Bicuspid Aortic Valve Behavior in Elite Athletes

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Abstract

Aims. To determine the prevalence and characteristics of BAV among elite athletes and to analyze the effect of long-term exercise training on their aortas.

Methods and results. Consecutive BAV and (TAV) elite athletes from a population of 5,136 athletes evaluated at the Sports Medicine Center of the Spanish National Sports Council were identified using echocardiography. A total of 41 BAV elite athletes were matched with 41 TAV elite athletes and 41 BAV non-athletic patients from 3 Spanish tertiary hospitals. Sixteen BAV elite athletes who had undergone at least 2 cardiac evaluations separated by more than 3 years were selected to assess their clinical course. The prevalence of BAV in elite athletes was 0.8%. The proximal ascending aorta was larger for both BAV groups in comparison to TAV athletes ($p=0.001$). No differences in aortic diameters were found between BAV athletes and BAV non-athletes. In BAV elite athletes, the annual growth rates for aortic annulus, sinuses of Valsalva, sinotubular junction, and proximal ascending aorta were 0.04 ± 0.24 mm/year, 0.11 ± 0.59 mm/year, 0.14 ± 0.38 mm/year, and 0.21 ± 0.44 mm/year, respectively. Aortic regurgitation was the only functional abnormality, but no significant progression was found.

Conclusion. High-intensity training and sports competition may not aggravate BAV condition during elite athletes' careers. BAV elite athletes with mild-to-moderately dilated aortas may engage in high-dynamic cardiovascular exercise without adverse consequences, although an echocardiographic follow-up is recommended.

Key words: Bicuspid aortic valve, athletes heart, echocardiography

Introduction

Bicuspid aortic valve (BAV) is the most common congenital cardiac condition in the general population (0.5 to 2%) and among competitive athletes (2.5%).[1] BAV is recognized as a valvulo-aortopathy because aortic valve dysfunction and ascending aorta dilation are the most frequent associated complications.[2] Aortic dilation is present in nearly half of all patients with BAV and is considered a risk factor for aortic dissection.[3] Although initial reports of aortic dissection in the BAV population estimated incidences of up to 8.6%,[4] more contemporary research has reported lower rates of dissection with excellent long-term survival.[5]

Both genetic and hemodynamic theories have been proposed as factors implicated in the progression of BAV valvulo-aortopathy,[6] and there is a belief that intense physical exertion may impair hemodynamic conditions and favor aortic dilation, placing athletes with BAV at a higher risk for aortic dissection or rupture.[7] Nevertheless, sports-related sudden cardiac death is very uncommon with aortopathy representing only 4.6% of cardiovascular causes of death.[8] Additionally, our group recently showed that aortic root measurements of healthy elite athletes are within the normal values for the general population, suggesting that athletic activity may not bring about an enlargement of the aorta.[9]

To date, studies evaluating the natural history of BAV in athletes are scarce and have only included competitive athletes.[1, 10-12] Therefore, the aims of this study are to determine the prevalence and characteristics of BAV among elite athletes and to analyze the effect of long-term high-performance exercise training on the aortas of BAV elite athletes.

Methods

Subjects and Study Protocol

From January 1997 through December 2015, a total of 5,136 consecutive elite athletes (3,355 males (65.3%) and 1,781 females (34.7%) were evaluated in the Cardiology Department of the Sports Medicine Center of the Spanish National Sports Council. All athletes were referred by their respective Spanish sports federations and had competed in Spanish sports leagues, European and World Championships, and/or the Olympic Games. For the purposes of this study, BAV elite athletes were identified through echocardiography.

Control Groups

To analyze the role of high-performance exercise training on aortic size and valve function in BAV elite athletes, two control groups were matched for comparison. A non-athlete BAV control group matched by sex, age, weight, and body surface area was selected from a multicenter cohort composed of consecutive BAV patients without other cardiovascular diseases, studied in 3 Spanish hospitals from 2005 to 2015. A second control group comprising elite athletes with normal tricuspid aortic valve (TAV) matched by sex, age, sport activity, height, weight, body surface, training regimen, training duration, and maximum oxygen consumption (VO_2max) was selected from the Spanish National Sports Council's cohort.

The study is included in the global project "Defining the Upper Limits of the Aortic Root Dimensions in Elite Athletes" approved by the Ethics Committee of Fundación Jiménez Díaz. All participants provided written informed consent.

Echocardiography

Echocardiographic measurements were performed as described previously[9] and then validated in accordance with revised guidelines from 2015[13] and stored in a magnetic-optical disk and server. Aortic valve morphology was evaluated in the parasternal long and short axis. The coronary ostium was visualized in all athletes. BAV was confirmed when 2 cusps were clearly identified in short-axis view (Figure 1); once presence of BAV was confirmed, we classified each as type 1 when right-left coronary cusp fusion (anteroposterior BAV with both coronary ostium at the anterior leaflet) was observed, type 2 for right-non-coronary cusp fusion (right-left BAV with right coronary ostium at the right leaflet and left coronary ostium at the left leaflet), or type 3 for left-non-coronary cusp fusion (left-non-coronary BAV with one ostium in each leaflet).[14, 15] Measurements were taken perpendicular to the axis of blood flow and included the largest aortic diameter. End-diastolic aortic measurements were made from a 2D parasternal long-axis view at the following sites using the inner edge-to-inner edge convention: (1) aortic valve annulus, (2) maximal diameter of the sinuses of Valsalva, (3) sinotubular junction, and (4) maximal diameter of the proximal ascending aorta. The presence of aortic regurgitation or stenosis was determined using Doppler echocardiography and was classified as mild, moderate, or severe according to published guidelines.[16]

Aortic dilatation morphotype was classified based on Z score ≥ 2 at any plane calculated from our published references values for elite athletes[9] as described by Evangelista et al. study.[15]

Cardiopulmonary Testing

The cardiopulmonary testing procedure has been detailed elsewhere.[9]

Follow-up

A total of 16 BAV elite athletes who had undergone at least 2 echocardiograms throughout their careers, with at least 3 years elapsed between echocardiograms and with no history of aortic surgery, were included in the follow-up analysis. Cardiovascular events, aortic root dimensions, aortic growth rate, and valve function were assessed at each visit. In addition, a clinical follow-up of all BAV elite athletes was performed.

