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ORIGINAL ARTICLE

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The relationship between serum apelin levels and aortic dilatation in bicuspid aortic valve patients*

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Abstract

Objective: The bicuspid aortic valve (BAV) is the most common congenital heart disease. The process of aortic dilatation is not completely clear in patients with the BAV. Apelin is a peptide found at high levels in vascular endothelial cells which has a role in vascular regulation and cardiovascular function. The aim of this study was to determine the relationship between serum apelin levels and ascending aortic dilatation in adult patients with BAV.

Design: This cross-sectional study included 62 patients with isolated BAV and to an age, gender, and body mass index-matched control group of 58 healthy volunteers with tricuspid aortic valve. Transesophageal echocardiography was performed on all patients to determine the type of BAV. Aortic diameters of the aortic root, sinus valsalva, sinotubular junction, and ascending aorta were evaluated with echocardiography. Patients with BAV were divided into two subgroups according to the aortic diameters, as the nondilated BAV group and the dilated BAV group. Serum apelin level was analyzed with ELISA method.

Results: The serum apelin levels of the BAV patients were significantly lower than those of the control group (833.5, 25th-75th percentile (713.5-1745) pg/dL vs 1669 (936-2543) pg/dL; $P = 0.006$). In the subgroup analysis, serum apelin level was significantly different between the nondilated BAV group and the dilated BAV group [977 (790-2433) pg/dL vs 737 (693-870) pg/dL, $P < 0.05$] and between the dilated BAV group and the control group [737 (693-870) pg/dL vs 1669 (936-2543) pg/dL, $P < 0.001$]. In multivariate logistic regression analysis apelin [7.27 (95% CI: 1.73-30.42), $P = 0.007$] and age [1.05 (95% CI: 0.99-1.20), $P = 0.049$] were determined as independent predictors for ascending aortic dilatation.

Conclusion: Low serum apelin level was associated with dilatation of ascending aortic in BAV patients. However, apelin was not relevant to BAV without aortic dilatation.

KEYWORDS

aortic aneurysm, aortic dilatation, apelin, bicuspid aortic valve

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1 | INTRODUCTION

Bicuspid aortic valve (BAV) is the most common congenital heart disease with a prevalence ranging between 0.5% and 2% in the general population.[1,2] BAV is often asymptomatic in childhood, although progressive valvular fibrosis and calcification may lead to valvular dysfunction in adults. BAV does not present solely with aortic valve involvement but also causes dilation of the different sections of the thoracic aorta.[3] According to Park's classification, three different patterns of bicuspid aortopathy can be distinguished based on the region involved in the dilatation: enlargement of only the tubular portion of the ascending aorta, enlargement of both the TP and root and enlargement confined only to the root (sinuses).[4,5] Although the relationship between BAV and aortic dilatation has been well established, the exact mechanism is still unknown. Earlier studies have suggested that abnormal flow from the stenotic valve causes aortic dilatation due to increased wall tension, but aortic dilatation is also observed in patients with normal hemodynamic flow.[4,6] Histopathological findings resembling those observed in patients with Marfan syndrome, such as medial degeneration, increased metalloproteinase, and fibrillin-1 activity, have been observed on the aortic wall of patients with BAV.[7,8] On the basis of these findings, BAV is currently considered as a clinical condition involving genetic disorders related to the aorta and/or heart tissue, and not simply a valvular disease.

Apelin peptide is a member of the adipokine family that was isolated from bovine stomach tissue extracts by Tatemoto et al in 1998, and it exerts its effects by binding to its G-protein-coupled angiotensin-like-1 receptor(APJ).[9] Apelin is known to regulate cardiovascular functions, fluid hemostasis, vessel formation, and cell proliferation.[10] While apelin has been reported to be profusely expressed in human endothelial cells of large conduction vessels, APJ receptor has also been detected in the tunica media.[11] Animal studies have shown that apelin decreases mean arterial pressure and exerts these effects through nitric oxide (NO). Apelin causes endothelium-dependent vasodilation through the Akt activation that phosphorylates endothelial-nitric oxide synthase (eNOS) and promotes NO release as well as increased cyclic-guanosine monophosphate levels.[12] Administration of apelin to animal models of aortic dilatation has been shown to reduce the diameter of the dilated aorta.[13] These animal studies have suggested that there is an inverse relationship between apelin and aortic dilatation. It is unclear whether there is a similar relationship between apelin and aortic dilatation in BAV anatomy in humans. Therefore, the aim of the present study was to evaluate the relationship between serum apelin levels and ascending aortic dilatation in adult patients with BAV.

