Archives of Cardiovascular Disease (2019) 112, 305—313

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

CLINICAL RESEARCH

Ten-year follow-up of unreplaced Valsalva sinuses after aortic valve replacement in bicuspid aortic valve disease

Suivi à 10 ans des sinus de Valsalva natifs après remplacement valvulaire aortique en cas de bicuspidie

Ramzi Abi Akar[a,b,*], **Noémie Tence**[a,b], **Jérome Jouan**[a,b], **Wassim Borik**[a,b], **Philippe Menasché**[a,b,c], **Jean-Noel Fabiani**[a,b], **Christian Latremouille**[a,b], **Paul Achouh**[a,b]

[a] *Department of Cardiovascular Surgery, Georges Pompidou European Hospital, AP—HP, 75015 Paris, France*
[b] *School of Medicine, Paris Descartes University, Sorbonne Paris Cité, 75006 Paris, France*
[c] *Inserm U970, PARCC, Paris Descartes University, Sorbonne Paris Cité, 75015 Paris, France*

Received 28 May 2018; received in revised form 24 October 2018; accepted 15 November 2018
Available online 14 February 2019

KEYWORDS
Bicuspid valve;
Valsalva sinus;
Heart valve disease;
Ascending aorta

Summary
Background. — Aortopathy is common in patients with bicuspid aortic valve (BAV).
Aim. — To evaluate the fate of unreplaced Valsalva sinuses in patients with BAV, 10 years after aortic valve replacement (AVR) with or without replacement of the ascending aorta (RAA).
Methods. — We retrospectively reviewed all surgical patients with BAV who were operated on between January 2005 and December 2007. Patients who underwent AVR with or without RAA were included. Surgical data were entered prospectively. Ten-year clinical and echocardiographic follow-up data as well as survival data were collected by contacting the patients and their personal cardiologists, and by consulting the French national mortality registry. Overall, 25% of the patients had computed tomography angiographic assessment of the aortic root at follow-up.
Results. — A total of 133 patients with BAV were operated on within the selected period. Thirty-two patients did not meet the inclusion criteria, and had primary Valsalva sinus surgery. Twenty-four patients underwent AVR with RAA and 77 patients had isolated AVR; all of these 101 patients

* Corresponding author. Department of Cardiovascular Surgery, Georges Pompidou European Hospital, 20, rue Leblanc, 75015 Paris, France.
E-mail address: ramzi.abiakar@aphp.fr (R. Abi Akar).

https://doi.org/10.1016/j.acvd.2018.11.014

were included in the study. The median follow-up was 9 years (up to 12 years). During follow-up, eight patients (7.9%) underwent late reoperation; two of them (2.0%) required root surgery. Ten-year freedom from reoperation was 86.2 ± 4.7%. Ten-year freedom from dilatation of the Valsalva sinuses (>45 mm) was 86.6 ± 5.2%. Ten-year cumulative survival was 83.5 ± 4%.
Conclusions. — Ascending aorta and Valsalva sinuses seem to have different fates after AVR in BAV disease. When the Valsalva sinuses are not dilated at the initial surgery, the risk of secondary dilatation at 10 years is low. Preservation of the sinuses is therefore justified in patients with BAV with a non-dilated root. In BAV with isolated aortic insufficiency, a more aggressive approach may be justified, especially in young patients.

MOTS CLÉS
Bicuspidie ;
Sinus de Valsalva ;
Valvulopathie cardiaque ;
Aorte ascendante

Résumé
Contexte. — L'atteinte de la paroi aortique est fréquente chez les patients ayant une valve aortique bicuspide. Nous avons évalué le devenir des sinus de Valsalva non remplacés chez les patients porteurs de bicuspidie aortique 10 ans un remplacement de la valve aortique (RVA), avec ou sans remplacement de l'aorte ascendante (RAA).
Méthode. — Nous avons examiné rétrospectivement tous les patients ayant une bicuspidie, opérés entre janvier 2005 et décembre 2007. Les patients qui ont bénéficié d'un RVA avec ou sans RAA ont été inclus. Les données chirurgicales ont été entrées prospectivement. Les données de suivi clinique et échocardiographique à dix ans ainsi que les données de survie ont été collectées en contactant les patients, leurs cardiologues et en consultant le Répertoire national français d'identification des personnes physiques (RNIPP) respectivement. Un quart des patients avaient un suivi de la racine aortique par angioscanner.
Résultats. — Cent trente-trois patients avec bicuspidie aortique ont été opérés durant cette période. Trente-deux malades ne répondaient pas au critères d'inclusion. Vingt-quatre patients ont été opérés de RVA avec RAA et 77 patients ont bénéficiés de RVA isolé. Le temps de suivi médian était de 9 ans et le suivi maximal de 12 ans. Durant le suivi, 8 patients (7,9 %) ont été réopérés dont deux pour dilatation du culot aortique (1,9 %). L'absence de réopération et l'absence de dilatation des sinus de Valsalva (> 45 mm) à 10 ans était de 86.2 ± 4.7 % et 86.6 ± 5.2 % respectivement. La survie cumulée à 10 ans était de 83.5 ± 4 %.
Concluison. — L'aorte ascendante et les sinus de Valsalva semblent avoir un destin différent après remplacement de la valve aortique dans la bicuspidie. Lorsque les sinus de Valsalva ne sont pas dilatés au moment de la chirurgie initiale, le risque de dilatation secondaire à 10 ans est faible. La conservation des sinus de Valsalva est donc justifiée chez les patients ayant une valve aortique bicuspide sans dilatation du culot aortique. Dans le cas de valve bicuspide avec insuffisance aortique isolée, une approche plus agressive pourrait être justifiée, notamment chez les patients jeunes.

