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Outcomes of microsurgical clipping vs coil embolization for ruptured aneurysmal subarachnoid hemorrhage

A multicenter real-world analysis of 583 patients in China

Hong-Yu Wang, MD[a], Jian Song, MD[b], Fei Gao, MM[c], Xu-Dong Duan, MM[d], Xuan Gao, MD[e], Yuan Wang, MM[a], Hong-Bo Cheng, MM[b], Cheng-Rui Nan, MM[b], Di Zhao, MM[f,*]

Abstract

Aneurysmal subarachnoid hemorrhage (SAH) is a complex neurovascular syndrome with high disability and mortality. SAH patients may be managed with surgical clipping or coil embolization. In this study, we provided a real-world analysis of the outcome and prognostic factors of aneurysmal SAH in patients treated with coil embolization or microsurgical clipping.

We retrospectively analyzed the medical records of aneurysmal SAH patients (n = 583) who underwent treatment at the First Hospital and the Second Hospital of Hebei Medical University, and Tangshan Worker's Hospital in China. All patients were evaluated by a combined neurosurgery and interventional neuroradiology team. Microsurgical aneurysmal clipping was performed using the skull base approach, while coil embolization was performed with bare platinum coils (with or without balloon assistance). The primary outcome was the Glasgow Outcome Scale (GOS) score at discharge.

A total of 583 patients were included in this study, of which 397 (68.1%) of them underwent clipping and 186 (31.9%) received coil embolization. The patient cohort consisted of both poor grade and good grade aneurysmal SAH: 441 (75.6%) patients had good-grade (Hunt and Hess grade II or III) and 142 (24.4%) had poor grade (Hunt and Hess grade IV or V). Overall, 123 (21%) patients had unfavorable neurologic outcome (GOS score 1–3) and 460 (78.9%) patients had favorable neurologic outcome (GOS score 4 or 5). The mean GOS score at discharge was comparable for patients who underwent clipping and those received coil embolization ($P > .05$). Multivariate analysis showed that clipping only [OR (95%CI): 0.03 (0.01, 0.36); $P = .000$] and clipping with CSF drainage [OR (95%CI): 0.41 (0.18, 0.89); $P = .001$] were independent factors of a favorable outcome in patients with aneurysmal SAH. Coil embolization with hematoma removal [OR (95%CI): 0.03 (0.01, 0.36); $P = .000$] was also an independent determinant of a favorable outcome. High baseline Fisher grades were associated with significantly increased risk of an unfavorable outcome [OR (95%CI): 2.08 (1.30, 3.33); $P = .002$].

Our findings suggested that both coil embolization and microsurgical clipping are viable treatment options for aneurysmal SAH patients. Procedures, such as CSF drainage and hematoma removal, performed in parallel with coil embolization and chipping should be considered when treating individual patients.

Abbreviations: CSF = cerebrospinal fluid, GOS = Glasgow Outcome Scale, SAH = subarachnoid hemorrhage.

Keywords: aneurysmal subarachnoid hemorrhage (SAH), coil embolization, microsurgical clipping

1. Introduction

Aneurysmal subarachnoid hemorrhage (SAH) is a complex neurovascular syndrome associated with high risk of disability and mortality. Majority of the non-traumatic SAH cases are due to rupture of an intracranial aneurysm.[1] Aneurysm rebleeding following treatment is also a major contributor to morbidity and mortality, particularly in patients with poor grade aneurysmal SAH (Hunt and Hess grade IV and V).[2] Prompt diagnosis (such as the use of computed tomography angiography) and surgical treatment are critical to successful management of aneurysmal SAH.[3] The standard treatment over the past few decades has been surgical clipping of the neck of the aneurysm. Recently, treatment with endovascular coil embolization has emerged. It is a percutaneous approach to treat an intracranial aneurysm from within the blood vessel without the need for a craniotomy.[4] Detachable coils were popular for occlusion of the aneurysm.[5] An emergency application of surgical clip placement or endovascular coiling could benefit patients with aneurysmal SAH by lowering the incidence of rebleeding.[6] Although there have been advances in therapeutic interventions, high proportions of patients with aneurysmal SAH still suffer from disability

Editor: Xiong Kun.

