Aortic valve dysfunction and dilated ascending aorta. A complex and controversial association

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Several pathogenetic mechanisms account for the association of the ascending aorta dilation with aortic valve dysfunction. Functional aortic insufficiency can derive from medial degeneration of the aortic wall and annuloaortic ectasia; leaflet structural disease can determine root dilation by increasing aortic wall stress in case of both regurgitation and stenosis; aortic valve disease and aortic aneurysm can however coexist due to two different intrinsic etiologies. In the attempt to best tailor the surgical correction of such conditions to the underlying causative mechanism, several technical options have already been developed including composite or separate aortic valve and root replacement, valve-sparing operations, and aortoplasty techniques. The criteria for surgical indication cannot leave the underlying pathogenesis out of consideration as well. The newly acquired knowledge in the basic research on this topic is expected to affect the approach to the individual patient in the future.

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The occurrence of an aortic valve disease associated with a dilation of the ascending aorta is frequent. In some cases the primary lesion may be identified and the associated disease may be considered as secondary; in some other cases a single pathogenesis underlies both lesions; in others the interpretation of the association is controversial. Similarly, the definition of the therapeutic indications with regard to the timing and technique of surgical treatment of the valve disease, aortic disease or both is debatable.

For several years a group of researchers from the Second University of Naples, Italy, has been focusing on this topic and the aim of the present review is to summarize the knowledge acquired so far.

Epidemiology

The normal dimensions of the aortic root and ascending aorta show a remarkable degree of variability and transthoracic and/or transesophageal echocardiography is still the main screening method. In both male and female normal subjects the diameters of the ascending aorta, of the sinuses of Valsalva and of the aortic annulus are related to age and body surface area: the body surface area is the main determinant of the aortic annulus and root dimensions, while the diameters of the sino-tubular junction and of the ascending aorta depend more strictly on age[1]. The expected aortic root diameter can be calculated from the subject's age and body surface area by means of the regression formula proposed by Roman et al.[1]. When the observed aortic diameter at echocardiography exceeds the expected measure the aorta is considered dilated: an aneurysm is defined as a measured diameter exceeding the expected one by 50%[2].

In 1991 Carrel et al.[3] reported an ascending aorta dilation to be found in about 15% of patients with an indication to aortic valve replacement. In a report by Prenger et al.[4] among 419 surgical patients undergoing aortic valve replacement 37 (8.8%) had an aortic size > 50 mm. It could be debatable whether those aortas should have been considered as being all really aneurysmatic or not, since one should think more in terms of ratios rather than absolute sizes; however, all cases of acute aortic dissection in the follow-up (0.6% of all aortic valve replacement procedures) were found in that subgroup of patients. It

is more difficult to define the average prevalence of ascending dilation in subgroups of patients with a definite valve dysfunction (stenosis versus regurgitation) or pathology (degenerative versus rheumatic), owing to the lack of up-to-date specific studies in the medical literature. The condition of a congenitally bicuspid aortic valve has been more closely investigated[5] and it is nowadays considered a predisposing factor to aortic dilation, dissection and other diseases both when the normal function is preserved as well as in the presence of valve dysfunction[6].

Pathophysiology: annuloaortic ectasia and medial degeneration

Several pathogenetic mechanisms may account for the association of a dilated ascending aorta and aortic valve dysfunction. Aortic insufficiency may either derive from the loss of central leaflet coaptation, due to a dilation involving the sino-tubular ridge (annuloaortic ectasia)[7,8] or, on the contrary, it may be a cause of backflow-related turbulences and of a wide pulse pressure associated with a hyperdynamic left ventricle and therefore of an increased aortic wall stress determining an aortic root dilation[9,10]. On the other hand, aortic stenosis may occasionally cause a post-stenotic dilation that, being related to the hemodynamic burden of the jet stream on the vessel wall, usually involves the tubular portion[10,11].

The term "annuloaortic ectasia" was first introduced in 1978 by Lemon and White[12] to define a primary dilation of the aortic annulus and of the ascending aorta. Today surgeons use the term "aortic annulus" to indicate the aorto-ventricular junction (surgical annulus) and consequently the term "annuloaortic ectasia" refers to dilation involving the fibrous portion of the aorto-ventricular junction, the aortic sinuses and the sino-tubular ridge with consequent aortic valve regurgitation[13]. The morphological substrate of this condition consists of varying degrees of medial (cystic) degeneration (MD) involving the medial layer of the vessel wall. MD lesions observed at morphology include: a) cystic spaces in which Alcian-positive and Pas-positive mucopolysaccharides are pooled; b) fragmentation and disarray of the lamellae formed by the elastic fibers; c) fibrosis (increase in collagen); and d) necrosis (a reduction in the number of smooth muscle cell nuclei). Since the anatomo-functional condition of an aortic dilation at the sino-tubular level with aortic valve incompetence may occur as a consequence of other diseases, among which atherosclerosis of the ascending aorta, syphilitic aortitis and extensive infective endocarditis, the term "non-inflammatory aortic root disease" (NIARD) has been introduced to indicate the primary form, in which MD is the culprit lesion. In NIARD a direct correlation has been found between the severity of MD (quantified according to the Schlatmann and Becker classification in three degrees[14]) and the aortic diameter at the site of dilation[15].

