

Keyhole Approach Combined With External Ventricular Drainage for Ruptured, Poor-Grade, Anterior Circulation Cerebral Aneurysms

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Abstract: Poor-grade ruptured anterior circulation cerebral aneurysms are frequently associated with severe vasospasm and high morbidity rates despite recent remarkable advances in endovascular coiling.

Here, we explored the feasibility of keyhole approach combined with external ventricular drainage for ruptured, poor-grade, anterior circulation cerebral aneurysms. We retrospectively assessed the records of 103 patients with ruptured, Hunt and Hess grade IV or V, anterior circulation cerebral aneurysms. The patients were divided into 2 groups (conservative group and surgical group). In surgical group, patients were divided into 2 subgroups according to surgical time (within 24 hours and at 24–48 hours). Clinical outcome was assessed at the 6-month follow-up and categorized according to modified Rankin Scale (mRS) score.

Twenty percent of patients (9/44) in conservative group obtained good outcome, while 54% (32/54) in surgical group ($P < 0.05$). Mortality was 73% in conservative group and 40% in surgical group, respectively. In surgical group, age, Hunt and Hess grade (IV or V), and timing of intervention (<24 hours or later) influenced the clinical outcome of the patients ($P < 0.05$), while sex, Fisher grade, hydrocephalus, the location of aneurysms, and cerebral vasospasm (CVS) not ($P > 0.05$). Furthermore, 65% of patients (22/34) operated within 24 hours after onset of hemorrhage had a good outcome compared with 20% of patients (5/25) operated at 24 to 48 hours in surgical group ($P < 0.05$).

The results indicate that keyhole approach combined with external ventricular drainage is a safe and reliable treatment for ruptured, poor-grade, anterior circulation cerebral aneurysms in early stage, which will reduce mortality.

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Abbreviations: 3D-CTA = three-dimensional CT angiography, 3D-DSA = three-dimensional digital subtraction angiography, aSAH = aneurysmal SAH, CSF = cerebrospinal fluid, CT = computed tomography, CVS = cerebral vasospasm, DC = decompressive craniectomy, DSA = digital subtraction angiography, EVD =

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external ventricular drainage, ICH = intracerebral hematoma, ICP = intracranial pressure, mRS = modified Rankin Scale, SAH = subarachnoid hemorrhage, TCD = transcranial Doppler monitoring.

INTRODUCTION

Poor-grade aneurysmal subarachnoid hemorrhage (SAH) had a high mortality and morbidity rate,¹ and the chance of survival in the patients received conservative treatment is almost nonexistent.² The management of patients with poor-grade aneurysmal SAH remains controversial. These patients are usually managed conservatively, and those who survive and show clinical improvement are selected for aneurysmal clipping.³ However, almost most patients finally die from rebleed or delayed ischemic events with nonoperative treatment.^{4–7} Recent studies have indicated that the outcome of patients with poor grade aneurysmal SAH (aSAH) may be improved by surgical clipping or endovascular coiling as soon as possible.⁵ Despite advances in neuroimaging techniques and development of microneurosurgical techniques, no effective treatments could be used to prevent occurrence and deterioration in poor-grade patients with aneurysmal SAH. And the percentage of poor outcome is up to 40%.⁸

Surgical clipping and endovascular coiling were equally likely to achieve a good outcome in patients with poor-grade aneurysmal SAH. The decision that a ruptured, poor-grade aneurysms should be treated with microsurgical or endovascular treatment should be made according to the aneurysmal morphology, vascular access, and branches related to the aneurysm.⁹ It was recognized that the development of cerebral vasospasm (CVS), which is associated with clinical deterioration in the poor-grade aneurysmal SAH, would be triggered by the hemoglobin of subarachnoid space.^{10–12} And we know that the space-occupying effect of intracerebral hematoma associated with aneurysmal SAH can lead to a raised intracranial pressure (ICP) and midline shift. Therefore, timely evacuation of the hemorrhage from the subarachnoid space or/and the intracerebral hematoma contributed to a good outcome of aneurysmal SAH, which could be easily obtained via surgical treatment and could be hardly achieved via endovascular treatment.

