CHAPTER 1

The failing aortic valve in adults: where do we stand?

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Introduction

In order to understand the physiology and pathophysiology of the aortic valve, one needs to be aware of the normal anatomy of the aortic valve and the most commonly seen structural deviations. This review will therefore first focus on the anatomy of the aortic valve and its most frequent abnormalities. Subsequently, the possible pathological conditions of the aortic valve will be discussed. Finally, the various treatment modalities for correction of the failing aortic valve will be presented. As this thesis focuses on reconstructive surgery of the adult aortic valve, this chapter will accordingly be limited to adults.

Anatomy and function of the normal aortic valve

The normal aortic valve is a structure consisting of three freely mobile cusps, located between the left ventricular outflow tract and the tubular portion of the aorta [1]. These three cusps together form a thin, mobile layer of tissue which, by opening, allows free flow of blood from the left ventricle into the aorta during systole, and which prevents, by closing during diastole, regurgitation of blood from the aorta back into the ventricle. The three aortic valve cusps are designated right, left and non-coronary cusp according to the respective coronary artery or the absence of an originating coronary artery from the sinus which they face. The size of the three cusps is usually unequal with the non-coronary cusp commonly being the largest and the right coronary cusp being the smallest [1-4]. In 16% of cases, the three aortic valve cusps are equal in size [1].

The aortic valve cusps are not attached in a circular horizontal plane to the aortic wall but in a semilunar fashion. This line of attachment, also called the annulus fibrosus, constitutes the physiologic ventriculo-arterial junction and is in fact a coupled sequence of three paraboloids [5] (Fig. 1). This physiologic ventriculo-arterial junction is different from the anatomical ventriculo-arterial junction being the straight horizontal circle where the fibro-elastic aortic wall joins the supporting structures of the left ventricle (Fig. 1) [6-7] or, beneath the non-coronary cusp, the aortic-mitral fibrous continuity. The area between the physiological and the anatomical ventriculo-arterial junction is made of fibrous tissue and forms three interleaflet triangles between the longitudinal limbs of the annulus fibrosus. These interleaflet triangles are thus situated underneath the line of attachment of the valve cusps and are therefore exposed to ventricular hemodynamics.

Each aortic valve cusp contains a hinge point, a body and a coapting surface (lunula) with a thickened central nodule, the nodule of Arantius. The hinge point is the area where the leaflet is attached to the aortic root in the earlier mentioned semilunar fashion. The top of these attachments is called the ‘commissure’ and is situated at the level of the sinotubular junction whereas the bottom (the so-called nadir) is situated below the anatomical ventriculo-arterial junction.

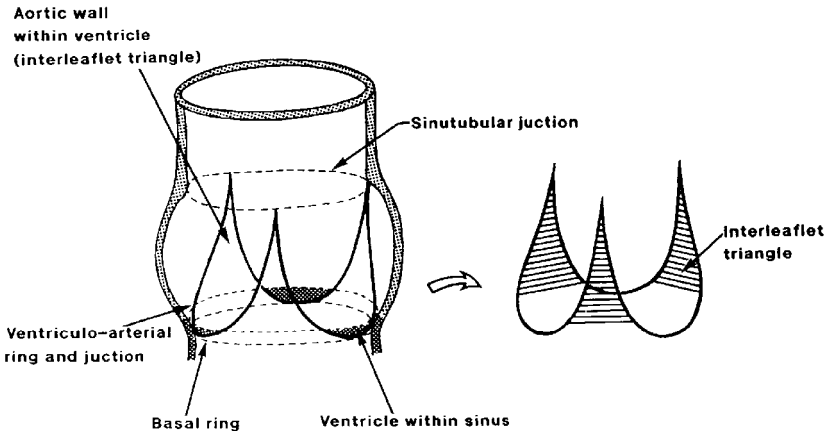

Figure 1: *Diagram of the aortic root. The coronetlike arrangement of the valvar attachments. (From: Sutton III JP, et al. The forgotten interleaflet triangles: a review of the surgical anatomy of the aortic valve. Ann Thorac Surg 1995;59:419-27. Reprinted with permission from The Society of Thoracic Surgeons).*

The function of the aortic valve cannot be separated from the more complex setting of the aortic root. The aortic root comprises the initial portion of the ascending aorta and is limited inferiorly by the anatomical ventriculo-arterial junction and superiorly by the sinotubular ridge or sinotubular junction which delineates the beginning of the proper ascending aorta. The components of the aortic root are thus the three sinuses of Valsalva, the interleaflet triangles and the valve cusps [6-9]. The three sinuses of Valsalva are designated left, right and non-coronary according to the aortic valve cusp they face and they are limited superiorly by the sinotubular ridge. The sinuses of Valsalva were already recognized by Leonardo da Vinci who realized their importance in correct aortic valve functioning [10]. Indeed, the aortic valve/root is a dynamic structure in which most geometric parts are continuously changing during a cardiac cycle in response to aortic pressure (which is also determined by the peripheral resistance), ventricular pressure and ventricular geometry [2, 11]. More precisely, due to the global left ventricular contraction during systole, there is an inward movement of the physiologic ventriculo-aortic junction, resulting in a reduction of its diameter. In addition there is an outward movement of the commissures. This change is supposed to facilitate systolic blood expulsion from the left ventricle [3, 9, 11]. During diastole, the opposite movement takes place and the aortic valve closes. The diastolic aortic pressure provides blood flow into the coronary arteries. The correct functioning of the aortic valve complex is an interaction of all of its components including the ventriculo-aortic junction, the aortic valve leaflets, the sinuses of Valsalva and the commissures with their apex reaching the sinotubular ridge. The importance of the diameter

of the sinotubular ridge was already recognized in 1832 by Corrigan who suggested that a dilatation of the sinotubular junction, frequently a result of ascending aortic aneurysm, was probably the cause of aortic regurgitation [12]. This pathophysiologic mechanism has been accepted since several years by cardiac surgeons and has recently been confirmed experimentally [13].

Anatomical variations

Congenital bicuspid aortic valve is the most frequent structural anomaly of the aortic valve. Its frequency in the general population however is not exceeding 0.4 to 2% [14]. There are two types of congenital bicuspid aortic valve: the cusps are either located right and left with the commissures being anterior and posterior or the cusps can be located anteriorly and posteriorly with the commissures being right and left [14-15] (Fig. 2).

