Ectasia of the ascending aorta at the time of aortic valve surgery: replace or relax?

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Background. **The fate of aortic ectasia associated with aortic valve disease is usually derived from the natural history of primitive aortic aneurysm. We evaluated the evolution of untreated aortic dilation following aortic valve replacement and analyzed risk factors for expansion.**

Methods. **Thirty-eight patients undergoing aortic valve replacement, with an aortic diameter 40 to 55 mm, were followed up for a mean of 42 ± 28 months (median 36 months). Freedom from adverse events, velocity of aortic expansion and correlation between velocity and several potential risk factors were evaluated.**

Results. **The mean aortic diameter did not change over time (43 ± 4 vs 44 ± 12, p = NS). Velocity of aortic expansion correlated significantly with the diameter of the ascending aorta at the time of operation, with faster growth in patients with ascending aorta diameter > 50 mm (p = 0.0004). Patients with aortic regurgitation had a tendency to a faster aortic dilation compared to those with aortic stenosis (p = 0.10).**

Conclusions. **In patients without other risk factors, prophylactic surgical treatment of the ectasic aorta seems advisable for diameters > 48 mm. For diameters < 43 mm no treatment is probably needed. Other aspects must be considered for appropriate surgical strategy in the interval between 43 and 48 mm. Patients with aortic regurgitation should be closely monitored.**

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A variable degree of ectasia of the ascending aorta is common in patients with aortic valve disease[1,2]. The natural history of this condition, and the factors predisposing to rapid dimensional increase, are not well known, and information is usually derived from studies addressing the evolution of primary, degenerative aortic aneurysms. If aortic dilation reaches the usual limits for the indication to substitution[3] at the time of aortic valve replacement (AVR), there are no doubts about the surgical strategy. When dilation is of moderate degree (< 55 mm), several options are suitable (aortoplasty, concomitant ascending aorta replacement, conservative approach), which rely often on the surgeon's opinion rather than on evidence-based guidelines. We tried to verify what is the natural history of this condition, once the primary cause is, at least partially, eliminated by AVR. Moreover, we attempted to identify preoperative factors that might influence the increasing rate of the ascending aorta diameter and therefore operative strategy.

Methods

Patients. Between February 1995 and December 2002, 971 patients were submitted to AVR at our Institution. Patients with aortic valve disease and concomitant dilation of the ascending aorta with preserved sinotubular junction, were submitted to AVR and reductive aortoplasty (n = 42) or ascending aorta replacement (n = 72). A minority of patients (n = 38) were not submitted to any treatment on the ectasic ascending aorta. They had a preoperative ascending aortic diameter comprised between 40 and 55 mm, and constitute the population of the present follow-up study. Their characteristics are summarized in tables I and II. Marfan syndrome affected none of them.

Follow-up. Pre- and postoperative echocardiography was performed in all patients. The follow-up period reaches 1545 patient/months, and is 98% complete. The mean duration is 42 ± 28 months (median 36 months).

Velocity of aortic diameter increase. The maximal aortic diameter recorded at the latest follow-up echocardiography was subtracted to the preoperative value, and the result was then divided for the length of the follow-up period, in order to achieve the mean velocity (mm/year) of the variation in the aortic diameter.

Table I. Patients' general characteristics.

Variable	Value	p
Age (years)	65 ± 10	0.44
Sex (M/F)	31/7	0.25
Height (cm)	168 ± 9	0.62
Weight (kg)	74 ± 12	0.35
Arterial hypertension (yes/no)	23/15	0.96
Diabetes mellitus (yes/no)	3/35	0.74
Smoke (yes/no)	25/13	0.77
Dyslipidemia (yes/no)	10/28	0.19

Table II. Characteristics of cardiovascular disease.

Variable	Value	p
Prevalent valve defect (AS/AR)	21/17	0.10
NYHA class (I/IV)	2.8 ± 1.2	0.27
Ejection fraction (%)	52 ± 11	0.97
LVEDD (mm)	59 ± 9	0.17
Ascending aorta diameter (mm)	43 ± 4	< 0.0001
Atrioventricular block (yes/no)	8/30	0.40
Associated cardiac disease* (yes/no)	11/27	0.98

AS = aortic stenosis; AR = aortic regurgitation; LVEDD = left ventricular end-diastolic diameter; NYHA = New York Heart Association. * requiring surgical treatment (coronary artery bypass grafting or mitral valve repair or replacement).