Traditional craniotomy or decompressive craniectomy (DC) has been applied to patients with poor-grade aneurysmal SAH.^{3,13,14} However, many complications in DC, such as herniation, infection, seizures, hydrocephalus, and large skull defects after surgery, restricted its application for aneurysmal clipping.¹⁵ In addition, decompressive craniectomy does not seem to be significantly associated with improved outcomes.¹⁶ Recent studies have indicated that simultaneous hematoma evacuation and aneurysmal clipping with or without craniectomy can be an effective treatment modality for poor-grade middle cerebral artery aneurysms.¹⁷ Along with the advances in

microneurosurgical techniques and development of microneurosurgical instrumentation, “keyhole” (mini bone flap) approach has been applied to aneurysmal clipping, and be equally likely to obtain a good outcome.¹⁸ Furthermore, external ventricular drainage (EVD) could reduce the intracranial pressure and has been proved to be indicative of increased likelihood favorable outcome for poor-grade aneurysms.^{19,20} Thus, the prognosis of poor-grade patients after onset of SAH may be improved by surgical invention via keyhole approach combined with sustained drainage of the bloody cerebrospinal fluid (CSF). We reviewed the clinical experience of keyhole approach combined with external ventricular drainage for ruptured, poor-grade, anterior circulation cerebral aneurysms at our institution from January 2005 to December 2014.

METHODS

Patient Population

This study was conducted at the First Affiliated Hospital of Fujian Medical University. The study protocol was approved by the ethics committee of the First Affiliated Hospital of Fujian Medical University. We retrospectively analyzed the clinical

materials of 103 patients with ruptured, Hunt and Hess grade IV or V (70 cases with Hunt and Hess grade IV and 33 with grade V), anterior circulation cerebral aneurysms at our institution from January 2005 to June 2014. Subarachnoid hemorrhage was confirmed by computed tomography (CT). All aneurysms were detected by three-dimensional CT angiography (3D-CTA) and/or three-dimensional digital subtraction angiography (3D-DSA) examinations. The patients presented with herniation and other cerebrovascular diseases (such as arteriovenous malformations or moyamoya disease) or treated by endovascular coiling were excluded. The population consisted of 103 patients. Forty-four patients were managed conservatively, and 59 patients were treated with microsurgical aneurysmal clipping via pterional or supraorbital keyhole approaches combined with placement of EVD within 24 hours (subgroup I) or at 24 to 48 hours (subgroup II) based on the time of admission after onset of SAH and/or intracerebral hematoma (ICH).

Management Protocol

Minimally invasive pterional or supraorbital keyhole approaches were performed in surgical group as previously described by the same neurosurgeon.^{21,22} A standardized

TABLE 1. Characteristics of Patients in 2 Groups

Characteristics	Control Group (n = 44)	Surgical Group (n = 59)	P Value
Age, yr			
Median	51.75	53.12	0.740
Range	25–75	25–80	
Sex, N (%)			
Male	20 (45)	23 (40)	0.510
Female	24 (55)	36 (60)	
Hunt and Hess grade, N (%)			
Grade IV	29 (66)	40 (68)	0.700
Grade V	15 (34)	19 (32)	
Fisher grade, N (%)			
Grade 2	11 (25)	10 (17)	0.342
Grade 3	24 (55)	30 (51)	
Grade 4	9 (20)	19 (32)	
Hydrocephalus, N (%)	9 (20)	13 (22)	0.847
Aneurysm location, N (%)			
ACA/AcomA	19 (43)	28 (47)	0.850
MCA	10 (23)	11 (19)	
ICA/PcomA	15 (34)	20 (34)	
Aneurysm size, N (%)			
<5 mm	26 (59)	27 (46)	0.221
5–15 mm	16 (36)	31 (53)	
15–25 mm	2 (4)	1 (2)	
Multiple aneurysms, N (%)	7 (16)	8 (14)	
Time to surgery			
<24 h	NA	34	NA
24–48 h	NA	25	
Rebleeding, N (%)	5 (11)	0 (0)	0.008
CVS, N (%)	7 (16)	10 (17)	0.888
mRS, N (%)			
0–3	9 (20)	32 (54)	0.008
4–6	35 (80)	27 (46)	
Total deaths, N (%)	32 (73)	24 (41)	0.001
Brain injury-related mortality, N (%)	23 (52)	5 (8)	0.000
Brain injury-unrelated, N (%)	9 (20)	19 (32)	0.185