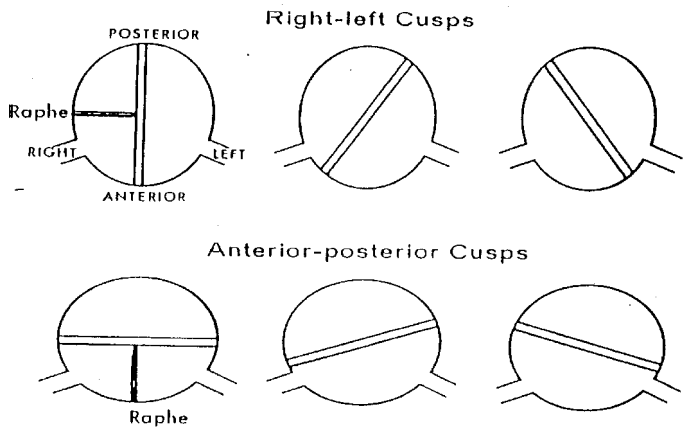

Figure 2: *Diagram showing the two basic types of congenitally bicuspid aortic valves. (From: Roberts WC. The congenitally bicuspid aortic valve: a study of 85 autopsy cases. Am J Cardiol 1970;26:72-83. Reprinted with permission from Exerpta Medica Inc.).*

Approximately 50% of congenital bicuspid valves have so-called false raphes [16]. A raphe is a ridge of tissue which partially divides one of the cusps of the bicuspid valve and which lies vertically in the wall of the aortic sinus. Although congenital bicuspid aortic valve is generally not considered to be inherited, there is a high incidence of familial clustering [17]. Besides the congenital bicuspid aortic valve, most authors also distinguish the so-called acquired bicuspid aortic valve. This type of valve originates from a trileaflet aortic valve in which fusion of two adjacent cusps occurred. This fusion constitutes a ‘new’ raphe,

and it is sometimes difficult to differentiate these two types of bicuspid aortic valves [14, 16, 18]. The majority of the bicuspid aortic valves belong to the acquired type of bicuspid valve as evidenced by the presence of three interleaflet triangles [7, 18].

Other anatomical variations are the unicuspid or quadricuspid aortic valve [16]. Unicuspid or quadricuspid valves occur very rarely but frequently develop stenosis or regurgitation throughout life.

Histology of the aortic valve and root wall

The aortic valve leaflet consists of three distinctive connective tissue layers covered by an endothelial cell layer on both the aortic and the ventricular side of the leaflet [19-20]. These three layers are the lamina fibrosa which is on the aortic side of the leaflet, the lamina spongiosa which is the middle layer and the lamina ventricularis which is on the ventricular side of the leaflet [21].

The lamina fibrosa is a dense layer of collagenous chords starting at the level of the commissures and running in circumferential direction towards the middle of the leaflet where the chords divide in smaller fibers forming a meshwork. The free edge of the leaflet is especially dense in collagenous fibers. The lamina fibrosa supports most of the diastolic pressure.

The lamina spongiosa is the middle layer which serves as a shock-absorber layer [21-22]. To fulfil this role, this layer contains only very few fibers but is composed of loose connective tissue mainly consisting of proteoglycans. The lamina spongiosa is relatively thick in the center of the leaflet but thins out towards the free edge.

The lamina ventricularis is a very thin layer consisting mainly of elastin fibers which are oriented in radial direction. Additionally, this layer contains smooth muscle cells. The lamina ventricularis is connected to the ventricular outflow tract [21].

The valve leaflet tissue is in constant tissue renewal and this tissue turn-over is maximal in the regions where stress is highest e.g. along the hinge point. This tissue turn-over is probably important to resist tissue wear [16].

A recent study demonstrated the vascularization of the aortic valve [23]. Vessels were found predominantly in the basal third of the cusps and extended in from the commissures almost to the level of the free edge. There was a significant difference between the presence of vessels in the basal part and the mid and free edge regions of the valve. There was no difference among the three cusps.

Innervation of the aortic valve arises from the ventricular endocardial plexus and is located in the lamina ventricularis [24]. The entire cusp contains nerve fibers with the exception of the coapting edge. The non-coronary cusp, which has no underlying ventricular endocardium, receives its innervation from the adjacent valve leaflets. Its innervation however is less dense than that of the two other cusps. The overall density of innervation decreases with age. It is unclear whether the innervation of the cusps plays a role in proper valve functioning [24].

The histology of the aortic root is characterized by a gradual shift from the muscular ventricle to the primarily elastic aorta [6]. The ascending aortic wall itself contains 3 layers which are, from intraluminal to extraluminal, the intima, the media and the adventitia. The media has a predominant circular 'lamellar' elastic architecture which is immediately proximal from the sinotubular ridge and further towards the aortic annulus, progressively interrupted by increasing amounts of collagenous tissue. The layers of elastic tissue eventually become thinner and subsequently disappear. It is at this level that the dense collagen bundles form the aortic annulus [6].

Pathological conditions of the aortic valve

These can either be aortic stenosis, aortic regurgitation or a combination of both, the so-called combined or mixed aortic valve disease. This paragraph will focus on the pathogenesis of aortic stenosis and aortic regurgitation. Mixed disease will not be discussed as this is a combination of both pathological conditions in a variable degree.

Aortic stenosis

Although aortic valves can become stenotic from several different causes, the large majority of them becomes stenotic because of congenital malformation or degenerative calcification [25-26]. Isolated aortic stenosis, in the absence of mitral valve disease, is uncommon in rheumatic heart disease [14, 16, 25-26]. The pathogenesis of rheumatic aortic valve disease is further explained in the section on aortic regurgitation.

Degenerative changes in the human body also affect the aortic valve and root. Aging causes a thickening of the collagen fibers in the aortic valve leaflets. These fibers also seem to lose their predominantly circumferential orientation [27]. In addition, aging aortic valves have an increased number of elastic fibers but this is most likely due to fragmentation rather than to an increase in the number of fibers present [28]. Other age-related changes include an accumulation of cellular degradation products such as lipids and calcium. This is probably due to an insufficient microvascular scavenging mechanism in the valve leaflets [29]. The presence of these cellular degradation products will increase the rate of calcification [29-30] and this phenomenon occurs initially at the sites of the highest mechanical stress in the aortic valve leaflets [31-32]. These areas are the hinge point of the aortic valve leaflet and the commissural area [31]. Once calcification is initiated at the leaflet attachment line, stress distribution on the remaining parts of the aortic valve leaflet is changed and the calcification then usually progresses along the line of coaptation [16].

These aging changes in the aortic valve leaflet result in an increasing valve thickening, stiffness and a decrease in extensibility of the valve leaflet [27, 29, 33-34].

Although up to 64% of patients with a bicuspid aortic valve have a normal life span without ever developing aortic valve pathology, about 50% of patients with aortic stenosis have a bicuspid aortic valve [25, 35-37]. The presence of a raphe might change the stress

distribution characteristics of the leaflet and therefore lead to calcification. However, the exact mechanism of calcification in bicuspid aortic valves is unknown. Edwards [38] suggested a mechanical trauma in the pathogenesis of bicuspid aortic valve stenosis. Indeed, the length of the free edge of the two valve leaflets is usually unequal. This unequal length creates abnormal contact between the two leaflets which in turn produces tension or mechanical trauma to the leaflet. This will result in focal fibrous thickening leading to dystrophic calcification. This hypothesis explains stenosis as a result of leaflet trauma but does not explain why other bicuspid aortic valves perform satisfactorily throughout a normal life span.

Aortic stenosis is considered the most frequent complication of a bicuspid aortic valve. Its clinical manifestation at a mean age of 56 to 59 years is earlier than in degenerative aortic stenosis (mean age of 62 to 72 years) whereas aortic stenosis in unicuspid valves occurs at an average age of 48 years [25].

Some other rare causes of aortic stenosis include Paget's disease, and end stage renal disease which both result in calcific aortic stenosis [39-40]. This subtype of aortic stenosis is an extreme form where the whole leaflet surface is calcified. Another rare cause of aortic stenosis is ochronosis, an inherited metabolic disorder [41].

