PERCUTANEOUS TRANSLUMINAL BALLOON CATHETER AORTIC VALVULOPLASTY IN ELDERLY PATIENTS

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Print: Haveka B.V., Alblasserdam, The Netherlands

PERCUTANEOUS TRANSLUMINAL BALLOON CATHETER AORTIC VALVULOPLASTY IN ELDERLY PATIENTS

VALVULOPLASTIEK VAN VERNAUWDE AORTAKLEPPEN BIJ OUDERE PATIENTEN DOOR MIDDEL VAN EEN PERCUTAAN INGEBRACHTE BALLON CATHETER

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Erasmus Universiteit te Rotterdam op gezag van de rector magnificus, Prof.Dr. C.J. Rijnvos en volgens het besluit van het college van dekanen. De openbare verdediging zal plaatsvinden op woensdag 21 november om 13.45 uur

door

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geboren te

Nispen

Commissieleden

Promotores	:	Prof.Dr. E. Bos
		Prof. P.G. Hugenholtz
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Financial support by the Netherlands Heart Foundation for the publication of this thesis is gratefully acknowledged

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CHAPTER 1
INTRODUCTION

Narrowing of the aortic valve by calcified deposits has been recognized for about 500 years, as seen in drawings by Leonardo da Vinci (1). The physiologic implications of such aortic valvular calcified deposits were only appreciated in the last 100 to 200 years. It was James Hope who in his " A Treatise on the Diseases of the Heart and Great Vessels", recognized that the contraction of the aortic valve must be very great to influence the vigor of the peripheral pulse (2).

At the beginning of this century, Tuffier attempted to treat aortic valvular stenosis by digitally invaginating a portion of the aortic wall through the opening of the stenotic aortic valve, thus creating a truly closed commissurotomy (3). Eleven years after this attempt the patient was reported living and his condition improved.

Beginning with Smithy and Parker (4) in 1947, a number of experimental operations have been reported, using a hooked blade initially, which was inserted into the ascending aorta, and, after passage through the stenotic valve, this thin-bladed knife was retracted, in order to lacerate one or more aortic valve cusps. Bailey and coworkers (5) used punchcutters, Goodell uterine dilators and a Brock-like valvulotome. This last instrument had an umbrella like configuration with three blades, which was advanced retro or antegradely through the stenotic aortic valve, opened and retracted. These investigators later developed a pencil-like instrument with a blunt point which could be opened and forced through the stenotic aortic valve. They felt that this instrument had insufficient dilating force, and that the forcible passage of the dilator head was unduly traumatic. Therefore they replaced the umbrella-like spring blades, by three parallel dilating bars with wedgelike cross sections, to dilate the valve, without retracting the instrument. The results left Bailey reflecting that " .... we do not accomplish much opening of the stenotic valve by any closed method. It is not surprising that many of our surviving patients are beginning to show evidence of recurrence of the stenosis" (6).

For this reason Bailey proposed an exclusive open method to remove the extremely calcified layer of the aortic cusps (6). This technique was initially hampered due to the time needed to perform a satisfactory "débridement". With the introduction of general hypothermia, which considerably extended the time available for a cardiac operation, more extensive and accurate sculpturing of the stenotic aortic leaflets became

possible, and was performed by Lewis and Shumway (7). Another milestone was attained with the introduction of extracorporeal circulation and the pumpoxygenator (8), which allowed surgeons ample time to perfect the débridement technique, and to attain more satisfactory results (9). At the same time, however, more definite alternatives came into vogue to completely replace the diseased aortic valve, and halted the era of operative valvuloplasty (10). Although surgical pioneers developed in the course of time many different prosthetic heart valves to improve durability and reduce thrombogenecity, no prosthesis proved ideal once subjected to the test of time.

As a result of these imperfections, techniques were developed to replace the aortic valve with homo and heterografts initially procured from post mortems and sewn into the descending aorta without the use of extracorporeal circulation (11). Later D. Ross (12) and Barratt Boyes (13) used freeze-dried aortic valve homografts, inserted below the coronary ostia. Heterografts, mainly consisting of pig or calf aortic valves were also employed in the same time period (14). Later Carpentier perfected these valves by employing a support ring (15), instead of suturing these valves directly to the aortic ring. Other biomaterials have been used to reconstruct or replace the diseased aortic valve, such as autologous fascia lata (16,17), heterologous pericardial tissue (18) and homologous dura mater tissue (19), with or without a supporting frame.

Nowadays aortic valve replacement or reconstruction is a widely accepted operation, which can be performed with an overall in hospital mortality of about 5% and an excellent life expectancy after the operation for the survivors (20). However several preoperative variables have been recognized that increase the operative risk of aortic valve replacement (21). Among these factors are age over 70 years, female gender, poor left ventricular function, concomitant coronary artery disease and emergency operation. Accumulation of several of these risk factors might lead to such a high expected operative risk, that patients, however severely symptomatic, are denied operation. Moreover the high age of some patients with severe aortic stenosis, can be a prohibitive factor in performing cardiac surgery.

In 1985, Cribier and coworkers from Rouen in France, extended the area of the interventional cardiologist, by applying percutaneously introduced balloon catheters to dilate acquired aortic valve stenosis in three elderly patients (22). Immediate results of these procedures appeared very encouraging, so that the authors subtitled their first publication with: "an alternative to valve replacement?". This balloon procedure had

been considered until then inconceivable for application in patients with longstanding, calcified stenotic aortic valves, although it had been preceded by the introduction of the balloon dilatation technique in young patients with congenital aortic valve stenosis for several years. This was the direct reason for the investigation laid down in this thesis.

On March 19, 1986, Cribier assisted Patrick Serruys and myself with our first percutaneous balloon valvuloplasty procedure in a male patient of 75 years old, with severe aortic stenosis. Till January 1, 1990, thirty seven other patients have been treated. The results obtained in these patients constitute the main topic of this thesis.

In chapter 2 we describe the pathology and etiology of the various forms of aortic valvular stenosis.

In chapter 3 we review the initial surgical attempts to relieve aortic valve stenosis with the help of remarkable instruments and later endeavors to replace the aortic valve, ultimately with prosthetic materials.

In chapter 4 we report our immediate and medium term results in elderly patients who underwent percutaneous balloon aortic valvuloplasty. Complications of the procedure and symptomatology of the patients after valvuloplasty were assessed systematically, by asking specifically about anginal symptoms, syncope or dizziness, dyspnea and daily activities.

In chapter 5 we describe the measurements obtained with echo Doppler techniques before and after valvuloplasty in these patients and we compare these data with catheter derived values.

In chapter 6 we describe experimental post mortem balloon aortic valve dilatations, evaluated with Computer Tomographic scans. We extrapolated these experimental data to actual relations between balloon design and valve anatomy.

In chapter 7 we report about the merits of a long introducer sheath inserted during the valvuloplasty procudure.

In chapter 8 we report the results of aortic valve replacement in patients with previous percutaneous balloon dilatation of the stenotic valve, and we describe the histologic changes in these valves excised during operation.

We conclude in chapter 9 with an inventarization of present and future indications for the procedure and some reflections on technical improvements to make the procedure safer and eventually more efficient.

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CHAPTER 2
ISOLATED AORTIC VALVE STENOSIS: HISTORY, ETIOLOGY, PATHOLOGY, PHYSIOLOGY

SUMMARY

Isolated aortic valvular stenosis has been recognized for about half a millennium. Many of the disputes around the etiology of this disease which have raged since, can be ascribed to changing prevalence of the different disease entities and gradual ageing of the population in general. While, only 40 years ago rheumatic fever was the principal cause of aortic valvular stenosis, nowadays this is only found in a small minority of patients in western countries. Thus the proportion of congenital aortic stenosis, or congenitally bicuspid aortic valves, which become gradually stenotic, has increased, and most of all the degenerative form prevalent in elderly patients is now the main cause. Calcification of aortic valves can occur in a congenitally abnormal aortic valve, after rheumatic valvulitis or as a degenerative process in an otherwise normal tricuspid aortic valve. This process of fibrosing and calcification of the valve leaflets regardless of cause, creates a resistance to ejection of blood from the left ventricle, which leads to cellular hypertrophy, hyperplasia and wall thickening in an effort to normalize wall stress. However sustained pressure overload eventually leads to a depression of the contractile state of the myocardium, usually late in the course of the disease, and then is attended by left ventricular dilatation. Thus symptoms usually appear late in the course of aortic valvular stenosis, and consist of angina pectoris, syncopal attacks, sudden death or dyspnea when patients enter the stage of cardiac failure. The onset of symptoms is an indicator of moderately severe aortic valvular stenosis, with an aortic valve orifice restricted to 1.0-0.7 cm^2. Sudden death is uncommon as a first symptom of aortic valve stenosis, and most patients remain asymptomatic until this critical value of an aortic valve area of less than 0.7 cm^2 is attained. Angina pectoris may occur earlier and is explained on the basis of subendocardial hypoperfusion. Syncope and sudden death are interpreted as a consequence of a malfunctioning baroreceptor mechanism rather than critical stenosis percentage. Dyspnea is caused by left atrial pressure elevation and pulmonary venous congestion in turn preceded by cardiac hypertrophy, dilatation and dysfunction in diastole. Evaluation of the natural course of aortic valve stenosis has become difficult because efforts at the objective

measurements of its severity over time by means of sequential left heart catheterization have been thwarted by operative treatment. Most studies on the natural history of this disease are therefore either based on early symptoms or on post mortem examinations, assessing retrospectively the symptoms of the deceased. Yet it is generally accepted that life expectancy in patients with critical aortic stenosis of ≤ 0.7 cm^2 is low, with more than 80% of patients dying within five years. Upon the occurrence of angina pectoris life expectancy is usually limited to three or four years, after syncope to three years or less and after signs of cardiac failure to one year.

The most important coexisting condition in aortic valve stenosis is coronary artery disease, which has a high prevalence among elderly people, the population predominantly affected by isolated aortic valve stenosis. Incidences of 24 to 52% of obstructive coronary artery disease have been reported in patients with severe aortic valve stenosis, the highest percentage being demonstrated in those over 80 years. As the absence of angina pectoris does not always indicate absence of coronary artery disease, selective coronary angiography should routinely be performed as part of a preoperative invasive evaluation in all patients.

HISTORY

The earliest description of aortic valvular stenosis is probably that of Riverius in 1647 who correlated the anatomic changes of aortic valvular stenosis, with the clinical features of a weak pulse and diminished arterial pulsations (1). Carolus Rayger (1672), annotated by Bonetus in his Sepulchretum, also contributed to the recognition of this disease (2). He noted that the aortic valves in a middle aged Parisian taylor who dropped dead on the street, had the consistency of bone. Many physicians, beginning with Corvisart, Napoleon's physician, recorded their impressions of the clinical manifestations of the disease (3). These early recordings led to various misconceptions about the physical signs of aortic valve stenosis. It was James Hope in his " A Treatise on the Diseases of the Heart and Great Vessels" who corrected these to a large extent. He noted that the "contraction of the aortic valves must be very great to render the pulse small, weak, intermittent and irregular". He also wrote that "irregularity of the pulse is not necessarily or usually produced by contraction of the aortic valves, unless extreme; nor are the size and strength of the pulse materially diminished by moderate

contractions"(4).

ETIOLOGY

Valvular aortic stenosis may be a congenital or acquired malformation (Table 1).

Age years	Disease prevalence listed in decreasing frequency
0-30	Unicuspid valve
	Bicuspid valve
30-70	Bicuspid valve
	Rheumatic valvulitis
	Unicuspid valve
> 70	Degenerative calcification
	Bicuspid valve
	Rheumatic valvulitis

Table 1 Etiology of isolated aortic valve stenosis (after Hurst (22)).

The pathogenesis and etiology of isolated aortic stenosis has long been a subject of great controversy. This controversy followed Mönckeberg's attempt to determine the pathogenesis of aortic stenosis in 1904 (5). He studied 32 cases between 26 and 84 years and concluded that either inflammation or degenerative calcification was the cause of aortic stenosis. This concept was the basis for numerous studies summarized by Karsner and Koletsky in 1947 (6). However, they concluded that out of 200 patients with aortic stenosis, 196 exhibited signs of rheumatic valvulitis (6), which view was supported by other cardiologists (7-9). Rheumatic fever is generally considered to be caused by an unusual response to a B hemolytic streptococcal infection. Cross-reactivity between membrane antigen determinants of B hemolytic streptococci (following a throat infection) and certain proteins present in the heart, may produce an immune- conveyed injury to cardiac tissues, evoking inflammation. This inflammatory reaction, in its acute stage, is dominated by edema. Fibrinoid necrosis of connective tissues and cellular reaction occur next. When the inflammatory process is located in

the heart valves, this valvulitis leads to verrucous fibrin deposits along the line of closure of the leaflets. Organization of the acute inflammatory reaction will go together with fibrosis and retraction or thickening. Recurrent attacks of rheumatic fever may thus produce repeated episodes of injury and repair leading to fibrosis of the valves and commissural fusion (10,11,12). This process may affect all three commissures, but is occasionally confined to only one cusp, leading to acquired bicuspidy of the aortic valve. Calcifications in the valve affected by rheumatic disease are as a rule a concomitant finding in patients over the age of 40. Campbell and Kauntze pointed out, that among congenital bicuspid aortic valves, aortic stenosis was more prevalent at a later age, observations which were confirmed by others (3, 13-17). This association, however, had already been recognized in 1858 by Peacock who indicated that bicuspid valves could develop "chronic inflammation" and become thick, unyielding and often ossified (18). Patients developing aortic stenosis over the age of 70, usually manifest degenerative calcifications of an in origin tricuspid aortic valve (19,20).

Many of the disputes around the etiology of valvular aortic stenosis can be ascribed to two causes. First of all the prevalence of several disease entities has changed over the years with for example a dramatic decrease in rheumatic fever especially in developed countries. While Karsner and Koletsky in 1947 described in 200 cases of autopsied aortic valve stenosis a 74% incidence of cases with commissural fusion (6), Petersen in 1985, found only a 10% incidence of the same phenomenon in 109 surgical patients with aortic valve stenosis (21). Secondly the longer survival of the population in general has had a great impact on the distribution of the different disease entities. As can be concluded from Table I, proposed by Willis Hurst (22), ageing of a population in general might favor the incidence of degenerative calcification as a cause of aortic valve stenosis.

PATHOLOGY

Calcific aortic stenosis is a term applicable in a broad sense to all varieties of adult aortic stenosis, but is now generally reserved for aortic stenosis with pure calcification of the valve leaflets. It is now clear that aortic stenosis does not have a single etiology, and in almost all cases can be attributed to one of three processes: calcification in a congenitally abnormal aortic valve, calcification following, usually rheumatic, valvulitis

and degenerative (or senile) calcifications in an otherwise initially normal tricuspid aortic valve (19, 23-25).

Congenital malformation of the aortic valve, includes unicuspidy, bicuspidy and tricuspidy. Unicuspid valves are usually the most common anatomical base for severe valvular aortic stenosis under the age of one year (26-28). Moreover, calcific aortic stenosis seen in children, teenagers and young adults will likely be due to either a unicuspid aortic valve or one with no obvious commissure (acommissural valve). Bicuspid valves may be stenotic at birth, but more commonly are initially not a serious impediment for aortic valve flow (29-31). Their abnormal architecture induces turbulent flow, which leads to trauma of the leaflets and later to rigidity of all cusps due to fibrosis, combined with calcification of the valves and narrowing of the valve orifice (32). The calcification usually develops at the free edges first, and then progresses to the base. If infective endocarditis develops on a calcified bicuspid aortic valve, the destructive inflammatory process renders the valve incompetent, leading to aortic regurgitation. However regurgitation is a rare finding in congenital bicuspid aortic valves without preceding infection. Also severe deposits of calcium do not occur in purely incompetent congenitally bicuspid aortic valves. Based on this observation Roberts states that valvular stenosis seems to be a prerequisite for the development of heavy deposits of calcium at this site. However, the inverse seems to be more plausible, i.e., only heavy calcifications cause stenotic aortic valves (33). Edwards (34), offers an attractive alternate explanation for a congenital bicuspid valve to become stenotic. In his view it is not mechanically possible for a congenitally bicuspid valve to open and close properly. The free margins of normal tricuspid valvular cusps are curved lines. Here the extra length allows the cusps to move freely during opening and closing of the valves. In contrast the distances between the lateral attachments of congenitally bicuspid valves are almost straight lines. Indeed if they were completely straight the valve could not even open during ventricular systole. Consequently at least one cusp is larger than the other, producing abnormal contact between the cusps. This in turn causes abnormal fibrous thickening, in the course of time progressing into calcification. Such an explanation does not elucidate why one congenital bicuspid aortic valve becomes stenotic, another incompetent, and yet another remains free of complications. Furthermore the congenitally bicuspid aortic valve induces calcific aortic

stenosis in patients 40 to 70 years old, yet also tricuspid valves may be congenitally misformed, with cusps of unequal size, which may lead, as in the case of bicuspid valves, to turbulent flows and fibrosis of the valve leaflets. In 20 percent of cases of aortic stenosis between the age of 15 and 65 years, tricuspid valves were found at autopsy, without signs of rheumatic fever. These cases must be considered to have been either congenital tricuspid malformed valves, or degenerative tricuspid valves, or a combination of both (35).

Rheumatic valvular disease is seen in the 30 to 50 age group, especially in women. The aortic lesion is almost always combined with mitral rheumatic valvular disease. Isolated aortic stenosis is a rare manifestation of rheumatic heart disease, accounting for only 5% of cases. Combined mitral and aortic disease occurs in about one third of patients with rheumatic heart disease often leading to the misrecognition of the other valve involvement (36). The stenosis of the aortic valve in this condition is initiated by recurrent episodes of valvulitis in due time leading to fibrosis of the valve leaflets and to fusion of commissures (10,11).

The fusion occurs most often between the left and right aortic leaflet converting the aortic valve into a bicuspid configuration, subjected to the same stresses as congenital bicuspid aortic valves (37). Thus, both for the pathologist and the surgeon it may be problematic to differentiate congenital bicuspid aortic valves from acquired bicuspidy. Osler (38), deduced characteristics to make this differentiation by macroscopic inspection. The raphe (false commissure or ridge) is located where the true commissure normally would be. The length of the free margin of the conjoint cusp, is slightly larger than the margin of the cusp without a raphe. The border of attachment of the conjoint cusp viewed from the ventricular aspect, presents either the contour of a single semilunar cusp or a shallow groove, indicative of the junction of two cusps. The raphe may be located on the aortic wall alone or extend onto the cusp for variable distances. According to Lewis and Grant (39) the subdivided cusp is larger than one normal cusp, but smaller than two normal cusps. As pointed out by Edwards (40) the raphe might also display macroscopic features suggesting fusion of two distinguishable separate cusps in infants with congenital bicuspid stenotic aortic valves. Lewis and Grant (39) considered gross examination to make a distinction between congenital and acquired bicuspid aortic valves unreliable, and supported their macroscopic

observations with histologic examination. They noticed that microscopically a "true" raphe is similar to the media of the aortic wall containing elastic fibres, while fused commissures lacked elastic fibres and consisted mainly of fibrous valvular tissue. Koletsky (24) pointed out that congenital raphes were devoid of vascular channels and inflammatory cells, whereas both were seen in acquired, fused commissures. However helpful these histologic criteria might seem, the experience is that by the time the patient suffers from the complications of his valve anomaly and the valves can be examined either after surgical excision or at autopsy, they will be so heavily scarred and calcified that histologic examination is often fruitless (33).

Primary degenerative calcification of otherwise initially normal tricuspid aortic valves. It appears that tricuspid aortic valves are rarely stenotic at birth. Possibly minor abnormalities in the size of the aortic valve cusps induce abnormal contact of the leaflets with one another, resulting in fibrosis and finally stenosis (41). According to Vollebergh and Becker three aortic valve cusps of equal size are the exception rather than the rule (42). Approximately 5 percent of aortic tricuspid valves show some degree of calcification by the age of 55, with an increase in incidence of 1 percent per year, up to 30% at the age of 85 (25). These degenerative changes were already recognized by Mönckeberg (5), but are not due to atherosclerosis as he suggested. In atherosclerosis the early lesion includes fatty macrophages, which are absent in the early stages of degenerative valvular calcification, the primary change in the latter condition being an alteration of connective tissue with extracellular droplets of neutral fat occurring within the collagen. This material serves as a precursor for calcium deposition. The bases of the cusps are the first sites to be affected with this alteration of the collagen, which later extends to the free margins of the cusps with progressive calcification. The calcification is entirely on the aortic side of the cusps, without fusion of commissures. Calcifications may also extend to the aortic wall while these three phenomena are rarely encountered in rheumatic aortic valve disease (15,19,37,43). The described changes are the same as those which occur at an earlier age in many bicuspid valves and are in the case of bicuspid valves ascribed to simple wear and tear as described earlier in this chapter. Support for the traumatic nature of the valve stenosis is found in the presence of the histologic counterpart of fatty deposits within the collagenous tissue and secondary calcifications in the supraspinatus tendon in

cases of subdeltoid bursitis (43). Although there is an overlap in the different age groups, the basic architecture of the aortic valve in general correlates with the age of the patient. Roberts noticed that there is a definite relationship between the number of cusps present at birth and the age at which aortic stenosis becomes manifest (33). Below the age of 15 years 60% of isolated aortic stenosis is due to unicuspidy and only 15% of these patients have tricuspid aortic valves. On the other hand 90% of patients above the age of 65 years with aortic stenosis manifest tricuspid valves, while none of these elderly patients have unicuspid valves. Aortic stenosis with underlying bicuspid anatomy was found in 20% of patients below the age of 15 years, 60% in patients between 16 and 65 years old, and in 10% of patients over the age of 65. (see Table I). We conclude therefore that congenital aortic stenosis is most frequently encountered with congenital unicuspidy.

INCIDENCE OF VALVULAR AORTIC STENOSIS

Unicommissural, unicuspid aortic valve stenosis

This type of valve is generally considered to be stenotic from birth on, and one of the common forms in very young children. Exceptionally this form of valve stenosis can be free of symptoms for a long period. The oldest reported patient with this type of lesion was 69 years old (12). The incidence of this congenital malformation is not known.

Bicuspid aortic valve stenosis

Congenital bicuspid aortic valves are not intrinsically stenotic (34). Campbell (25) stated that a bicuspid aortic valve occurred in 0.4% of live births, males dominating females in a ratio of 4 : 1. One quarter of these valves became calcified by the age of 40, and one half over the age of 50. Roberts (44) in 1800 autopsied hearts, without preexistent cardiac disease, found 17 congenitally bicuspid valves with normal appearance (1%). The same author concluded that the frequency of this malformation is as high as 2% of all human births (16). This incidence suggested by Roberts is far higher than that encountered by Becker (12) although he did not mention a specific percentage. Fenoglio reported that among children born with a bicuspid aortic valve one third will have normal function throughout life, one third will have calcific aortic

stenosis, and one third will have aortic regurgitation (29).

Rheumatic aortic stenosis

The incidence of isolated rheumatic aortic stenosis in a general population is not known. Of all patients affected with rheumatic heart disease, only 5% manifest isolated aortic valve stenosis (36). While the proportion of stenotic aortic valves with all commissures fused has been reported to be as high as 74% in autopsied hearts in 1947, in two recently reported series, from 1984 and 1985, it was only 27 and 10% (6,21,45).

Primary degenerative calcific aortic stenosis

This condition is now reported as accounting for 30% of surgical cases (21,45). As this disease affects the oldest people, the true incidence of the disease might be underestimated, because many patients are not candidates for surgery.

PATHOPHYSIOLOGY

Stenosis of the aortic valves creates resistance to the ejection of blood from the left ventricle. During systole a pressure difference develops between the left ventricle and the ascending aorta. The left ventricle adapts by hyperplasia and hypertrophy. Hypertrophy by definition is characterized by an increase in volume of the myocytes (12), but initially there is also hyperplasia, an increment in the number of cells. The cellular hypertrophy leads to a regular increase in thickness of the wall and left ventricular mass, known as concentric hypertrophy. This concentric hypertrophy without chamber dilatation normalizes the wall stress, and preserves normal left ventricular ejection function (46). Dilatation of the left ventricle does not occur until, in the more advanced stage of the disease, the contractile state of the myocardium is severely depressed. Eventually the increase in left ventricular volume and mass result in an elevation of the left ventricular end-diastolic pressure. Additionally atrial systole contributes more to the volume ejected by the left ventricle in severe aortic stenosis, as compared to the normal ventricle and so further raises end-diastolic left ventricular pressure (47). Such increases in end-diastolic pressure stretch the myocardial muscle fibres and so evoke a larger stroke volume by the Frank-Starling effect. Initially this will

aid left ventricular emptying (48). However, sustained pressure overload eventually leads to a depression of the contractile state (49). In turn the declining mechanical performance is attended by further dilatation of the left ventricle. This extra left ventricular dilatation will increase the left ventricular radius, and elevate wall stress to unsustainable degrees. Such consistently uncompensated and elevated wall stress jeopardizes coronary perfusion, leading to myocardial ischemia, especially in the subendocardial region. This event can be reinforced by the lengthening of the coronary capillaries in the dilated heart. Moreover, myocardial hypertrophy impairs oxygen delivery to the myocytes even more by increasing the diffusion distance from the capillaries to the center of the enlarged myocardial fibres. For all reasons stated above, myocardial fibres will suffer from ischemia, which not only will lower their performance, but may lead to cell death and fibrosis. This sequence of cellular events also occurs in patients with aortic stenosis without coronary sclerosis. However, it will be clear that in the case of even minor atherosclerotic narrowing of the coronary arteries the effective perfusion pressure of the coronary artery distally from the stenosis will decline even further, increasing the risk of developing ischemic damage to the myocytes.

Cellular malfunctioning can lead to a decline in ejection fraction, which implies a reduction in cardiac output. Reduced cardiac output will increase the left ventricular end-diastolic pressure, causing a rise of the effective left ventricular filling pressure, in its turn leading to left atrial pressure elevation. These events give cause for pulmonary venous dilatation and congestion, going together with dilatation of lymph vessels and edema of the intralobular septa. To protect the pulmonary capillary bed, temporarily a vasoconstriction of the arterial side of the pulmonary circulation will occur, leading to an increase in pulmonary resistance. Eventually this process will lead to structural changes in the pulmonary veins as well as in the pulmonary arteries and overload of the right ventricle.

Histologically myocardial hypertrophy is characterized by myocytes that have an enlarged cross sectional diameter, far exceeding the mean normal myocyte diameter of 12 microns. The nucleus of the hypertrophied cell is also increased in size and often shows a bizarre contour. Dilatation of the left ventricle leads to attenuation of the myocardial fibers and the cytoplasm of the cells is stretched along the enlarged nucleus leading to a discrepancy between nuclear size and fiber diameter. Myocardial

ischemic damage eventually may cause loss of myocytes. This goes together with a scarring reaction in which the lost myocytes are replaced by connective tissue (50). A variety of ultrastructural changes in the myocardium have been documented in patients with aortic stenosis. However, it must be kept in mind that these changes are by no means specific for aortic stenosis, and can also be found in other cardiac diseases. Loss of cellular elements, such as myofibrils and mitochondria, and proliferation of fibroblasts and collagen fibers in the interstitium, as part of the scarring reaction, have been described (51) in coronary artery disease and other inflammatory disorders.

Symptoms appear late in the course of aortic valve stenosis, and consequently patients may have severe stenosis, unrecognized for years. During this asymptomatic period a small percentage of the patients die suddenly (52,53). However the onset of angina pectoris, syncope or symptoms of left ventricular failure are the usual indicators of critical aortic stenosis. Critical in this sense, is commonly used by most authors as an aortic valve area of less than 0.7 cm^2, i.e. less than one quarter of the normal aortic orifice (54).

Angina pectoris is the most common initial symptom of severe aortic stenosis. The incidence of this symptom has been reported to be as high as 70 percent. The average life expectancy when this symptom appears is 5 years, with longer survival (10-20 years) noted only in 5 percent of the patients (7). This symptom can also occur in the absence of obstructive coronary lesions. It is explained on the basis of subendocardial hypoperfusion due to diminished coronary reserve, as described earlier (55,56).

Syncope and an increased risk of sudden death have long been considered to be unique features of aortic stenosis. Three hypotheses are being offered to explain the mechanism of syncope: arrhythmia, abrupt failure of the overloaded left ventricle and a faulty baroreceptor mechanism, leading to peripheral vasodilatation. In the series of patients with syncope observed by Schwartz, the first sign was always an abrupt fall in arterial pressure, followed by ventricular rhythm disturbances (57). It seems therefore that arrhythmias are secondary to a drop in pressure. It was Johnson who offered the hypothesis of baroreceptor mechanism malfunctioning in 1971, as the cause of syncope (58). He explained that an abrupt rise in pressure during exercise without a concomitant rise in aortic pressure, may stimulate left ventricular baroreceptors, to

produce a severe depressor effect. Very little support for the theory of abrupt left ventricular failure has been found in literature. One observation was published in 1967 by Flamm (59). Moreover Lombard (60) stated that syncope usually occurs at the time when left ventricular function is still normal. So it seems that up to now Johnson's hypothesis of baroreceptor mechanism malfunction is the most plausible explanation for syncope in patients with aortic stenosis. Sudden death has been related more to syncopal attacks which become irreversible, rather than to primary ventricular fibrillation (61).

Left ventricular function is well preserved in most patients, not only in the asymptomatic stage, but also in the patients with angina or syncope. Depression of left ventricular function may be caused by inadequate left ventricular hypertrophy and progression of the severity of aortic stenosis. Correction of the stenosis usually reverses hypertrophy and restores left ventricular function, mediated by regression of myocardial cellular hypertrophy. But even 6-7 years after valve replacement the regression of structural abnormalities of left ventricular hypertrophy is still incomplete, as recently demonstrated by left ventricular biopsies by Krayenbühl and co-workers. (62).

When left ventricular dysfunction is such that cardiac output is depressed, outflow obstruction becomes relatively more severe. These events might explain the rapid deterioration of patients with aortic stenosis, who enter the stage of cardiac failure (63). Progression of the severity of aortic stenosis can be accomplished either by a further reduction of the orifice size, or by restricting the mobility of the cusps. In congenital aortic valve stenosis the size of the orifice is determined at birth. The degree of stenosis may remain unchanged, progress, due to secondary degenerative changes, or possibly regress with the growth of the heart (64-66).

Rheumatic aortic stenosis develops in its early stages from cusp fibrosis and commissural fusion. Bland and Jones indicate that the stenotic process in the aortic valve is slower than in the mitral valve (67). A further decrease in the mobility of the movable portion of the cusps is achieved by calcium deposition, furthering progression of stenosis. This hypothesis is supported by findings at autopsy and surgery, where patients with rheumatic aortic valve stenosis show postinflammatory fibrosis and usually extensive calcifications (68).

In calcific aortic stenosis, a term usually applied to calcified bicuspid and tricuspid

aortic valves, the commissures are usually unaffected. The valve becomes more stenotic as the mobility decreases by fibrosis and deposition of calcium, as demonstrated by Wagner and Selzer in a serial study of 50 patients. Progression of stenosis was more rapid in older patients with calcific aortic stenosis (63). As stated by these authors, calculation of aortic valve area by means of cardiac output and mean transvalvular pressure gradient, constitutes a more reliable measure of progression of disease than the pressure gradient alone, because a decrease in valve opening force might reduce both cardiac output and transvalvular pressure gradient.

NATURAL COURSE

Evaluation of the natural course of aortic stenosis has been difficult because the objective assessment of its severity by means of left heart catheterization, and the initial attempts at correction by operative treatment, occurred almost simultaneously (52). Therefore most information on the natural history of aortic valve stenosis must be assembled from clinical and postmortem studies of the pre-surgery era. As mentioned earlier, the course of valvular aortic stenosis is characterized by a long asymptomatic stage. The normal aortic valve area in adults varies between 3 and 4 cm^2. Resistance to flow, manifesting itself by a transvalvular pressure gradient, appears when the aortic orifice is reduced to 1 to 1.5 cm^2. Symptoms seldom develop before the stenosis is at least moderately severe (0.7 to 1.0 cm^2), but even patients with critical aortic stenosis (< 0.7 cm^2) may remain asymptomatic (60).

Angina and syncope are early warning symptoms, present in about two thirds of patients with aortic valve stenosis. In the remaining one third congestive heart failure is the initial presentation (60). Also the age at which clinical symptoms present has changed. Ross and Braunwald in an overview of aortic stenosis collected several studies between 1934 and 1967, and found a mean age of clinical presentation of symptoms of 48 years (52). In the more recent study (1987) of Lombard and Selzer the age at presentation in symptomatic patients was 61.1 years (60). Many patients are not even considered for presurgical evaluation, due to other concomitant life expectancy limiting disease, so that the mean age at presentation might even be higher nowadays.

Only a few prospective clinical studies about the natural course and mortality in

aortic valve stenosis are available. Most of these studies, however, are based on symptoms, without evaluating the actual severity of the disease. Grant reported a 65% mortality in symptomatic patients at the end of 10 years follow up (69). Wood followed 32 patients, who were considered clinically to have severe aortic disease, for periods of one to seven years. Eighteen of these patients died during the observation period (7). Of Takeda's series of 60 patients admitted to the hospital with a diagnosis of isolated aortic valve stenosis, 82% were dead after 4 to 15 years (53). In the only reported series of 12 patients with critical aortic valve stenosis (valve orifice ≤ 0.7 cm^2), assessed by cardiac catheterization, without subsequent operation, 10 were dead, at the end of five years (70).

In various studies based on data obtained at post mortem examination the average duration of various symptoms was as follows: angina pectoris three years, syncope three years, dyspnea two years and congestive heart failure 1.5 to 2 years (52). Olesen and Wartburg showed a mean survival in the presence of angina of 4.7 years, in the presence of syncope of 3.2 years, and with concomitant cardiac failure of less than one year (71). The prognosis extracted from the literature might nowadays be more favorable, because the fatal outcome might have been modified by modern therapeutic measures. This is especially valid in the case of bacterial endocarditis, which counted for 15 to 20% of all deaths with isolated aortic valve stenosis in post mortem studies (52). Selzer recently stated that infective endocarditis is a rare complication of aortic valve stenosis, its incidence being known only for congenital aortic stenosis, and estimated to be 1.8 per 1000 patients-years (61,72).

COEXISTING CONDITIONS

The most important coexisting condition is coronary artery disease, which has a high prevalence among older people, which also happens to be the population predominantly affected by aortic stenosis. Roberts found a 48% incidence of a severe obstruction in at least one major coronary artery in 21 autopsied patients with severe aortic stenosis over the age of 65 years (20). Exadactylos et al. reported in 1984 a 34% incidence of coronary artery disease in a consecutive group of 88 patients with a mean age of 58 years requiring aortic valve replacement for isolated aortic valve stenosis. Interestingly, in view of current findings, they did not find significant coronary artery

disease when patients were free of angina (73). Bessone recently in a group of 219 patients, with a mean age of 74.8 years, identified 112 patients with concomitant coronary artery disease (52%) (74). In the same year, an incidence of only 24% was reported in a comparable population but with a lower age of 59 years (75). In another report from Emory, comprising 152 patients over the age of 70 who underwent aortic valve replacement, 41% of patients over the age of 70 underwent concomitant coronary bypass grafting, while under the age of 70 this figure was 31% (76). Although there is already a relatively high incidence of coronary artery disease in aortic stenosis, there is a tendency to an even higher incidence in older people. Angina pectoris is not always present in these patients. A study of Hancock revealed that, in a series of 45 patients with aortic stenosis without anginal complaints, 33% had significant coronary artery disease ! (77). Since coronary artery disease occurs so frequently in patients with aortic stenosis and may even exist without angina it is advisable to perform coronary arteriography in all patients with severe aortic valve stenosis, in need of aortic valve replacement.

An association between aortic stenosis and idiopathic gastrointestinal bleeding has been postulated for the first time in 1958 (78,79). Later reports more specifically related aortic stenosis to intestinal angiodysplasia (80,81). Although several case control studies on this subject have been reported (82-86), Imperiale and Ransohoff (87) recently concluded, after a critical review of the literature, that, due to methodological inadequacies, an association between aortic stenosis and angiodysplasia has not been demonstrated.

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CHAPTER 3
SURGICAL INTERVENTIONS FOR THE TREATMENT OF AORTIC VALVULAR STENOSIS

SUMMARY

In 1913 for the first time an attempt was made to dilate an aortic valve by digitally invaginating the aortic wall. Since then, the attention of, surgeons was initially more directed to dilating stenotic mitral valves, but around 1950 several instruments were developed to dilate, or separate stenotic aortic valves, without much success. In 1951 Hufnagel implanted an artificial valve in the descending aorta. With the introduction of cardiopulmonary bypass and the pumpoxygenator in 1954, techniques for surgical débridement of calcified aortic valves were developed, some of which still persist. Between 1950 and 1960 aortic cusp substitution, cusp extension and valve replacement, both by Starr - Edwards caged ball prostheses, as well as by homologous and later heterologous aortic valve grafts were the techniques used. These techniques were complemented by the use of auto and heterologous allografts, such as pericardium and dura mater. Homografts after cryopreservation appear to provide better results than nutrient medium preserved homografts. Some hospitals predominantly use aortic homografts for all age groups, with fairly good results, also in the long-term. Despite several large studies comparing biological valves with prosthetic valves, mainly Starr - Edwards and Björk - Shiley prostheses, the evidence is not yet decisive concerning failure rates into the second decade after implantation. For the first five years biological valves are superior, but in the second five year period results are equal for both valve types. Biological valves seem especially indicated in older patients, because they do not require anticoagulation, and results are better than in younger patients.

The evolution of prosthetic heart valves revolved around improvements of hemodynamic characteristics and durability, together with reduction of thrombogenicity. Caged-ball, disc-valve and bileaflet valve prostheses, are the valves most often employed. All patients need anticoagulation after implantation of these valves. There is also still a place nowadays for surgical valvuloplasty, which evidently does not need anticoagulation afterward.

Operative risk of aortic valve replacement has declined over the years, mainly due to better myocardial preservation techniques, but also by operating on patients earlier. Nevertheless there is an increasing demand for aortic valve replacement in the elderly, as the general population ages and because patients are better informed, and more often referred to cardiosurgical centers. Increasing age, advanced functional class, poor left ventricular function, female gender, urgent operation and the presence of coronary artery disease all are important independent predictors of operative mortality. It is advisable to calculate the operative risk, before discussing the options with the patient involved. After aortic valve replacement survival is improved in all age groups, especially if compared with a group of patients who were deferred or refused the operation. Linearized mortality rates were the same after aortic valve replacement for both mechanical and biological valves.

