diameter measurements. This opposes with the real time image aquisition of echocardiographically obtained images. A third explanation for the difference between the measurements at the proximal three levels may be related to the orientation of the sections with MRI; noncircular shape of the annulus and subannular region and different sizes of the sinuses may lead to a substantial variability. The last explanation may account for the differences between the sinus measurements: because the thickness of the slices at MRI was 10 mm, the largest diameter of two sinuses will probably be measured. This contrasts to the extremely thin echocardiographic 'slices' which may not cut both sinuses at their largest diameter.

The advantages of TEE over TTE in this study were the better image quality and the possibility of visualizing the entire pulmonary autograft. However, TEE is semi-invasive and in this study the probe could not be inserted in one patient. MRI is not invasive but the time required to finish the protocol is at least 40 minutes, due to long acquisition times (4 to 5 minutes) for each set of images. Contraindications for MRI may exclude patients, like the presence of a pacemaker or claustrophobic anxiety in our study. Furthermore, MRI is susceptible for artefacts due to respiration and metal sternal wires. TEE and MRI adequately

visualize the entire pulmonary autograft, with smaller variability compared to TTE. However, the standard deviation of MRI measurements may be somewhat smaller because it concerns a comparison of consensus measurements rather than measurements of separate observers. In general, when dilatation of the pulmonary autograft is the subject of a study and diameters of the entire autograft will be measured, it may be advisable to use MRI or TEE during follow-up. This will be done in our series in the future to make firm conclusions on the behaviour of pulmonary autograft diameters during follow-up and its relation to pulmonary autograft valve function.

Limitations to the study

This study compared three imaging modalities. However, a 'golden standard' for measuring the real pulmonary autograft diameters is lacking and the real bias for each technique is unknown.

Conclusion

The mean observed pulmonary autograft diameters are larger than native aortic and pulmonary diameters of a normal population of the same age group. TTE is inadequate for imaging the distal part of the pulmonary autograft. MRI diameter measurements are larger compared with echocardiographically obtained diameters, except for the autograft annulus in systole.

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Appendix

Table A Intramethod variability of the pulmonary autograft diameters.*

	TTE		TEE		MRI
	Obs.1	Obs.2	Obs.1	Obs.2	
Level	SD	SD	SD	SD	SD
Subannular region systolic	1.3	1.1	1.3	1.2	0.9
Subannular region diastolic	1.9	1.5	1.9	1.5	1.9
Annulus systolic	1.2	1.0	0.9	0.8	1.0
Annulus diastolic	1.6	1.4	1.3	1.2	1.1
Sinus systolic	1.3	1.0	0.8	0.6	0.9
Sinus diastolic	1.3	1.2	0.8	0.7	0.6
Sinotubular junction systolic	1.2	1.3	1.0	1.0	1.3
Sinotubular junction diastolic	0.9	0.9	1.0	1.0	0.9
Distal part autograft systolic	--	--	1.3	1.3	1.4
Distal part autograft diastolic	--	--	1.3	1.2	0.8

*: Intramethod variability is given as the mean standard deviation of the measurements (mm) of each observer; TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; MRI: magnetic resonance imaging; Obs.1 and Obs.2: observers 1 and 2; SD: standard deviation (mm).

Table B Interobserver variability of the pulmonary autograft diameters.*

	TTE		TEE	
Level	Diff	SD	Diff	SD
Subannular region systolic	0.6	1.2	0.3	0.6
Subannular region diastolic	0.8	1.4	1.0	1.5
Annulus systolic	-0.3	0.8	0.4	0.9
Annulus diastolic	1.1	1.1	0.0	1.0
Sinus systolic	1.2	1.2	0.2	0.7
Sinus diastolic	1.1	1.1	0.2	0.5
Sinotubular junction systolic	0.8	0.8	-0.3	0.9
Sinotubular junction diastolic	1.1	1.1	-0.2	0.9
Distal part autograft systolic	--	--	0.2	0.9
Distal part autograft diastolic	--	--	-0.6	1.3

*: Interobserver variability is given as the mean difference (mm) between the observers and its standard deviation; TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; Diff: difference (mm); SD: standard deviation.