Statistical Analyses

Analyses were conducted using SPSS 20.0. Normality was assessed with the Shapiro-Wilk test and confirmed by visual inspection. We assessed interobserver agreement for binary outcomes using the kappa statistic and for continuous outcomes using intraclass correlation. Normally distributed results are expressed as mean and standard deviation (SD); results that were non-normally distributed are described as median and interquartile range (IQR). The Kruskal-Wallis test with post hoc Bonferroni-Dunn correction and the Mann-Whitney U test were used to compare results between 3 and 2 non-normally distributed groups, respectively. Comparisons between 3 and 2 normally distributed groups were performed by one-way ANOVA with Tukey post hoc test or an independent Student t test, respectively. Differences between proportions were calculated by the chi-square test. To analyze the evolution of the size of the aorta and the progression of aortic regurgitation, a paired t-test and Wilcoxon rank-sum test were performed, respectively. Statistical significance was defined as $p < 0.05$ (two-tailed).

Results

Of the 5,136 elite athletes included in the population, BAV was diagnosed in 41 (83% males and 17% females), resulting in a prevalence of 0.8% and a male predominance of 5:1 (Figure 2). The mean duration of high competition training before the first echocardiogram at the Cardiology

Department of the Sports Medicine Center of the Spanish National Sports Council was 8.90±4.12 years for BAV elite athletes and 8.51±4.37 years for TAV elite athletes (p=0.679). The training regimen for BAV elite athletes was 17.12±9.20 hours/week and 18.73±9.64 hours/week for TAV elite athletes (p=0.442). The BAV non-athletic population was not involved in a structured exercise training regime. The BAV athletes competed in a total of 28 different sports. Using a modified version of Mitchell's system for sports classification[9] in which static and dynamic components were combined into 3 categories based only on the dynamic component, sports were classified as low or type A (<40% VO_2max), moderate or type B (40-70% VO_2max), and high or type C (>70% VO_2max). The cohort distribution was as follows: 9 (22%) participated in sports involving low dynamic demands, 8 (19.5%) engaged in sports with a moderate dynamic component, and 24 (58.5%) were involved in high-dynamic-component sports. None of the BAV athletes had arterial hypertension, dyslipidemia, diabetes, or a smoking habit. The demographic and echocardiographic characteristics of the BAV athletes and control groups (41 TAV elite athletes and 41 BAV non-athletic patients) are summarized in Tables 1 and 2. Five BAV elite athletes had a maximum aortic diameter > 45 mm at the beginning of the study. According to the recommended medical indications at the time of diagnosis,[17] two male BAV athletes with proximal ascending aortic diameters of 46.2 mm (a futsal goalkeeper with a type 3 pure BAV without raphe and high risk of trauma associated to his position) and 61.1 mm (a basketball player with type 1 BAV and playing in the center position) underwent elective aortic surgery (David technique). One resumed athletic activities 9 months after surgery and the others decided to quit professional sports after surgery. Also, a midfielder soccer player with type 1 BAV and severe aortic regurgitation underwent aortic valve replacement. Finally, a golf player with type 1 BAV, moderate aortic regurgitation and severe aortic root dilatation

underwent elective aortic surgery (aortic valve and root replacement). There were no cardiac events reported by any of the BAV athletes.

In males, the left ventricle, left atrium, and right atrium showed statistically significant greater dimensions in BAV and TAV elite athletes compared to non-athletes with BAV. The left atrial anteroposterior dimension was the only measurement that was statistically different between BAV and TAV male athletes, with smaller sizes found in the former. There were no significant differences between females. Reproducibility of echocardiographic aortic valve dysfunction expresses good agreement with a kappa value of 0.729 (CI95%: 0.905-0.553) p=0.0001. Reproducibility of echocardiographic aortic continuous measures expresses also good agreement: intraclass correlation is shown in Data Supplement.

Aortic Valve

Among BAV male athletes, BAV type 1 was the most common (85.3%), followed by type 2 (8.8%) and type 3 (5.9%). Pure BAV without raphe was observed in 14.7% of males. All BAV female athletes were type 1 and showed presence of a raphe. Aortic valve regurgitation was the only functional abnormality detected through Doppler echocardiography in BAV athletes (22 males and 5 females) and was less frequent (64.6%) compared to the non-athlete BAV population (83.9%). As seen in Table 3, no significant difference was observed between the two BAV groups regarding aortic regurgitation severity in both males ($p = 0.084$) and females ($p = 0.229$). Functional valve abnormalities were not identified in TAV elite athletes.

Aortic Diameter

According to the Tukey post hoc test, the size of the proximal ascending aorta was significantly larger for both BAV groups (elite athletes and non-athletes) compared to the TAV healthy elite

athletes, ($F(2,120) = 7.74$, $p = 0.001$). This analysis also revealed significant differences in the sinus of Valsalva ($F(2,120) = 4.07$, $p = 0.019$) and in the sinotubular junction ($F(2,120) = 3.22$, $p = 0.044$) between BAV elite athletes and the TAV group, and there were no differences at the aortic annulus level, where diameters were similar across groups ($F(2,120) = 2.93$, $p = 0.057$). No significant differences were found in the aortic root and proximal ascending aorta sizes between BAV athletes and BAV non-athletes in either sex (Table 4). Nevertheless, non-statistical significant differences were observed at the aortic annulus ($p=0.106$) and at the sinuses of Valsalva ($p=0.053$) between BAV elite athletes and BAV non-athletes. Further, Cohen's effect size values for aortic annulus ($d = 0.44$), sinus of Valsalva ($d = 0.44$), sinotubular junction ($d = 0.16$), and proximal ascending aorta ($d = 0.13$) suggested that athletic activities have low to moderate clinical significance for the aortic diameters of BAV elite athletes.

