

Predictive Value of the FDAPR Index for Ischemic Stroke in Patients with Coronary Heart Disease: A Machine Learning Study Based on a Multilayer Perceptron

Wei Lai¹, Jinbo Zhao², Juan Du¹, Changjiang Zhang¹

¹Department of Cardiology, Minda Hospital of Hubei Minzu University, Enshi, Hubei, People's Republic of China; ²Cardiovascular Disease Center, Central Hospital of Tujia and Miao Autonomous Prefecture, Hubei University of Medicine, Enshi, Hubei, People's Republic of China

Correspondence: Juan Du; Changjiang Zhang, Email 18671573125@163.com; zcj2008@163.com

Background: Ischemic stroke is a common and severe complication in patients with coronary artery disease (CAD), yet its early prediction remains challenging. This study aimed to investigate the association between the Fibrinogen–D-dimer to Albumin–Platelet Ratio (FDAPR) and the risk of ischemic stroke in CAD patients, and to develop a multilayer perceptron (MLP)–based machine learning model for stroke risk prediction.

Methods: Patients with confirmed CAD who underwent their first coronary angiography in two hospitals were retrospectively enrolled. The Boruta feature selection algorithm and multivariable logistic regression were used to identify independent predictors of ischemic stroke, which were subsequently incorporated into the MLP model. Model performance was evaluated using receiver operating characteristic (ROC) curves, area under the curve (AUC), and calibration plots. The Shapley Additive Explanations (SHAP) method was applied to quantify the contribution of each variable to model output, and two-dimensional contour plots were generated to explore the interaction effects between FDAPR and other key variables.

Results: A total of 1844 CAD patients were included in the analysis. Compared with the non-stroke group, patients with ischemic stroke were older, had higher FDAPR levels, and lower serum potassium concentrations. Boruta and multivariable logistic regression identified age, FDAPR, serum potassium (K), and total bilirubin (TBIL) as independent risk factors for stroke. The MLP model achieved an AUC of 0.71 in both the training and test datasets. SHAP analysis demonstrated that elevated FDAPR levels were positively associated with stroke risk. Contour plots further revealed synergistic interactions between FDAPR and age, potassium, and TBIL.

Conclusion: FDAPR is significantly associated with ischemic stroke risk among patients with coronary artery disease.

Keywords: FDAPR index, ischemic stroke, coronary artery disease, multilayer perceptron, prediction model

Background

Coronary heart disease (CHD) is one of the most prevalent cardiovascular disorders worldwide, primarily driven by atherosclerosis of the coronary arteries, leading to myocardial ischemia.¹ Patients with CHD are not only at risk of adverse cardiac outcomes such as myocardial infarction and heart failure^{2,3} but also of cerebrovascular complications, among which ischemic stroke (IS) is the most common and clinically devastating.^{4,5} IS results from vascular occlusion causing cerebral hypoperfusion and subsequent neuronal injury, often leading to disability or death and imposing a substantial public health and socioeconomic burden.⁶ Therefore, early identification of CHD patients at high risk for IS is critical for timely intervention and risk management.

In recent years, hematological parameters have shown substantial value in assessing the risk of thrombotic diseases.^{7–9} The FDAPR index, a novel composite biomarker that integrates coagulation function and nutritional status, reflects not only the prothrombotic state of the blood but also the patient's nutritional and inflammatory condition.¹⁰ It therefore represents a promising indicator for predicting ischemic stroke in individuals with coronary heart disease (CHD). However, current

research on the application of FDAPR in stroke risk prediction among CHD patients remains limited, and robust predictive models are still needed to validate its clinical utility.

Machine learning (ML) techniques have been increasingly applied in medical prediction research, as they are well suited to handle high-dimensional, nonlinear, and complex interaction data.^{11,12} The multilayer perceptron (MLP), a class of feedforward artificial neural networks, consists of an input layer, one or more hidden layers, and an output layer. Each neuron in a given layer is fully connected to those in the previous layer, processing information through weighted summation and nonlinear activation functions. Unlike traditional statistical approaches such as linear or logistic regression, MLP models do not rely on predefined distributional assumptions and can capture intricate nonlinear relationships and interactions among multiple variables, offering superior performance in complex predictive tasks.^{13,14} Moreover, by incorporating interpretability tools such as Shapley Additive Explanations (SHAP), MLP models can provide both accurate predictions and insights into variable interactions, enabling individualized risk assessment and supporting early clinical intervention.

Methods

Study Population

This retrospective study included patients who underwent their first coronary angiography (CAG) at Enshi Tujia and Miao Autonomous Prefecture Central Hospital and Minda Hospital of Hubei Minzu University between January 2024 and December 2024. The diagnosis of coronary artery disease (CAD) was defined as $\geq 70\%$ stenosis in a non-left main coronary artery or $\geq 50\%$ stenosis in the left main artery. As illustrated in Figure 1, patients were excluded if they had missing follow-up data, a history of malignancy or prior stroke, severe hepatic or renal dysfunction, or if more than 20% of key clinical variables were missing. Ultimately, 1844 eligible patients were included in the final analysis. The diagnosis of ischemic stroke was based on the AHA/ASA guidelines for the management of acute ischemic stroke.¹⁵