Chapter 8

General discussion

Anatomical considerations

The second chapter in this thesis provides an anatomical study of the aortic and pulmonary roots. The most striking structure in both roots is the annulus. We regard the annulus as the intricate collagenous structure, interposed between the vessel wall and the ventricular structures, to which the valve leaflets are attached. This collagenous structure is basically a circular band, its distal edge being formed like a three-peaked crown, while its proximal end is characterized by three fimbriated, less pronounced curves, the interleaflet triangles. These collagenous interleaflet triangles contain islets of elastic fibers. Sutton et al. arrived at similar findings.[1] The structure of the annulus, the semilunar valve leaflets, and the wall of the sinuses in both roots are quite similar. This may explain the success of the pulmonary root as a substitute for the diseased aortic root. However, there are some differences. The sinus walls and the interleaflet triangles of the pulmonary root are thinner. The annulus of the pulmonary root is proximally anchored in thin right ventricular myocardium along its entire circumference. This contrasts with the thick left ventricular myocardium and the proximal continuation of more than half of the aortic root annulus in fibrous structures: the membranous septum, the right fibrous trigone, the anterior leaflet of the mitral valve and the left fibrous trigone. Also with regard to the surrounding structures the aorta is better encased. The thick left ventricular myocardium bulges, forming a collar around the proximal part of the aortic root, and the aortic root is wedged between the right and left atrioventricular annuli and atrial myocardium. The pulmonary root is only slightly supported by the thin right ventricular myocardium and the adjacent aorta.

These anatomical findings support the surgical technique in the pulmonary autograft

procedure, consisting of trimming of the autograft to leave only a few millimeters of right ventricular myocardium as suture area. Autograft implantation at the level of the annulus is also obligatory to obtain maximal support of the fibrous structures of the left ventricular outflow tract and the surrounding ventricular and atrial myocardium. This is also stressed by others.[2,3] As a consequence, the supportive structures of the left ventricular outflow tract are regarded as insufficient by some, and the possibility of autograft dilatation was a reason for wrapping the autograft root[4,5] or using coronary buttons to replace native pulmonary sinuses.[6] The use of the intraaortic cylinder technique in aortic roots with normal dimensions is another possibility to ensure support (from the aortic wall).[2,7]

Pulmonary autograft: clinical results

After the introduction of aortic valve replacement with the pulmonary autograft technique by Ross, and its variants involving the subcoronary (1967), intraaortic cylinder (1982) and root replacement techniques (1986),[2,8] we started to use this last technique to treat aortic valve and aortic root pathology in children. Although the long-term results of Ross with subcoronary implantation are good with regard to structural valve degeneration,[9,10] we avoided the technically demanding subcoronary and intraaortic cylinder techniques with their risk of paravalvular leakage and anatomic malpositioning of the valves.[10-12] Another advantage of the root replacement technique is that a possible discrepancy between the aortic annulus diameter and the pulmonary autograft diameter is less important because the entire root is replaced. In addition, the disadvantages related to the use of mechanical, bioprosthetic and allograft valves are overcome. Reoperation for outgrowth is avoided. No structural degeneration, as in bioprosthetic valves and allografts, will occur. There are virtually no thromboembolic complications, and anticoagulants, obligatory with mechanical valves, with the intrinsic risk of hemorrhagic complications, are not necessary.

The feasibility of the procedure in the pediatric age group is shown by the absence of early mortality in our series (Chapter 3). During follow-up, one patient died due to recurrent chronic juvenile rheumatoid arthritis destroying the autograft.[13] Reoperation was necessary for a patient with recurrent acute rheumatic fever destroying the autograft.[14] The pulmonary autograft procedure is contraindicated in patients with chronic juvenile rheumatoid arthritis. In patients with acute rheumatic fever the procedure is relatively contraindicated, depending on the adequacy of antibiotic profylaxis for the disease. This corresponds to the concern of Kumar et al.,[15] who operated on 48 patients with rheumatic fever. After initially good results,[16] three patients had to be reoperated (one patient with recurrent rheumatic activity) despite continuous use of antibiotic prophylaxis.

The clinical outcome of the other patients in our pediatric series was good, and normal

increase of the pulmonary autograft diameter was obtained. The results of exercise capability testing were in accordance with those of age-matched normal children. Signs of left ventricular hypertrophy or myocardial damage on ECG were not found in our patients after 1 year of follow-up. Pulmonary autograft valve stenosis was not present and regurgitation was trivial or mild when present. This good valve function in the medium-term has been reported by others as well.[17] The report of Oury with regard to the Ross Procedure Registry also reports good valve function in the root replacement group in the majority of patients, children as well as adults.[18] However, this registry depends on voluntary participation of surgeons and may therefore not be representative for the entire experience.