Statistical analysis. Continuous data are presented as mean ± 1 SD, while discrete variables are presented as number and/or proportions. The Kaplan-Meier method was used to calculate the freedom from time-related unfavorable events (death, reoperation, anticoagulation-related complications, structural deterioration or non-structural failure). The association of velocity of aortic diameter increase (VADI) with continuous variables was tested with the regression analysis. The association with discrete variables was tested by the two-tailed Student's t-test for unpaired data or factorial ANOVA. The variables included in the statistical analysis are reported in tables I and II along with their respective p values.

Results

Unfavorable events. Two patients (5%) died early postoperatively, one for stroke and the other, operated on for active endocarditis, for septic shock. Three more patients died during the follow-up: two for sudden death (both of them suffered from aortic regurgitation and moderate dilated cardiomyopathy) at approximately 2 months after surgery, and the third died for malignancy at 40 months.

No structural deteriorations or thromboembolic events were recorded during follow-up. One patient on anticoagulant regimen had a non-fatal cerebral hemorrhage. Another patient was reoperated for prosthetic valve endocarditis. The probability of freedom from adverse events (death from any cause, reoperation and all valve-related complications) is plotted in figure 1.

Evolution of the ascending aortic disease. There are three main categories with respect to this aspect: 1) patients with no significant modification during follow-up; 2) patients who have reached an aortic diameter > 50-55 mm, with or without a high VADI; and 3) patients who experienced a VADI > 1 mm/year, without reaching an aortic diameter of ≥ 50 mm.

In general, the mean diameter of the ascending aorta remained stable following AVR (43 ± 4 vs 44 ± 12 mm, p = NS). The mean VADI was 0.2 ± 3.4 mm/year (median 0.0). Five patients out of 36 early survivors reached an aortic diameter of ≥ 50 mm: 3 exceeded the 55 mm limit, and were reoperated (one because of acute dissection and the other 2 on elective basis). The 2 patients with an aortic diameter 50 to 55 mm are on a close-interval follow-up protocol, to establish the timing for a possible replacement of the ascending aorta. In 2 more patients a VADI > 1 mm/year, that is the mean value reported for the expansion of chronic, degenerative, non-dissecting aneurysm located in the ascending aorta[4], was recorded: they both did not reach the limit of 50 mm at the moment. Nonetheless they were included in the close-interval follow-up protocol, their VADI being 1.1 and 1.5 mm/year, respectively.

Predictive factors of aortic dilation. A weak correlation between VADI and type of aortic valve disease, stenosis or regurgitation, was identified (Fig. 2). Patients affected by an aortic valve disease with exclusive

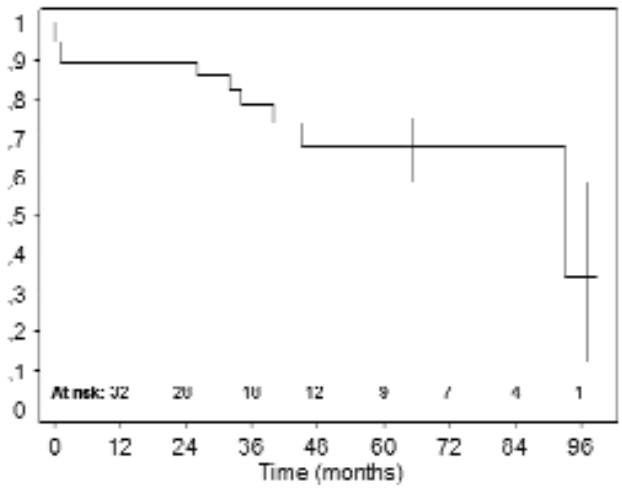

Figure 1. *Actuarial freedom from adverse events. Operative and late deaths from any cause, reoperation and prosthesis-related complications are included in the analysis. There were no instances of primary structural deterioration of the prosthetic valve. The* vertical bars *show the standard errors.*

