

Machine learning-based prediction of mortality and renal replacement therapy in ANCA- associated vasculitis: a single-center cohort study

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Abstract

Objectives

To analyze the clinical characteristics and prognosis of patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), identify independent risk factors for mortality and adverse renal outcomes, and construct machine learning prediction models to evaluate their prognostic value, thereby providing evidence for early diagnosis, risk stratification, and individualized treatment.

Methods

Using 14 baseline clinical variables (age, sex, systemic manifestations, pulmonary and renal involvement, dialysis requirement at diagnosis, BVAS score, hemoglobin, eGFR, serum creatinine, CRP, ESR, white blood cell count, and platelet count), we built four prediction models: logistic regression, LASSO, random forest, and XGBoost. Missing values were imputed with the median for continuous and the mode for categorical variables, and logistic and LASSO inputs were Z-score standardized. Models were evaluated by 5-fold stratified cross-validation, with AUC as the primary metric; sensitivity and specificity were calculated at the Youden-optimal threshold. Calibration curves, decision curve analysis (DCA), and SHAP analysis assessed calibration, clinical utility, and feature contributions, respectively. Analyses were run in Python 3.9 (scikit-learn 1.0.2; XGBoost 1.6.2) with a fixed random seed (random_state = 42) for reproducibility.

Results

Among 256 patients, microscopic polyangiitis (MPA) was the most common subtype (243 cases, 94.9%), followed by granulomatosis with polyangiitis (GPA) (12 cases, 4.7%) and eosinophilic granulomatosis with polyangiitis (EGPA) (1 case). MPO-ANCA was positive in 206 cases (80.8%) and PR3-ANCA in 49 cases (19.2%). Lung involvement occurred in 169 cases (71.0%) and renal involvement in 202 cases (79.2%). Compared with GPA, MPA patients had more frequent renal involvement and more severe renal impairment. Compared with PR3-ANCA-positive patients, MPO-ANCA-positive patients were older, predominantly female, and had more severe renal involvement. During a median follow-up of 26 months (range, 1-180 months), 60 patients died (29.9% among those with complete follow-up), 141 survived, and 54 were lost to follow-up. Multivariate analysis identified advanced age, systemic symptoms, dialysis requirement at diagnosis, and low eGFR as independent risk factors for mortality. For mortality prediction, the random forest model achieved the best performance (AUC = 0.863, sensitivity = 0.933, specificity = 0.730); for renal replacement therapy (RRT) prediction, XGBoost performed best (AUC = 0.949, sensitivity = 0.877, specificity = 0.884). Calibration and decision curve analyses supported the clinical value of the models across a wide range of threshold probabilities, and SHAP identified age, eGFR, and dialysis requirement at diagnosis as the top three predictors for both outcomes.

Conclusions

MPA was the predominant subtype in this cohort, with the lungs and kidneys the organs most often involved. Advanced age, dialysis requirement at diagnosis, and low eGFR independently predicted mortality. Machine learning models built on baseline clinical parameters showed good discrimination and clinical utility for both mortality and RRT, and may support risk stratification and individualized management of AAV patients.

1. Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune diseases characterized by serum ANCA positivity and necrotizing inflammation of small vessel walls, comprising three subtypes: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA) [1, 2]. The global annual incidence of AAV ranges from 2 to 12 per million population, with significant geographic variation: GPA and PR3-ANCA predominate in European and American populations, whereas MPA and MPO-ANCA are more common in Asian populations [3–7].

AAV can involve multiple organ systems, with the kidneys and lungs the most frequently affected. Renal involvement occurs in 70%-90% of patients and may progress rapidly to irreversible renal failure; pulmonary involvement, dominated by diffuse alveolar hemorrhage and interstitial lung disease, is a major cause of early mortality [8, 9]. Although induction remission therapy has significantly improved outcomes, the 5-year mortality rate remains as high as 20%-30%, and about 20% of patients require renal replacement therapy (RRT) at diagnosis [10, 11]. Identifying patients at high risk of a poor outcome early therefore remains an important step toward better long-term survival.

Advanced age, renal impairment, dialysis requirement at diagnosis, pulmonary hemorrhage, and ANCA subtype have all been reported as risk factors for mortality and end-stage renal disease in AAV[10]. Conventional logistic and Cox regression, however, can incorporate only a limited number of variables and do not readily capture nonlinear relationships among clinical parameters, which limits their ability to predict individual prognosis. Machine learning has shown promise in medical outcome prediction [12], but its application to AAV prognosis remains uncommon, and prediction models for AAV based on Chinese cohorts remain scarce.

We therefore reviewed the clinical data of AAV patients diagnosed at the Second Affiliated Hospital of Guangxi Medical University, described their clinical characteristics and outcomes, and identified independent risk factors for mortality and adverse renal prognosis. We then developed several machine learning models and assessed them with calibration curves, decision curve analysis, and SHAP, with the aim of supporting early risk stratification and individualized treatment.

2. Materials and Methods

2.1 Study Population

A total of 283 AAV patients diagnosed at the Second Affiliated Hospital of Guangxi Medical University between January 2005 and July 2022 were retrospectively and consecutively screened. After excluding 37 patients with incomplete clinical data, age < 18 years, concomitant malignancy, or connective tissue disease, 246 patients were ultimately included. An additional 10 prospectively registered MPA patients diagnosed between August 2022 and November 2023 were enrolled, yielding a total of 256 patients (243 MPA, 12 GPA, 1 EGPA). The single EGPA case was excluded from subtype comparison analyses due to insufficient sample size but was included in the overall cohort description and outcome analyses. All patients met the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides and the 2022 ACR/EULAR AAV classification criteria. The study was approved by the Ethics Committee of The Second Affiliated Hospital of Guangxi Medical University (approval No. 2024-(KY0028)), and all participants provided written informed consent.(Fig. 1)

2.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) meeting the above AAV diagnostic criteria; (2) treatment-naïve patients with complete clinical data and hospitalization > 24 hours.

Exclusion criteria: (1) concomitant other connective tissue diseases; (2) drug-induced secondary vasculitis; (3) concomitant hepatitis B, tuberculosis, or HIV infection; (4) concomitant malignancy; (5) age < 18 years.

2.3 Data Collection

Baseline demographic data, clinical manifestations, laboratory parameters (complete blood count, urinalysis, erythrocyte sedimentation rate, C-reactive protein, liver and renal function, eGFR, complement, immunoglobulins, ANCA subtype), and imaging data were collected. eGFR was calculated using the simplified MDRD equation [13, 14]. ANCA was detected by indirect immunofluorescence combined with immunoblotting, distinguishing MPO-ANCA from PR3-ANCA. Disease activity was assessed using the BVAS 2003 criteria [15].

2.4 Follow-up and Study Endpoints

Patients were followed up through inpatient and outpatient medical records combined with telephone interviews, with a cutoff date of November 30, 2023. The primary endpoint was all-cause mortality, and the secondary endpoint was renal replacement therapy (initiation of dialysis or eGFR < 15 mL·min⁻¹·1.73 m⁻²).

2.5 Statistical Analysis

Statistical analysis was performed using SPSS 24.0. Normally distributed continuous variables are presented as mean ± standard deviation and compared between groups using the t-test. Skewed variables are presented as median (interquartile range) and compared using the rank-sum test.

Categorical variables are presented as number (percentage) and compared using the χ^2 test. Multivariate logistic regression and Cox proportional hazards regression were used to identify independent risk factors for mortality. A two-tailed P value < 0.05 was considered statistically significant.