Abbreviations

AVR	aortic valve replacement
BAV	bicuspid aortic valve
CT	computed tomography
RAA	replacement of the ascending aorta
STJ	sinotubular junction
TAV	tricuspid aortic valve

Background

Bicuspid aortic valve (BAV) is the most common congenital valvular heart disease, affecting 0.9% to 2.0% of the general population [1,2]. In the community, asymptomatic patients with BAV who have no or minimal haemodynamic abnormality enjoy excellent long-term survival, but may experience frequent cardiovascular events, particularly with progressive early valve dysfunction [3]. BAV is also associated with

clinical aortopathy, and presents a higher risk of aneurysm formation and aortic dissection [4]. The development of BAV-related aortopathy has been attributed to genetic and haemodynamic factors. In surgical tissue specimens from patients with BAV, the aortic wall had significantly less fibrillin-1 compared with patients with tricuspid aortic valve (TAV), leading to vascular smooth muscular cell detachment from elastin and collagen, inducing apoptosis and loss of structural integrity. On the other hand, BAV-related haemodynamic factors, such as tensile and shear stresses, also play a role in the pathogenesis of cystic media necrosis [5]. The roles of each of these two factors (constitutional and acquired) are still a matter of debate [6,7].

Ascending aortic dilatation may progress even after successful aortic valve replacement (AVR) [8]. The risk of surgery on the aorta 25 years after BAV diagnosis is 25%, and rises to 53% in case of severe aortic valve stenosis [9]. As a consequence, in asymptomatic BAV, surgical intervention to replace the aortic sinuses or the ascending aorta has been advocated by the most recent American College of Cardiology/American Heart Association guidelines if the diameter is > 55 mm (50 mm in the presence of risk factors) [10]. Replacement of the moderately enlarged ascending aorta (>45 mm) is indicated in case of concomitant surgery for valvular heart disease [11]. However, neither European nor American guidelines differentiate between the aortic root and the supracoronary ascending aorta (tubular aorta) [12].

Older age at time of BAV diagnosis and baseline aortic dilatation seem to be predictors of aneurysm formation. In BAV, tubular ascending aorta dilatation is the most common pattern, and exhibits the fastest growing rate, irrespective of valve morphology and function [13]. Sinus growth rate is slower. Aortic dilatation progresses at the same speed in BAV as in Marfan syndrome, but a significantly higher proportion of patients with BAV do not progress at all [3,14].

After isolated BAV surgery, secondary dilatation of the tubular aorta is well documented [3,9], but the risk of dilatation of unreplaced Valsalva sinuses remains unclear. Very few publications seem to point out that it might be safe to preserve the aortic root in BAV disease [15,16].

Systematic replacement of the aortic root in BAV disease is associated with higher morbimortality compared with replacement of the valve and the tubular aorta, even in experienced hands. Furthermore, if subsequent reoperation is required secondary to bioprosthesis degeneration or mechanical valve complication, redo root replacement can be expected to carry a higher risk than simple redo AVR [17]. In these circumstances, separate valve and tubular aorta replacement seems to be a reasonable surgical option in the setting of AVR for BAV with ascending aortic dilatation, provided that the sinuses of Valsalva are not significantly enlarged [15].

The aim of this study was to evaluate the fate of unreplaced Valsalva sinuses 10 years after AVR for BAV disease.

Methods

The institutional review board of the George Pompidou European Hospital approved this study. All patients gave their consent for inclusion in clinical research projects, and study-specific consent was waived. Patients with BAV undergoing primary AVR with or without replacement of the ascending aorta (RAA) using graft replacement or aortoplasty, between 01 January 2005 and 31 December 2007, were identified via a search of our prospectively managed database. Patients with connective tissue disorders (Marfan syndrome or Ehlers-Danlos syndrome) were excluded, as were those with concomitant procedures on other valves and those operated on urgently for acute aortic syndrome. Perioperative data, including echocardiographic reports, and operative details were reviewed retrospectively. When possible, aortic root and ascending aorta sizes were determined from preoperative as well as the most recent echocardiograms or computed tomography (CT) scans. During the study period, there was no uniform departmental policy regarding size criteria for replacement of the sinuses. Perprocedural judgement was applied to decide whether the Valsalva sinuses were to be replaced or not. In general, sinuses were replaced based on size (>45 mm), age of the patient and ascension of the coronary ostia. Long-term follow-up was assessed using clinical surveys mailed to the patients' cardiologists. The most recent CT angiograms were reviewed and compared with baseline data for each patient, when available. Patients were considered lost to follow-up if their registered phone numbers were no longer valid, their postal addresses were modified without notifying our hospital registry and they did not check in with their cardiologist for follow-up. For these patients, the French national mortality registry was consulted. Patients were not considered dead unless the death certificate was found in the registry.