2 | MATERIAL AND METHODS

2.1 | Study group

Evaluation was made of 102 consecutive patients admitted to our outpatient clinic with suspected BAV or with a previous diagnosis of BAV between January 2014 and May 2015. BAV was identified when only two cusps were unequivocally identified in systole and diastole in the short axis view with a clear "fish mouth" appearance during systole on transthoracic echocardiography (TTE). For enrolment in the study, all patients underwent transesophageal echocardiography (TEE) to verify the diagnosis and identify valvular and aortopathy phenotypes. Patients with left ventricular (LV) systolic dysfunction (LV ejection fraction <55%) (n:5), moderate to severe valvular regurgitation or any degree of valvular stenosis other than the aortic valve (n:3), concurrent congenital cardiac disorder (ie, aortic coarctation, atrial septal defect, etc.) (n:9), patients with a past history of cardiac or vascular surgery (n:5), patients with a history of intervention to the aortic valve or aorta, patients with coronary artery disease requiring revascularization (n:4), patients with diabetes or uncontrolled hypertension (n:8), and those with chronic kidney disease (n:2) were excluded from the study. Patients unwilling to undergo TEE or participate in the study (n:3), or pregnant patients (n:1) were also excluded. Finally, 62 patients were enrolled in the study. The control group included 58 healthy volunteers subjects of similar age, gender and body mass index (BMI), who had no cardiac or ascending aortic disease on TTE in our cardiology department. The tricuspid aortic valve was clearly demonstrated using TTE and/or TEE (if the aortic valve was not well visualized on TTE) in all participants. The findings of patients with BAV were compared with the control group. All subjects aged over 40 years underwent additional exercise stress testing to exclude coronary artery disease. All subjects were in sinus rhythm. The study was approved by the Local Ethical Committee, and all patients provided informed consent for participation.

2.2 | Echocardiography

The echocardiographic study was performed by a single experienced cardiologist. TTE was performed using a Philips iE33×MATRIX device with the patient in the left decubitus position. LV internal systolic and diastolic dimensions, LV wall thickness, and the left atrial (LA) diameter were determined according to the recommendations of guidelines.[14] The aortic root diameters were measured at four levels (aortic annulus, sinuses of Valsalva (SOV), sinotubular junction, and ascending aorta (AA)) using a parasternal long-axis view at the largest diameter on TTE. All aortic measurements except for aortic annulus represented the maximal diameter at the end of LV diastole (as visualized using TTE) while the aortic annulus measurement was made at LV-end systole. In total, 3-5 measurements were made and averaged at each aortic level, then, the results were indexed for body surface area (BSA). In patients with a BSA ≤1.68 m^2, the indexed diameters of AA were used to assess whether the diameters exceeded the upper normal limits. When the indexed AA diameter exceeded two standard deviations of the normal limits, they were regarded as aortic dilatation (the upper limit was 22 mm/m^2 for the SOV and 19 mm/m^2 for the AA diameter).[15] Otherwise, an AA diameter exceeding 39 mm and an SOV diameter exceeding 40 mm was regarded as aortic dilatation.[16]