CVS = cerebral vasospasm; mRS = modified Rankin scale; NA = denotes not applicable.

clinical treatment protocol was used in management of poor grade aSAH patients, including dehydration, hemostatic, prevention of cerebral vasospasm, control of blood pressure. In addition, 44 patients in the conservative group were treated with oxygen free radical scavengers, nutritional support. And 59 patients in surgical group, operated within 24 hours or 24 to 48 hours after onset of SAH, were treated with pterional (50 cases) or supraorbital (9 cases) keyhole approach combined with placement of EVD. In addition, the surgical group was divided into 2 subgroups according to surgical time (within 24 hours and at 24–48 hours). The EVD was placed before craniotomy. The catheter inserted into the lateral ventricle was opened when brain swelling occurred, then intracranial pressure would be reduced and more working space was obtained. Furthermore, the sylvian fissure dissection would be performed smoothly. After the aneurysm and the proximal segment of parent artery were exposed, removal of the hematoma associated with a ruptured aneurysm in internal carotid artery pool, prechiasmatic cistern or brain parenchyma might be performed.

Postoperative Management and Evaluation

The patients were managed with a traditional treatment of aneurysmal subarachnoid hemorrhage postoperatively, including

“3H” (hypertension, hemodilution, hypervolemia), prevention of cerebral vasospasm, oxygen-free radical scavengers, nutritional support. CVS was detected by dynamic transcranial Doppler monitoring (TCD) and/or DSA. Routine brain CT for detecting postoperative complications has been achieved within 24 hours after surgical aneurysmal clipping. Postoperative DSA or CTA were performed within 72 hours to verify adequate clip placement. And neurological outcome was assessed at the 6-month follow-up and categorized according to the patient’s modified Rankin Scale (mRS) score (a good outcome was defined as mRS 0–3, and a poor outcome as mRS 4–6).

Statistical Analyses

Data analysis was performed in the Statistical Package for the Social Sciences version 19.0. Direct logistic regression analysis was applied to analyzing the prognostic impact of variables on the likelihood that a patient would receive a poor outcome rating. A probability of 0.05 or less was deemed statistically significant.

RESULTS

The population consisted of 103 patients, 43 men and 60 women, age ranging 21 to 80 years (average age of 52.5 years).

TABLE 2. Characteristics and Outcomes of Patients With Intracranial Aneurysm in Surgical Group

Characteristic	Time From Onset of Symptoms to Surgery		P Value
	Subgroup I <24 h (N = 34)	Subgroup II 24–48 h (N = 25)	
Age, yr			
Median	50.64	53.04	0.653
Range	35–65	25–80	
Sex, N (%)			
Male	12 (35)	7 (28)	0.554
Female	22 (65)	18 (72)	
Hunt and Hess grade, N (%)			
Grade IV	26 (76)	14 (56)	0.096
Grade V	8 (24)	11 (44)	
Fisher grade, N (%)			
Grade 2	6 (18)	4 (16)	0.867
Grade 3	18 (53)	12 (48)	
Grade 4	10 (29)	9 (36)	
Hydrocephalus, N (%)	8 (24)	5 (20)	0.747
Aneurysm location, N (%)			
ACA/AcomA	13 (38)	15 (60)	0.240
MCA	14 (41)	6 (24)	
ICA/PcomA	7 (21)	4 (16)	
Aneurysm size, N (%)			
<5 mm	17 (50)	10 (40)	0.412
5–15 mm	17 (50)	14 (56)	
15–25 mm	0 (0)	1 (4)	
Multiple aneurysms, N (%)	5 (15)	3 (12)	0.764
CVS, N (%)	5 (15)	5 (20)	0.592
mRS, N (%)			
0–3	22 (65)	5 (20)	0.001
4–6	12 (35)	20 (80)	
Total deaths, N (%)	7 (21)	17 (68)	0.000
Brain injury-related mortality, N (%)	2 (6)	3 (12)	0.404
Brain injury-unrelated, N (%)	5 (15)	14 (56)	0.001

CVS = cerebral vasospasm; mRS = modified Rankin scale.