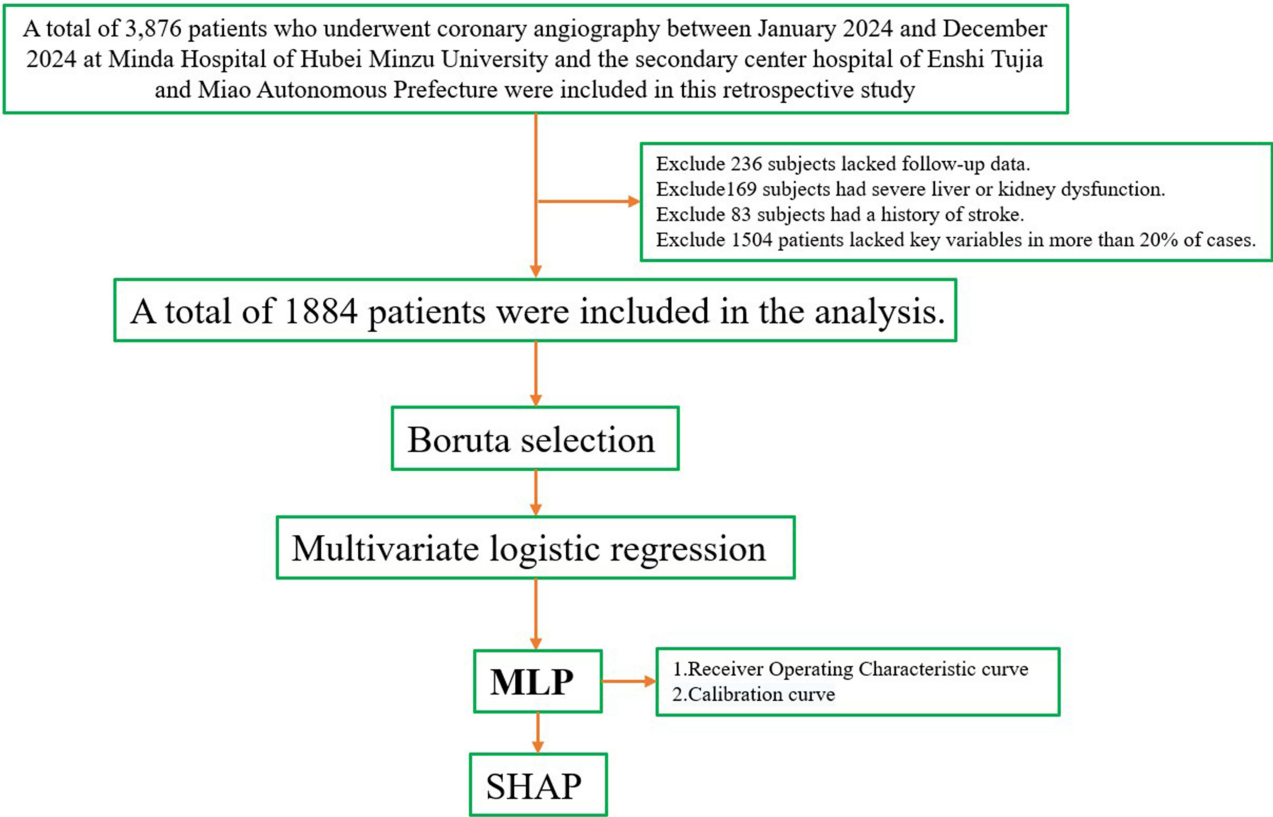


Figure 1 Flowchart of study population selection and inclusion.

All data were anonymized prior to analysis. This study was approved by the Ethics Committee of Enshi Tujia and Miao Autonomous Prefecture Central Hospital (Approval No. 2024–053-01). Given the retrospective design and use of de-identified clinical data, the requirement for informed consent was waived by the ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data Collection and Variable Definition

Clinical information was extracted from electronic medical records, including demographic characteristics (age, sex), medical history (hypertension, diabetes mellitus, atrial fibrillation, hyperuricemia, hyperlipidemia, and smoking status), and medication use (diuretics and anticoagulants). Laboratory data included hematological parameters (white blood cell count, red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, platelet count, mean platelet volume, and plateletcrit), lipid profiles (total cholesterol, triglycerides, high-density and low-density lipoprotein cholesterol), biochemical indices (serum potassium, alanine aminotransferase, aspartate aminotransferase, total and direct bilirubin, albumin, creatinine, uric acid, and urea), and coagulation-related markers (fibrinogen and D-dimer). The FDAPR index was calculated as: $(\text{Fibrinogen} \times \text{D-dimer} / \text{Albumin} \times \text{Platelet})$.¹⁰ Ischemic stroke was treated as a binary outcome (presence or absence) and was identified based on clinical diagnosis and neuroimaging findings documented in medical records during hospitalization or routine clinical evaluation. Uniform time-to-event information was not available for all patients; therefore, time-to-event analyses were not performed.

Feature Selection and Model Construction

To identify variables associated with ischemic stroke, the Boruta feature selection algorithm was first applied to all candidate variables. Boruta, based on a random forest framework, iteratively compares the importance of actual features with that of randomly permuted “shadow” features, retaining relevant predictors while minimizing redundancy and overfitting. Variables identified as “important” or “tentatively important” by Boruta were subsequently included in a multivariable logistic regression model to evaluate their independent associations with ischemic stroke and to enhance clinical interpretability. The features selected by Boruta were then used to construct the neural network model.