Statistical analysis

Data analysis was performed using SPSS Statistics software, version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics are expressed as medians (quartiles) for continuous variables and numbers (proportions) for categorical variables. The χ^2 test and Fisher's test were applied to compare subgroups, as appropriate, and Student's t test was used for continuous variables with a normal distribution. Estimates for long-term survival, freedom from reintervention and freedom from aortic dilatation were made using the Kaplan-Meier method. A Cox proportional hazard regression was performed to identify independent multivariable factors predictive of aortic dilatation. First, the log-rank test method and the univariate Cox regression analysis were used to determine univariable predictive factors of late aortic dilatation. Every variable with a P-value < 0.2 was entered into the multivariable Cox proportional hazards regression. Systemic hypertension was also forced into the model for clinical relevance, although it was not found to be associated with late aortic dilatation.

Results

Between January 2005 and December 2007, 133 patients with BAV were operated on in our institution. Twenty-two patients (16.5%) underwent full root replacement, and were excluded from the study. Ten patients (7.5%) who had partial replacement of the non-coronary sinus because of asymmetric enlargement were also excluded. The remaining 101

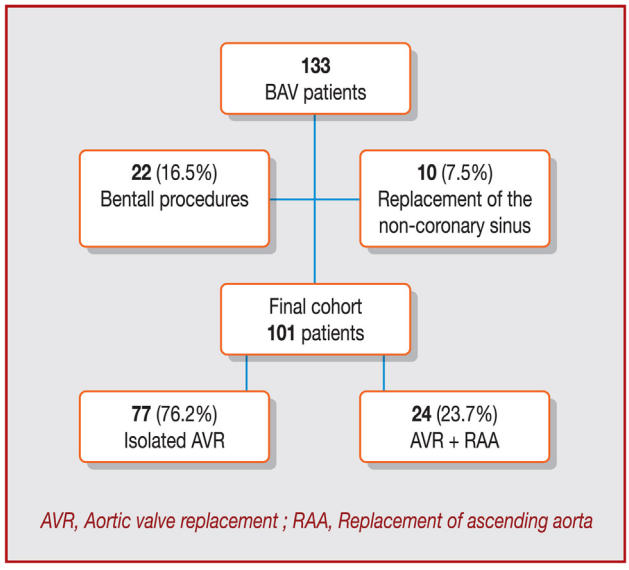

Figure 1. Flow chart of the study population. AVR: aortic valve replacement; BAV: bicuspid aortic valve; RAA: replacement of the ascending aorta.

Table 1 Baseline characteristics at time of surgery ($n = 101$).

Mean age (range) (years)	61.6 (27—87)
Men/women (n/n)	69/32
New York Heart Association	
1	25 (29)
2	44 (51.1)
3	18 (20.9)
4	1 (1.1)
Co-morbidities	
Diabetes mellitus	4 (3.8)
Hypertension	50 (49.5)
Smoking	
No	66 (65.3)
Active	13 (12.9)
Stopped	22 (21.8)
Renal failure	17 (16)
Type of valvulopathy	
Aortic stenosis	70 (69.3)
Regurgitation	20 (19.8)
Mixed	11 (10.9)

Data are expressed as number (%) unless otherwise indicated.

patients constitute the final study cohort (Fig. 1); baseline characteristics are shown in Table 1.

The mean age at the time of surgery was 61.6 ± 13.4 years. Among the 101 patients, 68.3% were male ($n = 69$), 49.5% ($n = 50$) had hypertension and 34.7% ($n = 35$) were smokers. New York Heart Association classification was noted in 86 cases (85.2%) out of the selected cohort.

Operative details

Patients had isolated AVR in 77 cases (76.2%) and AVR with RAA using a Dacron graft in 24 cases (23.8%) (Table 2); baseline characteristics according to type of surgery are shown in Table 3.

Table 2 Operative details.

Surgery	
Isolated AVR	77 (76.2)
AVR and replacement of ascending aorta	24 (23.8)
Type of implanted valve	
Biological	73 (72.3)
Mechanical	28 (27.7)
Cardiopulmonary bypass time, (minutes)	79 ± 21
Aortic cross-clamp time, (minutes)	46 ± 9

Data are expressed as number (%) or mean ± standard deviation.
AVR: aortic valve replacement.

The most frequent valvular dysfunction was aortic stenosis in 70 patients (69.3%), regurgitation in 20 patients (19.8%) and mixed dysfunction in 11 patients (10.9%). A biological valvular prosthesis was used in 73 patients (72.3%), and a mechanical valve prosthesis was used in 28 patients (27.7%). The median age was 64 (27—87) years for those receiving a biological prosthesis, and 53 (27—72) years for those receiving a mechanical valve.

