ORIGINAL ARTICLE

Mechanisms of Dysfunction and Prognostic Markers in Bicuspid Aortic Valve

Mecanismos de la disfunción y marcadores pronósticos en la válvula aórtica bicúspide

MARÍA C. CARRERO [1], GONZALO R. DÍAZ BABIO [1,2], GERARDO MASSON JUAREZ [1,2], IVÁN CONSTANTIN [1], FACUNDO VERÓN [1,3], MARÍA D.C. MEZZADRA [1,2], GUSTAVO L. VERA JANAVEL [1], PABLO G STUTZBACH [1]

ABSTRACT

Background: The most common complication of the bicuspid aortic valve (BAV) is aortic valve dysfunction, but it is difficult to predict which patients will develop aortic stenosis (AS) or significant aortic regurgitation (AoR) (moderate/severe).
Objectives: The aim of this work was to analyze the progression and the variables associated with the development of AS and significant AoR in adults with BAV.
Methods: Consecutive patients with BAV were studied between 2009 and 2017. The progression of their aortic valve dysfunction was analyzed and in the group without baseline dysfunction, significant predictors of AoR and AS were identified through univariate and multivariate analysis.
Results: Two hundred and forty-three patients (mean age 43±14.9 years, 73.2% men) were included in the study. The majority (n=194, 79.8%) with type I and raphe BAV (n=179, 73.6%). In the baseline echocardiogram, 111 patients presented mild (45.6%); 49, moderate (20.1%); and 10, severe (4.1%) AoR. Baseline AS was less frequent: 20 subjects had moderate (8.2%) and 12, severe (4.9%) AS.
Two patients died and 20 valve surgeries (8.2%) were performed in 4.7±1.7 follow-up years. Patients with significant baseline valve dysfunction presented a higher rate of progression requiring valve surgery (p<0.0001). There were 39 new cases (17.2%) of significant AoR or AS at follow-up. Aortic valve prolapse (p<0.001) and male sex (p<0.04) were associated with the development of significant AoR (p<0.001). Baseline calcification score was associated with significant AS (p<0.02).
Conclusions: A high proportion of patients with BAV and significant baseline aortic valve dysfunction required short-term surgery. Clinical and morphological characteristics associated with the development of significant aortic valve dysfunction were identified.

Keywords: Bicuspid aortic valve- Aortic regurgitation- Aortic stenosis- Aortic valve replacement

RESUMEN

Introducción: La complicación más frecuente de la válvula aórtica bicúspide (VAB) es la disfunción valvular aórtica, pero resulta complejo predecir qué pacientes desarrollarán estenosis aórtica (EAO) o insuficiencia aórtica (IAO) significativa (moderada/grave).
Objetivos: Este trabajo busca analizar la progresión y las variables asociadas con el desarrollo de EAO e IAO significativa en adultos con VAB.
Material y métodos: Se incluyeron pacientes consecutivos con VAB (2009-2017), se analizó la progresión de la disfunción valvular aórtica y en el grupo sin disfunción basal se identificaron variables predictoras de IAO y EAO significativas mediante análisis uni- y multivariados.
Resultados: Se incluyeron 243 pacientes (43±14,9 años, 73,2% hombres). La mayoría (n=194, 79,8%) con VAB tipo I y rafe (n=179; 73,6%). En el ecocardiograma basal, 111 pacientes presentaban IAO leve (45,6%); 49, moderada (20,1%); y 10, grave (4,1%). La EAO basal fue menos frecuente: 20 sujetos tuvieron EAO moderada (8,2%) y 12, EAO grave (4,9%).
Hubo 2 muertes y 20 cirugías valvulares (8,2%) en 4,7±1,7 años de seguimiento. Los pacientes con disfunción valvular significativa basal presentaron mayor tasa de progresión y requerimiento de cirugía valvular (p<0,0001). Hubo 39 nuevos casos (17,2%) de IAO o EAO significativas en el seguimiento. El prolapso valvular aórtico(p<0,001) y el sexo masculino (p<0,04) se asociaron al desarrollo de IAO significativa (p<0,001). El score de calcificación basal se asoció con EAO significativa (p<0,02).
Conclusiones: Los pacientes con VAB y disfunción valvular aórtica significativa basal requirieron cirugía en una elevada proporción a corto plazo. Se identificaron características clínicas y morfológicas asociadas con el desarrollo de disfunción valvular aórtica significativa.