Hemorrhage and thromboembolism are the most frequent valve related causes of morbidity after aortic valve replacement. It is concluded that age alone should not be a contraindication for surgical treatment of aortic valve disease, but that all factors pertinent to the operative risk and postoperative course should be included in the weighing process, before discussing the risks and potential benefits with the patient and his/her relatives.

A HISTORICAL REVIEW OF NOW DEFUNCT TECHNIQUES AND DESIGNS

Valvulotomy and débridement

The first referral to surgical repair of the aortic valve is by Allen and Graham who in 1922 divided the aortic valves in dogs by means of a cardioscope (1). Tuffier in 1913 made the first attempt to dilate a stenotic aortic valve in a patient, digitally invaginating the aortic wall (2). In 1924 this patient was reported to be still improved. In 1947 Smithy and Parker reported an animal study of aortic valvulotomy with open chest dogs using a hooked blade introduced through a sheath, which was inserted into the ascending aorta. They intended to perforate the normal aortic cusps in order to achieve a complete division of the free margin of the valve leaflet by retracting the barbed blade. More than one third of the animals died of bleeding from the ascending aorta, while division of the cusp could only be achieved in 30% of all surviving dogs (3). Bailey and coworkers stated that "only an entirely new valve could offer a reasonable solution" (4) and

continued the experiments of Smithy. To test this hypothesis they resected part of the aortic valve in mongrel dogs and replaced the valve action by inserting either an inverted vein graft, or direct valve grafts, or free aorta grafts between the left ventricle and the aorta. Later they redirected their attention towards punch resection of the aortic valve by a punchcutter either, from the left ventricle, retrogradely, or from the ascending aorta. As these methods produced an impressive amount of regurgitation they were abandoned. The same investigators later developed a Brock-like type of valvulotome, which had been used for division of the pulmonic valve in congenital pulmonary valve stenosis (5). The valvulotome has an umbrella like configuration, with three blades. They intended to cut through the posterior cusp and through the commissure between both anterior cusps. For this purpose the instrument was inserted in the left ventricle via the left ventricular apex and advanced through the aortic valve with retracted blades. Once the aortic valve was passed the instrument was opened and withdrawn into the left ventricle. On March 9, 1950, they performed this procedure for the first time in a 26 year old woman with severe aortic stenosis. Although they encountered problems crossing the valve, they ultimately succeeded in pulling back the partially opened instrument into the left ventricle. Directly after this manoeuvre, the patient died however. Autopsy revealed that the knife had been properly inserted, cutting the posterior valve leaflet for about one centimeter. Appreciable aortic regurgitation must have been produced by division of this cusp, leading to the fatal outcome. After this disappointing experience they devised an instrument shaped like a large pencil with a blunt point. This instrument was guided into the left ventricle via an incision in the left common carotid artery. After arriving in the left ventricle, the dilating mechanism was opened, to gradually dilate the narrowed orifice. Bailey and coworkers performed this procedure in 2 patients, and both withstood the procedure well. A third patient, however, died as a result of the procedure. This last event led to a change in approach to the aortic valve (4). In a later communication (6) they reported the use of this instrument in 11 patients, entering the aortic valve via an apical ventriculotomy. Two of these patients died in the hospital, one of them during operation. At autopsy this case manifested the degenerative type of valve stenosis, without any commissural fusion. The other patient died at day 13 of multiple peripheral arterial emboli. Two other patients died respectively at 12 days and one month after discharge, one due to cardiac failure the other due to septicemia. One further patient had, after several months, recurrence of anginal pain and myocardial

insufficiency. They felt that this instrument had insufficient dilating force and that forced passage of the opened, umbrella like dilatorhead back and forth through the valve orifice, was unduly traumatic (6).

By April 1952, a much superior instrument was developed to dilate stenotic aortic valves. The original umbrella spring type blades, had been replaced by three parallel dilating bars with wedgelike cross sections. It contained a beaded guidewire at the distal tip, and an operating control mechanism at the proximal end (7). The beaded wire was inserted into the left ventricular apex under purse string control, and advanced into the stenosed aortic valve. After setting of the control mechanism, so that the open diameter of the instrument would be slightly less than that of the aortic ring, and after aligning the instrument, so that the triradiate arms fitted into the commissures, the instrument was opened. In their first publication, 23 patients underwent aortic commissurotomy. In 13 patients this was combined with mitral commissurotomy. Only one patient died as a result of the operation (7). Aortic valve surgery had come of age.

In 1956, applying general hypothermia, Lewis and Shumway for the first time performed aortic valvulotomy under direct vision, after occluding the inflow of blood to the right heart. In their description of the first three patients, of whom one died due to a technical error, they state that an accurate separation of all three cusps was achieved under direct vision. They thought this would be a better operation than blind transaortic or transventricular procedures, especially in non calcified stenotic valves, with fused commissures (8). In the discussion of this paper, the superiority of "seeing being better than feeling" was questioned by Harken, who stated that lightly fused tricuspid aortic valves may best be managed by finger fracture. In the same discussion Larzelere showed an improved Donaldson instrument. This dilating instrument had about the same features as the one introduced by himself (7), but was advanced retrogradely, using a pouch or tunnel sewn onto the ascending aorta to control bleeding (9). The instrument was fingertip guided through the aortic valve and then opened (8).

With the introduction of cardiopulmonary bypass and the pumpoxygenator in 1954, a still more effective approach to the surgical treatment of aortic valve disease became possible.

Lillehei was one of the first to use total bypass of the heart and lungs together with retroperfusion of the coronary sinus, to retain a healthy pink color of the myocardium (10). The next logical step was to combine the advantages of extracorporeal circulation

with aortic valvulotomy and removal of calcareous deposits form the leaflets (débridement), a technique advocated by Bailey (11). Kirklin and Mankin described 14 patients operated upon in 1959, using extracorporeal circulation and valvulotomy combined with débridement for both isolated aortic stenosis and aortic stenosis combined with aortic incompetence (12). Thirteen out of 14 patients survived the operation; one died later, and another one was unimproved at short term follow-up. The débridement and other sculpturing techniques for restoring aortic valve anatomy were largely superseded by techniques involving valve replacement. However, already in 1967 Hurley et al reported their very disappointing results with débridement operations in a group of 76 patients. Thirteen out of the 61 patients with isolated aortic valve stenosis died during, or directly after the operation (21%), while another 6 died at follow-up. Although the majority of the surviving patients felt improved (60%), objective evaluation of this group at a mean of 46 months after operation, revealed a good or satisfactory result in only 5 patients (13%). They felt that débridement valvulotomy should no longer be considered as a suitable treatment (13). McGoon et al., however, had concluded two years earlier, that the method might have limited application, in patients where restoration of valve mobility could be anticipated (14). Indeed this surgical method has up to the present not been abandoned. Recently Mindich et al reported an increase in valve area from 0.55 cm^2 to 1.56 cm^2, using improved surgical valvuloplasty techniques in 23 patients with a mean age of 75 years. Follow-up ranged from 6 months to six years, in which period two patients died and two required reoperation. These authors conclude that aortic valvuloplasty, carefully performed, may be an excellent alternative in a select group of patients with aortic stenosis (15). Patients with a trileaflet valve, a small aortic valve annulus, a contra indication for oral anticoagulation and without significant aortic regurgitation are in their view candidates for this procedure.

Aortic valve replacement for aortic valve incompetence

In 1951, Hufnagel in Washington, developed a ball valve prosthesis for rapid insertion into the descending aorta just distal to the left subclavian artery to palliate severe aortic incompetence (16,17). Although palliation was observed in some patients, signs of aortic incompetence in the upper body became very severe (17,18). Some years later in 1961 a cusp-type valve prosthesis was developed by Hufnagel and Conrad, and was used widely after being commercially available (19). These authors introduced the technique

of topical cooling of the myocardium, combined with cardiopulmonary bypass. They stated that if the myocardial temperature could be reduced to between 5 and 8°C, periods of cardiac arrest of at least 100 minutes would be safe. A complete prosthetic valve consisted of 3 separate leaflets, made of terylene cloth impregnated with silicone rubber, while the free edge was sealed to prevent ingrowth of fibrous tissue. In over 100 patients with aortic incompetence, operated upon with replacement of the incompetent valve by this prosthesis, all except one resumed satisfactory cardiac output following topical cooling.

McGoon, also in 1961, employed a single unit prosthesis, consisting of a Teflon sleeve, fashioned from a piece of ordinary woven Teflon aortic prosthesis. Three of the first seven patients died in hospital (20). Further application of this valve in the Mayo Clinic proved to be rather unsuccessful because initial competence was sometimes not achieved, leading to an appreciable hospital mortality (21).

After several rather unsuccessful attempts to reduce aortic incompetence by circumclusion (narrowing of the aortic base by a woven silk band from the outside) and direct plastic procedures to provide a better apposition of incompetent valve cusps, Harken and coworkers directed their attention to cusp substitution, cusp extension and valve replacement (22). Teflon cloth used initially was subsequently abandoned for fear of ingrowth of fibrous tissue. A stiff woven Teflon patch for the cusp extension proved unsatisfactory.

They subsequently constructed a caged-ball valve, of stainless steel, with a Lucite ball, used since 1955 in human beings (23). This valve was quiet, atraumatic, competent, offered little resistance to flow (25 mm Hg pressure difference at a continuous flow of 20 l/min) and produced normal pulse contours, under laboratory conditions. However from the first five patients with massive aorta incompetence, only one survived implantation of this valve. The fatalities were ascribed to the preoperative grossly dilated left ventricles (22).

About one year later Starr and Edwards used a slightly modified caged-ball prosthesis with a silicone rubber ball and a vitallium like alloy cage. Out of their five first patients 4 died in hospital, one from valve suture dehiscence, one from hemolysis, one from cerebral thrombosis and one from preexistent left main coronary artery disease. The fifth patient died at 8 months due to a thrombus formed on the Teflon coated prosthesis ring and extending into the left coronary ostium. Afterwards they changed the sewing ring

from the rigid short Teflon cloth sleeve to a semirigid more compressible sewing margin. In 1962 this new type of valve was implanted in 11 patients. One patient died during operation, and there was one late death (24).

These efforts at replacing incompetent valves have strongly influenced the designs of valves utilized in replacing the stenotic valve.

Homo and heterologous aortic valve transplants

In 1956 Murray from Toronto reported the use of homologous aortic valve segments in three patients with severe aortic incompetence. Aortic valve segments were obtained from human postmortems and kept in saline gauze. Without extracorporeal circulation the segment was sewn into the descending aorta, just distal to the left subclavian artery. Circulation to the descending aorta was interrupted in the first case for 37 minutes. All three patients improved considerably following the operation (25). Six years after operation the first patient was reported to do well, while his cardio-thoracic ratio had decreased. Another 8 patients had been operated since 1956, of whom 3 died in the immediate post-operative period (26).

In Europe, D. Ross was the first to insert a freeze-dried aortic homograft below the coronary ostia. The patient did well after operation with a medication of anticoagulants and hydrocortisone (27). Barratt - Boyes from New-Zealand reported a series of 57 patients operated upon in 1962 and 1963, with the same technique as used by Ross. Four patients died in the post-operative phase, while three others died during follow-up. He used sterilized, freeze-dried valves, removed within 15 hours from the donor hearts (28).

The first use of a heterograft in a human being was reported in 1965 by Binet, Duran, Carpentier and Langlois. In their preliminary communication 5 patients were discussed who all had their stenotic or incompetent valves replaced by pig or calf aortic valves, all with good immediate results (29). A year earlier Duran and Gunning had transplanted a heterologous aortic valve in a very ill patient, who died 24 hours later from causes unrelated to the heterograft (30).

Carpentier used a support ring, instead of direct suturing of the heterologous valve graft; the support was subsequently modified into a frame on which the graft was mounted. He also modified the mode of preservation, from sterilization to electrodialysis, oxidation and cross linkage. These two combined changes improved the immediate as

well as long-term functioning of the graft. Grafts were stored in a gluteraldehyde solution (31).

Senning in Zürich used a strip of autologous fascia lata tissue to form three cusps. From his first series of 90 patients, 13 died within two months, most of them due to myocardial failure, coronary air embolism or myocardial infarction. Another 10 patients died 3 to 45 months postoperatively with a high incidence of endocarditis, while 4 patients were reoperated on due to valvular incompetence (32). Although no signs of fascia lata calcification or thromboembolism were found in Senning's patients, the high incidence of post-operative bacterial endocarditis led to the abandonment of this method.

From 1969 on Ionescu and Ross implanted autologous fascia lata valves, attached to a supporting frame (33). Ionescu later introduced heterologous pericardial tissue, also mounted on a frame as aortic valve replacement. In his first 80 patients with aortic stenosis, a 10% operative mortality is mentioned. Causes of death were heart failure, endocarditis, cerebral infarction and necrosis of the ileum. Another 8 patients died 2 to 15 months postoperatively, 3 of infective endocarditis, two of cardiac failure and one of mesenteric artery thrombosis (34). In two patients no cause of death was found. Because there is only limited time available in the operation theatre to construct these valves meticulously, Ionescu and coworkers later preferred stent mounted homologous fascia lata, or heterologous stent mounted pericardial tissue valves. These were prepared beforehand in the laboratory, sterilized and preserved, according to Carpentier's method (31).

Puig and Zerbini from Sao Paulo employed homologous dura mater tissue, prepared according to Ionescu's method. Dura mater was obtained at most 12 hours after the donor's death, and preserved in 98 per cent glycerin at room temperature for at least 12 days. After construction of the valve under aseptic conditions, it was preserved in a solution of physiologic saline with kanamycin and cephalothin, and stored at 4°C. Their initial results were satisfactory, but with a follow-up period of only 7 to 14 months no definite conclusions could be drawn as to the durability of these valves (35).

CURRENTLY USED SURGICAL TECHNIQUES FOR AORTIC VALVE REPLACEMENT OR RECONSTRUCTION

Aortic valve reconstruction

Although débridement was already described in 1967 by Hurley (13), with very disappointing results, McGoon stated that there still might be a very limited use of this method (14). In a well preserved three leaflet aortic valve, without commissural fusion, débridement of the individual leaflets might be performed, if for example the patients condition or age precluded valve replacement (15). In our own institute débridement has been conducted in 3 patients during the last year, with good direct results, a reduction of the maximal flow velocity measured with Doppler over the aortic valve, and good functional improvement (E. Bos, personal communication).

Homo and heterografts to replace the aortic valve

Homografts

After freshly procured aortic valves by Ross and Barratt - Boyes in the early sixties (27,28), preserved and sterilized valves came into use. However, irradiated and chemically sterilized valves showed a high incidence of cusp rupture, necessitating reoperations in a third of all patients within 6 years (36). In a later period valve failure was reduced when homografts were sterilized with antibiotics, and preserved in a nutrient medium (37). O'Brien recently compared the results of 124 allograft (nonviable) aortic valves, preserved by antibiotic sterilization and nutrient medium preservation at 4°C with 192 viable allografts cryopreserved at -196°C in liquid nitrogen. A total of 316 aortic valve replacement operations were performed from 1969 through 1986. Operative mortality was 6.0% while survival at 4 and 15 years was respectively 83 and 60%, without differences between the two groups (mean age at operation 51 years). Thirty eight patients underwent reoperation, 84% of the fresh valve group being at ten years without reoperation, while this was 92% for viable cryopreserved valves. Freedom from a thromboembolic event was the same between the two groups, being 97% at ten years and 96% at 15 years (38).

Aortic valve replacement with an aortic homograft sewn freehand in the aortic ring, is in some institutions, like the Green Lane Hospital in New Zealand, routinely used in all ages when no contraindications are present. The only real contraindications are

circumstances that predispose the patient to progressive dilatation of the aortic sinus, or aortic root, like aneurysms and media-necrosis, leading to aortic incompetence (21).

Heterografts

Since the introduction of the glutaraldehyde preservation technique by Carpentier, bioprostheses have provided an appealing alternative for mechanical valves, primarily because no long-term anticoagulant treatment is needed. A recently published randomized collaborative trial of 13 Veterans Administration hospitals compared 198 mechanical valves (Björk - Shiley), with 196 biological valves (Hancock) implanted in the aortic position. After a relatively short follow-up period of, on average, 5 years with a maximum of 8 years, a significantly higher proportion of patients with a biological valve proved to be free from all valve related complications, compared with the patients with mechanical valves, 63 vs 53%. This difference was entirely due to a higher hemorrhage rate with the mechanical valves (85 vs 67%). Thromboembolism rates were comparable with 9 and 10% respectively for mechanical and biological valves. No failure of one or another valve type had yet occurred at a relative short follow-up period of 5 years. Operative mortality was respectively 9.2 and 6.1% for implantation of a biological valve or mechanical valve in this group of patients with a mean age of 60.2 and 59.1 years respectively (39).

Another study compared three valve types implanted in the aortic position in 2074 patients in 3 different institutions. Results with the Starr - Edwards Silastic ball valve (Oregon), the Hancock (Stanford) and Carpentier - Edwards (Vancouver) porcine valves are compared with respect to treatment failure, defined as a valve-related death or permanent patient disability. Using this definition, biological valves are superior at 5 years; at 10 years the results are comparable. Structural failures of implanted valves had occurred at 7 years in 0% of Starr - Edwards prostheses, 5% of Hancock valves and 3% of Carpentier - Edwards valves. At 10 years no structural failure had occurred in the Starr - Edwards valves, while in 21% of Hancock valves a structural failure did occur. In the widely used Stanford definition of structural failure, which includes any valve related complication causing death or requiring valve removal, at 5 years respectively 95, 93 and 98% of all implanted aortic Starr - Edwards, Hancock and Carpentier - Edwards valves, were free of failure. At 10 years these numbers were 88 and 72% for Starr - Edwards and Hancock valves respectively, while follow-up time for

Carpentier valves was still less than 10 years (Table 1) (40).

	Aortic		
Variable	Starr	Hancock	Carpentier
Patient-years	3,310	4,747	2,532
Treatment failure-free			
At 5 years	93 (1)	96 (1)	97 (1)
At 7 years	91 (2)	94 (1)	93 (2)
At 10 years	90 (2)	87 (3)	.....
Structural failure-free			
At 5 years	100 (0)	98 (1)	99 (1)
At 7 years	100 (0)	95 (1)	97 (3)
At 10 years	100 (0)	79 (4)	.....
Valve failure- free			
At 5 years	95 (1)	93 (1)	98 (1)
At 7 years	94 (1)	88 (1)	95 (4)
At 10 years	88 (2)	72 (4)	.....

Table 1 Actuarial comparison of % of patients free from treatment, structural or valve failure at 5,7 and 10 years after implantation of Starr - Edwards, Hancock or Carpentier - Edwards valves in the aortic position (Standard error percentage)

Another analysis of biological versus mechanical valves, comparing total morbidity and valve related mortality significantly favored the biological valves in the first 5 years after implantation, and the mechanical valves in the ensuing five years, but the net 10 years results were not significantly different (41). This study included four different biological and five different mechanical types of valves, implanted in three different positions. These authors also noted an increased failure rate of biological valves in younger patients, as stated earlier by several authors (42-44).

A Spanish report compared long-term survival in 85 patients in whom 38 Björk - Shirley and 47 Hancock valves were implanted in 1975. Hospital mortality was 13 and 6% respectively. Unfortunately these authors did not state the age at which these patients were operated, as they only gave global figures of mean ages of the total group, which

also included mitral and double valve replacement. Mean survival at 10 years was 94 ± 4.2% and 89 ± 4.9% in patients with mechanical and biological valves respectively, a difference which is not significant. However in the 10 year follow-up freedom of reoperation was statistically significant higher in the Björk - Shirley valves than in the Hancock valves implanted in the aortic position, being 90 ± 5.2 and 63 ± 8.3% respectively (45).

Two studies from Scotland compared a mechanical valve prosthesis (Björk - Shiley) with a porcine aortic bioprosthesis (Hancock or Carpentier - Edwards) (46,47). Bloomfield et al randomized patients to a mechanical disc valve, or a porcine heterograft prosthesis. In hospital mortality was 7.6% for all patients undergoing aortic valve replacement, without significant differences between the three types of valves implanted. At a follow-up of 7 years no significant differences in actuarial survival were noted, survival being 69.6 ± 9.9% after 7 years for the whole group with aortic valve replacement. In the same follow-up period no significant differences in thromboembolic events were noted, all patients with a mechanical valve prosthesis and some of the patients with a porcine heterograft receiving anticoagulation therapy. Likewise reoperation was evenly distributed between the three types of valves being associated with a high operative mortality of 30%. The risks of anticoagulation in this trial were low with an overall incidence of complications of one per 100 patient years. These authors concluded that after a median follow-up period of 5.6 years no significant advantage of the use of any of the three prostheses studied had yet appeared, but that important differences might emerge later.

The other Scottish study, reported by Nashef et al, compared 169 Björk - Shiley aortic valves with 205 Carpentier - Edwards valves implanted in the same position. Hospital mortality in this study in patients with a mean age of 51 years was not statistically different being 5.9 and 4.9% respectively. At a mean follow-up of 3.2 and 3.5 years respectively no significant differences were found in overall incidence of thromboembolism, endocarditis, periprosthetic leak, anticoagulant related complications, incidence of reoperation, or late mortality.

Less information is available regarding the bovine pericardial valve implanted in the aortic position. At 10 years follow-up Ionescu et al found an actuarial survival of 85.8 ± 8.7%. In this group 83.0 ± 9.1% of all patients were valve failure free, and 72.5 ± 13.2% were free from all major complications. The linearized rate of embolism without

anticoagulant treatment is 0.55% per annum, with no deaths related to embolism (48). It is possible that newer generations of porcine and pericardial valves might improve the durability of these valves (49-51).

The evidence presented above establishes the fact that for the first five years tissue valves are superior to mechanical valves. They thus present an alternative choice when life expectancy is limited and anticoagulation problematic. In the second five year period results are equal for biological and mechanical valves, while beyond 10 years antibiotic treated homografts are definitely inferior compared to mechanical prostheses. Thus in younger patients and in areas where anticoagulant therapy is well controlled, this type of valve is preferred. Cryopreserved homografts show the same effectiveness as mechanical grafts, with 83% being free from intrinsic tissue disruption at 13 years (52). In children this appears to become the favoured approach. Another approach to treat valvular aortic stenosis in younger patients, introduced by D. Ross in 1967, is aortic valve replacement by pulmonary autograft (53). This technique, has also shown good results with an actuarial event free rate of 74.2% at 19 years. For the porcine valves no decisive figures concerning failure rates into the second decade are available.

Prosthetic heart valves

As pointed out earlier, Hufnagel and associates were the first to implant a caged ball prosthesis in the descending aorta in September 1951 (10). The subsequent history of prosthetic valves revolved around modification of the basic ball valve design, alteration of construction material and introduction of new valve designs.

The first caged ball valves to be widely used were the Starr - Edwards prostheses, which have undergone several refinements (54). The caged ball principle is also applied in the Smeloff - Cutter and Braunwald - Cutter valves, designed to diminish the stenotic nature of ball valves and problems associated with cloth covering (55,56).

Disc prostheses (Kay - Shiley, Kay - Suzuki and Cross - Jones) were developed to overcome problems of poppet inertia, by employing a light weight disc as an occluder and reducing the length of the cage (57,58). However, the incidence of thromboembolism remained high in these prostheses and led to the development of the Beall valve, a cloth covered disc prosthesis (59). However pressure gradients across these valves remained high as the valve orifice remained small (60).

To enlarge effective valve area, eccentric, monocusp, central flow prosthetic devices were introduced. First of these new types was the Wada - Cutter prosthesis which suffered intermittent fixation of the valve disc in an open position (61). One year later the Björk - Shiley design was introduced with a free floating and rotating disc (62). Although this model has been utilized in numerous patients, recently fracture of the struts restraining the disc has been reported in the convexo-concave valve types CC60 and CC70, especially with a 70 degree opening angle, leading to embolization of the disc and immediate massive aortic incompetence (63). The last two valves mentioned have an opening angle of 60° - 70°, while a third pivoting disc valve , the Lillehei - Kaster has an opening angle of 80°, which hopefully would lessen the incidence of thromboembolism (64).

The St. Jude bileaflet valve contains two valve discs which open vertically, and approach most closely normal physiological conditions. Haemodynamically superior, this valve also has a lower incidence of thromboembolic complications ranging in various reports from 0.3 to 2.5% per year and valve thrombosis between 0 to 1.2% per year. Rates are higher when anticoagulation is not given (65-70).

INDICATIONS FOR OPERATION IN PATIENTS WITH AORTIC STENOSIS

Patients with calcific aortic stenosis usually present because of symptoms, and when in such patients the presence of an important stenosis is confirmed by catheterization or echo Doppler measurements, i.e. a valve area of ≤ 0.7 cm^2, operation is clearly indicated. Signs and symptoms of left ventricular failure make the operation urgent. When symptoms are absent or trivial, and the stenosis is clearly important with a residual aortic valve area of ≤ 0.7 cm^2, operation is advisable. A positive exercise test lends weight to the decision to operate. In patients with predominantly anginal symptoms, who are found on cardiac catheterization to have a moderate to severe aortic stenosis (valve area 0.7 - 1.0 cm^2) and severe coronary artery disease, coronary artery bypass grafting should be performed, and the aortic valve replaced at the same time. Moderate to severe stenosis alone can also be a reason to replace the aortic valve, depending on the patients physical activities, and the diminished quality of life experienced.

OPERATIVE MORTALITY OF PROSTHETIC AORTIC VALVE IMPLANTATION AND MORBIDITY AFTER IMPLANTATION

The risk of aortic valve replacement depends on several, sometimes interrelated factors. Recognized risk factors are:

Operation decade

Acar reported a 19% early mortality in patients operated for aortic stenosis with or without aortic incompetence over the age of 65 in the period from 1968 to 1979 (71). Jamieson collecting his data in the same period found a 4.7% thirty day hospital mortality in aortic valve replacements for all causes in the age group over 65 (72). In his overview of the literature an overall operative mortality in the sixties was found of 13.3% for aortic valve replacement over the age of 60. In the seventies this figure dropped to 7% for the same condition in the same age group. Cormier reported a 8.1% operative mortality in a group of patients, with a majority having aortic valve replacement for aortic stenosis, before 1983, while this was 3.7% after 1983 (73). The year of operation was not a predictor for hospital mortality in Craver's review on operated aortic stenosis from 1975 to 1987, the overall death rate being 4.6% (74). So it seems reasonable to state that operative mortality for aortic valve replacement for mainly aortic stenosis is around 5% in 1989 taking all patients together, an experience matched by that of The Thoraxcenter.

Age at operation

Older age at the time of operation seems to contribute substantially to operative mortality. Deloche reported a 12% operative mortality in a group of 101 patients over the age of 70 with aortic valve replacement for aortic stenosis, between 1970 and 1980 (75). Düren showed a 10% hospital mortality in a comparable group of 20 patients, operated between 1977 and 1985 (76). Sethi found in male patients with comparable disease and operation, a 10.2% mortality in the age group between 60 and 70 years, and an 18.2% mortality in patients over 70 years (77). More recently Magovern reported a 5.9 % operative mortality for elective valve replacement in the age group over 70 (78), while in the age group over 80 a 28% early mortality (< 90 days) was seen (79). Craver found an in hospital mortality of 11.0% for aortic valve replacement for aortic stenosis above the age of 70, while this risk was 3.9% below the age of 70 years (74). Kay

reported earlier in 1981 an in hospital mortality of 14 and 6% in patients with aortic valve replacement over and under the age of 70 (80), while Rioux found a 10.1 % operative mortality in the same age group over 70, treated with aortic valve replacement mainly for aortic stenosis (81). In patients over 75 years, who underwent aortic valve replacement from 1982 to 1985 the same authors found an 8.8% mortality, while Teply gave a 23% operative mortality from 1964 to 1980 in the same age group (82). Most recently Levinson found a 9.4% in hospital mortality for the age group over 80, treated with aortic valve replacement for aortic stenosis (83).

It is concluded that the operative risk for patients over the age of 70 for aortic valve replacement for aortic stenosis ranges from 5.9 to 18.2%, over the age of 75 it is estimated as 8.8 to 23%, while in octogenarians the operative mortality risk varies from 9.4 to 28%.

Preoperative functional status and left ventricular ejection fraction

Although Rediker reported no mortality in 42 patients with ejection fractions less or equal to 45% undergoing aortic valve replacement of isolated aortic valve stenosis (84), impaired left ventricular function has been an independent predictor of operative mortality in patients over 70 years of age. In a recent report on 469 patients of whom 67% had aortic valve replacement New York Heart Association class IV was associated with increased risk of operative mortality compared with classes I, II and III (85). The group from Stanford also reported advanced functional class and the presence of congestive heart failure as univariate determinants of a higher operative mortality in patients with aortic valve replacement (86). In their multivariate analysis advanced functional class remained statistically the most significant independent determinant of operative mortality, although congestive heart failure was not a significant predictor. In a smaller group of 64 patients over the age of 80 who underwent aortic valve replacement for aortic stenosis, left ventricular ejection fraction was not a significant univariate predictor of a complicated postoperative course, nor of unfavorable outcome such as hospital death or permanent severe neurological deficit (83).

Functional status of the patient preoperatively also was an important determinant of mortality after aortic valve replacement in the experience from La Pitié Hospital in Paris between 1981 and 1984 (87). Another French study also showed a linear relationship between functional class and operative mortality, varying from 3.3% for patients in NYHA

class I or II to 16.4% for class IV patients (73). In the earlier mentioned series from Stanford, a collection of 1479 patients, with aortic valve replacement, a tendency to operate on patients in a lower functional class has been noted. While NYHA class III or IV patients constituted more than 60% of all patients operated on before 1974, this was about 10% less after 1974 (86). This difference in preoperative functional class, might account partly for the higher operative mortality noted before 1980,(see decade of operation), while improvement in surgical techniques in recent years, might also have lowered operative mortality.

Gender

Although female gender increased the risk for operative mortality in the series reported by the University of Toronto, which included 469 patients over 70 years, it is not clear from this report whether this was the case for all preoperative diagnoses, as only about 60% of all patients had isolated aortic valve procedures (85). The Stanford experience by univariate analysis did not reveal female gender to be associated with a higher operative mortality (86). In fact in the group with aortic valve replacement over the age of 80, women had a better chance to have an uncomplicated in hospital course than men, 56 vs 32% (83). On the other hand in the data reported by Lytle, female gender was the most important variable predictive of operative mortality for combined aortic valve replacement and coronary artery bypass grafting (88). The same factor has been identified as having a negative influence on operative mortality for isolated coronary artery surgery (89). So if there is an excess in mortality in female patients undergoing aortic valve replacement this could be due to a less favorable concomitant bypass operation result or to smaller aortic roots requiring smaller prostheses. The suggestion from the Coronary Artery Surgery Study (CASS) which compared medical and surgical treatment for relief of angina pectoris is, that small stature may be more important than female gender (89). Yet Sethi's large study analyzing predictors for operative mortality after valve replacement did this in males only (77). It confirmed however that a smaller body surface is independently related to a higher operative mortality.

Concomitant coronary artery disease

In Magovern's study, univariate analysis selected patients having combined aortic valve replacement and coronary artery bypass grafting as a high risk group, whereas

multivariate analysis did not (78). Here, unlike emergency operation and age greater than 70 years, the need for coronary bypass grafting in addition to aortic valve replacement had no independent effect on the mortality rate of the operation. Also in Scott's study concomitant coronary bypass grafting had no independent predictive value for operative mortality (86). Yet, in Fremes' experience, aortic valve replacement, with concomitant surgery for coronary artery disease, showed an elevated risk of operation. However this risk was lower when coronary arteries with significant stenoses were grafted than when left alone (respectively 8.0 and 10% operative mortality)(84). The same finding has been reported by Cormier for all age groups for aortic valve replacement. He recorded the lowest operative mortality in patients without significant coronary artery disease, a higher risk in patients with significant coronary artery disease and revascularization and the highest risk in patients with significant concomitant coronary artery disease without additional bypass grafting (73).

Urgent operation

A definition of urgent surgery is not given in the reported study populations but most authors include in this category patients with unstable angina, rapidly progressive heart failure, bacterial endocarditis and severe rhythm disturbances. Urgent surgery in these studies was associated with a higher operative mortality in most of the reported larger patient groups both old and young (74,78,85).

Urgent surgery was not, however, identified as a predictor of operative mortality in the Veterans Administration Cooperative Study (77), in the group over 80 years old reported by the Massachusetts General Hospital (83), in the Stanford University (86), or in the Cleveland Clinic study (88).

All these studies are not quite comparable as some contained all age groups (74,77,78,86,88), others only older patients (83,85); some comprised all valve replacements and combinations of these (77,85), others only aortic valve replacement (74,78,83,86,88); all incorporated both sexes, except the Veterans Administration study which included only male patients (77).

One study exclusively contained only older patients with aortic valve replacement comparing these two given data with urgent surgery as a variable (82). But the numbers in this last study were rather small: 54 patients undergoing elective and 10 patients undergoing urgent aortic valve replacement, so the absence of a predictive value of

urgent surgery for an unfavorable outcome in the last mentioned study is not very convincing.

Most probably urgent aortic valve replacement in elderly patients increases the operative mortality only moderately and to a lesser extent than urgent mitral valve replacement (85).

Combined valve surgery

In the patient series from the University of Toronto (85), aortic valve replacement combined with mitral valve replacement influenced operative mortality adversely only in the old patient group (> 70 years). Jamieson and associates (72) reported the same correlation in their patient population over 65 years of age, while a combined valve replacement had already been recognized as a risk factor for operative mortality in 1974 by Barnhorst and associates (90). The risk of double valve replacement is estimated to be 3 to 9 times higher than for aortic valve replacement alone.

Nature of underlying disease

The type of underlying valve disorder i.e. predominantly aortic stenosis, aortic insufficiency or combined defect, has been postulated to have an influence on operative mortality. Earlier studies had reported that operative survival was influenced adversely by aortic regurgitation (91). This relation was still manifest in Scott's series, from 1967 to 1981 (86). However in his latest publication, with patients undergoing surgery between 1982 and 1986, this relation was no longer manifest (85). The use of cardioplegia instead of anoxic arrest, and referral of patients earlier for surgical treatment must have outweighed the excess mortality associated with aortic valve replacement when aortic valve insufficiency was predominant (88).

Summarizing the previous data it is evident that, in the two largest series, comprising 1479 and 1148 patients respectively, with aortic valve replacement, analysis of the data such as advanced New York Heart Association functional class, renal dysfunction, type of underlying physiopathology, atrial fibrillation, older age and urgent operation showed, that all had independent predictive value for operative mortality. Only age emerged as a common predictor in both studies (86,74). In Magovern's smaller series also age in excess of 70 years and emergency operation were identified as independent predictors

of operative mortality (78). In a male population of 661 subjects having isolated aortic valve replacement and three vessel coronary artery disease, a higher left ventricular systolic pressure, presence of prior cardiac operation, smaller body surface area and lower cardiac index were all factors contributing independently to higher operative mortality (77). These studies included analysis of the most pertinent preoperative, and in two studies also intraoperative variables, which all had, except the ones mentioned previously, no independent predictive value for operative mortality.

Probability of operative mortality after aortic valve replacement based on logistic regression analysis.

The probability of an event is represented by the formula:

$$\ln = \frac{(p)}{(1-p)} = X$$

$$\frac{(p)}{1-p} = e^{X}$$

$$p = \frac{e^{X}}{1 + e^{X}}$$

where p = the probability of an event and

$$X = B_0 + B_1X_1 + B_2X_2 + ... B_nX_n$$

Where B_0 represents a constant, B_1, B_2, ... B_n represent coefficients for each of the risk variables X_1, X_2, ... X_n.

Fremes calculated factor adjusted odd ratios for the independent predictors of operative mortality (85). These factors are given in Table 2 for age groups below 70 and over 70. The probability of operative mortality ranges from 4.5 to 76% for patients below 70 years and from 0.9 to 40% in patients over 70 years (85).

	young patients < 70 years		old patients > 70 years	
	coefficient	factor - adjusted risk ratio	coefficient	factor -adjusted risk ratio
Intercept	-3.2274	....	-4.6823	...
Timing				
elective		1.00		1.00
urgent	1.29312	3.664	0.7196	2.05
NYHA class				
I		1.00		
II	-0.51659	0.60		
III	-0.93906	0.39		
IV	0.35488	1.43		
Tricuspid valve disease				
no		1.00		
yes	1.13876	3.12		
Left venticular EF %				
> 60		1.00		1.00
40 - 60	-0.02159	0.98	1.0598	2.89
20 - 40	0.80239	2.23	0.7465	2.22
< 20	0.77638	2.17	1.2553	3.51
Redo valvular surgery				
none		1.00		
previous repair	-0.59266	0.55		
previous replacement	0.75434	2.13		
Age				
< 40 years		1.00		
40 -60 years	0.17364	1.25		
60 -70 years	0.75965	2.15		
Position aortic				1.00
mitral			0.8126	2.25
double			1.5508	4.71
Coronary artery disease				
no				1.00
yes with CABG			0.7729	2.17
without CABG			1.2829	3.61
Gender				
male				1.00
female			1.0042	2.73

Table 2 Predictors of operative mortality in young and old patients, after aortic, mitral or double valve replacement.

Perioperative morbidity

Morbidity is significantly increased in the older population. Perioperative morbidity including myocardial infarction, postoperative low output syndrome, intra aortic balloon counterpulsation and cerebrovascular accident has been reported in 36% of patients > 70 years and in 23% of younger patients. The incidence of operative mortality was 28% after any major complication (85).

In a group of 64 patients aged 80 to 89 years, the following perioperative complications were recorded: six patients with debilitating neurological events, 15 with temporary encephalopathy, 9 with major technical difficulties in the operating room of whom two died, while 11 patients required additional surgical procedures after aortic valve replacement, of whom 4 died. Another 24 patients had postoperative complications, leading to a mean hospital stay of 18 days, with 3.5 days in intensive care, but with ultimately good outcome, although 9 were discharged to rehabilitation facilities. Six patients had devastating central nervous system events, and were permanently unable to take care of themselves. These last six patients spent on average 15 days in intensive care, with a mean total hospital stay of 48 days. Altogether 44% of the overall study group had no major complications and were discharged directly home after a mean hospital stay of 15 days, including 2.3 days in intensive care.So the mean stay in intensive care of the 58 operation survivors was 4.1 days, with a mean hospital stay of 19.7 days (83). Craver reported a 4.0% perioperative myocardial infarction rate in patients over 70 years after aortic valve replacement, while this complication occurred in 3.1% of younger patients. Neurological events in both age groups were recorded in 7.5 and 3.0% respectively (74). Age was the only independent predictor of neurological events in this last study, while length of stay in the hospital after aortic valve replacement was significantly longer with increasing age at time of surgery, emergency of the operation and the year in which surgery was performed. It is clear that advanced age and aortic valve surgery form a complex combination with major morbidity and mortality.