Regarding BAV athletes, 12 males (35.3%) and 2 females (28.6%) had enlarged aortas (raw diameters $\geq$ 2 SD from the reference values for elite athletes).[9] In 5 cases (12.2%), the aorta was enlarged at the aortic annulus, 10 (24.4%) at the sinuses of Valsalva, 6 (14.6%) at the sinotubular junction, and 11 (26.8%) at the proximal ascending aorta. Meanwhile, in the BAV non-athlete population, similar frequencies were found: 12 males and 3 females had diameters over these reference values. Specifically, 3 subjects (7.3%) showed enlargement at the aortic annulus, 6 (14.6%) at the sinuses of Valsalva, 9 (22.0%) at the sinotubular junction, and 12 (29.3%) at the proximal ascending aorta.

When analyzing, the aortic diameters of BAV elite athletes adjusted to body surface area, 15 males (44.1%) and 4 females (57.1%) had enlarged aortas (Z scores $\geq$ 2 from the reference values for elite athletes according to Mitchell's sports classification based on dynamic

components and/or ≥ 40 mm aortas in men/ ≥ 36 mm aortas in women). Suppl. Table 2 shows these results.

Follow-up

Over a period of 7.0±4.7 years of high-performance exercise training, the annual growth rate of the aortic root was as follows: aortic annulus 0.04±0.24mm/year, sinuses of Valsalva 0.11±0.59 mm/year, sinotubular junction 0.14±0.38mm/year, and proximal ascending aorta 0.21±0.44mm/year (Table 5). Only the proximal ascending aorta showed a statistically significant increase in diameter during follow-up, with mild clinical significance and high inter-individual variability for all aortic planes (Figure 3). There was no major change regarding aortic regurgitation, and none of the BAV athletes presented cardiovascular complications during follow-up.

Out of all 16 BAV elite athletes followed, 8 (50%) had Z scores ≥2 and/or ≥40mm (men)/ ≥36mm (women) at baseline. Four (25%) of them had Z scores ≥3.5 and 2 (12.5%) of them had ≥42mm (men) / ≥39 mm aortas (women). None of them were excluded from training or competition. From these 16 BAV elite athletes, 11 (68.8%) were engaged in high-dynamic cardiovascular exercise training (Mitchell's sports classification type C). Out of these athletes exposed to high-dynamic cardiovascular training regimes, five (45.5%) had a dilated aorta based on guidelines criteria (≥2 and/or ≥40mm aortas in men/ ≥36mm aortas in women). In addition, those same 5 (45.4%) athletes had a dilated aorta at the end of the follow-up period. No other elite athlete presented a dilated aorta at the end of the follow-up (Suppl. Table 2 and Suppl. Table 3).

A clinical follow-up was performed in 39 of 41 BAV elite athletes at the end of this study. The remaining two BAV elite athletes could not be located for the follow-up. The median total follow-up duration from baseline echocardiogram was 10.6 years (range 3 - 21). This broad range of time for the follow-up is explained by two factors. First, for some athletes there was a broad variability regarding the time of retirement from high-level sport competition and thus not continuing their follow-up in our center. And second, due to the nature of the study design, some BAV athletes underwent their first evaluation in September 2015, before the end of the recruiting period of the study. All 39 BAV elite athletes followed were alive and none of them had suffered an aortic dissection by the end of the clinical follow-up (October 2018).

Discussion

This is the first study describing the characteristics and behavior of BAV among elite athletes. We established that the prevalence of BAV in elite athletes (0.8%) is similar to that of the general population (0.5–2%).[18] We further demonstrate that the proximal ascending aorta, sinus of Valsalva, and sinotubular junction were larger in both BAV groups (elite athletes and non-athletes) compared to TAV healthy elite athletes. No significant differences in aortic root size were found between BAV elite athletes and a matched population consisting of BAV non-athletes. Regarding the clinical course of BAV elite athletes, aortic valve regurgitation showed a non-significant increase, and the proximal ascending aorta was the only diameter that increased significantly during the professional careers of these athletes, although we cannot rule out that a similar course may be observed in BAV non-athletes. The present study highlights the relevance of echocardiography in BAV elite athletes, mainly because of the high inter-individual variability depicted on aortic diameters during the evaluations.

Type-1 BAV (right-left BAV) was the most common phenotype evidenced by transthoracic echocardiography in athletes of both sexes, mirroring previous descriptions in the general population,[14] and aortic valve regurgitation was the only functional abnormality detected through Doppler ultrasound scans. Furthermore, none of the BAV athletes developed severe aortic regurgitation; this condition could be detrimental to athletic performance because it has been related with progressive left ventricle dilation and exercise intolerance.[7]

Among the possible complications of BAV, aortic dissection or rupture poses the most pressing challenge for clinical management of elite athletes with bicuspid aorthopathy.[3] Classically, aortic enlargement has been classified as a risk factor for dissection, and therapeutic interventions are indicated primarily on the aortic diameter. As described in previous studies,[1, 19] we found larger aortic diameters in both BAV groups in comparison to TAV controls, which may suggest underlying tissue disarrangement of the aortic root in the BAV population in combination with possible non-laminar flow. The only exception was the aortic annulus, possibly due to the fibrous nature of this location.[9] All measurements in absolute terms in BAV athletes were larger compared to BAV non-athletes but those differences were not significant in our study. On the other hand, a non-significant tendency of higher diameters was observed in the aortic annulus and the sinuses of Valsalva between BAV athletes and BAV non-athletes. These results do not discard that high training regimes might be involved in larger aortic diameter at both levels and further studies are needed to confirm these results or to explore a possible clinical impact.

