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Influencing Factors for Complication with Aneurysm Rupture of the Fetal Posterior Communicating Artery After Clipping Through the Lateral Supraorbital Approach and Prognosis

Yunxiang Chen, Yurong Cai, Huahui Chen, Xiafeng Lin, Gezhi Zhou, Jianlie Yuan and Yuejun Fan*

Abstract

Background: To explore the influencing factors for complication with aneurysm rupture of the fetal posterior communicating artery after clipping through the lateral supraorbital (LSO) approach and prognosis.

Methods: A total of 119 patients with posterior communicating artery aneurysm (PCoAA) accompanied by fetal posterior cerebral artery (fPCA), who underwent clipping through the LSO approach from January 2014 to December 2019, were selected. They were aged 50–70 years old, (60.5 ± 13.7) on average. The treatment outcome, incidence of complications and follow-up results were analyzed. Based on the follow-up results, univariate comparative analysis was conducted for the clinical data of patients with good or poor prognosis. The statistically significant factors were incorporated into multivariate Cox regression analysis, and the nomogram prediction model for prognosis was established. The accuracy of the model was assessed using the Hosmer–Lemeshow goodness-of-fit test.

Results: Clipping through the LSO approach was successful in all cases. Perioperative complications occurred in 41 patients. According to the follow-up results, 89 patients had good prognosis, while 30 had poor prognosis. Age of > 65 years old, history of hypertension, high Hunt–Hess grade and high modified Fisher grade were independent risk factors for the poor prognosis of patients with PCoAA accompanied by fPCA after clipping through the LSO approach. The results obtained by the established model were consistent with the actual ones.

Conclusion: Age, history of hypertension, Hunt–Hess grade and modified Fisher grade are independent risk factors for the prognosis of patients with PCoAA accompanied by fPCA after clipping through the LSO approach.

Keywords: Fetal posterior cerebral artery, Posterior communicating artery aneurysm, Lateral supraorbital approach, Clipping, Prognosis

1 Introduction

Posterior communicating artery aneurysm (PCoAA) is a clinically common internal carotid aneurysm, which refers to protrusion at the internal carotid artery-PCoA bifurcation, accounting for approximately 20–30% of intracranial aneurysms [1]. Ruptured intracranial aneurysm is mainly manifested as subarachnoid hemorrhage,

*Correspondence: dpljcs5903792@163.com
Affiliated Jinhua Hospital, Zhejiang University School of Medicine (Jinhua Municipal Central Hospital), Zhejiang Province, Jinhua 321000, China

sudden severe headache, nuchal rigidity, photophobia, nausea, and vomiting. The fatality rate of aneurysm hemorrhage is 25–50%, and nerve dysfunction may still occur in patients after treatment [2]. The treatment is difficult due to the complex anatomical structure of PCoA and existence of fetal posterior cerebral artery (fPCA) [3].

Intracranial aneurysm is mainly treated with craniotomy and interventional therapy. As a common method for treating intracranial aneurysm, clipping can be performed through the pterional, keyhole or lateral supraorbital (LSO) approach [4]. The formation of fPCA can be attributed to the absence or dysplasia of P1 segment of the ipsilateral brain PCA, so the blood supply of P2 segment originates from the thickened PCoA on the ipsilateral side. CT angiography shows that the diameter of PCoA is larger than that of P1 segment of the ipsilateral PCA, and the ipsilateral P1 segment is small or absent [5]. There is a higher risk of ischemic injury in the surgical treatment of PCoAA accompanied by fPCA than that of PCoAA alone [6]. Clipping aneurysms through the pterional or LSO approach is most common, and this approach has wide visual field which reduces the strain on brain tissues while separating each cistern during operation. Meanwhile, this method can well control bleeding during operation by fully exposing the A1 and A2 segments of bilateral anterior cerebral arteries simultaneously [7, 8]. Thereby motivated, we herein explored the efficacy of clipping through the LSO approach on PCoAA accompanied by fPCA, and the influencing factors for the prognosis, aiming to provide valuable evidence for clinical treatment.

