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# Risk Factors for Aortic Complications in Adults With Coarctation of the Aorta

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<b>OBJECTIVES</b>	We sought to determine the prevalence and predisposing condition for aortic wall complications in adults with either repaired or non-repaired coarctation of the aorta.
<b>BACKGROUND</b>	Aortic wall complications may develop in adults with coarctation of the aorta, despite successful surgical repair in childhood.
<b>METHODS</b>	A total of 235 adults with coarctation (mean age $27 \pm 13$ years) were retrospectively reviewed. Treatment had been performed by surgery in 181 patients (group I) or by balloon angioplasty or stenting in 28 patients (group II). No previous intervention had been carried out in 26 patients with mild coarctation at diagnosis (group III).
<b>RESULTS</b>	Forty-four aortic wall complications were found in 37 patients (16%). There were no differences among the three groups with respect to total complications (15%, 18%, and 15%, respectively), ascending aortic aneurysms (9%, 11%, and 12%), or descending aortic aneurysms (4% in all three groups). Multivariate analysis did not show a significant relationship between previous repair, type of repair, age at repair, residual Doppler pressure gradient, or systemic hypertension and the occurrence of aortic complications. Only aging (risk ratio [RR] 1.4 per decade of age, 95% confidence interval [CI] 1.1 to 1.8, $p = 0.002$ ) and bicuspid aortic valve (RR 3.2, 95% CI 1.3 to 7.5, $p = 0.005$ ) were significantly related to these complications.
<b>CONCLUSIONS</b>	Aortic wall complications are frequent in adults with coarctation of the aorta beyond that attributable to associated hemodynamic derangement or previous repair. The only independent risk factors appear to be advanced age and bicuspid aortic valve. (J Am Coll Cardiol 2004;44:1641-7) © 2004 by the American College of Cardiology Foundation

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Coarctation of the aorta is a common congenital defect whose natural history has substantially been changed by surgical repair in childhood. However, patients after successful repair of coarctation of the aorta still remain at high risk of late cardiovascular morbidity and mortality in adult life (1,2). Late cardiovascular complications include systemic hypertension (3), premature coronary artery disease (4), re-coarctation (5), left ventricular outflow tract abnormalities (6), and major aortic wall complications, such as true or false aortic aneurysm (7,8), rupture (9,10), dissection (11), endarteritis (12), and fistula (13). Aortic wall complications may occur at the site of previous repair or at a long distance from the aortic isthmus, mainly in the ascending aorta (14), and they may develop in both repaired or unrepaired patients (15). A high incidence of aneurysms at the site of repair, ranking from 5% to 50%, has been reported late after patch graft aortoplasty for coarctation (16-18), but this complication might also appear after subclavian flap angioplasty (19), end-to-end anastomosis (20), or bypass grafting (21). Aneurysm formation at or near the site of repair has been reported to be related not only to surgery but also to transcatheter relief of the coarctation

(22,23). Moreover, whether a significant relationship between age at repair and aortic complications exists remains a matter of debate. The aim of this study was to analyze the prevalence and risk factors for major aortic wall complications in a large series of adults with either repaired (by surgery or transcatheter) or untreated coarctation of the aorta.

## METHODS

**Study population.** The study population comprised 235 patients diagnosed with coarctation of the aorta seen between January 1990 and December 2002 in the Adult Congenital Heart Diseases Unit at La Paz University Hospital in Madrid. Only patients older than 15 years of age and who had at least one follow-up visit and a supportive Doppler echocardiographic examination were eligible for inclusion. There were 152 males and 83 females, with a mean age of  $27 \pm 13$  years (range 16 to 71 years). According to previous management, patients were classified into three groups: group I included 181 patients who had undergone surgery; group II had 28 patients with percutaneous intervention by balloon angioplasty or stenting; and group III had 26 patients with a non-repaired mild coarctation. The surgical technique of coarctation correction was patch graft aortoplasty ( $n = 76$ ), subclavian flap angioplasty ( $n = 20$ ), end-to-end anastomosis ( $n = 68$ ), or bypass grafting ( $n =$

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**Abbreviations and Acronyms**

BAV = bicuspid aortic valve  
CI = confidence interval  
RR = risk ratio  
TAV = tricuspid aortic valve

11). The operative procedure was not described in detail in six patients (Table 1). Over this period, indications for beta-blocker therapy in our population were hypertension at rest, hypertensive response to exercise, and any evidence of ascending or descending aortic dilation.