Current eligibility guidelines for competitive athletes suggest that the increase in blood pressure that takes place during intense physical exertion could raise the tension of the aortic wall, thus placing subjects with bicuspid aorthopathy at a greater risk for dilation and rupture. Likewise, athletes with BAV and mild-to-moderately dilated aorta are recommended to compete only in

sports of low and moderate cardiovascular demands (recommendation class IIb with evidence level C).[7] Nonetheless, available research in support of this theory is very limited[20] and, contrary to these beliefs, our data suggest that exercise training per se does not influence the size of the aorta. First, we did not find significant differences in the size of the aortic root between BAV elite athletes and BAV non-athletes, in conjunction to a small effect size; this suggests that athletic activities have a low clinical implication with regard to the aortic diameter of BAV elite athletes. Secondly, the mean and median aortic dimensions of male and female BAV elite athletes, respectively, were still within the limits established for healthy elite athletes and the general population.[9] Thirdly, 34% of all BAV elite athletes presented values over these limits (diameters ≥2SD), which is similar to the frequency observed in BAV non-athletes (36.7%). Moreover, in our cohort of BAV athletes, 58.5% of them were involved in sports with a high dynamic component (type C according to our modified Mitchell sports classification). Finally, aortic growth rates experienced by BAV elite athletes during follow-up were minimal. Although elite athletes usually train from 2 to 7 hours per day, the hemodynamic conditions generated by this exertion do not seem to accelerate aortic dilation during their professional sports careers. In a similar study, Detaint et al.[21] described slightly greater annual growth-rates for the aortic root in 353 non-athletic subjects in comparison to the present study. One explanation might be the age difference among both samples (48±15 years vs. 21.59±5.80 years). It has been shown in the past a direct relationship between aortic dilation and age, which may explain the slight differences on aortic annual growth-rates from both studies.[15]

It is worth noting that aortic diameter and/or growth rate may not be the best clinical tools to predict aortic dissection or rupture; indeed, distinct BAV phenotypes and pathways involved in the process of aortic wall disruption and repair have not yet been well characterized,[14, 15] and

while catastrophic aortic events may never occur in aortas over the threshold limit for dilation, these same events may occur in aortas with normal diameters.[2] In this study, no cardiovascular complications were detected among athletes with BAV, even in those who underwent elective surgery, and therefore we were unable to establish risk factors for aortic root dissection or rupture.

Aortic dilation is considered a pathological process that results from aging and, fortunately, aortic dissection in the younger population is extremely rare.[22] However, we cannot disregard the possibility of a delayed effect of intense physical activity after the fourth decade of life. Future studies should be performed to assess the evolution of the aorta in BAV elite athletes after they discontinue their high-intensity training regimes. One specific location to consider is the proximal ascending aorta, in the current study; this was the only location in which BAV athletes exhibited a significant increase during follow-up. Similarly, a recent study performed in former national football league players with TAV showed that the ascending aortic dimensions of these players were significantly higher in comparison to a non-elite group of athletes.[23]

Heart cavities were larger in both groups composed of elite athletes in comparison to the non-athlete group, a finding that has been extensively reported in the past.[24] The only exception was the smaller size of the anteroposterior left atrium dimension found in those elite athletes with BAV in contrast to those with TAV, which may be explained by the compression of a larger aortic root in the left atrium.

Limitations

All the aortic measures were performed using the inner edge-to-inner edge method as we have described previously.[9] Current 2015 guidelines for the general population recommend measuring

only inner edge-to-inner edge for the aortic annulus, employing the leading edge-to-leading edge convention for all other aortic root measurements. Regarding this concern, in elite athletes and young non-athletes, the aortic wall layers are not calcified, there is no acoustic blooming, and inner edge-to-inner edge measures are easily obtained. Finally, in case of doubt or when any aortic dimension is over 40 mm, confirmation by cardiac magnetic resonance imaging or cardiac computed tomography was performed as recommended.[2] Despite the small number of BAV elite athletes, to our knowledge, this is the largest study analyzing the association of BAV with elite competition. Future international multicentric studies based on larger populations are needed to confirm these results. The follow-up period lasted only until the conclusion of their elite athletic careers (7.0±4.7years), and future studies focusing on long-term evolution are needed to fully describe the behavior of BAV after retirement from professional competition. Regarding hemodynamic conditions, the use of a 3-dimensional, time-resolved, phase contrast cardiac magnetic resonance imaging would be ideal to characterize flow and to quantify aortic wall shear stress.[14] Our study did not include genetic information and only 3 of the BAV athletes referred family history of BAV aortopathy. This may limit the understanding of BAV heterogeneity in valvular dysfunction and aorta dilation among athletes.[15] Future studies are needed to improve individualized risk of aortic dilatation or BAV dysfunction based on genetic factors, among others[15]. Finally, the variability of aortic diameters between some BAV subjects was remarkable, and as stated by Longobardo et al.[6] and recently by Evangelista et al.,[15] we should view BAV as a condition best characterized as a clinical spectrum with different etiologies, where a detail analysis of valve morphotypes, cardiovascular risk factors, hemodynamic conditions and aortic dilation patterns may help to stratify the risk of valvular dysfunction and aortic dilation.

Conclusion

The findings of this study support the notion that athletic activities undertaken by BAV elite athletes may not trigger aortic enlargement or aortic valve dysfunction during their athletic careers. Despite current recommendations for competitive athletes with BAV and mild-to-moderately dilated aorta to limit athletic activity to sports with low and moderate cardiovascular demands, our results suggest that high-intensity cardiovascular exercise may not be detrimental to these individuals. Nevertheless, given the high inter-individual variability seen in aortic diameters throughout the clinical course of this condition, close echocardiographic follow-up should be mandatory for BAV competitive athletes. Long-term outcomes will require regular monitoring over time and the creation of a multicenter athlete database.