Initially this disease was observed in patients with Marfan's syndrome, Ehlers-Danlos syndrome or Osteogenesis imperfecta, in which a genetically inherited defect of the connective tissues is present. However, the incidence of idiopathic forms of NIARD, without the typical stigmata and comorbidities of those syndromes is constantly increasing[16]. Marfan's syndrome is caused by defects in the gene encoding fibrillin I, located on the short arm of chromosome 15: the consequent abnormal gathering of fibrillin molecules causes the loss of the microfibrillar coating on the elastin core as well as structural abnormalities in collagen fibers. The consequence of these abnormalities is the presence of typical MD lesions in the vessel wall, with consequent aneurysmal disease. No qualitative difference can be found between the media lesions in Marfan and non-Marfan patients with NIARD and annuloaortic ectasia; obviously clinical differences do exist (e.g. in the mean age at which surgery is indicated). Frequently a NIARD is associated with degenerative valve disease such as floppy mitral valve and floppy aortic valve[15,17]. In the latter condition a degeneration of the *lamina fibrosa* of the aortic leaflets with proteoglycan pooling is observed at morphologic examination. The association of an aortic valve dysfunction with a dilated intrapericardial aorta, apart from cases of annuloaortic ectasia with or without an associated floppy aortic valve, may be quite frequently observed. Indeed MD is found as the underlying lesion even in those cases not satisfying the anatomo-functional criteria for the definition of annuloaortic ectasia, such as post-stenotic dilations, aortic root or ascending aorta dilations associated with fibrocalcific or rheumatic aortic valve insufficiency, stenosis or mixed dysfunction. Schlatmann and Becker[14,18], who first graded MD lesions and investigated their occurrence even in elderly normal subjects, claimed the stress-origin of MD changes, interpreting them as the result of processes of hemodynamic injury to the aortic wall and of the related metabolic repair.

While the pathogenetic mechanisms underlying aortic dilations are still subject of active debate[19], insights on the nature and characteristics of MD lesions in the aorta of patients with aortic valve disease have been recently forwarded. After the recognition of the structural and functional complexity of the normal aortic root, which has been demonstrated to be an asymmetric structure[20,21], our group has shown that in case of aortic valve disease MD lesions vary in severity along the circumference of the ascending aorta. In particular, MD lesions have been found to be significantly more severe at the convex aspect (antero-lateral wall) of the ascending aorta than at the concavity[22,23]. This is likely to be due to the characteristics of the post-valvular flow in aortic valve disease. Furthermore, although not yet sufficiently supported by scientific data, the warning has been issued[24] that the clinical manifestation of MD

in patients with a bicuspid aortic valve may differ from that observed in those with a tricuspid valve. It has already been found[25,26] that significant differences among the pathologic pictures of these two forms of aortic disease may emerge mainly at morphometry rather than at standard histology examination (i.e. thinner elastic lamellae and greater distances between these structures in the aortas of bicuspid valve patients).

Surgical management

When and how? The ascending aorta is considered dilated if its diameters at any level exceed the values considered normal for a given age and body surface area of the patient. The expected root dimensions can be calculated using the formulas proposed by Roman et al.[1]. In view of the variability in the normal values of the aortic diameter, it is correct to refer to the aortic ratio (measured diameter/expected diameter) rather than to absolute values in centimeters, when deciding on the indication to surgical treatment.