TABLE 3. Characteristic and Outcome of Patients With Hunt and Hess Grade 4 or 5 in Surgical Group

Characteristic	Hunt and Hess Grade, N(%)		P Value
	Grade IV (N=40)	Grade V (N=19)	
Age, yr			
Median	50.25	54.63	0.108
Range	25–65	40–80	
Sex, N (%)			
Male	13 (33)	6 (32)	0.944
Female	27 (67)	13 (68)	
Fisher grade, N (%)			
Grade 2	6 (15)	4 (21)	0.840
Grade 3	21 (53)	9 (67)	
Grade 4	13 (32)	6 (32)	
Hydrocephalus, N (%)	11 (28)	2 (11)	0.142
Aneurysm location, N (%)			
ACA/AcomA	21 (53)	7 (37)	0.444
MCA	13 (32)	7 (37)	
ICA/PcomA	6 (15)	5 (26)	
Aneurysm size, N (%)			
<5 mm	19(47)	8 (42)	0.335
5–15 mm	21 (53)	10 (53)	
15–25 mm	0(0)	1 (5)	
Multiple aneurysms, N (%)	6 (15)	2 (11)	0.639
CVS, N (%)	5(13)	5 (26)	0.186
mRS, N (%)			
0–3	26 (65)	1 (5)	0.000
4–6	14 (35)	18 (95)	
Total deaths, N (%)	8 (20)	16 (84)	0.000
Brain injury-related mortality, N (%)	2 (5)	3 (16)	0.164
Brain injury-unrelated, N (%)	6 (15)	13 (68)	0.000

DIND = delayed ischemic neurologic deficit; mRS = modified Rankin scale.

Forty-four patients were enrolled in conservative group, and 59 patients were treated with microsurgical aneurysmal clipping via pterional or supraorbital keyhole approaches combined with placement of EVD within 24 hours (subgroup I) or at 24 to 48 hours (subgroup II) after onset of SAH and/or intracerebral hematoma (ICH). The characteristics of aSAH patients in the control group and surgical group are shown in Table 1. One hundred nineteen anterior circulation aneurysms in 103 patients were detected by CTA and DSA examinations. There were different amounts of hemorrhage in ambient cistern, sylvian fissures, interhemispheric fissure, brain parenchyma, or ventricular system. And there were 15 patients with multiple cerebral aneurysms and 38 patients with ICH in these patients. Aneurysm location is also shown in Table 1.

Nine patients (20%) in conservative group (44 patients) had a good outcome compared with 32 patients (54%) in surgical group (59 patients), and the difference was statistically significant ($P < 0.05$, Table 1). Thirty-five patients (80%) receiving conservative therapy had a poor outcome compared with 27 patients (46%) receiving surgical treatment. The difference was statistically significant ($P = 0.008$). In surgical group, it was shown that age, Hunt and Hess grade (IV or V), and timing of intervention (<24 hours or later) influenced the clinical outcome of the patients ($P < 0.05$), which was applied to predicting morbidity and mortality. However, sex, Fisher grade, hydrocephalus, and the location of aneurysms did not ($P > 0.05$).

Twenty-two patients (65%) in the subgroup I (34 patients) who were operated within 24 hours after onset of SAH had a good outcome compared with 5 patients (20%) in the subgroup II (25 patients) who were operated within 24 to 48 hours ($P < 0.05$, Table 2). In surgical group, 65% of patients (26/40) with Hunt and Hess grade IV had a good outcome compared with 5% (1/19) with Hunt and Hess grade V ($P < 0.05$, Table 3). And there were 7 patients (16%) with CVS in the conservative group compared with 10 patients (17%) in surgical group ($P < 0.05$, Table 1). The data for mortality were available for 32 (73%) in conservative group and 24 (40%) in surgical group, respectively ($P < 0.05$, Table 1). And the number of deaths due to brain injury (herniation) was 23 (52%) in the conservative group and 5 (8%) in surgical group, respectively ($P < 0.05$, Table 1). There was no intracerebral hemorrhage and infection associated with surgery. Case examples with edited videos are presented (Figures 1–3 and Videos 1–3, <http://links.lww.com/MD/A574>, <http://links.lww.com/MD/A575>, <http://links.lww.com/MD/A576>).