The natural history of aortic stenosis in the adult is characterized by a prolonged latent period in which morbidity and mortality are very low [42-44]. Medical therapy during this time interval mainly consists of afterload reduction. The rate of progression of aortic stenosis is impossible to predict for a specific patient but the decrease in valve area is usually around 0.12 cm^2 per year or an increase in pressure gradient across the valve of about 15 mm Hg per year [42]. The development of symptoms such as angina, syncope or heart failure identifies a critical point in the natural history of aortic stenosis [42-44]. After the onset of symptoms, survival averages two to three years. Patients in heart failure due to a deteriorating left ventricular function are dead within one to two years. Sudden death is also possible in patients with aortic stenosis but has hardly ever been documented in patients without prior symptoms. Deteriorating left ventricular function or the onset of symptoms are therefore strong indicators for operative management of aortic stenosis.

The diagnosis of aortic stenosis is usually confirmed by echocardiography and/or angiography. Stress tests have proved to be unreliable, especially with coexisting coronary artery disease. The severity of aortic stenosis is expressed as a pressure gradient between the left ventricle and the aorta as wel as a measurement of the (reduced) aortic valve orifice area. Currently, an aortic valve area < 1 cm^2 and/or a ventricular-aortic gradient of > 50 mm HG, are considered an operative indication in asymptomatic patients with normal left ventricular function. Symptomatic patients or patients with a deteriorating left ventricular function due to aortic stenosis should be operated within a short time frame, even though the above criteria might not be matched. Accordingly, patients with milder disease may undergo concomitant aortic valve surgery when other indications for heart surgery necessitate earlier intervention [42-44].

Aortic regurgitation

Aortic regurgitation may result from diseases from either the aortic valve, the ascending aorta or both [45]. The most common causes of aortic regurgitation in this study were aortic root dilatation (37%), postinflammatory or rheumatic disease (29%), incomplete closure of a congenitally bicuspid aortic valve (24%), and infective endocarditis (6%).

In rheumatic fever, the aortic valve cusps become infiltrated with fibrous tissue, and retract. This causes failure of cusp coaptation during diastole and consequently, central aortic regurgitation will result [46]. The associated fusion of the commissures may also restrict aortic valve opening, resulting in combined aortic valve stenosis and regurgitation. As stated earlier, associated mitral valve disease is the rule in rheumatic heart disease.

Other primary valvular causes of aortic regurgitation include incomplete closure and/or leaflet prolapse of a bicuspid aortic valve. It is true that the most frequent complication of a bicuspid aortic valve is stenosis [16, 25, 44] but nevertheless, bicuspid aortic valve is the major cause of isolated aortic regurgitation, especially in the absence of ascending aortic or aortic root dilatation [47]. Moreover, regurgitant bicuspid aortic valves tend to occur at a younger age than stenosis [35]. The cusp prolapse usually affects the leaflet containing the raphe since the free edge of this leaflet is longer. Although much less frequent, cusp prolapse may also occur in tricuspid aortic valves [48].

Infective endocarditis may destroy, or cause perforation of a leaflet; alternatively, vegetations on the valve leaflets may interfere with proper cusp coaptation. All of these will lead to massive aortic regurgitation [44].

Less common causes of aortic valve regurgitation include trauma, rupture of a congenitally fenestrated valve and aortic regurgitation associated with systemic diseases like lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, Syphilis and Takayasu's disease or associated with Whipple's and Crohn's disease [44]. Aortic regurgitation associated with prosthetic valve replacement will not be discussed here.

The incidence of patients undergoing surgery for pure aortic regurgitation secondary to aortic root disease with subsequent dilatation has steadily increased over the years and now accounts for about 50% of the cases [26]. Various conditions affecting the aortic wall produce dilatation of the sinotubular junction with secondary central aortic regurgitation [13]. Age-related changes affecting the aortic root and the ascending aorta include accumulation of ground substance, fragmentation of elastic fibers, gradual replacement of smooth muscle cells with collagen and focal medial necrosis [49]. The overall result is an increasing stiffness of the aortic root which also tends to dilate with age [50].

Other pathological conditions associated with dilatation of the aortic root include aortitis [51-54], Marfan syndrome [55], aortic dissection [56], hypertension [57], or other diseases associated with connective tissue abnormalities such as cystic medial necrosis [58], Ehlers-Danlos syndrome [59] or osteogenesis imperfecta [60]. All of these conditions do not primarily affect the aortic valve but the dilatation of the root and the resulting central aortic regurgitation may secondarily affect the valve leaflets which may thicken and retract,

thereby increasing the existing degree of regurgitation [44]. Interestingly, isolated dilatation of one or more of the sinuses of Valsalva without dilatation of the sinotubular junction does not cause aortic regurgitation [13]. Aortic regurgitation in association with a peri-membranous ventricular septal defect is an almost exclusively pediatric entity and will therefore not be discussed here.

The natural history of aortic regurgitation in patients with acute aortic regurgitation is different from patients with a gradual progressive 'chronic' aortic regurgitation [42-44]. Even a normal ventricle cannot sustain an acute severe volume overload. The risk of acute aortic regurgitation is therefore much higher than that of chronic aortic regurgitation and patients with acute regurgitation should promptly be referred for surgery since they will rapidly develop pulmonary edema and cardiogenic shock.

In contrast, chronic aortic regurgitation, even when severe, may be well tolerated for several years. Medical therapy in patients with normal left ventricular function should, besides diuretic therapy, also consist of afterload reduction since this diminishes the regurgitant volume and has been proven to delay the need for aortic valve replacement [43]. Patients with chronic aortic regurgitation should be followed echocardiographically at regular intervals to detect any progression of the disease, which is generally unpredictable. The onset of left ventricular dysfunction is an early marker of subsequent symptoms such as angina, dyspnea and heart failure. As in aortic stenosis, once the patient becomes symptomatic, the condition often deteriorates rapidly and survival in patients with heart failure generally does not exceed two years. Sudden death may occur but is not frequent and usually does so in previously symptomatic patients [42-44].

Aortic regurgitation is usually confirmed echocardiographically [61] and angio-graphically. Current indications for surgery include acute aortic regurgitation, severe regurgitation, whether or not in association with symptoms or a dilated left ventricle, left ventricular dysfunction and symptomatic patients [42-44, 62].

Surgical options for the failing aortic valve

Aortic stenosis

- Repair procedures

Although the majority of stenotic aortic valves will require valve replacement, there are some indications for 'alternative' techniques. Balloon aortic valvuloplasty initially relieves obstruction in most patients but restenosis due to scarring occurs in about half of the patients within 6 months [63]. Its role is currently limited to the management of severe aortic stenosis in non-surgical candidates such as patients requiring an urgent non-cardiac operation, in pregnant women, in patients refusing surgical treatment or as 'bridge' to aortic valve replacement in patients with severe heart failure, and an otherwise high operative risk [64-65].