2.6 Machine Learning Model Construction and Validation

Four prediction models (logistic regression, LASSO regression, random forest, and XGBoost) were constructed using 14 baseline clinical variables as predictive features (demographics, clinical manifestations, BVAS score, laboratory parameters, and dialysis requirement at diagnosis). Missing values for continuous variables were imputed with the median, and categorical variables with the mode. Z-score standardization was applied before input to logistic and LASSO models. Model performance was evaluated using 5-fold stratified cross-validation, with AUC as the primary metric, and sensitivity and specificity calculated at the optimal threshold determined by the Youden index. Calibration curves were used to assess the agreement between predicted probabilities and actual incidence rates. Decision curve analysis (DCA) was employed to evaluate clinical utility. The SHAP (SHapley Additive exPlanations) method was applied to the best-performing models for interpretability analysis, revealing the contribution of each feature to individual predictions.

3. Results

3.1 Comparison of Clinical Characteristics and Laboratory Parameters Between MPA and GPA Patients

Among 256 AAV patients, MPA was the most common subtype (243 cases, 94.9%), followed by GPA (12 cases, 4.7%), with only 1 case of EGPA. Renal involvement occurred in 202 of 255 patients with available renal data (79.2%), and pulmonary involvement in 169 of 238 patients with available pulmonary data (71.0%). Compared with GPA patients, MPA patients had more frequent renal involvement (81.9% vs. 25.0%, $P < 0.05$), higher positive rates of hematuria and proteinuria, more severe renal impairment (lower eGFR, higher serum creatinine, and urea nitrogen), more pronounced anemia, and lower platelet counts and complement C3 levels (all $P < 0.05$). No significant differences were observed in other clinical or laboratory parameters (all $P > 0.05$). (Table 1)

Table 1

Comparison of clinical characteristics and laboratory parameters between MPA and GPA patients

Parameter	MPA (n = 243)	GPA (n = 12)	Statistic	P value
Male/Female (n)	90/153	6/6	$\chi^2=0.82$	0.36
Age (years)	56.54 $\pm$ 15.26	54.17 $\pm$ 13.69	t = 0.53	> 0.05
Renal involvement [n(%)]	199 (81.9%)	3 (25.0%)	2 = 22.5	< 0.001*
Hematuria positive [n(%)]	192 (79.0%)	5 (41.7%)	2 = 9.1	0.01*
Proteinuria positive [n(%)]	188 (77.4%)	6 (50.0%)	2 = 4.7	0.05*
24h urinary protein (mg/24h), M(Q1,Q3)	1080.8(452.5,2019.7)	613.0(120.0,788.0)	z = 2.16	0.05*
Hemoglobin (g/L)	82.19 $\pm$ 24.38	99.79 $\pm$ 23.49	t=-2.44	0.05*
eGFR (mL/min/1.73m ²), M(Q1,Q3)	15.28(8.39,34.80)	80.17(56.67,112.51)	z=-3.48	< 0.001*
Serum creatinine (μ mol/L), M(Q1,Q3)	325.0(152.0,533.0)	86.5(52.0,126.5)	z = 3.27	0.01*
BUN (mmol/L), M(Q1,Q3)	15.72(8.60,24.98)	5.77(3.21,8.83)	z = 3.20	0.01*
Platelet count ($\times 10^9$ /L)	286.02 $\pm$ 131.04	387.92 $\pm$ 172.83	t=-2.59	0.05*
C3 (g/L)	0.93 $\pm$ 0.25	1.09 $\pm$ 0.20	t=-2.08	0.05*
Note: Systemic manifestations: body temperature $\geq 38^\circ\text{C}$, weight loss $\geq 2\text{kg}$; eGFR: estimated glomerular filtration rate; M(Q1,Q3): median (first quartile, third quartile); BUN: blood urea nitrogen. *: P < 0.05. Other parameters (systemic manifestations, pulmonary involvement, dialysis at diagnosis, BVAS score, serum albumin, CRP, ESR, WBC, neutrophil count, IgG, IgA, IgM, C4) showed no significant differences (all P > 0.05).				

3.2 Comparison of Clinical Characteristics Between MPO-ANCA and PR3-ANCA Positive Patients

Among 255 AAV patients with available ANCA data, 206 (80.8%) were MPO-ANCA positive and 49 (19.2%) were PR3-ANCA positive. Compared with the PR3-ANCA-positive group, the MPO-ANCA-positive group had a higher proportion of females (66.0% vs. 46.9%), older age [(57.33 $\pm$ 14.86) vs. (52.61 $\pm$ 16.02) years], more frequent renal involvement (84.5% vs. 57.1%), higher positive rates of hematuria and proteinuria, greater 24-hour urinary protein excretion, and more severe anemia and renal impairment (all P < 0.05). Other parameters were comparable between the two groups (all P > 0.05). (Table 2)

Table 2

Comparison of clinical characteristics between MPO-ANCA and PR3-ANCA positive AAV patients

Parameter	MPO-ANCA+ (n = 206)	PR3-ANCA+ (n = 49)	Statistic	P value
Male/Female (n)	70/136	26/23	$\chi^2=6.14$	0.01
Age (years)	57.33 $\pm$ 14.86	52.61 $\pm$ 16.02	t=-1.96	0.05
Renal involvement [n(%)]	174 (84.5%)	28 (57.1%)	$\chi^2=17.94$	0.01
Hematuria positive [n(%)]	164 (79.6%)	33 (67.3%)	$\chi^2=4.18$	0.04
Proteinuria positive [n(%)]	161 (78.1%)	33 (67.3%)	$\chi^2=3.95$	0.04
24h urinary protein (mg/24h), M(Q1,Q3)	1155.9(564.4,2131.1)	593.9(274.6,1318.5)	z = 2.23	0.02
Hemoglobin (g/L)	80.58 $\pm$ 23.46	93.30 $\pm$ 26.63	t = 3.27	0.01
eGFR (mL/min/1.73m ²), M(Q1,Q3)	11.70(7.91,23.82)	36.94(9.97,78.33)	z = 3.59	0.01
Serum creatinine (μ mol/L), M(Q1,Q3)	391.5(204.5,550.3)	173.5(86.8,510.0)	z = 3.22	0.01
BUN (mmol/L), M(Q1,Q3)	17.39(11.40,26.20)	9.44(5.04,22.22)	z = 2.71	0.01
Note: eGFR: estimated glomerular filtration rate; M(Q1,Q3): median (first quartile, third quartile); BUN: blood urea nitrogen. Other parameters (systemic manifestations, pulmonary involvement, dialysis at diagnosis, BVAS score, serum albumin, CRP, ESR, WBC, platelet count, neutrophil count, IgG, IgA, IgM, C3, C4) showed no significant differences (all P > 0.05).				