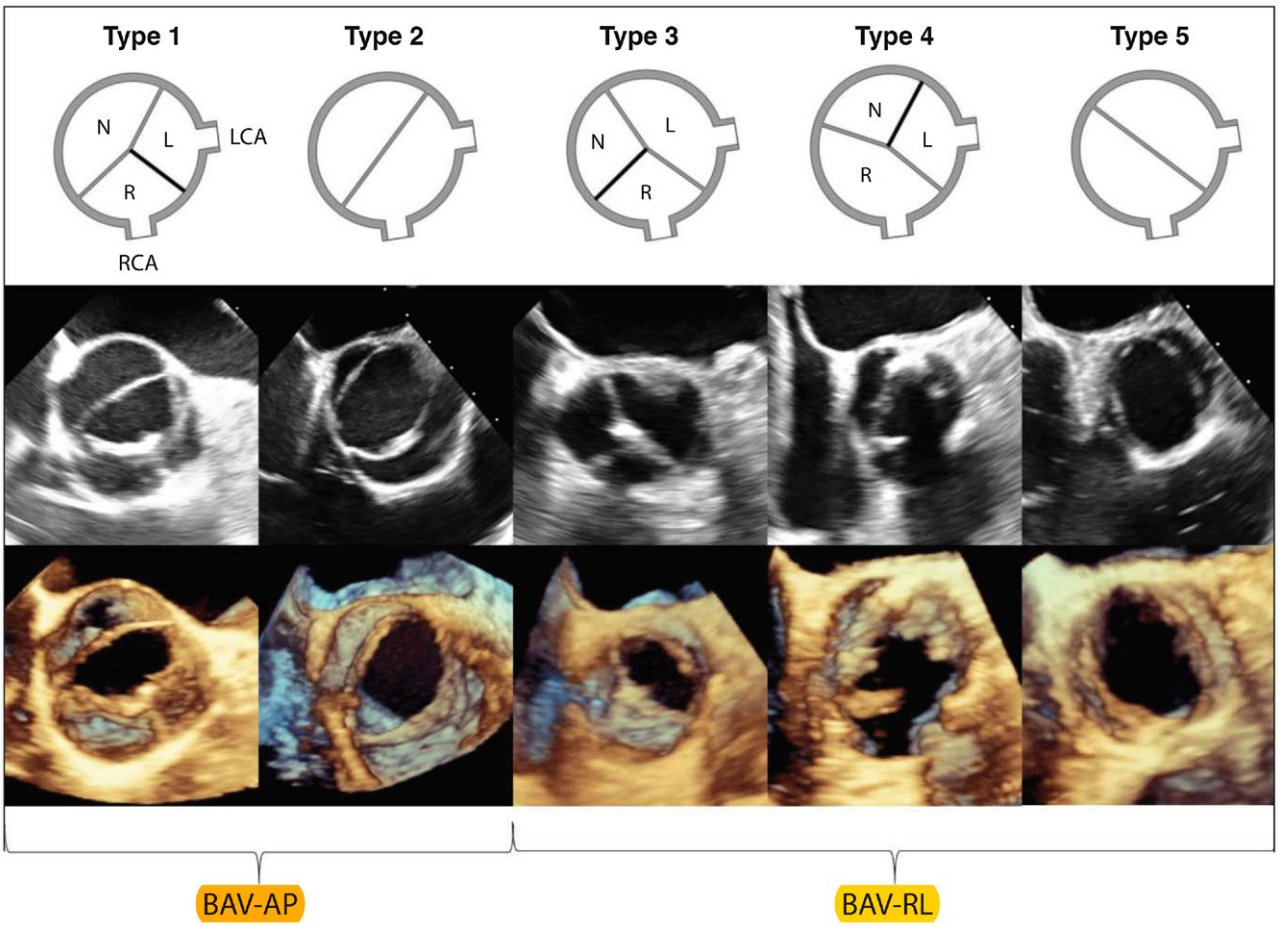

FIGURE 1 BAV phenotypes.[5] Top, Schematic diagram of the five different bicuspid aortic valve (BAV) phenotypes. Middle, Two-dimensional and three-dimensional TEE images of the five BAV phenotypes. Bottom, BAV phenotypes according to the Kang's classification

The pulsed-wave Doppler was placed at the tips of the leaflets to determine aortic velocities. Patients with an aortic jet velocity of 200-299 cm/s were considered to have mild aortic stenosis, and patients with aortic jet velocity of 300 cm/sec or higher were considered to have moderate or severe aortic stenosis. The degree of AR was defined by a composite evaluation of the ratio of proximal jet width to the left ventricular outflow tract (LVOT) diameter, vena contracta, and the presence and severity of holodiastolic aortic flow reversal, according to guidelines.[17] The ratio of proximal jet width to LVOT diameter and vena contracta were calculated in TEE examinations for more appropriate assessment of AR. TEE was performed using a multiplanar probe (Philips X7-2t; Philips Healthcare, Inc., Andover, Massachusetts). TEE views of the ascending aorta, aortic root, and the aortic valve were assessed at the high TEE long axis (at 120-150°) and short axis (at 30-60°). During TEE, the presence/absence of a raphe, orientation of the commissures, and coronary ostia were recorded. BAV was classified as either anterior-posterior (AP) or right-left (RL) according to the Kang classification[16] (Figure 1).