Initial attempts for the repair of calcific aortic valve stenosis were carried out in the late fifties and early sixties [66]. Cusp perforation and postoperative aortic regurgitation were frequent problems and the technique was abandoned when mechanical valve prostheses became available. However, with the increasing experience and improving results of mitral valve repair [67], renewed interest in aortic valve repair became apparent. This mainly included aortic valve repair for regurgitation of different origins (see further). Some authors also attempted aortic valve repair in calcific or degenerative aortic valve stenosis, either by manual debridement [68-69] or with the aid of electrohydraulic shock waves or ultrasonic therapy [70-73]. Although decalcification as such is technically feasible and has the benefit of avoiding oral anticoagulation, early recalcification is not prevented [74]. Restenosis after manual debridement may lead to reoperation in up to 25% of the patients at 5 years [69]. These unacceptable results currently exclude widespread use of manual aortic valve debridement. Aortic valve debridement with the aid of electrohydraulic shock waves or ultrasonic therapy equally leads to unacceptable results since restenosis or aortic regurgitation occur in the majority of patients at short-term follow-up [71-72].

Duran has been the proponent of aortic valve repair in a predominantly rheumatic patient population. Since most of his reports deal with valve repair for rheumatic aortic regurgitation, some with associated aortic stenosis, but not for pure aortic stenosis, this topic will be discussed in the section on valve repair for aortic regurgitation.

In summary, aortic valve repair for predominantly aortic stenosis has been disappointing, and largely abandoned in favour of valve replacement.

- Valve replacement options

The present paragraph aims to give a brief overview of the currently available valve substitutes while focussing on the main issues for each category rather than going into detail on all available types of valve substitutes for each category.

1) Mechanical aortic valve replacement. Since the first successful mechanical aortic valve replacement by Harken et al. in 1960 [75], a whole scala on mechanical valve prostheses has been developed and tested clinically. From all pioneering devices, only the Starr-Edwards® valve stood the test of time, and its Silastic ball valve model 1200 and 1260 is currently still implanted. The long-term performance (up to 31 years) of this valve was recently documented by Lund et al. [76]. No structural failures were seen in their series, and the incidence of valve related complications was as follows: thrombo-embolism 2%/patient-year (pt-year), valve thrombosis 0.06%/pt-year, anticoagulation related bleeding 2.08%/pt-year, endocarditis 0.38%/pt-year, paravalvular leak 0.26%/pt-year, hemolysis 0.1%/pt-year for a total of any valve related complication of 4.89%/pt-year. When only major complications were considered, the incidence was 2%/pt-year.

In order to further improve the clinical performance of mechanical heart valves, first the tilting disk [77-78], and later the bileaflet valve design was proposed which ultimately resulted in the St Jude Medical heart valve, clinically introduced in 1977 [79]. Intermediate and longer term follow-up of this model established its clinical domination [80-82], and

provoked competitors to design other bileaflet prostheses aiming to offer the patient a better and safer valve prosthesis [83-89]. Reported figures of valve related complications depend of course on the size and characteristics of the patient cohort and the duration of follow-up. Overall, the clinical performance of the currently available bileaflet aortic valve prostheses is rather good: structural failure is hardly ever reported; thrombo-embolic and anti-coagulation related bleeding events are both in the range of 1 to 1.5%/pt-year; valve thrombosis is rare and its incidence is around 0.06%/pt-year; endocarditis is less then 0.5%/pt-year; hemolysis accounts for approximately 0.1%/pt-year and paravalvular leak for approximately 0.25%/pt-year; finally, the aortic valve reoperation incidence is slightly less than 1%/pt-year.

In summary, the currently available mechanical aortic valve prostheses perform satisfactory but are not free from valve related complications. Patients need life-long anticoagulation and to date, it remains uncertain what the clinical impact will be on the very long-term.

2) Bioprosthetic valve replacement. Bioprostheses do not require permanent anticoagulation and therefore minimize the risk of trombo-embolism and anticoagulant related bleeding that is inherent to all mechanical prosthetic valves. Besides, they also obviate the practical inconveniences associated with permanent anticoagulation.

Numerous stented bioprostheses have been introduced in clinical practice during the past three decades. The second generation bioprostheses of the early eighties (Hancock II® porcine bioprosthesis, and the Carpentier-Edwards Perimount® pericardial bioprosthesis) have better hemodynamic features and appear to be more durable than the first generation bioprostheses of the seventies (Standard Hancock®, Hancock MO® and Carpentier-Edwards® porcine bioprostheses)[90]. Whether this can be solely attributed to the lower pressure fixation in the more recent series is beyond the scope of this review.

Myken et al. demonstrated a substantial reduction of valve related complications in bioprostheses when compared to bileaflet mechanical valve prostheses. The 10-year freedom from valve related complications in the bioprosthesis group was 74% versus 59% in the mechanical valve group [91].

The major problem with stented bioprostheses however is their limited durability. Cuspal tears, degeneration, perforation, fibrosis and calcification are possible complications which seem to occur more frequently in the younger patient population as opposed to a more elderly patient group [92-93]. This is probably due to the increased calcium metabolism in the younger patient group.

Currently, the Carpentier-Edwards® bovine pericardial valve is the most frequently used aortic valve bioprosthesis. Its low incidence of valve related complications, associated with a freedom of structural valve deterioration of 93% at 12 years in patients older than 65 years of age, makes this prosthesis the valve substitute of choice in this age group [94].

In order to improve the available stented bioprostheses, much attention and effort has been spent during the past decade in the development of stentless (mostly porcine) bioprostheses. These valves have better hemodynamic properties than stented bioprostheses,

and they also seem to have a more substantial beneficial effect on restoring left ventricular mass and function [90]. Besides, they may have a reduced medium-term mortality rate as compared to stented bioprostheses [95]. Whether the long-term durability will also be enhanced remains to be proven.

Stimulated by the favourable results with the Carpentier-Edwards® bovine pericardial valve, efforts have been undertaken to design a stented bioprosthesis made intra-operatively of autologous gluteraldehyde fixed pericardium. Results with this technique however have been disappointing and the idea was abandoned [96].

In summary, bioprosthetic valves obviate permanent anticoagulation, have a low incidence of trombo-embolic and bleeding complications but are limited by a substantial incidence of structural failure in patients of less than 65 years of age.

3) Homograft valve replacement. Homografts share the advantage of bioprostheses in avoiding the need of anticoagulation. Consequently, they have a very low thrombogenicity rate. Their hemodynamics are superior to those of stented bioprostheses and their clinical performance is excellent [97-99]. The incidence of valve related complications was given in the study by Lund et al. [99]: anticoagulant-related bleeding 0.09%/pt-year; embolism 1.4%/pt-year; endocarditis 0.6%/pt-year and tissue failure 4.5%/pt-year.

Limited availability and tissue failure restrict the use of homografts. Indeed, the overall freedom from tissue failure in the study from Lund et al. was 62 and 18% at 10 and 20 years respectively. This was however highly dependent on donor and recipient age with the best freedom of tissue failure obtained in a 70 year old recipient and a 30 year old donor. In this case, freedom from tissue failure was 91 and 64%, also at 10 and 20 years. Also, the technique of homograft insertion seems an important predictor. Basically, two techniques are used for homograft implantation: the subcoronary and the root replacement technique. In the paper by Lund et al. the root replacement group did significantly better with regard to tissue failure and subsequent aortic valve reoperation incidence. Freedom from tissue failure at 15 years in the root replacement group was 56% versus 33% with the subcoronary technique. The fact that their patient population mainly consisted of subcoronary implants may have adversely influenced the overall results of this study. Homografts are currently mainly indicated as root replacement in the treatment of native, or prosthetic valve endocarditis with excellent clinical results and a freedom from recurrent endocarditis of 98% at 5 years [100].