3.3 Clinical Characteristics of AAV Patients With and Without Lung Involvement

Among 238 AAV patients with available pulmonary data, 169 (71.0%) had lung involvement and 69 (29.0%) did not. Compared with patients without lung involvement, those with lung involvement were older, had more frequent systemic manifestations, a higher proportion of dialysis requirement at diagnosis, higher BVAS scores, more severe anemia and renal impairment, and higher CRP levels (all P < 0.05). The remaining parameters did not differ significantly between the two groups (all P > 0.05). (Table 3)

Table 3
Clinical characteristics of AAV patients with and without lung involvement

Parameter	Lung involvement (n = 169)	No lung involvement (n = 69)	Statistic	P value
Male/Female (n)	67/102	25/44	$\chi^2=0.24$	0.62
Age (years)	58.76 $\pm$ 14.51	51.75 $\pm$ 15.26	t = 3.33	0.01*
Systemic manifestations [n(%)]	83 (49.1%)	23 (33.3%)	2 = 4.9	0.05*
Dialysis at diagnosis [n(%)]	46 (27.2%)	9 (13.0%)	2 = 5.5	0.05*
BVAS score	18.17 $\pm$ 4.95	14.96 $\pm$ 4.77	t = 4.59	< 0.001*
Hemoglobin (g/L)	80.08 $\pm$ 21.66	90.64 $\pm$ 29.80	t=-2.67	0.01*
eGFR (mL/min/1.73m ²), M(Q1,Q3)	13.48(7.42,32.28)	24.50(10.46,63.08)	z=-3.33	< 0.001*
Serum creatinine (μ mol/L), M(Q1,Q3)	370.0(159.0,602.0)	207.0(102.0,415.0)	z = 3.30	< 0.001*
BUN (mmol/L), M(Q1,Q3)	18.20(8.96,27.60)	11.50(5.95,18.56)	z = 3.34	< 0.001*
CRP (mg/L), M(Q1,Q3)	23.96(7.18,66.30)	10.20(3.83,25.19)	z = 3.07	0.01*
Note: BVAS: Birmingham Vasculitis Activity Score; eGFR: estimated glomerular filtration rate; M(Q1,Q3): median (first quartile, third quartile); BUN: blood urea nitrogen; CRP: C-reactive protein. *: P < 0.05. Other parameters showed no significant differences (all P > 0.05).				

3.4 Clinical Characteristics of AAV Patients With and Without Renal Involvement

Among 255 AAV patients with available renal data, 202 (79.2%) had renal involvement and 53 (20.8%) did not. Compared with patients without renal involvement, those with renal involvement had significantly higher positive rates of hematuria and proteinuria, greater 24-hour urinary protein excretion, a higher proportion of dialysis requirement at diagnosis (28.2% vs. 0%), higher BVAS scores, more severe anemia, renal impairment, and inflammatory activity, and lower platelet counts, complement C3, and IgM levels (all P < 0.05). No other parameter differed significantly between the two groups (all P > 0.05). (Table 4)

Table 4
Clinical characteristics of AAV patients with and without renal involvement

Parameter	Renal involvement (n = 202)	No renal involvement (n = 53)	Statistic	P value
Male/Female (n)	75/127	21/32	$\chi^2=0.11$	0.73
Age (years)	57.26 ± 14.93	53.25 ± 15.80	t = 1.72	0.1
Hematuria positive [n(%)]	175 (86.6%)	22 (41.5%)	2 = 48.7	< 0.001*
Proteinuria positive [n(%)]	175 (86.6%)	19 (35.8%)	2 = 59.5	< 0.001*
24h urinary protein (mg/24h), M(Q1,Q3)	1219.0(596.0,2112.0)	302.4(110.5,609.4)	z = 4.73	< 0.001*
Dialysis at diagnosis [n(%)]	57 (28.2%)	0 (0.0%)	2 = 19.3	< 0.001*
BVAS score	18.09 ± 4.56	13.38 ± 5.33	t = 6.47	< 0.001*
Hemoglobin (g/L)	77.62 ± 22.31	103.59 ± 21.98	t=-7.56	< 0.001*
eGFR (mL/min/1.73m ²), M(Q1,Q3)	10.96(7.41,21.59)	91.04(76.41,110.52)	z=-11.18	< 0.001*
Serum creatinine (μmol/L), M(Q1,Q3)	420.0(256.0,602.0)	70.0(57.0,87.0)	z = 11.20	< 0.001*
BUN (mmol/L), M(Q1,Q3)	18.45(12.13,27.44)	4.69(3.43,5.80)	z = 10.26	< 0.001*
ESR (mm/h)	80.95 ± 39.45	61.27 ± 38.23	t = 3.08	0.01*
Platelet count (×10 ⁹ /L)	277.78 ± 128.29	340.53 ± 147.37	t=-3.07	0.01*
IgM (g/L), M(Q1,Q3)	0.91(0.62,1.42)	1.19(0.82,1.48)	z=-2.18	0.05*
C3 (g/L)	0.91 ± 0.23	1.06 ± 0.31	t=-3.04	0.01*
Note: BVAS: Birmingham Vasculitis Activity Score; eGFR: estimated glomerular filtration rate; M(Q1,Q3): median (first quartile, third quartile); BUN: blood urea nitrogen; ESR: erythrocyte sedimentation rate. *: P < 0.05. Other parameters showed no significant differences (all P > 0.05).				

3.5 Comparison of Clinical Characteristics Between Deceased and Surviving AAV Patients

As of the follow-up cutoff date of November 30, 2023, 60 patients had died, 141 had survived, and 54 were lost to follow-up, corresponding to a mortality rate of 29.9% (60/201) among patients with

complete follow-up, with a median follow-up of 26 months (range, 1-180 months). Of these, all 201 patients with complete follow-up (60 deceased, 141 surviving) were included in the deceased-versus-surviving comparison. Compared with the surviving group, the deceased group was older, had more frequent systemic manifestations and renal involvement, a higher proportion of hemodialysis requirement at diagnosis, higher BVAS scores, more severe anemia and renal impairment, and higher urea nitrogen (all $P < 0.05$), whereas neutrophil count did not differ significantly between groups ($P > 0.05$). Other parameters were similar between the two groups (all $P > 0.05$). (Table 5)

Table 5
Comparison of clinical characteristics between deceased and surviving AAV patients

Parameter	Deceased (n = 60)	Surviving (n = 141)	Statistic	P value
Male/Female (n)	25/35	55/86	$\chi^2=0.12$	0.72
Age (years)	67.12 $\pm$ 12.83	51.83 $\pm$ 14.98	t = 7.34	< 0.001*
Systemic manifestations [n(%)]	36 (60.0%)	58 (41.1%)	2 = 6.0	0.05*
Renal involvement [n(%)]	57 (95.0%)	91 (64.5%)	2 = 20.1	< 0.001*
Dialysis at diagnosis [n(%)]	30 (50.0%)	26 (18.4%)	2 = 20.9	< 0.001*
BVAS score	18.37 $\pm$ 4.87	16.70 $\pm$ 5.52	t = 2.13	0.05*
Hemoglobin (g/L)	73.19 $\pm$ 16.90	87.23 $\pm$ 26.36	t=-4.51	< 0.001*
eGFR, M(Q1,Q3) (mL/min/1.73m ²)	7.11(4.96,15.79)	24.44(9.88,76.49)	z=-6.01	< 0.001*
Serum creatinine, M(Q1,Q3) (μ mol/L)	618.0(302.8,945.2)	203.0(85.0,476.0)	z = 5.76	< 0.001*
BUN (mmol/L), M(Q1,Q3)	24.6(12.2,31.7)	11.8(5.1,23.3)	z = 4.28	< 0.001*
Neutrophil count ($\times 10^9$ /L)	7.09 $\pm$ 4.45	6.52 $\pm$ 3.55	t = 0.96	> 0.05

Note: BVAS: Birmingham Vasculitis Activity Score; eGFR: estimated glomerular filtration rate; M(Q1,Q3): median (first quartile, third quartile); BUN: blood urea nitrogen. *: $P < 0.05$. Other parameters showed no significant differences (all $P > 0.05$).