2 Materials and Methods

2.1 Subjects

A total of 119 patients undergoing vascular therapy in our hospital from January 2014 to December 2019 were retrospectively analyzed. Inclusion criteria: (1) patients diagnosed as PCoAA through CTA or DSA, (2) those with subarachnoid hemorrhage shown in head CT, (3) those with preoperative Hunt–Hess grade 1–3 undergoing clipping through the LSO approach, and (4) those with complete clinical data. Exclusion criteria: (1) patients complicated with severe diseases in the heart or lungs, (2) those with malignant tumors, (3) those with multiple intracranial aneurysms unable to be clipped by unilateral craniotomy, (4) those with modified Fisher grade III or above, or with brain swelling shown in head CT, (5) those with distal middle cerebral artery (M1) aneurysm or distal anterior cerebral artery (A2) aneurysm, or (6) those receiving conservative or endovascular treatment. This study was approved by the Hospital Ethics Committee, and the patients or their families were informed of the study and signed the informed consent.

2.2 Evaluation Criteria

The embolization of aneurysm was graded before operation according to the Raymond rating criteria [9]: grade I: there is basically no image developed in the aneurysm, grade II: there is image developed at the aneurysmal neck, and grade III: there is image developed in the aneurysmal body. Preoperative Hunt–Hess grading criteria [10]: grade 0: un-ruptured aneurysm, grade 1: asymptomatic or mild headache, and mild nuchal rigidity, grade 2: moderate–severe headache and nuchal rigidity, without other neurological deficits except cranial nerve palsy, grade 3: lethargy, confusion or mild focal neurological deficits, grade 4: stupor, moderate or severe incomplete paralysis, and possibly early decerebrate rigidity and vegetative nervous system dysfunction, and grade 5: deep coma, decerebrate rigidity, and dying state. Based on CT results, the subarachnoid hemorrhage of patients was graded using the modified Fisher scale before operation [11]: grade 0: no hemorrhage, or only intraventricular or intra-parenchymal hemorrhage, grade 1: hemorrhage only in the basilar cistern, grade 2: hemorrhage only in the surrounding cistern or lateral fissure cistern, grade 3: extensive subarachnoid hemorrhage accompanied by intraventricular hematoma, and grade 4: thick hematocele in the basilar cistern, surrounding cistern and lateral fissure cistern.

2.3 Imaging Examinations

The imaging data of all patients were assessed by more than two radiologists and neurosurgeons. Diagnostic criteria for PCoAA: filling defects in the cerebral veins were mainly shown in preoperative CTA, manifested as venous stenosis or no image development.

Diagnostic criteria for fPCA: it was observed in internal carotid angiography that PCoA was open, and PCA was mainly supplied by the internal carotid artery. The basilar artery angiography displayed little or no blood supply to PCA, accompanied by dysplasia or absence of P1 segment of PCA.

2.4 Surgical Methods

Under general anesthesia with tracheal intubation, the cutaneous muscle flap was turned to the orbital side, and a single bone hole was made at the temporal line of the temporal muscle attachment margin. A bone flap (about 3×4 cm) was dissociated with a milling cutter. The sphenoid ridge was partially abraded out, and the dura mater was cut open in an arc shape and hung on the edge of the bone window. In the case of high intracranial pressure, lumbar cistern drainage was performed to release the cerebrospinal fluid, the lateral fissure was separated under a microscope, and the upper segment

of the internal carotid artery was exposed. Then the frontal lobe was gently lifted using an automatic brain spatula, the skull base was opened, and the cerebrospinal fluid was aspirated to further cause brain tissue collapse. Afterward, the PCoA complex was fully exposed, and the aneurysmal neck was clipped, followed by indocyanine green angiography. The aneurysmal body was cut, hemostatized and washed before operation, and several gelatin sponges soaked with papaverine and hemocoagulase were placed to prevent vasospasm and bleeding in the operative region. Finally, the skull was routinely closed, and the patient was sent back to NICU for subsequent treatment.