4) Pulmonary autograft for aortic valve replacement (Ross procedure).The use of the autologous pulmonary valve to replace the aortic valve was first described by Ross in 1967 [101]. A homograft is then used in the pulmonary position to replace the patients' own pulmonary valve. The initial technique employed a subcoronary implantation, and long-term follow-up of the initial series showed a 23% reoperation rate for severe regurgitation of the autograft [102]. Currently, most authors use the root replacement technique while some favor the inclusion technique [103-104]. The advantages of the pulmonary autograft over the homograft include increased cellular viability and therefore possible enhanced

durability; an additional advantage is the growth potential of the autograft in children [103]. However, as this procedure implies a double valve replacement, the operation is technically much more complex and demanding than the homograft aortic valve replacement. Therefore, the Ross procedure is currently considered the valve substitute of choice in children and young adults. In a recent report by Elkins et al. [105] the freedom from autograft reoperation was 90% at 8 years and the freedom from reoperation on the homograft in the pulmonary position was 94%, also at 8 years. There were no other valve related complications such as thrombo-embolism, bleeding or endocarditis.

A point of concern exists with regard to dilatation of the pulmonary autograft when used as a root replacement. This dilatation occurs immediately postoperatively and progresses somewhat further during follow-up [106]. However, when the inclusion technique is used, the dilatation seems much less and growth potential is preserved [103].

Aortic regurgitation

- Repair procedures

Although some attempts were made in the early years of cardiac surgery to repair insufficient aortic valves [107-109], it is only in the eighties that recurrent interest resulted in consistent techniques with regard to specific pathological conditions.

The incidence of rheumatic fever has markedly decreased in Western Europe and Northern America [45], but in some parts of the world, it is still considerable. It is in this patient population that Duran developed his reconstructive techniques for predominantly regurgitant, rheumatic aortic valve disease. He applied these repair techniques in patients undergoing surgery primarily for mitral valve disease, and in whom it was desirable to save the aortic valve, particularly when a mitral valve repair had been possible. In a series of publications [110-114] he described his techniques. In rheumatic aortic valvular disease, regurgitation is mainly caused by decreased cusp mobility (Fig. 3). At the level of the commissure, increased mobility can be obtained by calcium excision and/or commissurotomy. Moderate leaflet edge retraction can be suppressed by free edge unrolling, or shaving whereas severe retraction will need cusp extension with autologous pericardium. Finally, Duran often adds a sinotubular ridge enhancement since this induces an earlier aortic valve closure [115] (Fig. 3).

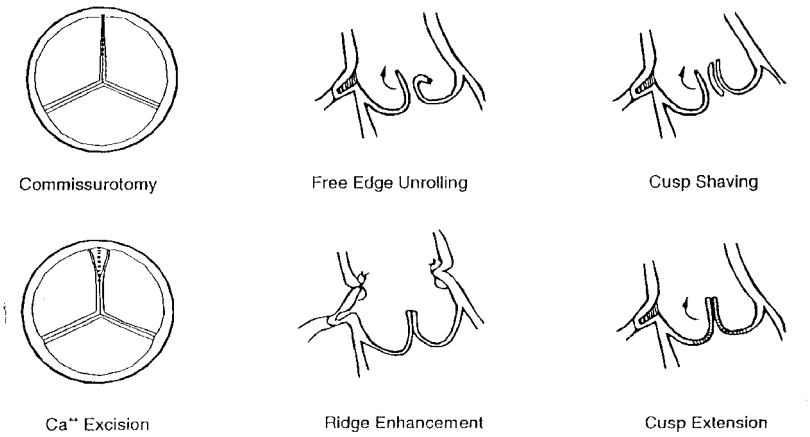

Figure 3: *Diagram of aortic valve lesions and corresponding repair techniques. Aortic regurgitation with decreased cusp mobility. (From: Duran CMG. Aortic valve repair and reconstruction. Oper Techn in Cardiothorac Surg 1996;1:15-29. Reprinted with permission from W.B. Saunders Company and CMG Duran).*

Although early and mid-term follow-up results reported by Duran were encouraging [110-114], and prompted further investigation of the applicability of these techniques, at least by himself, virtually no other authors have reported similar results on this topic which questions the reproducibility of these surgical strategies. In addition, a recent report by Bernal et al., who did a follow-up study of the initial patient population operated by Duran in Spain, showed a disappointingly low freedom from repaired aortic valve structural deterioration of 25.3% at 22 years [116].

For the above mentioned reasons, it is questionable whether there remains any place for aortic valve repair in rheumatic valvular heart disease, except in countries where adequate control of anticoagulation is not feasible.

Other pathological conditions leading to aortic regurgitation, such as cusp prolapse, aortic root and/or sinotubular dilatation regardless of the cause, are more amenable to repair and they constitute the basis of this thesis. Cusp perforation due to endocarditis, reparable with a patch of autologous pericardium, is not further described since this occurs only very seldom.

- Aortic valve replacement

All devices used for aortic valve replacement in aortic stenosis are also applicable in aortic regurgitation. However, results of the Ross procedure for pure aortic regurgitation show an increased rate of recurrent aortic regurgitation during follow-up when compared to aortic stenosis as operative indication [117]. At presence, it is yet unclear whether the Ross procedure should be limited to patients with aortic stenosis.

Combined aortic stenosis and regurgitation

The etiology and morphology in this group is similar to that of aortic stenosis. Accordingly, treatment principles and options follow [118].

Aim of the present thesis

Given the poor results of aortic valve repair in aortic stenosis, and rheumatic aortic regurgitation as discussed above, the present thesis focuses on possible indications for adult aortic valve repair in regurgitation due to other causes. Chapter 2 examines the results of bicuspid aortic valve repair for leaflet prolapse, whereas chapter 3 looks at the results of leaflet prolapse repair in tricuspid aortic valves. Chapter 4 studies the durability of aortic valve preservation in Type A dissection, and chapter 5 reports the initial results of the aortic valve reimplantation technique for the treatment of aortic regurgitation due to dilatation of the aortic root and sino-tubular junction. The present thesis investigates the feasibility and the durability of all these procedures. Essential in these reparative techniques is the presence of (near to) normal valve tissue in order to obtain the best result possible.

All of these techniques avoid the need for permanent anticoagulation. If durability of the techniques could be demonstrated, avoidance of anticoagulation might be an additional benefit, particularly if applied in young patients who still have a long life-expectancy. In order to study the incidence, frequency and severity of very long-term anticoagulation related complications, a follow-up study was undertaken of all patients undergoing a mechanical aortic valve replacement at the St. Antonius Hospital in Nieuwegein, The Netherlands between December 1963 and January 1st 1974, representing the first 10-year experience of mechanical aortic valve replacement at this institution. This study is the subject of chapter 6.

Chapter 7 is a discussion of the obtained results and a correlation with clinical practice. Finally, chapter 8 is a summary of the present thesis.