H-YW and JS contributed equally to this paper and should be treated as co-first authors.

The authors have no conflicts of interest to disclose.

[a] Department of Neurosurgery, Tangshan Gongren Hospital, Tangshan, Hebei, [b] Department of Neurosurgery, The Second Hospital of Hebei Medical University, [c] Hebei Provincial Procurement Centers for Medical Drugs and Devices, [d] Department of TCM Surgery, The Second Hospital of Hebei Medical University, [e] Hebei Medical University, [f] Department of Neurosurgery, The First Hospital of Hebei Medical University, Shijiazhuang, Hebei, China.

[*] Correspondence: Di Zhao, Department of Neurosurgery, The First Hospital of Hebei Medical University, No. 89 Donggang Road, Yuhua District, Shijiazhuang, Hebei 050031, China (e-mail: 179381749@qq.com).

Medicine (2019) 98:33(e16821)

Received: 9 November 2018 / Received in final form: 2 July 2019 / Accepted: 19 July 2019

http://dx.doi.org/10.1097/MD.0000000000016821

(33%) and succumb to deaths (44%).[7] Also, management of poor grade aneurysmal SAH with surgical clipping and coil embolization remains controversial.[8]

Continuous efforts have been made to investigate prognostic factors of SAH. Most of the studies focused on good grade aneurysmal SAH; also, patients were treated with variety of modalities.[9] Molyneux et al compared the safety and efficacy of endovascular coiling with standard neurosurgical clipping in 2143 patients with ruptured intracranial aneurysms in a randomized, multicentre trial (the International Subarachnoid Aneurysm Trial (ISAT)). The study demonstrated that endovascular coiling was superior to neurosurgical clipping with regards to survival free of disability at 1 year.[10] In the study, 88% of the patients in the ISAT study were of good-grade aneurysmal SAH (World Federation of Neurosurgeons [WFNS] grade I or II), and poor-grade aneurysmal SAH patients were largely excluded. Another meta-analysis showed that endovascular coiling yielded greater benefit in good grade aneurysmal SAH patients than poor grade aneurysmal SAH patients.[11] A recent systemic review also raised an uncertainty on the efficacy of endovascular coiling for poor grade aneurysmal SAH (Hunt and Hess grade IV or V or [WFNS grade III or V].[12]

In addition to treatment with clipping of the aneurysm or coil embolization, decompressive surgery is also important to achieve favorable outcomes by controlling elevated intracranial pressure in patients with poor-grade aneurysmal SAH. The presence of intracerebral hematoma in patients with aneurysmal SAH predicted an unfavorable outcome.[13] Decompressive surgery such as decompressive craniectomy and hematoma removal contributes to an improved outcome of patients with poor-grade aneurysmal SAH.[14] Hwang et al performed aneurysmal clipping in 40 patients with poor-grade aneurysmal SAH and coil embolization in 30 patients and found that early coil embolization followed by decompressive surgery led to a more favorable outcome.[15] A recent meta-analysis showed that drainage of the cerebrospinal fluid (CSF) also contributed to improved long term outcome of patients with aneurysmal SAH.[16]

In real-world scenarios, poor-grade aneurysmal SAH patients may be managed conservatively with surgical clipping or coil embolization,[17] supplemented with simultaneous decompressive surgery.[15] The learning from real-world data analysis may be different from those obtained from clinical trials. In this study, we analyzed the outcome and prognostic predictors of aneurysmal SAH in real-world settings, in which patients were heterogeneous in nature and the treatments were varied.