In children, left ventricular dimensions often remain abnormal after aortic valve surgery for congenital stenosis, probably related to the remaining pressure gradient across the valve.[19,20] In our study all variables related to left ventricular size and function were within normal limits, except in one patient, contrasting with the abnormal situation before operation. This is in agreement with the results of others.[4,21]

Following the good initial results of the use of the pulmonary autograft in the pediatric age group, the procedure was extended to adults (Chapters 4 and 5), by us as well as by others.[17,22,23] Except for the possibility of diameter increase, all other advantages of the use of a pulmonary autograft are valid for adults as well.

In our adult patient group, two patients died in hospital. This hospital mortality was not caused by the autograft procedure (Chapter 4). One of these suffered from Marfan's syndrome. Although this condition was not the cause of death, Marfan's syndrome is probably not a suitable condition for aortic root replacement using a pulmonary autograft because the disease may affect the pulmonary artery as well.[24] Like in the pediatric age group, thromboembolic complications were not registered in the absence of anticoagulant therapy, and reoperations for degenerative valve failure did not occur. Otherwise unexplained important autograft regurgitation and stenosis were not present.

Pulmonary autograft diameter increase

The most important advantage of the use of a pulmonary autograft in a pediatric population is its increase in diameter with age, suggesting a growth pattern.[17] The study in Chapter 3 confirms the increasing diameter of the pulmonary autograft in patients who were beyond the first postoperative year. Although, in most patients, this increase was less than 20%, there were three patients with an increase of more than 50% (>10 mm). Elkins reported a greater diameter increase of the (freestanding) pulmonary autograft compared to the increase of diameter using the intraaortic cylinder technique. He used the term dilatation for the 'extra' increase. Long-term follow-up is necessary to draw firm conclusions on the behaviour of the

pulmonary autograft diameter and whether there is an abnormal increase. Especially its relation to aortic regurgitation warrants a detailed follow-up. In our pediatric population, however, no correlation could be found between autograft annulus diameter increase and the severity of aortic regurgitation.

Strength and durability of the pulmonary valve under systemic pressures, when implanted subcoronary or as intraaortic cylinder, has been found adequate in the experimental as well as in the clinical situation.[8,25] However, when the pulmonary autograft is used as a root, the thinner pulmonary wall may be subject to an increase in diameter;[5,26-30] mechanical stretching of the pulmonary autograft and adaptation of the collagen and elastic fibers may play a significant role.[31] An increasing autograft diameter may be correlated with aortic regurgitation.[31-34] Therefore, pulmonary autograft diameter increase is not advantageous in the adult population.

When pulmonary autograft diameters are compared to the native pulmonary and aortic roots,[34-37] it is evident that most pulmonary autograft annulus diameters are not within the normal range. The question arises whether these diameters will increase with time and whether aortic regurgitation will develop.

Other studies with adult patients did not show autograft diameter increase, but diameters were compared with the first measurement when the patient was discharged.[22,38] In our study (Chapter 5), an increase of autograft annulus and sinus diameter occurred between the measurements after cardiopulmonary bypass and at follow-up, in absolute (5.1 and 7.4 mm respectively) as well as in relative terms (19 and 20% respectively). Fifty-nine percent of the annulus increase and 40% of the sinus increase was achieved at 7 to 10 days postoperatively. This is similar to the experiments of Kadoba et al., who implanted a cryopreserved pulmonary allograft in the descending aorta in sheep; 60% of the dilatation occurred in the first week and the remaining 40% in the following year.[26]

The increase of pulmonary autograft diameters in the adult population must be the consequence of dilatation rather than growth. This raises questions with regard to the diameter increase in pediatric patients; does it concern real growth (proliferation of cells) or is it merely dilatation due to mechanical stress? Our studies do not provide a solution to this problem. Histological studies in this regard may provide the answer. Because the increase in autograft diameter was the same for patients with a follow-up of less than 1 year compared with patients with a follow-up of over 1 year, we conclude that the increase of autograft diameters takes place largely in the first year after surgery and therefore suggest dilatation to be an important factor in diameter increase after the pulmonary autograft procedure. In our series, with limited follow-up, no association was found between increasing autograft diameter (absolute and relative) and severity of aortic regurgitation.