As no data could be found in literature related to the BAV-apelin relationship, first the entire BAV group was compared with the control. Then, the BAV patients were divided into two subgroups

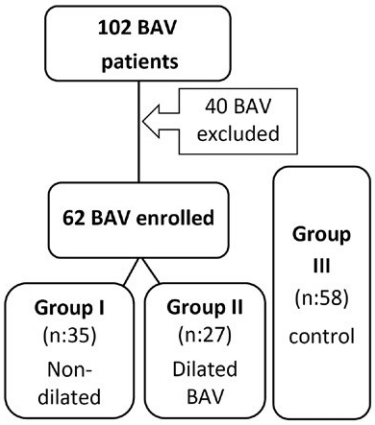

FIGURE 2 Schematic representation of the study population subgroups

according to the ascending aortic diameter to be able to accurately determine the relationship between apelin and ascending aorta dilatation (Figure 2). Patients without AA dilatation were included in the nondilated BAV group (Group I), and patients with dilatation of the AA were included in the dilated BAV group (group II). Patients

with aortic stenosis or aortic insufficiency were also assigned to the subgroups according to the aortic diameters.

2.3 | Laboratory analysis

A venous blood sample of 10 mL was obtained after at least 20 minutes of rest following an 8-hours fasting period for the analysis of serum apelin levels. The venous blood samples were transferred into 8.5 mL BD vacutainer tubes (Becton, Dickinson and Company, Franklin Lakes, New Jersey) in our institution's biochemistry laboratory. The samples were centrifuged at 2000 × g, portioned into Eppendorf tubes and stored at −20°C until analysis. All samples were randomly allocated for each assay and the assays were performed by personnel blinded to the participant's information. Serum apelin levels were measured with the ELISA method using YH Biosearch (Yehua Biological Tech. Co. Ltd, Shangai, China) human apelin kits (Lot No: 20150518; reference no: YHB20150518415). The intra- and inter-assay coefficients of variation (CV) of the kits were <10% and <12%, respectively. The reading range for the kit was 10-4000 pg/ml with a sensitivity of 5.21 pg/ml.

2.4 | Statistical analysis

All analyses were performed using SPSS for Windows Version 15.0 software (SPSS Inc., Chicago, Illinois). The assumption of normality was evaluated using the Shapiro-Wilk and Kolmogorov-Smirnov tests. If the variable was normally distributed, it was presented as the mean ± SD, otherwise, as median values (25th percentile, 75th percentile). The Mann–Whitney *U* test was used to compare continuous variables, as appropriate. Categorical variables were compared with the chi-square test. Continuous variables were compared between the groups using one-way analysis of variance for normally distributed variables and the Kruskal-Wallis test for nonnormally distributed variables. The receiver operating characteristics (ROC) curve analysis was used for determination of the optimal cutoff value of apelin for the prediction of ascending aortic dilatation. The best cutoff apelin level to predict ascending aortic dilatation was determined using the serum apelin values that provided the maximum sensitivity and specificity. According to the optimal cutoff value, the apelin levels were transformed into binary variables before being entered into the logistic regression analysis. For multivariate analysis, the possible factors identified with univariate analyses were further entered into the logistic regression analyses to determine independent predictors of ascending aortic dilatation. A value of $P < 0.05$ was considered statistically significant.

3 | RESULTS

The basic characteristics of the patient and control groups are presented in Table 1. The patients in the study group and subjects in the control group were comparable in terms of age, BSA, BMI, and gender distribution. No statistically significant difference was determined between the groups in respect of prevalence of hypertension

TABLE 1 Demographic characteristics and echocardiographic parameters of the BAV patients and the control group