Using mortality as the dependent variable and variables with $P < 0.05$ in univariate analysis as independent variables (excluding urinary protein, serum creatinine, urea nitrogen, and uric acid, which were highly correlated with eGFR), multivariate logistic regression analysis was performed. The results showed that age (OR = 1.102, 95%CI: 1.056–1.149, $P = 0.001$), systemic manifestations (OR = 2.643, 95%CI: 1.038–6.740, $P = 0.042$), dialysis requirement at diagnosis (OR = 4.200, 95%CI: 1.369–12.872, $P = 0.012$), and low eGFR (OR = 0.973, 95%CI: 0.949–0.997, $P = 0.028$) were independent risk factors for mortality in AAV patients. (Table 6, Fig. 2)

Table 6
Multivariate logistic regression analysis of risk factors for mortality in AAV patients

Variable	β	SE	OR	95% CI	P value
Age	0.097	0.022	1.102	(1.056, 1.149)	0.001*
Systemic manifestations	0.972	0.477	2.643	(1.038, 6.740)	0.042*
Dialysis at diagnosis	1.435	0.572	4.200	(1.369, 12.872)	0.012*
eGFR	-0.027	0.013	0.973	(0.949, 0.997)	0.028*
Note: β : regression coefficient; SE: standard error; OR: odds ratio; CI: confidence interval; eGFR: estimated glomerular filtration rate. *: P < 0.05.					

Multivariate Cox proportional hazards regression analysis showed that age (HR = 1.078, 95%CI: 1.054–1.103, P < 0.001), serum creatinine (HR = 1.001, 95%CI: 1.001–1.002, P < 0.001), systemic manifestations (HR = 0.588, 95%CI: 0.345–1.001, P = 0.048), and renal involvement (HR = 0.219, 95%CI: 0.065–0.738, P = 0.014) were independent prognostic factors for mortality in AAV patients. (Table 7)

Table 7
Multivariate Cox proportional hazards regression analysis of prognostic factors for AAV patients

Variable	β	SE	HR	95% CI	P value
Age	0.070	0.012	1.078	(1.054, 1.103)	0.001*
Serum creatinine	0.001	0.001	1.001	(1.001, 1.002)	0.001*
Systemic manifestations	-0.532	0.271	0.588	(0.345, 1.001)	0.048*
Renal involvement	-1.520	0.621	0.219	(0.065, 0.738)	0.014*
Note: β : regression coefficient; SE: standard error; HR: hazard ratio; CI: confidence interval. *: P < 0.05.					

3.6 Predictive Performance of Machine Learning Models for AAV Prognosis

To further evaluate the predictive value of baseline clinical parameters for adverse outcomes in AAV, we constructed four machine learning models (conventional logistic regression, LASSO regression, random forest, and XGBoost) using 14 baseline clinical variables as predictive features, and evaluated model performance using 5-fold stratified cross-validation. For all-cause mortality prediction (201 patients with complete follow-up data, including 60 deaths, event rate 29.9%), the random forest model performed best with an AUC of 0.863, sensitivity of 0.933, and specificity of 0.730; LASSO regression ranked second (AUC = 0.860), followed by logistic regression (AUC = 0.852) and XGBoost (AUC = 0.835). For renal replacement therapy prediction (255 patients, including 65 requiring RRT, event rate 25.5%), XGBoost achieved the best performance with an AUC of 0.949, sensitivity of 0.877, and specificity of 0.884; random forest ranked second (AUC = 0.938), followed by logistic regression (AUC = 0.914) and LASSO

regression (AUC = 0.909). Tree-based models (random forest and XGBoost) thus outperformed the conventional linear models for both outcomes. (Table 8, Fig. 3)

Table 8
Comparison of predictive performance of four machine learning models for mortality and renal replacement therapy in AAV patients

Outcome	Model	AUC	Sensitivity	Specificity	Optimal threshold
Mortality	Logistic regression	0.852	0.833	0.752	0.404
Mortality	LASSO regression	0.860	0.800	0.816	0.489
Mortality	Random forest	0.863	0.933	0.730	0.406
Mortality	XGBoost	0.835	0.850	0.745	0.150
RRT	Logistic regression	0.914	0.754	0.958	0.765
RRT	LASSO regression	0.909	0.738	0.953	0.797
RRT	Random forest	0.938	0.769	0.979	0.614
RRT	XGBoost	0.949	0.877	0.884	0.178
Note: AUC: area under the receiver operating characteristic curve; RRT: renal replacement therapy. Bold values indicate the best-performing model for each outcome.					

3.7 Model Calibration and Clinical Utility Evaluation

Calibration curves were used to assess the agreement between predicted probabilities and actual incidence rates of the best-performing models. Both the random forest model (mortality prediction) and the XGBoost model (RRT prediction) showed good agreement between predicted and observed probabilities, with near-ideal calibration for the XGBoost model across the full probability range. Decision curve analysis (DCA) indicated that the net benefit of the best-performing models exceeded that of both the "treat all" and "treat none" strategies across a wide range of threshold probabilities (approximately 5%-75% for mortality prediction and 5%-90% for RRT prediction), confirming the clinical utility of the models. (Figs. 4 and 5)

3.8 SHAP Interpretability Analysis

To interpret the models, we applied SHAP to the best-performing model for each outcome. For mortality (random forest), the top five predictors by mean SHAP importance were age (0.291), eGFR (0.196), hemoglobin (0.099), CRP (0.076), and systolic blood pressure (0.066), and the beeswarm plot showed that advanced age, low eGFR, dialysis at diagnosis, low hemoglobin, and high CRP increased mortality

risk. For RRT (XGBoost), dialysis at diagnosis, eGFR, hemoglobin, systolic blood pressure, and albumin ranked highest, with dialysis at diagnosis and low eGFR the strongest predictors. (Figs. 6 and 7)

4. Discussion

We reviewed the clinical features and outcomes of 256 AAV patients and, to our knowledge, are among the first to apply several machine learning models to mortality and renal replacement therapy (RRT) prediction in this disease. The cohort was predominantly MPA with MPO-ANCA positivity; pulmonary and renal involvement were common. Advanced age, dialysis requirement at diagnosis, and low eGFR independently predicted mortality. Random forest and XGBoost performed best for mortality and RRT, respectively, and SHAP identified age, eGFR, and dialysis at diagnosis as the strongest predictors.

AAV subtype distribution and ANCA specificity vary markedly by geography and ethnicity: GPA and PR3-ANCA predominate in Europe and North America, whereas MPA and MPO-ANCA are more common in Asia [16, 17]. MPA accounted for 94.9% and MPO-ANCA for 80.8% of our cohort, in line with multicenter Chinese reports[3]. As in previous studies, MPA patients in our cohort had more frequent and more severe renal involvement than GPA patients, consistent with the predominantly glomerular capillary injury seen in MPA, and MPO-ANCA-positive patients were older, more often female, and had more severe renal involvement than PR3-ANCA-positive patients. These differences support region-specific risk stratification in AAV.

The lungs and kidneys were the organs most often affected (71.0% and 79.2%, respectively), in line with previous reports[18]. Patients with lung involvement were older, had more systemic manifestations, higher BVAS scores, more severe renal impairment, and higher CRP, suggesting greater overall disease activity. Concurrent pulmonary-renal involvement may worsen prognosis: hypoxemia from alveolar hemorrhage can aggravate renal hypoxic injury, while systemic inflammation may accelerate fibrosis in both organs. Renal involvement was associated with more severe anemia, higher ESR, and lower complement C3 and IgM, reflecting the inflammatory burden of renal vasculitis.