DISCUSSION

Poor-grade aneurysmal subarachnoid hemorrhage is a cause of high morbidity and mortality. Nonoperative management is nearly fatal, whereas decompressive craniectomy, aneurysmal clipping, and early endovascular treatment can improve short- and long-term outcomes.^{13,23–25} However, many complications in DC, such as herniation, infection, seizures, hydrocephalus, and large skull defects after surgery, restricted its application for aneurysmal clipping.¹⁵ And although early endovascular treatment could lead to a better outcome due to a reduced chance of rebleeding, subsequent decompressive craniectomy should be performed.^{13,25} Here, we find that keyhole approach combined with external ventricular drainage is feasible and effective for hematoma evacuation and aneurysmal clipping in patients with poor-grade anterior circulation cerebral aneurysms.

It is generally accepted that keyhole approach is suitable for aneurysmal clipping.²⁶ The main problem of the keyhole approach for poor-grade ruptured aneurysm is whether ideal relaxation of the brain tissue and the exposure of the aneurysm and its parent artery can be easily achieved during operation. Hydrocephalus and brain edema will hamper the relaxation of the brain tissue, which is associated with intraoperative CSF drainage. The following ways are often used in CSF drainage: a preoperatively placed lumbar drain: as cerebral herniation may occur after placement of lumbar drain in the patients with intracranial hypertension, a preoperatively placed lumbar drain is a contradiction to the poor-grade patients with intracranial hypertension; Opening the sylvian fissure, carotid artery pool, prechiasmatic cistern, basal cistern, and cistern of lamina terminalis, which is easily blocked by blood clot following SAH; and drainage of CSF via ventricular system: according to the relationship between ICP and intracranial volume, removal of even a small amount of CSF can lower ICP significantly. In addition, and EVD has been proved to be effective in obtaining lower-grade condition in poor-grade patients.¹⁹ Therefore, EVD is the best scheme for CSF drainage. CSF drainage via ventricular system will reduce ICP, and provide more working space for surgery via keyhole approaches. Then the arachnoid can easily be dissected and the blood clot can be cleared from the subarachnoid cisterns. Finally, the ideal exposure of the aneurysm and its parent artery are obtained. It was shown that 9 patients (20%) in conservative group had a good outcome

