

Featured Article

A machine learning predictive model based on conventional two-dimensional echocardiography and serum biomarkers for early detection of ascending aorta dilation in BAV patients

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CITATION

Long X, Niu Y, Nie G, et al. A machine learning predictive model based on conventional two-dimensional echocardiography and serum biomarkers for early detection of ascending aorta dilation in BAV patients. *Psycho-Oncologie*. 2025; *Psycho-Oncology Research in China*: 4573.

ARTICLE INFO

Received:

Accepted:

Available online:

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Abstract: Objective: To compare echocardiographic parameters and lipid biomarker levels between patients with bicuspid aortic valve (BAV) associated with ascending aorta dilation and those without dilation using machine learning models, and to identify early diagnostic features for BAV-associated dilation. **Methods:** A retrospective cohort of 51 BAV patients (25 with ascending aorta dilation and 26 without) from the Ningxia Medical University Affiliated Hospital (January 2024–November 2024) was enrolled. Routine echocardiography and lipid profile measurements were performed. Lasso regression was applied to select key features, construct a predictive model, and develop a nomogram for individualized risk assessment. **Results:** BAV dilation group exhibited significantly higher AAOV and AAOMPG than the non-dilation group ($P < 0.05$ for both). HDL levels were also elevated in the dilation group ($P < 0.05$). Lasso regression identified five critical features: age, HDL, ApoB, LVMI, and AAOV, with the model formula: $Y = -0.02678133 + (0.10741491 \times \text{age}) + (0.25612267 \times \text{HDL}) + (-0.12903915 \times \text{ApoB}) + (0.14253473 \times \text{LVMI}) + (0.49063628 \times \text{AAoV})$. The model achieved an AUC of 0.825 (95% CI: 0.694–0.933). **Conclusion:** This study successfully identified key features using Lasso regression and developed an efficient predictive model for BAV-associated ascending aorta dilation. The model demonstrates strong diagnostic performance, interpretability, and clinical applicability. The nomogram provides a practical tool for individualized risk prediction, aiding early diagnosis, intervention decisions, and patient follow-up.

Keywords: bicuspid aortic valve; ascending aorta; echocardiography; lipid profile; machine learning

1. Introduction

Bicuspid aortic valve (BAV), the most prevalent congenital cardiac anomaly, is characterized by malformed aortic valve leaflets. Epidemiological studies report a global prevalence of 0.5%–2%, with a neonatal incidence of 0.77% documented in a Danish population-based study [1]. While BAV patients often maintain normal valvular function during early life, longitudinal evidence reveals substantial progression risks: 50%–70% develop aortic dilation [2], frequently accompanied by aortic valve dysfunction (stenosis/regurgitation), aortic dissection/aneurysm, or infective endocarditis. Notably, BAV-associated aortic pathologies exhibit distinct risk profiles, including an 8-fold elevated aortic dissection incidence versus the general population. Disease duration exceeding 25 years correlates with a 26%

aneurysm formation rate, and 32% of patients require surgical intervention. Critically, mortality from BAV-related aortic complications exceeds cumulative fatalities of other congenital heart defects [3], emphasizing the need for improved management strategies.

The predictive value of morphological assessment based on aortic diameter for aortic events remains limited. Since the mechanisms underlying aortic disease in BAV patients are not fully elucidated, other potential mechanisms may be involved. Studies have demonstrated that serum total cholesterol levels are closely associated with the progression of aortic stenosis and coronary artery calcification. In BAV patients, dyslipidemia may synergistically contribute to hemodynamics-related aortic dilation [4]. Additionally, low high-density lipoprotein (HDL) and high total cholesterol (TC) levels have been linked to accelerated abdominal aortic expansion [5]. In BAV, the synergistic effect of hemodynamic stress and dyslipidemia may drive disease progression.

To address diagnostic limitations, machine learning models integrating clinical, imaging, and biomarker data have gained prominence. Supervised algorithms (e.g., Lasso) enable identification of critical predictors for constructing prognostic frameworks. These models demonstrate utility in disease staging, risk stratification, and personalized therapeutic planning, offering novel avenues for optimizing BAV care.