The median follow-up was 26 months and the mortality rate was 29.9%, in keeping with the 70%-80% 5-year survival reported for AAV[5]. In multivariate analyses, advanced age, systemic manifestations, dialysis requirement at diagnosis, and low eGFR independently predicted mortality, and the association held in both logistic and Cox models. Age has repeatedly been linked to worse survival in AAV [10, 19], plausibly through immunosenescence-related infection, greater comorbidity, reduced organ reserve, and a higher risk of treatment-related complications. Dialysis at diagnosis indicates severe renal failure at presentation and carries a high mortality, reflecting both ESRD complications and drug toxicity. Low eGFR, an integrated measure of renal function and disease severity, has shown consistent prognostic value across AAV cohorts [20, 21].

Random forest achieved the best mortality prediction (AUC = 0.863) and XGBoost the best RRT prediction (AUC = 0.949), indicating that baseline clinical data carry substantial prognostic information in AAV and supporting the feasibility of prediction tools for this disease. Both tree-based models

outperformed the linear models for each outcome[22]. One likely reason is that tree models capture nonlinear relationships and higher-order interactions automatically, whereas such effects must be specified in advance in a regression framework. In a multisystem disease like AAV, interactions among prognostic factors are plausible (for example, age and renal function may act together on mortality beyond their individual effects), and tree models are better suited to detect them[23].

Calibration curves showed good agreement between predicted and observed event rates for the best-performing models, with near-ideal calibration for the XGBoost RRT model across the whole probability range [24, 25]. DCA confirmed clinical utility: across most threshold probabilities (5%-75% for mortality and 5%-90% for RRT), the models' net benefit exceeded both the "treat all" and "treat none" strategies [26, 27]. In practice, this means the models can help stratify patients at diagnosis, directing high-risk patients to closer follow-up and more intensive treatment while sparing low-risk patients from unnecessary therapy.

SHAP identified age, eGFR, hemoglobin, CRP, and systolic blood pressure as the top predictors of mortality, and dialysis at diagnosis, eGFR, hemoglobin, systolic blood pressure, and albumin for RRT[28]. The machine learning results agreed with the regression models in ranking age, eGFR, and dialysis at diagnosis as the most important prognostic factors. At the same time, machine learning drew attention to nutritional and inflammatory markers such as hemoglobin, CRP, and albumin [29, 30] that conventional regression may have underweighted, possibly because their effects are nonlinear or mediated through interactions[31]. Combining the two approaches therefore gives a fuller picture of what drives prognosis in AAV.

This study has several strengths. The cohort is relatively large for a single-center Chinese AAV series (256 patients) and includes ten prospectively registered cases. Both conventional regression and four machine learning models were used, with calibration curves, DCA, and SHAP for evaluation. Two clinically relevant endpoints (all-cause mortality and RRT) were modelled together, and the use of SHAP makes the models' behavior transparent rather than a "black box".

Several limitations should be noted. This is a single-center retrospective study, so selection bias is possible and the models need validation in multicenter prospective cohorts. Missing values were imputed with median/mode, which may bias estimates. Treatment details (e.g., corticosteroid dose, type of immunosuppressant) and renal histology (e.g., crescent proportion, interstitial fibrosis) were not included. Finally, only internal 5-fold cross-validation was performed, without an external cohort, so performance in other populations remains to be confirmed.

Despite these limitations, the results have practical implications. Models built on baseline clinical parameters can help stratify risk at the time of AAV diagnosis, directing high-risk patients toward intensive treatment and closer follow-up. Future work should focus on external validation in multicenter prospective cohorts, on incorporating treatment and histological variables, and, ultimately, on integrating the models into a clinical decision-support tool.

Declarations

Funding

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors upon reasonable request. The analysis dataset and data dictionary are available from the corresponding author on request.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of The Second Affiliated Hospital of Guangxi Medical University (approval No. 2024-KY(0028)). All participants provided written informed consent for participation in the study.

Consent for Publication

Not applicable.

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Author Contribution

L.P.C. conceived and designed the study, collected and interpreted the clinical data, performed the statistical analyses, and drafted the manuscript. C.X. supervised the study and critically revised the manuscript. B.Y. and F.X. contributed to data collection, statistical analysis, and machine learning model construction; F.X. also prepared the figures. L.L. contributed to data collection and clinical interpretation. B.N. performed the literature search and data organization. All authors read and approved the final manuscript.