**Definitions.** Diagnosis of an aortic wall complication, as suspected by clinical or echocardiographic examination, was confirmed by magnetic resonance angiography, computed axial tomography, or aortography. Only complications that resulted in death or the need for surgical or percutaneous intervention were included in the study. An aortic wall complication was diagnosed when one of the following criteria were present: 1) ascending and descending aortic aneurysm, defined as dilation of a diameter of 55 mm and  $\geq 40$  mm, respectively, in which elective repair was indicated; 2) intimal flap of aortic dissection at the ascending or descending aorta; 3) aortic false aneurysm at the site of coarctation or repair; 4) mycotic aneurysm at coarctation or previous repair site; 5) aortic fistulae into the bronchial tree or cardiac chamber; and 6) acute rupture of the aorta resulting in hypovolemic shock or sudden death (Table 2).

**Risk factors.** Clinical and echocardiographic records were retrospectively reviewed for the following variables: 1) gender; 2) current age; 3) age at coarctation repair; 4) type of repair (surgical or percutaneous); 5) surgical technique for correction; 6) time from repair to current age; 7) systemic hypertension; 8) trans-coarctation Doppler peak systolic pressure gradient; and 9) bicuspid aortic valve (BAV) or tricuspid aortic valve (TAV) morphology. Current age was considered to be the age at last follow-up visit or at the moment of an aortic wall complication occurrence. Systemic hypertension was considered to be present if a resting systolic blood pressure  $>150$  mm Hg or a resting diastolic

**Table 1.** Previous Management in 235 Patients  $>15$  Years Old With Coarctation of the Aorta

Group	Previous Management	Type of Repair	Number of Cases
I	Surgical		181
		Patch graft aortoplasty	76
		Subclavian flap angioplasty	20
		End-to-end anastomosis	68
		Bypass grafting	11
		Unknown	6
II	Balloon angioplasty or stenting		28
III	Not repaired		26

**Table 2.** Aortic Wall Complications in 235 Adults With Coarctation of the Aorta

Aortic Complication	BAV (n = 134, 57%)	No BAV (n = 101, 43%)	Overall (n = 235)
Ascending aortic aneurysm	19 (14%)	3 (3%)	22 (9%)
Descending aortic aneurysm	7 (5%)	3 (3%)	10 (4%)
Aortic rupture	3	1	4
False aneurysm	1	1	2
Aortic dissection	2	0	2
Mycotic aneurysm	2	0	2
Aortobronchial fistula	1	0	1
Fistula ruptured into right atrium	1	0	1
Overall	29 (22%)	8 (8%)	37 (16%)*

\*Five patients had two or more aortic complications.  
BAV = bicuspid aortic valve.