2.5 Postoperative Follow-up

Head CT was performed within 24 h after operation to determine whether there was new ischemic cerebral infarction, new intracranial hematoma and traction injury of brain tissues. The neurological prognosis of patients was evaluated using the Glasgow outcome scale (GOS) score before and 6 weeks, 6 months and 12 months after operation [12]: 5 points: well recovered, able to live normally, but accompanied by mild defects, 4 points: mildly disabled, but able to live independently and work under protection, 3 points: severely disabled, sober, and unable to live independently, 2 points: vegetative, with minimal responses, and 1 point: dead. The GOS score of 5 points indicates good prognosis, while that of 1–4 point(s) indicates poor prognosis.

2.6 Statistical Analysis

IBM SPSS 19.0 software was used for statistical analysis. The normality of continuous data was detected by Kolmogorov–Smirnov test. Normally distributed continuous variables were expressed as ($\overline{x} \pm s$), and t test was performed to compare whether there are statistical differences between two groups. Abnormally distributed continuous variables were expressed as median, and Mann–Whitney U test was performed to compare whether there were statistical differences between two groups. The difference in categorical variables was compared by χ^2 test. The influencing factors for the prognosis of PCoAA patients were explored through multivariate Cox regression analysis. Based on the independent risk factors for the prognosis of patients, a nomogram prediction model was established using R software and rms software package. The calibration of the model was assessed using the Hosmer–Lemeshow goodness-of-fit test. $P < 0.05$ suggested that a difference was statistically significant, and $\alpha = 0.05$ was set as the test level.

3 Results

3.1 General Conditions

A total of 119 patients were enrolled in this study, including 98 females and 21 males aged (60.5 ± 13.7) years old on average. The preoperative examination results and grading of patients are shown in Table 1.

3.2 Surgical Outcomes and Perioperative Complications

Head CTA conducted 7–10 d after operation confirmed that aneurysm clipping was successful in all cases. Perioperative complications occurred in 41 of 119 patients, including 5 cases of postoperative infarction, 7 cases of severe cerebral vasospasm, 18 cases of hydrocephalus and 11 cases of intracranial infection.

3.3 Follow-up Results

All patients were followed up for 12 months after operation, and their prognoses were assessed using GOS scores. There were 89 cases of good recovery, 28 cases of moderate disability, and 2 cases of severe disability. Besides, focal cerebral infarction and early hydrocephalus were found in 7 and 10 cases, respectively, which were mitigated through lumbar cistern drainage.

3.4 Univariate Analysis Results of Factors for Prognosis

The results of univariate analysis revealed that age, history of hypertension, Hunt–Hess grade and modified Fisher grade had significant differences between good and poor prognosis groups. The poor prognosis group was older, and the proportion of patients with history

Table 1 Preoperative conditions of patients ($n = 119$)

Item	Data
Female [*n* (%)]	98 (82.35)
Age ($\overline{x} \pm s$)	60.5 ± 13.7
History of hypertension [*n* (%)]	64 (53.78)
History of diabetes [*n* (%)]	6 (5.04)
Smoking history [*n* (%)]	12 (10.08)
Drinking history [*n* (%)]	5 (4.20)
Hunt–Hess grade [*n* (%)]	
Grade 1	25
Grade 2	35
Grade 3	59
Modified Fisher grade [*n* (%)]	
Grade 1	44
Grade 2	36
Grade 3	39
Raymond grade [*n* (%)]	
Grade I	112
Grade II	4
Grade III	3

of hypertension, high Hunt–Hess grade and high Fisher grade was higher in poor prognosis group than that in good prognosis group ($P<0.05$) (Table 2).

3.5 Cox Regression Analysis Results of Factors for Prognosis

The statistically significant factors in the above univariate analysis were incorporated into multivariate Cox regression analysis. It was found that age of > 65 years old, history of hypertension, Hunt–Hess grade 3 and modified Fisher grade 3 were independent risk factors for the prognosis of patients with PCoAA accompanied by fPCA (Fig. 1).