2. Patients and methods

2.1. Patients

We retrospectively analyzed the medical records of aneurysmal SAH patients who received treatment at the First Hospital and the Second Hospital of Hebei Medical University, and Tangshan Worker's Hospital between March 2013 and January 2016. All patients in this study were diagnosed with a ruptured aneurysm, and the aneurysm clipping procedure was performed within 24 hours after admission. Patients were excluded if they had a ruptured aneurysm of the vertebrobasilar system; received conservative therapy (or aneurysm clipping) more than 24 hours after admission. Other exclusion criteria included post-traumatic hemorrhage, intoxication, prior active cancer, infectious, systemic, hematological, or cardiovascular diseases. Patients were considered to have poor-grade aneurysmal SAH if they had Hunt and Hess grade IV and V.[18]

The study protocol was approved by the local institutional review boards The Second Hospital of Hebei Medical University. Patient consent was not required because of the retrospective nature of the study.

2.2. Patient evaluation

We retrieved the following data from the medical records: demographic variables including age and sex, presence of comorbidities, location, size, and multiplicity of aneurysm, Hunt-Hess scale scores, Fisher grade scores, and Glasgow Outcome Scale scores.[19] Morbidity was considered present in patients with neurological deficits and/or daily life dependency. Glasgow Outcome Scale at discharge was used to evaluate the outcome of patients. A favorable outcome was considered for a patient with a GOS score of 4 or 5 at discharge, while an unfavorable outcome was considered for a patient with a GOS score less than 4 at discharge. All patients were evaluated by both neurosurgery and interventional neuroradiology team. Cerebral angiography and CT angiography were used to identify the location of the ruptured aneurysm.

2.3. Treatments

Standardized procedures were followed for the preoperative and postoperative management. Surgical procedures were performed in the patients under general anesthesia and with neurophysiologic monitoring. The decision on clipping vs coiling of the aneurysm was made independently by the attending neurosurgeon, based on baseline Hunt-Hess grade, location and morphology of the aneurysm and dome/neck ratio. Microsurgical aneurysmal clipping was performed using the skull base approach and monitored under the microscope and fluorescence imaging technology. Coil embolization was carried out with bare platinum coils, with or without balloon assistance. Decompressive surgery was performed after coil embolization was completed. Intracerebral hematoma was removed via the transsylvian route or the transcortical approach. Hyperventilation, diuretics, and CSF drainage (including ventriculoperitoneal shunt and lumbar cistern drainage) were undertaken to minimize brain retraction.

Outpatient follow-up was performed at 1- and 3-month after surgery, and once yearly after discharge. CT angiography was performed on all patients within 3 months after discharge.

2.4. Statistical analysis

Data were expressed as mean ± SD or number (percentage). All data were analyzed using SPSS version 15.0 (SPSS Inc., Chicago, IL). Patient characteristics, treatments, and outcomes were tabulated. Univariate and multivariate logistic regression were performed to investigate the association of patient demographic and baseline variables with the primary outcome. Both unadjusted and adjusted logistic regression models were fitted. All probability values were 2-sided, and $P < .05$ was considered to be statistically significant.

3. Results

3.1. Patient demographic and baseline characteristics

A total of 583 patients were included in the study. The baseline and clinical characteristics were summarized in Table 1. The

Table 1

Characteristics of Patients (n=583) with Aneurysmal subarachnoid hemorrhage (SAH).

Characteristics	Values	Characteristics	Values
Age (yr), mean±sd.	56.6±10.4	CSF Drainage†	
Male-to-female ratio	1:1.69	Patients received Coil embolization, n (%)	60 (10.3)
Fisher Grade Scores		Patients received Clipping, n (%)	23 (4)
III (%)	75	**Hematoma**	
IV (%)	25	Patients received Clipping, n (%)	11 (1.9)
Hunt and Hess Grade		**Outcome**	
II or III (%)	75.6	Died, n (%)	6 (1)
IV or V (%)	24.4	Vegetative state, n (%)	81 (13.9)
Therapy received		Severely disabled, n (%)	36 (6.2)
Clipping, n (%)	397 (68.1)	Moderate disabled, n (%)	162 (27.8)
Coil embolization, n (%)	186 (31.9)	Good recovery, n (%)	298 (51.1)
Coiling to clipping, n (%)*	11 (1.9)		