Unfortunately, data were collected retrospectively, and bicuspid phenotype was not specified in our database during that time period.

Early follow-up (at 30 days)

During early follow-up, reoperation occurred in one patient (1.0%) for prosthetic valve dehiscence. Mortality was 2.0% ($n = 2$), and was related to cardiogenic shock in both cases. The first patient was 52 years old; he had severe low-flow low-gradient bicuspid aortic stenosis. The second patient died at the age of 55 years after his fourth surgical reintervention.

Late follow-up

The median follow-up was 9 years, up to a maximum of 12 years. Data concerning survival and freedom from reoperation were complete in 90.1% and 82.2% of patients, respectively. During late follow-up, eight patients (7.9%) underwent late reoperation (Table 4). Two patients (2.0%) required root surgery, and only one patient had a surgical indication for significant Valsalva sinus dilatation >55 mm. The remaining six patients underwent redo surgery for structural degeneration of the bioprosthesis ($n = 3$), perivalvular dehiscence ($n = 1$), aneurysm of the ascending aorta ($n = 1$) and endocarditis ($n = 1$). Three of the patients had RAA and one had transcatheter valve replacement. One patient needed coronary artery bypass surgery in addition to the redo AVR.

No aortic root dissection or rupture was reported during follow-up. The two cases of aortic root reoperation occurred after 6 and 10 years of follow-up, in patients aged 27 years and 36 years, respectively, at the time of the first surgery. Ten-year freedom from reoperation was $86.2 \pm 4.7\%$, as shown in Fig. 2. According to the type of surgery, freedom from reoperation at 10 years was $87.6 \pm 4.9\%$ in isolated

Table 3 Baseline characteristics according to type of initial surgery.

	AVR + RAA	Isolated AVR	*P*
Age (years)	60 [51; 68]	63 [57; 72]	0.14
Hypertension	15 (62.5)	35 (45.5)	0.15
Smoking			
No	15 (62.5)	51 (66.2)	0.94
Active	3 (12.5)	10 (13)	
Stopped	6 (25)	16 (20.8)	
Chronic renal failure	1 (4.2)	16 (21.1)	0.07
Diabetes mellitus	1 (4.2)	3 (3.8)	1.0
Initial pathology			
Aortic insufficiency	7 (29.2)	13 (16.9)	0.19
Aortic stenosis[a]	12 (50)	58 (75.3)	0.02
Aortic insufficiency + aortic stenosis	2 (8.3)	6 (7.8)	1.0
Aneurysm of the ascending aorta	20 (83.3)	6 (7.8)	<0.001
Cardiopulmonary bypass time[a]*, (minutes)*	84 [75; 112]	67 [55; 85]	0.01
Aortic cross-clamp time[a]*, (minutes)*	63 [56; 83]	50 [39; 61]	0.01
Prosthesis			
Mechanical	14 (58.3)	58 (76.3)	0.09
Biological	10 (41.7)	18 (23.7)	

Data are expressed as median [interquartile range] or number (%). AVR: aortic valve replacement; RAA: replacement of the ascending aorta.
[a] $P < 0.05$.

Table 4 Characteristics of patients who required redo surgery.

Age at first surgery (years)	Sex	Years after first surgery	Valsalva sinus dimensions	Initial diagnosis before first surgery	Valsalva sinus dimensions at redo	Reason for reoperation	Type of redo surgery
56	Male	4	ND	AS	38	Endocarditis	Biological AVR + CABG
53	Male	4	ND	AS	40	Valve degeneration + dilatation of the ascending aorta	Mechanical AVR + RAA
27	Male	6	44	AI	44	Valve degeneration	Mechanical Bentall's procedure
66	Female	10	40	AS	37	Valve degeneration	TAVR
36	Male	10	48	AI	65	Valsalva dilatation	Mechanical Bentall's procedure
60	Male	7	43	AS	41	Dilatation of the ascending aorta	RAA
58	Female	9	40	AS	41	Valve degeneration	Biological AVR + RAA
40	Male	0	ND	AI	ND	Perivalvular leak	Mechanical AVR

AI: aortic insufficiency; AS: aortic stenosis; AVR: aortic valve replacement; CABG: coronary artery bypass graft; ND: not determined; RAA: replacement of the ascending aorta; TAVR: transcatheter aortic valve replacement.

AVR, and 80 ± 12.6% in AVR associated with RAA, with no significant difference between the two groups ($P = 0.91$).