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DISCLOSURES

None

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FIGURE LEGENDS

Figure 1. Bicuspid aortic valves morphology in echocardiographic parasternal short axis. Bicuspid aortic valve was confirmed when 2 cusps were clearly identified in short-axis view. **A:** type 1 right-left coronary cusp fusion (anteroposterior bicuspid aortic valve with both coronary ostium at the anterior leaflet); **B:** type 2 right-non-coronary cusp fusion (right-left bicuspid aortic valve with right coronary ostium at the right leaflet and left coronary ostium at the left leaflet); **C:** type 3 left-non-coronary cusp fusion (left-non-coronary bicuspid aortic valve with one ostium in each leaflet). The coronary ostium was visualized in all athletes. (*) indicates coronary ostium and (arrow) indicates coronary cusp fusion.

Figure 2. Selection of study groups. The first group included all elite athletes in whom BAV was detected through echocardiography during their cardiovascular evaluation. The second group was a matched control group comprising elite athletes with TAV. The third group was also a matched control group, which included subjects with BAV from 3 different hospitals from Spain. In addition, a subpopulation of BAV elite athletes with a follow-up of at least 3 years were selected to assess the clinical course of their condition. BAV: bicuspid aortic valve; TAV: tricuspid aortic valve.

Figure 3. Aortic root and proximal ascending aorta: annual growth rate in BAV elite athletes. BAV: bicuspid aortic valve; AoA: aortic annulus; AoSV: sinuses of Valsalva; AoSJ: sinotubular junction; AoPxA: proximal ascending aorta. *p=0.018 between first and last control.

Table 1. Data are presented as mean (standard deviation) for normally distributed data and median (interquartile range) for non-normally distributed data, respectively. [a]: $p<0.05$ vs. TAV elite athlete; [b]: $p<0.05$ vs. BAV elite athlete. BAV: bicuspid aortic valve, TAV: tricuspid aortic valve, BSA: body surface area, VO_2max: maximal oxygen uptake.

Table 2. Data are presented as mean (standard deviation) for normally distributed data and median (interquartile range) for non-normally distributed data, respectively. [a]: $p<0.05$ vs. TAV elite athlete; [b]: $p<0.05$ vs. BAV elite athlete. BAV: bicuspid aortic valve, TAV: tricuspid aortic valve.

Table 3. Data are presented as frequency and percentage. BAV: bicuspid aortic valve.

Table 4. Data are presented as mean (standard deviation) for normally distributed data and median (interquartile range) for non-normally distributed data, respectively. [a]: $p<0.05$ vs. BAV elite athlete, [b]: $p<0.05$ vs. BAV non-athlete. BAV: bicuspid aortic valve, BSA: body surface area, TAV: tricuspid aortic valve.

Table 5. Data are presented as mean (standard deviation) and frequency (percentage). BAV: bicuspid aortic valve.

Bicuspid Aortic Valve Behavior in Elite Athletes

Word count: 5993

Table

Table 1. Demographic characteristics of BAV elite athletes, BAV non-athlete control group and TAV elite athlete control group.

	BAV Elite Athletes	**BAV Non-athletes**	**TAV Elite Athletes**	**P value**
	Mean (SD)	Mean (SD)	Mean (SD)	
Male	**n = 34**	**n = 34**	**n = 34**	
Age (yrs)	22.2 (6.0)	23.8 (6.7)	22.4 (6.1)	0.561
Height (cm)	179.4 (10.3)	174.7 (6.0) [a]	180.0 (7.0)	0.016
Weight (kg)	73.8 (9.9)	73.3 (8.6)	75.1 (9.3)	0.716
BSA (m^2)	1.9 (0.2)	1.9 (0.1)	1.9 (0.1)	0.202
Training Regimen (h/wk)	18.2 (8.5)	-	19.2 (9.5)	0.668
Duration of Training (yrs)	8.4 (4.2)	-	8.5 (4.7)	0.913
VO_2max (ml/kg/min)	56.6 (8.7)	-	56.6 (8.2)	0.965
	Median (IQR)	Median (IQR)	Median (IQR)	
Female	**n = 7**	**n = 7**	**n = 7**	
Age (yrs)	18.0 (5.0)	19.0 (6.0)	18.0 (5.0)	0.666
Height (cm)	165.5 (19.4)	164.0 (6.0) [a, b]	166.8 (10.0)	0.437
Weight (kg)	52.8 (15.6)	66.0 (9.5)	56.7 (25.2)	0.102
BSA (m^2)	1.6 (0.3)	1.7 (0.1)	1.6 (0.2)	0.185
Training Regimen (h/wk)	8.5 (15.0)	-	15.0 (16.0)	0.199
Duration of Training (yrs)	12.0 (2.0)	-	8.0 (5.0)	0.079
VO_2max (ml/kg/min)	47.6 (10.1)	-	51.2 (10.0)	0.155

Table 2. Echocardiographic characteristics of male and female elite athletes and BAV non-athletes.