Right-sided allograft function

The allograft implanted in the right ventricular outflow tract may raise some concern. Important pulmonary regurgitation did not develop in our population, but stenosis of the right ventricular outflow tract did occur. In one adult patient the distal anastomosis of the allograft was enlarged in a second operation with a patch in order to relieve an important stenosis (Chapter 4). Two children have important pressure gradients across the allograft (Chapter 3). Although right ventricular hypertrophy in these patients was not present and clinical function was good, reoperation for structural degeneration may be needed in the future. Pulmonary stenosis was reported in other series.[5,17,22] Fortunately, the long-term results of allografts in the pulmonary position are satisfactory. The long-term results of Ross with the use of antibiotically treated aortic allografts in this position revealed a freedom of reoperation of 80% at 16 years.[39,40] The performance of the cryopreserved pulmonary allografts, as commonly used nowadays, is expected to be better. Medium term results support their good function,[17,41] but long-term results must determine the length of the reoperation-free period. In this regard a distinction must be made between the function of the right-sided pulmonary allograft after the pulmonary autograft procedure and after implantation for right sided congenital heart defects, the latter group being less favourable.[41] However, a reoperation for replacement of the right-sided allograft probably cannot be avoided on the long-term.

Pulmonary autograft imaging

Follow-up with regard to pulmonary autograft diameter measurements is important for monitoring the increase of pulmonary autograft diameter. For this purpose different imaging modalities can be used. For this purpose we developed a magnetic resonance imaging (MRI) protocol, using gradient echo cine sequences. Although MRI has proven its value in aortic and pulmonary imaging[42-46] and diameter measurements distal to the aortic and pulmonary root,[47-50] few reports exist on measurements of the aortic root.[51,52] We tested the validity of the MRI measurements by comparing long-axis measurements of the sinus level in diastole with the short-axis measurements at this level. When the corresponding sinuses on the long and short-axis were compared, the correlation and agreement were very good. When all three possible sinus diameter combinations were averaged on the short-axis, correlation and agreement decreased, indicating that the sinuses are of different sizes. The pulmonary autograft diameter measurements obtained in this study with MRI can be repeated during follow-up. The same individual parameters can be used to perform the same measurements. This may be an appropriate method to evaluate the fate of the pulmonary autograft diameter in time. MRI is not invasive but the time required to finish the protocol was at least 40 minutes in a single

patient, mainly due to long acquisition times. Further development of MRI, in particular the development of 3D volume breathhold techniques, may reduce these acquisition times. Contraindications for MRI may exclude patients with for instance a pacemaker, patients with claustrophobic anxiety and young children. Artefacts due to respiration and metal sternal wires were always present, but in all patients these artefacts could be restricted to non important areas by selecting another set of slices with a different angle.

Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) are more routinely used imaging modalities for the aortic root. We compared the pulmonary autograft measurements at different levels in systole and diastole obtained with TTE, TEE and MRI. The advantages of TEE over TTE are the better image quality and the possibility of visualizing the entire pulmonary autograft, including the distal part. However, TEE is a semi-invasive imaging modality. For the proximal 3 levels, the diameters measured from TTE and TEE images were not statistically different in systole nor in diastole. The annulus measurements at systole with MRI were not statistically different from the echocardiographic measurements. This may be related to the collagenous structure of the annulus, resulting in a fixed maximum diameter in systole. Pulmonary autograft diameter measurements at the sinus level, the sinotubular junction and the distal part of the autograft, were larger on MRI than on echocardiography. This is in contrast with the agreement of MRI and TTE measurements of the native pulmonary artery reported by Fogel et al.[47]

The differences between the measurements obtained with MRI and echocardiography may be explained by four causes. Firstly, the use of cine sequences with MRI, in which outer boundaries of the bloodflow were measured rather than the inner side of the aortic wall as with two-dimensional echocardiography. The second explanation may be related to the construction of the MRI images, as they consist of many cardiac cycles. Differences in duration of the cardiac cycles may have led to different extensions and/or positional differences of the autograft wall, resulting in larger diameter measurements. A third explanation may be related to the orientation of the sections with MRI; noncircular shape of the annulus and subannular region and different sizes of the sinuses may lead to a substantial variability. The last explanation may account for the differences between the sinus measurements: because the thickness of the slices at MRI was 10 mm, the largest diameter of two sinuses will probably be measured. This contrasts with the extremely thin echocardiographic 'slices', which may not cut both sinuses at their largest diameter in one view.

TEE and MRI adequately visualize the entire pulmonary autograft, with smaller measurement variability compared to TTE. Therefore, when dilatation of the pulmonary autograft is the subject of a study and diameters of the entire autograft must be measured, MRI or TEE are the best techniques for imaging.