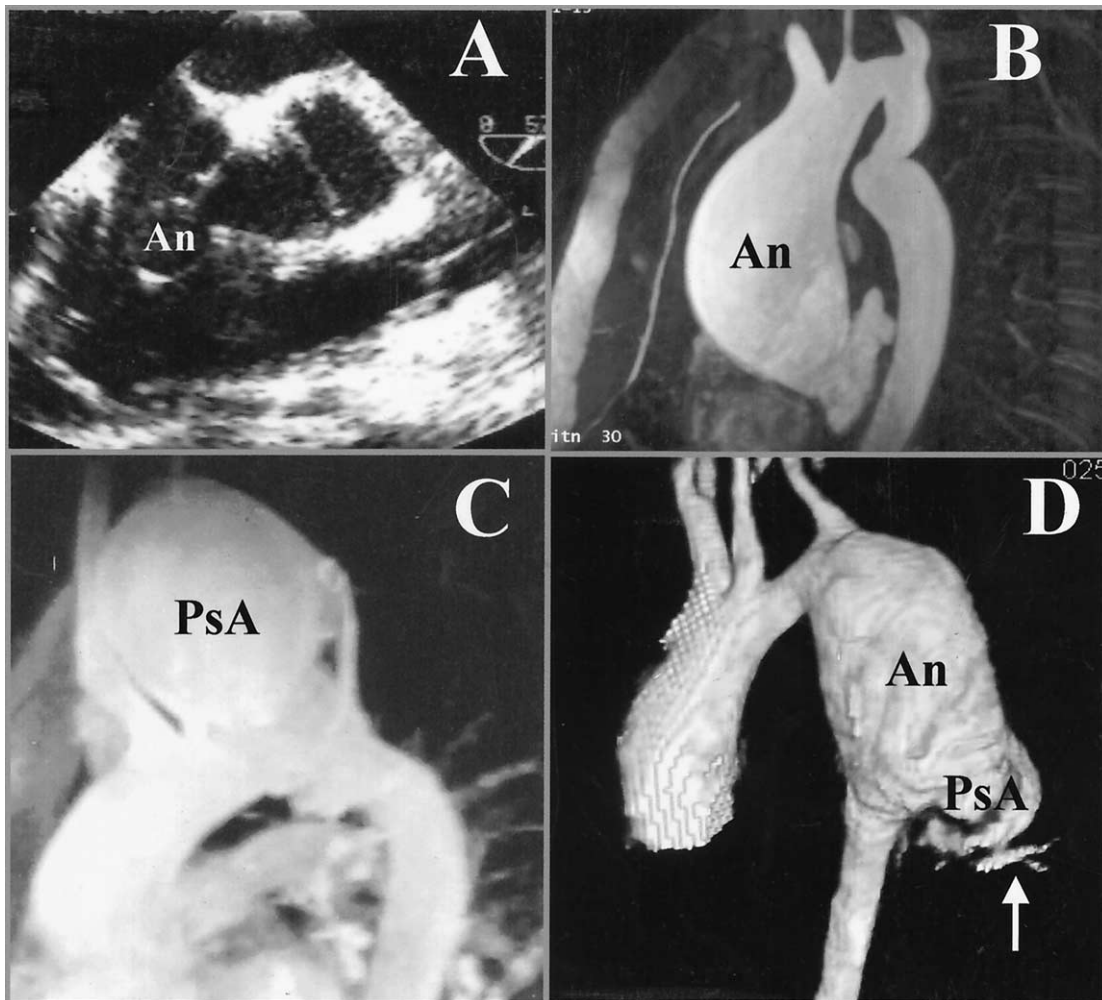
blood pressure  $>90$  mm Hg was measured at three separate readings. Echocardiographic examinations were reviewed for trans-coarctation peak systolic pressure gradient and evaluated by continuous wave Doppler using a 2-MHz imageless probe from the suprasternal view. The peak pressure gradient was determined by Bernoulli's equation. Aortic valve morphology (bicuspid or tricuspid) was assessed by parasternal short-axis two-dimensional echocardiography.

**Statistical analysis.** Data are expressed as the mean value  $\pm$  SD for continuous variables. The Mann-Whitney *U* test was used for comparison of non-normally distributed (as the Kolmogorov-Smirnov test) continuous variables. The Fisher exact test was used to compare noncontinuous variables expressed as proportions. Variables were entered into univariate and multivariate analyses, performed with a stepwise forward logistic regression model. The risk ratio (RR) and 95% confidence intervals (CIs) were calculated with Cox proportional hazards regression models, and  $p < 0.05$  (two-sided) was taken to be significant.

**RESULTS**

Forty-four major aortic wall complications resulting in death or the need for surgical or transcatheter intervention were found in 37 (16%) of 235 adults with coarctation of the aorta. Twenty-two patients (9%) developed an ascending aortic aneurysm, and 10 patients (4%) had a descending aortic aneurysm (Fig. 1). Acute aortic rupture occurred in four cases: two patients died suddenly while they were waiting for surgical intervention of an ascending aortic aneurysm, and two patients had a successful operation for acute rupture of the descending aorta. Other aortic wall complications were acute aortic dissection in two patients, aortic false aneurysm in two patients, mycotic aneurysm at the coarctation site in two patients, aortobronchial fistula in one patient, and right sinus of Valsalva aneurysm ruptured into the right atrium in one patient. Five patients had more than one type of aortic wall complication (Table 2).