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Figures

Figure 1. Flowchart of patient enrollment and follow-up

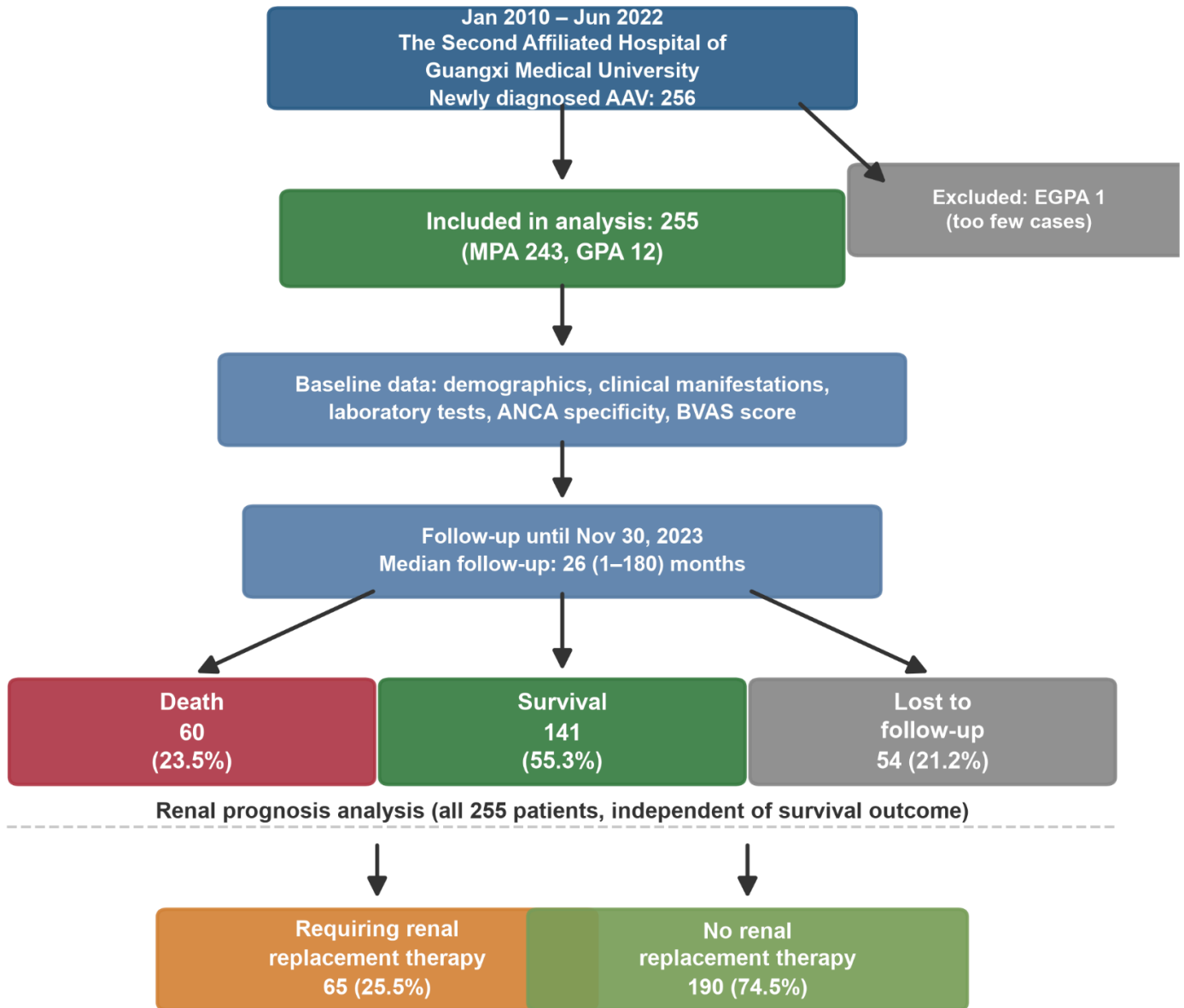


Figure 1

See image above for figure legend

Figure 2. Forest plot of independent risk factors for mortality in AAV patients (multivariate logistic regression)

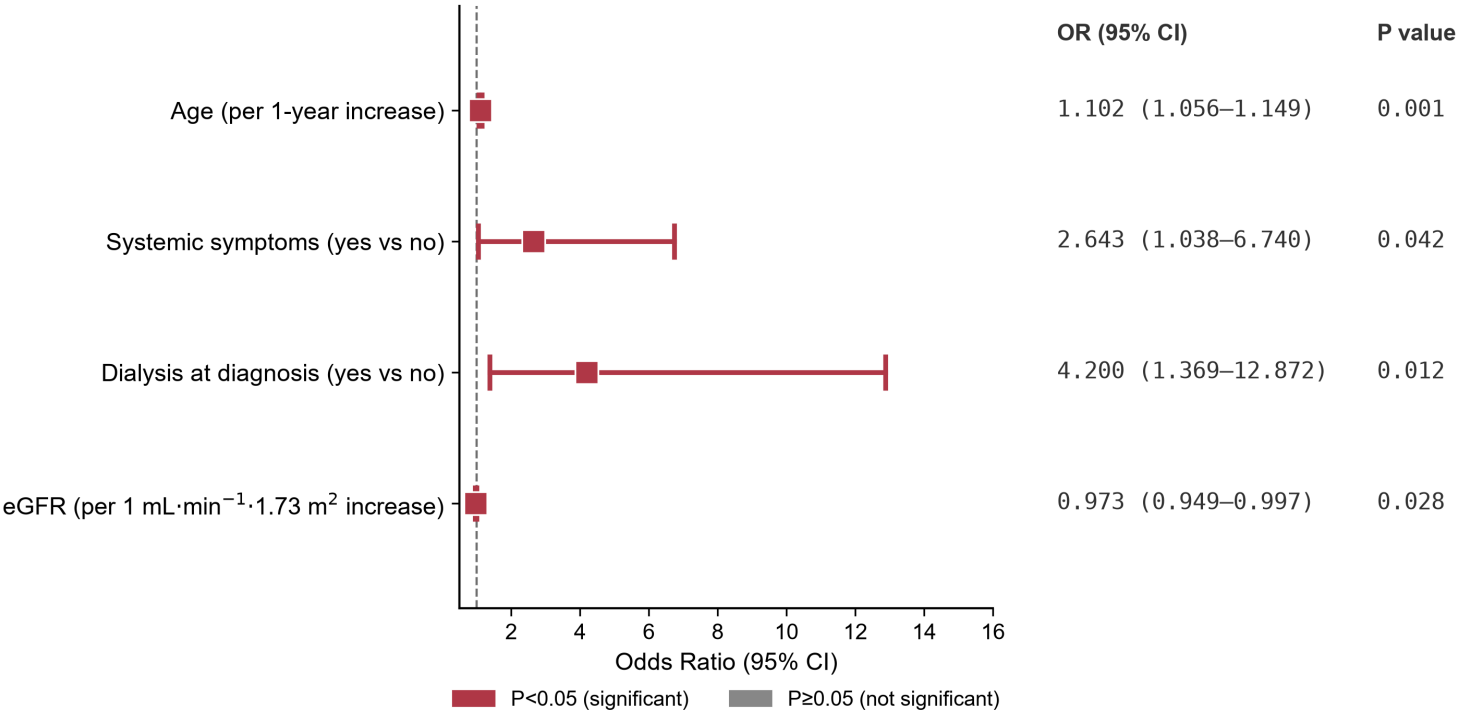


Figure 2

Forest plot of independent risk factors for mortality in AAV patients (multivariate logistic regression)

Figure 3. ROC curves of four machine learning models for predicting outcomes in AAV patients

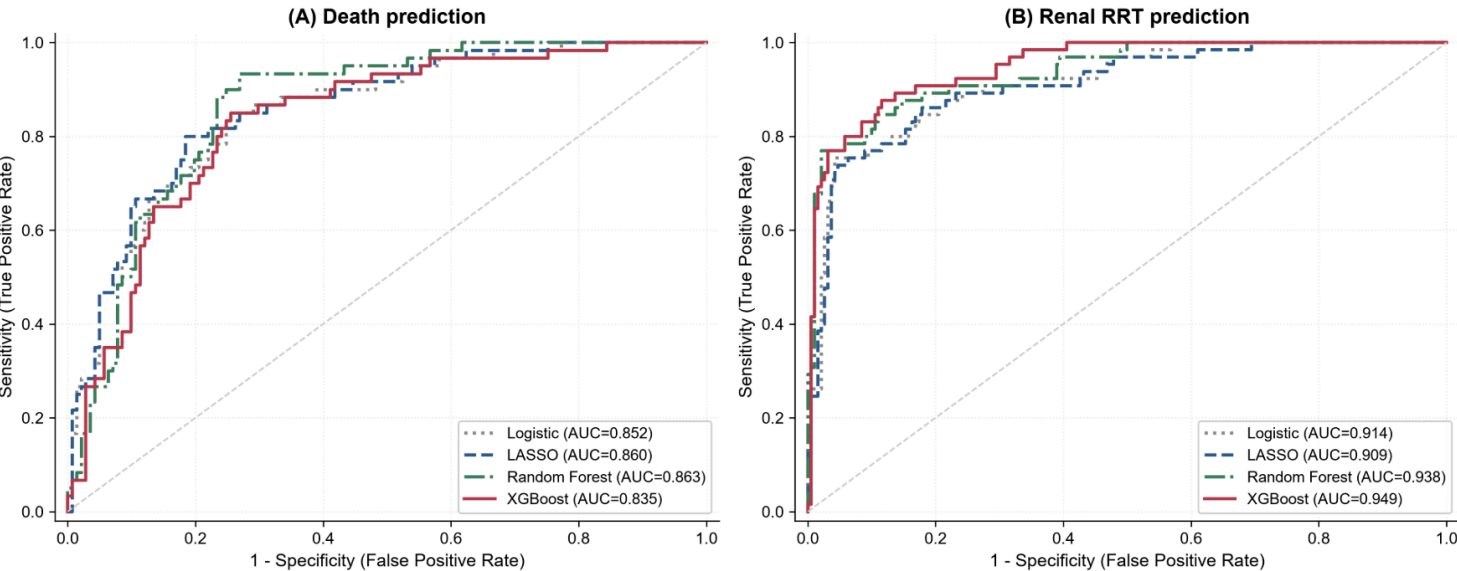


Figure 3

ROC curves of four machine learning models for predicting mortality and renal replacement therapy in AAV patients