* Patients were crossed over from coiling to clipping because of technical difficulty with the coiling procedure.
† CFS Drainage included ventricular shunt or lumbar cistern drainage.

mean age of the patients was 56.6±10.4 years (range 23–91 years) and the male-to-female ratio was 1:1.69 (217 males and 366 females). In addition, 437 (75.0%) of the patients had a Fisher grade of 3, and 146 (25.0%) patients had a Fisher grade of 4. There were 397 (68.1%) patients underwent clipping, and 186 (31.9%) received coil embolization. Eleven (1.9%) patients crossed over from coiling to clipping because of technical difficulty with the coiling procedure. CSF drainage, including ventricular shunt or lumbar cistern drainage, was done in 60 (10.3%) patients as an adjunct to coil embolization and in 23 (4%) patients as an adjunct to microsurgical clipping of the aneurysm. Hematoma was evacuated in 11 (1.9%) patients who received coil embolization.

Overall, 441 (75.6%) patients had good-grade aneurysmal SAH (Hunt and Hess grade II or III) and 142 (24.4%) had poor-grade aneurysmal SAH (Hunt and Hess grade IV or V). There were no statistically significant differences in demographic, baseline and treatment characteristics between good-grade and poor-grade aneurysmal SAH patients.

3.2. The primary outcome

Majority of the patients showed good recovery (n=298, 51.1%). The patient cohort had a mean Glasgow Outcome Scale score of 4.0 at discharge. The mean Glasgow Outcome Scale score at discharge was comparable for patients who underwent clipping and those who received coil embolization ($P>.05$). Overall, 123 (21%) patients had unfavorable neurologic outcome and 460 (78.9%) of them had favorable neurologic outcome (Table 2).

3.3. Predictors of treatment outcome

Univariate ordered logistic regression analysis showed that baseline Fisher grade was a significant adverse predictor of an unfavorable outcome [OR (95%CI): 2.78 (1.82, 4.17); $P=.000$] (Table 3). Baseline Hunt and Hess grade was a significant predictor of favorable outcome [OR (95%CI): 0.37 (0.26, 0.53); $P=.000$]. Furthermore, therapeutic intervention was associated with a favorable outcome [OR (95%CI): 0.75 (0.64, 0.88); $P=.000$]. Other variables such as gender, age or aneurysm size were not significant determinants of patient outcomes.

Table 2

Glasgow Outcome Scale scores at discharge for aneurysmal SAH patients.

	Glasgow Outcome Scale score	All patients
Unfavorable outcome		
1	1	6 (1.0)
2	2, 3	117 (20.1)
Favorable outcome		
3	4, 5	460 (78.9)

Multivariate analysis further showed that clipping only [OR (95%CI): 0.03 (0.01, 0.36); $P=.000$] and clipping with CSF drainage [OR (95%CI): 0.41 (0.18, 0.89); $P=.001$] were independent predictors of a favorable outcome in patients with aneurysmal SAH (Table 4). On the other hand, coil embolization only [OR (95%CI)1.15 (0.56, 2.09); $P=.636$], coil embolization with CSF drainage [OR (95%CI) 0.56 (0.29,1.10); $P=.091$], and coil embolization with CSF drainage and hematoma removal [OR (95%CI) 0.09 (0.008, 1.105); $P=.060$] were not statistically independent predictors of outcome. Coil embolization with hematoma removal [OR (95%CI)0.03 (0.01, 0.36); $P=.000$] was an independent determinant of a favorable outcome in patients with aneurysmal SAH. Overall, high baseline Fisher grades were associated with significantly increased risk of an unfavorable outcome in patients with poor-grade aneurysmal SAH[OR (95% CI): 2.08 (1.30, 3.33); $P=.002$] while baseline Hunt and Hess scale scores did not independently impact on patient outcome.