	BAV Elite Athletes	**BAV Non-athletes**	**TAV Elite Athletes**	**P value**
	Mean (SD)	Mean (SD)	Mean (SD)	
Male	**n = 34**	**n = 34**	**n = 34**	
Left ventricle end-diastolic dimensions (mm)	55.4 (6.5)	51.0 (7.2) [a, b]	54.8 (5.2)	0.011
Ventricular septum (mm)	9.8 (1.3)	10.0 (1.8)	9.6 (1.0)	0.420
Posterior free wall (mm)	9.4 (1.0)	9.4 (2.2)	9.2 (0.9)	0.793
Anteroposterior left atrium dimensions (mm)	31.8 (5.4) [a]	32.6 (6.1)	35.5 (5.5)	0.023
Superior-inferior left atrium (mm)	49.8 (7.6)	43.7 (6.3) [a, b]	51.7 (6.5)	<0.001
Superior-inferior right atrium (mm)	53.5 (5.0)	43.6 (5.4) [a, b]	53.1 (6.6)	<0.001
Left ventricle ejection fraction (%)	60.6 (6.8)	62.2 (5.7)	60.3 (6.0)	0.428
E wave (cm/s)	89.4 (18.0)	89.8 (20.0)	83.5 (15.7)	0.267
A wave (cm/s)	48.6 (11.6)	55.4 (21.0) [a]	41.3 (6.5)	0.001
	Median (IQR)	Median (IQR)	Median (IQR)	
Female	**n = 7**	**n = 7**	**n = 7**	
Left ventricle end-diastolic dimensions (mm)	49.4 (8.0)	41.0 (9.7)	46.5 (5.0)	0.103
Ventricular septum (mm)	8.7 (1.8)	8.3 (3.6)	7.6 (2.2)	0.690
Posterior free wall (mm)	8.5 (2.4)	9.0 (3.0)	7.3 (1.8)	0.974
Anteroposterior left atrium dimensions (mm)	27.4 (3.1)	26.0 (8.8)	33.2 (5.8)	0.099
Superior-inferior left atrium (mm)	46.0 (8.8)	47.8 (9.5)	48.3 (7.2)	0.074
Superior-inferior right atrium (mm)	43.4 (7.4)	40.0 (13.6)	47.0 (10.2)	0.117
Left ventricle ejection fraction (%)	69.0 (11.0)	61.0 (6.0)	61.0 (13.0)	0.190
E wave (cm/s)	76.8 (24.4)	93.0 (57.8)	97.6 (25.2)	0.062
A wave (cm/s)	52.3 (40.1)	71 (53.95)	39.5 (19.3)	0.175

Table 3. Aortic valve regurgitation in BAV elite athletes and BAV non-athletes.

	BAV Elite Athletes	**BAV Non-athletes**	**P value**
Aortic Valve Regurgitation	**n (%)**	**n (%)**	
Male			
Absence	12 (35.3)	5 (14.7)	0.084
Mild	13 (38.2)	18 (44.1)	
Moderate	8 (23.5)	6 (17.6)	
Severe	1 (2.9)	5 (14.7)	
Female			
Absence	2 (28.6)	5 (71.4)	0.229
Mild	4 (57.1)	2 (28.6)	
Moderate	-	-	
Severe	1 (14.3)	-	

Table 4. Raw and Corrected Values of Aortic root in BAV elite athletes, BAV non-athletes, and TAV elite athletes.

	BAV Elite Athletes	BAV Non-athletes	TAV Elite Athletes	P value
Aortic Diameter				
	Mean (SD)	Mean (SD)	Mean (SD)	
Total	**n = 41**	**n = 41**	**n = 41**	
Aortic annulus (mm)	26.5 (5.0)	24.9 (3.7)	24.4 (4.0)	0.074
Sinuses of Valsalva (mm)	34.1 (6.1)	31.6 (5.3)	30.8 (5.1) [a]	0.020
Sinotubular junction (mm)	28.4 (5.9)	27.5 (5.0)	25.6 (4.4) [a]	0.043
Proximal ascending aorta (mm)	31.1 (8.1)	29.9 (5.2)	26.1 (4.2) [a, b]	0.001
Aortic annulus/BSA (mm/m^2)	14.1 (2.3)	13.3 (2.0)	12.8 (1.6) [a]	0.007
Sinuses of Valsalva/BSA (mm/m^2)	18.2 (2.7)	17.1 (2.6)	16.8 (3.9)	0.091
Sinotubular junction/BSA (mm/m^2)	15.1 (2.6)	14.9 (2.8)	13.5 (1.8) [a, b]	0.004
Proximal ascending aorta/BSA (mm/m^2)	16.6 (3.6)	16.3 (2.8)	13.8 (1.8) [a, b]	<0.001
Male	**n = 34**	**n = 34**	**n = 34**	
Aortic annulus (mm)	27.0 (5.2)	25.9 (4.3)	25.2 (3.6)	0.155
Sinuses of Valsalva (mm)	34.7 (6.1)	33.0 (5.4)	31.9 (4.6)	0.066
Sinotubular junction (mm)	28.9 (6.1)	27.8 (5.2)	26.5 (4.2)	0.174
Proximal ascending aorta (mm)	31.6 (8.7)	29.6 (6.5)	26.8 (4.0) [a, b]	0.006
Aortic annulus/BSA (mm/m^2)	14.1 (2.4)	13.5 (2.1)	12.9 (1.6)	0.055
Sinuses of Valsalva/BSA (mm/m^2)	18.1 (2.8)	17.4 (2.7)	16.4 (2.0) [a]	0.024
Sinotubular junction/BSA (mm/m^2)	15.0 (2.7)	15.0 (2.8)	13.7 (2.0) [a, b]	0.043
Proximal ascending aorta/BSA (mm/m^2)	16.4 (3.9)	16.4 (2.7)	13.8 (1.9) [a, b]	<0.001
	Median (IQR)	Median (IQR)	Median (IQR)	
Female	**n = 7**	**n = 7**	**n = 7**	
Aortic annulus (mm)	23.4 (5.1)	21.7 (2.0)	19.1 (6.1)	0.196
Sinuses of Valsalva (mm)	28.6 (10.0)	27.0 (8.0)	24.2 (6.1)	0.144
Sinotubular junction (mm)	25.2 (6.2)	26.0 (4.6)	20.9 (4.0) [b]	0.029
Proximal ascending aorta (mm)	27.6 (7.2)	28.0 (7.0)	21.5 (4.0) [b]	0.035
Aortic annulus/BSA (mm/m^2)	14.1 (2.5)	12.4 (1.7) [a]	12.2 (4.4) [a]	0.036
Sinuses of Valsalva/BSA (mm/m^2)	19.4 (2.8)	15.6 (4.3)	15.5 (2.9)	0.057
Sinotubular junction/BSA (mm/m^2)	15.6 (1.7)	13.3 (3.4)	12.8 (1.3) [a]	0.008
Proximal ascending aorta/BSA (mm/m^2)	17.8 (2.0)	14.7 (5.9)	12.9 (1.4) [a]	0.017

Table 5. Follow-up of BAV elite athletes.