Machine Learning Model Development

The selected variables were used to construct a multilayer perceptron (MLP) neural network model. Data were randomly divided into training and validation sets in a 7:3 ratio. Hyperparameter tuning was conducted using a grid search strategy, exploring different network architectures and learning parameters, with the optimal model selected based on AUC performance. Model discrimination was assessed using receiver operating characteristic (ROC) curves and area under the curve (AUC) values, while calibration curves were plotted to evaluate the agreement between predicted probabilities and observed outcomes. To enhance interpretability, SHAP method was employed to quantify the contribution of each variable to stroke prediction. Variables were ranked according to their mean absolute SHAP values, and visualizations including feature importance plots and beeswarm plots were generated to illustrate the direction and magnitude of each predictor’s effect. Finally, two-dimensional contour plots (2D contour plots) were constructed based on MLP model outputs to explore the interaction effects between FDAPR and other key predictors, depicting ischemic stroke risk distributions under different variable combinations and revealing potential nonlinear synergistic effects.

All statistical analyses were conducted using R version 4.3.2 and Python version 3.9. Continuous variables were compared with the *t*-test or Mann–Whitney *U*-test, categorical variables with the χ^2 -test, and a *P* value <0.05 was considered statistically significant.

Results

As shown in Table 1, a total of 1844 patients were included, comprising 292 (15.8%) individuals with ischemic stroke (IS) and 1552 (84.2%) without stroke (non-IS). Patients in the IS group were significantly older than those in the non-IS group (median age: 70.00 vs 61.00 years, $p < 0.001$). Regarding comorbidities, hypertension was more prevalent among IS patients, whereas the prevalence of diabetes mellitus, atrial fibrillation, hyperuricemia, and hyperlipidemia showed no significant intergroup difference ($p > 0.05$). For medication use and lifestyle factors, both diuretic and anticoagulant use were more common in the IS

Table 1 Baseline Characteristics

Variable	Non IS (n=1552)	IS (n=292)	p-value
Age (median [IQR])	61.00 [53.00, 69.00]	70.00 [62.00, 74.25]	<0.001*
Sex=male (%)	952 (61.3)	187 (64.0)	0.384
HTN=yes (%)	930 (59.9)	208 (71.2)	<0.001*
DM=yes (%)	325 (20.9)	64 (21.9)	0.707
AF=yes (%)	71 (4.6)	19 (6.5)	0.16
HUA=yes (%)	153 (9.9)	35 (12.0)	0.27
HLP=yes (%)	330 (21.3)	61 (20.9)	0.886
Diuretic=yes (%)	334 (21.5)	88 (30.1)	0.001*
Smoking=yes (%)	1005 (64.8)	198 (67.8)	0.315
AC=yes (%)	506 (32.6)	118 (40.4)	0.01*
WBC (median [IQR])	6.11 [4.54, 9.49]	6.26 [4.56, 10.29]	0.33
RBC (median [IQR])	4.23 [3.73, 4.79]	4.12 [3.60, 4.65]	0.04*
FDAPR (median [IQR])	0.23 [0.12, 0.47]	0.36 [0.19, 0.72]	<0.001*
HGB (median [IQR])	131.00 [119.00, 144.00]	126.50 [114.00, 138.00]	<0.001*
Hct (median [IQR])	39.30 [35.88, 42.70]	38.05 [34.30, 41.20]	<0.001*
MCV (median [IQR])	91.40 [88.50, 94.60]	91.60 [88.40, 94.43]	0.741
MPV (median [IQR])	11.20 [10.40, 12.00]	11.20 [10.57, 12.20]	0.179
PCT (median [IQR])	0.21 [0.18, 0.25]	0.20 [0.16, 0.24]	<0.001*
TC (median [IQR])	4.30 [3.54, 5.06]	4.23 [3.57, 5.02]	0.865
TG (median [IQR])	1.52 [1.06, 2.37]	1.37 [0.94, 2.02]	0.001*
HDL-C (median [IQR])	1.17 [0.98, 1.41]	1.18 [1.00, 1.47]	0.203
LDL-C (median [IQR])	2.70 [2.14, 3.32]	2.71 [2.08, 3.28]	0.602
K (median [IQR])	3.80 [3.56, 4.02]	3.71 [3.45, 3.94]	<0.001*
ALT (median [IQR])	19.00 [14.00, 30.00]	19.50 [14.00, 26.00]	0.375
AST (median [IQR])	23.00 [18.00, 33.00]	24.00 [19.00, 34.00]	0.133
TBIL (median [IQR])	11.60 [9.10, 14.50]	11.70 [10.07, 14.90]	0.11
DBIL (median [IQR])	3.60 [2.70, 4.90]	3.60 [2.80, 5.03]	0.498
Cr (median [IQR])	72.00 [59.00, 91.00]	73.00 [61.75, 101.00]	0.058
UA (median [IQR])	323.50 [261.00, 394.00]	320.00 [250.75, 383.50]	0.3
Urea (median [IQR])	5.46 [4.35, 6.87]	5.37 [4.28, 7.24]	0.893

Note: *P <0.05.