This study hypothesizes serum lipid biomarkers as predictors of aortic dilation in BAV. Utilizing 2D transthoracic echocardiography (2D-TTE) and lipid profiles, we will develop Lasso models to evaluate their predictive performance. Through comparative analysis, we aim to establish an optimal model for early detection of aortic dilation, enhancing clinical risk assessment in BAV populations.

2. Material and methods

2.1. Patient selection

This study enrolled 51 patients with bicuspid aortic valve (BAV) who were admitted to the General Hospital of Ningxia Medical University from January 2024 to November 2024. Written informed consent was obtained from all participants, and the study was approved by the Ethics Committee of the General Hospital of Ningxia Medical University (approval number: 2020-280). BAV was diagnosed according to the International Consensus on Bicuspid Aortic Valve [6]. Patients were categorized into the BAV with ascending aorta dilation group (BAV-D, $n = 25$) and the BAV without dilation group (BAV-ND, $n = 26$) based on the diameter of the proximal ascending aorta measured by echocardiography. Exclusion criteria included: aortic stenosis, moderate or severe aortic regurgitation, significant aortic valve calcification, prior cardiac surgery, history of hypertension or other cardiovascular diseases, hyperlipidemia, diabetes mellitus, renal insufficiency, and end-stage diseases. Clinical data (age, height, weight, blood pressure, etc.) and 5 mL of fasting venous blood were collected from eligible participants.

2.2. Echocardiography

Participants were positioned in the left lateral decubitus or supine position and instructed to maintain quiet breathing. A GE Vivid E95 echocardiography system (S5-1 probe) was used with the pre-set “Adult Echo” protocol for routine echocardiographic examination. The following parameters were measured: diastolic interventricular septal thickness (IVSd), left ventricular end-diastolic diameter (LVIDd), and diastolic left ventricular posterior wall thickness (LVPWd). Left ventricular mass (LVM) and left ventricular mass index (LVMI) were calculated. Left atrial volume (LAV) was determined using the Simpson's method, and left atrial volume index (LAVI) was derived by dividing the measured value by body surface area (BSA). Pulse Doppler was applied to acquire flow spectra of the ascending aorta at rest, and manual tracing was performed to obtain the maximum velocity (AAoV) and mean pressure gradient (AAoMPG) of the ascending aorta.

2.3. Sample treatment

Venous blood was centrifuged at 3000 rpm for 10 min using a low-temperature centrifuge to obtain the supernatant. Biochemical analyses were performed using a Hitachi 7180 automated biochemistry analyzer. Triglyceride (TG) levels were measured using a GPO-PAP assay kit; total cholesterol (TC) levels were determined via a CHOD-PAP assay kit. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels were assessed using the direct peroxidase-based enzymatic method. Apolipoprotein A (ApoA) and apolipoprotein B (ApoB) levels were measured by immunoturbidimetry.

2.4. Machine learning model construction

One classification models based on patients' aortic valve morphology were established. Feature selection was performed using the Lasso algorithm via the glmnet package in R. Receiver operating characteristic (ROC) curves were generated using the pROC package, and model performance was evaluated based on accuracy, sensitivity, and specificity. A nomogram was finally developed using the rms package to predict event occurrence.

2.5. Statistical analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables with normal or approximately normal distributions were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and comparisons between groups were analyzed using the independent samples t-test. Non-normally distributed data were analyzed using nonparametric tests. A P value ≤ 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves were constructed to evaluate the diagnostic performance of each parameter.

3. Results

3.1. Comparison of clinical characteristics

There were no statistically significant differences in age, height, weight, body surface area (BSA), body mass index (BMI), or blood pressure between the two groups (all $P > 0.05$) (See **Table 1**).

Table 1. Comparison of characteristics between the two groups (Mean $\pm$ SD).