Palabras clave: Válvula aórtica bicúspide- Insuficiencia aórtica- Estenosis aórtica- Reemplazo valvular aórtico

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Address for reprints: María Celeste Carrero. dra.celestecarrero@gmail.com, von Wernicke 3031 - B1609JRA. San Isidro, Buenos Aires, Argentina. ICSI, Sanatorio Las Lomas. +54-11- 4129-5500.

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[1] Instituto Cardiovascular San Isidro (ICSI), Sanatorio Las Lomas, Buenos Aires, Argentina
[2] Instituto Cardiovascular San Isidro (ICSI). Nordelta Seat, Buenos Aires, Argentina
[3] Instituto Cardiovascular San Isidro (ICSI). Pilar Seat, Buenos Aires, Argentina

Abbreviations

AoR	Aortic regurgitation
AS	Aortic stenosis
AVD	Aortic valve dysfunction
AVR	Aortic valve replacement
BAV	Bicuspid aortic valve
BSA	Body surface area
IQR	Interquartile range
LVEDD	Left ventricular end-diastolic diameter
LVEF	Left ventricular ejection fraction
TAV	Tricuspid aortic valve
TDE	Transthoracic Doppler echocardiography

INTRODUCTION

More than five centuries ago, Leonardo Da Vinci described in one of his drawings the optimal geometry of a tricuspid aortic valve (TAV), as opposed to a quadricuspid and a bicuspid valve. But it was not until the 19th century that the bicuspid aortic valve (BAV) was associated with an increased risk of aortic valve dysfunction (AVD) and infective endocarditis. (1)

Bicuspid aortic valve is a common and clinically relevant entity, both for complications related with the aortic valve (AVD, infective endocarditis) as for its frequent association with aortic aneurysm; therefore, it is conceived as a valve-aortopathy. (2) However, not all patients with BAV develop complications throughout their lifetime. (3. 4)

Aortic valve dysfunction leads to the development of aortic stenosis (AS) or aortic regurgitation (AoR), or both, at much younger ages than in the general population. In fact, it is the first cause of aortic valve replacement (AVR) in patients under 65 years of age. (5) Although AoR is more frequent since the second decade of life, AS progresses significantly in patients with BAV since 40 years of age. The factors that lead a patient with BAV to develop valve dysfunction are still discussed. Those classically described include anatomical features such as valve phenotype, the presence of fusion raphe, valve calcification, dilatation of the aortic root and the aortic annulus and valve prolapse. (4-11)

At present, it is difficult to predict what the evolution of AVD will be in a patient diagnosed with BAV. There are few longitudinal studies that evaluate the history of the disease with the therapies available today. (3, 4) There is also little information on the prognosis of this pathology in Argentina, as well as on the incidence of AVD or its progression.

Although some recent studies analyze the impact of BAV phenotype on the evolution of AVD, there are almost no publications exploring all the mechanisms of AVD in patients with BAV who develop AS or AoR. (4, 5, 8) It is still unknown if there are valve characteristics that can be identified in the initial stages to predict the progression to AVD. (12)

Our working team considers that the identification of certain initial characteristics would allow early detection of those patients who will develop significant AoR or AS and would therefore require closer monitoring. Therefore, we proposed an observational and prospective study, with the following objectives:

- Analyze the baseline clinical and echocardiographic characteristics of adult patients with BAV
- Analyze the progression of aortic AVD
- Identify variables (anatomical and clinical) associated with the development of significant AVD during follow-up.

METHODS

Population

All consecutive patients with a confirmed diagnosis of BAV (2009-2017) were prospectively followed-up in our health network, which includes second and third level complexity institutions (ICSI Las Lomas, ICSI Nordelta and ICSI Pilar).

The inclusion criterion was BAV confirmed with transthoracic Doppler echocardiography (TDE). In cases with uncertain findings, another method was used to confirm the diagnosis (transesophageal echocardiogram, cardiac magnetic resonance imaging or cardiac multislice computed tomography). All the patients included signed an informed consent, approved by our institution. Patients under 18 years of age, who had previously undergone surgical procedures due to BAV, with familial aortopathies, Marfan syndrome or complex congenital heart diseases were excluded from the study.

Study protocol and endpoints

All procedures followed the principles of the Declaration of Helsinki and Good Clinical Practice standards.

All patients underwent baseline TDE and follow-up imaging studies. Baseline clinical characteristics, as age, gender, height, weight, presence of major cardiovascular risk factors (hypertension defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, diabetes, smoking and dyslipidemia), first-degree family history of BAV or aortopathy, symptoms (dyspnea according to the classification of the New York Heart Association, angina or syncope) and regular medications were analyzed. Body surface (BSA) was calculated with the DuBois formula ($m2=0.007184 \times$ height (cm)$0.725 \times$ weight (kg)0.425.

