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Early management of poor-grade aneurysmal subarachnoid hemorrhage: A prognostic analysis of 104 patients

Xiaofei Wang, Chao Han, Deguang Xing, Chengwei Wang, Xuan Ding*

Department of Neurosurgery, The Second Hospital of Shandong University, Jinan 250033, Shandong, China

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ABSTRACT

Objective: This study aimed to investigate the efficacy of early management for poor-grade aneurysmal subarachnoid hemorrhage (aSAH; WFNS grade IV and V), and analyze the prognostic factors.

Patients and methods: A total of 104 consecutive patients with poor-grade aSAH from the Department of Neurosurgery, the Second Hospital of Shandong University were enrolled between January 2010 and December 2017. All these patients underwent early microsurgical clipping or endovascular coiling within three days after onset. Microsurgical clipping or endovascular coiling was selected according to aneurysm patterns, patient clinical status, interdisciplinary consultation, and the decision-making of the family. The individual prognosis was evaluated using the modified Rankin scale (mRS), while the prognostic factors were analyzed using multivariate logistic regression analysis.

Results: There were 58 patients with grade IV aSAH and 46 patients with grade V aSAH. Microsurgical clipping was performed in 71 cases, while endovascular coiling was performed in 33 cases. According to the statistical results, microsurgical clipping was preferred by patients with CT Fisher grade III–IV, WFNS grade V, cerebral hernia, intracranial hematoma and preoperative rebleeding. At six months after onset, the overall rate of favorable outcome (mRS ≤ 2) was 36.5%. Furthermore, the favorable outcome rate was 56.9% in grade IV patients and 11.1% in grade V patients. Moreover, the univariate and multivariate logistic regression analyses revealed that CT Fisher grade I–II, WFNS grade IV and endovascular coiling were associated with a favorable prognosis, while the CT low-density area was slightly correlated to a poor prognosis.

Conclusion: The treatment of aSAH at the early stage by microsurgical clipping or endovascular coiling should be highlighted, especially for patients with WFNS grade IV. CT Fisher grade I–II, WFNS grade IV and endovascular coiling may predict a favorable prognosis, and the CT low-density area appeared to be a possible risk factor for poor prognosis.

1. Introduction

Patients with poor-grade aneurysmal subarachnoid hemorrhage (aSAH) usually have poor prognosis due to severe brain damage and complications, even though they are treated effectively [1,2]. Moreover, the mortality rate is nearly 100% in patients with poor-grade aSAH, who were conservatively treated [3]. Some studies have suggested that active surgical treatment should be applied to patients with poor-grade aSAH. However, its optimal time for operation remain controversial [4–6]. Intracranial hypertension, cerebral edema and focal hematoma increase the surgical challenges for early stage aSAH. Meanwhile, the early surgical removal of subarachnoid hemorrhage can reduce the occurrence rate of vascular spasm, and that this would be beneficial for subsequent vascular anti-spasm treatment. In recent years, with the development of microsurgical techniques and endovascular embolization technology, the prognosis of poor-grade aSAH has been greatly improved [7,8]. The present study aimed to investigate the efficacy of early management for poor-grade aSAH, and analyzed the prognostic factors.

2. Patients and methods

2.1. Patients

A total of 104 consecutive patients with poor-grade aSAH were enrolled from the Department of Neurosurgery, The Second Hospital of Shandong University between January 2010 and December 2017. The diagnosis of aSAH was made based on computed tomography (CT),

* Corresponding author at: Department of Neurosurgery, The Second Hospital of Shandong University, No. 247 Beiyuan Road, Jinan 250033, Shandong, China.
E-mail address: 15106983331@163.com (X. Ding).

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computed tomography angiography (CTA), or digital subtraction angiography (DSA). The World Federation of Neurological Surgeons (WFNS) grade IV and V were defined as poor-grade aSAH.

Inclusion criteria: (1) patients with aSAH assessed as WFNS grade IV or V after resuscitation; (2) patients who underwent early surgical treatment within three days after onset.