Future research

At present, the pulmonary autograft seems to be a good option for aortic valve or root replacement. However, attention must be focussed on the right sided allograft. A cryopreserved pulmonary allograft is at present the conduit of choice, but degeneration of this conduit will probably make a reoperation necessary. Future research on preservation techniques and patient related variables influencing allograft function should be conducted.

A definitive statement regarding the use of the pulmonary autograft in the aortic position is only possible when long-term results are available. Aortic regurgitation and left ventricular function are the ultimate parameters. In this respect, different surgical implantation techniques must be recognized, including the freestanding root as shown in our series, wrapping of the autograft and the use of the pulmonary autograft as intraaortic cylinder in an otherwise normal native aortic root. Possible differences with regard to indications for the use of these different techniques should be evaluated, depending on the functional results.

Increase of pulmonary autograft diameter, soon after implantation, is demonstrated in our studies, in children as well as in adults. The proportion of diameters at different autograft levels may be of importance in relation to aortic regurgitation. Further follow-up in this regard, with adequate imaging techniques, remains important, especially in the adult population. TEE and MRI should be used to visualize the entire autograft. Whether the increase in diameter is due to growth (proliferation of cells) or dilatation, and whether or not the young autograft behaves differently as compared to the adult autograft, should be a subject for future (histologic) investigation.

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Summary

Chapter 1 provides an introduction to this thesis describing the rationale for the use of the pulmonary autograft. The aim of the studies concerning this subject is explained and an outline is given.

Chapter 2 is a description of a thorough histologic comparison of the morphological characteristics of the pulmonary and aortic roots. For this purpose nine normal heart specimens (seven neonatal and two adult hearts) were studied. When the pulmonary autograft is used for aortic root replacement it should be trimmed to leave only a few millimeters of right ventricular myocardium as suture area, followed by implantation as proximally as possible to get the support from the fibrous structures of the left ventricular outflow tract and the surrounding ventricular and atrial myocardium.

Chapter 3 is a description of the results of aortic root replacement with a pulmonary autograft in children with aortic valve and/or root disease. In a 7-year period 26 patients were operated upon with a mean age of 10.9 years (range 0.3 to 16.9 years). There was no hospital mortality. The actuarial survival and actuarial event-free survival rates were 87% and 79% respectively, at both 5 and 7 years. Left ventricular function returned to normal within 1 year after the operation. Moderate or severe autograft regurgitation was not present in the patients with an autograft in situ. During follow-up, increasing autograft annulus diameters were observed, not related to the severity of autograft regurgitation. The autograft procedure may be contraindicated in patients with chronic juvenile rheumatoid arthritis and relatively contraindicated in patients with a history of acute rheumatic fever.

Chapter 4 is a description of a consecutive series of 42 patients with exclusively aortic root replacement using the pulmonary autograft. The mean age at operation was 19.3 years (range 0.3 to 41.4 years). Hospital mortality was 4.8%. The actuarial survival and actuarial event-free survival rates were 89% and 79% respectively, at 4 years. Moderate autograft regurgitation was present in one patient.

Chapter 5 is a description of the fate of the pulmonary autograft diameter over time in adults and its relation to aortic regurgitation in the setting of aortic root replacement. Pulmonary autograft annulus and sinus diameters increased during the first year after aortic root replacement with a pulmonary autograft. This occurred rapidly within 10 days postoperatively, with a further increase during follow-up, without causing significant aortic regurgitation during medium term follow-up. Diameter increase was neither associated with the length of follow-up (follow-up less than one year compared to a longer follow-up) nor

with the severity of aortic regurgitation.

Chapter 6 is a description of an MRI protocol to measure pulmonary autograft diameters after transplantation to the aortic root in adults. The MRI protocol selected proved to be eligible for measuring pulmonary autograft diameters. The agreement between long and short-axis measurements for sinus level values was very good. Cine gradient echo MRI is an appropriate technique to evaluate pulmonary autograft diameters during follow-up.

In **Chapter 7** a comparison is made between pulmonary autograft diameter measurements after transplantation to the aortic root using transthoracic echocardiography (TTE), transesophageal echocardiography (TEE) and magnetic resonance imaging (MRI). This may be useful for selecting the most eligible imaging modality during follow-up. The pulmonary autograft diameter was measured at 5 different levels in systole and diastole: the subannular region (1), the annulus at the hinge points of the valve leaflets (2), the sinus (3), the sinotubular junction (4) and the distal part of the autograft (5). The mean pulmonary autograft diameters with TTE, TEE and MRI were larger than native aortic and pulmonary diameters of a normal population in the same age group. Diameters of the distal 2 levels could not be imaged reliably with TTE. MRI diameter measurements were in general larger than those with echocardiography. With regard to follow-up of pulmonary autograft diameters, TEE and MRI are better imaging modalities with a lower variability.