Abbreviations: HTN, Hypertension; DM, Diabetes Mellitus; AF, Atrial Fibrillation; HUA, Hyperuricemia; HLP, Hyperlipidemia; Diuretic, Diuretic Use; AC, Anticoagulation; WBC, White Blood Cell Count; RBC, Red Blood Cell Count; HGB, Hemoglobin; Hct, Hematocrit; MCV, Mean Corpuscular Volume; MPV, Mean Platelet Volume; PCT, Plateletcrit; TC, Total Cholesterol; TG, Triglycerides; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; K, Potassium; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; TBIL, Total Bilirubin; DBIL, Direct Bilirubin; Cr, Creatinine; UA, Uric Acid.

group, while smoking rates were comparable between groups. Laboratory analyses revealed that IS patients had markedly higher FDAPR index values compared with the non-IS group (0.36 vs 0.23, $p < 0.001$). In contrast, red blood cell count, hemoglobin, hematocrit, and plateletcrit were significantly lower in the IS group ($p < 0.001$). Additionally, IS patients had reduced triglyceride (TG) and serum potassium (K) levels. Other parameters—including white blood cell count, mean platelet volume, cholesterol, liver and kidney function tests, and uric acid—did not differ significantly between groups ($p > 0.05$).

To identify key predictors of ischemic stroke among CAD patients, the Boruta feature selection algorithm was applied to all candidate variables. As illustrated in [Figure 2](#), Boruta successfully identified several variables strongly associated with stroke risk. These “confirmed important” (green) and “tentatively important” (yellow) features were subsequently entered into multi-variable logistic regression analysis ([Table 2](#)). Regression results indicated that age (OR = 1.066, 95% CI: 1.051–1.082, $p < 0.001$), FDAPR (OR = 1.097, 95% CI: 1.040–1.157, $p = 0.001$), serum potassium (OR = 0.640, 95% CI: 0.447–0.916, $p = 0.015$), and total bilirubin (TBIL) (OR = 1.027, 95% CI: 1.010–1.044, $p = 0.002$) were independent risk factors for ischemic stroke. Variables identified as relevant by the Boruta algorithm were used as input features for the subsequent neural network model.

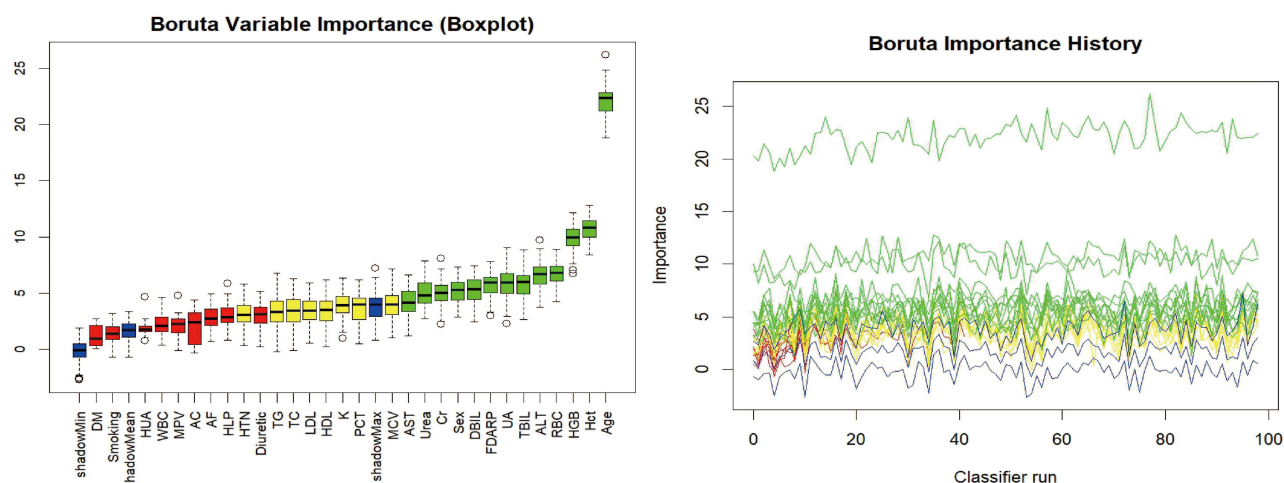


Figure 2 Feature selection and importance ranking identified by the Boruta algorithm. Green indicates confirmed important features, yellow indicates tentative features, red indicates rejected features, and blue represents shadow features.

As shown in Figure 3, the MLP model achieved an area under the ROC curve (AUC) of 0.71 in both the training and test sets, demonstrating robust generalizability and stability. The ROC curves indicated that the model effectively discriminated stroke events in the moderate- to high-risk range. The calibration curves showed close agreement between predicted and observed stroke probabilities, particularly within the 0.3–0.6 risk interval. A slight overestimation was noted at higher predicted probabilities, suggesting overall good calibration and discrimination of the MLP model.

To enhance interpretability, SHAP analysis was performed (Figure 4). Among all input variables, age had the greatest impact on model output (mean absolute SHAP value = 0.07), followed by serum potassium (K, +0.02), FDAPR (+0.01), and total bilirubin (TBIL, +0.01). The SHAP summary plot indicated that older age, higher FDAPR, and elevated bilirubin levels were associated with an increased predicted risk of ischemic stroke, whereas lower serum potassium values also contributed to higher predicted risk. To further explore potential interactions between FDAPR and other major predictors, two-dimensional contour plots were generated (Figure 5). In the FDAPR–Age plot, stroke risk increased markedly with simultaneous elevations in both FDAPR and age, with the highest predicted risk observed in older (≥ 70 years) patients with higher FDAPR levels, indicating a synergistic effect. In the FDAPR–K plot, the influence of FDAPR on stroke risk was more pronounced when serum potassium was below 3.6 mmol/L. Similarly, the FDAPR–TBIL plot demonstrated that both FDAPR and total bilirubin were positively correlated with stroke probability, and patients with high levels of both markers exhibited the greatest risk.