The elective treatment of the dilations of the intrapericardial aorta is meant to be prophylactic, aiming primarily at the prevention of lethal complications (spontaneous rupture and dissection) and of emergency operation. An aortic ratio of 1.5 (measured diameter exceeding the predicted one by 50%) is today considered the threshold value for the diagnosis of an aortic aneurysm[2]. Such a dilation may be cause of aortic regurgitation even in the presence of normal aortic leaflets[8,13] and exposes the patient to a higher risk of spontaneous rupture or dissection. This risk has been found to be strictly related to the aortic diameters and to the underlying wall pathology. The lack of accurate natural history studies makes a direct correlation of the dimensions with the incidence of major complications difficult and the current guidelines are to be considered improvable. It has been shown that an increased aortic diameter can carry a greater risk of postoperative dissection in patients undergoing aortic valve replacement[4]. With regard to the factor of wall disease, excluding cases of Marfan's syndrome and of chronic dissection, morphology studies aiming to characterize the heterogeneous group of morphostructural alterations that may underlie ascending aortic aneurysms are still being performed. This characterization is fundamental both for the determination of the correct surgical timing and for the choice of the adequate operative technique.

Nowadays, several surgical options are available in the management of these conditions. The choice of the appropriate strategy for the particular patient requires careful consideration of several factors including[2]: 1) the patient's age and expected survival; 2) the underlying pathology and structural state of the aortic wall; 3) the anatomic conditions of the aortic valve, sinuses and sino-tubular ridge; 4) the conditions of the distal aorta; 5) the risks related to postoperative anticoagulation; 6) the presence of active annular infection; and 7) the surgeon's experience. Regardless of the technique employed, elective root procedures should be performed if the associated operative risks, valve-related morbidity and late cardiac mortality are similar to those of routine aortic valve replacement[2].

Table I reports the current guidelines for establishing the indication to surgical repair of an aortic root/ascending aorta aneurysm, basing it on the aortic ratio and underlying disease, as recommended in 1999 by Ergin et al.[2].

Different approaches. *Separate replacement.* The first attempts to surgically correct ascending aortic aneurysms, before 1968, consisted of partial resections or external wrapping methods, characterized by poor long-term outcomes. Separate valve and supracoronary graft replacement was proposed by Wheat et al.[27] for aortic aneurysms involving the tubular portion of the ascending aorta, without sinus dilation, associated with aortic valve disease. This technique has been employed in both Marfan and non-Marfan patients as well as in dissections without aortic root involvement[2,3,10]. However, although considered a low-risk procedure by many authors[28], unsatisfactory results related to the high incidence of aneurysm or dissection/rupture at the level of the sinus have been reported in the long-term follow-up[29]. Using computer models simulating prosthetic separate aortic replacement, other authors have postulated that increased distension and wall stress in the aortic root occur in this condition, because of the loss of the normal ventriculo-arterial coupling: this could enhance the development of root complications[30]. It has been suggested that the indications to separate replacement be restricted, avoiding this technique in patients with a relatively long life expectancy[31].

The Bentall and modified Bentall operations. In 1968 the Bentall-De Bono technique introduced the concept of radical treatment by total prosthetic replacement of the aortic valve, root and ascending tract, with reimplantation of the coronary ostia on the composite prosthetic conduit[32]. The original technique included the longitudinal opening of the aneurysm, the prosthetic re-

Table I. Dimensional criteria for current surgical indications in ascending aortic aneurysms (adult, age < 40 years, body surface area 2 m^2).

	Diameter (cm)	Ratio
Marfan (or family history)	< 4.3	1.3
Chronic dissections	> 4.3	1.3
Degenerative without AI	> 4.8	1.5
Degenerative with AI	> 4.8	1.5
Bicuspid valve with dysfunction	> 4.5	1.4
Other cardiac surgery	> 4.8	1.5
Surgeon's experience	± 0.5	± 0.15

AI = aortic insufficiency.

placement of the valve and aorta and coronary ostia reimplantation without removing these structures from the aortic wall, followed by the reclosure of the native aortic wall around the prosthesis ("inclusion technique"). The technique was associated with better long-term results, due to the total removal of the diseased tissue. Nevertheless, complications involving the coronary anastomoses, such as bleeding due to the tension developing on the sutures for coronary attachment when an ample isolation and mobilization of the proximal coronary vessel was not performed, were frequent[33]. Periostial pseudoaneurysms or periprosthetic hematomas could result from this type of complication, even determining coarctations of the ascending aorta. With the aim of avoiding these complications, Cabrol et al.[34] proposed an end-to-end anastomosis of the coronary ostia to a Dacron vascular prosthesis which in turn was to be side-to-side anastomosed to the aortic prosthesis. Moreover, they proposed the connection, either through a direct anastomosis or by means of an interposed tubular prosthesis, of the ascending aorta wrapped around the aortic prosthesis with the right atrium, in order to allow for the drainage of the blood possibly oozing from the tissues or sutures. This variant allowed the achievement of a lower rate of pseudoaneurysm development, but increased the risk of coronary prosthesis kinking and/or thrombosis, resulting in massive acute myocardial infarction. Moreover, in some instances hemodynamically significant left-right shunts could develop.