**Relation to previous procedure.** There were no differences among the three groups of treatment with respect to the

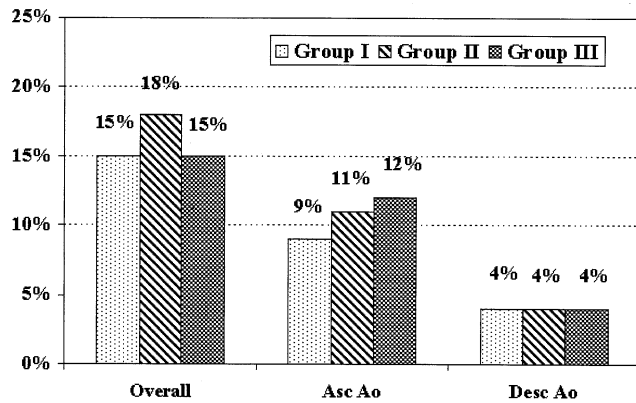


**Figure 1.** (A) Transesophageal echocardiography showing aortic bicuspid valve and right sinus of Valsalva aneurysm ruptured into the right atrium late after balloon dilation of coarctation of the aorta. (B) Magnetic resonance image (MRI) of an ascending aorta aneurysm in a patient with unrepaired mild coarctation of the aorta. (C) This MRI shows a descending aorta giant false aneurysm in another patient with unrepaired mild coarctation. (D) This MRI shows an abnormal bulge of aorta (aneurysm) and a false aneurysm (pseudoaneurysm) late after patch aortoplasty; aortobronchial fistula, causing massive hemoptysis, was also demonstrated (arrow). An = true aneurysm; PsA = false aneurysm.

development of aortic complications: group I had 28 patients (15%) who had operative repair; group II had 5 patients (18%) with percutaneous intervention; and group III had 4 patients (15%) with an unrepaired mild coarctation (Fig. 2). Moreover, a postsurgical aortic complication was observed in 11 of 76 patients (15%) who had correction by patch graft aortoplasty and in 17 of 99 patients (17%) treated by any other type of surgical technique, without a statistically significant difference between subgroups. On the other hand, neither the differences in the prevalence of ascending aortic aneurysms in the three groups (9% in group I, 11% in group II, and 12% in group III) nor the differences in the prevalence of descending aortic aneurysms (4% in the three groups) were statistically significant (Fig. 2). In fact, a descending aortic complication at the site of previous repair occurred in five patients treated by patch graft aortoplasty (6.6%) and in five patients with another type of repair (5%). False aortic aneurysm at or near the site of repair occurred in one patient in group I (patch graft aortoplasty) and one

patient in group III. Four patients had an acute aortic rupture: two in group I (end-to-end anastomosis and bypass grafting) and two in group III. Two patients had an acute dissection: one in group I (patch graft aortoplasty) and one in group II. An aortic mycotic aneurysm developed in one patient in group I (bypass grafting) and one patient in group III. Finally, a fistula from the aorta to right chambers or bronchi occurred in one patient in group I (patch graft aortoplasty) and one patient in group II.

**BAV.** In up to 57% (134 of 235 patients) of our patients with coarctation, a congenitally BAV was found (Table 2). The prevalence of aortic complications was 22% (29 of 134 patients) in those with a BAV, compared with 8% (8 of 101 patients) in those without a BAV ( $p < 0.01$ ). Aortic complications associated with a bicuspid valve account for 86% (19 of 22 patients) of ascending aortic aneurysms and 73% (11 of 15 patients) of descending aortic complications. Interestingly, of the 10 cases of aneurysms at the site of a previous repair, 8 patients had a BAV, as well.