	BAV-D ($n = 25$)	BAV-ND ($n = 26$)	<i>F</i>	<i>P</i>
Ages (year)	43.28 $\pm$ 9.81	38.53 $\pm$ 10.62	0.213	0.105
Height (m)	1.68 $\pm$ 7.00	1.69 $\pm$ 7.91	0.242	0.836
Weight (kg)	66.50 $\pm$ 11.04	69.67 $\pm$ 15.28	1.037	0.401
BSA (kg/m ²)	1.75 $\pm$ 0.16	1.79 $\pm$ 0.21	0.870	0.499
BMI	23.27 $\pm$ 0.88	24.10 $\pm$ 3.52	3.757	0.555
SBP (mmHg)	121.32 $\pm$ 10.19	123.38 $\pm$ 14.19	3.757	0.555
DBP (mmHg)	83.40 $\pm$ 8.30	80.80 $\pm$ 8.92	1.460	0.288

3.2. Comparison of 2D-TTE measurements between groups

No statistically significant differences were observed in LA-A4C, LA-A2C, LA, LAVI, LVMI, or EF between the two groups ($P > 0.05$ for all). In contrast, the BAV with dilation (BAV-D) group exhibited significantly higher values of AAOV and AAO MPG compared to the BAV without dilation (BAV-ND) group ($P < 0.05$ for both). See **Table 2** for details.

Table 2. Comparison of 2D-TTE measurements between groups (Mean $\pm$ SD).

	BAV-D ($n = 25$)	BAV-ND ($n = 26$)	<i>F</i>	<i>P</i>
LA-A4C (cm ²)	13.91 $\pm$ 3.27	12.90 $\pm$ 2.77	0.806	0.239
LA-A2C (cm ²)	14.25 $\pm$ 4.22	13.47 $\pm$ 3.29	2.201	0.465
LA(ml)	43.38 $\pm$ 15.41	38.46 $\pm$ 12.53	2.398	0.216
LAVI(ml/m ²)	24.57 $\pm$ 7.73	21.42 $\pm$ 6.07	1.777	0.116
LVMI	84.08 $\pm$ 11.84	78.94 $\pm$ 10.07	1.553	0.101
EF	66.56 $\pm$ 2.84	66.19 $\pm$ 2.60	0.128	0.632
AAoV	1.57 $\pm$ 0.44	1.29 $\pm$ 0.21	6.179	0.006*
AAoMPG	10.83 $\pm$ 6.80	6.76 $\pm$ 2.58	9.361	0.005*

3.3. Comparison of lipid biomarker levels between groups

No statistically significant differences were observed in TC, TG, LDL, ApoA, ApoB, levels between the two groups ($P > 0.05$ for all). However, the BAV with dilation (BAV-D) group exhibited significantly higher HDL levels compared to the BAV without dilation (BAV-ND) group ($P < 0.05$). See **Table 3** for details.

Table 3. Comparison of serum biomarker levels between groups (Mean $\pm$ SD).

	BAV-D (<i>n</i> = 25)	BAV-ND (<i>n</i> = 26)	<i>F</i>	<i>P</i>
TC (mmol/L)	2.86 $\pm$ 1.64	3.26 $\pm$ 1.46	3.038	0.370
TG (mmol/L)	2.73 $\pm$ 1.67	2.66 $\pm$ 1.53	0.657	0.877
HDL (mmol/L)	1.25 $\pm$ 0.29	1.07 $\pm$ 0.26	0.104	0.029*
LDL (mmol/L)	2.63 $\pm$ 0.58	2.91 $\pm$ 0.93	1.580	0.208
ApoA (g/L)	1.36 $\pm$ 0.22	1.26 $\pm$ 0.21	0.340	0.095
ApoB (g/L)	0.76 $\pm$ 0.13	0.82 $\pm$ 0.19	1.381	0.154

3.4. Feature selection

Features were extracted from clinical data, echocardiographic parameters, and serum biomarkers of the participants. The Lasso algorithm combined with 10-fold cross-validation was used to determine the optimal λ value and select the corresponding features. **Figure 1** illustrates the parameter selection process of the Lasso model using mean squared error (MSE) as the evaluation metric, which ultimately identified five features (**Table 4**).