3.6 Prediction Model for Prognosis and Efficacy Assessment

The nomogram prediction model for the prognosis of PCoAA patients was established based on the above independent risk factors (Fig. 2). As shown in the calibration curve of the model (Fig. 3), the gray diagonal line was the reference line, the blue curve was the prediction fitting line, and the gray shadow indicated 95%CI. When the event incidence rate was < 32% or > 78%, the risk of poor prognosis was underestimated by the model. When the rate was 32–78%, the risk was overestimated by the model. Overall, the result obtained by the nomogram prediction model was highly consistent with the actual ones, verifying a high accuracy.

4 Discussion

PCoAA refers to all aneurysms at the initial part of PCoA in a broad sense, and the aneurysm at the internal carotid artery-PCoA bifurcation in a narrow sense, accounting for 50% of internal carotid artery aneurysms [13]. As an important anatomical variation of PCoA, fPCA means that in the later stage of embryonic development, PCoA gradually becomes thinner with the development of brain tissues, and then its diameter is smaller than that of the P1 segment from the basilar artery. The blood to PCA is mainly supplied by the anterior circulation [14]. The incidence rate of fPCA is 7–36% in the population [15]. In terms of imaging, fPCA is manifested as the absence or dysplasia of P1 segment, and PCoA is the P2 segment of the ipsilateral PCA. Ruptured fPCA is a risk factor for PCoA. PCoAA complicated with fPCA, a complex type of aneurysm, easily leads to insufficient blood supply to the occipital lobe and even infarction during operation [16].

Table 2 Results of univariate analysis on influencing factors for prognosis ($n=119$)

Item	Good prognosis group ($n=89$)	Poor prognosis group ($n=30$)	t/χ^2	P
Age (Y)	59.2 ± 10.7	68.7 ± 3.9	4.746	0.000
Female [*n* (%)]	73 (82.02)	25 (83.33)	0.027	0.871
History of hypertension [*n* (%)]	42 (47.19)	22 (73.33)	6.169	0.013
History of diabetes [*n* (%)]	5 (5.62)	1 (3.33)	0.245	0.621
Smoking history [*n* (%)]	9 (10.11)	3 (10.0)	0.000	0.986
Drinking history [*n* (%)]	4 (4.49)	1 (3.33)	0.075	0.784
Side of aneurysm [*n* (%)]			0.074	0.786
Left	39 (43.82)	14 (46.67)		
Right	50 (56.18)	16 (53.33)		
Max diameter of aneurysm (mm)	6.95 ± 3.28	8.26 ± 4.13	1.768	0.080
Size of aneurysmal neck	3.58 ± 1.76	4.12 ± 1.23	1.555	0.123
Hunt–Hess grade [*n* (%)]			17.122	0.000
Grade 1	25 (28.09)	0 (0)		
Grade 2	29 (32.58)	6 (20.0)		
Grade 3	35 (39.33)	24 (80.0)		
Modified Fisher grade [*n* (%)]			21.897	0.000
Grade 1	43 (48.31)	1 (3.33)		
Grade 2	25 (28.09)	11 (36.67)		
Grade 3	21 (23.60)	18 (60.0)		
Raymond grade [*n* (%)]			1.481	0.477
Grade I	85 (95.50)	27 (90.0)		
Grade II	2 (2.25)	2 (6.67)		
Grade III	2 (2.25)	1 (3.33)		