Thirteen patients died during follow-up. Five patients (38.5%) died from diagnosed confirmed non-cardiovascular events. Two patients died from cardiovascular events, but aortic rupture and aortic dissection were ruled out. Four patients died beyond the age of life expectancy in western countries, aged 86, 89, 91 and 94 years, corresponding to 8, 7, 5 and 8 years after surgery, respectively. Hence, 11 of these 13 patients (84.6%) may be considered as having

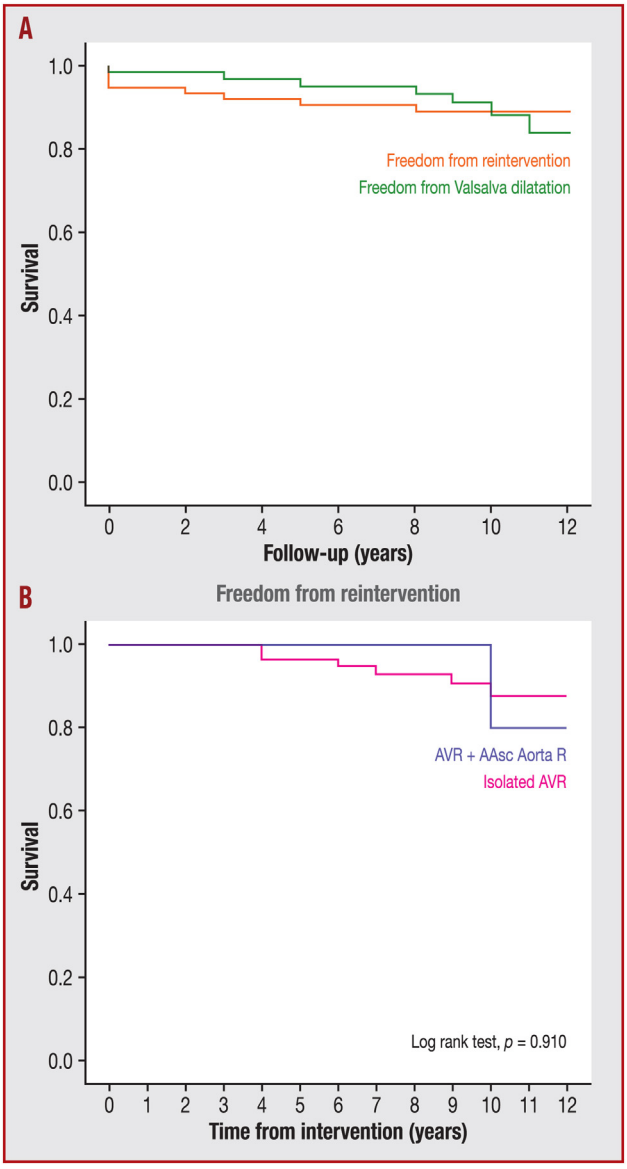

Figure 2. A. Freedom from reoperation and from Valsalva sinus dilatation in operated patients with bicuspid aortic valve. B. Freedom from reoperation for isolated aortic valve replacement (AVR) versus AVR + replacement of the ascending aorta (RAA).

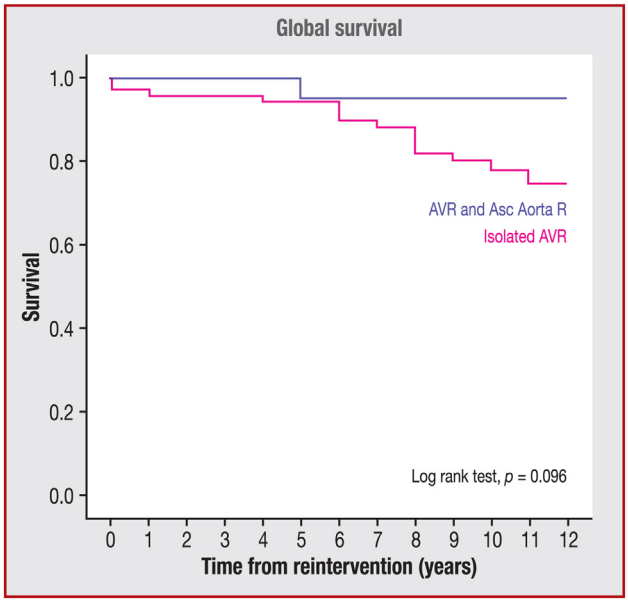

Figure 3. Global survival for isolated aortic valve replacement (AVR) versus AVR + replacement of the ascending aorta (AscAortaR).

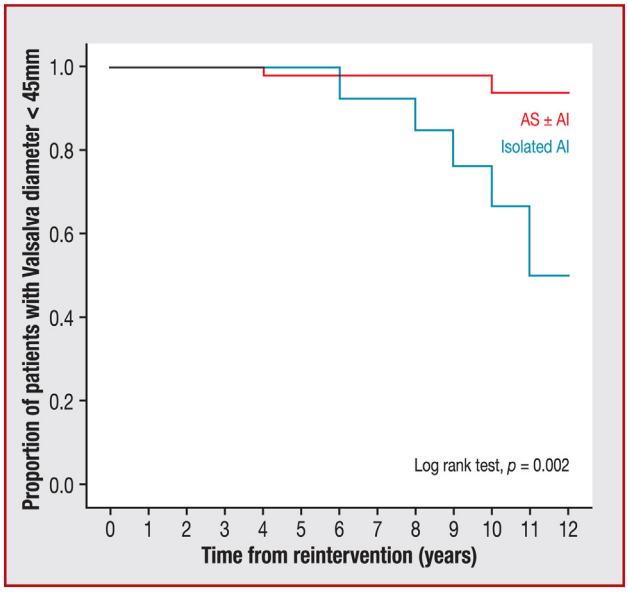

Figure 4. Freedom from Valsalva sinus dilatation in operated patients with bicuspid aortic valve according to initial diagnosis (isolated aortic insufficiency [AI] versus aortic stenosis [AS] ± AI).