The images were recorded in DICOM format for off-line audit by two experienced cardiologists (MCC and PS), masking previous measurements and patient data.

Follow-up was initiated at the time of the first TDE, with subsequent consultations by the valvulopathy team and studies analyzing the progression of AVD, valve calcification and aortic diameters. (20) Multislice computed tomography angiography or cardiac magnetic resonance imaging was performed on a subgroup of patients, and to unify measurements, the same cut-off points used for TDE were considered.

Through the analysis of the clinical history and direct communication with the patient or his family, or with the attending physician (by telephone contact), the progres-

	Total (n=243)	BAV Type I (n=195)	BAV Type II (n= 32)	p
Age, years	43.1 ± 14.9	41.9 ± 14.7	45.1 ± 15.3	NS
Men, n (%)	178 (73.2)	142 (72.8)	26 (81.2)	NS
European origin, n (%)	226 (93.2)	183 (93.8)	30 (93.7)	NS
Hypertension, n (%)	47 (19.4)	33 (18.8)	6 (18.7)	NS
Diabetes mellitus, n (%)	6 (2.5)	1 (0.5)	3 (9.3)	0.03
Smoking, n (%)	35 (14.4)	28 (14.3)	3 (9.3)	NS
Dyslipidemia, n (%)	28 (11.5)	20 (10.2)	4 (12.5)	NS
BAV as finding, n (%)	173 (71.2)	142 (72.8)	21 (65.6)	NS
Age at diagnosis, years	36.3 ± 15.7	35.6 ± 15.4	36.9 ± 17.1	NS
Weight (kg)	77.5 ± 15.5	77.1 ± 15.3	80.4 ± 16.5	NS
Height (cm)	172.5± 8.5	172.8 ± 8.5	171.9 ± 7	NS
BSA - Dubois (m2)	1.81 ± 0.21	1.80 ± 0.22	1.92 ± 0.18	NS
LVEF,%	64.2 ± 6.3	63.7 ± 6	63.5 ± 4.8	NS
LAV, ml/m2	26.3 ± 8.1	26.1 ± 8.2	26.5 ± 8.3	NS
Creatinine, mg/dL	0.90 ± 0.17	0.89 ± 0.17	0.93 ± 0.17	NS
Total cholesterol mg/dL	193.1 ± 39	191.9 ± 36.2	202.1 ± 55.2	NS

BAV: Bicuspid aortic valve. BSA: Body surface area. LVEF: Left ventricular ejection fraction. LAV: Left atrial volume indexed by body surface area. The results are expressed as mean ± SD.

Table 1. Baseline characteristics of patients according to valve phenotype

sion of AVD and the incidence of events were documented: AVR, aortic surgery or combined surgery, the cause of the intervention, aortic dissection, infective endocarditis and/or death.

The patient follow-up protocol included consultation and annual TDE in patients without AVD or with mild dysfunction, and in those with significant AVD (moderate / severe), a face-to-face visit every 3-6 months.

In all cases, the indication for surgical intervention was taken by the valve disease team and was performed mainly in the presence of symptoms. In asymptomatic patients, the surgical decision was made based on evident left ventricular dysfunction [left ventricular ejection fraction (LVEF) ≤55%, left ventricular end-diastolic diameter (LVEDD) ≥75 mm] or aortic diameters ≥55 mm. (14)

Echocardiographic examination

All patients underwent a conventional and complete baseline TDE with 2 to 4 Mhz transducer (Vivid S5, GE® Vingmed Ultrasound, Israel, and Vivid T8, GE® Medical Systems, China), in charge of a team of five cardiologists specialized in echocardiography and trained in aortic measurement (Level III).

Bicuspid aortic valve diagnosis was based on the detection in short axis parasternal projection at the level of the large vessels of an elliptical aortic valve opening and the identification of two leaflets in mid-systole and two commissures, and of eccentric aortic valve closure or aortic valve dome-shaped opening. Multiple views were obtained to corroborate the diagnosis.