Chapter 8 is a comprehensive discussion in which the most important results and conclusions of the studies in Chapters 2 to 7 are discussed as related to the aim of the studies presented in the introduction.

Uitgebreide samenvatting

Hoofdstuk 1 is een introductie voor dit proefschrift en beschrijft de achterliggende redenen voor het gebruik van de pulmonale autograft.

Hoofdstuk 2 is een beschrijving van een histologische studie van de pulmonaal- en aortawortels. Hiervoor werden zeven neonatale en twee volwassen hartpreparaten gebruikt.

De annulus in beide arteriële wortels is een complexe collagene structuur die is ingesloten door de elastine lamellen van de arteriewand en de ventriculaire structuren van het hart. In de sinuswand lopen de elastine lamellen van de arteriewand door aan de luminale zijde. De buitenkant van de sinuswand bestaat uit collageen. In de driehoekige structuur van de arteriewand tussen de commissuren is deze relatie omgekeerd. De driehoekige structuren, die voornamelijk uit collageen bestaan, bevatten aan de luminale zijde eilandjes van elastine. De hoeveelheid elastine lamellen in de arteriewand distaal van de commissuren was in beide arteriën hoger dan ter hoogte van het midden van de sinussen. Distaal van de commissuren bevatte de aortawand meer elastine lamellen dan de pulmonaal arterie. De annulus van de pulmonaalwortel is proximaal aan het relatief dunne rechterventrikel myocard gehecht, terwijl de annulus van de aorta proximaal is aanhecht aan het dikke linker ventrikel myocard en enkele fibreuze structuren. De pulmonaalwortel wordt nauwelijks gesteund door het rechter ventrikel myocard. De aortawortel wordt gesteund door het overbloezende dikke linker ventrikel myocard en de annuli van het linker en rechter atrium, waartussen de aortawortel gepositioneerd is.

In geval van een aortawortel vervanging met een pulmonale autograft moet deze gebruikt worden met een beperkte hoeveelheid rechter ventrikel myocard en zo proximaal mogelijk geïmplanteerd worden teneinde steun te verkrijgen van de fibreuze structuren van het linker ventrikel uitstroomgebied en het omgevende ventriculaire myocard en de atriale annuli.

Hoofdstuk 3 is een beschrijving van de resultaten van aortawortel vervanging met een pulmonale autograft bij kinderen met een aandoening van de aortaklep en/of wortel. In een periode van 7 jaar werden 26 kinderen geopereerd (18 jongens en 8 meisjes) met een gemiddelde leeftijd van 10,9 jaar (uitersten 0,3 en 16,9 jaar). De gemiddelde follow-up periode was 3,2 jaar (uitersten 0,2 en 7,5 jaar).

Drie patiënten overleden gedurende deze follow-up periode en één autograft werd vervangen door een mechanische klepprothese. De actuariële overleving en actuariële complicatie-vrije overleving na 5 en 7 jaar waren respectievelijk 87 en 79%. Alle patiënten

waren zonder klachten. Electrocardiografie toonde geen tekenen meer van myocard ischemie of linker ventrikel hypertrofie. Echocardiografie liet geen/triviale (n=17) of milde (n=5) autograft insufficiëntie zien. Er was geen autograft stenose. Gedurende follow-up was er een toename van de gemiddelde autograft diameter aanwezig, welke niet was gerelateerd aan de ernst van de eventueel aanwezige autograft insufficiëntie. Linker ventrikel dimensies en functie waren binnen de norm vanaf één jaar na de operatie. Twee patiënten hadden een matige pulmonaal stenose zonder rechter ventrikel hypertrofie.

De chirurgische resultaten, kliniek, pulmonale autograft en allograft functie en linker ventrikel functie zijn goed na aortawortel vervanging met een pulmonale autograft. Deze operatie is aan te bevelen bij kinderen die in aanmerking komen voor aortaklepvervanging.

Hoofdstuk 4 is een beschrijving van een serie van 42 patiënten waarbij de aortawortel vervangen werd door een pulmonale autograft. De gemiddelde leeftijd was 19,3 jaar (uitersten: 0,3 en 41,4 jaar).