BAV Elite Athletes (n=16)	**First Control**	**Last Control**	**P value**
	7.0 (4.7)years; range 3-15years		
Aortic Diameter	**Mean (SD)**	**Mean (SD)**	
Aortic annulus (mm)	26.5 (4.0)	26.8 (3.7)	0.352
Sinuses of Valsalva (mm)	34.3 (5.0)	35.5 (5.4)	0.098
Sinotubular junction (mm)	28.3 (3.8)	29.1 (4.2)	0.075
Proximal ascending aorta (mm)	30.7 (6.0)	32.2 (7.0)	0.018
Aortic annulus/BSA (mm/m^2)	14.3 (2.1)	14.1 (1.9)	0.462
Sinuses of Valsalva/BSA (mm/m^2)	18.6 (2.7)	18.7 (3.1)	0.620
Sinotubular junction/BSA (mm/m^2)	15.8 (2.5)	15.4 (2.5)	0.048
Proximal ascending aorta/BSA (mm/m^2)	16.6 (3.6)	17.1 (4.2)	0.174
Aortic Valve Regurgitation	**n (%)**	**n (%)**	
Absence	6 (37.5)	4 (25.0)	0.083
Mild	7 (43.8)	8 (50.0)	
Moderate	3 (18.8)	4 (25.0)	
Severe	-	-	-

Figure 1

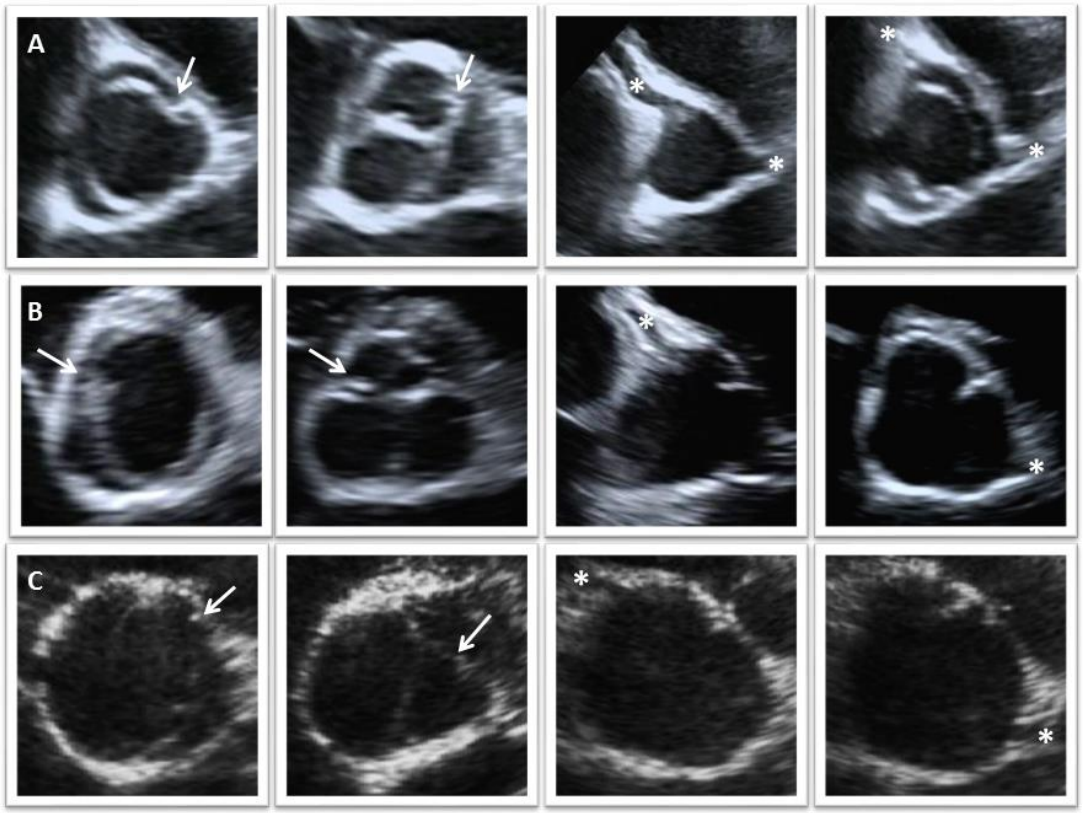

Figure 1. Bicuspid aortic valves morphology in echocardiographic parasternal short axis. Bicuspid aortic valve was confirmed when 2 cusps were clearly identified in short-axis view. **A:** type 1 right-left coronary cusp fusion (anteroposterior bicuspid aortic valve with both coronary ostium at the anterior leaflet); **B:** type 2 right-non-coronary cusp fusion (right-left bicuspid aortic valve with right coronary ostium at the right leaflet and left coronary ostium at the left leaflet); **C:** type 3 left-non-coronary cusp fusion (left-non-coronary bicuspid aortic valve with one ostium in each leaflet). The coronary ostium were visualized in all athletes. (*) indicates coronary ostium and (arrow) indicates coronary cusp fusion.