Measurements of routine echocardiographic variables (left ventricular diameters, LVEF, left atrial volume, aortic valve and left ventricular outflow tract velocities, and systolic pulmonary artery pressure estimation) were performed in all patients. Left ventricular mass indexed by BSA, relative wall thickness, left atrial volume indexed by BSA and the E/A ratio were recorded

Aortic stenosis was classified as mild [aortic valve area (AVA) >1.5 cm2, peak gradient <36 mmHg], moderate (AVA 1-1.5cm2, peak gradient 36-64 mmHg) or severe (AVA<1 cm2, peak gradient >64 mmHg). (13, 14) Aortic regurgitation was graded as mild, moderate and severe using a comprehensive diagnostic approach, which incorporated quantitative and semiquantitative criteria (left ventricular diameters, regurgitant jet to outflow tract ratio, pressure half time, presence of holodiastolic flow reversal in the descending aorta, vena contracta width and effective regurgitant orifice area). (15, 16) Moderate or severe dysfunction were consistent with significant AVD.

Risk factors for valve dysfunction

Patients were divided into two groups: those without or with significant baseline AVD (i.e., moderate or severe dysfunction). In the patients of the first group, different variables that could be associated with the development of AVD during follow-up were evaluated (valve phenotype, presence of raphe, valve prolapse, valve calcification, aortic dilatation, etc.).

The valve phenotype was classified as follows: I, fusion of the coronary leaflets; II, fusion of the right coronary and non-coronary leaflets; and III, fusion of the left coronary and non-coronary leaflet. (6)

The presence or absence of raphe was confirmed and the reviewers determined a posteriori the degree of calcification from 0 to 3 (absent, mild, moderate or severe). (9) In addition, in patients without significant baseline dysfunction, the Michelena score was calculated by adding the degree of calcification, valve thickening and baseline leaflet mobility restriction (this score ranged from 0 to 3, from normal to severe). (4)

A valve degeneration score was defined varying from 0 to 9 points. In all patients, the presence of aortic valve prolapse was established, defined as valve protrusion ≥1 mm through the aortic annulus plane in left parasternal view or in 5-chamber view (Supplementary material). (11)

Aortic dimensions were evaluated at 6 levels: aortic annulus, sinuses of Valsalva, sino-tubular junction, proximal ascending aorta, aortic arch and proximal descending aorta, with superior edge to superior edge technique at end-diastole. A diameter ≥23.5 mm defined annular dilatation and

