Predictors of Postoperative Cerebral Ischemia in Patients with Ruptured Anterior Communicating Artery Aneurysms

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■ OBJECTIVE: **Cerebral ischemia is a major contributor to poor outcome after ruptured anterior communicating artery aneurysms (ACoAs), and is not well classified. In this article, we develop a classification and identify risk factors of cerebral ischemia after ruptured ACoAs.**

■ METHODS: **Three hundred sixty patients with ruptured ACoAs undergoing microsurgical clipping were collected. Sex, age, smoking status, Hunt-Hess grade, Fisher grade, hospital stay, surgical timing, hypertension, diabetes, postoperative cerebral ischemia, and postoperative modified Rankin Scale score were collected. Postoperative ischemic changes are classified according to a novel grade (ischemic grade I—IV).**

■ RESULTS: **Predictive factors of postoperative ischemia (grade I—IV) included sex (odds ratio [OR], 1.956; 95% confidence interval [CI], 1.262—3.032; $P = 0.003$) and Fisher grade (OR, 1.813; 95% CI, 1.144—2.871; $P = 0.011$). Male sex had a tendency to develop postoperative cerebral ischemia (61.3% in the ischemia group vs. 45.7% in the nonischemia group), while surgical timing did not. However, in patients with postoperative ischemia, early surgery within 3 days (OR, 3.334; 95% CI, 1.411—7.879; $P = 0.006$) and advanced age greater than 55 years (OR, 2.783; 95% CI, 1.214—6.382; $P = 0.016$) were risk factors for postoperative neurologic deficits (grade III—IV).**

■ CONCLUSIONS: **Male sex and higher Fisher grade predict postoperative ischemia (grade I—IV), whereas surgical timing does not. However, in patients with postoperative cerebral ischemia, early surgery within 3 days and age greater than 55 years can increase the frequency of postoperative neurological deficits (grade III—IV). Older male patients undergoing early microsurgery had a tendency to develop neurologic deficits.**

INTRODUCTION

Anterior communicating artery aneurysms (ACoAs) are the most common, and more frequently associated with subarachnoid hemorrhage.[1] Marked difficulties were detected in both microsurgical and endovascular treatment because of frequent anatomical variations, deep location, and high frequency of triggering neurologic dysfunction resulting from many surrounding perforators.[2] And previous studies indicated that ruptured ACoAs were related to increased risk of cerebral ischemia,[3,4] which is a major contributor to poor outcome after ruptured ACoAs.[5,6] However, postoperative cerebral ischemia is not well defined and evaluated in previous studies. Although there are many studies of the risk factors of predicting poor functional outcome after subarachnoid hemorrhage (SAH),[7-9] there is much less information on predictors of postoperative cerebral ischemia. Furthermore, previous studies focused on the influence of clot burden, smoking status, and age on predicting mortality and poor functional outcome,[7,8,10] and indicated that sex was not associated with an unfavorable outcome.[11,12] However, sex is considered an independent risk factor for the growth of cerebral

Key words
- Cerebral ischemia
- Male
- Risk factor
- Ruptured anterior communicating artery aneurysms
- Surgical timing

Abbreviations and Acronyms
ACoA: Anterior communicating artery aneurysm
CT: Computed tomography
CTA: Computed tomography angiography
DSA: Digital subtraction angiography
ICA: Internal carotid artery
MRI: Magnetic resonance imaging
mRS: modified Rankin scale
SAH: Subarachnoid hemorrhage

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aneurysms,[13,14] and the influence of sex on predicting postoperative cerebral ischemia remains unknown. Another disputed factor affecting outcome was operation timing.[15] Most studies indicated that ultra-early surgery could avoid rebleeding of intracranial aneurysm[16,17]; however, higher mortality was detected in the early treatment group.[18] In the retrospective study, we developed a novel classification of cerebral ischemia and investigated the risk factors of cerebral ischemia, including sex and operation timing.

METHODS AND MATERIALS

The study protocol was approved by the ethics committee of the First Affiliated Hospital of Fujian Medical University. All patients provided written informed consent. Patients were eligible to enroll in the study if the following conditions were met: 1) subarachnoid hemorrhages were diagnosed with computed tomography (CT), and ACoAs were diagnosed with computed tomography angiography (CTA) or digital subtraction angiography (DSA), or both; 2) aneurysms were less than 2 cm in diameter; 3) all patients underwent microsurgery, and postoperative CTA or DSA, or both, were performed within 7 days. Routine brain CT for detecting postoperative complications has been achieved within 24 hours and at day 7 after surgical aneurysmal clipping. Postoperative DSA or CTA were performed within 72 hours to verify adequate clip placement. Patients with herniation, preoperative cerebral vasospasm, and other cerebrovascular diseases (e.g., arteriovenous malformations) were excluded. Patients with preoperative rebleeding, multiple intracranial aneurysms, postoperative delayed cerebral ischemia longer than 7 days, and Hunt-Hess grade V were excluded. Intraoperative motor-evoked potential (MEP) monitoring was performed in all patients as described previously.[19] Patients with accidentally iatrogenic occlusion of the perforating branches detected by intraoperative motor-evoked potential monitoring were excluded.