Table 2 Multivariate Logistic Regression

Variables	OR	95% CI	p-value
Age	1.066	1.051~1.082	<0.001*
FDARP	1.097	1.040~1.157	0.001*
HGB	0.985	0.963~1.008	0.193
Hct	1.057	0.984~1.136	0.131
PCT	0.713	0.059~8.665	0.791
K	0.64	0.447~0.916	0.015*
TBIL	1.027	1.010~1.044	0.002*

Note: *P<0.05.

Abbreviations: HGB, Hemoglobin; Hct, Hematocrit; PCT, Plateletcrit; K, Potassium; TBIL, Total Bilirubin.

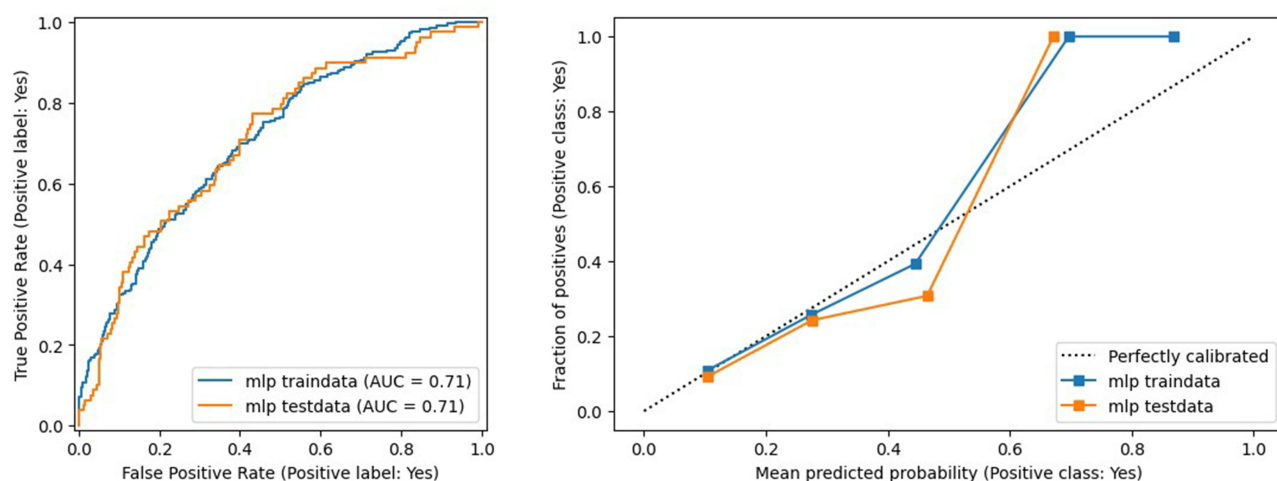


Figure 3 ROC curves and calibration plots of the MLP model in the training and testing sets.

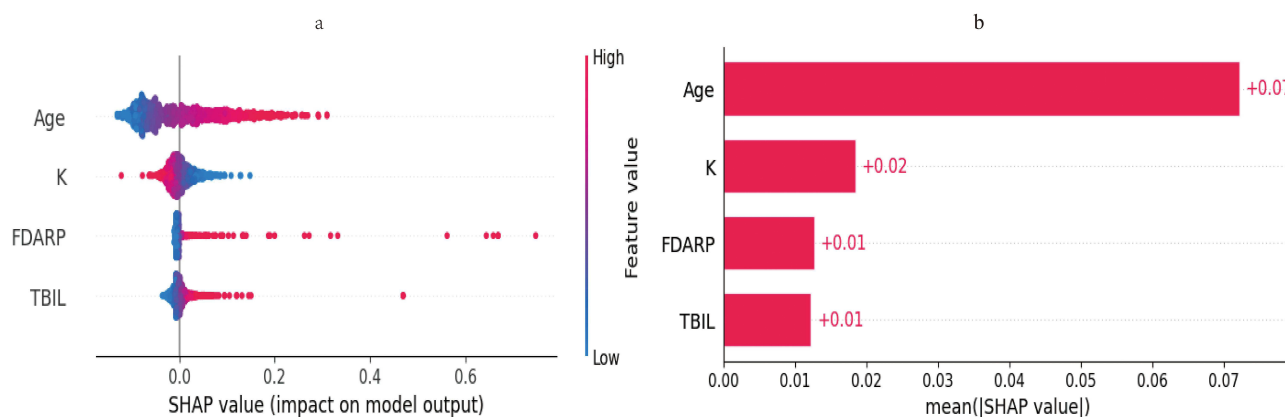


Figure 4 SHAP analysis of the MLP model showing feature importance and the direction of feature effects. (a) SHAP summary plot illustrating the impact of individual features on the model output, where each dot represents a sample and colors indicate feature values (low to high). (b) Bar plot showing the mean absolute SHAP values of the selected features, reflecting their overall importance in the model.