References

1. Silver MA, Roberts WC. Detailed anatomy of the normally functioning aortic valve in hearts of normal and increased weight. Am J Cardiol 1985;55:454-461.
2. Vollebergh FEMG, Becker AE. Minor congenital variations of cusp size in tricuspid aortic valves: possible link with isolated aortic stenosis. Br Heart J 1977;39:1006-1011.
3. Thubrikar M, Piepgrass WC, Shaner TW, Nolan SP. The design of the normal aortic valve. Am J Physiol 1981;241:H795-801.
4. Kunzelman KS, Grande KJ, David TE, Cochran RP, Verrier ED. Aortic root and valve relationships. Impact on surgical repair. J Thorac Cardiovasc Surg 1994;107:162-170.
5. Mercer JL, Benedicty M, Bahnson HT. The geometry and construction of the aortic leaflet. J Thorac Cardiovasc Surg 1973;65:511-518.
6. Sutton III JP, Ho SY, Anderson RH. The forgotten interleaflet triangles: a review of the surgical anatomy of the aortic valve. Ann Thorac Surg 1995;59:419-427.
7. Anderson RH, Devine WA, Ho SY, Smith A, McKay R. The myth of the aortic annulus: the anatomy of the subaortic outflow tract. Ann Thorac Surg 1991;52:640-646.
8. Zimmerman J. The functional and surgical anatomy of the heart. Ann R Coll Surg Engl 1966; 39:348-366.
9. Reid K. The anatomy of the sinus of Valsalva. Thorax 1970;25:79-85.
10. Robicsek F. Leonardo da Vinci and the sinuses of Valsalva. Ann Thorac Surg 1991;52:328-335.
11. Brewer RJ, Deck JD, Capati B, Nolan SP. The dynamic aortic root. Its role in aortic valve function. J Thorac Cardiovasc Surg 1976;72:413-417.
12. Corrigan DJ. Permanent patency of the mouth of the aorta. Edinburgh Med Surg 1832;37:111.
13. Furukawa K, Ohteki H, Cao ZL, et al. Does dilatation of the sinotubular junction cause aortic regurgitation ? Ann Thorac Surg 1999;68:949-954.
14. Roberts WC. The congenitally bicuspid aortic valve. A study of 85 autopsy cases. Am J Cardiol 1970; 26:72-83.
15. Campbell M. Calcific aortic stenosis and congenital bicuspid aortic valves. Br Heart J 1968; 30:606-616.
16. Thubrikar M. Diseases of the aortic valve. In Thubrikar M. 'The aortic valve' CRC press, Boca Raton FL, USA, 1990:157-174.
17. Huntington K, Hunter AG, Chan KL. A prospective study to assess the frequency of familial clustering of congenital bicuspid aortic valve. J Am Coll Cardiol 1997;30:1809-1812.
18. Angelini A, Ho SY, Anderson RH, et al. The morphology of the normal aortic valve as compared with the aortic valve having two leaflets. J Thorac Cardiovasc Surg 1989;98:362-367.
19. Deck JD. Orientation of endothelial cells on surfaces of aortic valve leaflets in dogs. Anat Rec 1979;193:518.
20. Deck JD. Endothelial cell orientation on aortic valve leaflets. Cardiovasc Res 1986;20:760-767.
21. Clark RE, Finke EH. Scanning and light microscopy of human aortic leaflets in stressed and relaxed states. J Thorac Cardiovasc Surg 1974;67:792-804.
22. Swanson WM, Clark RE. Dimensions and geometric relationships of the human aortic valve as a function of pressure. Circ Res 1974;35:871-882.
23. Weind KL, Ellis CG, Boughner DR. The aortic valve blood supply. J Heart Valve Dis 2000;9:1-8.
24. Marron K, Yacoub MH, Polak JM, et al. Innervation of human atrioventricular and arterial valves. Circulation 1996;94:368-375.
25. Subramanian R, Olson LJ, Edwards WD. Surgical pathology of pure aortic stenosis: a study of 374 cases. Mayo Clin Proc 1984;59:683-690.

26. Dare AJ, Veinot JP, Edwards WD, Tazelaar HD, Schaff HV. New observations on the etiology of aortic valve disease: a surgical pathologic study of 236 cases from 1990. Hum Pathol 1993;24:1330-1338.
27. Sell S, Scully R. Aging changes in the aortic and mitral valves. Am J Pathol 1965;46:345-365.
28. Fleg JL. Alterations in cardiovascular structure and function with advancing age. Am J Cardiol 1986;57:33C-44C.
29. Kim KM, Valigorsky JM, Mergner WJ, Jones RT, Pendergrass RF, Trump BF. Aging changes in the human aortic valve in relation to dystrophic calcification. Hum Pathol 1976;7:47-60.
30. Schoen FJ. Interventional and surgical cardiovascular pathology: clinical correlations and basic principles. W.B. Saunders Co., Philadelphia, 1989.
31. Thubrikar MJ, Nolan SP, Aouad J, Deck JD. Stress sharing between the sinus and leaflets of canine aortic valve. Ann Thorac Surg 1986;42:434-440.
32. Thubrikar MJ, Aouad J, Nolan SP. Patterns of calcific deposits in operatively excised stenotic or purely regurgitant aortic valves and their relation to mechanical stress. Am J Cardiol 1986;58:304-308.
33. Sahasakul Y, Edwards WD, Naessens JM, Tajik AJ. Age-related changes in aortic and mitral valve thickness: Implications for two-dimensional echocardiography based on an autopsy study of 200 normal human hearts. Am J Cardiol 1988;62:424-430.
34. Christie G, Baratt-Boyes B. Age-dependant changes in the radial stretch of human aortic valve leaflets determined by biaxial testing. Ann Thorac Surg 1995;60(suppl):156-159.
35. Fenoglio JJ, McAllister HA, DeCastro CM, Davia JE, Cheitlin MD. Congenital bicuspid aortic valve after age 20. Am J Cardiol 1977;39:164-169.
36. Hallgrimsson J, Tulinius H. Chronic non-rheumatic aortic valvular disease: a population study based on autopsies. J Chron Dis 1979;32:355-363.
37. Mills P, Leech G, Davies M, Leatham A. The natural history of a non-stenotic bicuspid aortic valve. Br Heart J 1978;40:951-957.
38. Edwards JE. The congenital bicuspid aortic valve. Circulation 1961;23:485-488.
39. Strickberger SA, Schulman SP, Hutchings GM. Association of Paget's disease of bone with calcific aortic valve disease. Am J Med 1987;82:953-956.
40. Maher ER, Young G, Smyth-Walsh B, et al. Aortic and mitral valve calcification in patients with end stage renal diseases. Lancet 1987;II:875-877.
41. Casselman F, Herijgers P, Meyns B, Daenen W. Aortic stenosis in endogenous ochronosis. J Heart Valve Dis 1999;8:445-446.
42. Bonow RO, Carabello B, de Leon AC Jr, et al. ACC/AHA Guidelines for the management of patients with valvular heart disease: executive summary. A report of the American College of Cardiology / American Heart Association task force on practice guidelines (Committee on management of patients with valvular heart disease). Circulation 1998;98:1949-1984.
43. Rahimtoola SH. Aortic valve disease. In Alexander RW, Schlant RC and Fuster V, Editors 'Hurst's - The Heart' McGraw-Hill, New York, 1998:1759-1785.
44. Braunwald E. Valvular heart disease. In Braunwald E 'Heart disease: A textbook of cardiovascular medicine' W.B. Saunders Co., Philadelphia, 1997:1007-1076.
45. Olson LJ, Subramanian R, Edwards WD. Surgical pathology of pure aortic insufficiency: a study of 225 cases. Mayo Clin Proc 1984;59:835-841.
46. Schoen FJ, St John Sutton M. Contemporary pathologic considerations in valvular disease. In Virmani R, Atkinson JB and Feuoglio JJ (eds.) 'Cardiovascular pathology' W.B. Saunders Co., Philadelphia, 199: 334.
47. Otto C. Aortic valve insufficiency: changing concepts in diagnosis and management. Cardiologia 1996;41:505-513.
48. Carter JB, Sethi S, Lee GB, Edwards JE. Prolapse of semilunar cusps as causes of aortic insufficiency. Circulation 1971;43:922-932.