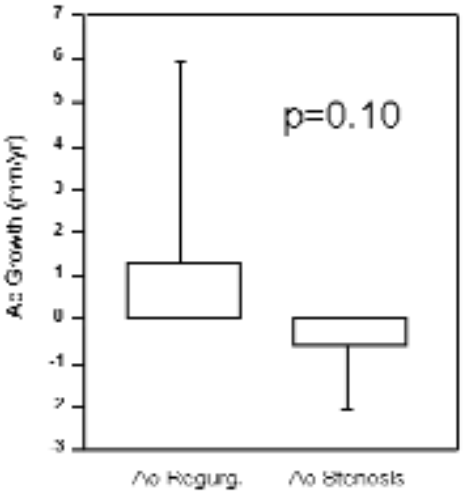

Figure 2. *Mean velocity of aortic diameter increase following aortic valve replacement in patients with aortic regurgitation or stenosis.*

or prevailing regurgitation were more prone to ascending aortic growth, with a mean VADI of +1.4 ± 4.8 mm/year. Patients with prevalent aortic stenosis showed a tendency to a decrease in aortic diameter following AVR, with a negative VADI of -0.6 ± 1.5 mm/year. This intriguing difference did not reach statistical significance (p = 0.10).

The only factor significantly associated with increased velocity of the aorta was the aortic diameter at the time of AVR. At linear regression analysis, VADI correlated with the aortic diameter (r = 0.60, p = 0.0004). The best fit for the description of VADI as a function of aortic diameter at the time of AVR was obtained with a third degree, polynomial regression function (Fig. 3). Plotting the calculated VADI against time we can see that ascending aortas with an initial diameter of ≥ 48 mm will probably reach the limit of 55 mm within 3 to 5 years from AVR. On the other hand, aortas with smaller diameters will probably increase to this limit in a much longer time, if ever.

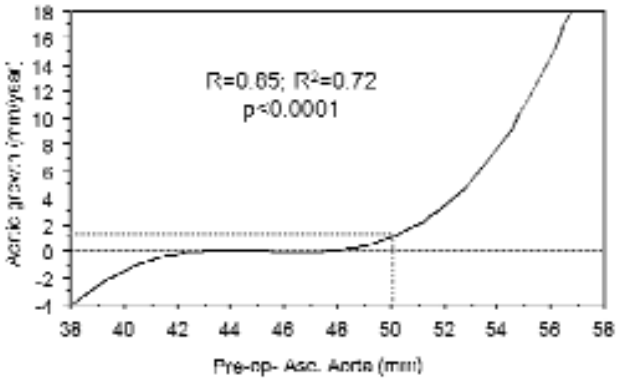

Figure 3. *Extrapolated, theoretical increase of the aortic diameter over time, based on the velocity of aortic diameter increase computed for different diameters obtained immediately before aortic valve replacement (see text for the equation derived from polynomial regression).*

Discussion

Although some degree of aortic dilation is a common finding in case of significant aortic valve disease, this ectasia cannot necessarily be classified as a primitive degenerative aneurysm of the ascending aorta, from a pathogenetic and clinical standpoint. Actually, while primitive degenerative aneurysms tend to constantly grow[3-5], aortic ectasia concomitant with aortic valve disease seems to have a different behavior in the majority of the cases, as reported also by others[2]. The most obvious hypothesis to justify this difference is that aortic ectasia associated with aortic valve disease is secondary to flow anomalies provoked by the valve disease itself: post-stenotic turbulence in case of aortic stenosis, and increased systolic ejection volume in case of aortic regurgitation. AVR causes an almost complete, instantaneous relief of flow abnormality in case of aortic stenosis, while a relative persistence of the underlying cause of aortic expansion could be hypothesized in case of aortic regurgitation. This could even partly justify the differences of VADI recorded in our study, although not statistically significant, that put forward a possible better outcome, in terms of aortic expansion, following AVR for aortic stenosis compared to regurgitation. These aspects remain to be further substantiated.