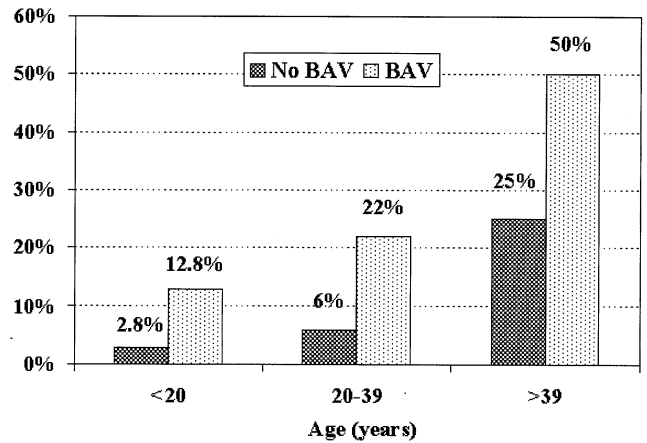


**Figure 2.** Prevalence of aortic complications and ascending (Asc Ao) or descending (Desc Ao) aortic aneurysm in adults with coarctation of the aorta, according to management: surgery (Group I), transcatheter intervention (Group II), or not previously repaired (Group III).

**Risk factors for aortic complications.** Clinical and echocardiographic variables were entered into univariate and multivariate analyses to assess predisposing conditions for aortic complications. A significant relationship between a previous intervention, residual trans-coarctation Doppler pressure gradient, or systemic hypertension was not found (Table 3). Aortic complications were univariately associated with age at intervention ( $16 \pm 15$  years vs.  $10 \pm 14$  years,  $p = 0.027$ ), current age ( $33 \pm 16$  years vs.  $26 \pm 12$  years,  $p = 0.006$ ), and the presence of a BAV (78% in patients with an aortic wall complication vs. 53% in patients without a complication,  $p = 0.005$ ), but they were independently predicted only by the age at the moment of the study (RR 1.4 per decade of age, 95% CI 1.1 to 1.8,  $p = 0.002$ ) and the association with a BAV (RR 3.2, 95% CI 1.7 to 7.5,  $p = 0.005$ ). The prevalence of aortic complications increased from 2.8% in patients younger than 20 years of age without a BAV to 50% in patients older than 39 years of age with BAV (Fig. 3).

**DISCUSSION**

This study shows that aortic wall complications, which result in death or the need for surgery, are frequent during adult life in patients with coarctation of the aorta. Neither surgical repair nor percutaneous intervention prevented the occurrence of aortic complications. Although associated



**Figure 3.** Prevalence of aortic wall complications in patients with coarctation of the aorta when these patients were classified according to age group and coexistence of the bicuspid aortic valve (BAV).

hemodynamic derangement, such as a residual gradient or systemic hypertension, might increase the risk of patients with coarctation of the aorta, they are not found to be related to the development of aortic complications. The only predisposing conditions appear to be advanced age and the coexistence of a BAV.

**Prevalence.** Previous studies have targeted aneurysm formation late after patch aortoplasty, a surgical technique associated with a reported prevalence up to 5% to 50% of aneurysm formation at the site of repair (16-18). Few studies have systematically examined aneurysm development after surgical repair of coarctation of the aorta. Therrien et al. (24) reported a prevalence of 14% in aneurysm formation in 84 adult patients after surgical repair or balloon angioplasty. Aneurysm was defined as a discrete bulging of the aorta at the repair site >150% of the diameter of the descending aorta at the level of the diaphragm. However, aortic aneurysms localized at a distance from the aortic isthmus or other aortic wall complications were not included. A recent report by von Kodolitsch et al. (14) noted that a significant proportion of aneurysms after coarctation repair had developed in the ascending aorta, with extensive aortic widening. In the present study, significant aortic complications resulting in death or the need for surgery are analyzed, including aneurysm formation at the ascending or descending aorta, true or false aneurysms, aortic dissection,

**Table 3.** Risk Factors for Aortic Complications in 235 Adults With Coarctation of the Aorta

Risk Factor	Aortic Complication (n = 37)	Nonaortic Complication (n = 198)	p Value (Univariate)	p Value (Multivariate)
Previous intervention	33 (90%)	178 (90%)	NS	—
Residual pressure gradient (mm Hg)	$22 \pm 12$	$23 \pm 14$	NS	—
Systemic hypertension (%)	6 (21%)	42 (21%)	NS	—
Age at intervention (years)	$16 \pm 15$	$10 \pm 14$	0.027	NS
Current age (years)	$33 \pm 16$	$26 \pm 12$	0.006	0.002
Bicuspid aortic valve (%)	29 (78%)	105 (53%)	0.005	0.005