Exclusion criteria: (1) patients with a WFNS grade that improved to I–III before surgical clipping or endovascular coiling; (2) patients who did not receive further treatment for aneurysms; or (3) patients who had a follow-up period of < 6 months.

2.2. T7reatment programmes

The early treatment of aneurysms was performed, except for patients who had organ failure or critical clinical condition. The treatment modality (microsurgical clipping or endovascular coiling) was selected according to aneurysm patterns, the clinical status of the patient, interdisciplinary consultation, and the decision-making of the family.

An emergency operation, including aneurysm clipping, hematoma clearance and decompressive craniectomy (DC), was performed in patients with cerebral hernia caused by intracranial hematoma. External ventricular drainage (EVD) was performed in patients with acute hydrocephalus or severe intra-ventricular hemorrhage (IVH). All patients received comprehensive postoperative pharmaceutical treatment, including vascular anti-spasm, improving cerebral perfusion and decreasing intracranial pressure. Repeated lumbar punctures or lumbar cistern drainage were performed to remove the subarachnoid hemorrhage.

2.3. Clinical data

A retrospective database was established, which included the following variables: demographic characteristics (age and gender), medical history (hypertension, diabetes, smoking, alcohol abuse, and obesity), radiological data (cerebral hernia, intracranial hematoma, IVH, CT Fisher grade, location of aneurysms, WFNS grade, preoperative rebleeding, CT low-density area, and hydrocephalus), and treatment modality (endovascular coiling, microsurgical clipping, decompressive craniectomy, EVD, and ventriculoperitoneal shunt).

The follow-up period ranged within 6–36 months after onset. Clinical outcomes were assessed using the modified Rankin Scale (mRS). At six months after onset, the prognosis was classified as favorable outcome (mRS ≤ 2) or poor outcome (mRS > 2).

2.4. Statistical analysis

The statistical analysis was performed using SPSS version 22.0 (IBM, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical values were presented in frequency (percentage, %). Chi-square test or Fisher's exact test was used for categorical variables, as appropriate. Furthermore, the adjusted odds ratio (OR) and 95% confidence interval (CI) were obtained by univariate and multivariate logistic regression analysis. $P < 0.05$ was considered statistically significant.

3. Results

The present study enrolled 39 male and 65 female patients, and the average age of these patients was 54.85 ± 11.92 years old (range: 23–78 years old). Among these patients, 58 patients were aSAH grade IV, while 46 patients were aSAH grade V. Furthermore, microsurgical clipping was performed in 71 patients, while endovascular coiling was performed in 33 patients. The detailed demographic data and clinical characteristics are summarized in Table 1.

According to the statistical results, microsurgical clipping was preferred by patients with CT Fisher grade III–IV, WFNS grade V, cerebral hernia, intracranial hematoma and preoperative rebleeding (Table 2).

Table 1
Demographic data and clinical characteristics of the 104 patients with aSAH.

Characteristics		Favorable outcome (*n*)	Poor outcome (*n*)
Gender	Male	11	28
	Female	27	38
Age	< 60	21	42
	≥60	17	24
Hypertension	Yes	22	39
	No	16	27
Diabetes	Yes	3	6
	No	35	60
Smoking	Yes	8	12
	No	30	54
Alcohol abuse	Yes	4	7
	No	34	59
Obesity	Yes	5	3
	No	33	63
Preoperative rebleeding	Yes	2	11
	No	36	55
Cerebral herniation	Yes	2	18
	No	36	48
Intracranial hematoma	Yes	3	20
	No	35	46
Decompressive craniectomy	Yes	3	21
	No	35	45
Intraventricular hemorrhage	Yes	4	21
	No	34	45
External ventricular drainage	Yes	0	10
	No	38	56
CT Fisher grade	I, II	19	2
	III, IV	19	64
Location of aneurysm	Anterior circulation	36	66
	Posterior circulation	2	0
WFNS grade	IV	33	25
	V	5	41
Low density area on CT	Yes	1	18
	No	37	48
Hydrocephalus	Yes	2	17
	No	36	49
Ventriculoperitoneal shunt	Yes	1	2
	No	37	64
Postoperative rebleeding	Yes	0	0
	No	38	66
Treatment modality	Endovascular coiling	20	13
	Microsurgical clipping	18	53

Note: WFNS, The World Federation of Neurological Surgeons.