4. Discussion

Aneurysmal SAH is a neurovascular disease with high morbidity and mortality. Although coil embolization has recently emerged as a popular therapeutic modality for aneurysmal SAH, its efficacy remains inconclusive in patient population with poor grade aneurysmal SAH. In this real-world study, we analyzed the clinical data of 583 aneurysmal SAH patients from three medical centers in China. Approximately one quarter (24.5%) of the patients had poor grade aneurysmal SAH. This was much higher than the proportion (12%) of poor-grade aneurysmal SAH patients in the ISAT study.[10] Majority (68.1%) of the patients in this study received microsurgical clipping of the aneurysm. We found that microsurgical clipping (with or without CSF drainage) of the aneurysm was independently associated with a significant reduction in the risk of unfavorable outcome. Coil embolization with hematoma removal was also associated with favorable outcome. Our findings suggested that both coil embolization and microsurgical clipping are viable treatment options for aneurysmal SAH patients.

Table 3

Univariate analysis of determinants of neurologic outcome of aneurysmal SAH patients.

Variables	β	Standard error	z	P	OR (95%CI)
Fisher grade at admission	1.02	0.22	−4.71	.000	2.78 (1.82,4.17)
Hunt and Hess grade at admission	−0.99	0.17	−5.58	.000	0.37 (0.26,0.53)
Therapeutic modality	−0.29	0.08	−3.58	.000	0.75 (0.64,0.88)

Our findings differ from the ISAT study which showed superiority of endovascular coiling in disability-free survival at 1-year and 10-year after treatment.[10] Our cohort consisted of higher percentage of poor grade aneurysmal SAH patients when compared with the ISAT study. Furthermore, 95% of the aneurysms in the ISAT were in the anterior cerebral circulation, and the size of the aneurysm was smaller than 10 mm in 90% of the patients, while our cohort included a heterogeneous group of aneurysmal SAH patients. Our finding was similar to that of the meta-analysis by Xia et al,[12] in which superiority of endovascular coiling vs. microsurgical clipping was not found in poor grade aneurysmal SAH patients. Schuss et al[20] analyzed the data of 111 aneurysmal SAH patients treated with clipping or coiling. The results showed a favorable outcome in 68% of patients with good grade aneurysmal SAH on admission (Hunt and Hess grade I-III) vs 23% of patients with poor grade aneurysmal SAH (Hunt and Hess Grades IV and V). Their multivariate analysis further revealed that poor grade aneurysmal SAH at admission was the only predictor of unfavorable outcome. Our multivariate analysis also showed that higher Fisher grade was an independent predictor of unfavorable outcome.

Decompressive surgery is performed to control elevated intracranial pressure in aneurysmal SAH patients. Poor grade aneurysmal SAH patients may have different clinical manifestations including intracerebral hemorrhage, cerebral swelling, and acute hydrocephalus that require additional management. Hwang et al showed that decompressive surgery following early coil embolization in poor grade aneurysmal SAH patients with elevated intracranial pressure contributed to a more favorable outcome.[15] The role of CSF drainage in poor-grade aneurysmal SAH is inconclusive.[21,22] In our study, 60 (10.3%) patients received CSF drainage as an adjunct to coil embolization, and our multivariate analysis failed to establish CSF drainage as a determinant of outcome.

Morbidity and mortality of SAH patients correlate with the volume of hemorrhage.[6–8] Fisher grade was first proposed in 1980 and modified in 2001; both of which initially were criteria for determining volume of hemorrhage by CT scan at the onset of SAH.[9–10] The clinical significance of Fisher grade has been recognized by numerous subsequent studies, which showed that higher Fisher grade predicted an adverse outcome and higher morbidity and mortality. Our clinical experiences, however, suggested that modified Fisher grades sometime did not correlate with Hunt-Hess grades. In some patients, CT scan indicated low modified Fisher grade (mostly grade II-III), but these patients subsequently developed acute respiratory failure and cardiac arrest. They maintained vital signs after vigorous preadmission resuscitation efforts, but their Hunt-Hess grades could be as high as grade V, and their CT scan showed SAH together with diffuse brain swelling. These patients were in deep coma without spontaneous respiration and their blood pressure was maintained by high dose vasoactive drugs. After reviewing these cases and thorough clinical analysis, we proposed the following explanations for the aggravated manifestations of aneurysmal SAH:

1) When SAH patients experience excruciating headache at the onset of SAH, they instinctively seek bed rest in a supine position. Blood rapidly enters the subarachnoid space and spreads over the brain surface and the cortex. Upon this intense stimulation, abnormal electric discharges may manifest as onset of seizures clinically. The loss of consciousness with seizure onset and vomit could cause asphyxiation and sudden cardiac arrest. We believe this could be the most important cause of the rapid death of SAH patients.