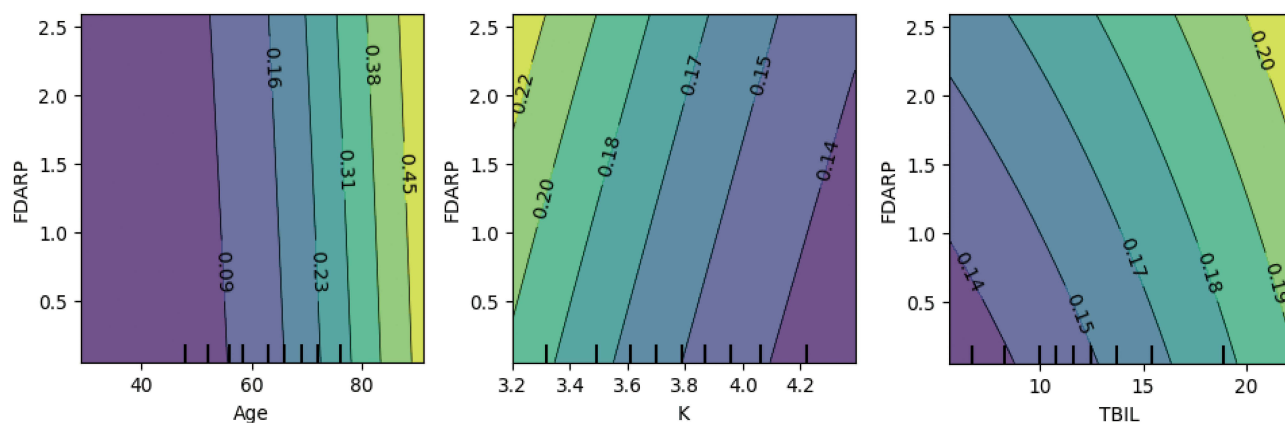


Figure 5 Effects of interactions between FDARF and key variables on ischemic stroke risk prediction.

Discussion

Our study revealed that, at baseline, patients in the ischemic stroke (IS) group were significantly older than those without stroke, and their FDAPR index values were markedly elevated. Both the Boruta feature selection and multivariable logistic regression analyses consistently identified FDAPR as an independent risk factor for ischemic stroke. The MLP model demonstrated robust predictive performance, with an AUC of 0.71 in both the training and validation sets, while calibration curves confirmed reliable probability estimation. SHAP analysis further indicated that FDAPR was the second most influential predictor within the model. Contour analysis revealed that elevated FDAPR, in combination with advanced age, hypokalemia, or metabolic dysfunction, markedly increased the predicted probability of stroke events.

FDAPR is a novel composite biomarker integrating indicators of coagulation, fibrinolysis, inflammation, and nutritional status, thus reflecting the multidimensional physiological balance of the body. It is derived from four key laboratory parameters (fibrinogen, D-dimer, albumin, and platelet count) and an elevated FDAPR value implies hypercoagulability, fibrinolytic imbalance, and compromised metabolic defense. Fibrinogen, as the principal substrate for clot formation, increases plasma viscosity and promotes platelet aggregation and vasoconstriction;^{16–19} its elevation reflects enhanced coagulation activity and inflammatory stimulation via cytokines such as IL-6 and CRP.^{20,21} D-dimer, a degradation product of cross-linked fibrin, indicates active coagulation and fibrinolytic imbalance, with persistently high levels suggesting endothelial dysfunction and microthrombotic activity that predispose to ischemic injury.^{22–24} Albumin, incorporated in the denominator of the FDAPR formula, represents the protective, anti-inflammatory, and antioxidative component; low albumin weakens vascular defense, increases blood viscosity, and facilitates thrombogenesis.^{25–28} Platelets contribute to thrombus formation and vascular inflammation through aggregation and the release of pro-inflammatory mediators such as thromboxane A₂ and platelet factor 4; however, in prothrombotic and inflammatory states, lower platelet counts may reflect platelet activation and consumption at sites of thrombus formation rather than a protective condition.^{29–32} Collectively, a higher FDAPR value denotes a state of hypercoagulability, impaired fibrinolysis, and weakened metabolic and anti-inflammatory defense, reflecting the multifactorial pathophysiology underlying ischemic stroke. By integrating these multidimensional disturbances into a single quantitative index, FDAPR provides a holistic measure of the coagulation–inflammation–metabolic axis, offering a potential biomarker for stroke risk stratification.

Previous studies first introduced FDAPR in 2022 by Çelikkol et al¹⁰ who demonstrated its prognostic value in predicting mortality among COVID-19 patients. Our findings expand this concept to the cardiovascular field. Consistent with prior evidence, advanced age was associated with increased stroke risk, likely due to vascular remodeling, endothelial dysfunction, and enhanced coagulation activity in older adults.³³ Likewise, hypokalemia may promote endothelial injury, augment vasoconstrictive responses, and increase arrhythmic potential, thereby elevating ischemic risk.³⁴ Hepatic dysfunction, characterized by impaired synthesis of coagulation factors and elevated inflammatory burden,³⁵ further disrupts the coagulation–fibrinolysis equilibrium, leading to increased D-dimer levels and platelet dysregulation—all of which promote thrombogenesis and indirectly heighten stroke susceptibility. Collectively, these results underscore the potential of FDAPR and its hematologic components as integrative biomarkers for assessing ischemic stroke risk among patients with coronary artery disease.