''non-aortic related death within general population life expectancy range''. Only two patients had an unknown reason for death, and were below the age of life expectancy; they were aged 68 and 70 years at the time of surgery, and died 6 and 8 years later, respectively. Only one patient had surgery before the age of 60 years; he died 6 years later, and the autopsy did not show aortic rupture or aortic dissection.

The 10-year cumulative survival rate was 83.5 ± 4%. The cumulative survival rates according to the type of surgery were 80 ± 5% for isolated AVR and 95 ± 4.9% for AVR and RAA. The difference did not reach statistical significance ($P = 0.10$) (Fig. 3).

Follow-up echocardiographic or CT angiographic diameters of the aortic root were collected 10 years after surgery in 59 patients (58.4%). Thirty-three patients had transthoracic echocardiography and 26 had CT angiograms. Ten-year freedom from dilatation of the Valsalva sinuses (>45 mm) was 86.6 ± 5.2%. Six patients (5.9%) had an aortic root diameter > 45 mm at the time of last follow-up, and one patient (1.0%) had a diameter > 50 mm. The proportion of patients with an aortic root > 45 mm at late follow-up was significantly higher in patients with an initial diagnosis of aortic insufficiency than in patients with aortic stenosis ($P = 0.002$) (Fig. 4). The univariate analysis also showed that age at initial surgery affected the proportion of patients with an aortic root > 45 mm at late follow-up ($P = 0.001$). In contrast, neither renal insufficiency ($P = 0.99$) nor the type of intervention ($P = 0.89$) seemed to be related to this variable. In the multivariable analysis, with hypertension as a forced

Table 5 Multivariable analysis for Valsalva dilatation > 45 mm.

	Hazard ratio	95% confidence interval	*P*
Age	1.08	1.02—1.15	0.01
Aortic insufficiency	3.01	0.45—20.11	0.26
Arterial hypertension	0.97	0.16—5.95	0.98

variable entered into the model ($P = 0.30$), only age at the time of the initial surgery was found to be correlated with late aortic root dilatation ($P = 0.013$) (Table 5).

Discussion

The present study shows that patients with BAV undergoing AVR with or without RAA have a 2.0% risk of reoperation for dilatation of the aortic root at 10-year mean follow-up. These findings confirm the Mayo clinic experience published recently by Park et al. [15]; in their report, freedom from root reoperation was 97.6%, 94.9% and 85.5% at 1, 5 and 10 years, respectively. All of their patients had undergone AVR and repair of the ascending aorta without root replacement, with significant reduction in the diameter of the sinotubular junction (STJ). The authors concluded that there was no significant dilatation of non-replaced sinuses of Valsalva in BAV up to 17 years after initial surgery. According to Park et al., the reduction in the STJ diameter may have been responsible for stabilization of the root over time, and the lack of subsequent root dilatation. In our study, 76% of the patients had isolated AVR (without RAA); still, most of the patients in our series did not develop a dilated aortic root. Therefore, stabilizing the STJ is not the only factor that prevents later dilatation. Restoring more uniform pressure distribution and flow patterns across the aortic orifice may also play a role in preventing root dilatation. In favour of the latter assumption is the study by Regeer et al. [18], who investigated the effect of AVR on aortic root dilatation rate in patients with BAV and TAV. In their report, faster annual dilatation of the aortic root was observed in patients with BAV compared with TAV before AVR. After AVR surgery, dilatation rates were similar in BAV and TAV, suggesting that an important role is played by haemodynamic factors in aortic root dilatation.

Juraszek et al. [19] showed, in an ex-vivo model, that BAV was associated with significant pressure differences in various locations within the ascending aorta compared with TAV. The altered pressure distributions and flow patterns in the ascending aorta may add further to the understanding of aneurysmal development in patients with BAV. It seems that dynamics after AVR simulate those found in native TAV. This hypothesis may explain the low rate of root dilatation in BAV in our study, even after isolated AVR.

If the aortic root is not dilated at the time of AVR in BAV, the risk of secondary dilatation is very low. That risk seems to be similar to TAV, according to Charitos et al. [20]. In their report, the sinus of Valsalva dimensions increased at a rate of 0.13 ± 0.04 mm/year. This increase in aortic root diameters was similar to that expected in an age-, sex- and body surface area-matched German general population (0.02 ± 0.02 z-values/year; $P = 0.22$). No difference in the initial Valsalva sinus diameters (Δintercept 0.6 ± 0.5 mm; $P = 0.2$) or in the rate of increase with time (Δslope 0.08 ± 0.05 mm/year; $P = 0.12$) could be observed between BAV and TAV.