Survival after aortic valve replacement

The data from the literature about survival after aortic valve replacement, including operative mortality are summarized in Table 3. Most authors used the actuarial survival method to calculate survival percentages (92).

Author (reference)	age group (years)	year of operation	number	survival percentage 1y	3y	5y	6y	8y	10y	12y
Jamieson (72)	> 65	1966 - 1979	320		68	56				
Cormier (73)	> 65	1968 - 1986	272			71			51	29
Rioux (81)	> 70	1971 - 1985	355	83	76	71	60	57		
Craver (74)	> 70	1975 - 1987	322	83				52		
Cabrol (87)	> 70	1981 - 1984	244			73				
Levinson (83)	> 80	1974 - 1987	64	83		67		49		

Table 3 Actuarial survival in elderly patients after aortic valve replacement

The results of aortic valve replacement on survival compare favorably with that recorded in 50 patients aged 60-89 years who while candidates for aortic valve replacement, did not undergo this procedure. The actuarial survival in these refusers was 57,37 and 25% after one, two and three years respectively (93).

Turina recorded a 2 year survival of only one patient, out of a group of 18 patients who were denied operation (94). Irrespective of age Ross and Braunwald found a 90% three year mortality in patients with unoperated aortic valve disease and angina or syncope, while those with heart failure died within two years (95).

Survival percentages in these patients after aortic valve replacement approximate the survival of the total apparently healthy population in the same age group (81). Some series have reported a better long-term survival after aortic valve replacement, than in the unselected general population of the same age (83). These differences must be ascribed to the preoperative selection process and the small numbers of patients at risk. Linearized rates of mortality were the same in patients over 70 years for mechanical valves and bioprostheses, being 6.12 and 5.71 per 100 patient years respectively (81). Causes of death most frequently encountered are thromboembolism, infective endocarditis, valve dysfunction and hemorrhage (74).

Valve related morbidity after aortic valve replacement

Thromboembolism and hemorrhage are the most frequent valve related causes of morbidity after aortic valve replacement. The linearized rate of non fatal thromboembolism for all age groups is reported as 0.96 and 1.14 per 100 patient years for bio and mechanical prostheses respectively, the latter with the use of oral anticoagulants (73). The incidence of non fatal bleeding of some importance was scored by the same authors as 0.3 and 1.06 per 100 patient years for bioprostheses and mechanical valves respectively. Hemorrhages in the mechanical valve group were twice as frequent with poor anticoagulation. Valve related morbidity in another French series in patients over 70 years was 1.5 and 1.3 per 100 patient years for mechanical and biologic aortic valve prostheses respectively (81). In an earlier series on results of aortic valve replacement in patients over 65 years, Jamieson reported a 2.63 and 2.76 non fatal morbidity rate per 100 patient years in mechanical and porcine aortic valves (72).

CONCLUSION

Most authors conclude that aortic valve replacement can be performed in elderly patients with an acceptable operative mortality, and that advanced age alone should not be a contraindication for surgical management. However identification of appropriate patients for aortic valve replacement remains quite difficult. These decisions involve ethical and social issues as well as economic realities. Consideration of the desires of the patient and the family is a prime consideration while advice from the surgeon, the cardiologist and other involved medical personnel is essential. Preoperative risk factor analysis as proposed by Fremes and summarized in Table 3 may simplify some of these decisions (85), and can provide a background risk profile in these patients, which can serve as a comparative standard for other interventions. Open discussions both within and outside the medical community can furnish preliminary answers to questions such as those raised by Edmunds (79). Among these are: Can we afford to offer expensive operations to elderly patients at high risk (96)? Is there a level of risk that precludes operation, and if so, who will decide what it is? Is it ethical to refuse to perform high risk operations when the alternatives have higher risks? Are surgeons and cardiologists justified in exercising preoperative selection criteria without including the patient in the decision process (97)? Can patients demand operations against medical advice (98)?

Only ongoing analysis, preferably with systematic registration of aortic valve replacement will be able to provide a useful reply.

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CHAPTER 4
PERCUTANEOUS BALLOON AORTIC VALVULOPLASTY FOR THE RELIEF OF ISOLATED AORTIC STENOSIS IN THE ELDERLY

SUMMARY

From March 1986 through December 1989 at the Thoraxcenter, 39 balloon aortic valvuloplasty procedures were performed in 38 patients. Mean age of these patients was 75.1 ± 7.1 years, male - female ratio was 15-23. Twenty five cases were considered as inoperable or high risk surgical candidates. Inoperability was judged to exist when poor left ventricular function, recently operated or unoperated carcinoma and severe pulmonary, neurological or renal disease were present. Very advanced age ($\geq$80 years) classified patients, in combination with other operative risk increasing factors, as high risk surgical candidates. Four patients died in hospital, two during the procedure and two within 8 days, one after dissection of the aortic base. In the remaining 35 cases, a satisfactory result (aortic valve area increase $\geq$25%) was obtained in 31. Mean aortic valve area increased from 0.47 ± 0.14 to 0.75 ± 0.19 cm^2 in the hospital survivors. Three patients were operated early (< 3 months), one for severe aortic incompetence, one after a failed procedure, and one for recurrence of symptoms. The other patients all experienced symptomatic improvement early after valvuloplasty, but thirteen had recurrence of symptoms and were then accepted for surgery, at a mean time of 15 months after valvuloplasty. No patient died after aortic valve replacement. Eight patients died during follow-up, which now extends to 45 months. Death occurred at a mean of 15 ± 5 months after valvuloplasty. The last eleven patients were alive and still improved at a mean follow-up time of 23 ± 12 months. Event free survival after one, two and three years was calculated as 62, 28 and 25% respectively. Total survival was 87, 68 and 68% after the same time intervals.

We feel that balloon aortic valvuloplasty is a palliative procedure which supplements surgical aortic valve replacement. In our view this new therapy is indicated in patients where surgical risk is prohibitive, or carries an unduly high risk.

INTRODUCTION

The use of a catheter for intracardiac therapeutic measures had appeared already in 1953, when Rubio-Alvarez and coworkers, used rigid catheters to dilate isolated cases of pulmonary valve stenosis (1). Charles Dotter in 1969 used rigid catheters of increasing size, to dilate acquired peripheral arterial stenoses (2). Apart from the isolated cases performed by Rubio-Alvarez, Rashkind was the first to introduce an intracardiac therapeutic procedure with a catheter to be used as a routine form of therapy. He published his atrial balloon septostomy, a crude, but often lifesaving procedure in the new born with transposition of the great arteries, in 1966 (3). After the introduction by Grüntzig in 1978 of small fixed diameter balloon catheters, which were inflated at high pressures to dilate coronary arteries (4) the same concept, but using larger balloons, was utilized in 1982 for the dilatation of pulmonary valve stenosis (5).

Dilatation of valvular aortic stenosis in infants and children was first performed in October 1982 by Lababidi, Wu and Walls and reported in 1984 (6). They percutaneously introduced balloons, with maximal inflatable diameters of 10-20 mm, and with a length of 40 mm, and positioned these balloons over a 0.035 inch guide wire in the aortic orifice. Care was taken to select an inflated balloon diameter at least one mm smaller than the aortic annulus. The balloon catheter was sequentially inflated to pressures of 80, 100 and 120 psi for 5 to 10 seconds. The results obtained in their first 23 patients, ranging in age from 2 to 17 years, were very promising. Peak systolic pressure differences between left ventricle and aorta ranged from 50 to 223 mm Hg before dilatation and from 11 to 80 mm Hg after dilatation. Cardiac index did not change after dilatation. No severe complications occurred, although 8 balloons ruptured and 10 patients showed a mild increase of aortic incompetence after dilatation. Two patients underwent open aortic commissurotomy, because peak systolic pressure difference was still 80 respectively 65 mm Hg after dilatation. At operation both aortic valves were bicuspid with small tears measuring 1 to 4 mm on the free ends of the commissures. Repeat catheterization in six patients 3 to 9 months after the procedure, showed no increase in pressure gradient over the aortic valve. The same favorable results were obtained by others, with increases in indexed aortic valve areas in children aged 10 days to 15 years from 0.48 to 0.65 cm^2/m^2 (7) and 0.44 to 0.73 cm^2/m^2 (8), the first authors using balloons always smaller

than the aortic annulus, while the second group employed sometimes larger balloons with a balloon/aortic annulus ratio, ranging from 0.67 to 1.1.

In September 1985, Cribier et al first applied percutaneous transluminal balloon valvuloplasty in three inoperable elderly patients with calcific aortic stenosis (9). The amazingly good results in these patients led to an extension of the technique to other patients with high surgical risk. Since then Cribier and other groups have published their indications, immediate results and complications of this technique (10-19). Later reports, also from our department, indicated a high restenosis rate, limited hemodynamic results, with a still high mortality rate and need for subsequent interventions, a fairly high immediate risk and a high number of complications, leading to a reevaluation of the indications of this technique (20-23). In this chapter we report our elderly patient population, that has undergone balloon aortic valvuloplasty, between March 1986 and January 1990.

PATIENTS AND METHODS

Since March 1986, a total number of 38 patients have undergone balloon aortic valvuloplasty, with a gradual decrease in the number of patients over the years, and a decrease in the proportion of operable patients (Table 1).

year	nr of patients	male/female ratio	mean age range	inoperable	high risk	operable
1986	10	6/4	72.4 (63 - 88)	3	1	6
1987	17	6/11	76.3 (60 - 88)	9	1	7
1988	8	3/5	74.8 (58 - 85)	6	1	1
1989	4	0/4	77.3 (72 - 81)	2	2	0
Total	39	15/24	75.1 ± 7.1 (58 - 88)	20	5	14

Table 1 Characteristics of balloon valvuloplasty patients

One patient underwent a second valvuloplasty, so 39 procedures were performed. All patients were discussed with the cardio-surgical team.

Patients were considered acceptable for a balloon valvuloplasty procedure if they

fulfilled one of the following criteria:

a) deemed inoperable after a combined cardio-surgical discussion

b) classified as a high risk case for surgical intervention

c) classified as a normal risk patient, but with preference of the patient for balloon valvuloplasty instead of surgical valve replacement or valvuloplasty.

All patients and a relative had to give their informed consent, after explanation of the experimental character of the procedure, and the potential risks and benefits. No patient was acceptable if during diagnostic angiography aortic insufficiency more severe than grade II was demonstrated.

The decision of inoperability was based on the following factors:
severe cardiac failure (Ejection Fraction $\leq$0.30) in 6 patients, moderate cardiac failure combined with neurological or renal disease or advanced age ($\geq$80 years) in 5 patients, recently operated or unoperated carcinoma in 5 patients, severe primary lung disease in 2 patients and gangrene of the toes in 2 cases (same patient). Patients were classified as high risk surgical candidates if the age was over 80, but no strict contraindication for surgery existed. This was the case in 5 patients. The other patients were considered as operable although a variety of concomitant diseases existed in these patients, as is not unusual in this age group (Figure 1).

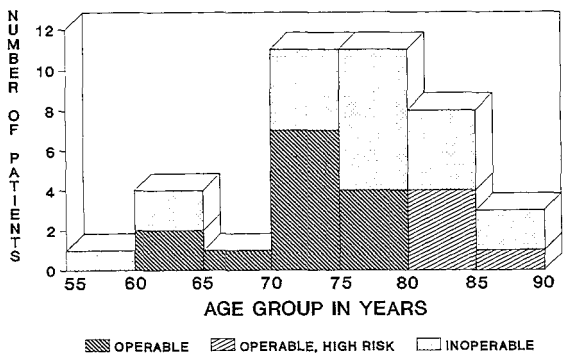

Figure 1: age distribution and estimated surgical risk of all aortic valvuloplasty patients

Before valvuloplasty 14 patients were in New York Heart Association validity class IV, while 25 were in class III. Angina on effort or at rest was noted in 33 patients while 11 patients reported syncopal attacks (Table 2).

Case No.	Follow-up time (months)	NYHA class		Angina		Syncope		Dyspnea		Aortic valve replacement After PBAV (months)
		Before PBAV	At FU	Before PBAV	At FU	Before PBAV	At FU	Before PBAV	At FU	
1	45	III	I	+++	--	+	--	--	--	6
2	45	III	I	++	--	--	--	+	--	13
3	44	III	II	++	--	--	--	+	--	36
4	18	III	#	+++		+		--		
5	39	III	II	++	--	--	--	+	+	1
6	39	III	I	++	--	--	--	+	--	10
7	37	IV	I	--	--	+	--	++	--	7
8	23	IV	#	++		--		++		
9	36	IV	I	++	--	--	--	++	--	9
10	36	III	II	++	--	--	--	+	+	
11	35	III	II	++	--	+	--	+	--	24
12	34	IV	I	--	--	--	--	+++	--	27
13	34	III	II	++	+	+	--	+	+	8
14	34	III	I	++	--	--	--	--	--	6
15	34	III	I	++	--	--	--	--	--	20
16	33	III	II	++	+	+	--	+	+	
17	33	III	I	++	--	--	--	--	--	13
18	33	III	II	++	--	--	--	++	+	
19	19	III	#	--		+		--		
20	31	III	III	++	++	--	--	++	++	
21	31	IV	II	+++	+	+	--	++	--	
22	31	III	II	++	+	--	--	++	+	
23	15	IV	#	--		+		+++		
24	8 days	IV	#	--		--		+++		
25	0 days	IV	#	++		--		+++		
26	14	III	#	++		--		+		
27	13	III	#	++		--		+		
28	23	III	I	+++	--	--	--	--	--	2,5
29	22	IV	II	++	+	+	--	+++	--	
30	5	III	#	++		--		++		
31	20	IV	I	++	--	--	--	+++	--	6
32	16	III	II	++	+	--	--	+	+	
33	16	III	III	++	--	--	--	++	++	13
34	16	IV	II	++	--	--	--	+++	+	
35	1 day	IV	#	--		--		+++		
36=26	0 days	IV	#	++		--		+++		
37	10	III	#	+++		--		--		
38	6	III	I	+++	--	--	--	--	--	
39	10 days	IV	II	+++	+	+	--	++	+	
Mean	26.3 (hospital survivors n = 35)									
± SD	11.9									

NYHA = New York Heart Association; PBAV = percutaneous balloon aortic valvuloplasty; At FU = at follow-up. # = Patient died
Angina: - = absent; + = angina on strenuous effort; ++ = angina on moderate effort; +++ = angina on minimal effort or at rest.
Syncope: - = absent; + = present
Dyspnea: - = absent; + = slight; ++ = moderate; +++ = severe also at rest.

Table 2 Validity class and severity of symptoms before and 0-45 months after balloon aortic valvuloplasty

Cardiac status of valvuloplasty patients

The ejection fraction was calculated from a 30° right anterior oblique left ventricular angiogram in all but two patients. Two patients had undergone previous open heart surgery, one with mitral valve replacement, while the other patient underwent previous bypass operation for three vessel disease with invalidating angina pectoris. Three patients had undergone previous coronary angioplasty.

The ejection fraction of the patients varied from 0.12 to 0.72. Individual ejection fractions, the grade of aortic insufficiency as assessed from a pre valvuloplasty supravalvular, 60° left anterior oblique, aortic root contrast injection, and the severity or absence of coronary artery disease are summarized in Table 3.

	Number of patients
EF $\geq$0.55	22
EF $\geq$0.40 - 0.54	6
$\geq$0.20 - 0.39	5
$\leq$0.19	4
not assessed	2
Aortic incompetence	
grade 0	10
grade I	20
grade II	9
Coronary artery disease	
Absent	24
1 vessel disease	7
2 vessel disease	2
3 vessel disease	5
left main disease	1

Table 3 Ejection fraction, severity of aortic incompetence and coronary artery disease in 39 valvuloplasty patients

Coronary artery disease was considered to be present if one of the three major coronary arteries i.e. right coronary, left anterior descending, left circumflex or the left main coronary artery showed a more than 50% diameter stenosis in one or more of multiple views.

In seven patients a grade II mitral insufficiency was present while in two other patients a mitral stenosis of moderate severity (ostium 1.5 - 2.0 cm^2) was demonstrated. Three cases had suffered a previous myocardial infarction. Other prevalvuloplasty hemodynamic data will be presented later, together with post valvuloplasty measurements.

Valvuloplasty procedure and hemodynamic evaluation

All procedures were performed using the femoral route and under local anesthesia except in one case, where general anesthesia was applied. Left ventricular and aortic pressures, and mean systolic transvalvular gradients were averaged and calculated on line after acquisition periods of 20 seconds. Cardiac output was computed from duplicate thermodilution measurements. A computerized system also provided instant calculation of the mean systolic aortic valve flow to compute aortic valve area (24)(fig 2) using the Gorlin formula (25):

$$\text{Aortic valve area } (cm^2) = \frac{\text{systolic valve flow (ml sec}^{-1})}{44.5 \sqrt{\text{mean pressure gradient (mm Hg)}}}$$

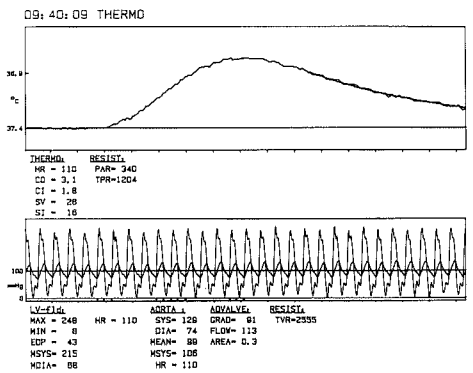

Figure 2: Example of computer output for calculation of cardiac output and aortic valve area. The 4 representative beats from which aortic valve area is calculated are marked under the respective beats, with small vertical bars, indicating beginsystole, endsystole and enddiastole.

Left ventricular enddiastolic and endsystolic volume indices were calculated from the diagnostic left ventricular angiogram, either performed just before the valvuloplasty procedure, or during a separate session. Volume indices were calculated using the area length method from a 30° right anterior oblique projection angiogram (26). A supravalvular aortic root injection of contrast was performed to grade the amount of aortic valve insufficiency ranging from 0 to IV. Aortic incompetence was scored as 0 when no contrast was visible in the left ventricle after supravalvular aortic contrast injection, as I when only minimal opacification of the left ventricle occurred, as II when the whole left ventricle was outlined with a density of contrast less than in the aortic root, as III when filling of the left ventricle was of the same density as the opacification of the aortic root and finally as grade IV when the contrast density of the left ventricle was higher than that of the aortic root.

After femoral venous and arterial puncture, 5000 I.U. of heparin and 1.0 mg of atropine was administered intravenously. A Swan - Ganz thermodilution catheter was introduced through the venous sheath into the pulmonary artery for measuring right heart pressures and cardiac output. In the first 17 patients a straight 0.038 inch, 260 cm long guidewire (Cordis Corporation, Miami), with its soft tip manually fashioned to a large J shape, was advanced into the left ventricle. In the remaining patients the distal part of a 0.035 inch, 300 cm long, "back-up" guidewire (Schneider - Shiley, Zurich) was introduced into the left ventricle, while over the proximal stiffer part of this guidewire a 16.5 French diameter, 100 cm long valvuloplasty introducer (Schneider - Shiley, Zurich) was positioned immediately above the aortic valve level, in an attempt to facilitate introduction and removal of multiple balloon catheters (see chapter 7). A balloon catheter was then pushed up along this wire and positioned across the aortic valve. Before insertion, particular care was taken to remove air from the balloon, by inflating and deflating the balloon before introduction with a mixture of contrast medium and saline (30/70). Inflations were performed by manual force, using a special 50 ml syringe with revolving piston, to increase the balloon pressure, under manometer control. Maximal inflation pressure ranged from 3 to 7 atmospheres. Single, double and trefoil balloons of increasing diameters and areas were used in an attempt to reduce the mean aortic transvalvular gradient to < 40 mm Hg, and to increase the aortic valve area to ≥ 1.0 cm^2. If this result was not accomplished oversized balloons (balloon/aortic annulus diameter

ratio > 1.0) were employed. Each inflation duration ranged from 15 to 260 s (mean 40 s) depending upon the individual tolerance. In most patients only a moderate decrease of systemic arterial pressure, continuously monitored throughout the procedure, was observed during balloon inflation (see also chapter 6). However, the maximal systolic pressure transiently fell to $\leq$60 mm Hg in 20 patients, resulting in dizziness and/or promptly reversible syncopal attacks in 7 cases. We instructed our last 14 patients to cough during balloon inflation to maintain minimal cerebral arterial flow. Since then only one patient fainted.

In some of the first patients, 80 mm long balloons were used, in order to achieve a stable position during inflation, but with the inherent disadvantage of longer inflation durations to achieve adequate intra balloon pressures. In the more recent patients shorter balloons could be used because to and fro motion across the aortic valve during inflation was prevented by the long sheath positioned immediately above the inflated balloon (Fig 3). At the end of the procedure hemodynamic results and aortic valve regurgitation were systematically reassessed.

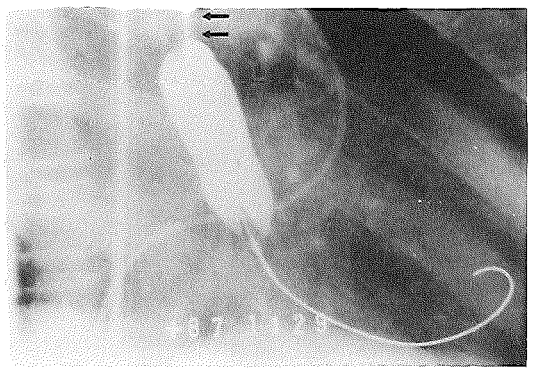

Figure 3: A 3 x 12, 40 mm long trefoil balloon (Schneider Medintag, Zürich) is inflated across the calcific stenotic aortic valve. The presence of the sheath (arrows) immediately above the balloon, prevents possible to-and-fro motion during inflation, allowing the use of shorter balloons.

Percutaneous balloon aortic valvuloplasty immediately followed the diagnostic catheterization in 8 patients, while valvuloplasty was performed in a separate session in the remaining 31 patients. The decision not to perform valvuloplasty directly after the diagnostic procedure was mainly taken in view of the old age of the patients, for whom a long procedure time is very uncomfortable.

Echocardiographic and Doppler measurements

These findings are detailed in chapter 5: Evaluation of percutaneous balloon aortic valvuloplasty in elderly patients with Doppler echocardiography.

Follow-up

Survival data and functional class of all patients discharged home were obtained mostly by telephone interview via general practitioners, referring cardiologists and the patients themselves. Follow-up coronary and left ventricular angiography was performed in 6 patients in five as a presurgery evaluation, and in one for assessment, before repeat valvuloplasty, after recurrence of symptoms.

Estimation of surgical operative risk

By means of the factor adjusted odds ratios for each risk variable, calculated by Fremes (27, see also chapter 3), the mortality probability of each patient as a surgical candidate was estimated. These risk variables included: gender, urgent/non urgent operation, ejection fraction of the left ventricle, the presence or absence of coronary artery disease and age below or over 70 years.

Statistical analysis

Student's *t*-test for paired data was used whenever appropriate.

Actuarial survival

Life - table analysis was performed using the Kaplan - Meier method (28). Both eventfree survival after valvuloplasty i.e. survival without further interventions, such as aortic valve replacement or revalvuloplasty, as total survival were calculated.

Analysis of risk factors for poor early or late outcome

The following three untoward events were defined.

1. Early mortality 2. Late mortality 3. Late events: revalvuloplasty or aortic valve replacement.

Eighteen variables, including all 13 hemodynamic parameters from Table 4, and age, gender, left ventricular ejection fraction, presence of coronary artery disease and

urgency of the procedure, were analyzed, to determine the relation between these preprocedural variables and untoward events. This relation between predictors and outcome was expressed as a relative risk or risk ratio, that is as the ratio of the rate of the respective outcome event observed in patients belonging to one category relative to that observed in the other category. For instance the risk associated with an urgent procedure is the rate of the outcome event after an urgent procedure divided by that rate after a "routine" procedure. Continuous variables were dichotomized. The 95% confidence limits of the relative risk estimates are also given (29).

RESULTS

Immediate hemodynamic results

Hemodynamic data before and after aortic balloon valvuloplasty are summarized in Table 4. In five cases no aortic valve area was calculated after the last balloon inflation. In cases 14 and 34 the aortic valve area could not be computed after aortic valve dilatation because of the development of grade III aortic insufficiency. In one case this complication occurred after a single 19 mm balloon inflation, in the other after inflation of a bifoil 2 x 19 mm balloon. The first patient, who was operated on 6 days later, showed a bicuspid aortic valve, with heavy calcifications and scarring in one of these cusps, while the other cusp was less affected by the degenerative process and manifested a tearing off of the aortic wall of 7 mm. After inflation of a bifoil 2 x 19 mm balloon the second patient showed a dissection of the aortic wall just distal to the opening of the left coronary ostium, together with severe aortic incompetence (Fig 4).

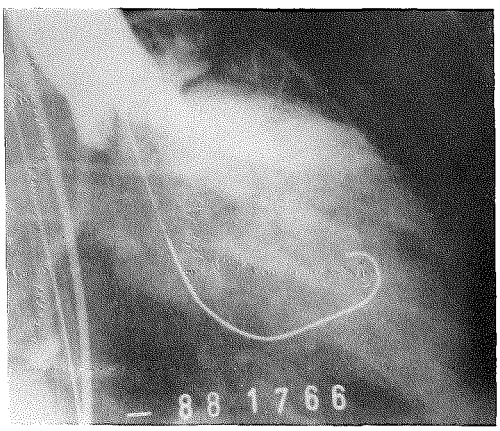

Figure 4: dissection of the aortic base (arrow) and aortic valve incompetence, (filling of the left ventricular cavity, after supravalvular contrast injection) after aortic valve dilatation with a bifoil 2 x 19 mm balloon.

Case No.	LVPSP B	LVPSP A	LVEDP B	LVEDP A	P-PSG B	P-PSG A	MSG B	MSG A	AF B	AF A	AVA B	AVA A	% Increase AVA
1	247	229	24	11	56	28	57	39	179	245	0.53	0.88	66
2	275	222	31	16	98	68	78	56	234	270	0.59	0.81	37
3	264	177	15	2	66	35	81	31	134	197	0.33	0.80	142
4	230	188	16	19	73	22	67	28	136	166	0.37	0.71	92
5	204	210	23	23	54	36	48	41	152	163	0.49	0.57	16
6	238	212	12	2	105	70	80	58	136	120	0.34	0.36	6
7	203	188	28	15	47	33	53	37	231	259	0.71	0.96	35
8	275	240	17	12	119	66	118	64	198	230	0.47	0.65	38
9	191	177	30	27	90	40	68	41	125	181	0.37	0.64	73
10	197	223	27	17	58	23	50	31	193	258	0.61	1.04	70
11	257	179	13	8	135	51	106	49	260	286	0.57	0.95	67
12	232	154	29	3	121	52	93	52	166	229	0.39	0.71	82
13	234	193	11	14	75	40	74	47	176	214	0.46	0.70	52
14	190	140	13	22	65	54	60	nc	226	nc	0.66	nc	
15	211	188	5	4	48	32	60	39	215	238	0.62	0.85	37
16	230	104	9	11	96	52	79	38	86	160	0.26	0.60	131
17	204	nr	28	nr	89	nr	82	nr	236	nr	0.59	nr	
18	218	192	9	8	83	47	74	53	144	205	0.35	0.67	91
19	219	164	7	6	103	83	67	60	238	253	0.65	0.72	11
20	232	156	13	3	89	46	72	31	180	198	0.48	0.80	67
21	207	199	28	12	96	24	75	54	119	140	0.31	0.44	42
22	303	193	12	17	124	59	115	62	145	231	0.30	0.66	120
23	180	181	11	11	72	37	89	49	139	151	0.33	0.49	48
24	157	123	11	14	60	28	39	30	169	200	0.61	0.82	34
25	105	nr*	27	nr*	35	nr*	36	nr*	90	nr*	0.34	nr*	
26	231	202	13	13	75	32	79	53	198	245	0.50	0.76	52
27	240	173	13	8	107	23	91	28	161	250	0.38	1.06	179
28	200	169	11	20	69	33	83	41	233	210	0.57	0.74	30
29	233	164	4	0	70	33	70	36	127	152	0.34	0.57	68
30	196	175	8	2	46	29	61	40	307	329	0.88	1.17	33
31	188	133	8	4	106	37	80	46	163	213	0.41	0.71	73
32	231	185	8	28	63	27	63	35	192	295	0.54	1.12	107
33	232	205	12	17	69	28	74	39	204	216	0.53	0.78	47
34	170	176	39	39	85	50	52	52	159	249	0.50	0.78	56
35	153	77	20	27	67	13	51	nc	88	nc	0.28	nc	
36=26	197	nr*	25	nr*	55	nr*	69	nr*	159	nr*	0.43	nr*	
37	242	184	9	0	86	33	84	45	136	145	0.33	0.49	48
38	231	148	11	3	108	44	95	46	228	193	0.53	0.64	21
39	230	150	14	10	117	58	94	27	192	175	0.45	0.76	69
Mean	217	177	16	12	82	41	74	43	176	214	0.47	0.75	63
± SD	37	34	9	9	24	15	19	10	50	49	0.14	0.19	38
p value	<0,05		<0.05		<0,05		<0,05		<0,05		<0,05		

AVA = aortic valve area (cm2); AF = systolic aortic valve flow (ml s-1); LVEDP = left ventricular end-diastolic pressure (mmHg); LVPSP = left ventricular peak-systolic pressure (mmHg); MSG = mean systolic aortic gradient (mmHg); P-PSG = peak to peak systolic gradient (mmHg); nc = not computed because of significant aortic valve insufficiency after valvuloplasty; nr = not recorded at the end of the last balloon inflation; nr* = not recorded because of patient's demise immediately after the first balloon inflation.
B = before; A = after.

Table 4 Hemodynamic data before and after 39 balloon aortic valvuloplasty procedures.

This patient, deemed inoperable, died 24 hours later of cardiac failure. At autopsy the dissection of the aortic wall seen on the angiogram was confirmed, compromising the left main coronary artery. No tears in the tricuspid aortic valve were observed, the aortic incompetence probably being caused by loss of support of the three heavily calcified cusps. Two patients died immediately after the first balloon inflation (nrs 25 and 36). The first patient was in severe cardiac failure, managed with dopamine infusion, with a left ventricular systolic pressure of 105 mm Hg, a left ventricular end diastolic pressure of 27 mm Hg, an ejection fraction of 0.14 and left main coronary artery disease. The second patient who died during the procedure (nr 36) had already undergone previous aortic valvuloplasty 14 months before, and previous coronary bypass operation 60 months earlier. During the first 25 mm balloon inflation the balloon "popped" out of the aortic valve possibly occluding the only remaining blood flow to the heart, i.e. the previously inserted jump graft with distal connections on 3 main coronary arteries. No autopsy was performed in these two last cases. In the last of the five patients without valve area calculation after the procedure, a severe epileptic fit occurred, with dislocation of the long wire from the left ventricle. In this patient no attempt was made to reposition the wire and measure the transvalvular aortic pressure gradient.

Comparison between pre and post valvuloplasty values in the remaining patients revealed highly significant changes in left ventricular peak systolic and end diastolic pressures, mean and peak systolic aortic valve gradients, mean systolic aortic valve flow, and aortic valve area (Table 4, figs 5 and 6).

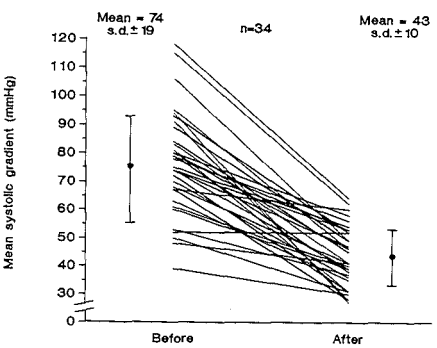

Figure 5: mean systolic aortic valve gradient before and after PBAV

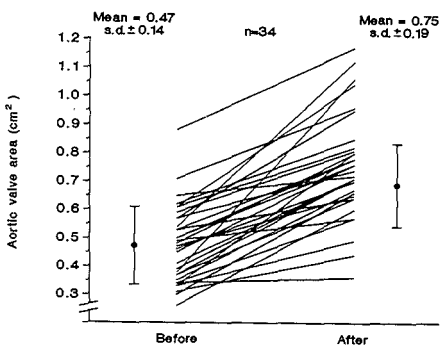

Figure 6: Aortic valve area before and after PBAV

However, when the individual absolute values after valvuloplasty are considered, the presence of a mean systolic gradient of > 40 mm Hg in 19 patients (49%), and an aortic valve area < 0.70 cm^2 in 12 patients (31%) should be emphasized. A less than 25% increase in valve area was obtained in 4 patients (10%). Increasing balloon sizes did not linearly affect the ultimate result of balloon aortic valvuloplasty, the increase in aortic valve area being 76 ± 37%, 52 ± 28% and 86 ± 53%, when a maximal single balloon size of 23 mm, trefoil 3 x 12 mm balloons or bifoil 2 x 19 mm balloons respectively were employed.

Complications

Mortality

In patient nr 24, a 77 year old man, admitted to the intensive care unit in cardiogenic shock, mentally confused and anuric with a left ventricular ejection fraction of 15%, the valve area was increased from 0.61 to 0.82 cm^2 as a result of valvuloplasty. Although temporary clinical benefit was observed for the first days after the procedure, all attempts at reducing the intravenous inotropic support were unsuccessful and the patient died in cardiogenic shock 8 days after the procedure. At autopsy no cardiac or vascular damage related to the procedure could be observed. Thus, in hospital mortality occurred in 4 patients or 10%.

Neurological

In patient nr. 10 a complete left hemiplegia developed at the end of the aortic valvuloplasty procedure, with persistent impairment of the mobility of the left arm at discharge from the hospital, but almost complete functional recovery at late follow-up. One patient developed complete left hemianopia during the procedure. At follow-up minimal residual defects were still present. Two patients (nrs 17 and 29) experienced syncopal attacks after balloon inflation. One of these patients had been known to have preexisting epilepsy, in the other patient syncope occurred after the balloon burst with possible air embolism in the cerebral circulation. Both patients recovered quickly and without sequelae.

Aortic valvular insufficiency

Apart from the two patients described under immediate hemodynamic results and complications, no patient experienced an increase in the severity of aortic insufficiency of more than one grade. In the patients where aortic incompetence after the procedure could be reassessed (n = 32), a grade I increase in aortic valve insufficiency was noted in 11 patients, in 7 of these from grade 0 to grade I and in 4 from grade I to grade II. In three other patients minimal aortic insufficiency was no longer detectable after the procedure.

Other cardiac complications

One patient developed complete atrioventricular block immediately after insertion of a "back-up" guide wire in the left ventricle, requiring implantation of a permanent pacemaker. One other patient developed a complete left bundle branch block during the procedure, disappearing during follow-up. Two patients had temporary ventricular fibrillation in the catheterization department; this was managed by DC countershock.

One patient had to be resuscitated for a short period after a prolonged fall in aortic pressure after balloon inflation, which led to an immediate fall in blood pressure to 20 mm Hg. One patient exhibited signs of severe pulmonary edema at the end of the procedure which was managed medically.

Vascular

Three patients required surgical interventions at the puncture site, two because of development of a femoral artery pseudo aneurysm, and one for the removal of a balloon remnant from the femoral artery after balloon rupture. Four patients developed large groin hematomata, requiring multiple blood transfusions in two cases. No hemorrhagic or other complications were observed at the puncture site in the last 21 procedures, after a long arterial valvuloplasty introducer was used (see chapter 7).

For all patients the procedure was free of the above complications in 23 cases (59%), this number being 61% after the use of a long sheath, and 57% before that period.

Estimated risk of surgical operative mortality

The patients that were deemed inoperable mainly on the basis of their cardiac condition (n = 16) had a calculated operative risk of 4 to 33% (mean 13.2 ± 7.4%). Three of these patients died in hospital for a calculated valvuloplasty risk of 18.8%. The other patients had a calculated mean risk of operative mortality of 4.4%. Eventually one died, i.e. a risk of valvuloplasty related mortality of 4.3%. Three other patients have died while waiting for their valvuloplasty procedure, which had already been planned in one case, while the other two were considered candidates and were evaluating the pro's and con's.

In hospital stay

Thirty five of the patients were discharged home, or referred to a rehabilitation center after a mean hospital stay of 6.1 ± 7.9 days. A prolonged hospital stay of more than six days was observed in 7 patients (range 7 to 37 days), mainly due to complications of the procedure or inability of these patients to take care of themselves and waiting for admittance to a recovery home. During this prolonged hospital stay also one pacemaker implant, one surgical aortic valve replacement and one surgical repair of a femoral artery pseudoaneurysm took place.

Follow-up catheterization

A total of six patients have been reinvestigated with left and right heart catheterization and left ventricular and aortic root angiography. Data obtained pre and post valvuloplasty and at follow-up catheterization are summarized in Table 5.