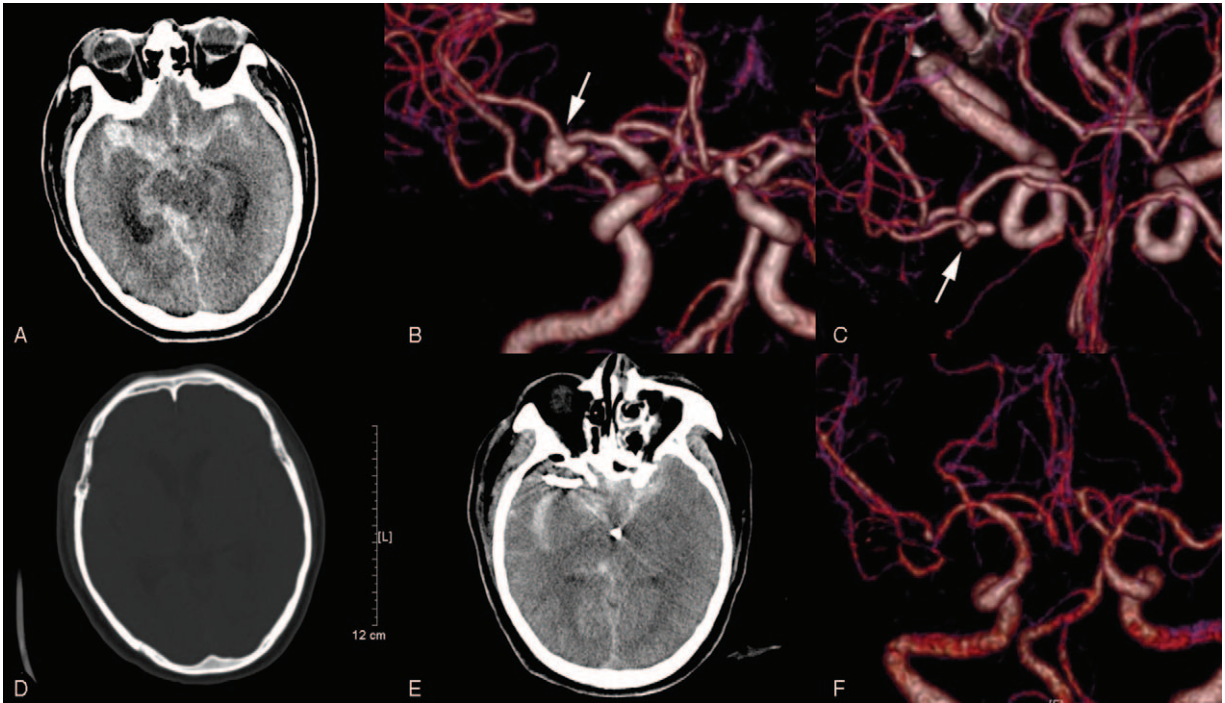


FIGURE 1. Case 1: A, Subarachnoid hemorrhage was detected on preoperative CT. B and C, Right MCA aneurysm was found on CTA. D, Postoperative CT displayed that the patient underwent surgery via right pterional keyhole approach. E, Postoperative CT displayed the MCA was clipped and no fresh bleeding was detected. F, Postoperative CTA showed MCA aneurysm was completely clipped. The surgical procedure was shown on Video, <http://links.lww.com/MD/A574>. CTA = computed tomography angiography.

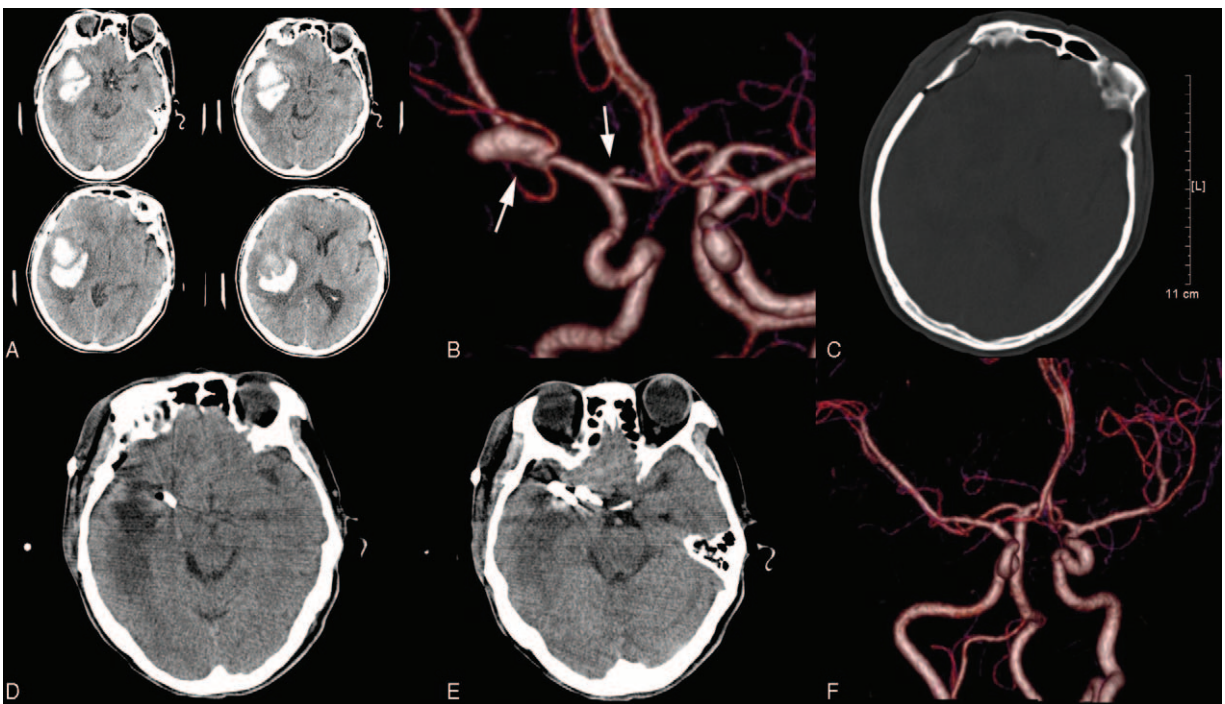


FIGURE 2. Case 2: A, Right temporal lobe sylvian fissure hematoma was detected on preoperative CT. B and C, Right MCA aneurysm was found on CTA. D and E, Postoperative CT displayed that the patient underwent aneurysm clipping and hematoma evacuation via right pterional keyhole approach. F, Postoperative CTA showed MCA aneurysm was completely clipped. The surgical procedure was shown on Video 2, <http://links.lww.com/MD/A575>. And the patient underwent aneurysm clipping with subsequent hematoma evacuation.