At six months after onset, the overall rate of favorable outcome (mRS ≤ 2) was 36.5% ($n = 38$), and the favorable outcome rate was 56.9% in grade IV patients and 11.1% in grade V patients. The univariate statistical analysis revealed that cerebral hernia, intracranial hematoma, IVH, hydrocephalus, CT low density area, CT Fisher grade III–IV and WFNS grade V were potential risk factors for poor prognosis, and that CT Fisher grade I–II, WFNS grade IV and endovascular coiling was associated with favorable prognosis. The prognostic factors are presented in Table 3.

The univariate and multivariate logistic regression analysis revealed that CT Fisher grade I–II ($P = 0.005$, OR = 12.102), WFNS grade IV

Table 2
Factors affecting the selection of either microsurgical clipping or endovascular coiling.

Characteristics	Microsurgical clipping	Endovascular coiling	*P* value
Preoperative rebleeding, *n* (%)	13 (18.3)	0	0.021
Cerebral herniation, *n* (%)	20 (28.2)	0	0.001
Intracranial hematoma, *n* (%)	23 (32.4)	0	< 0.001
Decompressive craniectomy, *n* (%)	24 (33.8)	0	< 0.001
Location of aneurysm, *n* (%)			0.099
Anterior circulation	71 (100)	31 (93.9)	
Posterior circulation	0 (0)	2 (6.1)	
CT Fisher grade, *n* (%)			0.001
I, II	8 (11.3)	13 (39.4)	
III, IV	63 (88.7)	20 (60.6)	
WFNS grade, *n* (%)			0.005
IV	33 (46.5)	25 (75.8)	
V	38 (53.5)	8 (24.2)	

Note: WFNS, The World Federation of Neurological Surgeons.

($P = 0.036$, OR = 3.852) and endovascular coiling ($P = 0.050$, OR = 3.581) were associated with favorable prognosis, while the CT low-density area was slightly correlated to a poor prognosis ($P = 0.042$, OR = 0.063) (Table 4).

4. Discussion

Conservative treatment is associated with a high mortality rate in patients with poor-grade aSAH, and an increasing number of scholars support the active treatment of aneurysms to improve the clinical prognosis [3,7,8]. However, the timing of surgical treatment for patients with poor-grade aSAH remains controversial [9], and the prognostic factors for poor-grade aSAH remain unclear [10]. In addition, the recovery course of poor-grade aSAH presently remains not well-understood. Previous evidence has shown that recovery following poor-grade aSAH is a dynamic process and early outcomes may not represent the long-term prognosis [11]. A recent meta-analysis containing 1111 patients exhibited no significant change in both functional outcome and mortality between ultra-early and delayed treatment, although ultra-early treatment may be associated with a lower rebleeding rate [4]. However, another meta-analysis that included a much larger cohort revealed that ultra-early treatment was associated with improved clinical outcomes [12]. Considering the poor outcomes of aneurysm rebleeding, the investigators prefer an ultra-early (< 24 h) or early microsurgical clipping or endovascular coiling for patients with poor-grade aSAH.

In the present study, a total of 104 consecutive patients with poor-grade aSAH were enrolled, and the potential prognostic factors were investigated. At six months after onset, the overall rate of favorable outcome (mRS ≤ 2) was 36.5% (56.9% in grade IV patients *vs.* 11.1% in grade V patients). Schwartz et al. assessed the long-term outcome of WFNS IV and V aSAH patients, and found that 40 of 97 patients (including 40/62 of long-term survivors) reached functional independence (mRS ≤ 2) [8]. Compared with the results reported by Schwartz, the prognosis was satisfactory in the present study, although the follow-up period was much longer in the study conducted by Schwartz.