	Patient group	Control group	
	n = 62	*n* = 58	*P*
Age (year)	39 ± 14	38.6 ± 9.9	0.874
Gender (F/M)	17/45 (27.4%/72.6%)	18/40 (31%/68.9%)	0.491
BSA (m^2)	1.90 (1.7-2.0)	1.91 (1.8-2.0)	0.563
BMI (kg/m^2)	26.5 ± 4.2	26 ± 4.5	0.648
Smoking (%)	10 (16%)	11 (19%)	0.450
Hypertension (%)	10 (16%)	8 (14%)	0.125
Left atrium (mm)	34.0 ± 4	34.0 ± 5.5	0.311
EDV (ml)	105 ± 29	103 ± 24	0.768
ESV (ml)	39 ± 15.2	35 ± 14.0	0.370
LVEF (%)	63 ± 7.0	66.0 ± 5.5	0.082
Aortic velocity (cm/s)	216 (156-298)	125 (118-138)	<0.001
Aortic VTI (cm)	44.7 (31-58)	25.3 (19.5-29.4)	<0.001
Aortic annulus (mm)	27.0 (24.7-31)	24.0 (21-26)	<0.001
Aort SOV (mm)	34.0 (30-37)	30.0 (28-32)	0.001
Aort STJ (mm)	29.0 (25-33)	26.0 (24-27)	0.003
Ascending aorta (mm)	38.7 (33-44)	28.0 (26-31)	<0.001

Abbreviations: EDV, end-diastolic volume; ESV, end-systolic volume; LVEF, left ventricular ejection fraction; SOV, sinuses of Valsalva; STJ, sinotubular junction; VTI, velocity time integral.
The data are expressed as mean ± SD for parametric tests, median (25th percentile, 75th percentile) values for nonparametric tests.

or of smoking. Of patients with BAV, 23 (37%) had moderate-to-severe AS and 20 (32%) had moderate-to-severe aortic insufficiency (AI). The echocardiographic parameters are shown in Table 1. The left ventricular end-diastolic diameter, left ventricular end-systolic diameter, end-diastolic volume, end-systolic volume, left atrium diameter, and left ventricular ejection fraction values were similar in the two groups ($P > 0.05$). Aortic velocities and AA diameters were higher in the study group than in the control group because of the aortic stenosis (AS) and dilatation of AA in the study group ($P < 0.05$). Serum apelin levels were significantly lower in the BAV group than in the control group [833.5 (713.5-1745) pg/dL vs 1669 (936-2543) pg/dL; $P = 0.006$] (Figure 3).

Of the patients with BAV, approximately equal proportions had the antero-posterior commissural line (52%) and right-left commissural line (48%). When the apelin levels were analyzed in the BAV patients according to BAV phenotype, there was no significant difference in apelin levels between patients with BAV-AP and BAV-RL (1136 ± 791 pg/dL vs 1143 ± 714 pg/dL, $P = 0.80$).

Demographic characteristics were also analyzed with two subgroups of BAV and the control group in multiple group comparisons (Table 2). There was a significant difference in the ages across the groups. The significant differences between the groups were as follows: nondilated BAV group vs control group; and dilated BAV group vs control group. The prevalence of hypertension in the dilated BAV group was higher than that in the other groups and this difference was of borderline statistical significance. There was a significant difference in the aortic velocity time integral (VTI) across the groups ($P < 0.001$ for dilated BAV group vs control group and for nondilated BAV group vs control group). No significant difference was determined in aortic VTI between the dilated BAV group and the nondilated BAV group. There was a significant difference between the three groups in terms of apelin levels (Table 2). This difference derived from the difference between the nondilated BAV group and the dilated BAV group and, between the dilated BAV group and the control group. There was no significant difference between the nondilated BAV group and the control group. In the ROC curve analysis, it was shown that apelin levels of 959 pg/ml had 83% sensitivity and 64% specificity for the prediction of ascending aortic dilatation (Figure 4).

To determine independent predictors of ascending aortic dilatation, univariate and multivariate logistic regression analysis was performed (Table 3). The univariate regression analysis showed that age, hypertension, BMI, aortic VTI, and low serum apelin level (≤959 pg/ml) were associated with the presence of ascending aortic dilatation. In the multivariate regression analysis only low apelin level [7.27 (95% CI: 1.73-30.42), $P = 0.007$] and age [1.05 (95% CI: 0.99-1.20), $P = 0.049$] remained as independent predictors for ascending aortic dilatation.