Genetic factors and histopathologic alterations can partially explain the aortopathy associated with BAV; they are both associated with abnormal regulatory pathways of smooth muscle cell in aortic media, causing apoptosis and disruption of the media layer, which adversely affect the structural integrity and flexibility of the aorta [7]. These alterations are well documented in the ascending aorta. Many studies have shown dilatation of the ascending aorta years after replacement of the BAV [4,9]. These alterations seem to affect the aortic sinuses to a lesser extent, as reflected in our results, as well as in those of Park et al. [15].

We did not notice any aortic rupture or dissection during follow-up. Such findings have also been reported by other groups [15,20]. Michelena et al. reported, while exploring the incidence of aortic complications in patients with BAV, that a baseline aortic diameter of $\geq$ 40 mm at diagnosis of BAV was an independent predictor of future elective aortic aneurysm repair. The incidence of aortic dissection in their series was 44.9 per 10,000 patient-years compared with 0.31 per 10,000 patient-years in the general population of Olmsted county [9]. We still need larger cohorts to study the protective effect of AVR and STJ stabilization on the incidence of aortic dissection.

On the other hand, the aortic root seemed to have a different fate depending on the culprit aortic valve disease at the time of initial surgery: patients with pure aortic insufficiency had a dilated sinus at 10-year follow-up more frequently then patients with aortic stenosis (with or without insufficiency) ($P = 0.011$). This difference between the two subgroups was not reported in earlier series. Larger series with preoperative and postoperative aortic measurements are needed to confirm these findings. We do not think that these findings will affect the threshold recommended in European and American guidelines for Valsalva sinus replacement in case of BAV disease. If confirmed by further studies, it might lower this threshold in patients with isolated aortic insufficiency who need surgery.

In a report by Charitos et al., patient age, male sex and the presence of pure aortic regurgitation were associated with increased initial aortic diameters. However, these factors did not influence the rate of diameter increase with time [20]. In contrast, Shan et al. studied the impact of valve function on haemodynamic status within the ascending aorta. The location of peak aortic wall shear stress and type of aortopathy remained homogeneous among patients with right-left BAV, irrespective of valve dysfunction. Severe aortic insufficiency or stenosis resulted in further elevated aortic wall shear stress and exaggerated flow eccentricity [21].

Our study supports a rather conservative strategy in dealing with non-dilated or moderately dilated sinus in the presence of BAV at the time of surgery for AVR. In the case of a non-significantly enlarged sinus of Valsalva, complications related to coronary implantation have been documented even in experienced hands. In our cohort, the overall

reoperation rate was 7.9%, and root-related reoperation did not exceed 2.0%. Considering the low risk of reoperation on the aortic root, systematic replacement of the aortic root is hardly justified. In this setting, separate valve and graft repair seems to be a reasonable surgical option in the setting of AVR for BAV with ascending aortic dilatation.

Furthermore, if subsequent reoperation is required secondary to structural valve deterioration of the bioprosthesis or mechanical valve complication, redo root replacement can be expected to carry a higher risk than simple redo AVR [17]. Indeed, in a study by Chiang et al. comparing biological versus mechanical aortic valves in patients aged between 50 and 69 years, the cumulative incidence of aortic valve reoperation at 15 years was 12.1% (95% confidence interval 8.8—15.4%) for the bioprosthesis group and 6.9% (95% confidence interval 4.2—9.6%) for the mechanical prosthesis group [22]. In another report by Glaser et al., aortic valve reoperation was needed in 2.2% (21/939) of the mechanical valve group, and in 5.2% (49/939) of the bioprosthetic valve group at 16-year follow-up [23]. A meta-analysis by Mookhoek et al. showed an annual linearized rate of 0.46% for aortic root reoperation after the Bentall procedure with a mechanical valve prosthesis [24].

Study limitations

Our study is subject to the limitations inherent in a single-centre retrospective cohort design. The main limitation is the lack of quantitative data about the dimensions of the sinuses at the time of surgery. Ultrasound was almost the only technique used to identify a dilated Valsalva sinus during the preoperative workout. The decision to replace the aortic root was based on a medicosurgical team consensus, and validated by the surgeon's eyeballing during the procedure, rather than specific preoperative CT root measurement. In addition, follow-up echocardiographic or CT angiographic measurements of the aortic root were collected in only 58.4% of cases. This heterogeneous data imaging made quantitative progression evaluation unfeasible. Nevertheless, this is a series of patients with a median follow-up exceeding 9 years, and we believe that the findings are clinically useful.

Conclusions

Ascending aorta and Valsalva sinuses seem to have different fates after AVR in BAV disease. When the Valsalva sinuses are not dilated at the initial surgery, the risk of secondary dilatation at 10 years is low. Preservation of the sinuses is therefore justified in patients with BAV with non-dilated root. In BAV with isolated aortic insufficiency, a more aggressive approach may be justified, especially in young patients. Further dedicated studies are needed to explore the quantitative rate of root size progression in this specific population.

