Aging Medicine

WILEY

Aging Medicine Open Access

ORIGINAL ARTICLE OPEN ACCESS

Risk Factors and Predictive Model for Ischemic Complications in Endovascular Treatment of Intracranial Aneurysms: Insights From a Large Patient Cohort

Jianwen Jia[1] | Zeping Jin[1] | Mirzat Turhon[2,3] | Yixin Lin[1] | Xinjian Yang[2,3] | Yang Wang[1] | Yunpeng Liu[1]

[1]Department of Neurosurgery, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, People's Republic of China | [2]Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, People's Republic of China | [3]Department of Neurointerventional Surgery, Beijing Neurosurgical Institute, Beijing, People's Republic of China

Correspondence: Yunpeng Liu (liuyunpeng6644@126.com)

Received: 2 July 2024 | **Revised:** 29 December 2024 | **Accepted:** 27 March 2025

Funding: This research was funded by the National Natural Science Foundation of China, grant number 82372058, and was also funded by the Scientific Research Fund of Beijing Chao-Yang Hospital.

Keywords: intracranial aneurysms | ischemic complications | predictive model | radiographic

ABSTRACT

Objectives: There remains a conspicuous absence of systematic analysis concerning the risk factors for the development of ischemic complications in the interventional treatment of IAs. Our study aimed to identify the risk factors for ischemic complications after the interventional treatment of IAs and to make an individualized prediction of the occurrence of ischemic complications, providing important reference guidance for clinicians.

Methods: This study encompassed a sample of 473 patients diagnosed with intracranial aneurysms (IA) and treated at our center between February 2022 and April 2024. Ischemic complications were identified via clinical symptomatology and corroborated with diagnostic subtraction angiography (DSA), computed tomography (CT), or magnetic resonance imaging (MRI). We used a machine learning (ML) approach to screen potential variables for ischemic complications and identify correlations between them, and subsequently constructed a logistic regression model to quantify these correlations.

Results: Patients were categorized based on the occurrence or absence of ischemic complications. A total of five potential factors were screened using LASSO regression, XGBoost, and Randomforest algorithms: hypertension, history of alcohol consumption, multiple IAs, rupture status, and antiplatelet agent. Multivariate analysis further disclosed that hypertension, history of alcohol consumption, ruptured aneurysms, and antiplatelet agent were independent risk factors for postoperative ischemic complications. The predictive model, derived from the multivariate regression analysis results, demonstrated robust reliability.

Conclusions: Hypertension, history of alcohol consumption, ruptured aneurysms, and antiplatelet agent as independent risk factors for ischemic complications following the interventional treatment of IAs. Accordingly, we constructed the first risk prediction model regarding ischemic complications of all IAs based on these factors, aiming to enhance prognostic judgment and treatment strategy planning.

Jianwen Jia, Zeping Jin, Yang Wang and Yunpeng Liu contributed equally to this study.

1 | Introduction

An intracranial aneurysm (IA) is a prevalent form of cerebrovascular disease, arising from tissue damage in the arterial wall due to inherited or acquired factors. It typically manifests as localized inflammatory infiltration and destruction of the internal elastic lamina, leading to potentially life-threatening complications [1]. This complex disease has been the focus of considerable clinical and research attention over the years.

The last few decades have witnessed a substantial shift in the management of IA, due in large part to the advent of innovative interventional technologies and materials. These advances have heralded a suite of new endovascular therapies, such as surface-modified coiling, balloon-assisted coiling, stent-assisted coiling, flow diversion, and flow disruption [2]. Consequently, endovascular treatment has emerged as the front-line therapeutic strategy for IA, often yielding favorable clinical outcomes [3, 4]. However, a notable caveat to this approach lies in its potential to precipitate ischemic complications, with ischemic stroke being cited as the most frequent complication following coiling of unruptured cerebral aneurysms [5].

Despite significant research efforts, the current understanding of risk factors [6] that predispose to complications primarily focuses on specific types of aneurysms [7–10]. There remains a conspicuous absence of systematic analysis concerning the risk factors for the development of ischemic complications in the interventional treatment of IAs. Relying solely on clinical intuition is insufficient for managing this complex condition. To address this knowledge gap, we collected data on a substantial cohort of patients with IAs who underwent endovascular embolization. Our study examined the incidence of ischemic complications and their associated risk factors, leading to the creation of a nomogram for individualized prediction of ischemic complications prognosis following interventional treatment of IAs. Our work's substantial diagnostic utility was validated, and we aim to offer critical reference guidelines to clinicians in the field.

2 | Methods

2.1 | Ethics Approval and Consent to Participate

The research protocol adhered to the ethical standards set out by the World Medical Association's Code of Ethics and was approved by the Institutional Ethics Committee of Beijing Tiantan Hospital, Capital Medical University (KY2023-261-01). All participants or their authorized relatives signed informed consent forms.

2.2 | Study Design and Participant Inclusion

We established a collected database containing data from patients undergoing interventional treatment of intracranial aneurysms at Beijing Tiantan Hospital and Beijing Chao-Yang Hospital. This database, in operation for 2 years from February 2022 to April 2024, was designed to improve patient survival quality and optimize aneurysmal patient care.

Patient evaluation included demographic information, medical history, lifestyle factors, family history, and clinical condition both pre- and post-treatment. Based on clinical and imaging conditions, patients underwent endovascular embolization treatment. We diligently recorded patient demographics, aneurysm characteristics, treatment modality, procedural details, and occurrence of cerebral vasospasm during aneurysm embolization. Aneurysm locations across various arteries were documented, and the patients were imaged one or more times within 14 days after surgery. We used these postoperative imaging findings to determine the presence of ischemic complications in the patients in the present study.

The inclusion criteria for this study were: (1) a confirmed diagnosis of IA via imaging scans (computed tomography (CT), magnetic resonance imaging (MRI)) or cerebral angiography, (2) age above 18 years and (3) received treatment at our center between February 2022 and April 2024. Exclusion criteria included: (1) no endovascular treatment, (2) the patient also has other central nervous system (CNS) diseases such as moyamoya disease, arteriovenous malformations, and brain tumors, and (3) missing follow-up data. Ultimately, a cohort of 473 patients was included in the present study, as depicted in the study flow diagram (Figure 1).

2.3 | Outcome Measures and Evaluation

The primary study outcomes were centered around ischemic complications associated with endovascular embolization treatment of intracranial aneurysms. Ischemic side effects primarily presented as new-onset neurological deterioration post-surgery, characterized by movement weakness and/or sensory abnormalities in the contralateral limb, alongside contralateral eyelid insufficiency and a shallow nasolabial sulcus. On the emergence of such symptoms, a digital subtraction angiography (DSA) or diffusion-weighted MRI was promptly performed, with confirmation made by qualified imaging professionals. Ischemic complications included severe ischemic strokes persisting for more than 7 days, mild neurological strokes lasting less than 7 days, transient ischemic attacks (TIA), and abnormalities in postoperative brain imaging, such as low-density lesions on CT scans or high signal intensity lesions on diffusion-weighted MRI.