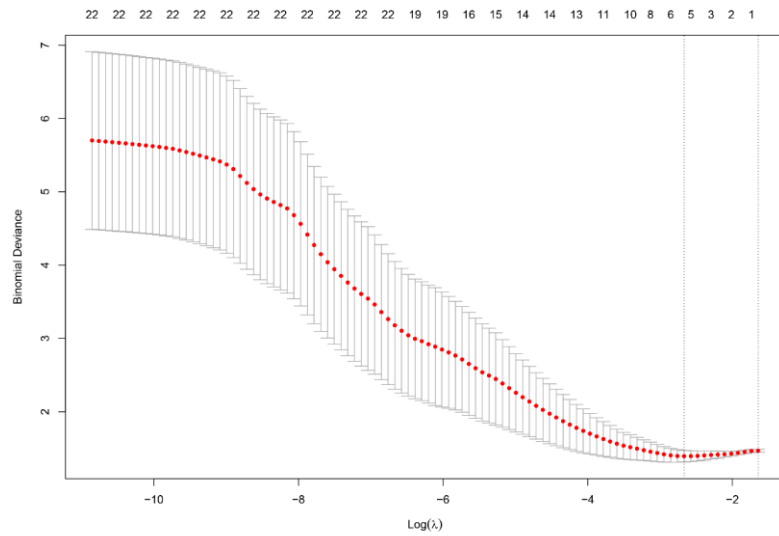


Figure 1. Feature selection process via lasso algorithm in R.

Table 4. Feature selection results.

Feature	Coefficients
Ages	0.10741491
HDL	0.25612267
ApoB	-0.12903915
LVMi	0.14253473
AAoV	0.49063628

A Lasso model was constructed using the selected features and their coefficients to predict BAV-associated ascending aorta dilation. The receiver operating characteristic (ROC) curve for predicting BAV-associated ascending aorta dilation is

shown in **Figure 2**. The model exhibited an AUC value of 0.825 (95% CI: 0.694–0.933), with an accuracy of 0.745, sensitivity of 0.720, and specificity of 0.769.

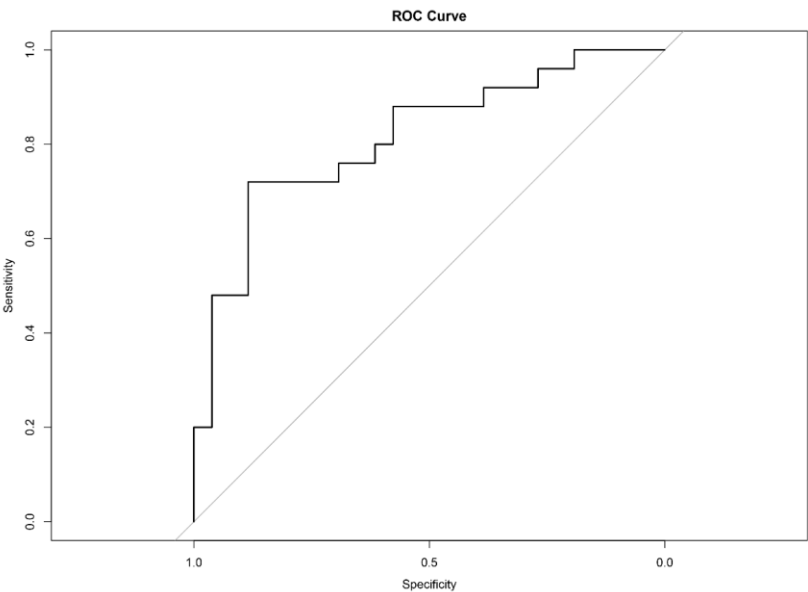


Figure 2. ROC curve of the lasso model.

To individualize the prediction of ascending aorta dilation risk in BAV patients, this study identified five variables selected by the Lasso model as independent predictors. A nomogram was constructed using the R software package based on the coefficients of these features, enabling personalized calculation of the risk probability for ascending aorta dilation in BAV patients (**Figure 3**).