Figure 2

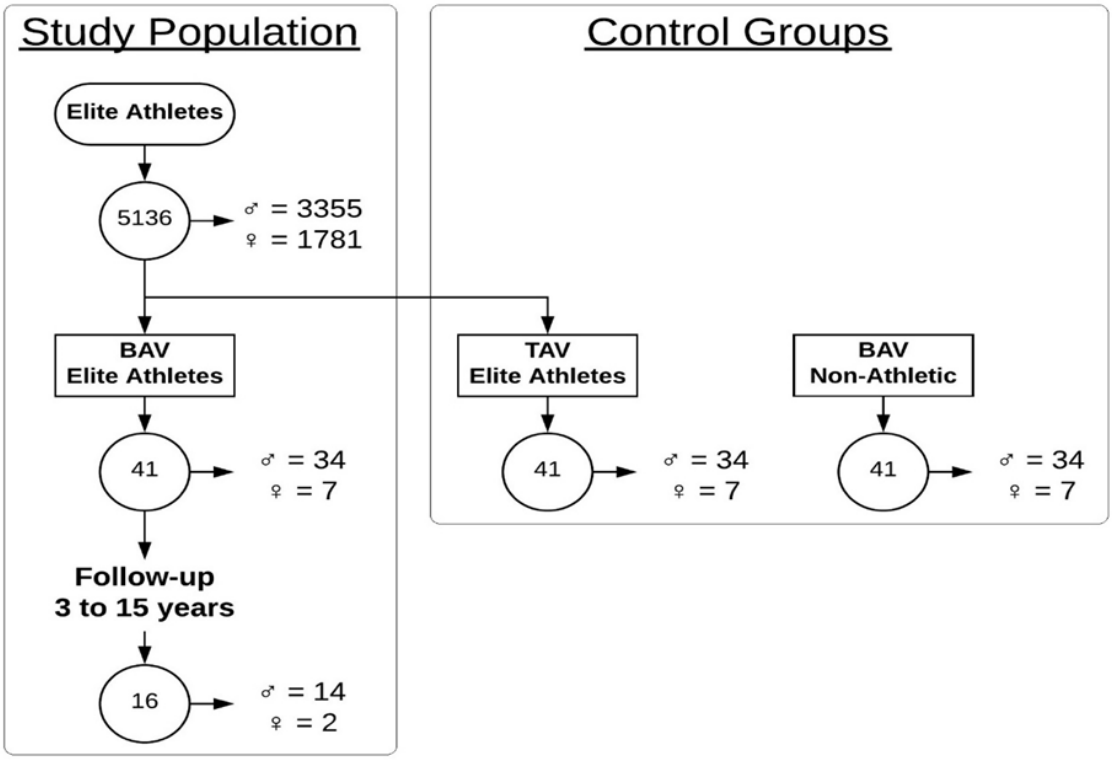

Figure 2. Selection of study groups. The first group included all elite athletes where BAV was detected through echocardiography during their cardiovascular evaluation at the Sports Medicine Center of the Spanish National Sports Council. The second group was a matched control group composed by elite athletes with TAV selected from the Spanish National Sports Council's database. The third group was also a matched control group, which included subjects from 3 different hospitals from Spain, with the diagnosis of BAV. In Addition, a subpopulation of BAV elite athletes with a follow-up of at least 3 years were selected to assess the evolution of their condition.
BAV: bicuspid aortic valve; TAV: tricuspid aortic valve.

Figure 3

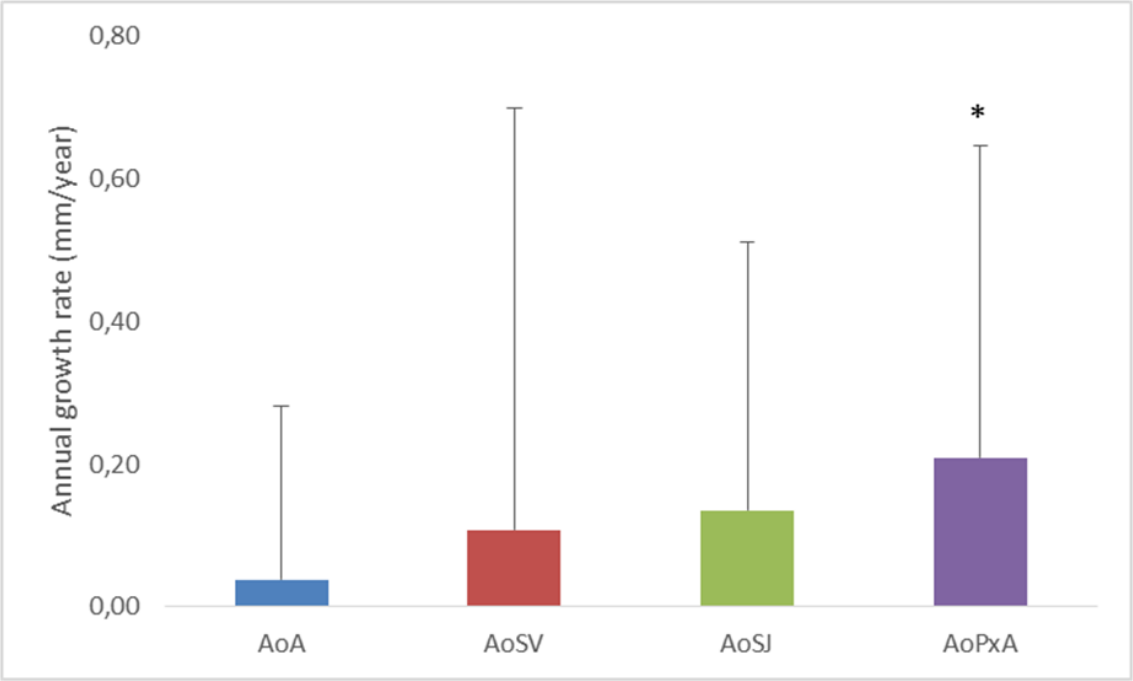

Figure 3. Aortic root and proximal ascending aorta annual growth rate of BAV Elite Athletes. *Significantly different diameter between first and last control. BAV: bicuspid aortic valve; AoA: aortic annulus; AoSV: sinuses of Valsalva; AoSJ: sinotubular junction; AoPxA: proximal ascending aorta.