Twee patiënten overleden in het ziekenhuis (4,8%; 70% betrouwbaarheidsinterval: 0,0% tot 8,2%). Deze mortaliteit was niet gerelateerd aan de autograft procedure. De gemiddelde follow-up bedroeg 30 maanden (uitersten: 3 en 70 maanden; SD: 20 maanden). De late mortaliteit betrof twee patiënten; een hiervan had een ernstige insufficiëntie van de pulmonale autograft ten gevolge van chronisch juveniele rheumatoïde arthritis. De geschatte 4 jaars overleving was 88,8% (70% betrouwbaarheidsinterval: 83,3% tot 94,5%). Morbiditeit betrof drie patiënten. Eén patiënt had postoperatief een totaal AV-blok waarvoor pacemaker implantatie noodzakelijk was. Twee patiënten werden gereopereerd: één patiënt voor ernstige autograft insufficiëntie ten gevolge van recidiverend acuut rheuma en de andere voor ernstige stenose ter hoogte van de distale anastomose van de pulmonale allograft. Tromboembolische complicaties en endocarditis traden niet op. Reoperaties ten gevolge van technische of degeneratieve oorzaken waren niet noodzakelijk. De geschatte 4 jaars complicatie-vrije overleving was 78,7% (70% betrouwbaarheidsinterval: 71,0% tot 86,4%). Postoperatieve echocardiografie (n=28) toonde een significante toename van de autograft annulus diameter van 2,9 mm (SD: 2,7 mm). Vijfendertig van de 37 patiënten met een autograft in situ waren in NYHA-klasse I en twee patiënten in klasse II. Kleuren Doppler echocardiografie tijdens het laatste follow-up bezoek liet matige aorta insufficïentie zien bij één patiënt en geen, triviale of milde insufficiëntie bij 36 patiënten. Autograft stenose werd niet geconstateerd.

Deze middellange termijn resultaten zijn veelbelovend met betrekking tot mortaliteit, morbiditeit en autograft functie. De autograft procedure is gecontraïndiceerd bij patiënten met chronisch juveniele rheumatoïde arthritis en relatief gecontraïndiceerd bij patiënten met acuut rheuma in de voorgeschiedenis. Langere follow-up is nodig om eventuele progressie van de autograft annulus dilatatie en de klinische consequenties daarvan te onderkennen.

Hoofdstuk 5 is een beschrijving van de pulmonale autograft diameter in de tijd bij volwassenen na aortawortel vervanging en de relatie hiervan met autograft insufficiëntie. Van

januari 1989 tot mei 1995 ondergingen 36 opeenvolgende volwassenen een aortawortel vervanging met een pulmonale autograft voor aortaklep pathologie. De gemiddelde leeftijd van 20 mannen en 16 vrouwen was 29,1 jaar (uitersten: 19,3 en 52,1 jaar). De gemiddelde follow-up was 2,3 jaar (uitersten: 0,3 en 6,0 jaar). Twee patiënten overleden in het ziekenhuis.

Pulmonale autograft annulus en sinus diameters werden gemeten met epicardiale echocardiografie voor (alleen annulus) en na cardiopulmonale bypass, met transthoracale echocardiografie bij ontslag uit het ziekenhuis, en met transoesophageale echocardiografie gedurende follow-up. Er was geen toename van de gemiddelde annulus diameter na cardiopulmonale bypass (26,2 mm voor en 26,4 mm na cardiopulmonale bypass). De gemiddelde autograft sinus diameter na cardiopulmonale bypass bedroeg 36,5 mm. De gemiddelde autograft annulus diameter gedurende follow-up bedroeg 31,5 mm, een toename van 5,1 mm (19%). De gemiddelde autograft sinus diameter bedroeg gedurende follow-up 43,9 mm; een toename van 7,4 mm (20%). Negenenvijftig procent van de toename van de annulus diameter en 40% van de toename van de sinus diameter was al opgetreden bij ontslag uit het ziekenhuis (7 tot 10 dagen postoperatief). De diameter toename was niet geassocieerd met de lengte van follow-up (follow-up minder dan 1 jaar vergeleken met langere follow-up) of de ernst van de aorta insufficiëntie.

Er vindt toename plaats van de pulmonale autograft annulus en sinus diameters gedurende het eerste jaar na aortawortel vervanging met een pulmonale autograft. Deze toename vindt vooral plaats in de eerste postoperatieve week met een verdere toename gedurende follow-up. Deze toename is op de middellange termijn niet gerelateerd aan aorta insufficiëntie.