Four patients (nrs 3,12,26,33) had a return to pre valvuloplasty values, one had a moderate restenosis (nr 9) while one did not show signs of restenosis (nr 28). Nevertheless this last patient (85 years old) who had undergone angioplasty of the left anterior descending coronary artery one month before aortic valvuloplasty , and angioplasty of the left circumflex artery one month after valvuloplasty, was accepted for aortic valve replacement and a coronary bypass operation, due to persisting symptoms of angina pectoris. Four of the other patients underwent aortic valve replacement as well, while the last (inoperable) patient underwent revalvuloplasty.

case	LVPSP			LVEDP			MSG			AF			AVA			I-D		EF		AI			Interval	Coronary
number	B	A	FU	B	A	FU	B	A	FU	B	A	FU	B	A	FU	I	D	B	FU	B	A	FU	V-FU (months)	artery disease
3	264	177	273	15	2	16	81	31	93	134	197	151	0.33	0.80	0.35	142	128	0.63	0.60	I	I	I	33	1 VD
9	191	177	215	30	27	30	68	41	72	125	181	199	0.37	0.64	0.53	73	30	0.19	0.38	I	II	I	9	none
12	232	154	221	29	3	9	93	52	n.a.	166	229	n.a.	0.39	0.71	n.a.	38	n.a.	n.a.	0.37	II	II	III	27	none
26	231	202	197	13	13	25	79	53	69	198	245	159	0.50	0.76	0.43	52	77	0.51	0.37	II	II	II	14	3 VD open jump graft
28	200	169	181	11	20	21	83	41	56	233	210	257	0.57	0.74	0.77	30	-4	0.60	0.60	0	I	I	1	2 VD
33	232	205	234	12	17	18	74	39	70	204	216	203	0.53	0.78	0.55	47	42	0.58	0.61	I	I	II	13	none

LVPSP = left venticular peak systolic pressure (mm Hg); LVEDP = left venticular enddiastolic pressure (mm Hg); MSG = mean systolic aortic valve gradient (mm Hg); AF = systolic aortic valve flow (ml s^{-1}); AVA = aortic valve area (cm^2); I-D = increase, respectively decrease; in AVA (%); EF = ejection fraction of the left venticle; AI = grade of aortic incompetence; B = before valvuloplasty; A = after valvuloplasty; FU = at follow-up; 1-2-3 VD = single, double, triple vessel disease; V = valvuloplasty; n.a. = not assessed

Table 5 Hemodynamic and angiographic data before and after balloon valvuloplasty and at follow-up catheterization

Clinical follow-up

Mortality

Eight patients died 5 to 23 months after hospital discharge (mean 15 ± 5 months). With the exception of a 58 year old man, who was refused surgery on the basis of a pleural mesothelioma, and one other 70 year old male patient who rejected surgery, all other 6 patients were deemed inoperable on the basis of their age and cardiac and general condition (mean age 83 ± 5 years). They all experienced some relief of their anginal symptoms and dyspnea, while two patients with syncopal attacks did not report this complaint in the follow-up period before they died of natural causes.

Aortic valve replacement

A total of sixteen patients underwent aortic valve replacement, one after a complicated aortic valvuloplasty, two for failed valvuloplasty and thirteen for clinical, hemodynamic and echocardiographic signs of restenosis. All but one of these patients had been classified as inoperable or high risk cases. Six cases, previously deemed inoperable, were acceptable for surgery, after improvement of left ventricular function, or elimination of other diseases which had caused the decision of inoperability. Nine other patients, initially classified as high risk cases, were after a second discussion, when valvuloplasty had proved to be ineffective, accepted for surgical valve replacement. These 16 patients will be discussed in a separate chapter (chapter 8). At a mean follow-up of 34 (± 8) months after valvuloplasty and 22 (± 11) months after aortic valve replacement, none of these patients have died. Eleven patients are in New York Heart Association validity class I, four are in class II, while one is in class III. Thirteen patients are taking oral anticoagulants, three digoxin and six are on diuretics.

Patients without further interventions

Eleven patients were alive after a one-off balloon aortic valvuloplasty, at a follow-up time of 10 days to 35 months (mean 23 ± 12 months). One patient is in validity class I, 9 are in class II and one is in class III. The last patient is 31 months after valvuloplasty in the same validity class as before valvuloplasty, and is now waiting for reevaluation and eventually revalvuloplasty. The other patients have experienced an increase in validity class of on average 1.5. Syncopal attacks which were present in 4 of these

patients before valvuloplasty, were not reported after valvuloplasty. Anginal symptoms and dyspnea improved as well after the procedure. The mean age of this group of patients was at the time of valvuloplasty 76.6 years.

Symptoms and validity class before intervention and at follow-up are summarized in Table 2. One patient is taking oral anticoagulants, nine are on diuretics, 5 on digoxin and three are taking long-acting nitrates. Table 6 summarizes some clinical and hemodynamic data of patients dying early (in hospital mortality), late deaths and long-term survivors with and without aortic valve replacement.

	Age (years)	Male/Female ratio	Follow-up (months)	Aortic valve area (cm2) Before	Aortic valve area (cm2) After	Aortic valve area Increase (%)	Validity class Before III	Validity class Before IV
Survivors operated (n = 16)	72.1 ± 5.6	6/10	34 ± 8	0.51 ± 0.11	0.75 ± 0.15	52 ± 32	12	4
Survivors not operated (n = 11)	76.7 ± 6.6	4/7	23 ± 12	0.42 ± 0.11	0.73 ± 0.19	77 ± 31	7	4
Late deaths (n = 8)	78.7 ± 9.5	3/5	15 ± 5	0.49 ± 0.18	0.76 ± 0.23	67 ± 48	6	2
Early deaths (n = 4)	76.2 ± 1.5	2/2	2 ± 3 days	0.42 ± 0.12			0	4

Table 6 Clinical and hemodynamic data at the time of percutaneous balloon aortic valvuloplasty in patients with early and late mortality and in survivors, with and without aortic valve replacement. Data are given as mean values ± standard deviation

Figure 7, depicting the relation between aortic valve area increase and late outcome, indicates a trend for better long-term results if the aortic valve area is increased by at least 50%.

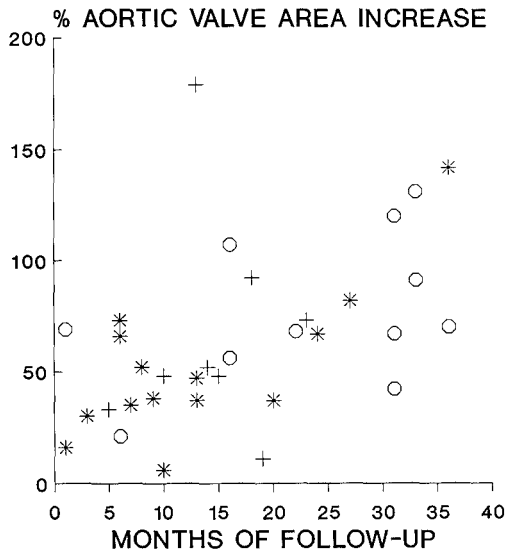

Fig 7: Relation between percentage aortic valve area increase during valvuloplasty and late outcome

○ UNEVENTFUL
\+ MORTALITY
✳ AORTIC VALVE REPLACEMENT

Actuarial survival analysis

Actuarial survival for 38 patients was 87% after one year, and 68% after two as well as three years. Excluding patients who had a reintervention an eventfree survival of 62, 28 and 25% after 1,2 and 3 years respectively was found (fig 8).

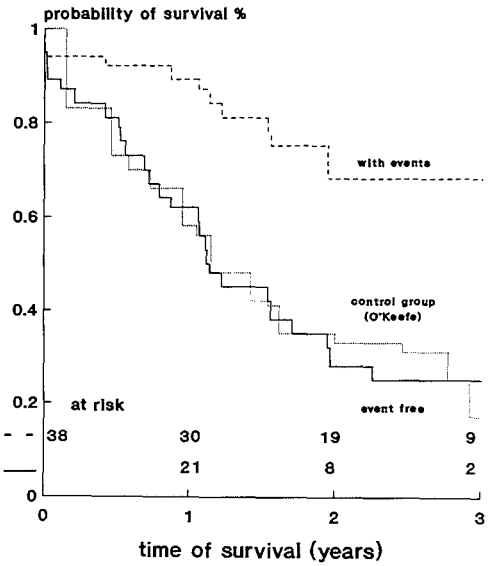

Fig 8: Kaplan - Meier survival curve for 38 patients after percutaneous balloon aortic valvuloplasty. Survival curves with and without reinterventions are shown. For comparison, survival in a group of 50 patients with severe aortic stenosis who did not undergo surgical treatment or aortic valvuloplasty is also shown (ref 62).

Predictors of early and late mortality and events after valvuloplasty

Table 7 summarizes predictors for periprocedural and late mortality, as well as for late events. Procedural mortality was higher in patients with a left ventricular pressure < 200 mm Hg, a peak and mean systolic aortic gradient of < 75 mm Hg, an ejection fraction of less than 0.55 and in cases of an urgent procedure. The risk of aortic valve replacement during follow-up is higher in patients with a less than 50% aortic valve area increase after aortic valvuloplasty.

Unfavorable outcome	Variable*	Risk ratio	95 % confidence limits
Early mortality	Left venticular peak systolic pressure < 200 mm Hg	1.5	1.0 - 2.2
	Peak systolic gradient < 75 mm Hg	1.3	1.0 - 1.6
	Mean systolic gradient < 75 mm Hg	1.2	1.0 - 1.5
	Ejection Fraction < 0.55	1.3	1.0 - 1.8
	Urgent valvuloplasty	1.4	1.0 - 2.0
Late mortality	none		
Late events	Aortic valve area increase < 50 %	2.0	1.0 - 4.0

* only the significant variables are tabulated

Table 7 Univariate analysis to predict immediate and late unfavorable outcome after aortic valvuloplasty

DISCUSSION

Procedural risk

Mortality

Comparison of in hospital mortality rates following aortic valve replacement versus percutaneous balloon valvuloplasty, may be somewhat misleading, as all calculated risks for valve replacement are by definition obtained from operated patients only (27,30,31). In fact we do not know what the operative risk of these patients would have been, had they been accepted for surgery as a first choice. Also we do not know how the factors that make patients unsuitable candidates for aortic valve replacement, would influence operative mortality. Another part of the problem of estimating surgical risk is that results obtained in one hospital may not be applicable in another. Finally the calculated risk probabilities for operative mortality, were derived by Fremes (27) from a study group of 315 patients with aortic valve replacement who had a mean age of 74 ± 3.4 years. Although the higher risk for operative mortality in patients over 80 is well recognized, compared to the age group over 70 (30,31), we could not adjust our calculated probabilities for patients over 80 years. In fact we have calculated the risk probabilities in these patients as those belonging to Fremes' group over 70 years old.

With these limitations in mind operative mortality was found to be 8.0% for the whole group, while the actual valvuloplasty mortality was 10.3%. Other authors have reported valvuloplasty related mortalities in hospital to range from 3.5% (23) to 9.6% (32) in a series comprising 170 and 104 patients respectively. It might well be, that after the initial "Samson feeling, the Delilah of restenosis" (33) tempered the enthusiasm among interventional cardiologists, and the procedure is now reserved as palliation for patients with severe symptoms who are denied surgery, resulting in an inherent higher procedural risk. But the opposite could also be true, as pointed out by Cribier (34). He found in the French Registry a mortality of 13% in the first 215 patients, while this figure dropped to 4% in the following 237 patients.

Other complications

a) Vascular complications at the introduction site

The most frequent complication of the procedure, is local trauma to the femoral artery

at the puncture site. In particular prior to the availability of introducer sheaths, and with balloons which had a high profile even when deflated, local vascular injury was encountered in about 10% of patients, while 23.5% of all patients required blood transfusion (23). Our vascular complication rate was 7.7%, while only 5% of patients were in need of blood transfusions. Vascular complications did not occur in our series in the last 21 procedures when a long introducer sheath was used (see chapter 7). Skillman et al found in 7333 patients undergoing percutaneous left heart catheterization 75 operative repairs of catheterization related vascular complications (1%). For diagnostic heart catheterization, percutaneous transluminal coronary angioplasty and balloon valvuloplasty the percentages were 0.6, 0.9 and 5.2% respectively (35).

b) Embolic complications

Embolic events produced by calcific emboli, dislodged from the calcified leaflets during valvuloplasty are rare, but serious. In the French registry a 2% incidence of stroke was noted (34). Embolization to the coronary arteries, with ensuing myocardial infarction is even more rare (< 1%) (23). Neurological complications with residual impairment at follow-up, occurred in our series in two patients, in one a complete stroke occurred, while the other patient exhibited signs of hemianopia. Davidson et al systematically investigated the occurrence of emboli associated with percutaneous mitral and aortic valvuloplasty by computed tomography of the head, funduscopy and electrocardiography in 32 patients. They demonstrated signs of old cerebral infarction in nine patients, with three patients showing a new cerebral abnormality after valvuloplasty. Two of these three episodes were symptomatic, and occurred in patients with bicuspid aortic valves. Serial electrocardiograms were unchanged in all patients (36). Detachment of a large calcific fragment from the aortic valve was recently described in a case report. The calcific embolus was recovered from the abdominal aorta during operative aortic valve replacement (37).

c) Aortic valve and aortic root complications

Complications at the level of the aortic valve were observed in two patients, in both instances leading to severe aortic incompetence, one due to a tear in one of the leaflets of a bicuspid valve, the second caused by aortic root dissection (fig 4). Severe aortic incompetence has been reported previously but with a remarkably low incidence, mostly as case reports (38-40). In larger series the incidence of severe aortic valve incompetence ranged from 1 to 2% (23,34). Two papers addressing specifically the

problem of aortic valve insufficiency after aortic valvuloplasty came to the same conclusion in that the procedure neither produces significant increases nor decreases in aortic valve regurgitation (41,42).

Although the use of balloons larger than the aortic annulus has been shown to lead to a greater increase in aortic valve area (43), a balloon - aortic annular area ratio of more than 1.2 led to aortic annular tears in 2 out of 100 patients, while this complication did not occur with ratios below 1.2 (44). If for example a trefoil balloon with 3 parallel balloons of 12 mm diameter mounted on a single catheter, is inflated, the radius is 14.2 mm, the area occupied is 633 mm^2, and the effective circumference 89 mm. If the aortic annulus diameter is 24 mm, the aortic annulus area is 452 mm^2, and the circumference 75 mm. So this balloon causes in a relatively large annulus diameter of 24 mm, already an overstretching of 19% of the aortic wall, where as a single balloon with a 25 mm diameter overstretches it by only 3%. Assuming a tricuspid valve, with equal cusp margin lengths in the previous example of a 24 mm diameter annular ring, the cusps are overstretched by 25%. In our patient whose aortic annulus was 20 mm with severe aortic incompetence after a single 19 mm balloon inflation, only one of the bicuspid leaflets was heavily calcified. The radial force of the inflated balloon must have been exerted eccentrically, overstretching the half of the annulus with the more supple valve by 56 %, which led to a tearing of the aortic attachment of this valve leaflet.

Calculated circumferences, leaflet free margin lengths and annular areas are summarized in Table 8, for annular diameters varying from 20 to 26 mm in trileaflet valves. These values are compared with the same data derived from inflated balloons with increasing diameters. Leaflet length at the time of balloon inflation is derived from dividing the balloon circumference by 3. Maximal advisable balloon sizes are for annulus diameters of 20, 22, 24 and 26 mm: trefoil 3 x 10 mm, single 25 mm, trefoil 3 x 12 mm and trefoil 3 x 13 mm respectively.

The application of double balloons for mitral valve dilatations, has also encouraged the use of this type of balloon in aortic valve stenosis (45-47). Calculations such as shown in Table 8 can also be performed for bifoil balloons. The circumferences of bifoil 2 x 15, 2 x 17 and 2 x 19 mm balloons are respectively 77, 87 and 98 mm. By the nature of its design this balloon exerts more force on one leaflet than on the other two in tricuspid valves, so the result is more unpredictable. In bicuspid valves a 2 x 15 mm

balloon overstretches the leaflet edges in a 20 mm aortic annular ring by (30/20-1) x 100 = 50%. The use of a bifoil 2 x 19 mm balloon in patient nr 35 with an aortic annulus diameter of about 22 mm must have overstretched the wall circumference by 42%, causing fatal laceration and dissection of the aortic wall.

	Aortic annulus diameter											
	20 mm			22 mm			24 mm			26 mm		
	cf	ll	area	cf	ll	area	cf	ll	area	cf	ll	area
	mm	mm	mm2	mm	mm	mm2	mm	mm	mm2	mm	mm	mm2
	63	20	314	69	22	380	75	24	452	82	26	534
Balloons												
Single 20 mm	63	21	314									
Overstretch (%)	0	5	0									
Single 23 mm	72	24	415	72	24	415						
Overstretch (%)	14	20	32	4	9	9						
Trefoil 3 x 10 mm	74	25	439	74	25	439						
Overstretch (%)	17	25	40	7	14	16						
Single 25 mm	79	26	491	79	26	491	79	26	491			
Overstretch (%)	25	30	56	14	18	29	5	8	9			
Trefoil 3 x 12 mm	89	30	633	89	30	633	89	30	633	89	30	633
Overstretch (%)	41	50	101	29	36	66	19	25	40	8	15	19
Trefoil 3 x 13 mm	97	32	745	97	32	745	97	32	745	97	32	745
Overstretch (%)	54	60	137	41	45	96	29	33	65	18	23	40
Trefoil 3 x 14 mm	104	35	860	104	35	860	104	35	860	104	35	860
Overstretch (%)	65	75	174	51	59	126	39	46	90	27	35	62
Trefoil 3 x 15 mm	111	37	989	111	37	989	111	37	989	111	37	989
Overstretch (%)	76	85	215	61	68	160	48	54	119	35	42	86

cf = circumference; ll = length of free margin of leaflet

Table 8 Comparison of aortic annulus circumference, leaflet length and area for annulus diameters of 20 to 26 mm in tricuspid aortic valves, with the same data for inflated balloons of increasing sizes. Percentage overstretch is the ratio of the three calculated parameters for the balloons and the aortic annulus -1 (x 100). The balloons above the drawn line in the table can be used with an overstretch of < 20% of the aortic annular circumference.

The fact that we obtained a larger increase in valve area with bifoil 2 x 19 mm balloons is of some interest, but one has to keep in mind that these balloons were only employed in patients where trefoil 3 x 12 balloons gave unsatisfactory results. One has to weigh the

higher risk of an oversized balloon in each individual against an unsatisfactory valvuloplasty result.

d) Incidental complications

Other complications mentioned in the literature were mitral valve rupture by balloon inflation while the balloon was entrapped in the chordae tendineae (48) and in another case report, the rupture of an aberrant chorda, crossing the left ventricular outflow tract (49).

Direct hemodynamic results

In our experience balloon aortic valvuloplasty resulted in an increase in aortic valve area from 0.47 ± 0.14 to 0.75 ± 0.19 cm^2 with an average increase of 63 ± 38% (fig 6). This increase in valve area resulted in a significant higher systolic aortic valve flow and a significant lower mean systolic pressure difference between the left ventricle and the aorta (fig 5). Larger series from Rouen (50) and Boston (23) reported increases in aortic valve area of 0.53 ± 0.18 to 0.97 ± 0.34 cm^2 and from 0.6 ± 0.2 to 0.9 ± 0.3 cm^2 respectively, representing an increase of 83 and 50% respectively. These two series comprising 300 and 170 patients respectively of the same mean age as our series, also contained some younger patients, the youngest being 30 and 35 years old respectively. The technique of valvuloplasty used, was also comparable, the largest balloon used was no bigger than in our institution. Letac (50) like others, noticed a significant correlation between the initial and post dilatation valve area. He also found that patients with an increase in valve area of less than 75% were younger (mean age 71 years) than those with an increase $\geq$75 % (mean age 75 years). On the other hand Cribier, the pioneer from the Rouen group, states that "best results were usually obtained in younger patients" (34), a finding confirmed by Safian (23). Sex, etiology of valve disease, clinical symptoms, ejection fraction of the left ventricle or bi or tricuspidy were not predictive for a good result (50). Although the difference in the relative increase in valve area between Letac's and our own patient series is obvious (83 and 63%), we have no explanation for their better results, albeit that the Rouen group applied longer and more inflations than we did. Although this group calculates valve area from mean gradients between aorta and left ventricle, they never mentioned in their last or previous publications the actual

values of the mean gradients. If we had used peak systolic gradients across the aortic valve for our calculations as they did, the increase in valve area would have been about 10% higher.

Restenosis and clinical results

After the initial enthusiasm for this new technique, Dancy was one of the first to point out the high frequency of early recurrence after balloon aortic valvuloplasty (20). Later reports confirmed this finding, Grollier (51) e.g. routinely recatheterized 24 out of 30 patients 8 days after aortic valvuloplasty. Eight of these patients must be considered as failed valvuloplasties, with a less than 25% increase in aortic valve area, 9 had a persistent more than 25% increase while 7 had not. Of note is that 4 patients with failed procedures had a more than 25% increase in valve area at recatheterization. The same finding has been reported by Davidson, using echo Doppler measurements routinely in 20 consecutive patients 2-4 days after valvuloplasty. The 50% increase in aortic valve area directly after the procedure, had been reduced to 25% in a few days (52). Spielberg found signs of restenosis at recatheterization in all but one of 23 patients who had undergone valvuloplasty 6-9 months earlier (53). Letac, routinely recatheterized 45 patients, at 5 months, but excluded 8 patients from his analysis, because they had incomplete dilatations, and thus could not be taken into account for restenosis (54). Of the 37 remaining patients, 9 (24%) showed restenosis. At 5 months follow-up, Bashore found signs of restenosis in 30 out of 44 patients, measured invasively (68%) (55). Desnoyers recorded a return to prevalvuloplasty measured aortic valve flow velocities in 52% of patients at 9 months follow-up (56). So the rate of restenosis whether measured invasively or not is very high, ranging from 24 to 96%, depending on the definition of restenosis and selection of patients. We did not routinely measure invasively the result of valvuloplasty at follow-up, mostly in view of the age and "brittleness" of these patients. Echo and Doppler measurements where available during follow-up will be discussed in a separate chapter (chapter 5).

In contradistinction with these disappointing data, the functional improvement encountered in most of these patients is good. An improvement in functional class was noted in the series from Rouen in 84% of all patients, at a mean follow-up of 8 months (54). This improvement was reflected in a reduction of the severity of all symptoms, present before valvuloplasty: syncopal attacks from 26% to 0%; dyspnea class III-IV from

69 to 12%; severe angina pectoris from 24 to 6%. In the series from Boston (23), 26% of patients had a recurrence of symptoms, treated with revalvuloplasty in 9%, aortic valve replacement in 10%, while 7% were managed on medical therapy, after a mean follow-up time of 9 months. In our patient group improvement in clinical symptoms was present initially in all patients after a successful procedure (31 out of 35 hospital survivors). Event free improvement on the contrary persisted only in 26% of patients, at a mean follow-up time of 22.5 months. Of the remaining 74% of patients, 10% died in hospital, 41% underwent aortic valve replacement after a mean of 13 months, 20.5% died out of hospital on average 15 months after valvuloplasty, while one inoperable patient is now waiting for revalvuloplasty.

The literature (23,53,54,57.58,59,60,61,62) is summarized in fig 9 with data on event free and total survival.

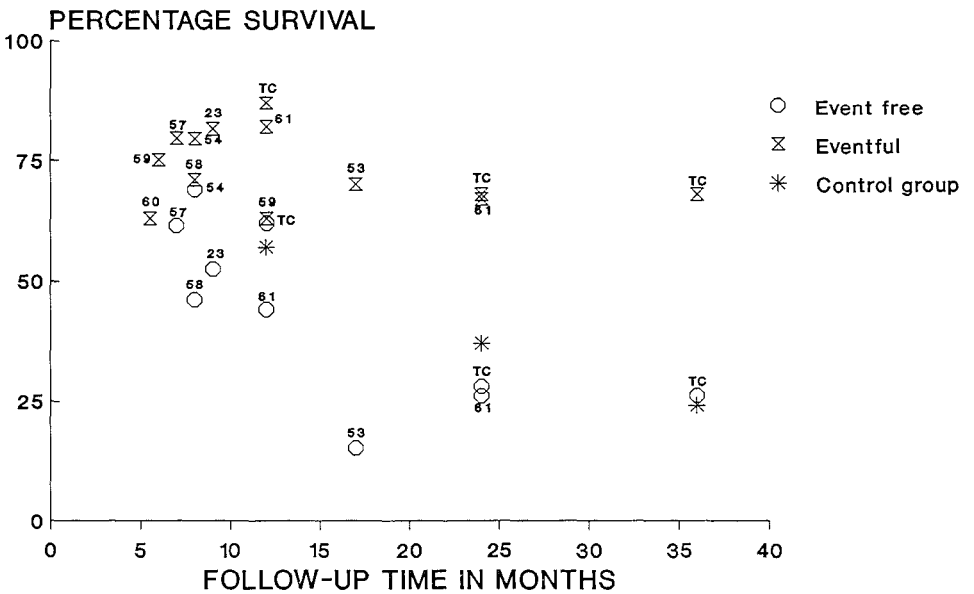

Figure 9: Survival data from literature reports (with reference numbers) and present data, indicated by TC. Control data again derived from O'Keefe (ref 62). Total survival, including survival of patients who underwent aortic valve replacement after aortic valvuloplasty, and event free survival data are given.

For comparison survival data are given from a group of 50 patients with severe aortic stenosis in whom operation was either declined by the patient or deferred by the physician. Survival at one, two and three years in this last group was 57,37 and 25%

respectively, with 5 patients having aortic valve replacement (62). All reported data show better total survival at any time of follow-up after balloon aortic valvuloplasty, but data beyond twelve months are scanty.

Left ventricular function after valvuloplasty

Three patients from our study population, in whom surgery was deferred on the basis of poor left ventricular function, had improved ejection fractions after valvuloplasty, and were operated on when symptoms recurred. Impaired left ventricular function is a common phenomenon in patients with long standing, severe aortic valve stenosis. This depression of the ejection fraction may be reversible after aortic valve replacement (63). Safian et al (64) noted a significant increase in ejection fraction after aortic valvuloplasty in almost half of 28 patients with low ejection fractions before valvuloplasty. The increase was from 34 to 58%, three months after the valve dilatation in these responders. These authors found no differences between responders and non responders with respect to aortic valve area after valvuloplasty. Berland et al published immediate results and one year follow-up in a group of 55 patients with ejection fractions < 40%, who subsequently underwent valvuloplasty. In hospital mortality was 5.5%, while at a mean follow-up of 11 months, another 40% of patients died. Recatheterization was carried out in 20 patients from this study group. Ejection fraction rose only significantly in 11 patients without restenosis (65).

The value of valvuloplasty in patients who have low ejection fractions and urgently need valve replacement is hard to establish. According to Fremes, urgent surgery and a low ejection fraction together, increase predicted probability of operative mortality in elderly patients by a factor 4 to 6 and in younger patients by a factor 6 (27). So it might be worthwhile performing valvuloplasty as an initial procedure, and make a subsequent operation less risky. A similar line of reasoning goes for coronary artery dilatation and the ultimate need for bypass grafting. But one has to add to the total risk, the risk of the valvuloplasty procedure itself, which is certainly not negligible (around 5-10%) in these patients. One has to individualize these decisions, also explaining to patients what the dilemmas and options are, because some of the preoperative variables that increase the surgical risk also increase the risk of valvuloplasty (Table 7).

Very old patients and indications

In a consecutive series of 26 patients aged 80 years or older undergoing aortic valvuloplasty, Brady et al (66) determined the in hospital mortality as 7.5%, mortality at 6 months at 32%, and functional improvement occurred in 63% of all patients. Letac reported in the same age group in 92 patients, a perioperative mortality of 6.5%, a late mortality at 13 months of 29%, and functional improvement in about 85% of patients (67).

The improvement in symptoms is impressive in both studies, and it is the most important result obtained in these patients. While death is inevitable, and life expectancy is probably not changed in this very old age group, no comparative group with the same amount of disease and without valvuloplasty is available. We fully agree with Cheitlin (33) who wrote in a recent Editorial in Circulation: "In this elderly age group with severe aortic stenosis, the quality of the last months of life can be miserable, with unremitting congestive heart failure, angina and syncope and multiple hospitalizations. If balloon valvuloplasty can alter these last years and improve the quality of life for these patients, then the procedure, even though its benefits are temporary, should be used in at least this one group of patients as the primary procedure " From our own series of patients, 11 were older than 80 years at the time of valvuloplasty. Five of these patients died a mean of 16 ± 4.5 months after the dilatation procedure. One patient underwent aortic valve replacement, while the other five all still experience an improvement in symptoms at a mean follow-up time of 24 ± 12 months. The same improvement in validity class has also occurred before the demise of those patients who died. So although we can probably not offer them a longer life, at least a better quality of their remaining life span is in perspective.

Aortic valvuloplasty is also indicated in that group of patients who are initially denied cardiac surgery. It provides a bridge for non cardiac surgical procedures (68,69), and is also indicated as a palliative treatment during pregnancy (70). Finally we feel that the procedure could be used in all patients with urgent need for relief of aortic valvular stenosis, as well as those who present with poor left ventricular function, as a bridge to surgical aortic valve replacement.

In conclusion, just as previous attempts at surgical aortic valvuloplasty with dilating instruments were only partly or temporarily successful (71) and recent intraoperative studies of balloon valvuloplasty showed only a minimal or moderate increase in the

functional aortic orifice in a minority of patients (72), percutaneous balloon aortic valvuloplasty remains a technique which is lifesaving in selected patients with an acceptable procedural risk and marked functional improvement at medium term follow-up in the majority of patients.

We would recommend percutaneous valvuloplasty in patients over the age of 80, in those considered too high at risk for open heart surgery, in those with unoperated or recently operated carcinoma and finally in all patients who are denied cardiac surgery for other reasons. In chapter 9 these recommendations will be detailed.

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CHAPTER 5
EVALUATION OF PERCUTANEOUS BALLOON AORTIC VALVULOPLASTY IN ELDERLY PATIENTS WITH DOPPLER ECHOCARDIOGRAPHY

(This chapter has been accepted in a slightly different format for publication in the Netherlands Journal of Cardiology, 1990. Authors are: van den Brand M, Bellerse L, Vletter WB, Plante S, Serruys PW, de Feyter PJ, Suryapranata H, Roelandt JR)

SUMMARY

From March 1986 through December 1989, 38 patients underwent 39 percutaneous balloon aortic valvuloplasty (PBAV) procedures, for isolated severe aortic valve stenosis. Mean age of these patients was 75 years, range 63-88. Nineteen of these patients were considered to be inoperable either due to cardiac or extracardiac conditions. Five patients were classified as high risk cases (age over 80 years), while the remaining 14, although presenting with several operative risk increasing factors, were acceptable candidates for aortic valve replacement. Aortic valve area calculated by the Gorlin formula increased, from 0.47 (± 0.14) to 0.75 (± 0.19) cm^2 after PBAV. Four patients died in hospital, eight patients died out of hospital 5-23 months after valvuloplasty (mean 15 ± 5 months). Sixteen patients underwent aortic valve replacement 6 days to 36 months after valvuloplasty (mean 13 ± 9 months), while 11 patients are still without events at a mean follow-up period of 23 ± 12 months.

Thirty-one patients had maximal aortic valve flow velocity measured with echo Doppler techniques both immediate before and 24-48 hours after valvuloplasty.

Conversion of this maximal velocity to millimeters mercury and comparing these values with the pressure difference between peak left ventricular and peak aortic pressure, when estimated hemodynamically, showed poor correlations both before and after valvuloplasty (r = 0.49 and 0.55 respectively). The Doppler technique tended to overestimate aortic valve pressure drops over 74 and 25 mm Hg, when hemodynamically derived, and to underestimate pressure drops below that value respectively before and after PBAV. After valvuloplasty the maximal velocity over the aortic valve was significantly reduced from 4.6 ± 0.7 m/sec to 4.1 ± 0.8 m/sec.

Twenty two patients had immediate Doppler evaluation after valvuloplasty as well as at a mean follow-up time of 10 ± 7 months. Maximal velocity over the aortic valve increased in that period from 4.1 to 4.4 m/sec (not significant), with the highest increase in velocity in the group of patients dying late, 4.0 to 4.5 m/sec (not significant).

Comparing catheter derived aortic valve areas calculated by the Gorlin formula directly post PBAV, with echo Doppler derived areas calculated with the continuity equation at follow-up, showed a good correlation in 6 patients with persisting clinical improvement ($r = 0.94$).

It is concluded that the echo Doppler derived aortic valve areas, show a better correlation with hemodynamically derived aortic valve areas, than maximal aortic valve flow velocities with peak to peak pressure aortic valve gradients. Although both techniques have their inherent limitations, the outcome of both estimations for aortic valve area is very similar.

INTRODUCTION

Percutaneous balloon aortic valvuloplasty is recently being performed with increasing frequency for the relief of severe calcified aortic stenosis in selected elderly patients. Most investigators now believe that aortic valvuloplasty is a palliative procedure, that should be limited to patients who are not surgical candidates for whatever reason (1-5). In patients with severe congestive heart failure, balloon aortic valvuloplasty may improve the patient's condition, as a bridge to later aortic valve replacement.
The procedure can produce moderate increases in aortic valve area, generally from 0.4-0.6 before to 0.7 to 0.9 cm^2 after valvuloplasty and can be performed with an acceptable periprocedural risk (1,2).

Unfortunately, the mortality of these patients remains high after the procedure and mortality rates of 15 to 28% after 6 to 9 months have been reported (1,2). This high mortality is probably caused by restenosis, whose rate has been shown to be high both after invasive and non invasive assessment (6,7). Doppler echocardiography is a noninvasive method, especially convenient for elderly people with a low validity class, the population mostly referred for valvuloplasty. Symptomatic improvement and a non invasively measured reduction in the severity of aortic valve stenosis might indicate a persisting good result (8).

Previous studies using Doppler echocardiography have shown a fair or good correlation between pre and post valvuloplasty measured aortic valve areas, with catheterization data using the Gorlin formula (7,9-15).

We studied the correlation between the drop in pressure across the stenotic aortic valve as well as valve area, measured during catheterization and estimated by Doppler echocardiography technique before and after aortic valvuloplasty. Long-term follow-up Doppler measurements were performed to correlate changes in maximal valve flow velocity with clinical events, mortality, aortic valve replacement, and functional status.

PATIENTS AND METHODS

From March 1986 through December 1989, 38 patients underwent 39 aortic valvuloplasty procedures. All patients were diagnosed as having severe aortic valve stenosis by physical examination, Doppler echocardiography and heart catheterization. All patients were discussed with the cardio-surgical team. Patients were acceptable candidates for a balloon valvuloplasty procedure if they fulfilled one of the following criteria:

a) deemed inoperable in a combined cardio-surgical discussion
b) classified as a high risk case
c) classified as a normal risk patient, but with preference of the patient for balloon valvuloplasty instead of surgical valve replacement or surgical valvuloplasty.

All patients and a relative had to give their informed consent, after explanation of the experimental character of the procedure, and the potential risks and benefits. No patient was acceptable if during diagnostic angiography aortic insufficiency more severe than grade II was demonstrated.

Clinical characteristics and the cardiac condition of these patients before valvuloplasty are summarized in tables 1 and 2.

Nr of Patients	39
Female sex	24
Mean age (years)	75.1 ± 7.1
Inoperable	20
High risk case	5
Acceptable risk case	14
Validity class IV	14
Validity class III	25

Table 1 Clinical characteristics of balloon aortic valvuloplasty patients

	Number of patients
EF $\geq$0.55	22
EF $\geq$0.40 - 0.54	6
$\geq$0.20 - 0.39	5
$\leq$0.19	4
not assessed	2
Aortic incompetence	
grade 0	10
grade I	20
grade II	9
Coronary artery disease	
Absent	24
1 vessel disease	7
2 vessel disease	2
3 vessel disease	5
left main disease	1

Table 2 Ejection fraction, severity of aortic incompetence and coronary artery disease in 39 valvuloplasty patients

Table 3 summarizes the hemodynamic data of these patients before and after balloon aortic valvuloplasty.

	LVPSP		LVEDP		P-PSG		MSG		AF		AVA		% increase
	B	A	B	A	B	A	B	A	B	A	B	A	AVA
Mean	217	177	16	12	82	41	74	43	176	214	0.47	0.75	63
± SD	37	34	9	9	24	15	19	10	50	49	0.14	0.19	38
p value	<0,05		<0.05		<0,05		<0,05		<0,05		<0,05		

AVA = aortic valve area (cm2); AF = systolic aortic valve flow (ml s-1); LVEDP = left ventricular end-diastolic pressure (mmHg); LVPSP = left ventricular peak-systolic pressure (mmHg); MSG = mean systolic aortic gradient (mmHg); P-PSG = peak to peak systolic gradient (mmHg); B = before; A = after.

Table 3 Hemodynamic data before and after 39 balloon aortic valvuloplasty procedures.

The direct result of balloon aortic valvuloplasty, and the clinical follow-up of these patients are combined in table 4.

	Age (years)	M/F ratio	Follow-up time (months)	Aortic valve area (cm2) Before	Aortic valve area (cm2) After	Aortic valve area Increase (%)	Validity class Before III	Validity class Before IV
Survivors operated (n = 16)	72.1 ± 5.6	6/10	34 ± 8	0.51 ± 0.11	0.75 ± 0.15	52 ± 32	12	4
Survivors not operated (n = 11)	76.7 ± 6.6	4/7	23 ± 12	0.42 ± 0.11	0.73 ± 0.19	77 ± 31	7	4
Late deaths (n = 8)	78.7 ± 9.5	3/5	15 ± 5	0.49 ± 0.18	0.76 ± 0.23	67 ± 48	6	2
Early deaths (n = 4)	76.2 ± 1.5	2/2	2 ± 3 days	0.42 ± 0.12			0	4

Table 4 Clinical and hemodynamic data at the time of percutaneous balloon aortic valvuloplasty in patients with early and late mortality and in survivors, with and without aortic valve replacement. Data are given as mean values ± standard deviation

Doppler echocardiography was performed in 34 patients within two weeks before and in 35 patients 24-48 hours after balloon aortic valvuloplasty. 1-27 months after valvuloplasty 24 patients were re-investigated (mean 10 ± 7 months).

Patients were examined in the supine left lateral position. The continuous wave Doppler

examination was performed using a Toshiba SSH160 or a Diasonics Vingmed ultrasound unit. Peak aortic valve blood flow velocity was obtained by a non imaging continuous wave Doppler probe, placed in various positions to obtain apical right, left parasternal and suprasternal views. Spectral velocity traces were recorded on strip charts at a speed of 50 mm/s.

The maximal instantaneous transvalvular pressure difference was estimated from the maximal aortic Doppler velocity by the modified Bernoulli equation:

$$\text{Pressure difference} = 4 \times \text{max. velocity}^2$$

Aortic valve area (AVA) was calculated from two dimensional echo and Doppler data with the continuity equation as follows:

$$AVA = \frac{A_{LVOT} \times (TVI)\ LVOT,}{(TVI)\ AV} \quad (11)$$

where AV = aortic valve, A_{LVOT} = area of left ventricular outflow tract in cm^2, AVA = aortic valve area in cm^2, LVOT = left ventricular outflow tract and TVI = time velocity integral. Time velocity integrals were obtained by integrating the respective Doppler velocity spectra on a digitizing tablet, connected to an Olivetti computer. Aortic valve area was calculated before and after valvuloplasty in one patient and in six other patients after valvuloplasty using echo and Doppler data.

In two patients transoesophageal echocardiography was performed, in one during valvuloplasty under general anaesthesia, and in one other patient before and after valvuloplasty. The transoesophageal probe (5 MHz, single plane transverse transducer) was inserted through the oropharynx into the oesophagus. Two dimensional images were obtained in the standard transoesophageal echocardiographic planes.