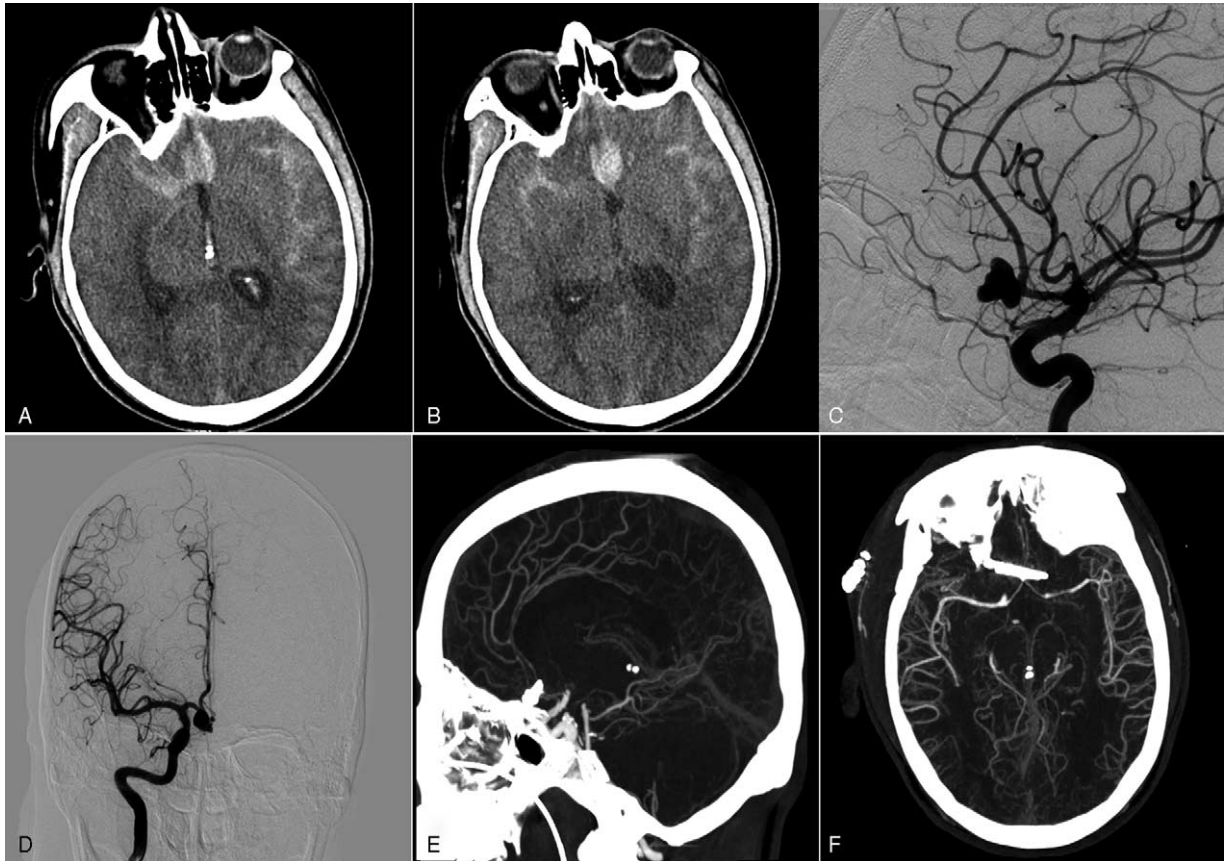


FIGURE 3. Case 3: A and B, Subarachnoid hemorrhage was detected on preoperative CT. C and D, AcomA aneurysm was found on preoperative DSA. E and F, Postoperative CTA showed AcomA aneurysm was completely clipped. The surgical procedure was shown on Video 3, <http://links.lww.com/MD/A576>. DSA = digital subtraction angiography.