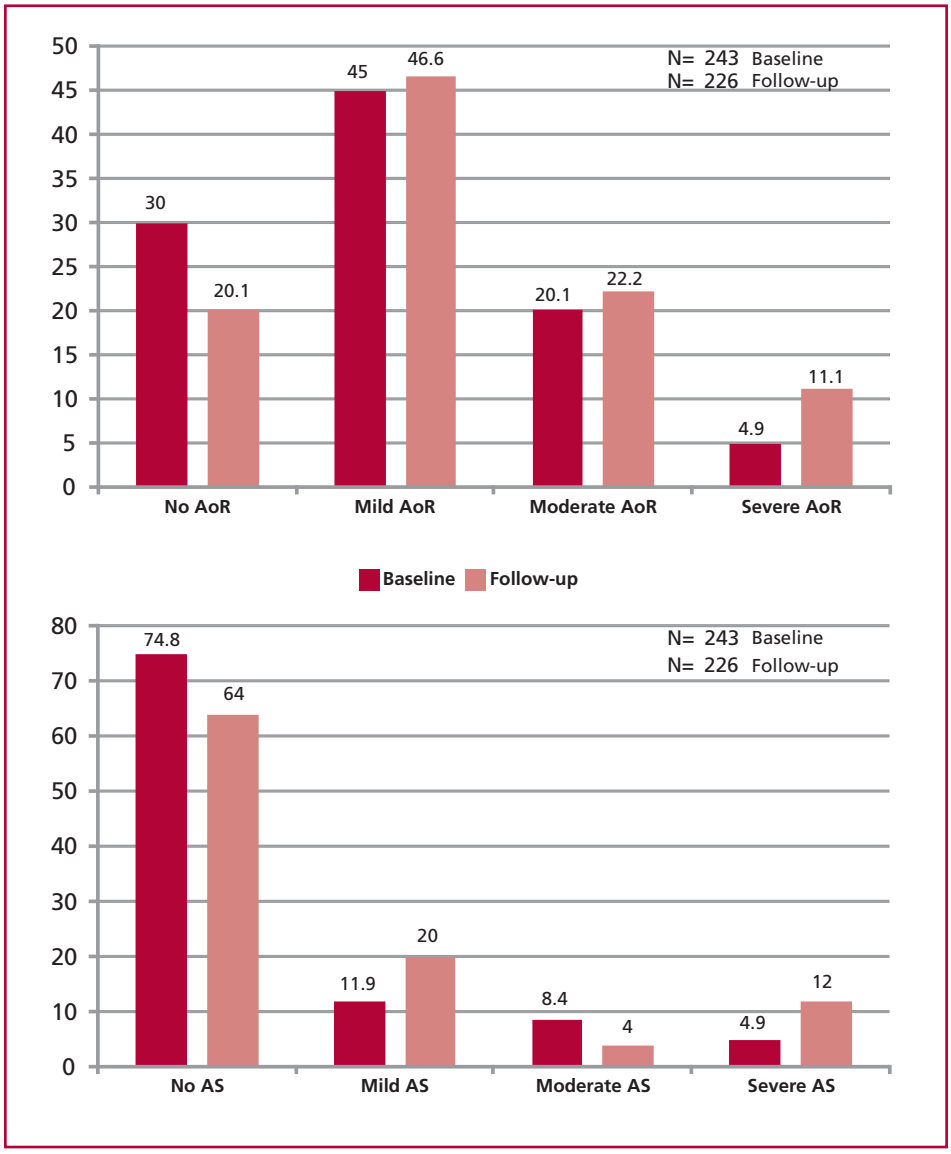

Fig. 1. Percent aortic regurgitation and stenosis and severity at the beginning and end of follow-up

AS: Aortic stenosis, AoR: Aortic regurgitation.

a diameter ≥36.1 mm sinus dilatation; both measurements correspond to a Z-score ≥2 in our population. (17) Aortopathy was defined as a diameter ≥40 mm or ≥21 mm/m2, and aortic aneurysm as a diameter ≥45 mm. (3, 18) Aortopathy was classified into three types: I, dilatation of the tubular portion and the sinus portion; II, dilatation of the tubular portion; and III, dilatation of the sinus portion. (19)

Statistical analysis

Continuous variables were compared using two-tailed Student´s t test and categorical variables using the chi-square test with Yates correction or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation, median and interquartile range (IQR) or prevalence (in percentage), as appropriate.

In the group without significant baseline AVD, univariate analysis of all parameters obtained during patient recruitment was carried out to predict the development of significant AoR and AS at follow-up. Then a multivariate analysis was performed and the criteria for introducing variables were their clinical relevance and statistical significance in the univariate analysis.

Two multivariate logistic regression models were built to identify independent predictors of significant AoR and AS. The first one considered the following factors: age, gender, annular dilatation, sinus dilatation, valve phenotype, baseline calcification score, hypertension, smoking, presence of raphe and valve prolapse. The second included the covariates age, gender, valve phenotype, baseline calcification score, hypertension, smoking and presence of raphe.

The results were reported as RR (univariate) and OR with 95% confidence intervals.

The statistical analysis was carried out with Sofastat R and Evan Miller-Wizard softwares, with Macintosh system. A p value <0.05 was considered significant.

RESULTS

Baseline characteristics and events

A total of 243 patients with confirmed BAV diagnosis, 6.5% of whom had family history of BAV, were in-

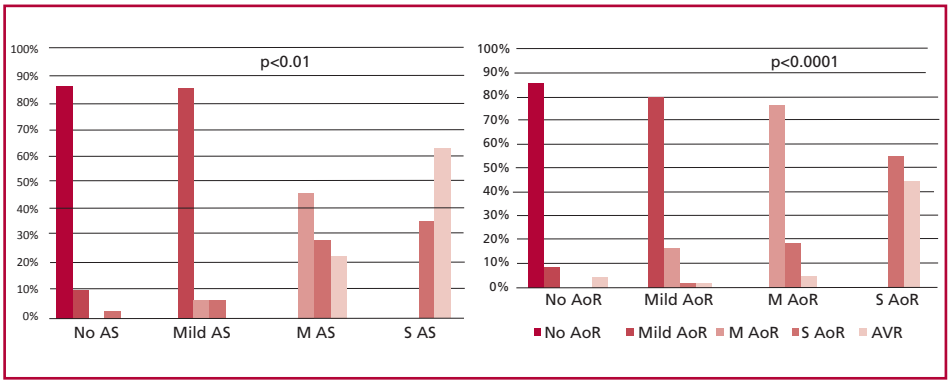

Fig. 2. Progression of the degree of aortic valve dysfunction and requirement of aortic valve replacement during follow-up

AoR: Aortic regurgitation. AS: Aortic stenosis. M: Moderate. S: Severe AVR: Aortic valve replacement, FU: Follow-up