Collectively, our findings highlight that FDAPR serves as an integrated biomarker reflecting both hypercoagulable status and nutritional condition, serving as an important predictor of ischemic stroke risk in patients with CHD.

Limitations

This retrospective, single-center study has several limitations, including limited generalizability and the inability to infer causality. A substantial proportion of patients were excluded due to missing laboratory data required for FDAPR calculation, potentially introducing selection bias, and no multiple imputation or sensitivity analyses were performed. Ischemic stroke was analyzed as a binary outcome because uniform time-to-event data were unavailable, precluding survival or competing-risk analyses. Despite hyperparameter tuning using grid search, the predictive performance of the MLP model was moderate (AUC = 0.71), suggesting that FDAPR should be interpreted as a complementary rather than

a standalone predictive marker. External validation was not conducted, limiting model robustness, and residual confounding cannot be entirely excluded, particularly regarding hypokalemia and its potential association with diuretic use.

Disclosure

The authors report no conflicts of interest in this work.

References

- Kraler S, Mueller C, Libby P, Bhatt DL. Acute coronary syndromes: mechanisms, challenges, and new opportunities. *Eur Heart J*. 2025;46(29):2866–2889. doi:10.1093/eurheartj/ehaf289
- Chen J, Xu C, Qiu L, et al. Heparin administration at first medical contact vs immediately before primary percutaneous coronary intervention: the HELP-PCI trial. *Eur Heart J*. 2025;46(39):3888–3901. doi:10.1093/eurheartj/ehaf481
- Welén Schef K, Tornvall P, Lindahl B, Nordenskjöld AM, Jernberg T. Angina pectoris prevalence and sick leave burden 1 year after myocardial infarction with nonobstructive coronary arteries. *J Am Heart Assoc*. 2025;14(14):e037264. doi:10.1161/jaha.124.037264
- Lee G, Malik A, Vervoort D, et al. Revascularisation in left ventricular systolic dysfunction: a meta-analysis of kaplan-meier reconstructed individual patient data. *Can J Cardiol*. 2024;40(11):2188–2200. doi:10.1016/j.cjca.2024.05.023
- Suh S, Soh S, Song JW, Kwang-Sub K, Kwak YL, Shim JK. Association between ex vivo thrombogenicity and ischemic outcome in off-pump coronary surgery. *Ann Med*. 2025;57(1):2514079. doi:10.1080/07853890.2025.2514079
- Ran J, Liu Y, Ma H, Zhang Y. Accuracy of NT-proBNP for predicting mortality amongst patients with ischemic stroke: a systematic review and meta-analysis. *BMC Med*. 2025;23(1):476. doi:10.1186/s12916-025-04299-1
- Yatsenko T, Us I, Korolova D, et al. Placental dysfunction is associated with dysregulated fibrinolytic system activation. *Int J Mol Sci*. 2025;26(19):9339. doi:10.3390/ijms26199339
- Liu Y, Li F, Sun H, et al. Combined prognostic significance of D-dimer level and platelet count in acute ischemic stroke. *Thromb Res*. 2020;194:142–149. doi:10.1016/j.thromres.2020.05.021
- Prasad MK, Marandi S, Mishra B, et al. Association of fibrinogen with ischemic stroke: a systematic review and meta-analysis. *Cureus*. 2023;15(1):e34335. doi:10.7759/cureus.34335
- Celikkol A, Dogan M, Guzel EC, Erdal B, Yilmaz A. A novel combined index of D-dimer, fibrinogen, albumin, and platelet (FDAPR) as mortality predictor of COVID-19. *Niger J Clin Pract*. 2022;25(9):1418–1423. doi:10.4103/njcp.njcp_1633_21
- Rajkomar A, Dean J, Kohane I. Machine Learning in Medicine. *N Engl J Med*. 2019;380(14):1347–1358. doi:10.1056/NEJMra1814259
- Efthimiou O, Seo M, Chalkou K, Debray T, Egger M, Salanti G. Developing clinical prediction models: a step-by-step guide. *BMJ*. 2024;386:e078276. doi:10.1136/bmj-2023-078276
- Alghamdi FA, Almanaseer H, Jaradat G, et al. Multilayer perceptron neural network with arithmetic optimization algo rithm-based feature selection for cardiovascular disease prediction. *MAKE*. 2024;6(2):987–1008. doi:10.3390/make6020046
- Diamzon J, Venturi D. Uncertainty propagation in feed-forward neural network models. *Neural Netw*. 2025;194:108178. doi:10.1016/j.neunet.2025.108178
- Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50(12):e344–e418. doi:10.1161/str.0000000000000211
- Boateng NKK, Wimberley RM, Rose JP, et al. Tissue transglutaminase drives fibrin β -chain cross-linking: a novel fibrin modification observed in trauma patients. *Blood*. 2025;147(1):87–92. doi:10.1182/blood.2025029458
- Ząbczyk M, Ariëns RAS, Undas A. Fibrin clot properties in cardiovascular disease: from basic mechanisms to clinical practice. *Cardiovasc Res*. 2023;119(1):94–111. doi:10.1093/cvr/cvad017
- Risman RA, Belcher HA, Ramanujam RK, Weisel JW, Hudson NE, Tutwiler V. Comprehensive Analysis of the Role of Fibrinogen and Thrombin in Clot Formation and Structure for Plasma and Purified Fibrinogen. *Biomolecules*. 2024;14(2):230. doi:10.3390/biom14020230
- Nencini F, Bettiol A, Argento FR, et al. Post-translational modifications of fibrinogen: implications for clotting, fibrin structure and degradation. *Mol Biomed*. 2024;5(1):45. doi:10.1186/s43556-024-00214-x
- McCabe JJ, O'Reilly E, Coveney S, et al. Interleukin-6, C-reactive protein, fibrinogen, and risk of recurrence after ischaemic stroke: systematic review and meta-analysis. *Eur Stroke J*. 2021;6(1):62–71. doi:10.1177/2396987320984003
- Dobson DA, Holle LA, Lin FC, et al. Novel genetic regulators of fibrinogen synthesis identified by an in vitro experimental platform. *J Thromb Haemost*. 2023;21(3):522–533. doi:10.1016/j.jth.2022.10.027
- Bonaventura A, Vecchié A, Dagna L, et al. Endothelial dysfunction and immunothrombosis as key pathogenic mechanisms in COVID-19. *Nat Rev Immunol*. 2021;21(5):319–329. doi:10.1038/s41577-021-00536-9
- Zheng Z, Mukhametova L, Boffa MB, et al. Assays to quantify fibrinolysis: strengths and limitations. Communication from the International Society on Thrombosis and Haemostasis Scientific and Standardization Committee on fibrinolysis. *J Thromb Haemost*. 2023;21(4):1043–1054. doi:10.1016/j.jth.2023.01.008
- Buzza MS, Pawar NR, Strong AA, Antalis TM. Intersection of Coagulation and Fibrinolysis by the Glycosylphosphatidylinositol (GPI)-Anchored Serine Protease Testisin. *Int J Mol Sci*. 2023;24(11):9306. doi:10.3390/ijms24119306
- Sun Y, Deng J, Ding Y, et al. Serum albumin, genetic susceptibility, and risk of venous thromboembolism. *Res Pract Thromb Haemost*. 2024;8(5):102509. doi:10.1016/j.rpth.2024.102509
- Sastre-Oliva T, Corbacho-Alonso N, Rodríguez-Sánchez E, et al. Albumin redox modifications promote cell calcification reflecting the impact of oxidative status on aortic valve disease and atherosclerosis. *Antioxidants*. 2024;13(1):108. doi:10.3390/antiox13010108
- Diebel LN, Liberati DM, Carge M. Effect of albumin solutions on endothelial oxidant injury: a microfluidic study. *Surgery*. 2023;173(3):876–882. doi:10.1016/j.surg.2022.08.043