There is presently no consensus on the treatment modality for aneurysms in patients with poor-grade aSAH. The International Subarachnoid Aneurysm Trial (ISAT) suggested that interventional coiling is superior to surgical clipping [13,14]. However, the number of patients with poor-grade aSAH was limited in this study, and the efficacy of embolization treatment considerably varied. In the Barrow Ruptured Aneurysm Trial (BRAT) study, the difference in outcomes between the coiling and clipping groups was present at six months and one year, postoperatively, and this difference disappeared at the 3-year time point [15]. At postoperative three years, the rate of poor outcome did not significantly differ between the coiling and clipping groups (35.8% *vs.* 30%; OR: 1.30; 95% CI: 0.83–2.04; $P = 0.25$), suggesting that initial differences in outcomes may not persist [15]. A recent meta-analysis that contained 4506 patients revealed that favorable neurological outcome rates were similar between surgery and endovascular treatment in patients with poor-grade aSAH [12]. In the present study, the statistical results revealed that the surgeons preferred microsurgical clipping for patients with CT Fisher grade III–IV, WFNS grade V, cerebral hernia, intracranial hematoma and preoperative rebleeding. The prognostic analysis suggested that early endovascular coiling is associated with favorable prognosis. It was speculated that patients in the microsurgical clipping group might be accompanied by a more severe clinical status, such as cerebral hernia and intracranial hematoma, which may explain the relatively poor prognosis.

Table 3
Prognostic factors evaluated at six months after onset for favorable outcome.

Characteristics		Favorable outcome (*n*)	OR	95% CI	*P* value
Treatment modality	Microsurgical clipping	18	0.221	0.092–0.532	0.001
	Endovascular coiling	20			
Cerebral herniation	Yes	2	0.148	0.032–0.680	0.006
	No	36			
Intracranial hematoma	Yes	3	0.197	0.054–0.717	0.008
	No	35			
Intraventricular hemorrhage	Yes	4	0.252	0.079–0.803	0.014
	No	34			
External ventricular drainage	Yes	0	NA	NA	0.029
	No	38			
WFNS grade	IV	33	10.824	3.735–31.367	< 0.001
	V	5			
CT Fisher grade	I, II	19	32.000	6.830–149.922	< 0.001
	III, IV	19			
Low density area	Yes	1	0.072	0.009–0.565	0.002
	No	37			
Hydrocephalus	Yes	2	0.160	0.035–0.737	0.009
	No	36			

Note: WFNS, The World Federation of Neurological Surgeons; CI, confidence interval; NA, not available due to the small sample size.

Table 4
Results of the univariate and multivariate logistic regression analyses.

Risk factor	Univariate analyses			Multivariate analyses		
	P value	Odds ratio	95% CI	*P* value	Odds ratio	95% CI
Cerebral hernia	0.006	0.148	0.032–0.680	0.861		
Intracranial hematoma	0.008	0.197	0.054–0.717	0.447		
Decompressive craniectomy	0.005	0.184	0.051–0.666	0.452		
Intraventricular hemorrhage	0.014	0.252	0.079–0.803	0.254		
External ventricular drainage	0.029	NA	NA	0.999		
CT Fisher grade I–II	< 0.001	32.000	6.830–149.922	0.005	12.102	2.101–69.712
WFNS grade IV	< 0.001	10.824	3.735–31.367	0.036	3.852	1.094–13.562
Low-density area on CT	0.002	0.072	0.009–0.565	0.042	0.063	0.004–0.900
Hydrocephalus	0.009	0.160	0.035–0.737	0.849	NA	NA
Endovascular coiling	0.001	4.530	1.880–10.915	0.050	3.581	0.999–12.835

Note: WFNS, The World Federation of Neurological Surgeons; CI, confidence interval; NA, not available due to the small sample size.