compared with 32 patients (54%) in surgical group. In this study, the rate of favorable outcome in surgical group (54%) is higher than that in patients with coil embolization followed by decompression (22.5%).¹³ Furthermore, the mortality in patients with keyhole approach combined with EVD has been reduced to 40% (Table 1), which is similar to that in patients with coil embolization followed by decompression (36.7%).¹³ Therefore, keyhole approach combined with EVD was a feasible treatment for ruptured, poor-grade, anterior circulation cerebral aneurysms, and it reduced the morbidity and mortality effectively. In the surgery, adhesion between the dome of the aneurysm and surrounding tissue usually occurs following SAH, which will cause premature rupture of the aneurysm before confirmation of the vascular anatomy. Therefore, sharp division is recommended to execute while dissecting of cerebral gyri and cisterns. In addition, the aneurysms and their parent arteries are recommended to be exposed with little or no brain retraction which may minimize the risk of mechanical injury to brain tissue and cerebral vasculature,²⁷ when the ideal drainage of CSF from ventricular system occurs.²⁷ If the intracranial hypertension is mainly associated with the ICH, we may partly remove the hematoma first to lower ICP.

Direct logistic regression analysis was applied to analyzing the prognostic impact of variables in surgical group, including age, sex, Hunt and Hess grade (IV and V), Fisher grade, (2,3,4) hydrocephalus, aneurysmal location, time to surgery, and CVS.

And it was shown that age, Hunt and Hess grade (grade IV or V), and timing of intervention (<24 hours or at 24–48 hours) influenced the clinical outcome of the patients ($P < 0.05$), which was applied to predicting morbidity and mortality. However, sex, Fisher grade, hydrocephalus, and the location of aneurysms did not ($P > 0.05$). It is doubted whether mechanical stimulation of early surgical intervention for ruptured aneurysms might aggravate brain damage produced by cerebral vasospasm. However, it is recognized that hemoglobin is a key factor in the production of cerebral vasospasm.²⁸ More and more evidence indicated that CVS can be prevented and reduced by increased blood clot clearance from the subarachnoid space after SAH,¹² and timely removal of red blood cells and hemoglobin from subarachnoid space may potentially reduce or even prevent CVS.²⁹ Twenty-two patients (65%) in subgroup I who were operated within 24 hours after onset of SAH had a good outcome compared with 5 patients (20%) in subgroup II who were operated at 24 to 48 hours ($P < 0.05$, Table 2). Consequently, it tells us that the good outcome may be obtained, if the poor-grade, anterior circulation cerebral aneurysm had been treated in the first 24 hours after SAH.³⁰ Twenty-six patients (65%) in patients with Hunt and Hess grade IV had a good outcome compared with 1 patient (5%) patients with Hunt and Hess grade V ($P < 0.05$, Table 3). Hence, it also tells us that Hunt and Hess grade IV in surgical group will lead to a much better prognosis than grade V. Certainly, the amount of removed

blood clot in subarachnoid space and surrounding aneurysms may be a little part of intracranial hematocoele following SAH. And bloody CSF might be continuously drained after surgery for reducing the stimulation of hemoglobin on cerebral vasculature. With fluctuations in ICP continuously observed and timely adjusting the usage of mannitol, the rating of mannitol-induced acute renal failure was decreased.^{31,32} In addition, real-time detection of changes in ICP could be useful in alerting clinicians to the application of timely intervention measures, such as assistant examination for detection of intracranial hemorrhage or CVS and medical management or surgical intervention for elevated ICP.

As our conclusions were drawn from a single institution experience, and the conclusion that CVS is associated with poor outcome is not inconsistent with the previous report,³³ a larger sample is needed to verify our findings.

In conclusion, keyhole approach combined with external ventricular drainage is a safe and reliable treatment for ruptured, poor-grade, anterior circulation cerebral aneurysms, and it will reduce morbidity and mortality effectively. It is recommended that the poor-grade, anterior circulation cerebral aneurysm should be treated in the first 24 hours after SAH, and the Hunt and Hess grade IV will lead to a much better prognosis than grade V.

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