Data are presented as the mean value  $\pm$  SD or number (%) of subjects.  
NS = not significant.

rupture, mycotic aneurysm, or fistulization. Neither previous repair nor untreated coarctation nor type of surgical or percutaneous intervention was distinguished when the prevalence of aortic complications was analyzed. A total of 44 aortic complications were found in 37 of 235 patients, bringing the prevalence of aortic complications among adults with coarctation of the aorta to 16%. Ascending aortic aneurysms were the most frequently encountered complications with an increase of two-fold in prevalence with respect to that of a descending aortic aneurysm. However, the number of aortic complications in either the ascending or descending aorta could be underestimated because noninvasive screening methods for early detection of complications were not performed.

**Previous repair.** Comparisons of aortic complications between repaired or unrepaired adults with coarctation of the aorta or between surgical or transcatheter repair of the coarctation have not been previously reported. In this study, surgical repair of the coarctation of the aorta had been performed in 77% of patients, balloon angioplasty or stenting in 12%, and the remaining 11% with mild coarctation at diagnosis had not undergone a previous intervention. Remarkably, the prevalence of aortic complications was quite similar in the three groups, and we have not found statistically significant differences in the prevalence of aortic complications between patients corrected by patch graft aortoplasty or other surgical procedures. Several studies have shown that advanced age at coarctation repair may be a significant predictor of late survival and aneurysm formation (1,2,14), but the effect of age at repair might be influenced by the older age at follow-up of patients with late repair. In previously repaired patients of our series, age at repair was significantly older in patients with than in those without aortic complications. However, this difference did not achieve statistical significance in multivariate analysis, probably because the age at repair was directly related to current age, and an advanced age at the moment of the study was the most important risk factor for aortic complications in this study group.

**Predisposing conditions.** Aortic complications may be related to the technique of coarctation repair, hemodynamic derangement imposed by residual coarctation or re-coarctation, intrinsic abnormalities of the aortic wall, or any combination of these three factors. Previous studies have mainly focused on the effect of the repair procedure and emphasized the high prevalence of aneurysm formation at the site of repair in patients with patch graft aortoplasty (16-18). However, aneurysm formation in relation to other techniques of surgical repair, complications localized at a distance from the repair site or even in unrepaired patients, and aortic complications other than aneurysms have not been well characterized to date. In line with previous reports (14), we found that there was no association between the remaining hemodynamic derangement and the development of aortic complications. Although we do not have complete data on catheterization pressure gradients or

arm-leg pressure gradients, neither trans-coarctation peak pressure gradient nor persistent systemic hypertension were significantly related to aortic complication in our series. The only conditions that independently predicted an aortic complication were advanced age and the coexistence of a bicuspid aortic valve. The prevalence of aortic complications was lower than 3% in patients younger than 20 years old without a BAV, but it increased up to 50% in patients older than 39 years old with a BAV (Fig. 3).

**BAV.** Previous studies have shown that aortic dimensions are larger in patients with a BAV than in control subjects with comparable degrees of TAV disease (25). Aortic enlargement in people with a BAV occurs independent of hemodynamic abnormalities (26). Patients with a BAV have thinner elastic lamellae of the aortic media and greater distances between the elastic lamellae than do patients with a TAV (27). Premature medial layer smooth muscle cell apoptosis could be part of a genetic program underlying aortic disease in these patients (28,29). Intrinsic weakness of the aortic wall beyond that predicted by hemodynamic factors might also be responsible for aortic complications in adults with coarctation of the aorta. Coarctation of the aorta is associated with a BAV in more than 50% of patients, and this association has been demonstrated to be a risk factor for ascending aorta aneurysms after coarctation repair (14). However, we did find that the bicuspid valve is also associated with other types of aortic complications in adults with either repaired or non-repaired coarctation of the aorta. The prevalence of a BAV was 86% in an ascending aortic aneurysm, 73% in descending aortic complications, and 80% in an aortic aneurysm at the site of previous surgical repair, compared with 53% in patients without aortic wall complications. Although the study is not powered enough to statistically analyze the small group of patients with complications at the site of previous repair and descending aortic aneurysms, our data show that the BAV might also be a predisposing factor for non-ascending aortic wall complications. Furthermore, marked media degeneration of the aortic wall has been reported in more than 50% of aneurysm wall at the site of surgical repair using patch graft angioplasty (30), suggesting that intrinsic abnormalities of the aortic wall may be responsible, at least in part, for local aneurysm formation after surgery. Recently, it has been noted that the association of coarctation of the aorta and BAV might represent part of the spectrum of a diffuse arteriopathy (31). Unfortunately, a systematic pathologic examination was not available in many of the cases that were sent for surgery in our retrospective series to address these issues, but our findings are also consistent with the hypothesis that intrinsic abnormalities of the aortic wall could be responsible for many aortic complications in patients with coarctation of the aorta.