4 | DISCUSSION

To the best of our knowledge, the present study is the first clinical study which demonstrates low serum apelin level as an independent predictor of dilatation of the ascending aorta (AA) in adult patients with BAV. In BAV subgroups those with dilatation of the AA had

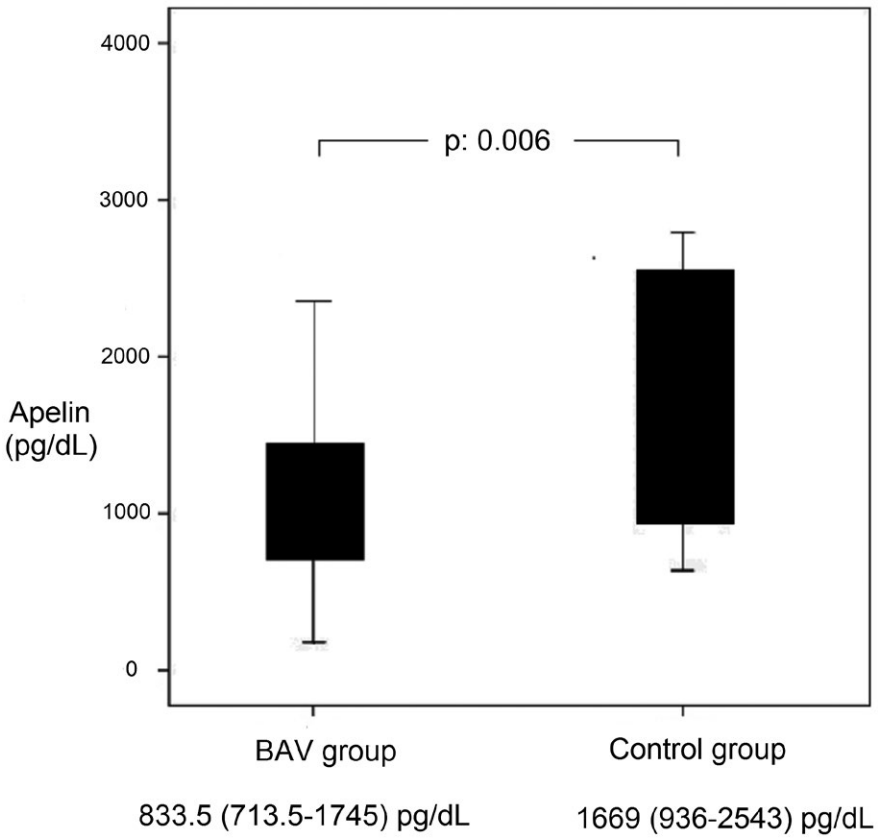

FIGURE 3 Serum apelin levels in the BAV and control group. The data are expressed as median (25th percentile, 75th percentile)

TABLE 2 Distribution of demographic data and apelin levels after separating patients into the nondilated BAV and dilated BAV subgroups

	Group I (nondilated BAV)	Group II (dilated BAV)	Group III (control)	
	n = 35	*n* = 27	*n* = 58	*P* value
Age (years)	33.8 ±12.7	45.9 ± 12.8	38.6± 9.9	0.001[af]
BMI (kg/m^2)	25.6 ± 4.1	27.7± 4.0	26.0 ± 4.5	0.127[f]
Hypertension	4 (%12)	6 (22%)	8 (14%)	0.06
LVEF (%)	63.0 ± 7.2	62.8 ± 6.7	66.0 ± 5.5	0.151[f]
Aortic VTI (cm)	36.6 (30.5-56.8)	48.8 (32.0-61.6)	25.3 (19.5-29.4)	<0.001[bcg]
Apelin (pg/mL)	977 (790-2433)	737 (693-870)	1669 (936-2543)	<0.001[deg]

Abbreviations: BAV, bicuspid aortic valve; BMI, body mass index; LVEF, left ventricular ejection fraction; VTI, velocity time integral.
The data are expressed as mean ± SD for parametric tests, median (25th percentile, 75th percentile) value for nonparametric tests.
[a]Nondilated BAV vs control *P* < 0.001; Tukey test.
[b]Dilated BAV vs control *P* < 0.001; Tukey test.
[c]Dilated BAV vs control *P* < 0.001; Mann-Whitney *U* test.
[d]Nondilated BAV vs control *P* < 0.001; Mann-Whitney *U* test.
[e]Nondilated BAV vs dilated BAV *P* < 0.001; Mann-Whitney *U* test.
[f]Dilated BAV vs control *P* < 0.001; Mann-Whitney *U* test.
[g]ANOVA test.
[h]Kruskal-Wallis test.