2) The rupture in patients with long term arteriosclerosis and posterior circulation aneurysm may rapidly lead to formation of hematoma around the brain stem. This causes spasm of the arterioles on the surface of the brain stem, leading to brain stem ischemia, suppressing the respiratory center with presentation of respiratory cessation and cardiac arrest.

3) Patients may have cardiac disease and develop cardiac arrhythmia or myocardial infarction as a consequence of stress response to aneurysm rupture; these patients are very difficult to resuscitate. We also observed that many patients had very high admission Fisher grade or modified Fisher grade but low Hunt and Hess grade; these patients are at a high risk for development of delayed cerebral vascular spasm and poorer prognosis. These observations suggested that acute respiratory arrest and cardiac arrest following the onset of SAH are mostly due to asphyxiation,

Table 4

Multivariate ordered logistic regression analysis of predictors of treatment outcome.

Variables	β	SE	z	P	OR (95%CI)
Clipping					
Clipping only	−3.56	0.85	−4.17	.000	0.03 (0.01,0.36)
Clipping + CSF drainage	−1.56	0.46	−3.40	.001	0.41 (0.18,0.89)
Coil embolization					
Coiling only	0.14	0.30	0.47	.636	1.15 (0.56,2.09)
Coiling +hematoma removal	−3.56	0.85	−4.17	.000	0.03 (0.01,0.36)
Coiling + CSF drainage	−0.57	0.34	−1.69	.091	0.56 (0.29,1.10)
Coiling + hematoma removal + CSF drainage	−2.35	1.25	−1.88	.060	0.09 (0.008,1.105)
Baseline Fisher grade	0.73	0.24	−3.02	.002	2.08 (1.30,3.33)

acute cerebral vascular spasm and other systemic diseases. The arrest may not necessarily be due to SAH itself. The use of Hunt and Hess grade only to assess severity of SAH may not be sufficient. Fisher grade, modified Fisher grade and Hunt and Hess grade should all be considered to determine whether a patient has severe aneurysmal SAH.

One of the limitations of the present study is the lack of outcome data at the follow up visits. Except in prospective controlled studies, patients in China are seldom followed up. Another limitation is the tertiary care setting for all three centers in the study. The findings may not be totally applicable to secondary or primary care settings. In addition, no safety data was reported in the current study. Future prospective studies with a larger population size are warranted to investigate whether coil embolization is superior to microsurgical clipping in terms of both efficacy and safety for poor grade aneurysmal SAH patients.

In conclusion, microsurgical clipping of the aneurysm is associated with significantly improved outcome in aneurysmal SAH patients. Our findings suggest that both coil embolization and microsurgical clipping are viable treatment options for aneurysmal SAH patients. Therapeutic choice for poor grade aneurysmal SAH should be tailored to individual patients (e.g., addition of CSF drainage and hematoma removal).

Author contributions

Conceptualization: Hong-Yu Wang, Di Zhao.
Data curation: Jian Song, Fei Gao, Xu-Dong Duan.
Formal analysis: Jian Song, Fei Gao, Xu-Dong Duan, Hong-Bo Cheng.
Investigation: Xuan Gao, Yuan Wang, Hong-Bo Cheng, Cheng-Rui Nan.
Methodology: Xuan Gao, Yuan Wang, Cheng-Rui Nan.
Validation: Yuan Wang.
Writing – original draft: Hong-Yu Wang.
Writing – review & editing: Di Zhao.

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