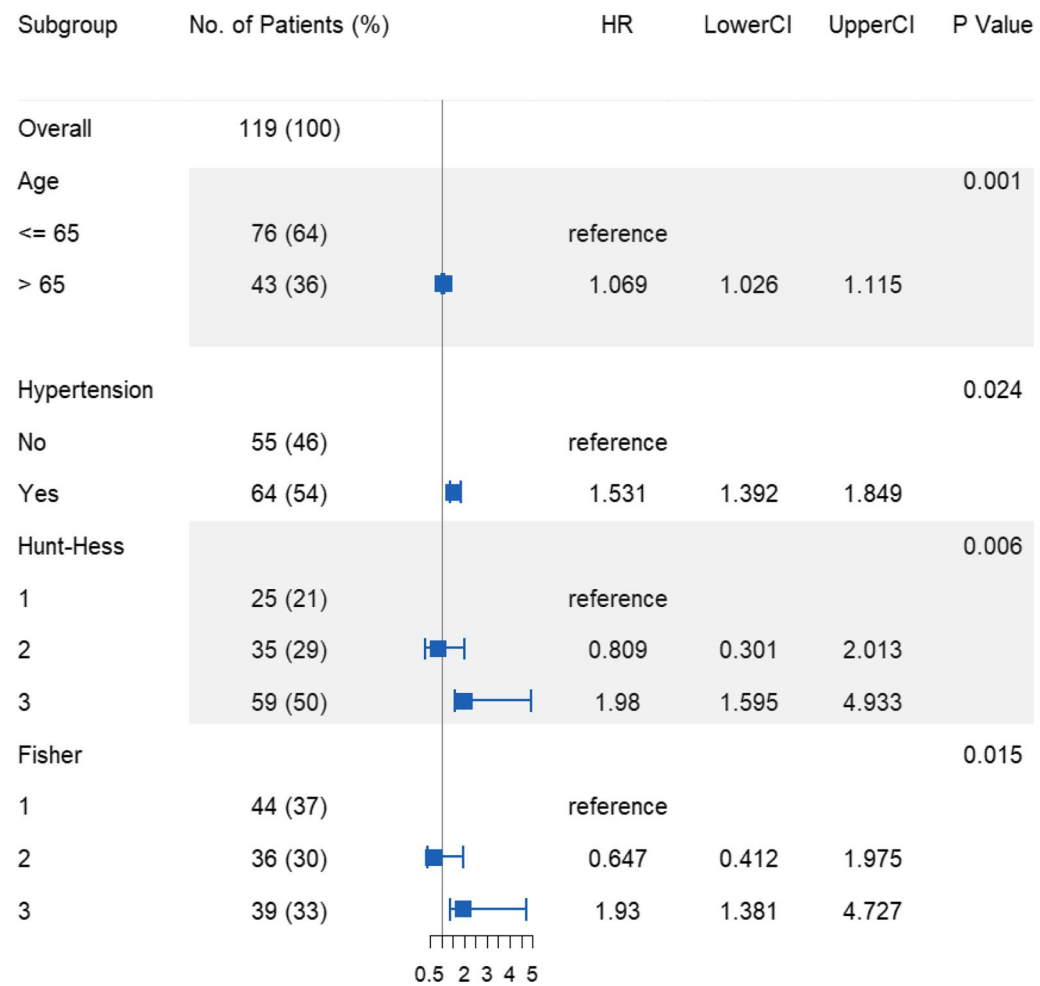

Fig. 1 Forest plot of Cox regression analysis on influencing factors for prognosis

Clipping through the LSO approach was first modified by Hernesniemi based on that through the pterional approach. Incision through the pterional approach starts in front of the tragus, so the main superficial temporal artery is prone to damage. In contrast, the lower edge of incision through the LSO approach starts above the main superficial temporal artery, thereby avoiding damage and reducing bleeding [17]. Compared with the pterional approach, the LSO approach is characterized by more exposure of frontal base, less exposure of lateral fissure temporal lobe, short surgical incision, small scope of temporal muscle dissection, and decreased bone window size and defects. Moreover, the incidence rate of postoperative complications, such as intracranial infection, cerebrospinal fluid leakage, temporal muscle atrophy and facial paralysis, declines.