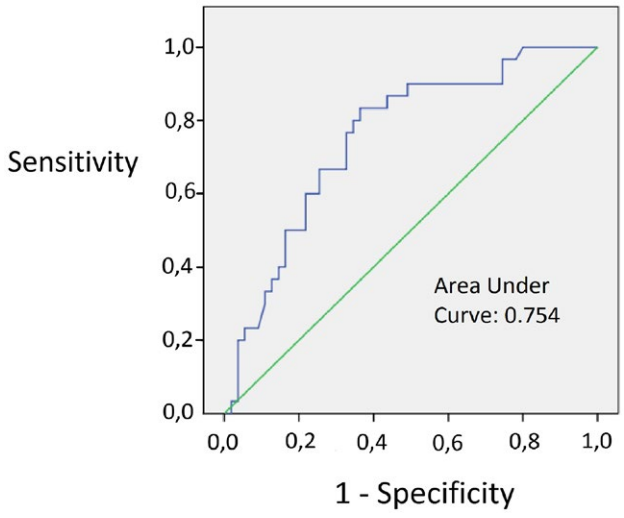

FIGURE 4 ROC curve analysis of apelin for the prediction of ascending aortic dilatation

significantly lower serum apelin levels when compared to both BAV patients without dilatation of the AA and control subjects. In addition to apelin, age was also shown to be an independent predictor of dilatation of the AA.

Although the current opinion is that beta-blockers and ACE-inhibitors reduce the progression of aortic aneurysms by improved control of the blood pressure in Marfan syndrome, the role of these agents is not yet clear in aortic aneurysms associated with BAV.[18,19] In some patients, BAV is accompanied predominantly by valvular pathologies, whereas some patients have concurrent aortic pathologies such as an aneurysm and dissection. It is not clear through which mechanisms these different manifestations occur. Differences at the molecular level that have not yet been identified may be responsible for these differences. Apelin is an adipokine that serves as an endogenous ligand for orphan G protein-coupled APJ receptor. The finding that intravenous administration of apelin-13 to rats decreased systolic and diastolic blood pressure was the first evidence reflecting the effects of apelin on cardiovascular system functions.[20] The disappearance of this effect with the addition of NO synthase inhibitor by Tatemoto et al suggested that the vasoactive effects of apelin are mediated by nitric oxide (NO).[12] Endothelial function abnormalities caused by the altered expression of endothelial NO synthase (eNOS) have been shown to play a role in the development and progression of aortic dilatation in previous studies.[21,22] Interestingly, animal studies have shown a higher prevalence of congenital BAV in eNOS knockout mice. This finding points to the potential role of NO in the development of the heart. In a study of 40 patients with bicuspid and tricuspid aortic valve that underwent aortic surgery, Aicher et al evaluated eNOS in aortic wall samples and reported a remarkable decrease in eNOS levels in aortic endothelial cells of patients with BAV compared to patients with the tricuspid aortic valve. Furthermore, a negative correlation was reported between eNOS levels and aortic root and AA diameters.[22] In the present study, serum apelin levels were found to be significantly lower in BAV patients with dilatation of the AA when compared to the control subjects and BAV patients without dilatation of the AA. It can be considered that a deficiency of apelin, similar to eNOS, may have caused changes in the aortic wall and led to the development of aneurysms in patients with BAV.

One of the most likely mechanisms for altered aortic dimensions in BAV patients is altered fluid mechanics, such as abnormal flow from the stenotic valve.[23] However, some studies have shown that

TABLE 3 Univariate and multivariate analysis using the logistic regression method for dilatation of ascending aorta

	Univariate regression analysis		Multivariate regression analysis	
Variables	**Odds ratio (95% CI)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Age	1.07 (1.03-1.12)	0.001	1.05 (0.99-1.20)	0.049
BMI (kg/m^2)	1.13 (1.00-1.27)	0.050	1.93 (0.93-1.29)	0.293
Hypertension	1.93 (1.04-3.63)	0.063	1.12 (0.18-6.93)	0.901
Apelin level	5.11 (1.93-13.52)	<0.001	7.27 (1.73-30.42)	0.007
[a]≤ 959 vs >959 pg/ml				
Aortic VTI (cm)	1.03 (1.01-1.06)	0.011	1.00 (0.97-1.03)	0.735

Abbreviations: BMI, body mass index; CI, confidence interval; VTI, velocity time integral.
[a]The apelin levels were modeled into a binary outcome as a ≤959 or >959 pg/ml before being entered into the logistic regression analysis.