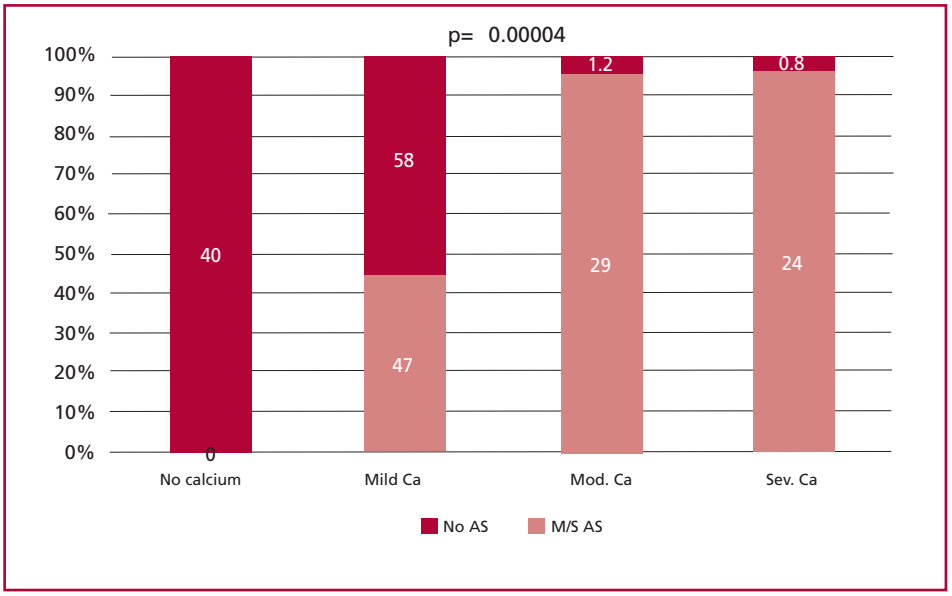

Fig. 3. Association between the degree of baseline aortic valve calcification and the development of significant aortic stenosis during follow-up

Ca: calcification, AS: Aortic stenosis, Mod: moderate; Sev: Severe

	OR (IC95%)	p
Moderate/severe aortic regurgitation during follow-up		
Male gender	15.5 (1.2-197.2)	<0.04
Aortic valve prolapse	15.6 (3.5-69.9)	<0.001
Moderate/severe aortic stenosis during follow-up		
Baseline valve calcification score	47.7 (5.7-107.5)	<0.001

Table 2. Independent predictors of significant AoR and AS during the follow-up (logistic regression analysis)

Variables included in the logistic regression analysis. 1) AoR model: age, gender, annulus dilatation, sinus dilatation, valve phenotype, baseline calcification score, hypertension, smoking, presence of raphe and valve prolapse; 2) AS model : age, gender, valve phenotype, baseline calcification score, hypertension, smoking and presence of raphe.

cluded in the study at our institution between 2009 and 2017. Mean follow-up was 4.7±1.7 years, and was completed in 226 cases (93%). Raphe was observed in 179 patients (73.6%), without significant differences in their baseline characteristics between valve phenotype I and II (Table 1).

Twenty patients (8.2%) underwent AVR during follow-up, mainly due to symptomatic valve dysfunction. Mean time from follow-up initiation to AVR was 4.95±2.6 years. Men were more frequently operated on for symptomatic severe AoR (n=5) (100% vs. 33%, p=0.001), and were younger (35.4±7.3 years vs. 60.8±8.1 years, p=0.0001), with higher LVEDD (6.5±0.5 cm vs. 4.7±0.8 cm, p=0.0007), larger annulus diameter (2.7±0.3 cm vs. 2.1±0.3 cm, p=0.02) and ascending aorta diameter (4.2±0.3 cm vs. 3.4±0.3 cm, p=0.01) than those operated for symptomatic AS (n=9). All patients undergoing AVR due to severe AoR had aortic valve prolapse in the baseline TDE.

Progression of valve dysfunction

In the baseline TDE, 170 patients (69.9%) had some degree of AoR, which was significant in 25% of cases. On the other hand, AS was present in 1 of every 4 patients at the beginning of follow-up and was significant in 13% of cases. Figure 1 shows the proportion of each valve disease and its degree of severity at the beginning and end of follow-up.

During follow-up of patients without significant baseline AVD, 39 patients (17.2%) developed significant AVD: 26 (11.5%) with significant AoR (mean progression time: 4.2±2.3. years) and 13 (5.3%) with significant AS (mean progression time: 5.1±2.4 years).

The majority of patients without significant baseline AVD did not progress during follow-up. Patients with significant baseline AS or AoR had a higher rate of progression and of AVR during follow-up (p<0.001, Figure 2).