2.4 | Machine Learning Algorithms

A total of 473 patients were assigned to the training and validation sets in a 7:3 ratio using computer-generated random sampling; 70% of the patients were assigned to the training set and the remainder to the validation set. The validation set is applied to verify the predictive efficacy of the predictive model constructed using the training set.

We selected four machine learning (ML) algorithms from a variety of ML algorithms because they are more suitable for developing clinical models. Logistic regression is designed to analyze multiple variables simultaneously and can solve a wide range of binary classification problems. Least absolute shrinkage and selection operator (LASSO) regression is capable of

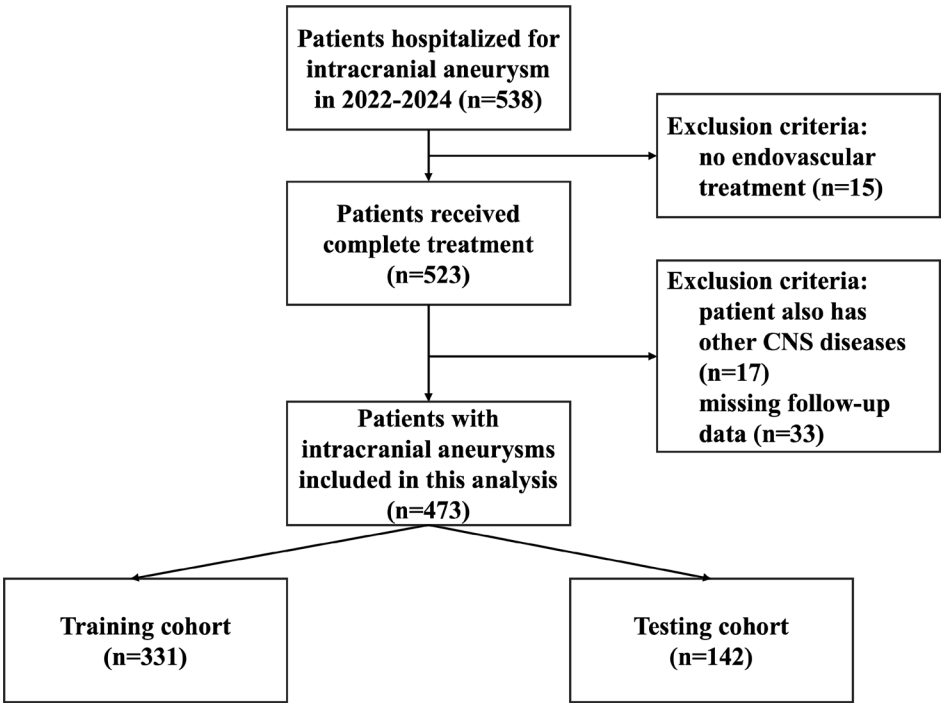

FIGURE 1 | Study flow diagram.

removing unimportant variables by penalizing regression coefficients for parameter size. The response variable of LASSO regression is a binary variable, and alpha is 1. LASSO regression shrinks the coefficient estimates to zero; the degree of shrinkage depends on the additional parameter λ. To determine the optimal value of λ, 10-fold cross-validation was used, and we selected λ by a minimum criterion. Secondly, we made use of the Extreme Gradient Boosting Algorithm (XGBoost), which is designed to minimize the loss function by adjusting the weights of the samples and the features. The most important relevant variables are finally filtered out. Random forests allow us to understand the importance of each feature for prediction and ultimately pick the top 10 important factors. Finally, the potential factors screened by LASSO regression, XGBoost, and Random Forest are intersected to obtain the pivotal factors, which will be incorporated into the logistic multiple regression and ultimately result in the predictive model for ischemic complications.

We use the "glmnet (version: 4.1.8)," "xgboost (version: 1.7.7.1)," "randomForest (version: 4.7.1.1)," "ggvenn (version: 0.1.10)," "stats (version: 4.3.3)," and "autoReg (version: 0.3.3)" packages to perform these ML algorithms in R.

2.5 | Statistical Approach

Statistical analyses were conducted using R version 4.3.3 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were represented as mean ± standard deviation (SD) for normal distributions and median (range) for skewed distributions. Categorical variables were presented as number (%), and binary variables as median with interquartile range (IQR).

Subsequently, we constructed a nomogram using the rms package in R to validate the predictive capacity of the logistic regression model. Calibration curves were plotted to evaluate the nomogram's calibration ability, which assesses the congruence between the nomogram predictions and actual observed outcomes.

The model's predictive ability was evaluated through the area under the receiver operating characteristic curves (AUC), with an AUC over 0.700 indicating good discrimination. The Hosmer-Lemeshow test assessed each model's calibration, where lower p values suggest a poorer fit. Decision curve analysis (DCA) was used to assess the net benefit of our established nomogram.

3 | Results

3.1 | Patient Demographics and Baseline Characteristics

Between February 2022 and April 2024, a total of 473 patients with intracranial aneurysms (IAs) were enrolled in our study. The characteristics of the patients, aneurysms, and treatment procedures are detailed in Table 1. Of these participants, 192 (40.506%) were male and the median age was 59 years, ranging from 19 to 89 years. The prevalence of smoking was noted in 83 individuals, while 35 reported alcohol consumption. In total, postoperative ischemic complications were diagnosed in 48 patients. Regarding medical history, 201 (42.405%) patients had hypertension. We noted that 32 patients (6.751%) had multiple IAs, while 164 (34.599%) presented with ruptured IAs. At the same time, we made statistics on the form of aneurysms, including 362 (76.533%) saccular aneurysms, 47 (9.937%) fusiform

TABLE 1 | Baseline characteristics of patients, aneurysms, and treatment procedures.