Side by side with the improvements in surgical methods, advancements in anesthetic techniques, in extracorporeal circulation, in methods of coagulation control and above all in vascular prosthetic tissue production have taken place.

The availability of very low porosity prosthetic tissue allowed for the introduction of the "open technique"[35]. This consists of the detachment of the coronary ostia from the aorta together with a "button" of aortic wall about 0.5 cm in radius, generously mobilizing the proximal tract of the coronary main stems. The aortic root and the diseased tract of the ascending aorta are resected and the valved conduit is implanted on the aortic annulus. Then, two circular openings in the Dacron graft opposite the coronary orifices are made and the coronary buttons are sutured onto them. Before performing the distal anastomosis of the graft to the distal ascending aorta or aortic arch, the hemostasis of the coronary sutures is checked by inspecting them accurately even from the inside of the prosthesis. The open technique has the advantage of reducing the tension on the coronary anastomoses and hence the development of pseudoaneurysms[36]. Last generation prostheses have strongly decreased the risks of bleeding and the sutures employed to implant the prosthesis can be made more accurately without having to resort to the inclusion technique.

Despite the improvements of this technique, it still carries some risks, mostly related to the susceptibility of the non-included prosthesis to possible mediastinal infections and to the development of excessive tension on the coronary arteries with late thrombosis. The incidence of infection is today estimated at about 4-5% in patients who have been followed for 14-17 years[35] and that of coronary complications at about 3%[37]. Coronary stretching could be reduced by providing the proximal part of the tubular prosthesis with radial extensibility. This could be achieved by employing a new type of tubular prosthesis recently introduced in surgical practice. This prosthesis has been designed with a proximal longitudinally corrugated and bulging tract (named "skirt"), resembling the sinuses of Valsalva[38]. This type of prosthesis could be even more useful in valve-sparing operations, described below, in view of the importance of preserving the structure of the sinus in order to avoid valve leaflet structural deterioration[39].

The valve-sparing operations. Aortic valve incompetence may occur even in the presence of normal valve leaflets, when the correct coaptation of the free margins is prevented by the dilation of the sino-tubular junction with a subsequent increase in the distance between the commissures[7,8,10,13]. This condition is more commonly observed in elderly (sixth or seventh decade of life) patients, often with hypertension and degenerative aneurysms of the ascending aorta. In such patients ascending aortic replacement with a tubular prosthesis, restoring the normal sino-tubular diameter, can itself correct the valvular competence.

In annuloaortic ectasia, either isolated (aortic wall degeneration in elderly patients) or in the context of Marfan's syndrome, the sino-tubular junction and the fibrous portion of the aortic annulus (accounting for 55% of its diameter) are dilated, causing aortic regurgitation. In such cases both the aortic annulus and sino-tubular junction have to be included in the surgical repair. Besides the above reported techniques for the radical replacement of the aortic valve, root and ascending aorta, surgical options also include the so called "valve-sparing operations", that have been introduced with the purpose of avoiding postoperative anticoagulation and all valve-related complications.

Valve-sparing operations consist of the replacement of the aortic root with reimplantation of the coronary ostia; either the commissures of the aortic valve leaflets are suspended inside the graft (reimplantation technique, proposed by David et al.[40]) or the prosthesis is scalloped at its proximal end to produce three neo-sinuses of Valsalva to be sutured to the remnants of the native sinuses surrounding the attachments of the aortic valve leaflets (remodeling technique, proposed by Yacoub et al.[41]). The David operation implies the proximal implantation of the tubular prosthesis at the level of the aortic annulus, the diameter of which is therefore reduced to that of the prosthesis, while the Yacoub procedure can be associated with an aortic annuloplasty with a Dacron felt strip if it is retained necessary that

a dilated aortic annulus be reduced. The remodeling technique exposes the patient to a higher risk of bleeding. It necessitates associated annuloplasty in most cases, but seems to achieve a more physiologic condition due to the presence of the sinus-like structures. This should prevent the hemodynamic stress-related damage to the aortic leaflets occurring when the valve opens into a cylindrical structure such as the Dacron prosthesis, impacting during systole against the prosthetic wall[39]. David et al.[42] have recently reported an 8-year freedom from significant aortic insufficiency of 90 ± 3% after the technique of reimplantation and of 55 ± 6% after the technique of remodeling. The new model of tubular prosthesis introduced by De Paulis et al.[38], showing a proximal radially expansible tract, could restore a condition similar to the presence of normal sinuses of Valsalva when employed in a David procedure, and it has been claimed that this variant could carry better long-term results in terms of valve competence.