During catheterization the aortic valve area was calculated using the Gorlin formula (9).

RESULTS

Gradients and flow velocity

Comparison of the peak to peak systolic aortic valve pressure drop measured before and after valvuloplasty by catheterization, and maximal velocity over the aortic valve measured with Doppler, revealed poor correlations (fig 1).

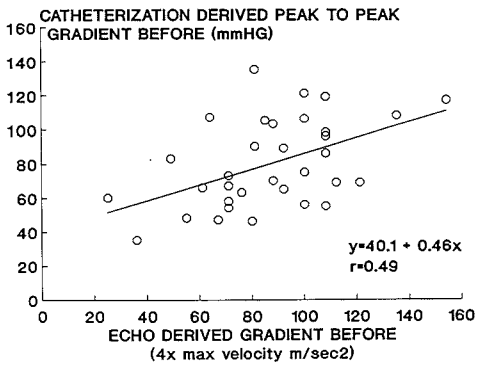

Figure 1a

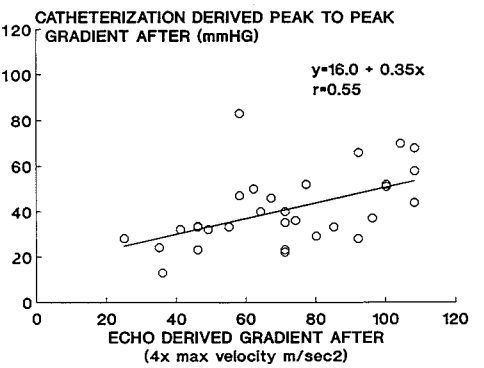

Figure 1b

Figure 1: Regression analysis of catheter and echo Doppler derived pressure drop over the aortic valve, (a) before and (b) after percutaneous balloon aortic valvuloplasty

This proved also to be true for a regression analysis of the change in pressure drop. The maximal flow velocity over the aortic valve fell significantly after valvuloplasty from 4.6 ± 0.7 to 4.1 ± 0.8 m/sec ($p < 0.05$) (fig 2).

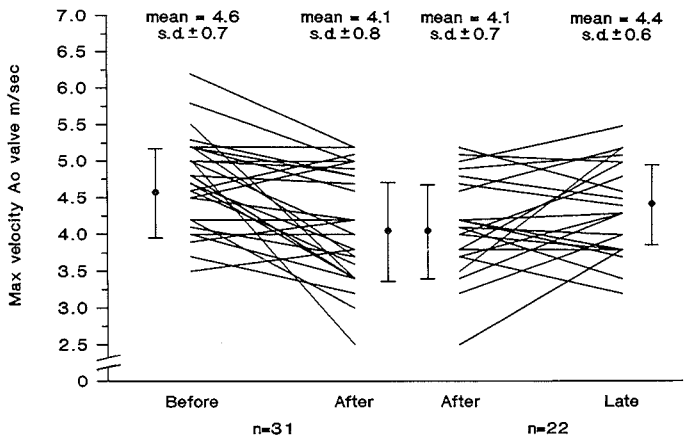

Figure 2: Maximal flow velocity over the aortic valve, before and after balloon valvuloplasty and at late follow-up. The decrease in flow velocity after valvuloplasty is significant ($p < 0.05$), while the increase in flow velocity at late follow-up is not significant

The highest aortic valve flow velocity after valvuloplasty was recorded in the group with subsequent aortic valve replacement (Table 5). At a mean follow-up of 10 ± 7 months an increase in aortic valve flow velocity to 4.4 ± 0.6 m/sec was recorded (fig 2, table 5). This increase was not significant. The increase was on average highest in patients dying late, and lowest in patients who underwent late aortic valve replacement, although in none of the subgroups was this increase significant.

		All patients (n = 39)	AVR (n = 16)	Late mortality (n = 8)	Uneventful FU (n = 11)
Examined		(n = 31)	(n = 16)	(n = 7)	(n = 6)
Max. Ao Velocity (m/sec)					
before PBAV	mean ± SD	4.6 * 0.7	4.7 * 0.5	4.6 * 0.5	4.9 * 0.9
after PBAV	mean ± SD	4.1 0.8	4.2 0.8	4.1 0.5	4.2 0.7
		(n = 22)	(n = 11)	(n = 5)	(n = 6)
Interval (months)	mean ± SD	10 7	8 6	8 4	16 8
after PBAV	mean ± SD	4.1 0.7	4.3 0.8	4.0 0.4	3.9 0.3
late FU	mean ± SD	4.4 0.6	4.3 0.7	4.5 0.7	4.2 0.5

* $p < 0.05$

Table 5 Comparison between maximal Doppler measured aortic valve flow velocity before and after PBAV and at follow-up in all patients, and in three different outcomes: valve replacement (AVR), late mortality and uneventful follow-up (FU)

Prevalvuloplasty aortic valve flow velocities were also compared between groups (Table 5). The values measured directly before and at late follow-up after valvuloplasty were not significantly different in the total group, nor in any subgroup.

Echo Doppler estimated aortic valve area

The only patient with prevalvuloplasty estimated echo Doppler aortic valve area showed an increase from 0.41 cm^2 to 0.44 cm^2 after valvuloplasty. If aortic valve area before and after valvuloplasty was measured with pressure difference and cardiac output

this increase was from 0.53 to 0.64 cm^2. Six other patients had echo Doppler estimated aortic valve areas at a mean follow-up of 13 months after valvuloplasty. Aortic valve area varied from 0.47 to 1.22 (Table 6).

Case number	1	2	3	4	5	6
Catheter measured AVA post PBAV (cm^2)	0.67	0.80	0.57	0.78	1.12	0.78
Echo Doppler estimated AVA at follow-up (cm^2)	0.75	0.96	0.47	0.85	1.22	0.96
Follow-up period (months)	22.5	21.0	12.5	9	6.5	5.5

Table 6 Echo Doppler estimated aortic valve area (AVA) at follow-up, and catheter measured aortic valve area directly after valvuloplasty

Only patient nr 4 underwent aortic valve replacement, 4.5 months after this measurement, because of recurrent symptoms of angina pectoris. This patient had undergone coronary angioplasty for two vessel disease as well as aortic valvuloplasty. Regression analysis of echo Doppler estimated aortic valve areas at follow-up with aortic valve areas calculated from hemodynamic data at the end of the valvuloplasty procedure shows that AVA (cath) = 0.18 + 0.70 AVA (echo). There was a good correlation between both values, with a r value of 0.94. Below a hemodynamic derived AVA of 0.60 cm^2, echo Doppler measurements underestimated aortic valve area, while above a hemodynamic derived AVA of 0.60 cm^2, echo Doppler tended to overestimate the AVA.

Transoesophageal echocardiography

In two patients transoesophageal echocardiograms were performed. In the first patient a tricuspid heavily calcified aortic valve with very limited cusp mobility was documented before valvuloplasty. After valvuloplasty an improved mobility of predominantly the non coronary cusp was seen. Five months later, after recurrence of symptoms, the mobility of the non coronary cusp was similar to prevalvuloplasty. This patient subsequently underwent valve replacement. In the other patient transoesophageal echocardiographic monitoring was performed under general anaesthesia during valvuloplasty. A heavily calcified tricuspid aortic valve, with a big calcified lump in the left coronary cusp was present and valve opening was solely confined to the non coronary cusp. After valvuloplasty no apparent difference in cusp mobility was noted. This patient showed an increase in echo Doppler estimated aortic valve area from 0.41 cm^2 to 0.44 cm^2 and in hemodynamic derived aortic valve area from 0.53 to 0.64 cm^2. These values are in agreement with the minimal changes observed during transoesphageal echocardiography.

DISCUSSION

Transvalvular pressure gradients

Several studies have shown the usefulness of Doppler echocardiography in assessing the systolic transvalvular pressure drop in aortic stenosis (10, 16-28). Although the systolic pressure gradient is an important determinant of aortic valve area, transvalvular flow is even more important. In our study a poor correlation was found between maximal Doppler estimated flow velocity and peak to peak systolic gradients measured at catheterization, both before and after aortic valvuloplasty. Doppler measured maximal instantaneous systolic transvalvular pressure differences before valvuloplasty were on average 7 mm Hg higher than catheter derived peak to peak systolic gradients. After aortic valve dilatation the mean difference between the two methods increased to 29 mm Hg, with again the higher values for Doppler derived pressure differences. Danielsen (29) comparing maximal Doppler and maximal catheter derived pressure differences, found these gradients both to be significantly higher than peak to peak systolic gradients, recorded during catheterization. Defined this way the Doppler technique systematically underestimated the maximum catheter derived pressure difference (29).

Both Doppler and catheterization measurements have several sources of inaccuracy for deriving the pressure drop over a stenotic valve. For catheterization derived values, the acquisition mode is very important. Calculations from left ventricle to aorta pull back tracings, can be misleading in failing to achieve a good superimposition of left ventricular and aortic pressure recordings (30). This is more the case if any irregularity of the heart rhythm exists. Also measuring pressure differences with tipmanometered catheters instead of fluid filled catheters might result in different values, because fluid filled catheters overestimate especially the left ventricular pressure, and lead to an overestimation of the catheter derived instantaneous maximal pressure difference.

Danielsen (29) for example calculated in 80% of his patients pressure drops across the aortic valve from pull back tracings, while we always used simultaneous recorded pressures, derived mostly from fluid filled catheters. Introducing a catheter in the left ventricle through the aortic valve further reduces the aortic orifice. An 8F catheter for example occupies an area of $3.14 \times (4F)^2 = 5.6\ mm^2$, reducing the actual aortic valve area in severe aortic stenosis by about 10%. An additional variability in the catheter data is introduced by the pressure recovery. In a region distal to an obstruction the pressure gradually increases. Clark (31) using aortic stenosis models, demonstrated that pressure recovery extended to 9 cm downstream of the stenotic area. Pressure recovery is determined by the flow velocity at the site of the obstruction, and the ratio between the cross sectional flow area at the obstruction site, and that of the flow channel distal to the obstruction. In order to obtain a fully recovered pressure, the catheter must be positioned outside the turbulent area, which is at a variable distance from the stenotic valve.

The application of the Bernoulli equation in its most simple form (pressure drop = $4 \times (\text{fluid velocity})^2$) has also several assumptions as put forward by Rijsterborgh and Roelandt (32).

It is assumed that the conversion of potential energy into kinetic energy takes place without energy losses. Also a uniform velocity distribution at the cross sectional flow area in the obstruction is assumed, which might not be the case. A standard Doppler instrument measures the maximum velocity at the site of the obstruction. It is conceivable that especially after valvuloplasty, non uniform flow velocities across the stenotic aortic valve exist, resulting in overestimation of actual velocities, by measuring only maximal velocities. Also the energy losses may not be negligible and vary with the

shape and size of the obstruction, underestimating the pressure drop by Doppler echocardiography. These two potential errors partly compensate for each other by operating in opposite directions. The simplified Bernoulli equation will overestimate the actual pressure drop in mild aortic stenosis and underestimate it in severe aortic stenosis (32). This theory is confirmed by the data of several reports. Below a peak catheterization pressure drop of 50 mm Hg, the simplified Bernoulli equation tends to overestimate the pressure drop, while above a pressure difference of 50 mm Hg the same equation underestimates the pressure difference obtained by catheter (16-28). One technical aspect of measuring maximal velocities across the aortic valve by Doppler echocardiography deserves attention. The Doppler beam must be derived as parallel as possible to the blood flow jet across the stenotic valve (24,29). This requires the use of a small non imaging transducer with multiple angulations from various positions. Nonetheless experienced echocardiographers can assess accurately aortic valve gradients (24). Finally the measured difference might well be real, because measurements were not made simultaneously. In the post valvuloplasty situation alterations in aortic valve flow might partly be responsible for the demonstrated differences.

Aortic valve area calculations

Data from previous studies indicate that for a given, catheter calculated valve area, a wide scatter of peak Doppler derived pressure gradients exists especially for mild to moderate aortic stenosis (29). This scatter is the result of variation in transvalvular flow, which is unknown. A peak aortic flow velocity of $\geq$4.5 m/sec for example was highly specific for severe aortic stenosis, but had a low sensitivity. Half of the 70 patients described by Oh with a peak aortic flow velocity of $<$ 4.5 m/sec had severe aortic stenosis (15), by hemodynamic measurements. These authors found good correlations between catheter and Doppler derived mean gradients ($r = 0.86$; $y = 0.89x + 2.3$).

With use of the continuity equation, relating the flow velocity with the cross sectional area of flow at a given flow volume, it was demonstrated in several studies that aortic valve area can be reliably estimated (11-13). The same equation has been applied to calculate aortic valve area both before and after aortic valvuloplasty (7,14,15). According to these authors the Doppler continuity equation can accurately predict the severity of aortic stenosis pre and post valvuloplasty. Pre valvuloplasty correlation coefficients

between catheter and Doppler derived aortic valve areas were 0.72, 0.71 and 0.80. Two of these studies also correlated postvalvuloplasty valve areas and found correlation coefficients of 0.61 and 0.85 respectively (7,14).

It is rather remarkable that two techniques, each with their inherent sources of errors, show such good correlations. Catheter measured aortic valve area, measured with aortic valve flow and mean transvalvular pressure gradient, has also been questioned, especially when assessing severe stenotic valves with low transvalvular flow rates (33,34). During dobutamine and isoproterenol infusion, aortic valve areas calculated by the Gorlin formula (9), increased from 0.67 to 0.81 cm^2 and from 0.86 to 1.09 cm^2 respectively. In one of these studies, aortic valve area was calculated during dobutamine infusion in five patients simultaneously using the continuity equation. In these patients calculated aortic valve area echo Doppler derived changed from 0.69 ± 0.23 cm^2 to 0.71 ± 0.21 cm^2.

These findings suggest flow dependence of the Gorlin formula. Come et al recording two sets of catheter derived aortic valve areas before valvuloplasty, found only a moderate correlation between the two sets of values (r = 0.42) (35). Catheter derived aortic valve area can therefore not be considered as the "gold standard" (32).
Although there was a time delay of several months in our patients in whom aortic valve area was measured both with echo Doppler and with catheter derived methods, good agreement existed between the values calculated in this way. As all patients mentioned in table 6 were free of clinical symptoms of restenosis, we might assume that aortic valve areas measured at the end of the valvuloplasty procedure did not change much during the follow-up period. Moreover none of these patients showed an increase in maximal aortic valve flow velocity, measured repeatedly during this follow-up period.

Transoesophageal echocardiography

One literature report adresses the usefulness of transoesophageal echocardiography during aortic valvuloplasty (36). The potential advantages are: readily visible anatomy of the stenotic aortic valve, monitoring of left ventricular function during and after balloon inflation and assessment of aortic incompetence after dilatation.

Transoesophageal echocardiography can be of help in deciding whether further valve dilatation with a larger balloon is warranted, evaluate directly the effect of balloon inflation on valve cusp mobility and space balloon inflations till left ventricular function has

returned to preinflation values.

We feel that in patients with symptomatic aortic valve stenosis, echo Doppler evaluation with aortic valve area calculation is indicated. In surgical candidates, presurgical evaluation should include coronary angiography. In non surgical candidates coronary angiography and valvuloplasty could be performed in the same session. The procedure is preferably performed under general anaesthesia while transoesophageal echocardiography may become a major monitoring technique. After valvuloplasty, follow-up investigations should include echo Doppler aortic valve area measurements at regular intervals e.g. every three months. If recurrence of symptoms occurs and aortic valve area measured this way returns to prevalvuloplasty values, the mentioned investigation scheme should be repeated. In patients without symptoms, or with moderate symptoms and with signs of restenosis documented objectively by calculating aortic valve area with echo Doppler, a conservative attitude is justified, with more frequent follow-up visits, because asymptomatic patients with moderate to severe aortic stenosis are at relatively low risk for sudden death as recently documented by Kelly et al (37). If complaints persist or recur in patients without objective signs of restenosis, alternative explanations for the clinical deterioration should be sought before the patient is subjected to recatheterization.

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CHAPTER 6
AORTIC VALVULOPLASTY OF CALCIFIC AORTIC STENOSIS WITH MONOFOIL AND TREFOIL BALLOON CATHETERS: PRACTICAL CONSIDERATIONS

(This chapter has been published in the Int J Cardiac Imaging 1990; 5:249. Authors are: Plante S, van den Brand M, van Veen L, di Mario C, Essed CE, Beatt KJ, Serruys PW)

SUMMARY

In order to evaluate the relation between balloon design (monofoil, trefoil) and valvular configuration, experimental aortic valvuloplasty was performed in four post-mortem hearts with calcific aortic stenosis of various morphology. The degree of obstruction of the aortic orifice was assessed by computed axial tomography during inflation of monofoil 15 and 19 mm and trefoil 3 x 12 mm balloon catheters. We also evaluated the hemodynamic repercussion of balloon inflation (fall in systolic aortic pressure) in four elderly patients with acquired aortic stenosis who underwent a percutaneous transluminal aortic balloon valvuloplasty, with stepwise increasing balloon sizes of 15 mm, 19 mm and 3 x 12 mm, as during our in vitro experiments, and who underwent aortic valve replacement later on. In these patients, we correlated the anatomy of the excised aortic valves with the retrospective analysis of aortic pressure curves recorded during previous valvuloplasty procedures.

Our experimental and clinicopathological observations showed that the degree of obstruction of the aortic orifice in post-mortem specimens and the tolerance to balloon inflation in live patients are dependent of the valvular configuration. Although trefoil balloons have the theoretical advantage to avoid complete obstruction of the aortic orifice during inflation, we observed that in presence of a tricuspid configuration, they could be potentially more occlusive than monofoil balloons since each of the 3 individual components of the trefoil balloon occupied the intercommissural spaces while inflated. However, they offered more residual free space when inflated in aortic valves with a bicuspid configuration (i.e. congenitally bicuspid valves or tricuspid valves with one fused commissure).

In our opinion, these observations are relevant, since degenerative disease of the aortic valve (i.e. tricuspid valve without commissural fusion) is now recognized as the most common etiology of aortic stenosis in the elderly.

INTRODUCTION

Percutaneous transluminal balloon aortic balloon valvuloplasty (PBAV) for acquired aortic stenosis (AS) has been introduced a few years ago as an alternative for valve replacement in patients with high surgical risk or for those who refused surgical intervention (1,2). Procedure-related complications, limited hemodynamic improvement and the high recurrence rate reported until now (3-16) have decreased the initial enthusiasm for this relatively new technique.

Despite these current limitations, PBAV is currently regarded by many cardiologists as a palliative treatment in a subset of patients with prohibitive surgical risk. Some authors recently advocated PBAV as a "bridge" procedure to improve left ventricular function before aortic valve replacement or non-cardiac surgery (17,18).

However, other shortcomings of the procedure are 1) the largely unpredictable individual tolerance to balloon inflation (hypotension) and 2) the unpredictable immediate hemodynamic results in an individual patient. The incidence of non-responding or poorly responding patients (aortic valve area still < 0.7 cm^2 at the end of the procedure) is ranging from 18.7% to 38.2% (12). These facts suggest that some morphological aspects (bicuspid or tricuspid valve, fused or non-fused commissures) or other factors like the volume occupied by nodular calcifications and residual elasticity of some leaflets (19) can adversely influence the hemodynamic results of the procedure. Furthermore, it seems conceivable that balloon catheters of different shapes (monofoil, bifoil, trefoil) operate with distinct mechanisms of dilatation in the presence of a specific valvular morphology.

To circumvent hypotensive responses during balloon inflation, trefoil balloon catheters have been introduced recently. Attractive advantages of this device have been demonstrated in animal experiments (20) and it has been effective in allowing continuous blood flow during inflation in the setting of pulmonary valvuloplasty in adults (21), aortic valvuloplasty in children and young adults (22), and in mitral and aortic valvuloplasty in adults (23-24). However, the degenerative, remodeling and calcifying

process peculiar to acquired AS in elderly patients differs largely from the pathological changes observed in congenital and rheumatic valvular diseases; this may explain why some of these patients still present abrupt and severe falls in aortic pressure, even when PBAV is performed with trefoil balloon catheters.

In order to achieve better hemodynamic results and to obtain technical refinements in the valvuloplasty material, we have to improve our knowledge of the operational mechanisms of dilatation. Intra-operative, post-mortem and experimental studies on the mechanisms of aortic valvuloplasty have been reported until now, based mainly on visual inspection and low-energy x-ray techniques (19,25-27). In order to obtain detailed quantitative information on the intravalvular calcium distribution before and after valvuloplasty and to further elucidate the operational mechanisms of dilatation, we have performed thin-slice computed tomographic scanning in post-mortem hearts with calcific AS before, during and after balloon valvuloplasty (28). This technique avoided superimposition of structures and provided vastly superior density resolution compared to conventional x-ray techniques. In our study, fracture of nodular calcifications, commissural separation and central raphe splitting were the observed mechanisms of balloon valvuloplasty. However, calcium redistribution (27) could not be recognized as an operational mechanism, since no dilatation-related modification in density and volume of the calcific deposits was observed with computed tomographic scanning. Furthermore, computed axial tomography provided useful informations concerning the relations between balloon size and shape and valvular configuration. To our knowledge, few reports have focused on this particular aspect of aortic balloon valvuloplasty.

In this chapter, we describe our experimental and clinicopathological observations related to aortic valvuloplasty performed with single circular (monofoil) and trefoil balloon catheters in human hearts with acquired AS. We will present a review of our previous experimental findings and we will correlate these results with our recent clinicopathological observations, based on retrospective analysis of valvuloplasty procedures performed in some patients who underwent subsequently a valve replacement and from whom excised aortic valves were available for anatomopathological evaluation. For more detailed information concerning our in vitro experiments, the reader is referred to our previous publication (28).

EXPERIMENTAL VALVULOPLASTY

Material and methods

Four hearts with calcific, stenotic aortic valves and intact aortic rings were selected from our collection of autopsy specimens (Pathology Department 1, Erasmus University). The mean heart weight was 583 $\pm$ 78 g (range: 538-700 g). The average thickness of the left ventricular wall was 19.5 $\pm$ 1.9 mm.

Case 1: This specimen was obtained from a 67 year-old female who died suddenly. The aortic valve was tricuspid, with extensive nodular calcifications of the valve cusps projecting into the valve sinuses, but without commissural fusion. These findings were compatible with a degenerative etiology.

Case 2: The second specimen came from a 71 year-old male patient in whom a pre-mortem cardiac catheterization had shown a mean systolic aortic gradient and a valve area of 70 mm Hg and 0.6 cm^2, respectively. Mild aortic regurgitation, moderate combined mitral valve disease and subocclusive stenoses of the left anterior descending and circumflex arteries were also present. This patient died after having sustained a large anterior myocardial infarction. At pathological examination, the coexisting mitral valve disease and the tight, heavily calcified commissural fusion between non-coronary and right coronary aortic cusps were in accordance with a rheumatic etiology. Although originally tricuspid, the aortic valve had a bicuspid configuration, owing to the tightly fused commissure. Nodular calcifications on the aortic aspects of the cusps were also observed.

Case 3: Irreversible cardiogenic shock occurred in this 73 year-old male patient, as a consequence of a posterior myocardial infarction. Post-mortem examination revealed a congenitally bicuspid aortic valve. The larger anterior cusp was divided by a central calcified raphe, extending across the floor of the aortic sinus from aorta to the free edge. The valve had moderate nodular calcifications, but no commissural fusion.

Case 4: The fourth heart was obtained from a 50 year-old female in whom a previous catheterization had demonstrated a mean systolic aortic gradient of 77 mm Hg and a calculated valve area of 0.7 cm^2. This patient, while awaiting surgical correction, developed fatal acute pulmonary edema. At autopsy, the valve was also congenitally bicuspid, but with an almost symmetric configuration, a moderate bilateral commissural fusion, and diffuse calcifications confined to the leaflets. In the anterior

cusp, a calcified central raphe was also observed.

Specimens were originally preserved in a 10% formalin solution but were kept in water for 30 days before the experiment. Cylindrical calipers of increasing diameter (range: 3-30 mm) were used to assess the aortic orifice area, while the aortic annulus diameter was measured directly. All specimens were examined on a Tomoscan 350 clinical unit (Philips, Phillips Medical Systems, Best, Netherlands). Three radiopaque markers were sutured to the aortic wall at the leaflet level and used as reference points in the scanning procedures. Axial scan series, covering the entire aortic valve region, were performed with contiguous scans of 1.5 mm thickness. Off-line evaluation was performed on a Philips Stand Alone Viewing System, enabling sagittal reconstruction, contour detection of the region of interest, and calculation of volumes and mean computed tomographic attenuation values (Hounsfield Units) of calcium deposits. In all specimens the region of interest contour mode was used to determine the residual orifice area during each inflation. Evaluation of all the axial scans was used to assess the minimal free space between leaflets and balloon.

Post-mortem aortic valvuloplasty was performed with balloons of increasing diameter, passed retrogradely from the aorta into the left ventricle. First, a monofoil 15 mm balloon (inflated cross-sectional area: 1.8 cm2) was manually inflated across the aortic valve with a pressure of 3 atmospheres. Thereafter, a second and third dilatation were performed with a monofoil 19 mm (area: 2.8 cm^2) and a trefoil 3 x 12 mm (3.4 cm^2) balloon catheter, both inflated to a pressure of 3 or 4 atmospheres. Balloons were inflated until complete disappearance of indentation of the valves on the balloons. Leaflet avulsion, valve ring disruption or liberation of valvular debris did not occur in any specimen. Experimental valvuloplasty with bifoil-designed balloon catheters was not assessed in this study, since they were not commercially available at that time in our institution.

Measurement of the aortic valve orifice by cylindrical calipers was performed at the beginning and after each dilatation. Visual inspection, photographs and axial computed tomographic scans were obtained before, during and after each balloon inflation. Figure 1 provides an example of computed axial tomography scans obtained at the level of the aortic valve orifice during experimental valvuloplasty in a post-mortem specimen.

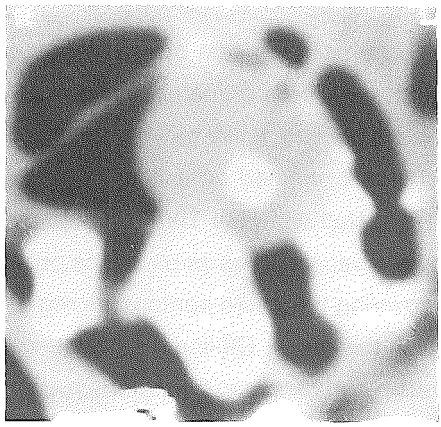

Figure 1A

Figure 1: Axial scans of a post-mortem specimen (case #1) performed at the level of the aortic valve orifice, during inflation of 15 mm, 19 mm and trefoil 3 x 12 mm balloons (enlargement factor: 4 X). This valve was the most heavily calcified. The density is decreasing from white areas (calcium deposits, catheters, radiopaque markers), to the grey (heart and valve soft tissue, water in inflated balloons), and the black areas (air). During inflation, the 15 mm balloon was displaced towards the less calcified left aortic cusp (Fig.1A). Minimal increment in valve area was achieved. The inflated 19 mm balloon occupied also an asymmetrical position in the aortic orifice, but the displacement of the free edges of the cusps was greater than with the previous dilatation, involving also the most heavily calcified leaflet (Fig.1B). Fracture of nodular calcifications was noted at visual inspection. During inflation of the trefoil balloon (Fig.1C), a rotating movement was observed. At the end of inflation, the three intercommissural spaces were occupied by the 3 individual components of the balloon, almost totally occluding the aortic orifice. At visual inspection, the increase in cusps mobility was associated with full-thickness fracture of the heavy nodular calcifications. L: left; R: right.

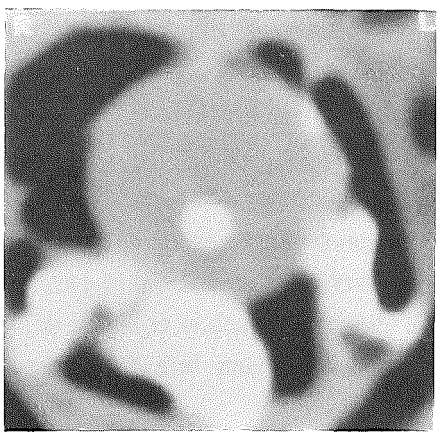

Figure 1B

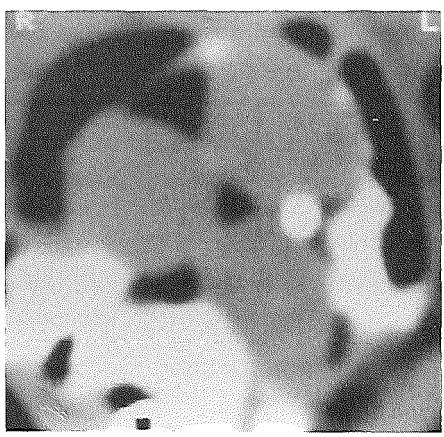

Figure 1C

Results and comments

Table 1 summarizes clinical data and macroscopic aspects of the four valves. Volumes and mean computed tomographic attenuation values of the calcific deposits are also tabulated.

						Calcium Deposits	
				Valve Ring			
Case	Sex	Age	No Cusps	Commissural Fusion	Diameter (mm)	Volume (cm^3)	CT Value (HU)
1	F	67	3	No	24	1.21	948
2	M	71	3	Yes	24	0.29	132
3	M	73	2	No	22	0.19	281
4	F	50	2	Yes	20	0.17	121

CT value = computed tomographic attenuation value; HU = Hounsfield Units; F = female; M = male

Table 1 Clinical data, macroscopic aspects and computed tomographic evaluation of valve calcium deposits of the four post-mortem specimens.

Table 2 shows the aortic valve area (AVA) obtained before and after dilatation with 15 mm, 19 mm and 3 x 12 mm balloons in each case, as calculated by cylindrical calipers.

Balloon Size	Case 1	Case 2	Case 3	Case 4
BASAL	0.20	0.78	0.95	0.95
15 mm	0.28	1.76	0.95	0.95
19 mm	0.50	2.26	1.76	1.76
3 x 12 mm	0.95	3.14	2.83	2.54

Table 2 Aortic valve area (cm2) before experimental valvuloplasty and after dilatation with 15 mm, 19 mm and 3 x 12 mm balloons, as calculated by cylindrical calipers.

Figure 2 represents the minimal free space (residual aortic orifice) observed during inflation, as determined by the region of interest contour mode.

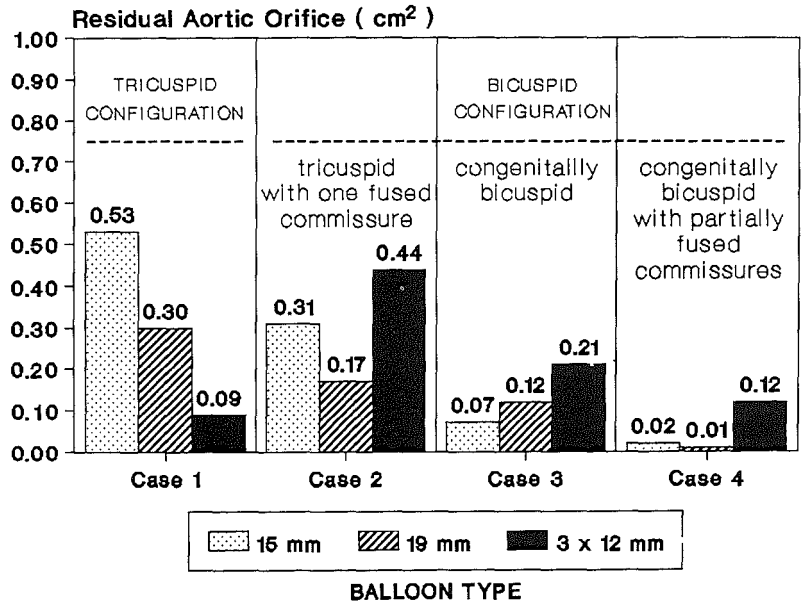

Figure 2: Computed tomographic evaluation of the residual aortic orifice (cm^2) during inflation of 15 mm, 19 mm and 3 x 12 mm balloons in the four post-mortem specimens, as determined by the region of interest contour mode. In cases where a bicuspid configuration was present (cases 2, 3 and 4), the trefoil 3 x 12 mm balloon allowed more free space between balloon and leaflets, while the monofoil 15 mm and 19 mm balloons were both more occlusive, despite their smaller cross-sectional surfaces. Conversely, when the valve had a tricuspid configuration (case 1: tricuspid valve without fused commissure), the trefoil balloon was much more occlusive (residual aortic orifice: 0.09 cm^2) than monofoil 15 mm and 19 mm balloons (residual aortic orifice: 0.53 and 0.30 cm^2, respectively).

During inflation of the 15 mm balloon, a residual free space between the balloon and the aortic cusps of at least 0.30 cm^2 was observed in cases 1 and 2. However, in presence of a congenitally bicuspid valve (cases 3 and 4), balloon inflation resulted in an almost complete obstruction of the aortic orifice (0.07 and 0.02 cm^2, respectively). No gross fracture of nodular calcifications nor commissural or raphe splitting were observed in any specimen. A moderate increase in AVA occurred only in case 2, while minimal or no changes were achieved in the remaining cases (Table 2). It should be noted that in none of the specimens did the inflated 15 mm balloon occupy a central

position in the aortic orifice. The stretching induced by the balloon was more important on the less calcified, more flexible valve leaflets.

Concerning the 19 mm balloon, a significant increment in AVA was achieved in all the specimens. Although the balloon still occupied an asymmetrical position in the aortic orifice, larger displacement of the free edges of the cusps were observed, involving the most heavily calcified leaflets. Except in case 1, which was a tricuspid valve without commissural fusion, this balloon was almost occlusive in the remaining cases. The better residual free space observed in case 1 (0.30 cm^2) can be explained by a wider opening of the leaflets, which in turn created an increment in intercommissural spaces. Fracture of nodular calcifications were noted in cases 1 and 2 at visual inspection. Partial commissural separation or central raphe splitting occurred in cases 2, 3 and 4.

Conversely, despite the larger transverse diameter and cross-sectional area of the inflated 3 x 12 mm trefoil-shaped balloon, the residual orifice during inflation was paradoxically greater than with previous dilatations in all cases except in case 1, due presumably to the peripheral and central spaces generated by the trefoil configuration. This advantage of the trefoil shape was already known, but we remarked that it was mostly evident when a "bicuspid" configuration could be observed (case 2: tricuspid valve with one fused commissure; cases 3 and 4: congenitally bicuspid valves). However, in presence of a tricuspid morphology (case 1), the opposite effect was observed. This may be explained by the rigidity of the leaflets related to the degenerative process, which have oriented passively the individual parts of the inflating trefoil balloon to engage each of the three intercommissural spaces.

CLINICOPATHOLOGICAL OBSERVATIONS

In order to compare the results of experimental valvuloplasty to the clinical situation, we analysed retrospectively aortic pressure curves recorded during dilatation at the time of PBAV in patients who underwent subsequently a valve replacement and we have correlated these hemodynamic data with the anatomopathological evaluation of the surgically excised aortic valves.

Methods

From March 1986 to October 1988, thirty-five elderly patients underwent PBAV in our institution. The technique of the valvuloplasty procedure itself in our institution has been described earlier by our group (10). Ten of these patients underwent subsequently an aortic valve replacement (7 for restenosis, 2 for a failed procedure and one patient for severe aortic regurgitation). In four of these surgical patients, a stepwise dilatation with 15 mm, 19 mm and trefoil 3 x 12 mm balloons had been performed, in the same sequence as during our in vitro experiments described above. Two of these patients underwent surgery for failed PBAV, since increments in AVA achieved by valvuloplasty were only minimal, without significant symptomatic improvements. The two other patients underwent valve replacement for recurrence of stenosis, defined as a clinical recurrence of symptoms with either a return of maximal aortic valve flow velocity to pre-valvuloplasty values on echo Doppler flow measurements, or an invasively measured AVA which was less than 25% larger than before PBAV.

The hemodynamic repercussion of aortic orifice obstruction generated by balloon inflation was assessed by the systolic aortic pressure, continuously recorded throughout the procedure by a 7 F pigtail catheter positioned in the descending aorta. Systolic aortic pressure values were obtained by reviewing the aortic pressure tracings recorded on paper during the PBAV procedures. The pressure curves recorded during dilatation were analyzed and the lowest systolic aortic pressure values (nadir) were selected. Since the pressure scale on the recording paper grid was 4 mm Hg / mm, the lowest systolic aortic pressure value was arbitrarily rounded to 5 mm Hg (for example: 12 mm = 48 mm Hg; rounded to 50 mm Hg). In cases where more than one inflation was performed with the same balloon, the pressure curve showing the lowest systolic aortic pressure value was selected. Figure 3 gives an example of the aortic pressure curves recorded during a valvuloplasty procedure.

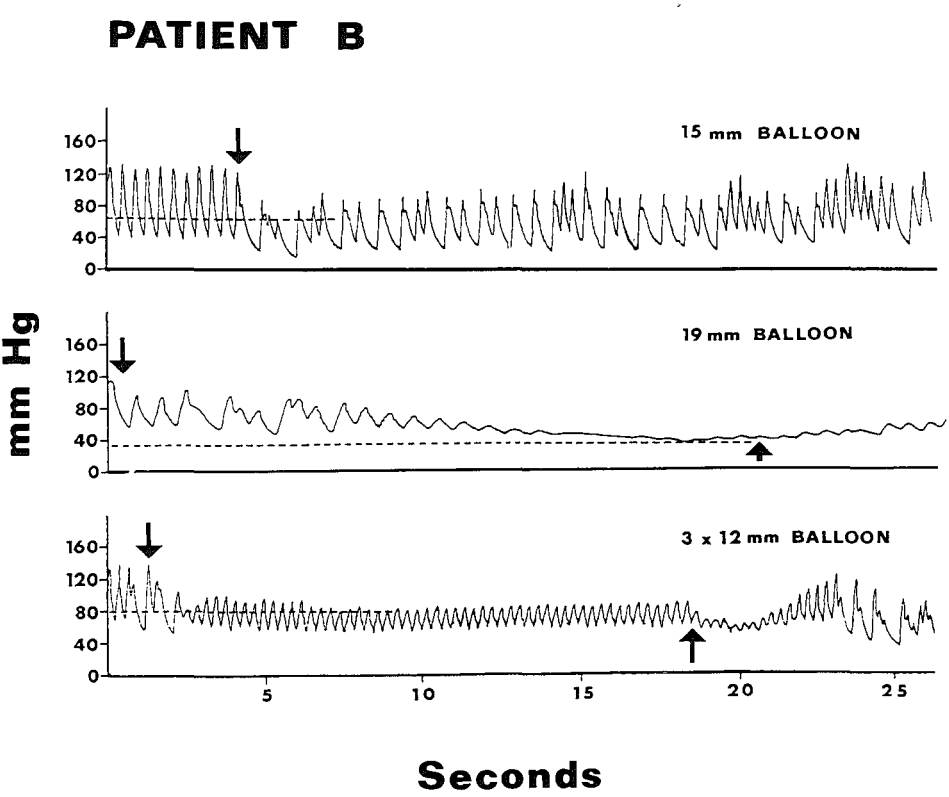

Figure 3: Patient B: Aortic pressure curves recorded at the time of percutaneous aortic valvuloplasty during dilatation with 15 mm, 19 mm and 3 x 12 mm balloon catheters. In this patient, anatomopathological evaluation revealed a congenitally bicuspid calcified aortic valve. Balloon inflation is represented by downward arrows (↓) and deflation by upward arrows (↑). The dotted lines show the point on the curves where the lowest systolic aortic pressure values were selected. During dilatation with the 15 mm balloon (upper tracing), blood pressure dropped rapidly to 60 mm Hg, but an increase to 80 mm Hg was noted shortly after. However, the inflated monofoil 19 mm balloon (center tracing) was very occlusive, resulting in a marked fall in blood pressure (30 mm Hg) and disappearance of the systolo-diastolic waves. The balloon was rapidly deflated after 20 seconds and blood pressure returned almost immediatly to 120 mm Hg (not shown). No loss of consciousness occurred. During inflation of the 3 x 12 mm balloon (lower tracing), the lowest systolic pressure was 80 mm Hg and was well tolerated, even if that balloon had the largest inflated cross-sectional area. A transient decrease in blood pressure occurred at the time of deflation. This phenomenon is relatively common during deflation, although not completely understood.