We retrospectively analyzed the predictors of cerebral ischemia in 360 patients with ruptured ACoAs undergoing microsurgery between January 2002 and December 2015. Long-term neurologic outcome was assessed at the 6-month follow-up and categorized according to the patient's modified Rankin Scale (mRS) score. A favorable outcome was defined as an mRS score of 0–3, and a poor outcome was defined as an mRS score of 4–6. Orientation of ACoAs was divided into 2 types (inferior and superior) according to the classification described by Kobayashi et al.[20]

Cerebral vasospasm was diagnosed with postoperative CTA or DSA. Cerebral infarction was defined by the development of a hyperintensity on postoperative magnetic resonance imaging (MRI) or hypodensity on postoperative CT with or without neurologic deficits within 7 days, and performed by a blinded reviewer. If significant cerebral infarction were detected in postoperative CT, postoperative MRI might not be performed in the study. Postoperative neurologic deficits were diagnosed after daily neurologic examination, including emerging or aggravating motor dysfunction, decreased consciousness, and dysphasia. Postoperative ischemic changes are classified as follows (ischemic grade):

1. Grade 0—no ischemic changes (without cerebral vasospasm, infarction, and neurological deficits)
2. Grade I—instrumental vasospasm (cerebral vasospasm without cerebral infarction and neurological dysfunction)
3. Grade II—asymptomatic MRI ischemic changes (without neurologic deficits)
4. Grade III—transient ischemic neurologic deficits (cerebral vasospasm or infarction combined with temporary neurological dysfunction)
5. Grade IV—permanent ischemic neurologic damage (cerebral vasospasm or infarction combined with permanent neurologic dysfunction)

Grades I–II were named *nonsymptomatic ischemia*, and grades III–IV were named *symptomatic ischemia*. All patients with cerebral vasospasm were treated with moderate induced hypertension and hypervolemia combined with intravenous nimodipine in an attempt to optimize collateral circulation.

Sex, age, smoking, Hunt-Hess grade, Fisher grade, hospital stay, surgical timing, hypertension, diabetes, postoperative ischemia, and postoperative mRS score were collected. Surgical timing was defined as the onset of hemorrhage to the time of operation.

Statistical Analysis

Measurement data were expressed as mean ± SD. Univariate analysis of continuous data was performed with one-way analysis of variance and Student *t* test. Qualitative data were analyzed using a χ^2 test or Fisher exact test. Multivariate logistic regression analyses included all variables significant at $P < 0.15$ in univariate analysis. For inclusion in the multivariate model, age was dichotomized as "less than 55 years" and "more than 55 years," Hunt-Hess grade was "low grade (grade I–III)" or "high grade (grade IV)", Fisher grade was "low grade (grade 1–2)" or "high grade (grade 3–4)", surgical timing was "less than 3 days" or "more than 3 days", and ischemic events were graded as "No (grade 0, group I)" or "Yes (grade I–IV, group II)." In patients with postoperative ischemia (grade I–IV), ischemic events were divided into subgroup I (grade I–II, without neurologic deficits) or subgroup II (grade III–IV, with neurologic deficits). Adjusted odds ratios and 95% confidence intervals were analyzed to represent the relative risk of predictive variables. $P < 0.05$ was considered statistically significant.

RESULTS

Three hundred sixty patients (190 men and 170 women) were collected between January 2002 and December 2015 in this retrospective study. There were 360 ruptured ACoAs undergoing adequate surgical clipping via pterional keyhole approaches. Univariate analysis indicated that significant differences in sex, surgical timing, and Fisher grade were detected between the nonischemia and ischemia groups. High frequency (45.3%) of cerebral ischemia (grade I–IV) was detected in the study. However, neurologic deficits (grade III–IV) were detected in 11.1% of patients. Male patients had a tendency to develop postoperative cerebral ischemia (61.3% in the ischemia group vs. 45.7% in the nonischemia group; $P = 0.003$). Prolonged hospital stay and high rate of poor outcome were observed in ischemia group (Table 1).