Hoofdstuk 6 is een beschrijving van de pulmonale autograft diameters na aortawortel vervanging met een pulmonale autograft in volwassenen. Een 'magnetic resonance imaging' (MRI) protocol, waarbij gebruik gemaakt wordt van gradiënt echo cine sequenties werd ontwikkeld om pulmonale autograft diameters te meten in 27 volwassenen, 2,3 jaar postoperatief (uitersten: 0,3 en 6,2 jaar). De gemiddelde leeftijd ten tijde van de operatie was 29 jaar (uitersten: 19,0 en 54,0 jaar). Systolische en diastolische metingen van de autograft werden verricht op een lange as afbeelding op 5 niveau's: subannulair (1), annulus ter hoogte van de aanhechting van de klepblaadjes (2), sinussen (3), sinotubulaire overgang (4) en 10 mm distaal van de sinotubulaire overgang (5). Voor validatie werden korte-as afbeeldingen op sinusniveau gebruikt. De gemiddelde systolische lange as metingen voor de verschillende niveau's waren respectievelijk 36,4; 32,5; 45,2; 36,7 en 37,0 mm. De gemiddelde diastolische metingen waren respectievelijk 33,9; 31,1; 44,1; 36,3 en 36,3 mm. De correlatiecoëfficiënt (r^2) tussen lange-as en korte-as metingen voor corresponderende sinussen was 0,97.

Het gemiddelde verschil (lange-as minus korte-as) was 0,3 mm met een SD van 1,3 mm. Het geselecteerde MRI protocol is geschikt gebleken voor het meten van pulmonale autograft diameters. Overeenstemming tussen lange-as en korte-as metingen voor het

sinusniveau was goed. MRI met gradiënt echo cine sequenties is een geschikte techniek om pulmonale autograft diameters gedurende follow-up te vervolgen.

Hoofdstuk 7 is een beschrijving van de vergelijking van pulmonale autograft diameter metingen, na aortawortel vervanging met een pulmonale autograft, met transthoracale echocardiografie (TTE), transoesophageale echocardiografie (TEE) en 'magnetic resonance imaging' (MRI). Hiermee zou de beste techniek geselecteerd kunnen worden voor metingen gedurende follow-up. Eenendertig patiënten met een pulmonale autograft werden onderzocht met TTE (n=31), TEE (n=27) en MRI (n=27) binnen een zo kort mogelijke periode, maximaal 3 maanden. De gemiddelde leeftijd ten tijde van operatie was 28,7 jaar (uitersten: 19,0 en 52,0 jaar) en de gemiddelde follow-up periode was 2,8 jaar (uitersten 0,8 en 6,7 jaar). De diameter van de pulmonale autograft werd op 5 verschillende niveau's gemeten in systole en diastole: subannulair (1), annulus ter hoogte van de aanhechting van de klepblaadjes (2), sinus (3), sinotubulaire overgang (4) en 10 mm distaal van de sinotubulaire overgang (5).

Met TEE waren de gemiddelde systolische metingen op niveau's 1 tot en met 5 respectievelijk 32, 31, 42, 35 en 34 mm. De corresponderende diastolische metingen waren kleiner, respectievelijk 25, 28, 42, 35 en 34 mm. Met TTE konden de niveau's 4 en 5 niet goed in beeld gebracht worden. Er was geen significant verschil tussen de TTE en TEE metingen van het proximale deel van de autograft (niveau's 1 tot 3). Met MRI werden de diameters 1 tot 3 mm groter gemeten vergeleken met TTE en TEE (p<0.05), behalve voor de annulus in systole (p>0.3).

De gemiddelde pulmonale autograft diameters waren groter dan natieve aortale en pulmonale diameters van een normale populatie in dezelfde leeftijdsgroep. Autograft diameters van het distale gedeelte konden niet betrouwbaar worden gemeten met TTE. Autograft diameters gemeten met MRI waren in het algemeen groter vergeleken met de metingen met echocardiografie. Met betrekking tot de follow-up van pulmonale autograft diameters zijn TEE en MRI betere afbeeldingstechnieken.

Hoofdstuk 8 is een algemene discussie waarin de belangrijkste resultaten en conclusies van de studies in hoofdstukken 2 tot en met 7 worden besproken, gerelateerd aan de doeleinden zoals gesteld in de inleiding.

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Curriculum vitae

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