Results and comments

Table 3 summarizes clinical data, pathological findings related to the excised valves and hemodynamic data of the PBAV procedures.

			Patient A	Patient B	Patient C	Patient D
CLINICAL	Age (years)		65	73	64	74
	Interval* (months)		1	9	9	9
	Reason for Surgery		F	F	R	R
PATHOLOGY	Valve Anatomy		T	B	B	T
	Commissural Fusion		--	--	--	+ **
	Calcifications		3+	3+	2+	3+
	Tearing of Leaflets		--	--	--	--
VALVULOPLASTY	Gradient (mean)	PRE	48	80	68	74
		POST	41	58	41	47
	A.V.A. (cm^2)	PRE	0.5	0.3	0.4	0.5
		POST	0.6	0.4	0.6	0.7

B = bicuspid;F = failed valvuloplasty; R = restenosis; T = tricuspid; A.V.A. = aortic valve area, calculated with the Gorlin's formula; PRE = before valvuloplasty;POST = after valvuloplasty

* Time elapsed between aortic valvuloplasty and valve replacement
** PBAV did not result in commissural separation in patient D

Table 3 clinical data, pathological findings related to the excised valves and hemodynamic data obtained before and after PBAV, in patients who underwent valve replacement after PBAV.

Figure 4 illustrates the lowest systolic aortic pressure recorded in the four patients, when the different balloons were fully inflated.

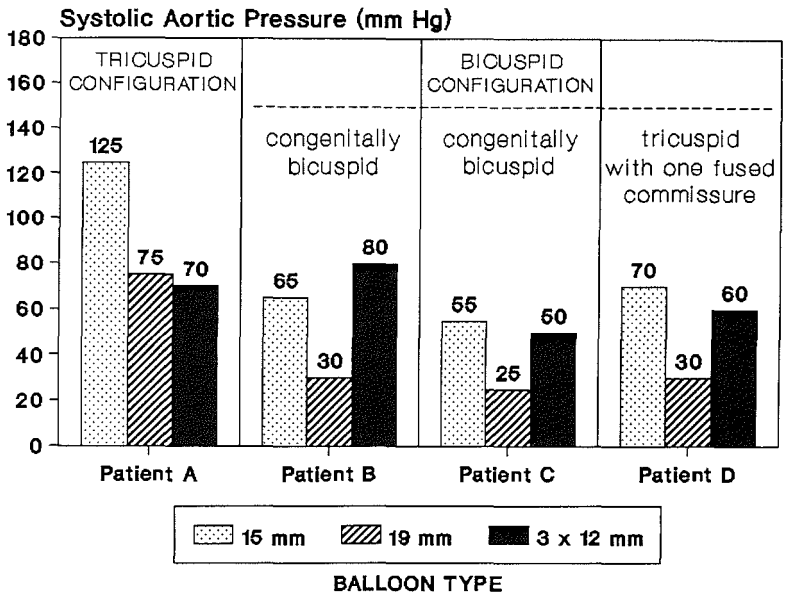

Figure 4: Lowest systolic aortic pressure values recorded during inflation of monofoil 15 mm, 19 mm and trefoil 3 x 12 mm balloons in four patients who underwent elective percutaneous aortic valvuloplasty 1 to 10 months before valve replacement. In cases where more than one inflation was performed with the same balloon catheter, the curve showing the lowest systolic pressure value was selected. In patients in whom a bicuspid configuration was present (B and C: congenitally bicuspid valves; D: tricuspid valve with one commissural fusion not separated by balloon valvuloplasty), the 19 mm balloon generated a more dramatic fall in blood pressure and was less tolerated than the larger trefoil 3 x 12 mm balloon (30 vs 80 mm Hg, 25 vs 50 mm Hg, and 30 vs 60 mm Hg, respectively). Conversely, in patient A (tricuspid valve without commissural fusion), the trefoil balloon offered no advantage compared to the 19 mm balloon, as reflected by the slightly lower blood pressure observed during the 3 x 12 mm balloon inflation.

The mean age was 69.0 years (range: 64-74 years) and the mean time interval between PBAV and valve replacement was 7.0 months (range: 1-9 months). Despite the limited number of patients available, we noted that in patients in whom a bicuspid valve configuration was present (patients B and C: congenitally bicuspid valves; patient D: tricuspid valve with one fused commissure in which PBAV did not result in commissural separation), dilatation with the single circular 19 mm balloon was less well

tolerated than with the larger 3 x 12 mm trefoil balloon, as revealed by the systolic aortic pressure during inflation (Figure 4). These observations correlated well with our experimental findings, which have shown that inflated trefoil-shaped 3 x 12 mm balloons allowed more residual free space in presence of a bicuspid configuration.

Conversely, pathological examination of the aortic valve in patient A revealed a calcified tricuspid valve without commissural fusion (i.e. tricuspid configuration), in accordance with a degenerative etiology. In this case, dilatation with the 3 x 12 mm balloon did not appear to offer any advantage, being as occlusive as the 19 mm circular balloon (Figure 4). These findings do not confirm but suggest strongly that intercommissural spaces may have been obstructed by each of the three individual parts of the trefoil balloon, as observed in our in vitro experiments.

DISCUSSION

In contrast with other valvular heart diseases in which balloon valvuloplasty has been applied, acquired AS in the elderly is characterized by a broad spectrum of valvular morphology. We have assessed qualitatively and quantitatively the effects of dilatation with different balloons in aortic valves of various morphology (bicuspid, tricuspid, fused and non-fused commissures) and etiology (degenerative, congenital and rheumatic), but the extrapolation of our experimental results to other cases with different anatomy should be made with caution.

The increments in AVA achieved after experimental valvuloplasty were much greater than those reported in clinical trials. It seems unlikely that this discrepancy was related to the effects of formalin fixation. In fact, formalin preservation alters valvular fibrous proteins and leads to stiffening of the valve leaflets and reduction of the elastic properties of the aortic cusps, resulting in increased rigidity of the aortic valve leaflets. Thus, it seems conceivable that smaller increments in AVA would have been obtained after formalin fixation. However, it should be noted that previous reports (26) compared the effects of balloon dilatation on 27 calcific, stenotic aortic valves dilated after variable periods of fixation in formalin and on 12 non-preserved valves dilated either at post-mortem examination or in the operating room and observed no apparent difference in results. In our experimental study, the greater increments in AVA, compared to those

achieved in the clinical situation, are rather explained by: 1) easy and optimal positioning of the balloon in a non-beating heart, 2) the possibility to perform prolonged inflation time without creating adverse effects such as hypotension and 3) direct measurement of AVA by cylindrical calipers, which differs greatly from the Gorlin's formula used in live patients.

Our experimental observations have demonstrated that use of balloons with diameter smaller than 19 mm resulted generally in minimal or no increment in aortic valve area. The radial forces of the inflating 15 mm balloon were initially applied on the less calcified and more flexible leaflets and the space occupied by the fully inflated balloon was not sufficient to displace substantially the free edges of the more rigid leaflets. This was depicted by the asymmetrical position of the inflated 15 mm balloon observed in all the experimental cases. Clinical experience has also shown that better hemodynamic improvements can usually be achieved with balloons of larger diameter (29). Some authors advocate the use of oversized balloons (i.e. larger than the aortic ring) to obtain better hemodynamic results (30) but some controversies still exist, based mainly on the fear of producing catastrophic complications such as tearing of aortic leaflets or aortic wall dissection, resulting in major aortic regurgitation, cardiac tamponnade or fatal aortic rupture (31,32). Furthermore, acquired aortic stenosis is frequently associated with extensive calcific vegetations, protruding into the valve sinuses. During balloon inflation, this calcium bulk may prevent the complete apposition of the aortic leaflets against the aortic wall. If oversized balloons are used in this situation, the trapped calcific vegetations can further increase the mechanical stress generated by the inflating balloon on the aortic wall, which may lead to disastrous consequences. Extensive calcifications may also provide additional explanations on the limited hemodynamic improvements achieved by PBAV in a non negligeable proportion of patients (19). For instance, the lowest obtained AVA in our experimental study occurred in the most heavily calcified valve (case 1), reflected by the largest volume and the highest density on computed tomographic scanning (Table 1). In our clinical observations, the failed PBAV procedures occurred in patients A and B, in whom aortic valves were also heavily calcified.

Trefoil balloons have been developed in attempt to avoid complete interruption of blood flow during inflation and to reduce the frequency of marked hypotension during valvuloplasty procedures. This advantage has been observed during inflation across the aortic valve in dogs, in pulmonary valvuloplasty in adults, aortic valvuloplasty in children and young adults, and in mitral and aortic valvuloplasty in adults (20-24). Our experimental and clinical observations suggest that trefoil balloons allow a larger residual orifice and can provide a better blood flow during inflation in presence of a bicuspid configuration, despite its superior inflated cross-sectional area (3.4 cm^2) compared to the circular 19 mm balloon (area: 2.8 cm^2); on the contrary, the trefoil-shaped balloon does not appear to offer the same advantages in presence of a tricuspid aortic configuration. In order to compare the trefoil 3 x 12 mm balloon with a single circular balloon of equivalent diameter, experimental valvuloplasty using a monofoil 25 mm balloon would have been interesting, but this size was not commercially available at the time of our in vitro experiments. Nevertheless, it seems conceivable that the obtained results would have been similar in cases where a bicuspid configuration was present, since the 19 mm balloon was already almost completely occlusive.

Balloon catheters with a bifoil design have also been introduced recently. As mentioned previously, bifoil balloons were not assessed in our study, since they were not commercially available in our institution at the time of our in vitro experiments and they have not been used during valvuloplasty procedures in patients from whom our clinicopathological observations were derived. In a recent report of Voudris et al. (33), it has been stated that bifoil balloons offered better hemodynamic results and a better tolerance during inflation than monofoil and trefoil balloon catheters. The balloon catheters assessed in that study were monofoil 19 mm (inflated area: 2.8 cm^2), bifoil 2 x 15 mm (area: 3.5 cm^2) and trefoil 3 x 10 mm (area: 2.4 cm^2). The better hemodynamic results achieved may be related simply to the greater inflated area of the bifoil balloon used in that study. They also reported a higher rate of marked hypotension in the group of patients in which a 3 x 10 mm trefoil balloon was used. However, this subgroup had the more depressed left ventricular function before PBAV; thus, the relatively poorer tolerance of inflation observed might not be entirely related to the trefoil design. Furthermore, since the valvular configuration was not known, it

may be speculated that some of these patients had indeed aortic valves with tricuspid configuration and according to our observations, use of trefoil balloons in this situation can lead to an almost complete interruption of aortic flow and severe hypotension. Further experimental studies with monofoil, bifoil and trefoil balloon catheters of equivalent inflated cross-sectional areas, assessed in different valvular configurations, would certainly be very useful for improving our knowledge of the balloon - leaflets relationship in PBAV.

CONCLUSION

Our experimental and clinicopathological observations have shown that the degree of aortic orifice obstruction during inflation of a monofoil or a trefoil balloon is dependent on the underlying valvular morphology. In our opinion, these observations are relevant, since degenerative disease of the aortic valve is now recognized as the most common etiology of aortic stenosis in the elderly, based on the knowledge of the changing natural history of aortic stenosis observed since a few decades (34). Some authors have also reported that heavily calcified congenitally bicuspid aortic valves were at higher risk for complications from PBAV, such as irreversible hypotension (35). These findings demand that, in clinical practice, a careful assessment of the valvular anatomy should be attempted in patients in whom PBAV is planned, in order to individualize the choice of the valvuloplasty material and to optimize the tolerance of the procedure. Unfortunately, accurate characterization of the valvular morphology of stenotic aortic valves in elderly patients can be often misleading, due to the remodeling of the valve architecture by the degenerative process and calcium deposition. Until now, conventional techniques such as contrast angiography and precordial echocardiography have not been proved to be reliable for assessing accurately the valvular morphology of acquired AS. Transoesophageal (36) or intravascular echocardiography (37) can be valuable techniques to provide useful images of valvular anatomy and represent promising solutions to this diagnostic problem, especially in obese or emphysematous patients. Fiberoptic angioscopy can also provide diagnostic informations on aortic valvular morphology (35), but probably with a lesser degree of accuracy and applicability, compared to transoesophageal and intravascular ultrasound imaging.

However, all these techniques have the major disadvantage to be relatively invasive. But recently, ultrafast computed tomography has been used in the diagnosis of aortic valve stenosis and assessment of its severity in a small number of patients (38,39). Good correlations with catheterization-derived AVA have been obtained and in some patients, heavily calcified bicuspid and tricuspid aortic valves were clearly identified. Even if the overall accuracy is not yet defined, this noninvasive technique seems very promising as a diagnostic adjunct to improve the safety of PBAV.

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CHAPTER 7
ASSESSMENT OF THE "LONG SHEATH" TECHNIQUE FOR PERCUTANEOUS AORTIC BALLOON VALVULOPLASTY

(This chapter has been published in Cathet and Cardiovasc Diagn 1990; 19: 129. Authors are: Plante S, Beatt KJ, van den Brand M, di Mario C, Meier B, Serruys PW)

SUMMARY

A 100 cm long 16.5 F valvuloplasty catheter introducer was assessed as an adjunct for percutaneous transluminal aortic valvuloplasty (PBAV) via the femoral artery in 31 patients with severe aortic stenosis. Observed improvements in peak systolic gradient (81.6 ± 29.9 mm Hg vs 35.5 ± 16.0 mm Hg, $p < 0.000001$) and aortic valve area (0.6 ± 0.4 cm^2 vs 1.0 ± 0.6 cm^2, $p < 0.00001$) were similar to those achieved in a control group (C) of 17 patients in which no femoral sheath was used. However, a shorter procedure duration (211 ± 81 min. vs 117 ± 30 min., $p < 0.001$) and a reduced rate of vascular complications at the femoral puncture site (41% vs 6.5%) were observed in patients in whom the long sheath (LS) technique was used. The frequency of other PBAV-related complications was comparable (C = 35%, LS = 29%, p = n.s.).

Other technical advantages of this device are: 1) prevention of looping and bending of the balloon catheter in tortuous vessels and easy positioning of the balloon across the aortic orifice provided by the LS trackability, 2) stabilisation of the balloon during inflation, 3) monitoring of supravalvular aortic pressure provided by the side-arm of the LS and reliable measurement of systolic gradient and 4) the ability to perform aortograms without the need of another catheter in the ascending aorta. Thus, in our experience, the long sheath technique is a valuable adjunct for PBAV.

INTRODUCTION

Percutaneous transluminal aortic balloon valvuloplasty (PBAV) is currently regarded as a palliative treatment for elderly patients with critical aortic stenosis (AS) not suitable for open-heart surgery (1,2). Although the limited immediate hemodynamic improvement, inherent procedure-related complications and possible development of late valve restenosis have decreased the initial enthusiasm for this alternative technique

(3-6), PBAV remains the only therapeutical tool available for severely symptomatic patients with unacceptably high or prohibitive surgical risk. These current limitations of PBAV demand simplification of the technique, in order to decrease the duration of the procedure and the rate of vascular complications, and to facilitate passage of balloon catheters through tortuous vessels and across severely narrowed aortic orifices. The device described here has been developed in an attempt to achieve these objectives.

Long sheaths are currently used in catheterization laboratories for trans-septal catheterization and myocardial biopsy by the femoral vein. Recently, they have been used to help the performance of PBAV (7). In a previous report (8), we have presented results of PBAV performed in 12 patients with severe AS, using this 100 cm long introducer especially designed for retrograde PBAV via the femoral artery. In this article, we report the results of PBAV procedures performed with this device in 31 patients and we compare the observed results and complications with our previous experience with the conventional percutaneous femoral artery approach.

METHODS

Introducer design

The introducer consists of a polyurethane inner dilator and a 100 cm long Teflon sheath (Schneider AG) with a 15 F internal lumen and a 16.5 F external diameter, connected to a proximal valve system to prevent retrograde bleeding. This proximal adjustable adaptor is formed by a self-sealing diabolo-shaped silicon valve and a proximal screw-seal. A side-arm, connected to the transparent chamber in which the silicon valve is located, allows intermittent flushing of both the silicon valve and the internal lumen of the sheath and enables the recording of the hydraulically transmitted pressure from the distal tip of the sheath.

Patients

From March 1986 to April 87, 17 patients (47% male; mean age $\pm$ SD: 73.2 $\pm$ 6.8 years) underwent PBAV in our institution, using a conventional technique of direct percutaneous introduction of the valvuloplasty balloon catheters through the femoral

artery, as previously described (2). These patients, in whom no femoral sheaths were used, served as our control group.

Thereafter, PBAV was performed with the use of the long sheath technique in 31 patients (42% male; mean age ± SD: 66.5 ± 22.5 years) from two catheterization centers. The AS etiology was presumed degenerative in twenty-four patients (77%) and congenital (bicuspid) in the remaining cases. Informed consent was obtained before each procedure.

Technique

In the 17 patients who served as our control group, a conventional approach was used, consisting of direct introduction and removal of various balloon catheters through the femoral artery. In the long sheath group, the valvuloplasty introducer was inserted through the femoral artery, following adequate positioning of a 0.035 inch, 300 cm exchange guidewire across the aortic valve orifice. The guidewire is designed with a stiff proximal part to facilitate the insertion of the introducer and to provide a better trackability when attempting to cross the aortic orifice with the balloon catheter. The distal tip of the guidewire (7-12 cm) is soft and flexible to prevent ventricular wall trauma. The gradual tapering of the tip of the inner dilator combined with the support provided by the stiff guidewire allowed easy introduction into the femoral artery. Progression up the ascending aorta and positioning of the distal end of the sheath just above the aortic valve is also facilitated, despite the frequently tortuous iliac and femoral vessels commonly seen in elderly patients. After removal of the inner dilator, multiple balloon catheters were easily positioned across the aortic valve orifice, over the exchange guidewire with its tip in the left ventricular cavity. The side-arm was used for pressure monitoring, performance of aortograms and for irrigation and intermittent flushing with heparinized solution; this was mandatory since blood clots can form rapidly in the large dead space of the sheath (Figure 1). At the end of the procedure, after reversal of the residual effect of heparin, the sheath was removed and hemostasis achieved by careful inguinal compression.

In the control group, the largest balloon catheter used was 15 to 20 mm in 8 patients, trefoil 3 x 9 mm in one patient and 3 x 12 mm in the remaining cases. In the long sheath group, the largest balloon catheter used was 23 to 25 mm in two cases, trefoil 3 x 8 in one, 3 x 9 mm in four and 3 x 12 mm in 19 patients. In two cases, the

bifoil 2 x 19 mm balloon was the largest balloon used.

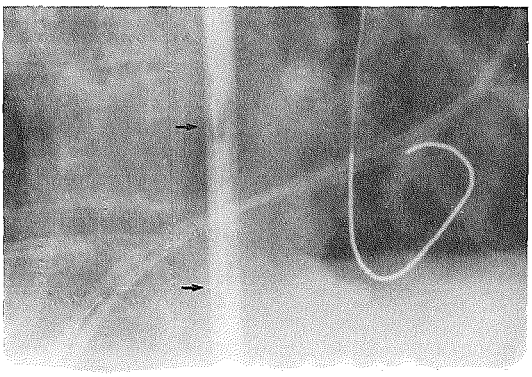

Figure 1: Blood clots in the lumen of the long sheath. After two balloon dilatations, the contrast injector was connected to the side-arm of the long sheath, for the performance of an aortogram. During pre-filling by contrast medium, large clots were observed in the lumen of the long sheath (arrows). The screw-seal was removed, allowing spontaneous expulsion of the thrombi. After, the sheath was irrigated with heparinized solution and a supplementary dose of I.V. heparin was given. The procedure was continued without complications.

Statistical analysis

Means and standard deviations were calculated for each group of data. Unpaired and paired Student's t test, Chi square test and Fisher's exact test were used whenever appropriate.

RESULTS

Table 1 shows the hemodynamic variables measured immediatly before the procedure and after the last balloon dilatation in the two groups. The procedure duration is also tabulated. The two groups were comparable for age, sex, peak systolic gradient and aortic valve area before and after the procedure. Significant improvements in peak systolic gradient and aortic valve area were achieved in both groups. However, the mean procedure duration was much shorter in the long sheath group (117 ± 30 min. vs 211 ± 81 min., $p < 0.001$), as reliably assessed in 14 patients (82%) of the control group and in 23 patients (74%) of the long sheath group. This was calculated

as the time elapsed from femoral puncture to the last recorded intra-aortic pressure, just before removal of the sheath and catheters. This included the time required for complete diagnostic catheterization (control group: 5 cases; long sheath group: 4 cases) and transluminal coronary angioplasty (long sheath group: 2 cases) in the same session. To achieve hemostasis after removal of the long sheath, the mean inguinal compression time was 43 minutes (range 30-70 min., as assessed in the first 14 patients), which was comparable to the time usually required to achieve hemostasis after a conventional PBAV procedure.

	Control Group	Long Sheath Group	
No. Patients	17	31	
Age (years)	73.2 ± 6.8	66.5 ± 22.5	(p = n.s.)
Sex (% Male)	47 %	42 %	(p = n.s.)
Peak Systolic Gradient (mm Hg)			
Before	83.8 ± 28.8	81.6 ± 29.9	(p = n.s.)
After	39.6 ± 17.0	35.5 ± 16.0	(p = n.s.)
Aortic Valve Area (cm2) *			
Before	0.5 ± 0.1	0.6 ± 0.4	(p = n.s.)
After	0.7 ± 0.2	1.0 ± 0.6	(p = n.s.)
Duration of Procedure (min.) **	211 ± 81	117 ± 30	p <.001

* Assessed with the Gorlin's formula

** The procedure duration (minutes) was calculated as the time elapsed from femoral puncture to the last recorded intra-aortic pressure, just before removal of the sheath and catheters. For some patients (see text), this included the time required for complete diagnostic catheterisation or transluminal coronary angioplasty in the same session.

Table 1 Age, sex, hemodynamic data and procedure duration

In the control group, unsuccessful introduction of a 3 x l2 mm trefoil-shaped balloon catheter into the femoral artery or across the aortic valve occurred in 3 patients (17.6%), mainly due to tortuous vessels and lack of pushability. Such unsuccessful attempts were not encountered in any patient of the long sheath group; in only one

case, we experienced a relatively difficult retrieval of a 2 x 19 mm bifoil-shaped balloon after rupture. The use of the long sheath technique in patients with tortuous vessels has facilitated the manipulation of the catheters and the exchange procedures, by preventing looping and bending of the balloon catheters. A good example of facilitated positioning of the balloon catheter across the aortic valve provided by the long sheath is shown in Figure 2.

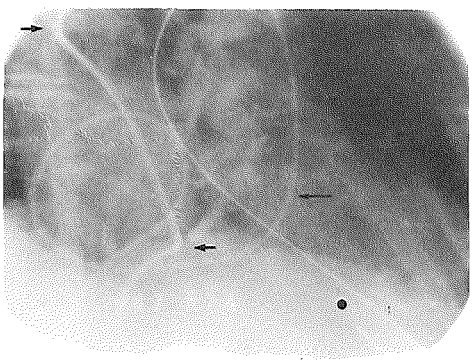

Figure 2a

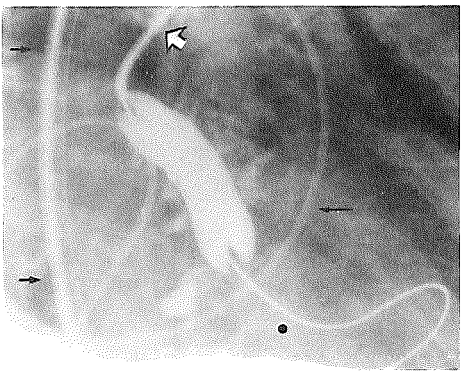

Figure 2b

Figure 2: Fig.A: This 80 year-old female patient with severe aortic stenosis (aortic valve area: 0.4 cm^2; peak systolic gradient: 66 mm Hg) was scheduled for an elective PBAV. After introduction of a 23 cm 16.5 F sheath into the right femoral artery, a 0.035 inch exchange guidewire was positioned in the left ventricle. However, multiple attempts at crossing the stenotic valve with a 3 x 8 mm trefoil balloon catheter were unsuccessful, due to bending of the catheter in the descending aorta. The procedure was aborted, but the short sheath was left in place and irrigated with a heparinized solution. We urgently ordered a long sheath, which was provided by the manufacturer within 24 hours. (Thick arrows: bendings of the shaft of the 3 x 8 mm trefoil balloon catheter in the descending aorta; thin arrow: Swan-Ganz catheter; black dot: exchange guidewire in the left ventricle.)

Fig.B: The following day, a second PBAV was attempted. After positioning of the guidewire into the left ventricle, the short sheath was removed and replaced by a 100 cm long sheath. The aortic orifice was easily crossed and consecutive dilatations with trefoil-shaped 3 x 8 mm and 3 x 12 mm balloon catheters were performed, without bending of the balloon catheters. The procedure was uncomplicated and satisfactory (aortic valve area: 0.7 cm^2; peak systolic gradient: 47 mm Hg). (Thick arrows: shaft of the 3 x 8 mm trefoil balloon catheter inside the long sheath; open arrows: distal tip of the long sheath above the inflated balloon; thin arrow: Swan-Ganz catheter; black dot: exchange guidewire in left ventricular cavity.)

The procedure-related complications observed in the two groups are summarized in Table 2.

VASCULAR COMPLICATIONS AT PUNCTURE SITE			
CONTROL GROUP		LONG SHEATH GROUP	
Femoral pseudoaneurysm	(2)	Surgical repair of damaged femoral artery	(1)
Surgical removal of balloon remnant	(1)	Femoral intimal dissection with mural thrombosis	(1) *
Groin hematoma	(4) **		
Total	7 (41 %)	Total	2 (6.5 %) $p < 0.05$
OTHER PBAV-RELATED COMPLICATIONS			
CONTROL GROUP		LONG SHEATH GROUP	
Left hemiplegia	(1)	Procedure-related death	(2) *
Left hemianopia	(2)	Pericardial tamponnade	(1)
Grade 3 Aortic insufficiency	(1)	Third degree AV block	(1)
Ventricular fibrillation	(2)	Grade 3 Aortic insufficiency	(1) *
		Stroke	(1)
		Acute pulmonary edema	(1)
		Embolic myocardial infarction	(1)
		Ventricular tachycardia	(1)
Total	6 (35 %)	Total	9 (29 %) p = n.s.

* These complications occurred in the same patient (see text for details).

** Large groin hematomas requiring multiple blood transfusions in two patients.

Table 2 Procedure - related complications

Seven patients (41%) of the control group developed vascular complications at the femoral puncture site: three required surgical intervention (2 for pseudoaneurysm

formation and one for removal of a balloon remnant after balloon rupture) and large groin hematomas developed in 4 patients, requiring multiple blood transfusions in two cases.

Vascular complications occurred only in 2 patients (6.5 %) of the long sheath group. A 22 year-old male patient needed surgical repair of the femoral artery for severe bleeding after unsuccessful attempts at introducing the long sheath over a conventional guidewire. The other vascular complication occurred in a 73 year-old female patient in functional class IV (N.Y.H.A.). The procedure was uncomplicated with a single circular 19 mm balloon (2 inflations) and a 23 mm balloon (3 inflations). In an attempt to achieve better hemodynamic results, the balloon catheter was exchanged for a 2 x 19 mm bifoil-shaped balloon. After the second inflation with the latter, an aortogram showed severe aortic regurgitation with evidence of contrast extravasation around the left main coronary artery. In the following hours, her clinical condition deteriorated and she died one day after the procedure in a state of irreversible cardiogenic shock. Before death, signs of right leg ischemia were noted, suggesting a procedure-related complication. Post-mortem examination showed congested lungs and liver, along with signs of hypoperfusion in both kidneys. Examination of the heart revealed a hypertrophied and dilated left ventricle, moderate atherosclerosis of the coronary arteries and a calcified tricuspid stenotic aortic valve showing severe iatrogenic aortic insufficiency. An aortic intimal dissection was found, originating at the junction of the right and left coronary cusps, with extension to the proximal part of the left coronary artery. Inspection of the right leg vasculature revealed a mural dissection with occlusive thrombosis originating at the level of the right femoral artery puncture site.

The rate of other PBAV-related complications (cardiac, neurological, etc.) was similar in the two groups (35% vs 29% for the long sheath group, p = n.s.). One intra-operative death (long sheath group) occurred in a 77 year-old patient, with coexistent severe stenosis of the left main coronary artery, an occluded right coronary artery and a left ventricular ejection fraction of 14%, who developed irreversible cardiogenic shock at the end of the first inflation. Post-mortem examination did not reveal any cardiac or vascular damage that could have been related to the procedure itself.

DISCUSSION

Cribier et al (1) reported that tortuosity of the iliac arteries or aorta impeded balloon exchanging procedures in 16 of 82 patients (19.5%) in whom the femoral route was used, preventing further dilatations with larger sized balloons, and possibly leading to suboptimal results. Drobinski et al. (4) also reported that a right axillary percutaneous arterial approach has to be used in 4 of 37 patients (11%) for the same reasons. We observed a similar rate of unsuccessful attempts in our control group (17.6%), but such difficulties were not encountered in the long sheath group.

It should be noted that, although many patients had tortuous iliac and femoral vessels, none of them had severe narrowings or subtotal occlusions, a condition which appears less amenable to the proposed technique. Nevertheless, the combined use of a stiff guidewire and a long sheath was able to straighten the vessels, allowing more easy passage of balloon catheters up to the ascending aorta. Stiffer guidewires were introduced almost simultaneously with the use of the long sheath and may have had an independent effect in facilitating negotiations of tortuous vessels and passages of balloon catheters across the aortic valve orifice.

The improvement in procedure duration observed in the long sheath group was mainly related to the facilitated balloon catheters manipulations and exchange procedures, especially in presence of tortuous vessels. However, other factors may have influenced these results. For instance, the long sheath technique has been introduced after the performance of 17 conventional PBAV procedures in our institution. Therefore, the operators's previous experience (the "learning curve" effect) may have influenced favorably and independently the duration of the PBAV procedures in the long sheath group. Another bias may also arise from the small number of patients in the study and the incomplete data collection, since it was not possible to reliably assess the procedure duration in all cases, for various reasons. Other groups have reported procedure duration of less than 2 hours with a standard approach (4,9), but the time interval used for the assessment of the procedure duration was not clearly defined. Nevertheless, we observed a dramatic reduction in the time required for performing PBAV with the long sheath technique in our institution. It should be emphasized that patients undergoing PBAV are often severely ill or in poor general condition and improvement in procedure duration with easier and quicker access to

the ascending aorta may be crucial in reducing the inherent complication rate.

Since the introduction of PBAV for calcific AS, the most frequently reported procedure-related complication has been related to local damage at the femoral puncture site, due to multiple insertions and removals of large balloon catheters and to the use of larger balloons required to achieve better hemodynamic results. The rate of vascular complications reported in the literature varies from 11.7% up to 32%, depending upon the severity of complications described (10-13). According to data obtained from the French Registry (more than 600 patients) (14), this rate was approximately 12%. In the present series, we observed a rate of 41% in patients treated with the standard approach, compared to only 6.5 % when the long sheath was used. A shorter sheath, of course, would suffice for reducing the rate of vascular complications at the femoral puncture site, since others have reported a reduction from 14.8 % to 4.9%, using a shorter 14 F femoral sheath (9).

The observation of such a low frequency of vascular complications with a 16.5 F arterial sheath may be unexpected, since the reported incidence of peripheral vascular damage related to the use of insertion sheaths of similar size for intraaortic counterpulsation balloons varies from 10% to 20% (15). However, this may be more related to the duration of use rather than the size of the catheter itself. On the other hand, the potential damage to the artery wall caused by multiple insertions and removals of balloon catheters frequently presenting irregular shapes and/or sharp edges after several inflations or after balloon rupture may be greater than that induced by the single insertion of a long sheath over its well-tapered inner dilator. Long sheaths with 14, 11.5 and 10 F diameter were also available at the time of our study. A 16.5 F sheath was selected in order to accommodate easily the shafts of the largest balloon catheters commercially available, to avoid difficult retrieval of deflated or ruptured balloons and to avoid damping of the aortic pressure tracing when deflated balloon catheters were pulled back in the lumen of the sheath. In some cases, a 14 F sheath might have been of sufficient size, but after having experienced a relatively difficult retrieval of a ruptured 2 x 19 mm bifoil balloon in one of our first patients, it was decided not to use sheaths smaller than 16.5 F.

Other advantages of the long sheath technique should be emphasized. First, the long sheath provides stability during inflation (Figure 3), allowing the use of shorter balloons and preventing the to-and-fro motion of the balloon across the aortic valve,

which is frequently observed during inflation and may be implicated as a factor of ventricular perforation.

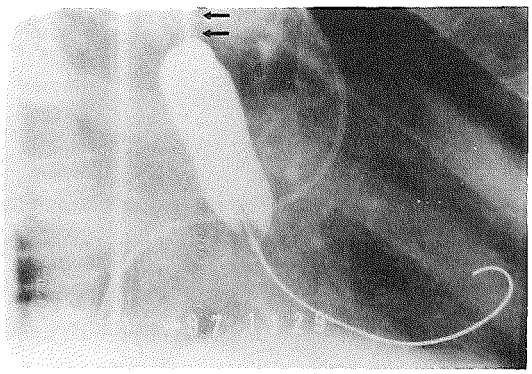

Figure 3: Trefoil-shaped 3 x 12 mm, 40 mm long balloon (Schneider AG) inflated across the stenotic aortic valve. The presence of the distal end of the sheath (arrows), just above the balloon, prevents possible to-and-fro motion during inflations.

Second, the side-arm located in the proximal part of the sheath enables recording of the hydraulically transmitted supravalvular aortic pressure, allowing reliable measurement of the aortic gradient. Even during balloon inflation, high quality pressure tracings were obtained. In a few cases, damped pressure curves were observed and obstruction of the distal tip of the sheath by the the inflated balloon was suspected. In those cases, immediate injection of contrast via the side-arm revealed that the distal end of the sheath was free and that the recorded aortic pressure, which correlated with patients's symptoms, was rather related to aortic orifice obstruction by the inflated balloon. Third, iatrogenic aortic valve regurgitation can be assessed easily, since good quality aortograms can be obtained by contrast injection either by the side-arm or via a pigtail catheter inserted through the long sheath. Finally, as with the use of shorter sheaths, the exchange procedures are performed without bleeding or the need of a second person to compress the punctured artery throughout the procedure.

A major disadvantage of the long sheath is the fact that its position in the ascending aorta provides a potential source for cerebral/peripheral air or clot embolism, although we observed more cerebrovascular complications in the control group (3 patients) than in the long sheath group (1 patient) (Table 2). In the latter, air embolism from the balloon itself was more likely, since the patient had a stroke almost immediatly after

balloon rupture. This patient was discharged a few days later, after partial recovery. In another patient however, a clot embolization in the left circumflex coronary artery, resulting in a non-fatal myocardial infarction, was probably related to the use of the long sheath. Meticulous purging and adequate heparinization are thus crucial.

CONCLUSION

In our experience, the long sheath technique provides easier and quicker access to the aortic orifice, especially in patients with tortuous vessels. It gives additional support for the passage of the balloon catheters and offers a better stability during balloon inflation. In our hands, the long sheath technique has been associated with a decrease in the number of unsuccessful attempts, a decrease in procedure duration and a reduction in the frequency of vascular complications at the femoral puncture site. However, since the two groups have been compared in a sequential way, a direct comparison with our previous experience may be misleading, as the improvements observed with the long sheath technique may be related in part to the "learning curve" effect.

With the commercially available balloons catheters, the long sheath technique is a valuable adjunct for the performance of PBAV, despite its large diameter. Technological improvements are needed for manufacturing balloon catheters with smaller shafts and with effective balloon cross-sectional area, in order to use femoral sheaths with a smaller diameter and eventually further decrease the rate of vascular complications related to the performance of PBAV.

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CHAPTER 8
AORTIC VALVE REPLACEMENT AFTER FAILED OR COMPLICATED BALLOON AORTIC VALVULOPLASTY, OR AFTER RESTENOSIS. IMMEDIATE RESULTS, FOLLOW-UP COURSE AND HISTOLOGIC FINDINGS

(Part of this chapter has been submitted for publication to the American Journal of Cardiology under the title: Histologic changes in the aortic valve after balloon aortic valvuloplasty: evidence for a delayed healing process. Authors are: van den Brand M, Essed CE, Plante S, Mochtar B, de Feyter P, Suryapranata S, Serruys PW).