In the present study, 119 PCoAA patients were treated with clipping through the LSO approach. It was confirmed that aneurysm clipping was successful in all cases, and perioperative complications were observed in 41 patients. All patients were followed up for 6 months, of whom 89 patients had good prognosis (GOS score = 5 points) while the remaining 30 had poor prognosis (GOS score = 2–4 points). The univariate analysis results revealed that age, history of hypertension, Hunt–Hess grade and modified Fisher grade were influencing factors for the prognosis of patients.

There were more female patients than male patients in this study. However, the prognosis of patients showed no statistically significant difference in terms of gender. The higher incidence rate of PCoAA in female patients may be related to the estrogen level. The risk of degenerative lesions in organs rises with aging, and the incidence rate of underlying diseases, such as hypertension, diabetes mellitus and cardio-cerebrovascular diseases, is higher in the elderly [18]. Elderly patients have decreased ability of cerebrovascular auto-regulation and weakened compensatory ability of collateral circulation, so they are prone

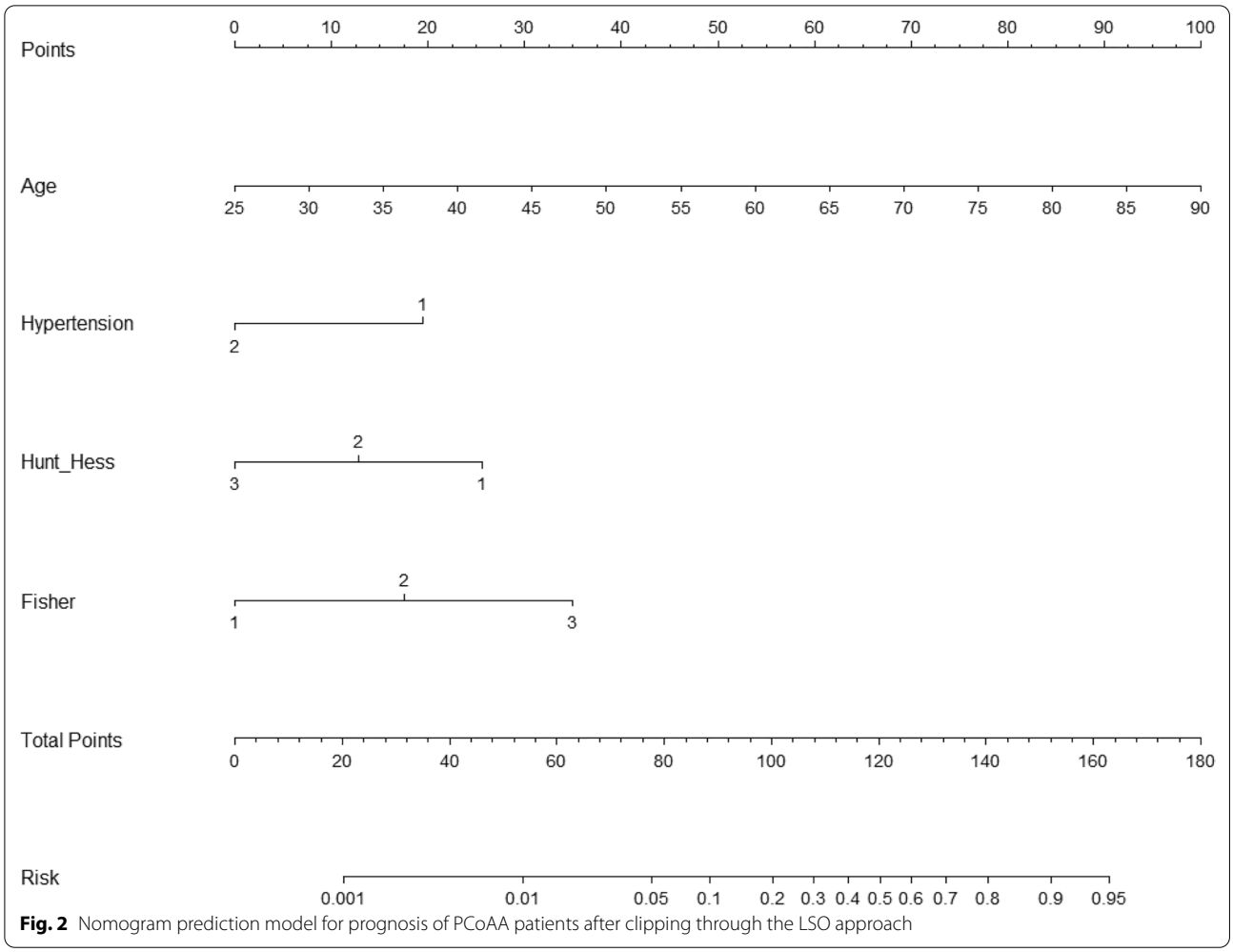

Fig. 2 Nomogram prediction model for prognosis of PCoAA patients after clipping through the LSO approach

to cerebral ischemia after clipping through the LSO approach [19]. History of hypertension is an influencing factor for the poor prognosis of patients with aneurysms. Hypertension can lead to vascular sclerosis and even calcification in patients, thus increasing the operation difficulty and risk of aneurysm clipping and inducing aneurysm rupture in the perioperative period [20]. The