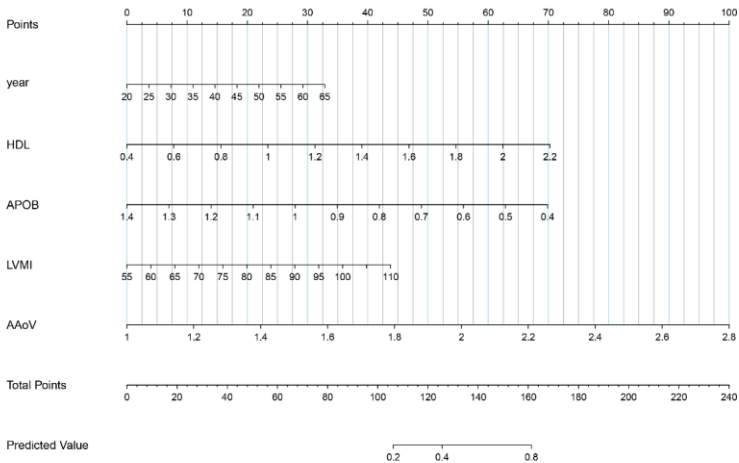


Figure 3. Nomogram for predicting BAV-associated ascending aorta dilation.

The model equation was formulated using the coefficients of the selected features as follows:

$$Y = -0.02678133 + (0.10741491 \times \text{year}) + (0.25612267 \times \text{HDL}) + (-0.12903915 \times \text{APOB}) + (0.14253473 \times \text{LVMI}) + (0.49063628 \times \text{AAoV}).$$

4. Discussion

The current study compared clinical parameters between BAV patients with and without aortic dilation, highlighting the potential roles of hemodynamic indices and lipid metabolism in BAV-associated aortic dilation. Although no significant differences were observed between the groups in baseline characteristics (age, body surface area), cardiac structure (LA, LVMI), and function (EF), the dilated group exhibited higher aortic valve velocity (AAoV), mean aortic pressure gradient (AAoMPG), and high-density lipoprotein (HDL) levels, suggesting that these parameters may contribute to pathological remodeling of the aorta in BAV patients.

Hemodynamic abnormalities are considered key drivers of aortic dilation in BAV patients. Compared to lipid metabolism, hemodynamic abnormalities (e.g., AAoV and AAoMPG) may play a more direct role in BAV-associated aortic dilation. This finding supports the hypothesis that abnormal blood flow shear stress contributes to the degenerative remodeling of the aortic wall. Mechanistically, hemodynamic indices such as pressure gradients and velocity reflect real-time mechanical stress loads on the aortic wall, which can directly degrade vascular matrix structure by activating matrix metalloproteinases (MMP-2/9) and inflammatory pathways [7]. In contrast, elevated high-density lipoprotein (HDL) levels may represent a secondary compensatory response with delayed and indirect effects. As a sensitive indicator of hemodynamic load, increased AAoMPG may signal early compensatory remodeling of the aortic wall, consistent with the mechanical injury mechanism observed via 4D flow MRI in BAV-specific vortical flow patterns [8]. The Lasso regression model employs L1 regularization to select five critical features from candidate variables: age, HDL, ApoB, LVMI, and AAoV. This process significantly reduced model complexity while enhancing interpretability. The sparsity of Lasso regression enables it to excel in high-dimensional data analysis by identifying the most influential variables for prediction. The selected features have been validated in prior studies for their associations with cardiovascular disease. For instance, age is an independent risk factor for cardiovascular disease [9], HDL and ApoB are lipid metabolism markers linked to atherosclerosis [10], and LVMI and AAoV reflect cardiac remodeling and aortic valve function as structural parameters [11]. The advantages of the Lasso model include: (1) Interpretability: Its linear structure allows straightforward interpretation of feature coefficients, facilitating clinical evaluation of their impact on predictions; (2) Computational Efficiency: Low computational complexity ensures ease of implementation and deployment, making it suitable for rapid clinical application; (3) Widespread Utility: As a classical statistical method, Lasso is broadly accepted and extensively applied in medical research.

Based on the five features selected by the Lasso model, a nomogram was developed to enable personalized prediction of BAV-associated ascending aorta dilation risk. The nomogram translates complex statistical models into an intuitive visual tool to aid clinical decision-making. It is user-friendly, requiring clinicians only to mark and sum scores based on patients' feature values to rapidly calculate risk

percentages. This approach facilitates early identification of high-risk patients and guides the implementation of preventive and therapeutic interventions.

Overall, this study identified five critical features using the Lasso regression model and developed an efficient predictive model for BAV-associated ascending aorta dilation. By constructing a nomogram, an individualized risk prediction approach was established, providing a practical tool for early clinical diagnosis, intervention guidance, and patient follow-up.

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