Variables associated with the development of significant aortic valve dysfunction

Patients who developed significant AoR were younger than those who developed significant AS (44.9±13.1 years vs. 51.2±11.2 years, p=0.03).

In the baseline echocardiogram, 41 patients (16.8%) were diagnosed with valve prolapse. This subgroup showed greater progression to significant AoR than those without prolapse [RR=4.45 (3.02-6.57), p<0.001].

In 10% (17 patients) of cases, patients with some degree of AoR presented valve calcification as the only mechanism of dysfunction and, of these, 3 also presented moderate AS.

The degree of calcification was significantly and linearly associated with age. Patients with a baseline calcium score of 0 (n=87, 36%) were significantly younger than those with grade 3 calcification (37.2±3.1 years vs. 60.2±4.3 years, p<0.001). Patients with significant AS at follow-up had a greater degree of baseline valve calcification (p<0.001, Figure 3).

Likewise, in patients with a baseline valve degeneration score ≥1, the development of significant AS was more frequent [RR=2.17 (1.86-2.52), p<0.001, Figure 4]. None of the patients with a baseline score of 0 developed significant AS.

Logistic regression analysis

1) Significant AoR prediction model: Independent predictors were male gender [OR=15.5 (1.2-197.2), p<0.04] and valve prolapse [OR=15.6, (3.5-69.9), p<0.001].

2) Significant AS prediction model: The only independent predictor was baseline aortic valve calcification score [OR 47.7 (5.7-107.5), p<0.001] (Table 2).

All other variables were not significantly associated with the development of significant AVD during follow-up (p=NS).

DISCUSSION

Main findings

The present study provides evidence of the contemporary clinical evolution of a cohort of adult patients with BAV in Argentina. The rate of progression to significant AVD and AVR was high, despite being a young population with a mean follow-up of almost 5 years. These findings reinforce the concept that BAV is a pathology that is associated with the development of significant AVD at an early age. (3, 4)

Bicuspid aortic valve is one of the first causes of AVR and usually occurs with valve calcification at a young age. Calcification is an active inflammatory, slowly progressive process that evolves in its initial stages restricting leaflet mobility and developing AS. (21, 22) It is associated with age, as confirmed in our findings, but it was not related to the valve phenotype in our series. The semiquantitative evaluation of the degree of aortic valve calcification, even with certain limitations, has proved to be useful, as previously published. (4, 9, 23) As already suggested, (23) an increased baseline calcium score or a Michelena score ≥1 were associated with greater risk of developing significant short-term AS.

Some recently published results suggest that the presence of raphe would be associated with a higher prevalence of AVD and a higher rate of AVR. (8) In our study, the presence of raphe was not independently associated with the development of significant AS. Our group maintains that the presence of raphe could accelerate the degree of valve calcification, so in the multivariate analysis it does not become independent of the baseline calcification score.

Although prolapse has been described as a mechanism of AoR, there are few publications that analyze this characteristic as a predictor of AVD in patients with BAV. (11, 23) Our results indicate that prolapse is independently associated with greater risk of developing significant short-term AoR, especially in men.

In our study, we found that patients who underwent surgery for symptomatic AoR were significantly younger than those who underwent AVR for symptomatic AS. This suggests a rapidly progressive behavior of significant AoR.

Study limitations

A limitation of the study is the still short follow-up period, considering it is a congenital pathology. Moreover, there may also be limitations to extrapolate these results to larger populations.

The quantification of the degree of valve calcification by TDE presents limitations and was carried out a posteriori by the review group. However, we believe that our results constitute a significant contribution to the current knowledge of this disease. Future studies with a greater number of patients could confirm or not the present findings.

CONCLUSIONS

The results of our study show that a high percentage of patients with BAV and moderate to severe baseline AVD progressed and required AVR, despite being a young population with a limited follow-up of only a few years.

On the other hand, we identified valve prolapse and male gender as variables associated with the development of significant AoR, while an increased valve calcification score was associated with the development of significant short-term AS.

These findings would allow the identification of subgroups of patients at higher risk, in which cardiologic follow-up should be intensified.