Characteristic	Patients ($n = 473$)
Baseline characteristics	
Age, year	59 (19–89)
Gender, male	192 (40.592)
Hypertension	201 (42.495)
Hyperlipidemia	6 (1.268)
Diabetes	30 (6.342)
Heart comorbidities	21 (4.440)
Cerebral infarction	42 (8.879)
Smoking	83 (17.548)
Drinking	35 (7.300)
Characteristics of aneurysms	
Maximum diameter, mm	5.690 (1.3–25)
Multiple aneurysms	32 (6.765)
IA rupture	164 (34.672)
IA location	
ACA	10 (2.114)
ACoA	95 (20.085)
AChA	11 (2.326)
MCA	38 (8.034)
ICA	97 (20.507)
VA	28 (6.131)
BA	26 (5.497)
PCA	9 (1.903)
PCoA	176 (37.209)
IA form	
Saccular	362 (76.533)
Fusiform	47 (9.937)
Lobulated	19 (4.017)
Dissecting	12 (2.537)
Irregular	33 (6.977)
Treatment related	
Chief complaint	
Discovered during physical examination	116 (24.524)
Symptoms of cerebral hemorrhage	280 (59.197)
Postoperative recurrence	5 (1.057)
Others	72 (15.222)
Modality of treatment	
Coiling only	130 (27.484)
Balloon/stent-assisted coiling	314 (65.962)
Double microcatheter technique	22 (4.651)
PAO	9 (1.903)
Degree of embolism	
Complete embolism	287 (60.677)
Proximal total embolism	110 (23.256)
Most embolism	53 (11.205)
Partial embolism	23 (4.863)
Antiplatelet agent	357 (75.476)

Abbreviations: ACA, anterior cerebral artery; AChA, anterior choroidal artery; ACoA, anterior communicating artery; BA, basilar artery; IA, intracranial aneurysm; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; PCoA, posterior communicating artery; VA, vertebral artery.

aneurysms, 19 (4.017%) lobulated aneurysms, 12 (2.537%) dissecting aneurysms, and 33 (6.977%) irregular aneurysms.

The most frequently treated aneurysm locations were the anterior communicating artery (ACoA, 20.042%), internal carotid artery (ICA, 20.464%), and posterior communicating artery (PCoA, 37.131%). A majority of patients (59.072%) sought medical assistance due to symptoms of cerebral hemorrhage, such as limb weakness and speech disorders. The primary treatment techniques included coiling only (27.426%), balloon or stent-assisted coiling (65.823%), double Microcatheter Technique (4.641%), and parent artery occlusion (1.899%). Postoperative evaluation indicated that complete embolization was achieved in 287 (60.549%) patients. In terms of medication, 357 (75.476%) patients received antiplatelet therapy.

By comparing the two groups with and without ischemic complications, we found statistically significant differences in hypertension ($p < 0.001$), smoking ($p < 0.001$), history of alcohol drinking ($p < 0.001$), IA rupture ($p < 0.001$), and antiplatelet agents ($p < 0.001$) (Table 2). There were no significant differences in other factors.

3.2 | Identifying Predictors for Ischemic Complications

Plot the binomial deviation curve versus log (λ), where λ is the tuning hyperparameter. The vertical solid line represents the binomial deviation ± standard error (SE). The vertical dashed line is plotted at the optimum value using the minimum criteria and 1-SE criteria. The optimal value of λ was selected for the LASSO model by using a 10-fold cross-validation of the minimum criterion (Figure 2A). We chose the optimal λ value of 0.01878406. A coefficient distribution plot was generated based on the log (λ) sequence (Figure 2B). Eight relevant factors were finally selected, including

TABLE 2 | Clinical characteristics of ischemic complications subgroups.

Characteristics	Ischemic complications incurred ($n = 48$)	Ischemic complications non-incurred ($n = 425$)	p
Age, mean (year)	59.104	58.802	0.869
Gender, male	19 (39.583)	173 (40.706)	0.999
Hypertension	38 (49.167)	163 (38.353)	< 0.001
Hyperlipidemia	0 (0)	6 (1.412)	0.882
Diabetes	3 (6.250)	27 (6.353)	0.999
Heart comorbidities	4 (8.333)	17 (4.000)	0.312
Cerebral infarction	2 (4.167)	40 (9.412)	0.346
Smoking	18 (37.500)	65 (15.294)	< 0.001
Drinking	12 (25.000)	23 (5.412)	< 0.001
Characteristics of aneurysms			
Maximum diameter, mm	6.152	5.638	0.397
Multiple aneurysms	6 (12.500)	26 (6.118)	0.172
IA rupture	34 (70.833)	130 (30.588)	< 0.001
IA location			
ACA	1 (2.083)	9 (2.118)	0.999
AcoA	13 (27.083)	82 (19.294)	0.277
AChA	1 (2.083)	10 (2.353)	0.999
MCA	6 (12.500)	32 (7.529)	0.357
ICA	5 (10.417)	92 (21.647)	0.101
VA	3 (6.250)	25 (5.882)	0.999
BA	2 (4.167)	24 (5.647)	0.926
PCA	3 (6.250)	6 (1.412)	0.077
PCoA	15 (31.250)	161 (37.882)	0.457
IA form			
Saccular	31 (64.583)	331 (77.882)	0.072
Fusiform	7 (14.583)	40 (9.412)	
Lobulated	3 (6.250)	16 (3.765)	
Dissecting	0 (0)	12 (2.824)	
Irregular	7 (14.583)	26 (6.118)	
Treatment related			
Chief complaint			
Discovered during physical examination	11 (22.917)	105 (24.706)	0.431
Symptoms of cerebral hemorrhage	32 (66.667)	248 (58.353)	
Postoperative recurrence	1 (2.083)	4 (0.941)	
Others	4 (8.333)	68 (16.000)	

(Continues)

TABLE 2 | (Continued)

Characteristics	Ischemic complications incurred ($n = 48$)	Ischemic complications non-incurred ($n = 425$)	p
Modality of treatment			
Coiling only	8 (16.667)	122 (28.706)	0.205
Balloon/stent-assisted coiling	37 (77.083)	275 (64.706)	
Double microcatheter technique	3 (6.250)	19 (4.471)	
PAO	0 (0)	9 (2.118)	
Degree of embolism			
Complete embolism	21 (43.750)	266 (62.588)	0.054
Proximal total embolism	16 (33.333)	94 (22.118)	
Most embolism	9 (18.750)	44 (10.353)	
Partial embolism	2 (4.167)	21 (4.941)	
Antiplatelet agent	26 (54.167)	90 (21.176)	< 0.001

Abbreviations: ACA, anterior cerebral artery; AChA, anterior choroidal artery; ACoA, anterior communicating artery; BA, basilar artery; IA, intracranial aneurysm; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; PCoA, posterior communicating artery; VA, vertebral artery.