BAV is associated with an alteration of aortic dimensions even in the absence of hemodynamically significant aortic valve stenosis or regurgitation.[24] In the present study, there was a significant difference in the aortic VTI across the groups. While the values of the dilated BAV group and nondilated BAV group were significantly higher than that of the control group ($P < 0.001$), there was no statistically significant difference between the dilated BAV group and the nondilated BAV group ($P > 0.05$). In the regression analysis, the relationship between aortic VTI and ascending aortic dilatation was not an independent relationship, which suggested the impact of other possible confounding factors, such as apelin.

The binary classification of BAV-AP and BAV-RL types has persisted even though it is well known that BAV is characterized by variable patterns of leaflet fusion. Although BAV-AP has been shown to be significantly more common in the general population according to previous reports,[25,26] some studies have reported that the prevalence of both types is approximately equal.[16] In the current study, despite the comparable prevalence of both types, BAV-AP type was slightly higher than BAV-RL type (52% BAV-AP, 48% BAV-RL). Some recent animal studies have shown that different BAV phenotypes (BAV-AP and BAV-RL) are different embryological entities. These studies suggest that BAV-AP is caused by the defective formation of the outflow tract (OFT) cushion, which might be a result of an alteration in the neural crest, whereas BAV-RL seems to be the result of defective OFT septation, which might occur during the nitric oxide-dependent stage of endothelial-to-mesenchymal transformation.[25,27] However, in the current study population, no difference was detected between the BAV-AP and BAV-RL groups with regard to apelin levels. This might suggest that animal models for BAV are not compatible with humans. In a previous study of BAV patients with normally functioning valves by the current authors, no difference was detected between myocardial functions and aortic diameters when BAV-RL patients were compared with BAV-AP patients, which might also reflect that these two entities might not be embryologically different.

Recent clinical investigations have reported that age was a predictor of aortic dilatation in BAV patients.[28] In the current study groups, age was statistically significantly higher in the dilated BAV group. The difference in age between the three groups could be a possible confounding factor for the results. Therefore, to determine independent predictors of dilatation of AA, univariate and multivariate logistic regression analyses were performed and both age and low apelin level were shown to be independent predictors for ascending aortic dilatation in BAV. The determination of age as a predictor of aortic dilatation in the current study was in concordance with the previous data. In addition, the ROC curve revealed that serum apelin levels of ≤959 pg/ml are optimal for the prediction of ascending aortic dilatation. A low serum apelin level (≤959 pg/ml) was also found to be associated with a 7.3-fold greater likelihood of aortic dilatation than a high apelin level (>959 pg/ml).

The small number of patients in the study is the main limitation of this study. A consequence of the sample size was the statistical imprecision of the odds ratio estimates for serum apelin which had very wide 95% confidence intervals. Another limitation is that the study was conducted at a single center and only on adult patients, so further multicenter studies including children with BAV are needed to be able to generalize the results to all BAV patients. Finally, as this clinical study was cross-sectional in design, it does not provide any evidence of a cause and effect relationship. Nevertheless, these data provide additional evidence of aortic dilatation in BAV and apelin may be a potential therapeutic target in BAV aortopathy. The hypothesis of this study could be confirmed with evaluation of the levels of APJ receptors and eNOS in the same patient group. Further studies are required to explain the extent of apelin deficiency in patients with BAV and to verify its role as a predictor for aortic dilatation.

In conclusion, serum apelin was decreased in BAV patients with ascending aortic dilatation and apelin was an independent marker of ascending aortic dilatation. The current findings may lead to further studies researching the therapeutic potential utility of apelin in BAV patients with aortopathy whose treatment is not yet clarified.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

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Analysis and/or interpretation: Kami Tuluce, Ersin Cagri Simsek, Selcen Yakar Tuluce.

Critical revision of article: Kami Tuluce, Selcen Yakar Tuluce.

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