In the presence of annuloaortic ectasia without associated structural disease of the aortic valve, or in patients with ascending aneurysms and secondary aortic valve incompetence, valve-sparing operations are to be considered among the available surgical options. The widespread use of these techniques has been limited by some concerns regarding the long-term aortic valve function and above all regarding the increased technical complexity and the related longer learning curve required when compared with the more standardized Bentall procedure.

Techniques of aortoplasty. Several authors proposed aortoplasty techniques in order to avoid such an extensive procedure as the Bentall operation, and to restore a normal diameter through a conservative approach. The first attempt to reduce the aortic diameter conservatively dates back, according to Carrel's report[3], to 1966, with the studies by Senning, whose procedure was resumed in 1979 by McCready and Pluth[43].

The technical variants proposed so far substantially amount to four: simple aortoplasty, aortoplasty with external wrapping, shawl lapel aortoplasty, and "S"-aortoplasty.

Simple aortoplasty has been described in the literature as consisting of the excision of an oval portion of aortic wall from the supracoronary ascending aorta followed by aortotomy closure with a simple running suture, in some cases reinforced with Teflon felt strips. The most important weakness of this tailoring aortoplasty procedure was the use of a single suture line: the hemodynamic stresses in the ascending aorta are predominantly borne by the anterior aortic wall, where the suture line lies[9,44]. The high rates of recurrent aneurysms after simple aortoplasty could be related to this technical limitation[43]. In 1982 Robicsek[45] proposed a technique of aortoplasty, referred to as the "external wrapping" procedure, consisting of a reduction aortoplasty associated with aortic valve replacement, similar to the simple aortoplasty described by McCready and Pluth[43]: a segment of Dacron conduit was longitudinally incised, accurately tailored to fit the ascending aortic geometry, and placed around the reconstructed aortic wall in order to reinforce it. The "wrapping" method still exposed the patient to the risks associated with the presence of a foreign body in the mediastinum; furthermore, the proximal tailoring and anchoring of the external Dacron graft could be difficult, with the risk of displacement and impinging on the coronary arteries at their origin[9,46]. In order to avoid the implantation of prosthetic material as suggested by Robicsek[45] to support the reconstructed aortic wall, Harrison and Heck[47] in 1996 and Baumgartner et al.[48] in 1998 developed modified aortoplasty procedures, namely the "shawl lapel aortoplasty" and the "S"-aortoplasty respectively. Very few data have been provided to validate the use of these techniques in clinical practice. Several authors[49-51] have reported controversial results with aortoplasty procedures; their series, although with heterogeneous techniques and indications, all share the policy of a conservative approach, confirming that significantly shorter cardiopulmonary bypass and aortic clamp times, as well as lower rates of bleeding can be achieved, with particular benefit for aged patients requiring associated cardiac procedures. Nevertheless, the old aortoplasty techniques incompletely addressed the hemodynamic pathogenetic aspects of aortic dilations associated with aortic valve disease and neglected the underlying aortic wall pathology characteristics. Indeed, they have been applied in series including poststenotic dilations, in which the hemodynamic stress is the most important among the causative factors in the development of the aneurysm, as well as annuloaortic ectasia in Marfan's syndrome, aortic dissections and ascending aneurysms associated with a bicuspid aortic valve[11,51] in which the main pathogenetic factor is represented by idiopathic wall disease.

On the basis of our above-mentioned findings on the asymmetrical distribution of MD lesions along the ascending aortic circumference with more severe involvement of the convex wall[23,24], we have developed a specific procedure of aortoplasty for asymmetrical dilations of the ascending aorta associated with aortic valve disease, named "waistcoat aortoplasty". The sinus dilation is repaired by folding up the subcoronary redundant aortic wall using the anchoring sutures of the valve prosthesis (plication of the sinuses of Valsalva). Through a triangular resection the most involved portion of the aortic wall (convexity) is removed and the aorta is reconstructed with a double layer technique, thus achieving an autologous reinforcement of the convex wall and stress reduction on the aortotomy suture line. The short-term good clinical and echocardiographic results have already been published[52]; further studies will ascertain the validity of this technique in the long term.

Conclusions

The clinical condition of a dilated ascending aorta associated with aortic valve dysfunction includes several diseases which differ from one another for their pathophysiologic mechanisms, underlying structural morphology and, therefore, surgical approach. The surgeon's mindset should be in compliance with such a variety of disease forms, in order to achieve a patient-tailored management. As several questions remain unanswered, surgical guidelines and protocols of treatment are expected to undergo further modifications and updating in the future, side by side with the advances in basic medical research.

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