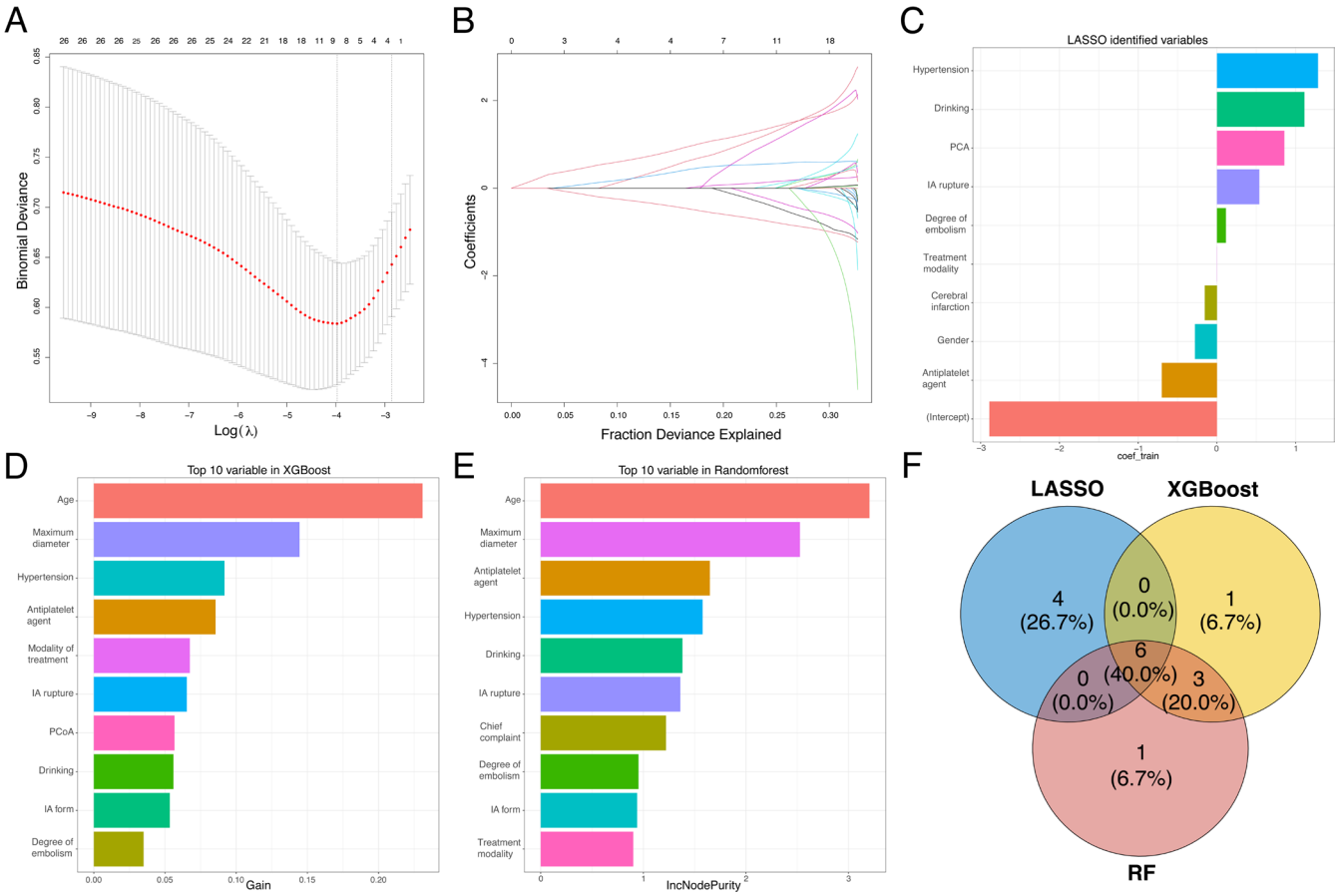

FIGURE 2 | Machine learning and variable screening. (A) Cross-validation results. The two dashed lines on the left and right are the range of positive and negative standard deviations of log(λ). The dashed line on the left indicates the value of the harmonic parameter log(λ) when the model error is minimized. (B) LASSO coefficient curves for 25 variables. (C) Variables screened by LASSO regression. (D) Top 10 features selected using XGBoost and the corresponding variable importance score. (E) Top 10 important features selected using randomForest. (F) The factors screened by LASSO regression, XGBoost, and Random Forest methods are summarized, and the figure shows the hub variables.

gender, hypertension, history of cerebral infarction, history of alcohol drinking, multiple IAs, rupture status, location as PCA, treatment modality, degree of embolism, and antiplatelet agent, with coefficients of −0.280, 1.284, −0.155, 1.110, 0.539, 0.857, 0.002, 0.114, and −0.700, respectively (Figure 2C). We screened the variables based on the contribution of the XGBoost model to each

factor, and Figure 2D demonstrates the top 10 important factors, which are age, maximum diameter of IAs, hypertension, antiplatelet agent, treatment modality, rupture status, location as PCoA, history of alcohol drinking, IAs form, and degree of embolism. We used Random Forest to analyze the correlation factors and sorted them according to IncNodePurity values, and finally we filtered the top 10 important factors as age, maximum diameter of IAs, antiplatelet agent, hypertension, history of drinking, rupture status, chief complaint, degree of embolism, IAs form, and treatment modality (Figure 2E). We combined the factors screened by LASSO regression, XGBoost modeling, and random forests to identify hub factors associated with ischemic complications, including hypertension, history of drinking, rupture status of IAs, and antiplatelet agent (Figure 2F). We then performed multivariate logistic regression analysis of these six potential correlated factors.

Table 3 depicts the outcomes of the multivariate logistic regression analyses. Our multivariate analysis identified hypertension as an independent risk factor for postoperative ischemic complications, with an odds ratio (OR) of 6.468 (95% confidence interval [CI]: 2.673–18.292, $p < 0.001$), and history of drinking with an OR of 4.476 (95% CI: 1.525–12.622, $p = 0.005$). Ruptured IA (OR = 2.746, 95% CI: 1.137–6.882, $p = 0.027$) and antiplatelet agent (OR = 0.417, 95% CI: 0.177–0.974, $p = 0.044$) were also a potent independent risk factors.

3.3 | Nomogram Construction and Validation for Predicting Ischemic Complications

Utilizing the independent risk factors identified by the multivariate logistic regression analysis, a nomogram was constructed to predict the prognosis of ischemic complications. Each variable was assigned a point score from 0 to 100, which corresponded to the coefficients of the independent risk factors. The total score was determined by summing the scores associated with each factor. The higher the overall nomogram score, the greater the influence of the contributing variables. As indicated by the developed nomogram, hypertension exerted the most substantial influence on ischemic outcomes, followed by history of drinking, ruptured aneurysms, and antiplatelet agent (Figure 3).

3.4 | Evaluation of Nomogram Prediction Efficacy

The receiver operating characteristic (ROC) curve demonstrated the nomogram's high diagnostic utility, with an area under the curve (AUC) of 0.826, signifying that the model exhibited good discrimination (Figure 4A). At the same time, we apply this model in the validation set for verification, and the AUC of the ROC curve plotted using the validation set data is 0.836 (Figure 4B). This proves that the predictive effectiveness of this prediction model is relatively stable.