**Management considerations.** Evaluation of aortic dilation must be treated as a continuum. We have focused on aortic complications that resulted in death or the need for surgery, but many patients have ascending aortic dilation <55 mm

or descending aortic bulging <40 mm, and they might be at risk for further dilation or even dissection and rupture. Adults with coarctation of the aorta, either repaired or not, especially when associated with a bicuspid aortic valve, should be closely followed up for detecting progressive aortic dilation. Whether or not beta-blockers might help to prevent aortic dilation, as demonstrated in Marfan's syndrome (32), is still undetermined. Because most of the patients with aortic dilation in our series, including those with severe aortic complications, were receiving preoperative beta-blockade therapy, our data do not allow us to explore whether beta-blockers were effective in slowing the progression or decreasing the number of events. The timing of surgical repair of aortic dilation in patients with coarctation of the aorta also remains uncertain. Our data suggest that a more aggressive surgical approach should be required when both coarctation and BAV coexist.

**Study limitations.** The retrospective nature of this study may be considered an important limitation, and data should be confirmed by prospective studies. The most confusing factor to be noted in data analysis is the different profile of the three compared groups of patients. The prevalence of systemic hypertension was lower in patients with non-repaired mild coarctation of the aorta (group III), but there were few distinguishable differences in current age, gender, trans-coarctation peak pressure gradient, or prevalence of BAV among the three groups. Furthermore, surgical procedures performed on patients changed over time when a high prevalence of aneurysm formation late after patch aortoplasty was reported (16–18). Despite this fact, we have not found significant differences in the prevalence of aortic complications between patients treated by patch graft aortoplasty or other surgical procedures. Although Doppler pressure gradients based on the Bernoulli equation might not be reliable for detecting re-coarctation, this variable was assessed in our study because complete data on catheterization or arm-leg pressure gradients were not available. Finally, the prevalence of aortic complications might be underestimated because noninvasive screening tests for early detection of aortic complications were not performed. Only those patients with a suspected aortic complication by clinical or echocardiographic examination underwent magnetic resonance angiography, computed axial tomography, or aortography. Although a combination of radiologic and clinical assessment plus transthoracic echocardiography and magnetic resonance angiography in patients with positive results may be an acceptable alternative for detecting aortic complications (21), systematic magnetic resonance screening is a "cost-effective" approach for early detection of aortic complications in adults with coarctation of the aorta, especially when a BAV coexists.

**Conclusions.** Severe aortic complications are prevalent in adults with repaired or non-repaired coarctation of the aorta. The most commonly encountered ones are ascending and descending true aortic aneurysms. However, false aneurysm, aortic rupture, dissection, mycotic aneurysm, and

fistulae also should be considered. The risk of the development of aortic complications increases with age, and it is independently related to coexistence of a BAV. Intrinsic abnormalities of the aortic wall beyond that attributable to associated hemodynamic derangement or previous repair might be responsible for aortic complications. The association between a BAV and coarctation of the aorta would identify a more severe form of aortic wall disease. In the light of these results, close follow-up of all adults with coarctation of the aorta, either repaired or non-repaired, irrespective of hemodynamic status, should be advised for the early detection of aortic wall complications.

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