SUMMARY

Out of a consecutive series of 39 elderly patients who underwent percutaneous balloon dilatation of a severely stenotic aortic valve, 4 died within 28 days. In four other patients a less than 25% increase in valve area was achieved. Two of them underwent surgery at 1 and 9 months after valvuloplasty, the third patient died 19 months after valvuloplasty, while the fourth patient is in validity class II without operation. One other patient had severe aortic incompetence due to tearing off of one aortic valve leaflet, and was operated on within one week. Of the remaining 30 patients, 13, showing signs of restenosis, after an initial increase in valve area of at least 25%, have also been operated on 3 to 36 months after valvuloplasty (mean 17 months). None of the 16 operated patients died, the in hospital postoperative course being mostly uncomplicated, with a mean hospital stay of 16.9 days (range 10-62 days). At a mean follow-up of 22.0 months after operation (range 3-39 months) none of the patients died. Macroscopic inspection of previously dilated aortic valves showed a tear off of the aortic wall of 7 mm in one case. In all other valves no macroscopic changes attributable to previous valve dilatation could be detected. Histology of the resected valves was available in 12 patients and was compared with histology of resected non-dilated aortic valves from 10 patients in a matching age group. Microscopically the dilated aortic valves showed small tears or lacerations of the collagenous valve stroma, fractures in the calcifications and splitting of commissures that were all filled up by young scar tissue. This scarification may play a role in the development of restenosis.

However, it seems that organization and collagenisation of the scar tissue takes longer to develop in these aortic valves as compared to other tissues. Young scar tissue without collagenisation was still seen 24 months after dilatation. It is suggested that due to this belated collagenisation of scar tissue, restenosis might develop more slowly than is expected.

INTRODUCTION

Balloon valvuloplasty of the aortic valve has been advocated by several authors as an alternative for aortic valve replacement in patients with high surgical risk, or as an intermediate procedure to improve left ventricular function, before aortic valve replacement (1-8). A recent Editorial by Block stated that one has to weigh the benefits of a single intervention with a higher risk (operation) against a palliative procedure with a high recurrence rate and cumulative risks (valvuloplasty) (9). Recurrence rates, both clinically defined and measured invasively or noninvasively are indeed high, varying from 24 to 67% (6-10). With this high restenosis rate, subsequent procedures are numerous. Two recently published series reported reinterventions in about a quarter of the patients, after a mean follow up of six months, while another quarter did not survive this follow-up period (6,8). As the vast majority of patients undergoing balloon valvuloplasty for aortic valve stenosis are poor surgical candidates, operative mortality and postoperative course should be documented in these patients, both after unsuccessful or complicated procedures, as well as after restenosis of the dilated valve.

The mechanisms and effects of aortic valve dilatation by inflated balloons depend on the underlying anatomy. "Calcific aortic stenosis" is applicable to all varieties of aortic stenosis in adults, but is usually reserved for the late calcification of bicuspid or tricuspid aortic valves (11). In these forms the principal mechanism of dilatation might be fracture of nodular calcifications, with an increased leaflet mobility. In the types of aortic stenosis where there is concomitant fusion of commissures, like in rheumatic valvular disease, separation of these commissures at dilatation might have a beneficial effect (12,13). Little is known about the effects of balloon dilatation at a microscopical level and possible change in microscopic anatomy with time (10,14,15). To obtain an insight into the frequency and magnitude of these potential changes and the alterations

these induced damages undergo in time after dilatation, 12 valves excised during valve replacement were histologically examined and compared with histology of resected non-dilated aortic valves of patients in a matching age-group.

PATIENTS AND METHODS

From March 1986 through December 1989, 39 elderly patients underwent percutaneous balloon dilatation of the aortic valve (PBAV). Sixteen of these later underwent aortic valve replacement. Characteristics of all patients undergoing aortic valve dilatation and of the group with subsequent aortic valve replacement are summarized in Table 1.

	BAV	AVR	non AVR
Number	39	16	19
Male/female	15/24	6/10	7/12
Mean age (years)	75.1	72.1	77.3
Range	58-88	63-85	58-88
Ejection fraction $\geq$0,55	22	10	12
0.40-0.54	6	2	4
0.20-0.39	5	1	2
$\leq$0.19	4	1	1
not assessed	2	2	0
Aortic valve area before dilatation (cm^2)	0.47 ± 0.14	0.51 ± 0.11	0.45 ± 0.15
Aortic valve area after dilatation (cm^2)	0.75 ± 0.19	0.75 ± 0.15	0.74 ± 0.21
Aortic valve area increase (%)	63.0 ± 38.0	52.0 ± 32.0	64.0 ± 33.0

Table 1 Characteristics of all patients undergoing balloon aortic valvuloplasty (BAV) and of patients with and without subsequent aortic valve replacement (AVR). Data are given as mean values ± standard deviation.

Valvuloplasty procedure

The technique of the valvuloplasty procedure itself in our institution has been described earlier (16). All procedures were performed using a percutaneous femoral approach. After recording of baseline values to calculate on line aortic valve area, by measuring mean transvalvular pressure gradient and aortic valve flow, balloons of increasing size were introduced to increase the aortic valve area by at least 50%. The maximal balloon diameter employed in the first 29 patients was a trefoil 3 x 12 mm balloon, while in the last 10 patients a bifoil 2 x 19 mm balloon was used in six (manufactured by Schneider-Shiley, Zürich). The bifoil balloons were employed after examination of the results obtained with these larger balloons in other institutes (17-19). In the first seventeen patients a balloon was positioned in the aortic valve area over a 260 cm long 0.038" diameter guide wire with a soft tip (Cordis Corporation, Miami). In the last 22 patients a 0.035" diameter, 300 cm long back up guide wire was used (Schneider-Shiley, Zürich). Over this wire a 100 cm long, 16.5 French diameter valvuloplasty balloon introducer (Schneider-Shiley, Zürich) was positioned immediately above the aortic valve. This introducer sheath facilitates the exchange of balloon catheters, restricts the balloon movement during inflation, enables a check for aortic incompetence by injecting contrast through it after dilatation, and reduces the trauma of multiple balloon insertions (20) (see also chapter 7). A successful procedure was arbitrarily defined as an increase in aortic valve area of at least 25%, without death or major complications necessitating urgent surgery. Restenosis was defined as a clinical recurrence of symptoms with either, on echo Doppler flow measurements, a return of maximal aortic valve flow velocity to pre valvuloplasty values, or an invasive measured aortic valve area which was less than 25% larger than before valvuloplasty. Hemodynamic data before and after valvuloplasty are summarized in Table 2.

	LVSP (mmHg)	LVEDP (mmHg)	MSG (mmHg)	SAVF (ml/sec)	AVA (cm2)	AVA increase(%)
Before (N = 39)	218 ± 37	16 ± 9	74 ± 19	176 ± 50	0.47 ± 0.14	
After (N = 34)	177 ± 34	12 ± 9	43 ± 10	214 ± 49	0.75 ± 0.19	63 ± 38

LVSP = left ventricular systolic pressure; LVEDP = left ventricular enddiastolic pressure; MSG= mean systolic aortic valve gradient; SAVF = systolic aortic valve flow; AVA = aortic valve area

Table 2 Hemodynamic data of 39 patients before and after balloon aortic valvuloplasty

In five patients no valve area could be calculated after the procedure: two patients died after the first balloon inflation, two patients had severe aortic regurgitation after valvuloplasty, which precluded aortic valve area calculation, while in a fifth patient data were not recorded due to neurological complications.

Mortality and procedural failure

Four patients died within 28 days after balloon valvuloplasty. Two patients in severe failure died during the procedure after the first balloon inflation. One other patient, also with severe failure, had a successful procedure but died one week later due to progressive failure. The fourth patient had signs of aortic base dissection after inflation of a bifoil 2 x 19 mm balloon, and died 24 hours after the procedure. One patient was operated on within one week after the procedure, because of severe aortic incompetence (Table 3, nr 7). Of the remaining 34 patients, 4 must be considered as failures, with an increase in valve area after dilatation of less than 25% (see chapter 4). Two of these patients have been operated upon (Table 3, nr 3,4). One was operated on within one month, the other one experienced some relief of symptoms and was operated on 10 months later. Of the other two with failed procedures, one died 19 months after the procedure, while the last patient is in validity class II, 6 months after valvuloplasty. Of the remaining 30 patients, 13 cases with clinical signs of restenosis, i.e. recurrence of symptoms such as angina and/or syncope and/or dyspnoea which were present before dilatation and had improved afterwards were acceptable for operation. Six of these 13 cases had been classified as inoperable before valvuloplasty, three for poor left ventricular function (Table 3, nr 5, 6, 13), one for possible dementia, one for unoperated carcinoma uteri and one for advanced age combined with intestinal angiodysplasia. Another six had been classified as increased risk candidates and one patient preferred valvuloplasty. They all exhibited an increase in Doppler measured aortic valve velocities at the time of recurrence of symptoms compared with post valvuloplasty measurements. Hemodynamic and clinical details of these 16 operated patients are given in table 3.

Nr	Age	Sex	EF	LVEDP (mmHG)		Maximal Balloon size	AVA (cm2)		% AVA Increase	Interval Valvuloplasty Operation	Concomitant Disease
			B	B	A	(mm)	B	A		(months)	
1	63	M	0.42	31	16	20	0.59	0.81	37	13	---
2	76	M	0.65	24	11	20	0.53	0.88	66	6	Coronary artery disease diabetes, nephrolithiasis
3	74	F	0.63	12	2	3 x 12	0.34	0.36	6	10	Rheumatoid arthritis, anemia
4	5	F	0.56	23	23	3 x 12	0.49	0.57	16	1	Mitral prosthesis, COPD
5	75	M	0.27	25	13	20	0.71	0.96	35	7	COPD
6	64	M	0.19	40	39	3 x 12	0.37	0.64	73	9	Usual interstitial pneumonitis
7	72	F	0.72	13	22	19	0.66	AI grade III		6 days	Rheumatoid arthritis, anemia
8	74	F	0.60	11	14	3 x 12	0.46	0.70	52	8	Hypertension, ulcus duodeni, polyposis recti
9	85	F	0.55	11	20	2 x 19	0.57	0.71	30	3	Coronary artery disease, intestinal angiodysplasia
10	73	M	0.64	28	n.a.	3 x 12	0.59	n.a.		13	Epilepsia tarda
11	64	F	0.63	15	2	20	0.33	0.80	142	36	Cholelithiasis, dysbasia, hypertension
12	75	M	0.60	13	8	20	0.57	0.95	67	24	Intestinal angiodysplasia and bleeding
13	75	F	n.a.	27	3	3 x 12	0.39	0.71	82	27	Congestive heart failure
14	72	F	n.a.	5	4	15	0.62	0.85	37	20	COPD, hypertension, coronary artery disease
15	71	F	0.43	8	4	23	0.41	0.71	73	6	Sjögren's disease, dementia?, coronary artery disease
16	77	F	0.60	12	17	3 x 12	0.53	0.78	47	13	Adenocarcinoma uteri

EF = ejection fraction of the left ventricle; LVEDP = left ventricular enddiastolic pressure; AVA = aortic valve area; B = before valvuloplasty; A = after valvuloplasty; COPD = chronic obstructive pulmonary disease; n.a. = not assessed;

Table 3 Clinical characteristics and outcome of balloon aortic valvuloplasty in 16 patients subsequently operated on

Surgical procedure

All patients operated on in our hospital (n = 14) were treated according to the same standard surgical protocol. Extracorporeal circulation was started combined with moderate (28°C) hypothermia and hemodilution. After aortic cross clamping cold crystalloid potassium cardioplegia was infused either in the aortic root or directly into the coronary ostia. Topical cooling was applied. Left ventricular venting was routinely instituted via the right upper pulmonary vein. After incision of the aortic root special attention was given to macroscopic inspection of the previously dilated valve, specifically looking for tearing of valve leaflets, fracture of calcific deposits and rupture of previously fused commissures. The underlying valve anatomy was established as mono-, bi- or tricuspid. The amount of calcification was scored as + to +++, indicating, minimal, moderate or extensive involvement. After inspection, the valve leaflets were excised and stored for microscopic examination in twelve cases. Optimal decalcification of the valve ring was performed. Eleven valves were replaced by St Jude Medical bileaflet valves ranging in size from 21 to 25 mm. (St Jude Medical Inc., Minnesota, USA). Three valves were replaced by Carpentier-Edwards bioprostheses size no 23. (Edwards Laboratories AG, Switzerland) in one case a Mitroflow bioprosthesis no 23 was implanted (Symbiom Inc, Arizona, USA), while in the last patient surgical débridement of the tricuspid aortic valve was performed. All devices were implanted with interrupted Ticron 2-0 sutures. In four cases concomitant coronary artery bypass grafting was carried out. Mean cardiopulmonary bypass time was 122 minutes (± 32, range 72-192) while mean aortic cross-clamping time was 90 minutes (± 24, range 48-135).

Histological technique

The fragmented resected valves from patients 2 through 12 and 15 (Table 3) were fixed in 10% formalin and decalcified in rapid bone decalcifier (RDO: Dupage Kinetic Laboratories Inc, Plainfield, USA). Subsequently a routine paraffin processing cycle was applied and 5μm sections were stained with hematoxylin and eosin and elastic-van Gieson stain.

RESULTS

Operation and postoperative course

As can be concluded from Table 3, one of these patients (nr 7) had aortic valve replacement after a complicated valvuloplasty procedure, resulting in severe aortic incompetence. Two other patients must be considered as failed procedures, with less than 25% aortic valve area increase, while the last 13 patients had restenosis.

Nr.	Valve anatomy	Commissural fusion	Calcifi-cations	Tearing of leaflets	Implanted valve	In hospital stay (days)	In hospital rehabilitation (weeks)
1	B	No	3 +	No	StJ 25	12	
2	B	No	3 +	No	StJ 23	11	4
3	B	No	3 +	No	StJ 21	14	2
4	T	No	3 +	No	StJ 21	12	
5	B	No	3 +	No	StJ 23	16	3
6	B	No	2 +	No	StJ 23	11	
7	B/T	Yes/No	2 +	Yes	StJ 19	21	
8	T	Yes	3 +	No	StJ 21	14	2
9	T	No	3 +	No	CE 23	11	3
10	B	No	3 +	No	CE 23	11	
11	T	No	3 +	No	StJ 21	13	
12	T	No	3 +	No	CE 23	10	
13	n.a	n.a	3 +	n.a	StJ 21	15	
14	T	No	3 +	No	surgical valvuloplasty	11	
15	T	No	3+	No	StJ 21	62	10
16	n.a	n.a	3+	n.a	M 23	26	

B = Bicuspid aortic valve; T = Tricuspid aortic valve; StJ = St Jude Medical valve prosthesis; CE = Carpentier Edwards biological valve prosthesis; M = Mitroflow biological valve prosthesis;

Table 4 Peroperative findings and early postoperative course after inadequate valvuloplasty and subsequent aortic valve replacement

Gross anatomical findings and in hospital course in these 16 operated patients are summarized in Table 4. Six patients had an, in origin bicuspid valve, seven a tricuspid

valve and in 1 patient bicuspidy or tricuspidy could not be established with certainty. Two patients were operated on in another hospital. In these cases macroscopy (and microscopy) was not available(nr 13 and 16). Macroscopic findings attributable to the previous valve dilatation could be demonstrated in one patient only. In this case (nr 7, Table 4), the original valvular anatomy could not be established with certainty. There were two cusps, the one posteriorly situated was thickened and heavily calcified. The other cusp, probably a fusion of the left and the right cusps, was remarkably unaffected by the degenerative process, but exhibited a tearing off of the aortic wall over 7 mm on the right side. It must be assumed that, through the rigidity of the posterior cusp, all radial balloon force had been exerted on the more pliable cusp, with subsequent tearing.

Fracturing of calcific deposits was not macroscopically noticed in any case.

The in hospital course of all patients was favorable. No patient died after the procedure, while the post-operative course was uncomplicated in eleven patients. In four patients the postoperative recovery was prolonged, once due to a sternal hematoma, once due to pneumonitis, once due to urinary tract infection, mental confusion and a Colles fracture, and in one patient due to intrathoracic bleeding necessitating rethoracotomy 5 days after the operation. One other patient had a rethoracotomy on the day of operation for intrathoracic bleeding, which did not prolong the recovery period. After discharge 6 patients were rehabilitated in a convalescent home for 2 to 10 weeks, mainly due to the social situation of these patients (older, unattached people).

At a mean follow-up of 22.0 months after operation (range 3-39) no patient has died. Eleven patients are in validity class I (NYHA), four are in class II, and one is in class III. Thirteen patients are taking anticoagulants, three digoxin and six diuretics. The other medication of these patients is mainly determined by coexistent disease, such as hypertension, rheumatoid arthritis and epilepsia.

Microscopy

The control group consisted of 4 female and 6 male patients. They underwent aortic valve replacement for critical aortic stenosis. Microscopically the valves basically presented the picture that is seen in calcific aortic stenosis (21). They showed marked fibrosis, with nodular calcifications in a hypocellular dense collagenous connective tissue stroma (Fig 1).

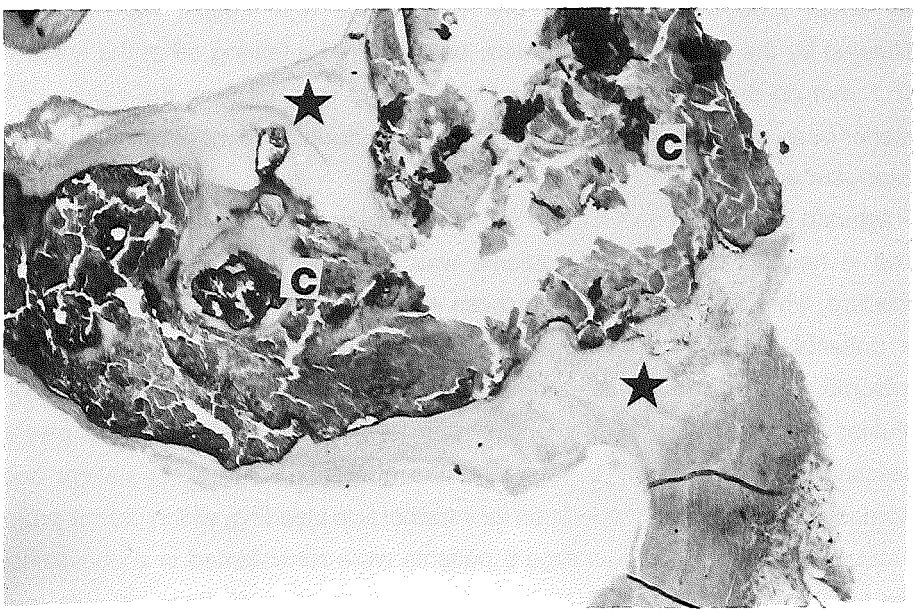

Figure 1: Histologic segment of non dilated aortic valve leaflet after excision, shows nodular calcifications (C), in a hypocellular collagenous tissue stroma (*).

Lymphocytes, plasmacells and capillaries could be present in the more loose connective tissue stroma surrounding the collagenous stroma. Where calcifications eroded the valve surface fibrin deposits were present between the protrusions. Small hemorrhages and iron laden macrophages were present subendothelially. The hemorrhages are considered to be an effect of manipulation during valve excision.
All resected dilated valves showed the basic histologic changes that were also seen in the control group (Table 5). In two patients degenerative bone formation was present in the calcifications. However, a few striking differences with the control group are noticed. In 11 of the 12 patients, young scar tissue, consisting of a rather cell-rich

Patient Nr.	Interval Months	Nature stenosis	"Pre-existent" pathology collagenary stroma	calcification	bone formation	superficial fibrin deposits	superficial hemorrhages
2	6	R	++	++	+	++	--
3	9	F	++	++	--	--	--
4	3 weeks	F	++	++	--	--	--
5	6	R	++	++	+	--	+
6	9	R	++	++	+	--	+
7	6 days	C	++	++	--	--	--
8	9	R	++	++	+	--	--
9	2	R	++	++	--	+	+
10	13	F/R?	++	++	--	--	--
11	36	R	++	++	--	--	+
12	24	R	++	++	--	+	+
15	6	R	++	++	--	--	--

Patient Nr.	Interval Months	Nature stenosis	pathology as result of valvuloplasty young scar in collagenous stroma	young scar in calcified nodule	calcium fragments in scar	Iron laden macrophages	hemorrhages deep in stroma	Interstitial fibrin
2	6	R	+	--	+	--	+	+
3	9	F	++	--	++ histiocytic infiltrate	--	--	--
4	3 weeks	F	--	--	++	--	+	+
5	6	R	++	--	++	+	--	--
6	9	R	++	++	+	--	+	--
7	6 days	C	+++	++	++	--	--	--
8	9	R	++ with sealed commissure	++	++	+	--	+
9	2	R	+	+	--	--	--	+
10	13	F/R?	+ superficial	+ superficial	+	--	--	--
11	36	R	--	--	--	--	--	--
12	24	R	++	++	+	--	--	--
15	6	R	++	+	+	--	--	--

R = Restenosis C = Complicated valvuloplasty F = Valvuloplasty Failure

Table 5 Histologic findings in 12 excised aortic valves operated on after PBAV

pattern of fibroblasts, capillaries and an inflammatory infiltrate composed of lymphocytes, plasmacells and histiocytes was present. This scar tissue seemed to fill up small tears or lacerations in the dense collagenous tissue stroma (11 patients) (Fig 2a) and it also filled up fractures in the calcified nodules (7 patients) (Fig 2b).

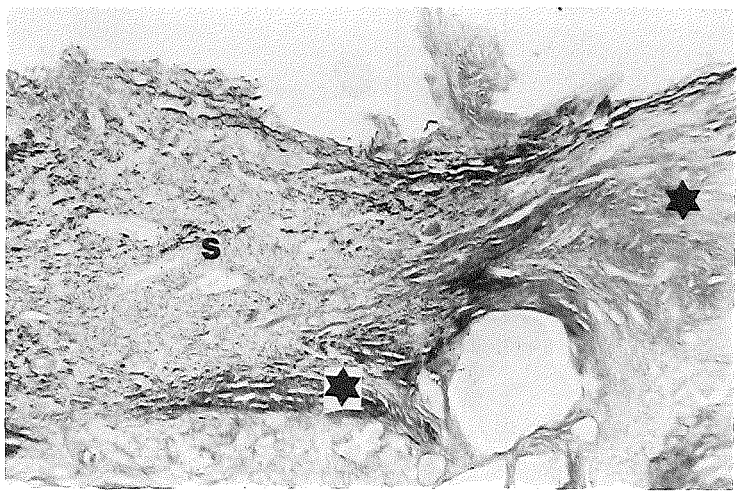

Figure 2a: Histologic segment of aortic valve leaflet after balloon dilatation.
Small laceration in the dense collagenous tissue stroma (*), filled up with scar tissue (S).

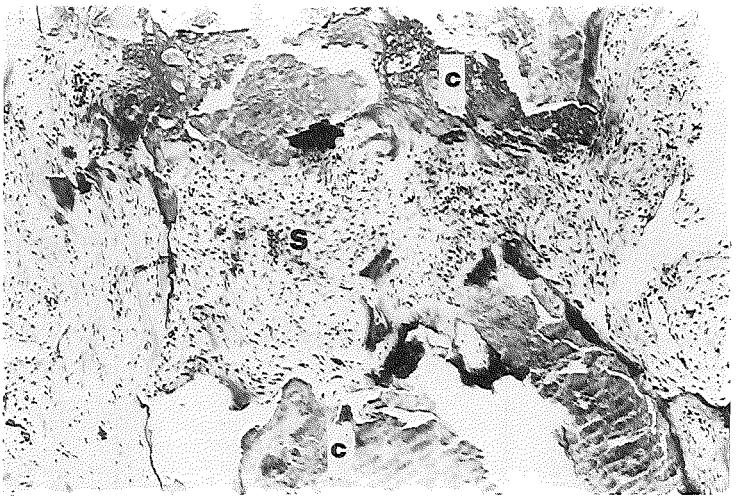

Figure 2b: Histologic segment of aortic valve leaflet after balloon dilatation.
Scar tissue (S) filling up fractured calcified nodule (C).

Fragments of calcium embedded in the young scar tissue were seen in 10 patients (Fig 2c).

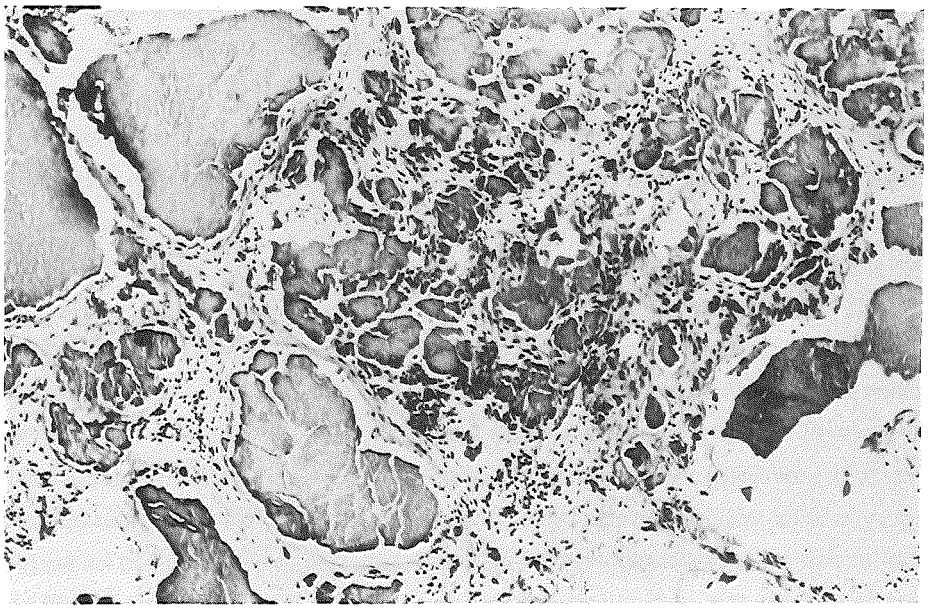

Figure 2c: Histologic segment of aortic valve leaflet after balloon dilatation. Calcium fragments embedded in young scar tissue.

In one patient a commissure was identified to be sealed together again with recent scar tissue. Hemorrhages and fibrin, more deeply in the valve stroma were seen in 6 patients. Superficial fibrin deposits and hemorrhages might very well be, but were not considered as an effect of dilatation because they were also seen in the control group. One patient only showed the basic pathology of calcified aortic stenosis and no recent scar tissue. However, this patient was operated on 36 months after dilatation and it may very well be that by that time the scar tissue is completely organized and not recognizable as "new". There was no clear difference in microscopical appearance between the successfully and the 2 non-successfully dilated patients, although 1 of the non-successfully dilated patients showed, in addition to the presence of young scar tissue in the collagenous valve stroma, an extensive histiocytic reaction around severely fragmented calcifications (nr 3). The second patient only showed scar tissue between fragmented calcifications (nr 4).

DISCUSSION

The reasons not to operate on these sixteen patients as a first choice were manifold. One patient, 85 years old, who had recently undergone hemicolectomy for angiodysplasia, had angioplasty of the left anterior descending artery in a previous session, without much improvement of her predominantly anginal symptoms. After valvuloplasty as a second procedure she experienced no improvement of her symptoms and she underwent a second angioplasty of the left circumflex artery in a third session. When symptoms did not improve afterwards, she was ultimately operated on, despite her age.

Three other patients were declined surgery for poor left ventricular functions with ejection fractions of respectively 0.19 and 0.27 (one not assessed). After valvuloplasty their ejection fractions were respectively 0.38 ,0.42 and 0.37 and after recurrence of symptoms they were subsequently operated on. Two other patients were declined surgery, one for unoperated carcinoma and one for possible dementia. After operation in the former, and reevaluation in the latter case they both were accepted for surgery. Another nine patients all had concomitant disease such as diabetes, nephrolithiasis, coronary artery disease, previous mitral valve replacement, lung disease, epilepsia, arthritis and hypertension, or a combination of these, which together with advanced age made surgery less desirable. However, after recurrence of symptoms or after unsuccessful valvuloplasty they were nevertheless accepted for surgery. The last patient preferred valvuloplasty as a first choice, but underwent valve replacement after restenosis.

Without intervention life expectancy is limited in patients with symptomatic aortic valve stenosis. Natural history data are only available from the pre-surgery era and show a life expectancy of 3 to 4.7 years in the presence of angina and/or syncope (21-23). In patients with cardiac failure the expectancy is from less than one year to two years (21-23).

None of the patients died after surgical replacement of the severely stenotic aortic valves. The risk of valve replacement is hard to establish in this heterogeneous group of patients. Acar reported a 19% early mortality in patients operated on for aortic stenosis with or without aortic incompetence over the age of 65 in the period from 1968 to 1979 (24). Jamieson collecting his data in the same period found a 4.7% thirty

day hospital mortality in aortic valve replacements for all causes in the age group over 65 (25). In his overview of the literature an overall operative mortality was found of 13.3% for aortic valve replacement over the age of 60 in the sixties. In the seventies this figure dropped to 7% for the same condition in the same age group. Deloche reported a 12% operative mortality in a group of 101 patients over the age of 70 with aortic valve replacement for aortic stenosis, between 1970 and 1980 (26). Düren reported a 10% hospital mortality in a comparable group of 20 patients, operated on between 1977 and 1985 (27). More recently Magovern reported a 4.3% operative mortality for aortic valve replacement in the age group over 70, while it was 26,7% when combined with bypass surgery for the same age group (28). In the age group over 80 a 30% early mortality (< 90 days) has been reported (29). Preoperative selection must be the most important determinant of peri-operative mortality as stated correctly by the last author. So it is at least remarkable that in this group with more than average risk factors no in hospital mortality occurred, and the post-operative course was so favorable. This is the more the case as these operations were performed in three different hospitals, with five surgeons operating. Two authors reported in hospital mortality after aortic valve replacement in patients with previous balloon aortic valvuloplasty, the mortality being 13 and 14 % respectively (30,31).

After aortic valve replacement the prognosis for patients with severe aortic valve stenosis is considerably improved. An annual mortality after operation of 2.0% to 11.3% has been reported (25). In our series at a mean follow-up of 22 months after operation no patient who had undergone previous balloon aortic valvuloplasty died. It is very unlikely that this group of patients constituted a selected group with a more favorable prognosis with or without surgery, because they were all but one considered high risk candidates for aortic valve replacement.

Several reports mention the percentage reinterventions after balloon aortic valvuloplasty after different follow-up periods. After 7 to 10 months percentages are noted from 12 to 29% (6,31,32). At a longer follow-up period of 17 and 24 months these percentages were 36 and 48% respectively (33,34). Revalvuloplasty is less influenced by the time of follow-up, and varies between 10 and 18 % (7,33), probably more reflecting local policy, or different patient populations, than differences in restenosis percentages. Our proportion of patients operated upon after valvuloplasty was 41% at a mean of 17 months after valvuloplasty, while one patient underwent

revalvuloplasty after 14 months. Combining the operation and revalvuloplasty numbers yields a 44% reintervention rate. It has been our policy to refer patients for surgery in case of restenosis, if they are operable. Of five inoperable patients presenting with signs of restenosis all but one refused redilatation.

It is difficult to appreciate these outcomes in different hospitals. Selection of patients, definition of inoperability, and acceptability for (re)valvuloplasty must at least in part be responsible for these divergencies. Also local and national logistics and availability of cardiac surgery might influence operative mortality. In our country with excellent cardiac surgical facilities, balloon aortic valvuloplasty seems only justified in very old patients, patients with untreatable infections, patients with unoperated or recently operated carcinoma, while it is open for debate whether patients with very poor left ventricular function should undergo balloon aortic valvuloplasty first as a bridge to surgery.

The morphologic substrate of calcific aortic stenosis in the elderly is, irrespective of the mechanism initiating it, represented by severe fibrosis and heavy calcifications of the valve leaflets sometimes in combination with commissural fusion. These pathologic changes render the valve rigid and immobile (35,36).

As was seen in our study, and supported by other workers (12,14,37) the effect of balloon valvuloplasty lies in decreasing this immobility in three ways:

1. Cleavage or tearing of the dense collagenous valve stroma.
2. Fracture and/or fragmentation of calcifications.
3. Cleavage of fused commissures.

It seems that the final outcome of PBAV mainly depends on the severity of the basic pathologic changes in the valve and the extent of the injury the balloon is able to create. In the 2 patients that had insufficient dilatation procedures with an increase of the aortic valve area of less than 25%, we indeed saw some injury in the valve leaflets, but apparently it was not extensive enough. Commeau et al (10) made a comparable observation in a peroperative study. They noticed, that when the valve was extensively calcified, dilatation macroscopically hardly showed any effect. On the other hand, a too extensive injury, holds the risk of creating too severe a damage to the valve with a chance of aortic insufficiency, as happened in one of our patients, where a valve leaflet was actually torn off the aortic wall.

The injury inflicted to the aortic valve, appears to be followed by a scarring reaction.

We saw that small tears or lacerations in the collagenous valve stroma and fractures in the calcifications as well as cleavages of commissures were filled up with young scar tissue. Our observations find support in literature (14,37). Scarification is recognized as a possible mechanism for restenosis (14,15). Indeed, development, organization and collagenisation of the young scar tissue, in the tears and fractures in the valve, will in the course of time restore the valve's immobility, and so have the potential to lead to restenosis.

However, from our study it appears that organization and collagenisation of the scar tissue in these valves takes longer to develop as compared to other tissues. We saw non-collagenous scar still present in the valves 24 months after dilatation. Normally a scar should be completely organized and collagenised within 6 weeks. This observation shows the potential for restenosis to develop slowly, so that the patient may expect to enjoy an acceptable complaint-free episode.

Another conclusion that could be drawn from our observations is that the per- and post-operative risk of surgery in valvuloplasty patients might be overestimated. After all, one of the more important spin offs of the introduction of balloon valvuloplasty, so far has been a more liberal attitude of surgeons to operate on patients with an increased but acceptable risk.

We feel that PBAV still has a place in relieving aortic stenosis in the inoperable elderly with severe aortic stenosis, albeit on strict indications.

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CHAPTER 9
MECHANISMS, NEWER TECHNIQUES AND INDICATIONS FOR PERCUTANEOUS BALLOON AORTIC VALVE DILATATION

MECHANISMS

Several mechanisms for successful dilatation have been proposed. These mechanisms include fracture of nodular calcifications, separation of fused commissures, or stretching of rigid valve leaflets, all with the aim of restoring some of the valve's normal mobility (1-3). Most data have been derived from inspection after balloon dilatations in the operating theatre (1,4), after postmortem dilatations (1,3,5), or from inspection of aortic valves which have previously undergone balloon valvuloplasty (2,6,7). Our own histologic observations, described in chapter 8, suggest fragmentation of calcific deposits, also on a microscopic level, with filling of the cleavage line with fresh scar tissue. This scarring reaction may play a role in the development of restenosis, although organization and collagen deposition of the scar tissue occurs over a prolonged period. Becker and Hoedemaker state that the nature of the damage inflicted on these valves, almost by necessity dictates that restenosis must occur (8).

Kennedy et al. noted in five postmortem examinations of aortic valves previously subjected to balloon dilatation that in the two tricuspid valves increase in cusp mobility was greater than in the two bicuspid valves (9). Here the difference in outcome could be explained by the underlying anatomy. Unfortunately the exact anatomy of a stenotic aortic valve can only be ascertained before operation in a minority of patients. The creation of hinge points by fracturing calcific deposits by the inflated balloon, might be one of the more important working mechanisms of successful percutaneous valvuloplasty. If correct, more mobility of the valve leaflets might be achieved, by applying more force on the calcified, scarred valve leaflets.

NEWER BALLOON TECHNIQUES

Balloons with larger diameters and inflated to higher pressures, exert a greater stress on the wall than smaller balloons. On the other hand, oversized balloons have the intrinsic disadvantage of possibly dissecting the aortic wall, resulting in less support of

the valve leaflets on the aortic wall, with ensuing aortic valve leaflet incompetence. A recent publication from Dorros et al. showed a greater valve area increase after employment of double balloons than after the use of single balloons (10). The number of complications appeared not to increase with this alternative method although medium term results were not much better than with single normal sized balloons. So while a slightly better direct result is obtained with these larger balloons, the procedure is potentially more hazardous, and the medium term outcome is still at its best, only fair, with a high mortality and high recurrence rate after the procedure. It might be inferred that overstretching accelerates the restenosis process.

Recently a new device has been described for valvuloplasty in calcified aortic stenosis (11). The system consists of 3 expandable prongs mounted on a freely movable catheter tip. The prongs can be manipulated into an expanded position from outside of the body. No obstruction of bloodflow occurs as with conventional balloon dilatation. Use of this instrument in the operating room in 10 patients, just prior to aortic valve replacement, yielded a substantial increase in planimetered aortic valve area, primarily due to improved splitting of fused commissures. Unfortunately commissural fusion is encountered only in a minority of cases of calcified aortic valve stenosis in elderly patients. Evenso, the instrument has certain potential by virtue of the fact that it does not obstruct aortic valve flow during expansion. Its disadvantage is that it fractures calcific deposits to a lesser extent. The design of the instrument has a high resemblance to the instruments developed around 1950 by the surgeons Brock, Bailey and Larzelere, as discussed in chapter 3.

Other techniques have been advocated to create a greater cusp mobility by fracturing calcific deposits, retained within leaflets. Worley et al (12) described a technique to decalcify aortic valves by electrohydraulic shock waves. They reported their experiences with a lithotripsy electrode in four postmortem specimens and in five living patients undergoing aortic valve débridement valvuloplasty for severe aortic stenosis. Under both circumstances the hand held lithotriptor fragmented the calcifications contained within the valve leaflets, leading to less rigidity of the valve as estimated by palpation. In the surgical cases subsequent removal of calcific deposits was facilitated after the lithotriptor had been used, by creating a cleavage plane between fragmented calcifications and the surrounding valve tissue. No perforations of valve cusps were seen. One patient was operated on at 6 months follow-up for

severe aortic incompetence, the other four still experienced a measurable improvement, with mild or moderate aortic incompetence in all patients. Potential problems in the application of this technique in the operating theatre include perforation in the area of previously existing ulcerations, or burning and distortion of aortic valve cusps by direct contact between spark and tissue.

The use of electrohydraulic shock waves is not necessarily the optimal means of decalcification. The use of ultrasonic destruction and aspiration of calcium fragments from the valve cusps, might improve the results of surgical débridement techniques, and decrease aortic cross-clamp time. Other energy sources will undoubtedly be introduced and might make the procedure safer (12).

Erny and Waller (13) constructed a balloon catheter which incorporated an electrohydraulic lithotripsy probe at its tip. In three of five postmortem human specimens with severe aortic valve stenosis, a slight increase in valve area was apparent after utilization of this device. No apparent increase in calcium nodule fracturing over a conventional balloon technique was noted, nor was there a perceptible release of calcific fragments from the valves. In a calcified porcine aortic valve this lithotripsy balloon catheter resulted in massive release of calcific fragments, when compared to conventional balloon dilatation.