28. Aldecoa C, Llau JV, Nuvials X, Artigas A. Role of albumin in the preservation of endothelial glycocalyx integrity and the microcirculation: a review. *Ann Intensive Care*. 2020;10(1):85. doi:10.1186/s13613-020-00697-1
29. Yang M, Jiang H, Ding C, et al. STING activation in platelets aggravates septic thrombosis by enhancing platelet activation and granule secretion. *Immunity*. 2023;56(5):1013–1026.e6. doi:10.1016/j.immuni.2023.02.015
30. Mack A, Vanden Hoek T, Du X. Thromboinflammation and the Role of Platelets. *Arterioscler Thromb Vasc Biol*. 2024;44(6):1175–1180. doi:10.1161/atvbaha.124.320149
31. Leiter O, Brici D, Fletcher SJ, et al. Platelet-derived exerkine CXCL4/platelet factor 4 rejuvenates hippocampal neurogenesis and restores cognitive function in aged mice. *Nat Commun*. 2023;14(1):4375. doi:10.1038/s41467-023-39873-9
32. Wienkamp AK, Erpenbeck L, Rossaint J. Platelets in the NETworks interweaving inflammation and thrombosis. *Front Immunol*. 2022;13:953129. doi:10.3389/fimmu.2022.953129
33. Liu L, Zhao B, Yu Y, et al. Vascular Aging in Ischemic Stroke. *J Am Heart Assoc*. 2024;13(15):e033341. doi:10.1161/jaha.123.033341
34. Wang A, Cao S, Tian X, et al. Lower serum potassium levels at admission are associated with the risk of recurrent stroke in patients with acute ischemic stroke or transient ischemic attack. *Cerebrovasc Dis*. 2022;51(3):304–312. doi:10.1159/000520052
35. Ghanem HB, Elderderly AY, Alnassar HN, et al. Study of coagulation disorders and the prevalence of their related symptoms among COVID-19 patients in Al-Jouf Region, Saudi Arabia during the COVID-19 Pandemic. *Diagnostics*. 2023;13(6):1085. doi:10.3390/diagnostics13061085

International Journal of General Medicine

Publish your work in this journal

The International Journal of General Medicine is an international, peer-reviewed open-access journal that focuses on general and internal medicine, pathogenesis, epidemiology, diagnosis, monitoring and treatment protocols. The journal is characterized by the rapid reporting of reviews, original research and clinical studies across all disease areas. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-general-medicine-journal>

Dovepress
Taylor & Francis Group