Hunt–Hess scale is used for the grading of clinical symptoms of patients with subarachnoid hemorrhage. It is recommended that patients with low grade should be treated with early surgery, and those with high grade should undergo late surgery after the vasospasm stage due to obvious clinical symptoms including peripheral nerve injury and neurological impairment [21]. Besides, the modified Fisher scale is used for the head CT grading of patients with subarachnoid hemorrhage, which can reflect the bleeding site, presence or absence of hematoma, and hematoma volume [22]. The higher modified Fisher grade corresponds to severer cerebral injury of patients, in which blood clot surrounding the aneurysm in the subarachnoid space triggers vasospasm and induces aneurysm re-rupture [23]. Ding et al. [24] analyzed the clinical data of 80 PCoAA + fPCA patients undergoing microsurgical clipping. They found that age, preoperative Hunt–Hess grade and modified Fisher grade were independent risk factors for the surgical outcomes and prognosis, and the risk of poor prognosis of patients with high-grade aneurysm was 2.1 times that of patients with low-grade aneurysm. The aneurysm size is a risk factor for aneurysm rupture, and the diameter of aneurysm > 7 mm is a risk factor for incomplete aneurysm clipping and second operation [25, 26]. Herein, good and poor prognosis groups had similar aneurysm sizes. Probably, PCoA was adjacent to the oculomotor nerve, and the patients visited the hospital due to oculomotor nerve palsy in the early stage, so the aneurysm developed for a short time.

In a study involving 55 ruptured fPCA aneurysm patients, Mardjono et al. [27] found that clipping through the LSO approach was safe and effective, being