49. Schlatmann TJ, Becker AE. Histologic changes in the normal aging aorta: implications for dissecting aortic aneurysm. Am J Cardiol 1977;39:13-20.
50. Dobrin PB. Pathophysiology and pathogenesis of aortic aneurysms. Current concepts. Surg Clin North Am 1989;69:687-703.
51. Heggtveit HA. Syphilitic aortitis: a clinicopathologic autopsy study of 100 cases, 1950 to 1960. Circulation 1964;29:346-355.
52. Honig HS, Weintraub AM, Gomes MN, Hufnagel CA, Roberts WC. Severe aortic regurgitation secondary to idiopathic aortitis. Am J Med 1977;63:623-633.
53. Akikusa B, Kondo Y, Muraki N. Aortic insufficiency caused by Takayasu's arteritis without usual clinical features. Arch Pathol Lab Med 1981;105:650-651.
54. How J, Strachan RW. Aortic regurgitation as a manifestation of giant cell arteritis. Br Heart J 1978;40:1052-1054.
55. Roberts WC, Honig HS. The spectrum of cardiovascular disease in the Marfan syndrome: a clinico-morphologic study of 18 necropsy patients and comparison to 151 previously reported necropsy patients. Am Heart J 1982;104:115-135.
56. Fann JI, Glower DD, Miller DC, et al. Preservation of aortic valve in Type A aortic dissection complicated by aortic regurgitation. J Thorac Cardiovasc Surg 1991;102:62-75.
57. Waller BF, Zoltick JM, Rosen JH, et al. Severe aortic regurgitation from systemic hypertension (without aortic dissection) requiring aortic valve replacement: analysis of four patients. Am J Cardiol 1982;49:473-477.
58. Ferlic RM, Goott B, Edwards JE, Lillehei CW. Aortic valvular insufficiency associated with cystic medial necrosis: surgical and pathologic considerations. Ann Surg 1967;165:1-9.
59. Leier CV, Call TD, Fulkerson PK, Wooley CF. The spectrum of cardiac defects in the Ehlers-Danlos syndrome, types I and III. Ann Intern Med 1980;92:171-178.
60. Stein D, Kloster FE. Valvular heart disease in osteogenesis imperfecta. Am Heart J 1977;94:637-641
61. Perry G, Helmcke F, Nanda N, Byard C, Soto B. Evaluation of aortic insufficiency by Doppler color flow mapping. J Am Coll Cardiol 1987;9:952-959.
62. Klodas E, Enrique-Sarano M, Tajik AJ, Mullany CJ, Bailey KR, Seward JB. Optimizing timing of surgical correction in patients with severe aortic regurgitation: role of symptoms. J Am Coll Cardiol 1997;30:746-752.
63. Otto CM, Mickel MC, Kennedy JW, et al. Three-year outcome after balloon aortic valvuloplasty: insights into prognosis of valvular aortic stenosis. Circulation 1994;89:642-650.
64. Moreno PR, Jang IK, Newell JB, et al. The role of percutaneous aortic balloon valvuloplasty in patients with cardiogenic shock and critical aortic stenosis. J Am Coll Cardiol 1994;23:1071-1075.
65. Angel JL, Chapman C, Knuppel RA. Percutaneous balloon aortic valvuloplasty in pregnancy. Obstet Gynecol 1988;72:438-440.
66. Mulder DG, Kattus AA, Longmire WP. The treatment of acquired aortic stenosis by valvuloplasty. J Thorac Cardiovasc Surg 1960;40:731-743.
67. Carpentier A. Cardiac valve surgery: the 'French correction'. J Thorac Cardiovasc Surg 1983; 86:323-337.
68. Shapira N, Lemole GM, Fernandez J, et al. Aortic valve repair for aortic stenosis in adults. Ann Thorac Surg 1990;50:110-120.
69. Weinschelbaum E, Stutzbach P, Oliva M, Zaidman J, Torino A, Gabe E. Manual debridement of the aortic valve in elderly patients with degenerative aortic stenosis. J Thorac Cardiovasc Surg 1999;117:1157-1165.
70. Worley SJ, King M, Edwards WD, Holmes DR. Electrohydraulic shock wave decalcification of stenotic aortic valves: postmortem and intraoperative studies. J Am Coll Cardiol 1988;12:458-462.

71. Freeman WK, Schaff HV, Orszulak TA, Tajik AJ. Ultrasonic aortic valve decalcification: serial Doppler echocardiographic follow-up. J Am Coll Cardiol 1990;16:623-630.
72. McBride LR, Naunheim KS, Fiore AC, et al. Aortic valve decalcification. J Thorac Cardiovasc Surg 1990;100:36-43.
73. Kellner HJ, Pracki P, Hildebrandt A, Binner C, Eisele G, Struck E. Aortic valve debridement by ultrasonic surgical aspirator in degenerative, aortic valve stenosis: follow-up with Doppler echocardiography. Eur J Cardiothorac Surg 1996;10:498-504.
74. Dahm M, Dohmen G, Groh E, et al. Decalcification of the aortic valve does not prevent early recalcification. J Heart Valve Dis 2000;9:21-26.
75. Harken DE, Soroff HS, Taylor WJ, Lefemine AA, Gupta SK, Lunzer S. Partial and complete prostheses in aortic insufficiency. J Thorac Cardiovasc Surg 1960;40:744-762.
76. Lund O, Pilegaard HK, Ilkjaer LB, Nielsen SL, Arildsen H, Albrechtsen OK. Performance of the Starr-Edwards aortic cloth covered valve, track valve, and silastic ball valve. Eur J Cardiothorac Surg 1999;16:403-413.
77. Daenen W, Nevelsteen A, van Cauwelaert P, de Maesschalk E, Willems J, Stalpaert G. Nine years' experience with the Bjork-Shiley prosthetic valve: early and late results of 932 valve replacements. Ann Thorac Surg 1983;35:651-663.
78. Daenen W, Van Kerrebroeck C, Stalpaert G, Mertens B, Lesaffre E. The Bjork-Shiley monostrut valve. Clinical experience in 647 patients. J Thorac Cardovasc Surg 1993;106:918-927.
79. Emery RW, Mettler E, Nicoloff DM. A new cardiac prosthesis: the St Jude Medical cardiac valve. In vivo results. Circulation 1979;30:48-54.
80. Duncan MJ, Cooley DA, Reul GJ, et al. Durability and low thrombogenicity of the St Jude Medical valve at 5-year follow-up. Ann Thorac Surg 1986;42:500-505.
81. Czer LSC, Chaux A, Matloff JM, et al. Ten-year experience with the St Jude Medical valve for primary valve replacement. J Thorac Cardiovasc Surg 1990;100:44-55.
82. Fernandez J, Laub GW, Adkins MS, et al. Early and late-phase events after valve replacement with the St Jude Medical prosthesis in 1200 patients. J Thorac Cardiovasc Surg 1994;107:394-407.
83. de Luca L, Vitale N, Giannolo B, Cafarella G, Piazza L, Cotrufo M. Mid-term follow-up after heart valve replacement with Carbomedics bileaflet prostheses. J Thorac Cardiovasc Surg 1993; 106:1158-1165.
84. Copeland JG. The Carbomedics prosthetic heart valve: a second generation bileaflet prosthesis. Semin Thorac Cardiovasc Surg 1996;8:237-241.
85. Van Nooten G, Caes F, Francois K, Missault L, Van Belleghem Y. Clinical experience with the first 100 ATS heart valve implants. Cardiovasc Surg 1996;4:288-292.
86. Westaby S, Van Nooten G, Sharif H, Pillai R, Caes F. Valve replacement with the ATS open pivot bileaflet prosthesis. Eur J Cardiothorac Surg 1996;10:660-665.
87. Flameng W, Vandeplas A, Narine K, Daenen W, Herijgers P, Herregods M. Postoperative hemodynamic study of two bileaflet heart valves in aortic position. J Heart Valve Dis 1997;6:269-273.
88. Casselman F, Herijgers P, Meyns B, Flameng W, Daenen W. The Bicarbon heart valve prosthesis: short-term results. J Heart Valve Dis 1997;6:410-415.
89. Borman JB, Brands WGB, Camilleri L, et al. Bicarbon valve – European multicenter clinical evaluation. Eur J Cardiothorac Surg 1998;13:685-693.
90. David TE. Aortic valve surgery : where we are and where we shall go. J Heart Valve Dis 1999; 8:495-498.
91. Myken P, Caidahl K, Larsson P, Larsson S, Wallentin I, Berggren H. Mechanical versus biological valve prosthesis: a ten year comparison regarding function and quality of life. Ann Thorac Surg 1995;60(suppl):447-452.