The calibration curve for both the training and validation sets displayed favorable alignment (Figure 4C,D). The training set decision curve indicated that if the threshold probability is > 0% and < 70%, the nomogram used in this study to predict risk of poor recovery added more benefit than either the intervention-all-patients scheme or the intervention-none-patient scheme (Figure 4E). On the other hand, the decision curves in the validation set showed that nomograms used to predict the risk of poor recovery in the range added more benefit than either the intervention-all-patients scheme or the intervention-none-patient scheme, with the threshold probability greater than 0% and less than 70% were more beneficial (Figure 4F).

TABLE 3 | Multivariable logistic analysis for ischemic complications.

	Multivariate analysis	
Characteristics	**OR (95% CI)**	***p***
Hypertension	6.468 (2.673–18.292)	< 0.001
Drinking	4.476 (1.525–12.622)	0.005
Ruptured IA	2.746 (1.137–6.882)	0.027
Antiplatelet agent	0.417 (0.177–0.974)	0.044

Abbreviations: CI, confidence interval; IA, intracranial aneurysm; OR, odds ratio.

4 | Discussion

Intracranial aneurysms (IAs) have a prevalence of approximately 2% within the general population [11]. Since the advent of the 21st century, endovascular therapy has been progressively favored over surgical procedures for the treatment of IAs [12]. Despite the refinement and maturation of these technologies, complications during endovascular treatment persist, with thromboembolic events representing a principal concern following endovascular coiling [13].

Current research on postoperative ischemic complications tends to concentrate on aneurysms that are specific to certain arteries. These include the ophthalmic segment aneurysms [14], anterior choroidal artery (AChA) [8], and intracranial vertebral artery dissecting aneurysms [15]. While some studies have examined overall clinical outcomes, they have yet to develop comprehensive models or hypotheses [16]. All patients with IAs at different sites were included in this study and screened for clinical and imaging indicators using ML. We identified three independent risk factors that were significantly associated with these ischemic complications: hypertension, drinking, and history of rupture. These three independent risk factors are eventually used to construct a risk prediction model, which shows stable prediction performance in both the training and validation sets.

Hypertension has been associated with the formation, growth, and rupture of IAs [17]. The increased risk of ischemic complications in hypertensive patients can potentially be attributed to the following reasons: (1) Increased risk of arteriosclerosis: Hypertensive patients have a higher risk of developing arteriosclerosis. Changes in hemodynamics during and after surgery may trigger the detachment of plaques or thrombosis, thereby leading to cerebral embolism. (2) Propensity for cerebral vasospasm: Patients with hypertension are more likely to experience cerebral vasospasm [18], although induced hypertension is an important therapeutic approach to maintain cerebral blood flow when cerebral vasospasm occurs [19, 20]. (3) Induction of aneurysm enlargement: Hypertension can lead

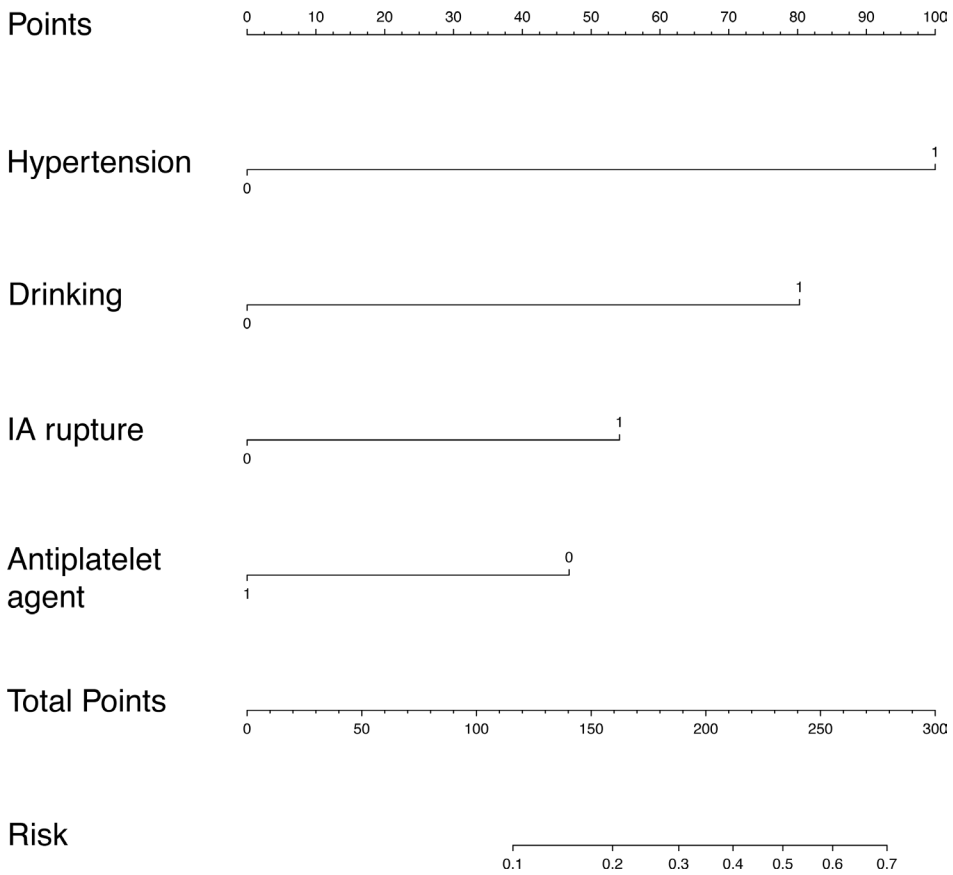

FIGURE 3 | Nomogram for predicting ischemic complications in patients with intracranial aneurysm. IA, intracranial aneurysm.

to the enlargement of arterial aneurysms. Larger aneurysms have a higher likelihood of forming thrombi in the lumen, which may result in cerebral embolism if the thrombi dislodge [21, 22].

Alcohol abuse may lead to the development and rupture of cerebral aneurysms, resulting in aneurysmal subarachnoid hemorrhage (aSAH). In a study that included 6411 patients with intracranial aneurysms, univariate and multivariate logistic regression found that alcohol consumption was associated with aneurysm rupture and that alcohol consumption increased the risk of aneurysm rupture [23]. Aneurysmal subarachnoid hemorrhage resulting from aneurysm rupture can cause vasospasm and delayed cerebral ischemia. This was confirmed by a study that included 236 patients with aneurysmal subarachnoid hemorrhage, which found that alcohol abuse can lead to an increased risk of vasospasm and delayed cerebral ischemia [24]. Related previous studies have shown that alcohol can cause vessel constriction in several ways. Alcohol can increase sympathetic nervous system activity as well as catecholamine release, which ultimately leads to vessel constriction [25, 26]. Alcohol abuse can also lead to a higher procoagulant state by stimulating the production of fibrinogen activator inhibitor 1 (PAI-1), which inhibits fibrinolytic activity [27]. In addition, an animal study has demonstrated that alcohol can increase the risk of thrombosis. This study showed that serum sulfatide level was significantly decreased in mice fed alcohol. And, sulfatide has anti-thrombotic properties [28]. These related mechanisms help to explain why alcohol consumption was an independent risk factor for ischemic complications after endovascular treatment of IA in the present study.