Laser balloon valvuloplasty has also been tried recently in normal canine aortic valves (14). Simultaneous application of pressure and heat might be more effective than pressure alone to prevent elastic recoil. For this purpose two optical fibers were inserted in the central portion of a balloon catheter, terminating in a cylindrical diffuser. During balloon inflation and laser activation in vitro, a 70°C temperature was measured at the aortic adventitial surface. Laser balloon valvuloplasty increased (normal) aortic valve area more than balloon valvuloplasty. No loss of integrity of valve leaflets and aortic wall or charring was evident. We must point out, however, that normal aortic valves are hard to compare to severely stenotic valves, especially in in vitro experiments. The temperature recorded in this experiment will certainly be lower during in vivo balloon valvuloplasty, by the cooling effect of the bloodstream. And finally if recoil is prevented by heat application, severe valve insufficiency might ensue. Nevertheless experiments which aim at preventing recoil after aortic valve dilatation, should continue. After all, during a 20 mm balloon inflation, without a visible waist, aortic valve area is temporarily 3.14 cm^2. Research should be directed to develop

instruments to stent the aortic valve area, which might ultimately lead to percutaneous implantable artificial aortic valves.

NEWER INTRODUCTION TECHNIQUES

As described in chapter 4, arterial complications at the balloon insertion site are numerous. With the introduction of long and short arterial sheaths, as described in chapter 7, arterial complication rate dropped from 41 to 6.5 %, due to less trauma from smooth surface sheaths, rather than sliding multiple, uneven balloons over a wire through the femoral artery wall. The availability of polyethylene balloons, which deflate to a lower profile, and pass through 12 French (4.0 mm) sheaths, has also diminished the arterial introduction complication rate (15). Another approach to reduction of vascular complications of percutaneous valvuloplasty has been reported by Cole and Krone (16). They advise placement of the large-bore arterial sheath in the common femoral artery, and to confirm this by introducing first a 5 French catheter, and inject 8-10 cc of non ionic contrast through this catheter. Should the catheter be in the superficial femoral artery, than a more cephalad puncture site is selected, and the angiogram repeated. Puncturing the common femoral artery however, bears a potentially higher risk of retroperitoneal bleeding, especially if the posterior wall of the common femoral artery above the inguinal ligament is perforated during the puncture.

NEWER MONITORING TECHNIQUES

The usefulness of transoesophageal echocardiography, has been mentioned in chapter 5. The advantages are: readily visible anatomy of the stenotic aortic valve, monitoring of left ventricular function during and after balloon inflation, assessment of aortic incompetence after balloon inflation, and measurement of the aortic annulus and inflated balloon diameter (17). Especially when the procedure is performed under general anaesthesia, this method of monitoring the patient is without problems in our experience of three cases. Afterload reduction during general anaesthesia by injecting nitroglycerin intravenously just prior to balloon inflation, has also proven in our experience to make balloon inflations better tolerated, with the option of longer duration of balloon inflation, and quicker return to pre inflation left ventricular function.

Also recently the use of a percutaneously introduced intravascular ultrasound catheter during percutaneous balloon valvuloplasty has been reported (18). These investigators were able to record not only the nature of the underlying anatomy of the stenotic aortic valve, but also the improved mobility of the aortic valve leaflets post valvuloplasty, with visualisation of a crack in a calcific aortic valve nodule post valvuloplasty. Also the extent of the atrial septal defect after mitral balloon valvuloplasty, was clearly visible with this new instrument. Thus transoesophageal echocardiography and intravascular ultrasound catheters, may become important adjunctives to monitor valve anatomy before and after balloon valvuloplasty.

NEWER CIRCULATORY SUPPORT

Balloon valvuloplasty for the management of aortic valvular stenosis is generally performed in patients who are high risk operative candidates, or in whom surgery is actually contraindicated. Unfortunately these patients are also at high risk during valvuloplasty, because balloon inflation across the aortic valve is linked with a substantial reduction in cardiac output, leading to hypotension.

Recently percutaneous cardiopulmonary support systems have been introduced, and the use of this technique during aortic valvuloplasty has been reported (19). The long valvuloplasty sheath and a venous sheath are introduced on one side, as described in chapter 4. The femoral vein and artery in the other groin were used for introducing 20 French sheaths. Via the femoral venous sheath on this side, an 18 or 20 French multihole catheter was passed over a guidewire into the right atrium. Via the arterial sheath an 18 or 20 French catheter was positioned in the distal abdominal aorta. Both cannulae were then connected to the cardiopulmonary support system, which consisted of a pump and oxygenator. Cardiopulmonary support was achieved by pumping blood from the right atrium to the distal aorta at a maximal flow rate of 5.0 liters/min. After attaining satisfactory cardiopulmonary support, valvuloplasty was performed in the usual manner. Vogel (19) reported 6 patients undergoing aortic valvuloplasty with such an approach. Aortic valve areas increased as a result of valvuloplasty at least twofold in all patients. In two patients self terminating ventricular tachycardia lasting 10 seconds was noted. No other major problems were encountered during these support procedures. Declining filling pressures during cardiopulmonary

support required fluid administration. At the termination of the procedure approximately 1.5 liters of blood remained in the bypass system, which could not be pumped back into the patient. Consequently blood transfusions were required in all patients to compensate for this blood loss. The femoral vein and artery were closed by suture after removal of the cardiopulmonary support catheters at the end of the procedure. One patient died 12 hours after valvuloplasty following sudden ventricular fibrillation.

Such support during aortic valvuloplasty could extend the application of aortic valvuloplasty to patients with severely diminished left ventricular function and hemodynamic instability. It also permits the use of extended balloon inflation times, which might improve the results of valvuloplasty. We agree with Vogel's statement (19): "As interventional cardiology advances into the treatment of more complex and advanced coronary and valvular disease, circulatory support procedures are likely to bridge the gap between standard transcatheter interventions and open heart surgery". Moreover, cardiopulmonary support, installed in the interventional catheterization room, also allows for less urgency during transfer of the patient to the operating room, should the need arise. Nevertheless these decisions depend on local policies and the willingness of the surgical team to accept patients for valve replacement, even if they are in a poor cardiac condition. It has not been demonstrated that supported valvuloplasty, eventually followed by aortic valve replacement offers these patients a more favorable outlook for the future, than direct aortic valve replacement.

INDICATIONS FOR PERCUTANEOUS BALLOON AORTIC VALVULOPLASTY

It should be stressed that at least in the group of elderly patients described in this thesis, the valve area increases only minimally, and can not compete with the effects achieved by aortic valve replacement. Looking at these heavily calcified, fibrous, scarred valves in the operating theatre, makes this conclusion hardly unexpected. But as pointed out in chapter 4, even minimal or temporary improvements in valve area can lead to a better quality of life and to a better hemodynamic situation, albeit temporary, by diminishing the afterload which an already severely hypertropied ventricle has to overcome. Minor improvements have yielded major effects. So the paradoxical fact presents itself that elderly patients, who are at high risk during aortic

valve replacement, are also the very patients who by the nature of their disease might expect to benefit the least from a percutaneous balloon dilatation. Balloon dilatation creates a greater valve area, especially if the commissures are fused. Unfortunately this is only the case in a minority of the elderly population described here. This is in contradistinction with congenital aortic stenosis, where commissural fusion is rather the rule than the exception. In such patients better results have been obtained. A particular matter of discussion could be the group of adult patients with congenital aortic stenosis, who are not yet symptomatic. It could be expected that in this group of patients, the best results could be obtained by reducing effectively and early on, the pressure overload on these ventricles. As hypertrophy is a process which is only partly reversible as shown by Krayenbühl and coworkers (20), it might be worthwhile to prevent the more severe forms of hypertrophy, by dilating these valves in younger patients at the right moment. If the procedural risk were to become negligible, then even presymptomatic patients might be candidates for this procedure.

For the elderly age group the procedure should be restricted to severely symptomatic patients who for whatever reason, are inacceptable for aortic valve replacement. These reasons could include recently operated, or inoperable malignancies, provided such patients are not in a terminal phase of their malignant disease, or very advanced age with diminished cerebral function. Infectious diseases precluding the implantation of an artificial valve, the necessity of performing major non cardiac surgery, and very poor left ventricular function are other reasons. In the last instance one has to weigh the risk of the palliative valvuloplasty procedure itself, against the diminished risk of valve replacement, once left ventricular function has improved.

As most risk factors and the relative importance of these individual risk factors for aortic valve replacement are well known, a more accurate risk profile should be calculated in each patient before making an individual decision for aortic valve replacement or percutaneous balloon aortic valvuloplasty. These considerations should be discussed with the patients and their relatives in a frank and open manner.

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SAMENVATTING

Aortastenose is een term die algemeen gebruikt wordt voor de aandoening, waarbij de aortaklep vernauwd is. De aortaklep bevindt zich tussen de linker kamer en het opstijgende deel van de lichaamsslagader, en heeft als functie het terugstromen van bloed uit de lichaamsslagader naar de linker kamer te beletten.

Ongeveer 500 jaar geleden maakte Leonardo da Vinci schetsen van deze klep en trachtte hij zich met glasmodellen een inzicht te verwerven in de stroompatronen die optreden als het bloed vanuit de linker hartkamer deze klep passeert.

Een eerste beschrijving van vernauwde aortakleppen vinden we terug in 1647 in het werk van Riverius.

Ongeveer 200 jaar later vinden we de eerste min of meer complete beschrijving van aortastenose en de invloed die deze aandoening uitoefent op het overige deel van de bloedsomloop. Toen reeds werd vastgesteld dat een normale aortaklep, die ongeveer tot 3 à 4 cm^2 oppervlakte kan openen, ernstig vernauwd moet zijn aleer deze vernauwing leidt tot een vermindering van de bloedstroom door deze klep.

In het algemeen kan het ziektebeeld samenhangend met vernauwing van de aortakleppen ingedeeld worden in twee hoofdgroepen: de aangeboren en de verworven aortastenose. Bij de aangeboren vorm is de meest voorkomende onderliggende anatomie een aortaklep die bestaat uit één of twee slippen, in plaats van de normale drie slippige klep. Behalve dat deze aangeboren afwijking al kan leiden tot vernauwing van de klepopening bij de geboorte, kan een aangeboren afwijking in het aantal klepslippen ook met een normale wijdte van de opening gepaard gaan, en pas op latere leeftijd aanleiding geven tot een vernauwing. Naast deze aangeboren vorm door een te gering aantal klepslippen, kan het dus ook voorkomen dat deze aangeboren afwijking in de aanleg van de normaal voorhanden zijnde drie klepslippen, pas op latere leeftijd leidt tot aortastenose. In het algemeen geldt dat hoe geringer het aantal klepslippen, hoe eerder de verschijnselen van aortastenose zich zullen manifesteren. De verkregen vorm van aortastenose kan zowel bij een abnormaal aantal klepslippen als ook bij een in aanleg drieslippige klep optreden. De meest voorkomende oorzaak van vernauwing van een in aanleg normale klep was acuut rheuma, maar door een verminderd voorkomen van dit ziektebeeld in westerse landen, is nu een degeneratieve afwijking van de aortaklep, die zich manifesteert op oudere leeftijd, de meest voorkomende oorzaak in onze samenleving, doordat de bevolking steeds ouder wordt. In alle drie de ziektebeelden die

zich op latere leeftijd voordoen, dus vernauwing van congenitaal misvormde aortakleppen, rheumatische ontsteking van de aortakleppen en degeneratieve vernauwing van in aanleg "normale" aortakleppen kunnen verkalkingen optreden, die de reeds verdikte en vergroeide klepslippen nog minder beweeglijk maken. Dit proces van verdikking en verkalking leidt to een verhoogde weerstand voor de uitstoot van bloed uit de linker hartkamer, hetgeen weer leidt tot een verdikking van de spierwand van de hartkamer. In een later stadium kan deze voortdurende overbelasting leiden tot een verminderde samentrekking van de hartkamer. Verschijnselen samenhangend met een vernauwde aortaklep treden meestal pas laat op in het beloop van de ziekte en bestaan uit pijn op de borst, aanvankelijk vooral bij inspanning, duizeligheid en flauwvallen, terwijl kortademigheid meestal pas optreedt bij falen van de linker hartkamer. Het optreden van plotse dood is zeldzaam als eerste symptoom van aortastenose. Symptomen doen zich voor als de aortaklepopening tot minder dan 1.0 cm^2 is teruggebracht, terwijl de meerderheid van alle patiënten zelfs zonder verschijnselen blijft zolang de klepopening meer dan 0.7 cm^2 bedraagt. Het natuurlijke beloop van deze ziekte is moeilijk vast te stellen, omdat de mogelijkheid tot het vaststellen van de ernst van de aortaklepafwijking door middel van hartcatheterisatie samen viel met de eerste pogingen een dergelijke afwijking door middel van een hartoperatie te behandelen. Toch wordt algemeen aangenomen, onder andere door retrospectief onderzoek van overleden patiënten, dat de levensverwachting van patiënten met symptomen wijzend op aortastenose beperkt is tot enkele jaren. Omdat vooral oudere mensen in onze westerse samenleving getroffen worden door dit ziektebeeld, is het begrijpelijk dat een groot aantal patiënten in de oudere leeftijdscategorie, ook afwijkingen aan de kransslagaderen vertonen. Het zichtbaar maken van de kransslagaderen door middel van hartcatheterisatie en selectieve coronaire angiografie behoort dan ook routine matig te geschieden bij deze groep patiënten.

In 1913 werd door Tuffier voor het eerst een poging gedaan een vernauwde aortaklep op te rekken door met de vinger de aortaklepopening te verwijden door instulpen van een deel van de aortawand, juist boven het klepniveau. In de vijftiger jaren werden door chirurgen vaak ingenieuze instrumenten ontwikkeld om een vernauwde aortaklep in te snijden of op te rekken. Tegelijkertijd werden pogingen ondernomen tot het verwijderen van kalkneerslagen in de aortaslippen en het losmaken van aan elkaar vergroeide

klepslippen, welke techniek verder werd verfijnd na de invoering van de hart-long machine, waardoor de operatie tijd aanzienlijk kon worden verlengd. Deze techniek aangeduid met de Franse term " débridement", bestaat nog tot op de dag van vandaag en wordt toegepast bij patiënten met drieslippige kleppen, redelijk behouden normale anatomische verhoudingen, zonder aortaklep lekkage en bij wie behandeling met antistollingsmiddelen, zoals gebruikelijk na implanteren van een kunststofklep, minder gewenst is.

In 1951 werd door Hufnagel voor het eerst een kunststofklep in de afdalende aorta geïmplanteerd bij een patiënt met aortaklep insufficiëntie. Deze kunstklep bestond uit een metalen ring met een kooi, waarin een metalen bal op en neer kon bewegen. Dit ontwerp werd later vervolmaakt door Starr en Edwards door gebruik te maken van een siliconen bal en bekleding van de stalen poten van de kooi. Ook werden in dezelfde periode kunststof klepprothesen ontwikkeld, gelijkend op de natuurlijke aortaklep, welke terplaatse van de insufficiente aortaklep werden ingehecht.

In dezelfde periode werd door Murray in Canada en D. Ross in Europa voor het eerst gebruik gemaakt van klepsegmenten van humane oorsprong. Later werden deze donor kleppen eerst gesteriliseerd, ingevroren en gedroogd, welke techniek vooral door Barratt Boyes in Nieuw Zeeland werd ontwikkeld. Ook niet-humane kleppen werden voor transplantatie gebruikt, alsook andere humane of dierlijke weefsels, al of niet met gebruikmaking van een frame waarop deze klep vervangende weefsels werden gemonteerd. Ook prothesen uit kunststof vervaardigd ondergingen de afgelopen 40 jaar vele veranderingen, alle bedoeld om de kunstklep minder thrombogeen te maken, duurzamer en minder belemmerend voor de bloedstroom.

Momenteel worden zowel de "débridement" techniek, verschillende homo- en heterografts, als kunststof kleppen gebruikt om zieke vernauwde aortakleppen te remodelleren of te vervangen. De controverse of biologische kleppen van humane of dierlijke oorsprong beter zijn dan kunstkleppen is niet in het voordeel van een van beide beslecht. Biokleppen hebben ongetwijfeld het voordeel dat na implantatie geen antistollingstherapie vereist is, maar het nadeel dat de duurzaamheid in de tweede decade na implantatie mogelijk minder is dan van artificiële kleppen.

Hoe dit ook zij, vast staat dat chirurgische vervanging van de aortaklep, met welke prothese dan ook, nog steeds een niet onaanzienlijke kans op sterfte met zich meebrengt, vooral bij oudere patiënten, met een verminderde linker kamerfunctie. Het

risico van overlijden ten gevolge van het chirurgisch vervangen van de aortaklep kan variëren van 5 tot 25% afhankelijk van de aanwezigheid van een aantal risicofactoren die door retrospectief onderzoek van geopereerde patiënten konden worden vastgesteld. Hoewel de vooruitzichten zowel wat betreft de levensduur als de kwaliteit van dit resterende leven na een succesvolle operatie zeer gunstig zijn, heeft met name het risico van overlijden ten gevolge van de operatie er toe geleid dat alternatieve behandelingsmethoden werden aangewend, vooralsnog in de groep patiënten die zich presenteren met ernstige symptomen van aortaklepstenose, en bij wie het operatie risico of door de chirurg of door de patiënt zelf als onaanvaardbaar hoog werd ingeschat.

In 1966 werd door Rashkind voor het eerst een catheter met een ballon aan het distale einde gebruikt om een levensreddende behandeling toe te passen in pasgeborenen met een volledige transpositie van de long en de lichaamsslagader om een betere menging van beide bloedsomlopen te creëren. De ballon werd in lege toestand door het nog open zijnde foramen ovale van de rechter in de linker voorkamer gebracht, en na gevuld te zijn met contraststof teruggetrokken naar het rechter atrium om zo door een grotere opening tussen beide voorkamers de menging tussen beide bloedstromen te verbeteren. Na de introductie door Grüntzig in 1978 van kleinere opblaasbare ballonnen om kransslagadervernauwingen op te rekken, werd hetzelfde concept ook toegepast om aanvankelijk longslagader en later aortakleppen te dilatateren, vooral bij aangeboren vernauwingen van deze kleppen, met een bevredigdend resultaat. En hoewel pogingen van 30 jaar geleden vooral door chirurgen ondernomen om vernauwde en verkalkte aortakleppen op te rekken meestal tot een onbevredigend resultaat leidden, en werden achterhaald door betere chirurgische technieken, is het concept van het oprekken van vernauwde aortakleppen nu door percutaan ingebrachte ballon catheters bij volwassenen in 1985 door Cribier uit Rouaan opnieuw geïntroduceerd. Zijn inspanningen richtten zich vooral op de groep patiënten met een onaanvaardbaar hoog operatie risico, zoals zeer oude mensen.

In maart 1986 hebben wij met Cribier samen de eerste patiënt door middel van deze techniek, die in de internationale literatuur de naam: percutane ballon aortavalvuloplastiek heeft meegekregen (PBAV), behandeld. Tot januari 1990 hebben wij 39 van dergelijke procedures uitgevoerd in 38 patiënten, 23 vrouwen en 15 mannen. De gemiddelde leeftijd van deze patiënten bedroeg 75 jaar. Van deze groep patiënten

werden 25 beschouwd als inoperabel of zij vertegenwoordigden een zeer hoog operatie risico. Deze inschatting was gebaseerd op de leeftijd van de patiënten, hun linker kamerfunktie en het bestaan van andere bijkomende, vaak de levensverwachting ernstige beperkende ziekten, zoals de aanwezigheid van een geopereerd of met geopereerd carcinoom, ernstige longfunctie stoornissen of infecties. De overige 13 patiënten werden niet als inoperabel beschouwd, maar hadden een aantal bijkomende afwijkingen die operatie minder gewenst maakten, of de patiënten gaven zelf de voorkeur aan ballondilatatie. Van deze groep patiënten zijn er vier in het ziekenhuis overleden, twee tijdens de procedure na een eerste ballon inflatie, een derde patiënt overleed een dag na de procedure ten gevolge van ernstige aortainsufficiëntie veroorzaakt door een dissectie van de aortabasis na ballondilatatie, terwijl de laatste patiënt 8 dagen na de procedure is overleden aan onomkeerbaar hartfalen. Een toeneming van de aortaklep opening met tenminste 25% kon worden bereikt in 31 van de overige 35 patiënten. Bij de patiënten die het ziekenhuis konden verlaten nam het klepoppervlak toe van 0.47 cm^2 voor tot 0.75 cm^2 na de dilatatie, terwijl het gemiddelde drukverval over de aortaklep afnam van 74 naar 43 mm Hg.

Bij 3 patiënten vond binnen 3 maanden een chirurgische vervanging van de aortaklep plaats, bij één van hen wegens ernstige aortainsufficiëntie na de procedure, bij één wegens een onvoldoende resultaat van de ballondilatatie, terwijl de derde patiënt al snel tekenen van restenose vertoonde. De overige patiënten ondervonden allen een symptomatische verbetering na aortaklepdilatatie, syncopale aanvallen bijvoorbeeld, die tevoren bij acht patiënten voorkwamen, deden zich na dilatatie niet meer voor. Ook klachten van angina pectoris en kortademigheid waren bij de meeste patiënten verdwenen of verminderd na de procedure, resulterend in een betre validiteitsklasse. Vooral in de beginperiode ging de procedure vaak gepaard met soms ernstige complicaties. Complicaties ten gevolge van het invoeren en wisselen van ballon catheters in de arteria femoralis kwamen frequent voor, voordat een lange invoerschede werd gebruikt. Deze lange schede werd opgevoerd tot juist boven het aortaklepniveau en verhinderde dat de opgeblazen ballon uit de aortaklep opening kon schieten. Een ander voordeel van deze lange schede was een aanzienlijke vermindering van plaatselijke complicaties in de lies. Het opvoeren van ballon catheters door deze schede geeft aanzienlijk minder beschadiging van het gepuncteerde vat, dan het wisselen van balloncatheters over een ingebrachte voerdraad. Het aantal plaatselijke arteriële

complicaties verminderde dan ook van 41 naar 6,5%, zoals in een onderzoek in samenwerking met de universiteitskliniek van Genève werd aangetoond. Ook de tijd benodigd voor een procedure verminderde aanzienlijk van 211 maar 117 minuten, nadat gebruik werd gemaakt van deze invoermethode. Zoals vermeld konden 35 patiënten het ziekenhuis verlaten, na een gemiddelde opname duur van 6 dagen. Acht van dezen zijn overleden gemiddeld 15 maanden na de dilatatie, voor een groot deel ten gevolge van hun hartlijden, voor een deel ten gevolge van andere ziekten, welke andere ziekten een aortaklepvervanging minder gewenst maakten. De gemiddelde leeftijd van deze overledenen bedroeg 79 jaar. Behalve de drie eerdergenoemde patiënten, ondergingen nog 13 anderen een aortaklep vervanging, gemiddeld 17 maanden na de klepdilatatie, ten gevolge van het opnieuw optreden van ernstige klachten en tekenen van restensose. De gemiddelde leeftijd van alle geopereerde patiënten bedroeg 72 jaar. Van de dertien patiënten geopereerd drie maanden of meer na valvuloplastiek, waren 6 in eerste instantie als inoperabel beschouwd, 3 vanwege een sterk verminderde linker kamerfunctie, één vanwege een niet geopereerd uterus carcinoom, één wegens dementie, en één wegens hoge leeftijd gecombineerd met angiodysplasieën. Niettemin werden zij in tweede termijn geaccepteerd voor operatie. Een inoperabele patiënt met tekenen van restenose onderging een revalvuloplastiek. De zeven overige geopereerde patiënten werden in eerste instantie geaccepteerd voor ballondilatatie vanwege bijkomende ziekten, of een voorkeur van de patiënt voor deze ingreep in plaats van operatie. Van alle zestien geopereerde patiënten is er geen enkele overleden tijdens het ziekenhuisverblijf, noch gedurende een vervolg periode van gemiddeld 22 maanden. Het feit dat het hier een oudere groep patiënten betreft met een groter of kleiner aantal risicofactoren voor sterfte tijdens of na de operatie, en de omstandigheid dat deze patiënten door minstens vijf verschillende chirurgen in drie ziekenhuizen werden geopereerd, maakt dit uitstekende resultaat nog opmerkelijker.

Een groep van 11 patiënten tenslotte, met een gemiddelde leeftijd van 77 jaar is gemiddeld 23 maanden na een eenmalige klepdilatatie nog steeds in leven, en op één na, met aanzienlijk minder klachten.

Van de gehele groep patiënten was 87, 68 en 68% in leven na respectievelijk één, twee en drie jaar, terwijl deze percentages 62, 28 en 25% bedroegen indien alleen patiënten die geen vervolg ingrepen ondergingen, worden beschouwd. Alles bijeen

verdient chirurgische therapie de voorkeur boven klepdilatatie bij patiënten bij wie het operatierisico aanvaardbaar laag wordt ingeschat (bv. < 10%). Voor ernstig symptomatische patiënten die niet voor operatie geaccepteerd worden, vanwege hun algemene, cardiale of extracardiale conditie, verdient valvuloplastiek overwogen te worden, omdat deze ingreep tot symptomatische verbetering leidt, ondanks het frequent optreden van restenose, welke dan opnieuw met valvuloplastiek behandeld kan worden, indien patiënten nog steeds inoperabel worden geacht.

De beslissing om tot operatie of valvuloplastiek over te gaan bij een groep patiënten met een hoog operatierisico, zoals te verwachten is bij zeer oude patiënten of patiënten met een sterk verminderde linker kamerfunctie, dient genomen te worden in een overleg tussen patiënt, cardiochirurg en cardioloog. Ook kan valvuloplastiek bij sommige patiënten leiden tot een verbetering van de verminderde linker kamerfunctie, hetgeen een latere klepvervanging minder riskant maakt. Deze beslissingen zullen mede bepaald worden door plaatselijke omstandigheden, zoals de beschikbaarheid en de kwaliteit van chirurgisch handelen.

Doppler echocardiografie is een niet invasieve methode om de ernst van aortaklepstenose vast te stellen. Vooral bij hogere bloedstoomsnelheden over de aortaklep is deze methode specifiek voor het vaststellen van ernstige aortaklepstenose, bij lagere snelheden is een ernstige aortastenose niet uit te sluiten indien tevens een verminderde linker kamerfuctie bestaat. De stroomsnelheid kan via de vereenvoudigde Bernoulli formule omgerekend worden tot millimeters kwik en zo vergeleken worden met het tijdens hartcatheterisatie gevonden drukverval over de vernauwde aortaklep. Metingen bij 31 patiënten voor en na ballonvalvuloplastiek, toonden een matige correlatie tussen de met Doppler techniek gemeten maximale stroomsnelheid en het piek systolische drukverschil tussen linker kamer en aorta, hemodynamisch geëvalueerd. Indien met behulp van echo Doppler en catheterisatie technieken het resterende aortaklep oppervlak wordt berekend tonen deze waarden een zeer goede correlatie, al heeft elk van beide technieken zijn specifieke tekortkomingen. Niettemin daalde de maximale stroomsnelheid over de aortaklep met Doppler techniek gemeten van 4,6 tot 4,1 meter per seconde onmiddellijk na ballondilatatie. Bij Doppler metingen gemiddeld 10 maanden na ontslag uit het ziekenhuis nam deze snelheid weer toe tot 4,4 meter per seconde, wijzend op een partiële restenose. Evaluatie van patiënten na aortaklepdilatatie door middel van Doppler stroomsnelheid metingen, gecombineerd met het registreren

van veranderingen in het klachtenpatroon, lijkt de aangewezen methode om deze patiënten te vervolgen.

De eerste catheters die gebruikt werden om aortakleppen te dilateren, bevatten aan het einde een enkele ballon, van verschillende lengte en met verschillende doorsneden. Modificaties in dit ontwerp leidden tot de ontwikkeling van twee of drie parallel geplaatste ballonnen aan het einde van de catheter. In hoofstuk zes hebben wij getracht nadere informatie te verkrijgen omtrent de relatie tussen het model van de toegepaste ballon en de onderliggende anatomie van de te dilateren aortaklep. De mate van de theoretische belemmering van de bloedstroom door opgeblazen enkelvoudige en drieweg ballonnen werd door middel van computer tomografie gemeten in vier vernauwde aortakleppen van overleden patiënten. Het bleek dat drieweg ballonnen, die theoretisch het voordeel hebben enige bloedstroom langs de opgeblazen ballonnen toe te laten, in deze experimenten tot een meer complete afsluiting van de aortaklepopening konden leiden dan enkelvoudige ballonnen, indien de te dilateren aortaklep drieslippig was. Deze theoretische beschouwingen werden geëxtrapoleerd naar de werkelijkheid door metingen van de daling van de aortadruk bij opblazen van verschillende ballonontwerpen in vier aortakleppen die twee- of drieslippig waren. De anatomie van deze kleppen was bekend doordat deze vier patiënten na aortaklepdilatatie later een aortaklep vervanging ondergingen. Deze observaties toonden een goede correlatie met onze in vitro experimenten, in die zin dat dilatatie van tweeslippige kleppen met een drieweg ballon beter werd verdragen en tot minder aortadruk daling leidde dan oprekking door enkelvoudige ballonnen, en omgekeerd het gebruik van drieweg ballonnen geen voordeel opleverde ten opzichte van enkelvoudige ballonnen bij drieslippige aortakleppen.

In hoofstuk acht worden naast de resultaten behaald met operatie van patiënten die eerder een ballondilatatie hadden ondergaan, en die eerder zijn besproken in deze samenvatting, macroscopische en microscopische bevindingen bij geopereerde patiënten gerapporteerd. Voor deze evaluatie waren 12 kleppen, die bij operatie waren verwijderd, beschikbaar. Slechts bij één patiënt werden macroscopisch afwijkingen gevonden die toegeschreven kunnen worden aan de voorafgaande klepdilatatie. Bij deze patiënt was een klepslip over een lengte van 7 mm losgescheurd van de aortawand, resulterend in ernstige aortaklep insufficiëntie, welke spoedoperatie

noodzakelijk maakte. Histologische afwijkingen in de gereseceerde kleppen, werden vergeleken met afwijkingen bij een controle groep van 10 patiënten die tevoren geen klepdilatatie hadden ondergaan en ook werden geopereerd vanwege een ernstige aortaklepstenose. De niet tevoren met ballondilatatie behandelde kleppen toonden een aanzienlijke fibrose, met knobbelige verkalkingen ingebed in een celarm dicht collageen bindweefsel. Bij alle kleppen die verwijderd werden na voorafgaande percutane valvuloplastiek werden de afwijkingen die ook in de controle groep werden gezien, waargenomen, en bovendien in 11 van de 12 verwijderde kleppen een celrijk litteken weefsel, welk weefsel de breuklijnen in kalkophopingen en scheurtjes in het collagene bindweefsel opvulde. Dit litteken weefsel werd tot 24 maanden na voorafgaande dilatatie aangetroffen, en was bij één patiënt, 36 maanden na valvuloplastiek niet meer aantoonbaar. Dit zou de suggestie kunnen wekken dat organisatie van dit litteken weefsel laat optreedt en dat deze vertraagde omzetting van litteken in collageen weefsel het opnieuw optreden van vernauwing van de aortaklep vertraagt. Fragmentatie van kalkneerslagen in de klepslippen, het losmaken van aanelkaar vergroeide klepslippen en oprekking van starre klepbladen zijn waarschijnlijk gezamenlijk verantwoordelijk voor een grotere klepopening na dilatatie door middel van een ballon catheter.

Diverse technieken zijn de laatste jaren aangeprezen om de resultaten van percutane dilatatie te verbeteren. Naast ballonnen met een grotere diameter in opgeblazen toestand, welke het gevaar van overrekking en verscheuring van klepslippen of de aortawand met zich meebrengen, werd recent een metalen dilatator geïntroduceerd. Dit instrument, dat veel gelijkenis vertoont met de in vroeger tijden door chirurgen à vue gebruikte dilatator, bestaat uit drie ijzeren armen die van buitenaf geopend kunnen worden. Het voordeel van dit instrument is dat het minder belemmerend werkt op de bloedstroom en dat een grotere kracht kan worden uitgeoefend op de verkalkte en soms vergroeide klepslippen. Een nadeel is dat het minder invloed heeft op het kraken van kalkophopingen in de klepbladen. Andere methoden om de kleppen op te rekken maken gebruik van een vergruizer tip op een catheter gemonteerd, of catheters met een laser tip welke plaatselijk de opgerekte aortaklep kunnen verhitten, om zo een betere fragmentatie van kalkneerslagen te verkrijgen of elastische recoil na dilatatie te voorkomen. Voorlopig lijken deze technieken geen betere resultaten op te leveren dan ballon catheters.

Het gebruik van een lange invoerschede is reeds besproken, en biedt naar ons idee aanzienlijke voordelen, zowel om het aantal complicaties van ballonvalvuloplastiek te verminderen, als ook om de duur van de ingreep te bekorten. Behalve het voordurend meten van de aortadruk om het effect van ballondilatatie op de bloedstroom langs de opgeblazen ballon te kunnen vaststellen, verdient transoesophageale echocardiografie overweging tijdens de procedure. Naast een beter inzicht in de anatomie van de aortaklep en de invloed die ballondilatatie uitoefent op de beweeglijkheid van de klepslippen, kan deze methode ons een goed inzicht verschaffen in de samentrekking van de linker hartkamer. Met een volgende balloninflatie zou dan gewacht kunnen worden, totdat de linker kamerfunctie zich weer hersteld heeft. Ook de toepassing van een hart-long machine in het catheterisatie laboratorium tijdens percutane valvuloplastiek is recent gerapporteerd. Het voordeel hiervan is dat de bloedcirculatie op peil blijft tijdens afsluiting van de aortaklepopening met een opgeblazen ballon, en de ballon dus langer opgeblazen kan blijven, zonder dat de patiënt bewusteloos raakt. Deze techniek kan overwogen worden als tijdelijke ondersteuning van de circulatie, vooral bij patiënten met een sterk verminderde linker kamerfunctie. Dit houdt wel in dat de hulp van een perfusionist in de catheterisatie kamer onontbeerlijk wordt, hetgeen tot wrijvingen met de afdeling cardiochirurgie, het normale werkterrein van perfusionisten, kan leiden.

Concluderend zijn wij van mening dat percutane ballon valvuloplastiek een nuttige aanvulling kan zijn op de reeds zijn waarde bewezen hebbende chirurgische klepvervanging, indien patiënten om wat voor reden dan ook niet aanvaardbaar zijn voor operatie. De techniek biedt deze groep patiënten een redelijke kans op een betere kwaliteit van het resterende leven, al wordt de levensduur door deze ingreep waarschijnlijk vooralsnog niet verlengd. Ballondilatatie kan ook overwogen worden bij patiënten met een sterk verminderde linker kamerfunctie, omdat zelfs minimale vergroting van het aortaklepoppervlak kan leiden tot een verbeterde linker kamerfunctie, en zo een latere aortaklep vervanging minder riskant kan maken.

In ieder geval dient het risico van operatie en ballondilatatie vrijelijk met de patiënten besproken te worden, om zo tot een beslissing te geraken welke ingreep bij deze individuele patiënt de voorkeur verdient.

EEN WOORD VAN DANK

Het enthousiasme van Prof. P.G. Hugenholtz en Prof.Dr. J. Roelandt voor hun vakgebied, hebben mij in 1971 doen besluiten mijn opleiding tot internist om te zetten in een opleiding tot cardioloog. Prof.Dr. G.T. Meester leerde mij al tijdens mijn opleiding de magie van het catheteriseren ondergaan. Samen met Prof.Dr. A. Querido die mijn interne vooropleiding verzorgde, wil ik hen danken, voor mijn opleiding tot cardioloog.

Patrick Serruys dank ik voor zijn grote kennis van zaken en de aanstekelijke manier waarop hij de introductie van nieuwe technieken nastreefde.

Pim de Feyter, Harry Suryapranata, Gert-Jan Laarman en Ivan De Scheerder dank ik voor hun collegialiteit.

In de personen van Susan Veldhof en Nico Vogelaar wil ik mijn dank overbrengen aan de verpleegkundige en de technische staf van de catheterisatie afdeling, welke van onschatbare waarde was bij de behandeling van de patiënten.

Eveneens dank ik de verpleegkundigen van de afdelingen intensive care, 3 zuid en 1200 voor hun voortreffelijke zorg aan de patiënten besteed.

Deze dank wil ik ook overbrengen aan de cardiologen en cardiologen in opleiding werkzaam in het Thoraxcentrum, voor hun bereidheid deze kwetsbare groep patiënten mede te begeleiden. Speciaal dank ik hiervoor René Geuskens.

De afdeling cardiochirurgie onder leiding van Prof.Dr. J. Nauta en Prof.Dr. E. Bos en de afdeling cardioanaesthesie onder leiding van Dr. O. Prakash ben ik veel dank verschuldigd voor de steun die zij mij gaven bij het betreden van het onontgonnen terrein van de interventie cardiologie, en het aandeel dat zij in mijn opleiding hebben gehad. Ook de overige medewerkers van de operatiekamers dank ik voor hun bereidheid om bij voorkomende problemen klaar te staan en ingewikkelde situaties op te lossen.

Zonder vooral de hulp van Marjolein Wapenaar, maar ook van Claudia Sprenger de Rover en Laetitia Bautz, was dit boek nooit in druk verschenen. Hartelijk dank voor de vanzelfsprekendheid van jullie inzet.

Nienke Essed was het meest actief betrokken bij het tot stand komen van dit proefschrift. Kritiek van jou leek altijd meer op een lofzang.

Ook Aida Azar, Louise Bellersen, Ron van Domburg, Albert McNeill, Marie-Angèle Morel, John de Kuyper, Sylvain Plante, Jan Tuin en Wim Vletter ben ik zeer erkentelijk voor hun daadwerkelijke bijdrage aan de tekst, de illustraties en het onderzoek van de patiënten.

Marianne Eichholtz was van onschatbare waarde bij het vinden van de weg in de

bureacratische doolhof rondom een promotie.

Tot slot dank ik allen die mij het schrijven van dit proefschrift hebben mogelijk gemaakt. Niet in het laatst geldt dat voor mijn kinderen Eva, Igor, Jurriaan, Mischa, Crispijn en Charlotte. Door jullie liefderijke houding en niet aflatende belangstelling hebben jullie me aangespoord dit werk te beginnen en af te maken. Ik ben er trots op jullie vader te mogen zijn.

CURRICULUM VITAE

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