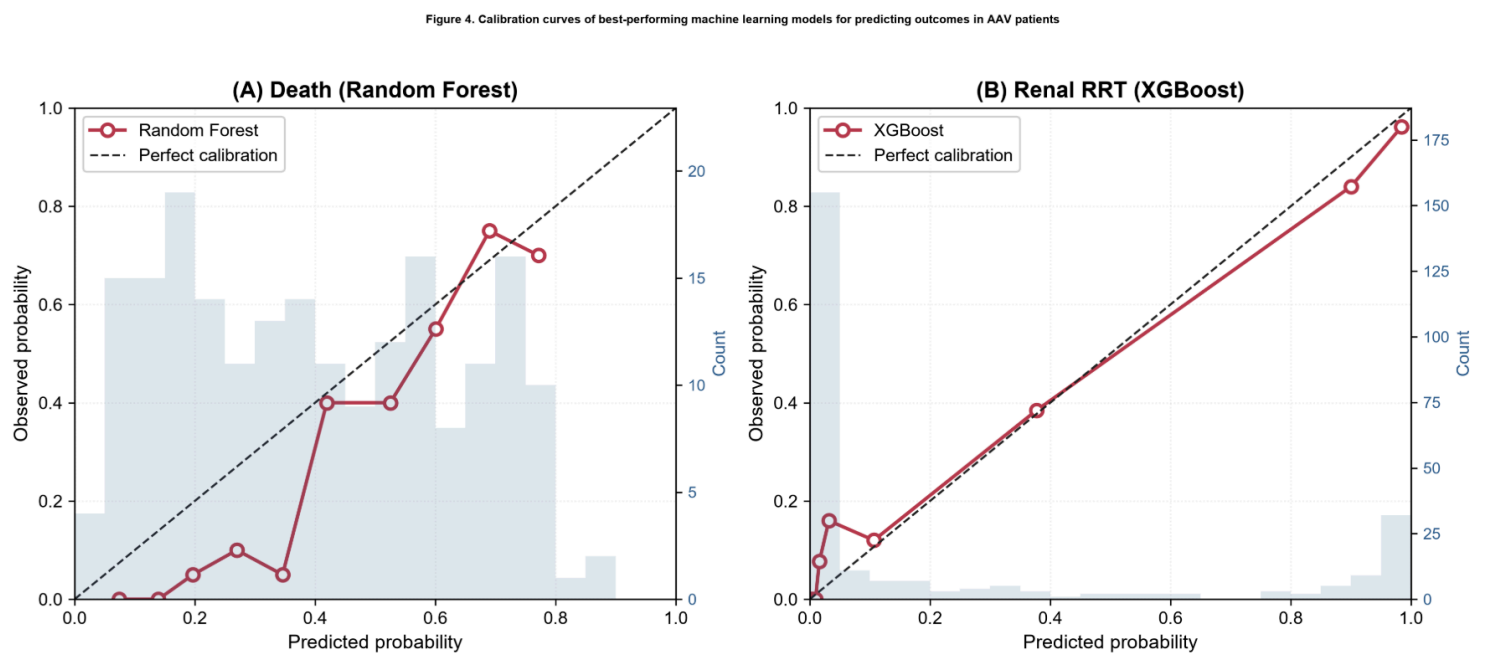


Figure 4

Calibration curves of best-performing machine learning models for predicting outcomes in AAV patients

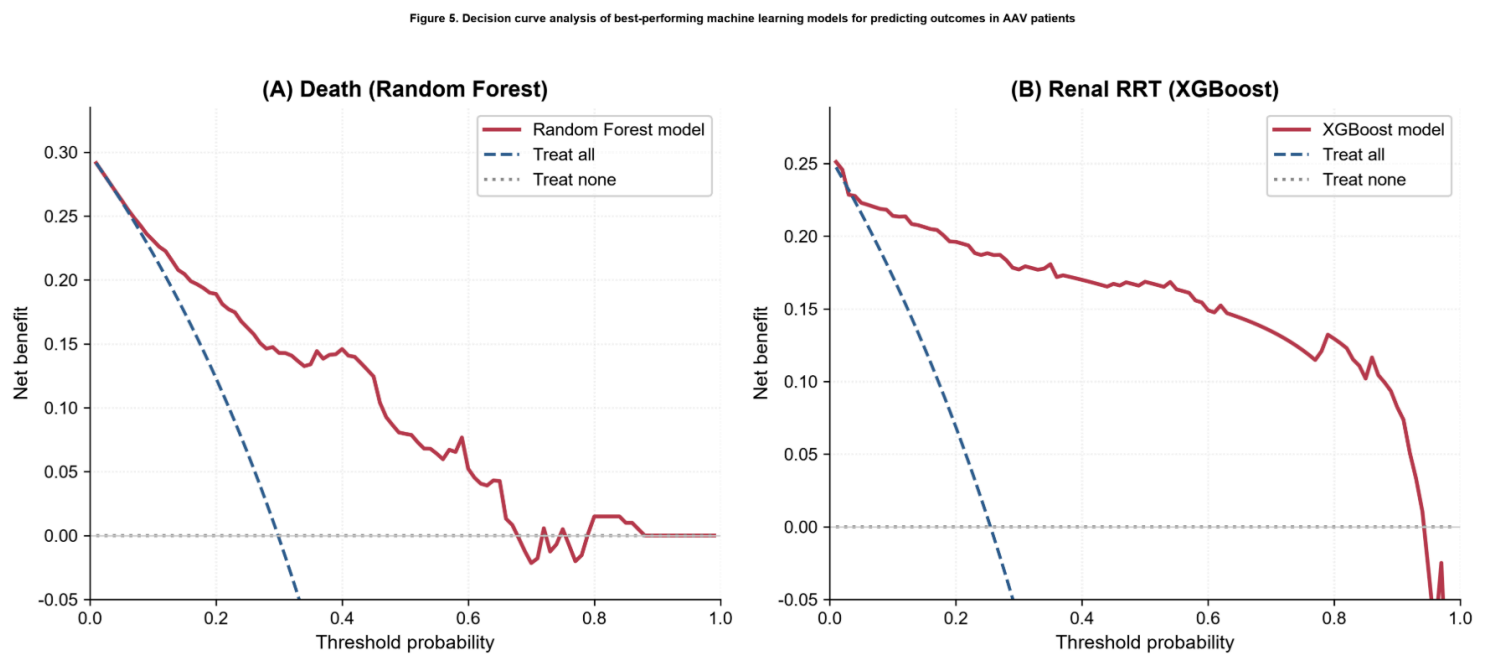


Figure 5

Decision curve analysis of best-performing machine learning models for predicting outcomes in AAV patients