The status of rupture emerged as a major independent predictor for ischemic complications of IAs, a finding that is in alignment with previous research [29–31]. Previous studies have investigated the potential mechanisms by which aneurysm rupture increases the risk of ischemic complications. First, aneurysmal hemorrhage leads to aneurysmal subarachnoid hemorrhage, which results in cerebral arterial vascular tissue thromboplastin activation and focal type of disseminated intravascular coagulation [32, 33]. Secondly, subarachnoid hemorrhage causes excessive neuroinflammation, which may be one of the potential mechanisms contributing to vasospasm. Toll-like receptors (TLR) play an important role in neuroinflammation, and upregulation of TLR4 is associated with activation of NF-κB signaling and ultimately leads to vasospasm. High levels of TLR4 in peripheral blood mononuclear cells have also been shown to be an independent predictor of vasospasm and poor prognosis due to subarachnoid hemorrhage in a clinical study [34]. These potential mechanisms could explain the rupture state as a potential risk factor for ischemic complications.

Based on our research findings, perioperative antiplatelet therapy is associated with ischemic complications following aneurysm interventional treatment. The use of antiplatelet therapy can be helpful in preventing and managing ischemic complications. However, there are still certain limitations, particularly

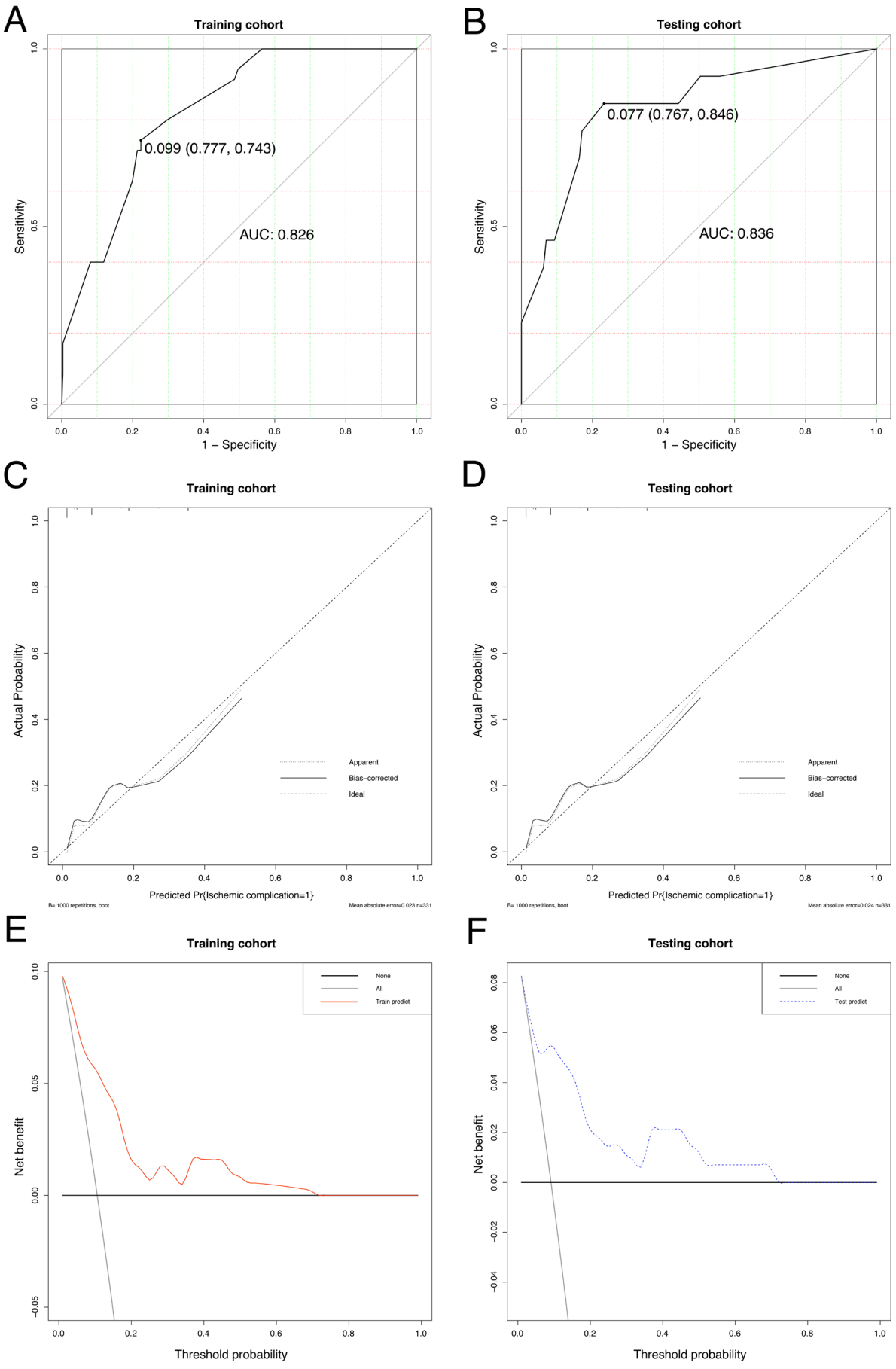

FIGURE 4 | Legend on next page.

FIGURE 4 | Evaluation of Nomogram prediction efficacy. (A) The receiver operating characteristic (ROC) curve of the predictive value of ischemic complications according to the risk score in train sets. (B) The ROC curve of the predictive value of ischemic complications according to the model in test sets. (C) Calibration curve for predicting ischemic complications in training cohort. (D) Calibration curve for predicting ischemic complications in testing cohort. (E) Decision curve analysis (DCA) for nomogram in training cohort. (F) DCA for nomogram in testing cohort.

in patients with ruptured aneurysms, where the application of antiplatelet therapy remains controversial. In a study on ischemic and hemorrhagic complications in patients treated with Pipeline embolization devices, the authors found that high-dose acetylsalicylic acid therapy and clopidogrel treatment for at least 6 months were associated with a reduced incidence of ischemic events, without affecting the risk of hemorrhagic events [35]. Another study on coil embolization of ruptured aneurysms suggested that antiplatelet therapy significantly reduced the incidence of immediate thromboembolic events after the procedure but was not significantly associated with delayed ischemic complications [36]. Although the use of antiplatelet therapy may increase the risk of postoperative hemorrhagic complications, it remains the preferred approach for preventing ischemic complications [37]. Therefore, the types and dosages of antiplatelet drugs, as well as the timing of their use, should be explored through large-scale clinical trials.