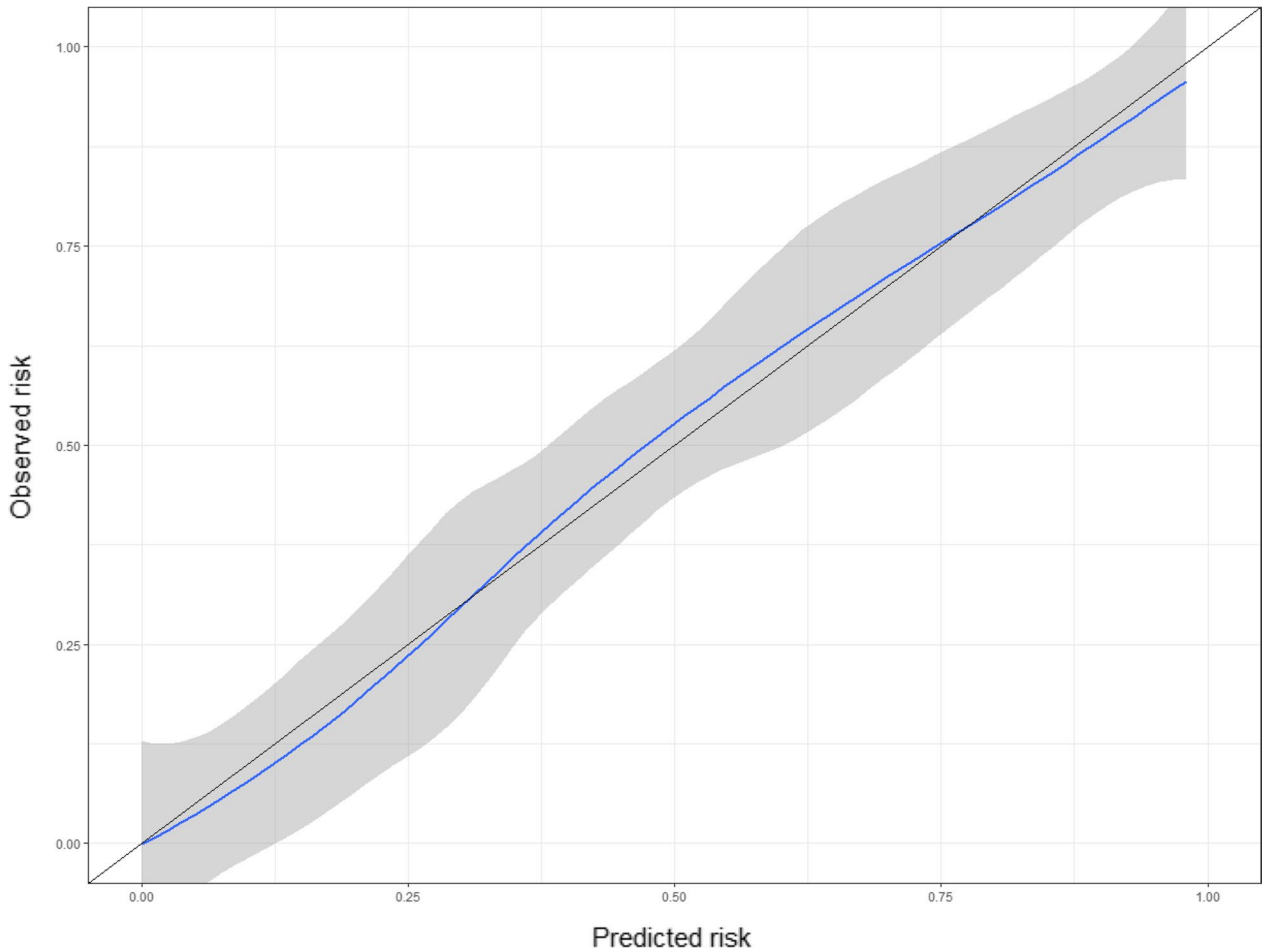

Fig. 3 Calibration curve of nomogram prediction model for prognosis of PCoAA patients after clipping through the LSO approach. When the event incidence rate is < 32% and > 78%, the model underestimates the risk of poor prognosis; when the rate is 32–78%, the model overestimates the risk of occurrence

consistent with the results in this study. We herein found through multivariate Cox regression analysis that age of > 65 years old, history of hypertension, high Hunt–Hess grade and high modified Fisher grade were independent risk factors for the prognosis of PCoAA + fPCA patients undergoing clipping through the LSO approach. The nomogram prediction model established with the above factors had high accuracy and effectively predicted the prognosis after clipping through the LSO approach.

5 Conclusion

In conclusion, age, history of hypertension, Hunt–Hess grade and modified Fisher grade are independent risk factors for the prognosis of patients with PCoAA accompanied by fPCA after clipping through the LSO approach.

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Author Contribution
Y.X.C. and Y.J.F. designed this study and prepared this manuscript; Y.R.C., H.H.C., X.F.L., G.Z.Z. and J.L.Y. collected and analyzed clinical data. All authors approved the submission and publication of this manuscript.

Data Availability
The data that support the findings of this study are available from the corresponding author, Y.J.F., upon reasonable request.

Declarations

Conflict of interest
The authors declare they have no conflicts of interest.

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