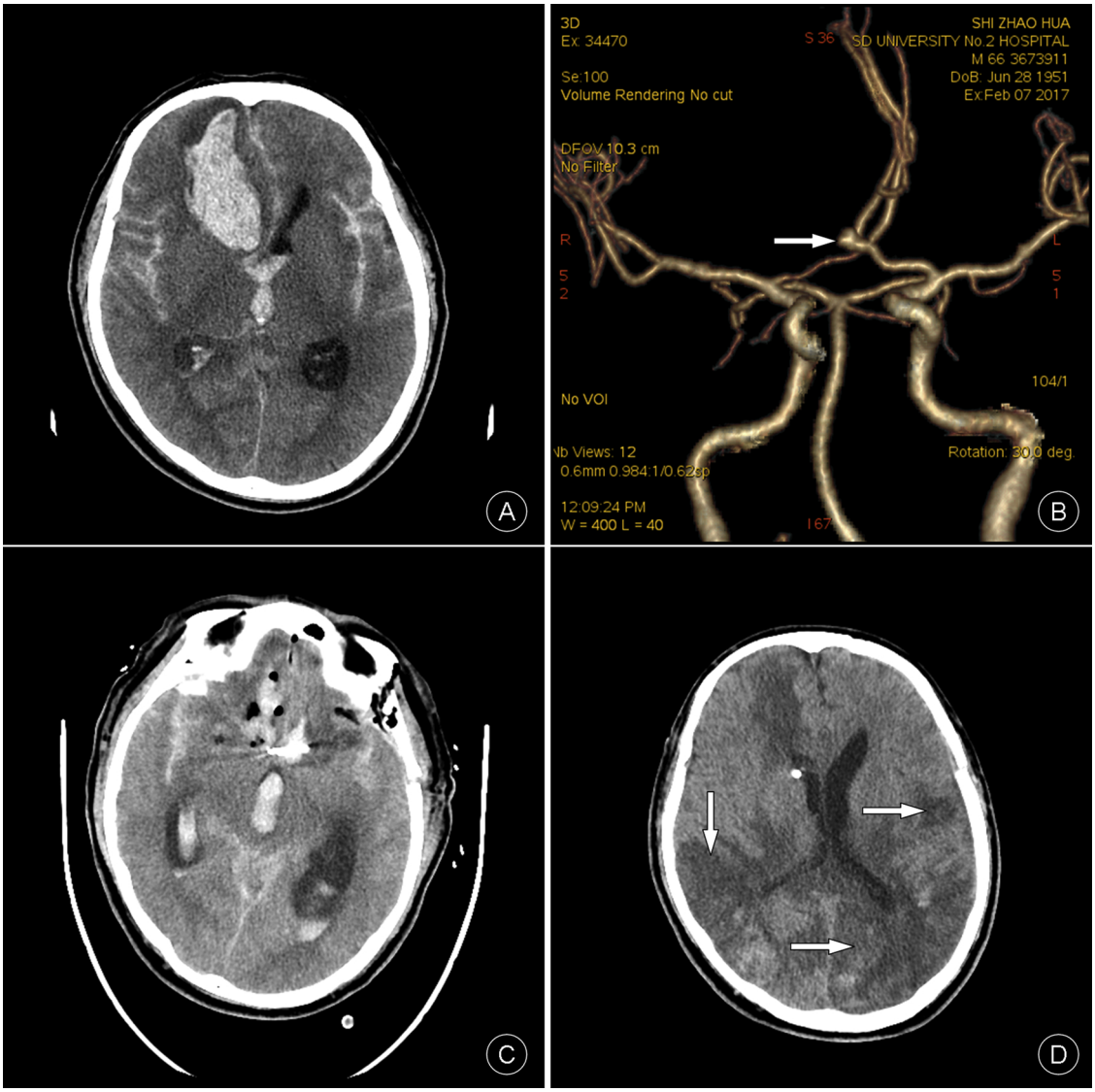

Fig. 1. The CT image shows the ruptured anterior communicating artery aneurysm (CT Fisher grade IV; WFNS grade V) and intracranial hematoma. (A) Preoperative CT imaging; (B) preoperative CT angiography showing an anterior communicating artery aneurysm (arrow); (C) CT imaging after the microsurgical clipping of the aneurysm; (D) the postoperative CT image presents the multiple low-density areas (arrow).