5 | Limitation

However, there are still some limitations in this study. Firstly, this study was retrospective. In the future, this predictive model should be applied to prospective studies to better reflect the efficacy of the model and improve the predictive model. Secondly, the threshold range of DCA curves in the training set was narrowed, which may be limited by the sample size. Therefore, the sample size should be further expanded to improve this prediction model so that it can have a more stable and better prediction ability.

6 | Conclusion

In conclusion, this study successfully developed an individualized prediction model for assessing the risk of ischemic complications in patients with intracranial aneurysms (IA). The model accurately identifies patients at higher risk, enabling proactive measures to reduce the overall impact of ischemic complications. Implementation of this prediction model in clinical practice has the potential to improve patient care and outcomes in IA treatment. Further validation and integration of the model can enhance the precision and effectiveness of interventions, benefiting patients with IA.

Author Contributions

Writing-original draft preparation and data curation, J.J.; methodology, software, and writing-original draft preparation, Z.J.; data curation, M.T. and Y.L.; supervision, X.Y.; and supervision and writing-review and editing, Y.W. and Y.L.

Acknowledgments

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Any data associated with this review article will be made available upon reasonable request to the corresponding author.

References

1. R. G. Tawk, T. F. Hasan, C. E. D'Souza, C. E. D'Souza, J. B. Peel, and W. D. Freeman, "Diagnosis and Treatment of Unruptured Intracranial Aneurysms and Aneurysmal Subarachnoid Hemorrhage," *Mayo Clinic Proceedings* 96, no. 7 (2021): 1970–2000, https://doi.org/10.1016/j.mayocp.2021.01.005.

2. M. Blecha and V. Gahtan, "Modern Endovascular Therapy," *World Journal of Surgery* 45, no. 12 (2021): 3493–3502, https://doi.org/10.1007/s00268-020-05875-7.

3. K. S. Lee, J. J. Y. Zhang, V. Nguyen, et al., "The Evolution of Intracranial Aneurysm Treatment Techniques and Future Directions," *Neurosurgical Review* 45, no. 1 (2022): 1–25, https://doi.org/10.1007/s10143-021-01543-z.

4. R. Li, F. Lin, Y. Chen, et al., "In-Hospital Complication-Related Risk Factors for Discharge and 90-Day Outcomes in Patients With Aneurysmal Subarachnoid Hemorrhage After Surgical Clipping and Endovascular Coiling: A Propensity Score-Matched Analysis," *Journal of Neurosurgery* 137, no. 2 (2021): 381–392, https://doi.org/10.3171/2021.10.JNS211484.

5. J. S. McDonald, R. J. McDonald, J. Fan, D. F. Kallmes, G. Lanzino, and H. J. Cloft, "Comparative Effectiveness of Unruptured Cerebral Aneurysm Therapies: Propensity Score Analysis of Clipping Versus Coiling," *Stroke* 44, no. 4 (2013): 988–994, https://doi.org/10.1161/STROKEAHA.111.000196.

6. T. Koiso, Y. Komatsu, D. Watanabe, et al., "The Influence of Aneurysm Size on the Outcomes of Endovascular Management for Aneurysmal Subarachnoid Hemorrhages: A Comparison of the Treatment Results of Patients With Large and Small Aneurysms," *Neurologia Medico-Chirurgica (Tokyo)* 63, no. 3 (2023): 104–110, https://doi.org/10.2176/jns-nmc.2022-0253.

7. J. Han, F. Liu, J. Chen, et al., "Periprocedural Cerebrovascular Complications and 30-Day Outcomes of Endovascular Treatment for Intracranial Vertebral Artery Dissecting Aneurysms," *Journal of Neurosurgery* 138, no. 6 (2023): 1–9, https://doi.org/10.3171/2022.10.JNS221953.

8. T. Maeda, H. Ooigawa, K. Suzuki, et al., "Predictors of Ischemic Complication in Anterior Choroidal Artery Aneurysm Repair," *World Neurosurgery* 167 (2022): e157–e164, https://doi.org/10.1016/j.wneu.2022.07.111.

9. H. J. Lee, J. H. Choi, B. S. Kim, and Y. S. Shin, "Symptomatic Ischemic Complications Following Endovascular Treatment of Vertebral Artery Dissecting Aneurysms," *Acta Neurochirurgica* 164, no. 6 (2022): 1645–1651, https://doi.org/10.1007/s00701-022-05223-9.

10. Q. Wu, S. Xu, C. Wang, et al., "Endovascular Management of Vertebrobasilar Trunk Artery Large Aneurysms: Complications and Long-Term Results," *Frontiers in Neurology* 13 (2022): 839219, https://doi.org/10.3389/fneur.2022.839219.

11. B. Radić, A. Blažeković, I. Jovanović, A. Jurišić-Kvesić, E. Bilić, and F. Borovečki, "Diagnostic and Therapeutic Dilemmas in the

Management of Intracranial Aneurysms," *Acta Clinica Croatica* 60, no. 4 (2021): 758–764, https://doi.org/10.20471/acc.2021.60.04.24.

12. C. S. Lozano, A. M. Lozano, and J. Spears, "The Changing Landscape of Treatment for Intracranial Aneurysm," *Canadian Journal of Neurological Sciences* 46, no. 2 (2019): 159–165, https://doi.org/10.1017/cjn.2019.7.

13. Y. K. Ihn, S. H. Shin, S. K. Baik, et al., "Complications of Endovascular Treatment for Intracranial Aneurysms: Management and Prevention," *Interventional Neuroradiology* 24, no. 3 (2018): 237–245, https://doi.org/10.1016/j.mayocp.2021.01.005.

14. R. B. Qu and H. Jin, "Endovascular Treatment of Intracranial Ophthalmic Segment Aneurysms: A Series and Literature Review," *Turkish Neurosurgery* 26, no. 2 (2016): 223–228, https://doi.org/10.5137/1019-5149.JTN.7710-12.1.

15. H. S. Oh, J. W. Bae, C. E. Hong, et al., "Flow Diverter in Unruptured Intracranial Vertebral Artery Dissecting Aneurysm," *Frontiers in Neurology* 13 (2022): 912863, https://doi.org/10.3389/fneur.2022.912863.

16. H. Henkes, S. Fischer, W. Weber, et al., "Endovascular Coil Occlusion of 1811 Intracranial Aneurysms: Early Angiographic and Clinical Results," *Neurosurgery* 54, no. 2 (2004): 268–280, https://doi.org/10.1227/01.neu.0000103221.16671.f0.