Future directions

Our working team is currently conducting a substudy to evaluate the usefulness of cardiac multislice computed tomography combined with TDE for calcium quantification and early identification of valve characteristics in adults with BAV. On the other hand, these results reflect the first follow-up years of this cohort, which still continues.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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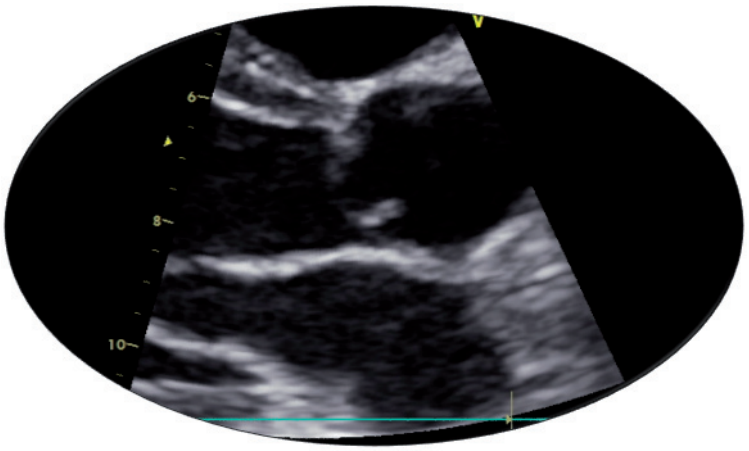
Baseline characteristics of patients who did not complete the follow-up.

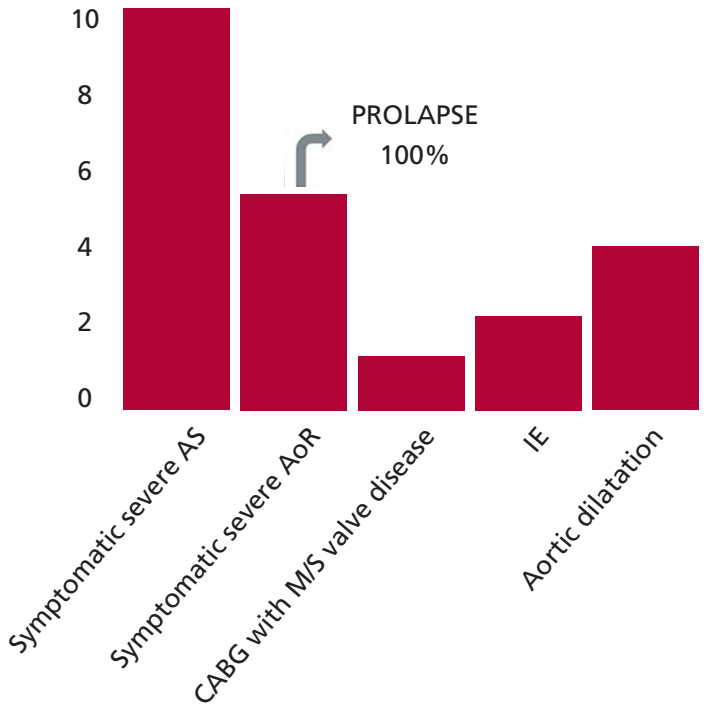
	n=17
Age, years	32± 14
Male gender, n (%)	16 (94.2%)
Type I BAV, n (%)	16 (94.2%)
Aorta >40 mm, n (%)	5 (29%)
Associated lesion, n (%)	2 (11.7%)
Family history, n (%)	1 (5.8%)
LVEF, %	62.9 ± 7.4
Serum creatinine, mg/dL	0.9 ± 0.21
Total cholesterol, mg/dL	190.2 ± 32.4
Mild aortic regurgitation, (n (%)	5 (29.5%)
Moderate aortic regurgitation, (n (%)	3 (17.6%)
Severe aortic regurgitation, n (%)	1 (5.8%)
No aortic regurgitation, n (%)	8 (47.1%)
Mild aortic stenosis, n (%)	1 (5.8%)
Moderate aortic stenosis, n (%)	0 (0%)
Severe aortic stenosis, n (%)	0 (0%)
No aortic stenosis, n (%)	16 (94.2%)

BAV: Bicuspid aortic valve. LVEF: Left ventricular ejection fraction.

Aortic valve prolapse. Aortic valve prolapse was defined as cusp protrusion ≥1 mm through the aortic annulus plane in left parasternal view (as in this case) or in 5-chamber view.



Incidence of events in patients with BAV: Twenty patients (8.2%) underwent AVR during follow-up, mainly due to symptomatic valve dysfunction. Two patients died (1 in the postoperative period and 1 due to an acute coronary syndrome) and 2 developed infective endocarditis, without aortic dissections. All patients with AVR due to severe AoR had aortic valve prolapse in the baseline TDE.



AS: Aortic stenosis. AoR: Aortic regurgitation. CASBG: Coronary artery bypass grafting. M: Moderate. S: Severe. IE: Infective endocarditis