Figure 6. SHAP summary plot — Death prediction

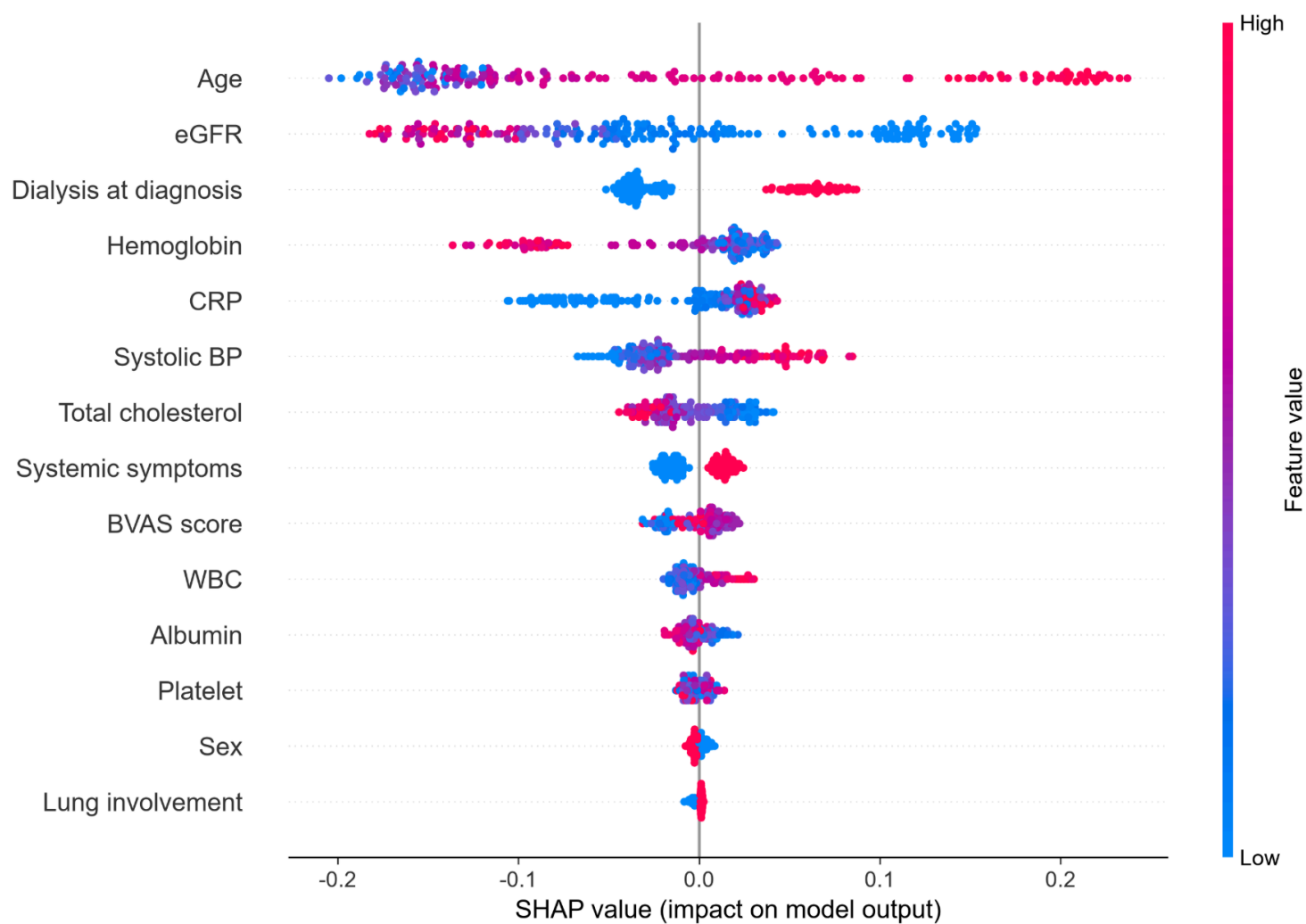


Figure 6

SHAP summary plot (beeswarm plot) of the mortality prediction model (random forest)

Figure 7. SHAP summary plot — Renal RRT prediction

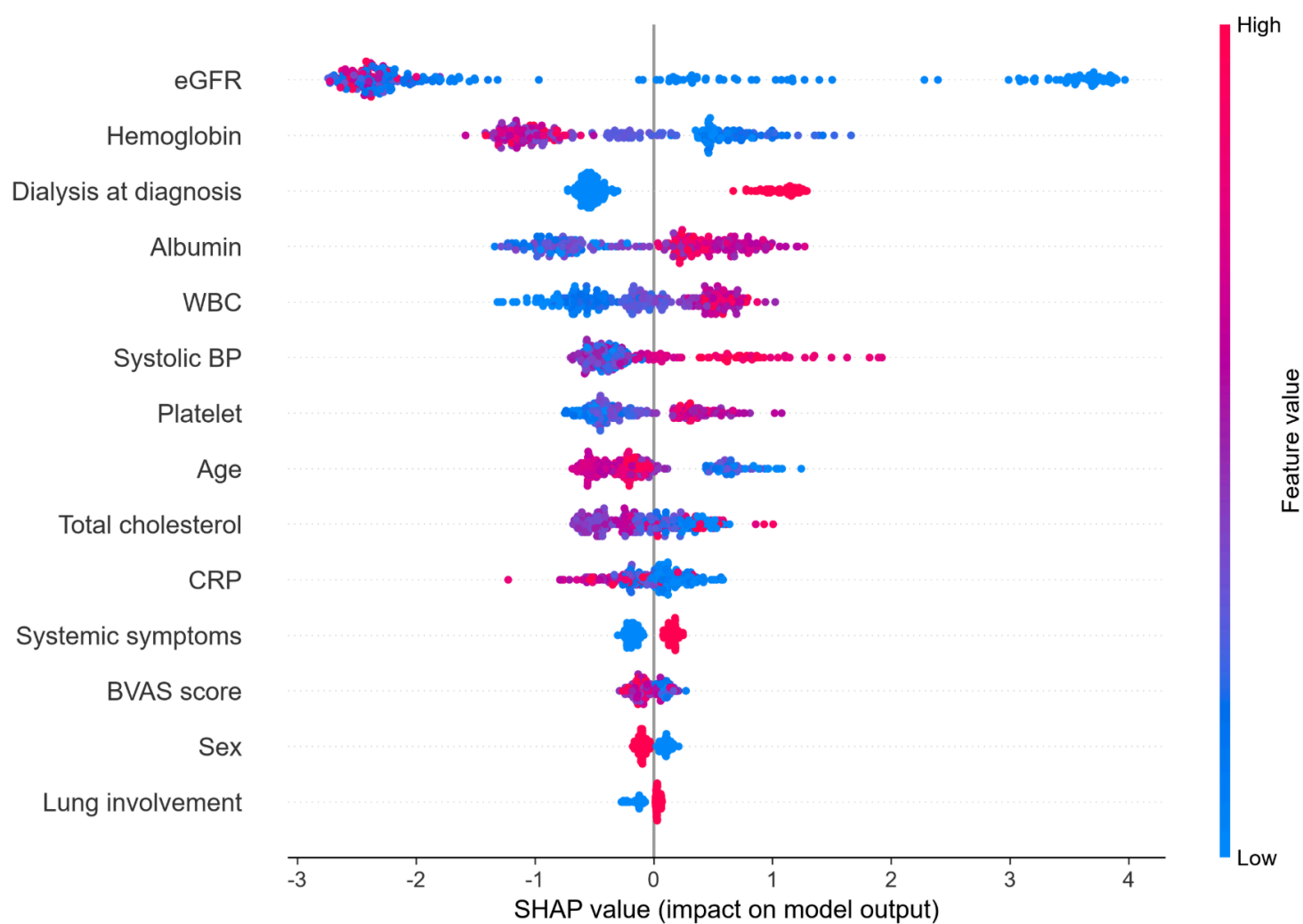


Figure 7

SHAP summary plot (beeswarm plot) of the renal replacement therapy prediction model (XGBoost)