17. S. Zaremba, L. Albus, A. Hadjiathanasiou, H. Vatter, U. Wüllner, and E. Güresir, "Aneurysm Size and Blood Pressure Severity in Patients With Intracranial Aneurysms and Sleep Apnea," *Journal of Clinical Sleep Medicine* 18, no. 6 (2022): 1539–1545, https://doi.org/10.5664/jcsm.9906.

18. C. D. Baggott and B. Aagaard-Kienitz, "Cerebral vasospasm," *Neurosurgery Clinics of North America* 25, no. 3 (2014): 497–528, https://doi.org/10.1016/j.nec.2014.04.008.

19. K. Lakhal, A. Hivert, B. Rozec, and J. Cadiet, "Induced Hypertension or Intravenous Milrinone for Cerebral Vasospasm: Why Choose?," *Neurocritical Care* 35, no. 3 (2021): 922–923, https://doi.org/10.1007/s12028-021-01378-y.

20. M. R. Harrigan, "Hypertension May Be the Most Important Component of Hyperdynamic Therapy in Cerebral Vasospasm," *Critical Care* 14, no. 3 (2010): 151, https://doi.org/10.1186/cc8983.

21. T. Y. Cras, D. Bos, M. A. Ikram, et al., "Determinants of the Presence and Size of Intracranial Aneurysms in the General Population: The Rotterdam Study," *Stroke* 51, no. 7 (2020): 2103–2110, https://doi.org/10.1161/STROKEAHA.120.029296.

22. C. P. Derdeyn, D. T. Cross, C. J. Moran, et al., "Postprocedure Ischemic Events After Treatment of Intracranial Aneurysms With Guglielmi Detachable Coils," *Journal of Neurosurgery* 96, no. 5 (2002): 837–843, https://doi.org/10.3171/jns.2002.96.5.0837.

23. A. Can, V. M. Castro, Y. H. Ozdemir, et al., "Alcohol Consumption and Aneurysmal Subarachnoid Hemorrhage," *Translational Stroke Research* 9, no. 1 (2018): 13–19, https://doi.org/10.1007/s12975-017-0557-z.

24. L. Zhao, C. Cheng, L. Peng, et al., "Alcohol Abuse Associated With Increased Risk of Angiographic Vasospasm and Delayed Cerebral Ischemia in Patients With Aneurysmal Subarachnoid Hemorrhage Requiring Mechanical Ventilation," *Frontiers in Cardiovascular Medicine* 9 (2022): 825890, https://doi.org/10.3389/fcvm.2022.825890.

25. R. Russ, A. R. Abdel-Rahman, and W. R. Wooles, "Role of the Sympathetic Nervous System in Ethanol-Induced Hypertension in Rats," *Alcohol* 8 (1991): 301–307, https://doi.org/10.1016/0741-8329(91)90433-w.

26. A. D. O'Connor, D. E. Rusyniak, and A. Bruno, "Cerebrovascular and Cardiovascular Complications of Alcohol and Sympathomimetic Drug Abuse," *Medical Clinics of North America* 89 (2005): 1343–1358, https://doi.org/10.1016/j.mcna.2005.06.010.

27. H. S. Ballard, "The Hematological Complications of Alcoholism," *Alcohol Health and Research World* 21 (1997): 42–52, https://doi.org/10.1111/j.1530-0277.1989.tb00408.x.

28. H. Kanbe, Y. Kamijo, T. Nakajima, et al., "Chronic Ethanol Consumption Decreases Serum Sulfatide Levels by Suppressing Hepatic Cerebroside Sulfotransferase Expression in Mice," *Archives of Toxicology* 88, no. 2 (2014): 367–379, https://doi.org/10.1007/s00204-013-1132-3.

29. T. Altay, H. I. Kang, H. H. Woo, et al., "Thromboembolic Events Associated With Endovascular Treatment of Cerebral Aneurysms," *Journal of NeuroInterventional Surgery* 3, no. 2 (2011): 147–150, https://doi.org/10.1007/s11910-012-0326-z.

30. N. P. Brooks, A. S. Turk, D. B. Niemann, B. Aagaard-Kienitz, K. Pulfer, and T. Cook, "Frequency of Thromboembolic Events Associated With Endovascular Aneurysm Treatment: Retrospective Case Series," *Journal of Neurosurgery* 108, no. 6 (2008): 1095–1100, https://doi.org/10.3171/JNS/2008/108/6/1095.

31. H. Hadeishi, A. Suzuki, N. Yasui, J. Hatazawa, and E. Shimosegawa, "Diffusion-Weighted Magnetic Resonance Imaging in Patients With Subarachnoid Hemorrhage," *Neurosurgery* 50, no. 4 (2002): 741–747, https://doi.org/10.1097/00006123-200204000-00010.

32. S. C. Stein, K. D. Browne, X. H. Chen, D. H. Smith, and D. I. Graham, "Thromboembolism and Delayed Cerebral Ischemia After Subarachnoid Hemorrhage: An Autopsy Study," *Neurosurgery* 59, no. 4 (2006): 781–787, https://doi.org/10.1227/01.NEU.0000227519.27569.45.

33. Y. Fujii, S. Takeuchi, O. Sasaki, T. Minakawa, T. Koike, and R. Tanaka, "Hemostasis in Spontaneous Subarachnoid Hemorrhage," *Neurosurgery* 37, no. 2 (1995): 226–234, https://doi.org/10.1227/00006123-199508000-00006.

34. Q. Wang, Q. Luo, Y. H. Zhao, and X. Chen, "Toll-Like Receptor-4 Pathway as a Possible Molecular Mechanism for Brain Injuries After Subarachnoid Hemorrhage," *International Journal of Neuroscience* 130, no. 9 (2020): 953–964, https://doi.org/10.1080/00207454.2019.1709845.

35. H. Saber, R. Y. Kherallah, M. O. Hadied, S. Kazemlou, P. Chamiraju, and S. Narayanan, "Antiplatelet Therapy and the Risk of Ischemic and Hemorrhagic Complications Associated With Pipeline Embolization of Cerebral Aneurysms: A Systematic Review and Pooled Analysis," *Journal of NeuroInterventional Surgery* 11, no. 4 (2019): 362–366, https://doi.org/10.1136/neurintsurg-2018-014082.

36. H. Takase, J. Tatezuki, M. M. Salem, et al., "Antiplatelet Therapy for Standalone Coiling of Ruptured Intracranial Aneurysms: A Systematic Review and Meta-Analysis," *Journal of NeuroInterventional Surgery* 14, no. 12 (2022): 1207–1212, https://doi.org/10.1136/neurintsurg-2021-018346.

37. B. M. Meyer, J. K. Campos, J. C. de Collard Beaufort, et al., "Trends in Dual Antiplatelet Therapy Use for Neurointerventional Procedures for the Management of Intracranial Aneurysms," *Biomedicine* 11, no. 8 (2023): 2234, https://doi.org/10.3390/biomedicines11082234.