Nonetheless, there are some cases in which the alteration of the aortic wall probably reaches the limit beyond which a recovery is not allowed anymore, and the further evolution is quite similar to that of primitive expanding aneurysms. Indeed, although the mean aortic diameter is similar at baseline and during follow-up, still a proportion of patients develop a significant ascending aortic disease requiring surgical revision or inducing sudden complications, such as acute dissection. The rate of such patients is consistently around 10% in the different series[2,6,7], as well as in ours. The real question is how to identify these patients at higher risk. Several risk factors are now widely accepted as markers of probable quick expansion of the aortic aneurysms, such as connective tissue disorders (typically the Marfan syndrome) or bicuspid aortic valve[5,8,9], or familial syndromes[10], thus influencing critically the surgical timing for ascending aorta replacement[5]. Although in our series none of these well documented risk factors is associated with an increased VADI or with a higher reoperation rate, we strongly believe that this is due to an underestimation, secondary to the small sample size. We would therefore strongly recommend to establish an aggressive policy in patients with connective tissue disease or bicuspid aortic valve, following the dimensional indications reported by Ergin et al.[5] for primitive degenerative aortic aneurysms: we actually believe that these observations can undoubtedly be applied to aortic ectasia associated with aortic valve disease.

Although most of the studies in the literature focused actually on primitive aortic aneurysms, several different risk factors, like baseline aortic diameter[3-5]

and arterial hypertension[11], have been reported to be significantly associated with aortic expansion. Beside the type of aortic valve disease, our data show that preoperative diameter of the ascending aorta is indeed a reliable predictive factor of quick aortic expansion, also in the subset of patients with concomitant aortic valve disease and aortic ectasia, with a rapidly increasing VADI for aortic diameters > 48-50 mm. We would therefore recommend an aggressive, prophylactic treatment of aortic dilation (aortoplasty or replacement) at an early level, around 48 mm at the time of AVR, regardless of any other clinical consideration, since a significant expansion (up to 55 mm) would be reached in a short period, probably comprised between 3 and 5 years. This dimensional limit should be lowered to 45 mm in the presence of other demonstrated risk factors[5], and probably in case of AVR for aortic valve insufficiency.

In our series, smaller aortas are probably prone to remain stable over time, or even to partially recover, as reported also by others[2]: therefore, for diameters not exceeding 43 mm we would advise a conservative approach on the ascending aorta. A gray area remains, in which surgical strategy cannot rely simply on the aortic dimensions. Beside the above-mentioned risk factors, other aspects should be taken into appropriate account. Quality and thickness of the aortic wall, anatomic shape of the expanded aorta, patient's younger age, increased operative risk due to an expanded operation (additional anastomoses, increased cardiopulmonary bypass time, risk of bleeding) and surgeon's experience may all contribute to influence the therapeutic strategy in the case of ectasic aortas 43 to 48 mm in diameter.

Study limitations. The small sample size might have masked the relevance of some risk factors, such as the presence of a bicuspid valve that in our series is not associated with an increased risk of aortic expansion. This problem is partly due to the fact that we limited the analysis only to patients with an aortic diameter > 40 mm, in contrast to other series in which all aortas with a diameter ≥ 35 mm were included[2]. Furthermore, another cohort of patients with similar aortic diameters was submitted to reductive aortoplasty (with or without periaortic wrapping) or direct replacement of the ascending aorta, based on intraoperative observation and decision-making, and therefore excluded from the study. This leads to further considerations. First of all, one may speculate that the inclusion of the mildly dilated ascending aortas (i.e. with a diameter 35 to 40 mm, which is probably the most common case) would have provoked a potentially confounding effect, since in these cases, further dilation after removal of the primary cause is quite unlikely. Therefore, the conclusion could be more optimistic than it would be actually appropriate, and induce a relatively unjustified sense of safety when renouncing to treat the ascending aortic ectasia.

Finally, by excluding all patients who were submitted to adjunctive treatment on the ascending aorta, we might have introduced a selection bias. Indeed, the population of our study was judged by the surgeons to have different features, mainly inherent to the apparent quality of the aortic wall (thickness, absence of calcification, apparently preserved elasticity, dimension of the aorta probably appropriate for patients with greater body surface area) that would have made unlikely an evolution toward progressive dilation or rupture. Although this could actually have created a subgroup with scarce tendency to expansion, it also supports the idea that, in the case of moderate aortic dilation, other aspects, beside the mere aortic diameter, must be appropriately considered in the decision-making process about whether or not to repair or replace the ascending aorta.

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