92. Kopf GS, Geha AS, Hellenbrand WE, Kleinman CS. Fate of left-sided cardiac bioprosthesis valves in children. Arch Surg 1986;121:488-490.
93. Pupello DF, Bessone LN, Hiro SP, et al. Bioprosthesis longevity in the elderly: an 18-year longitudinal study. Ann Thorac Surg 1995;60(suppl):270-275.
94. Banbury MK, Cosgrove DM, Lytle BW, Smedira NG, Sabik JF, Saunders CR. Long-term results of the Carpentier-Edwards pericardial aortic valve: a 12-year follow-up. Ann Thorac Surg 1998;66(suppl):73-76.
95. David TE, Puschmann R, Ivanov J, et al. Aortic valve replacement with stentless and stented porcine valves: a case-match study. J Thorac Cardiovasc Surg 1998;116:236-241.
96. Gross C, Simon P, Grabenwoger M, et al. Midterm results after aortic valve replacement with the autologous tissue cardiac valve. Eur J Cardiothorac Surg 1999;16:533-539.
97. O'Brien MF, Stafford EG, Gardner MAH, et al. Allograft aortic valve replacement: long-term follow-up. Ann Thorac Surg 1995;60(suppl):65-70.
98. Yacoub M, Rasmi NRH, Sundt TM, et al. Fourteen-year experience with homovital homografts for aortic valve replacement. J Thorac Cardiovasc Surg 1995;110:186-194.
99. Lund O, Chandrasekaran V, Grocott-Mason R, et al. Primary aortic valve replacement with allografts over twenty-five years: valve-related and procedure-related determinants of outcome. J Thorac Cardiovasc Surg 1999;117:77-91.
100. Dossche KM, Brutel de la Riviere A, Morshuis WJ, Schepens MA, Ernst SM. Aortic root replacement with human tissue valves in aortic valve endocarditits. Eur J Cardiothorac Surg 1997;12:47-55.
101. Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. Lancet 1967;2:956-958.
102. Chambers JC, Somerville J, Stone S, Ross DN. Pulmonary autograft procedure for aortic valve disease: long-term results of the pioneer series. Circulation 1997;96:2206-2214.
103. Elkins RC, Knott-Craig CJ, Ward KE, McCue C, Lane MM. Pulmonary autograft in children: realized growth potential. Ann Thorac Surg 1994;57:1387-1394.
104. David TE, Omran A, Ivanov J, et al. Dilatation of the pulmonary autograft after the Ross procedure. J Thorac Cardiovasc Surg 2000;119:210-220.
105. Elkins RC, Knott-Craig CJ, Ward KE, Lane MM. The Ross operation in children: 10-year experience. Ann Thorac Surg 1998;65:496-502.
106. Hokken RB, Bogers AJJ, Taams MA, et al. Does the pulmonary autograft in the aortic position in adults increase in diameter? An echocardiographic study. J Thorac Cardiovasc Surg 1997; 113:667-674.
107. Taylor WJ, Thrower WB, Black H, Harken DE. The surgical correction of aortic insufficiency by circumclusion. J Thorac Surg 1958;35:192-205.
108. Cabrol C, Guiraudon G, Bertrand M. Le traitement de l'insuffisance aortique par l'annuloplastie aortique. Arch Mal Cœur 1966;59:1305-1312.
109. Frater RWM. The prolapsing cusp. Experimental and clinical observations. Ann Thorac Surg 1967;3:63-67.
110. Duran CMG, Alonso J, Gaite L, et al. Long-term results of conservative repair of rheumatic aortic valve insufficiency. Eur J Cardiothorac Surg 1988;2:217-223.
111. Duran CG. Reconstructive techniques for rheumatic aortic valve disease. J Card Surg 1988;3:23-28.
112. Duran C, Kumar N, Gometza B, Al Halees Z. Indications and limitations of aortic valve reconstruction. Ann Thorac Surg 1991;52:447-454.
113. Duran CMG. Present status of reconstructive surgery for aortic valve disease. J Card Surg 1993; 8:443-452.
114. Duran CMG. Aortic valve repair and reconstruction. Oper Techn in Cardiothorac Surg 1996;1:15-29.
115. Duran CMG, Balasundaram S, Bianchi S, et al. Hemodynamic effect of supraaortic ridge enhancement on the closure mechanism of the aortic valve and its implication in aortic valve repair. Thorac Cardiovasc Surgeon 1990;38:6-10.

116. Bernal JM, Fernandez-Vals M, Rabasa JM, Gutierrez-Garcia F, Morales C, Revuelta JM. Repair of nonsevere rheumatic aortic valve disease during other valvular procedures: is it safe? J Thorac Cardiovasc Surg 1998;115:1130-1135.
117. Dossche KM, Brutel de la Riviere A, Morshuis WJ, Schepens MA, Ernst SM, van den Brand JJ. Aortic root replacement with the pulmonary autograft: an invariably competent aortic valve ? Ann Thorac Surg 1999;68:1302-1307.
118. Kirklin JW, Baratt-Boyes BG. Aortic valve disease. In Kirklin JW, Baratt-Boyes BG eds. 'Cardiac surgery', Churchill Livingstone Inc., New York, 1993:491-571.