There is a high incidence of acute intracranial hypertension in patients with poor-grade aSAH. In clinical practice, urgent EVD has been widely used in patients with acute hydrocephalus or severe IVH. Studies have shown that decreasing intracranial pressure can improve cerebral perfusion without increasing the rebleeding risk of aneurysms [16]. In the present study, EVD was performed in patients with acute hydrocephalus or severe IVH prior to the surgery or clipping for aneurysms. The CT Fisher grade reflects the quantity and location of hemorrhage in

patients with aneurysms. Previous evidence has shown that CT Fisher grade IV is associated with poor prognosis [17]. Irreversible periventricular cerebral damage caused by IVH has been considered as a possible reason. In the present study, EVD was performed in 10 patients with severe IVH, and all of them were diagnosed as aSAH with CT Fisher grade IV. However, the prognosis of these patients was poor. These present results were consistent with previous findings, in which CT Fisher grade III–IV is associated with poor outcomes.

Cerebral vasospasm is a common complication after aSAH, and it is also the major cause of death and disability. Patients with WFNS grade IV have normal or focally abnormal perfusion. However, patients of WFNS grade V often have severe symptomatic vasospasm, which induces hypoperfusion and remarkable brain damage [18]. Although most patients with reversible cerebral vasoconstriction syndrome (RCVS) had favorable outcomes, the clinical deterioration of aSAH may result in permanent neurological deficits [19]. Therefore, early microsurgical treatment or lumbar cistern drainage for eliminating aSAH should be emphasized. Studies have suggested that severe cerebral vasospasm can lead to delayed cerebral ischemia, which was found to be an independent predictor for the poor prognosis of aSAH [11,19–22]. It was speculated that severe symptomatic and irreversible vasospasm may eventually lead to a low-density area on CT imaging in patients with poor-grade aSAH (Fig. 1). In the present study, the occurrence rate of a CT low density area in the favorable prognosis group and poor prognosis group was 2.6% and 27.3%, respectively. It was also noted that the CT low density area, which is a sign of severe cerebral vasospasm, appeared to be a possible risk factor for poor prognosis.

Studies regarding the relationship between the location of aneurysms and clinical prognosis in patients with poor-grade aSAH remain scarce. Zheng et al. conducted a multicenter study on prognostic factors for one-year outcomes in patients with poor-grade intracranial aneurysm after early treatment, and they found that anterior circulation aneurysms were associated with an unfavorable prognosis [23]. In the present study, merely two posterior circulation aneurysms were enrolled. However, a statistical analysis was not available due to the small sample size.

5. Limitations

There are some limitations to the present study. First, the present study had a retrospective design, and the sample size was small. Second, the follow-up duration was not long enough to monitor the long-term outcomes. Third, there was no control group (delayed treatment group). Fourth, the single-center experience limited the generalization of the present preliminary conclusions, and a multicenter study involving a large cohort is warranted.

6. Conclusion

The treatment of aSAH in the early stage by microsurgical clipping or endovascular coiling should be highlighted. Poor-grade aSAH is not necessarily associated with poor outcome, and clinical outcomes can be satisfactory in patients with WFNS grade IV aSAH. Furthermore, CT Fisher grade I–II, WFNS grade IV and endovascular coiling may predict a favorable prognosis, and the CT low-density area appeared to be a possible risk factor for poor prognosis.

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Conflict of interests

The authors have no conflicts of interest to disclose.

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