Funding

None.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Nkomo VT, Enriquez-Sarano M, Ammash NM, et al. Bicuspid aortic valve associated with aortic dilatation: a community-based study. Arterioscler Thromb Vasc Biol 2003;23:351—6.
[2] Roberts WC. The congenitally bicuspid aortic valve. A study of 85 autopsy cases. Am J Cardiol 1970;26:72—83.
[3] Michelena HI, Desjardins VA, Avierinos JF, et al. Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. Circulation 2008;117:2776—84.
[4] Keane MG, Wiegers SE, Plappert T, Pochettino A, Bavaria JE, Sutton MG. Bicuspid aortic valves are associated with aortic dilatation out of proportion to coexistent valvular lesions. Circulation 2000;102 [III35—9].
[5] Tadros TM, Klein MD, Shapira OM. Ascending aortic dilatation associated with bicuspid aortic valve: pathophysiology, molecular biology, and clinical implications. Circulation 2009;119:880—90.
[6] Girdauskas E, Borger MA, Secknus MA, Girdauskas G, Kuntze T. Is aortopathy in bicuspid aortic valve disease a congenital defect or a result of abnormal hemodynamics? A critical reappraisal of a one-sided argument. Eur J Cardiothorac Surg 2011;39:809—14.
[7] Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. N Engl J Med 2014;370:1920—9.
[8] Yasuda H, Nakatani S, Stugaard M, et al. Failure to prevent progressive dilation of ascending aorta by aortic valve replacement in patients with bicuspid aortic valve: comparison with tricuspid aortic valve. Circulation 2003;108 [II291-4].
[9] Michelena HI, Khanna AD, Mahoney D, et al. Incidence of aortic complications in patients with bicuspid aortic valves. JAMA 2011;306:1104—12.
[10] Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;70:252—89.
[11] Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Thorac Cardiovasc Surg 2014;148:e1—132.
[12] Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur J Cardiothorac Surg 2012;42:S1—44.
[13] Schaefer BM, Lewin MB, Stout KK, et al. The bicuspid aortic valve: an integrated phenotypic classification of leaflet morphology and aortic root shape. Heart 2008;94:1634—8.
[14] Detaint D, Michelena HI, Nkomo VT, Vahanian A, Jondeau G, Sarano ME. Aortic dilatation patterns and rates in adults with bicuspid aortic valves: a comparative study with Marfan syndrome and degenerative aortopathy. Heart 2014;100:126—34.
[15] Park CB, Greason KL, Suri RM, Michelena HI, Schaff HV, Sundt TM. Fate of nonreplaced sinuses of Valsalva in bicuspid aortic valve disease. J Thorac Cardiovasc Surg 2011;142:278—84.

[16] Sundt TM, Mora BN, Moon MR, Bailey MS, Pasque MK, Gay Jr WA. Options for repair of a bicuspid aortic valve and ascending aortic aneurysm. Ann Thorac Surg 2000;69:1333—7.
[17] Etz CD, Plestis KA, Homann TM, et al. Reoperative aortic root and transverse arch procedures: a comparison with contemporaneous primary operations. J Thorac Cardiovasc Surg 2008;136:860—7 [7e1-3].
[18] Regeer MV, Versteegh MI, Klautz RJ, et al. Effect of aortic valve replacement on aortic root dilatation rate in patients with bicuspid and tricuspid aortic valves. Ann Thorac Surg 2016;102:1981—7.
[19] Juraszek A, Dziodzio T, Stoiber M, et al. The influence of bicuspid aortic valves on the dynamic pressure distribution in the ascending aorta: a porcine ex vivo model. Eur J Cardiothorac Surg 2014;46:349—55 [Discussion 55].
[20] Charitos EI, Stierle U, Petersen M, et al. The fate of the bicuspid valve aortopathy after aortic valve replacement. Eur J Cardiothorac Surg 2014;45:e128—35.
[21] Shan Y, Li J, Wang Y, et al. Aortic shear stress in patients with bicuspid aortic valve with stenosis and insufficiency. J Thorac Cardiovasc Surg 2017;153 [1263e1—1272e1].
[22] Chiang YP, Chikwe J, Moskowitz AJ, Itagaki S, Adams DH, Egorova NN. Survival and long-term outcomes following bioprosthetic vs mechanical aortic valve replacement in patients aged 50 to 69 years. JAMA 2014;312:1323—9.
[23] Galser N, Jackson V, Holzmann MJ, Franco-Cereceda A, Sartipy U. Aortic valve replacement with mechanical vs. biological prostheses in patients aged 50—69 years. Eur Heart J 2016;37:2658—67.
[24] Mookhoek A, Korteland NM, Arabkhani B, et al. Bentall procedure: a systematic review and meta-analysis. Ann Thorac Surg 2016;101:1684—9.