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Original Article

Factors Influencing 1-year Functional Outcome after Surgery in Aneurysmal Subarachnoid Hemorrhage Patients: A Single-center Series

I-sorn Phoominaonin, Somkiat Wongsuriyanan

Department of Surgery, Neurosurgery Unit, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand

Abstract

Objective: The objective of the study was to evaluate the outcome and related factors in patients with aneurysmal subarachnoid hemorrhage (aSAH). **Materials and Methods:** Clinical data of 221 patients who were diagnosed with spontaneous SAH due to ruptured intracranial aneurysm and surgically treated at Vajira Hospital between January 2013 and May 2016 were retrospectively reviewed. Patient and aneurysm characteristics, clinical status at presentation, treatment, and status at discharge and 1 year after discharge were recorded. Outcomes 1 year after surgery were assessed using the Glasgow Outcome Scale (GOS). Patients were divided into two groups according to the GOS score: the favorable outcome group (GOS scores 4 and 5) and unfavorable outcome group (GOS scores 1–3). **Results:** Among the 221 study patients, 158 were classified in the favorable outcome group and 63 in the unfavorable outcome group. Patient age, Hunt and Hess grade, aneurysm size, use of Vitamin C solution irrigation in the subarachnoid space, and GOS score 1 year after surgery significantly differed between the two groups. **Conclusions:** Numerous factors analyzed in this study were significantly associated with 1-year outcome in surgically treated aSAH patients, including subarachnoid Vitamin C irrigation. Further study of subarachnoid Vitamin C irrigation is warranted.

Keywords: *Aneurysm clipping, aneurysm trapping, aneurysmal subarachnoid hemorrhage, ruptured intracranial aneurysm*

Introduction

Clinical outcomes of ruptured intracranial aneurysms vary widely and depend on several factors.[1-4] Long-term outcome is affected by the severity of initial presentation, amount of blood on computed tomography (CT) at presentation, initial resuscitation, and patient management. At our hospital, aneurysmal subarachnoid hemorrhage (aSAH) is treated with surgical obliteration of the aneurysm by direct clipping, trapping with or without bypass, or aneurysmal wrapping or coating. This retrospective study aimed to analyze factors affecting 1-year outcome in aSAH patients who underwent surgical aneurysm treatment.

Materials and Methods

Patient selection

Two hundred sixty-five patients diagnosed with spontaneous SAH and intracranial aneurysm who were treated at Vajira Hospital between January 2013 and May 2016 were eligible for study inclusion. We included only those with ruptured intracranial aneurysms that were surgically treated. Forty-four patients were excluded because of unruptured or undetectable intracranial aneurysm or treatment with a modality other than surgical obliteration. Ruptured aneurysm patients were surgically treated within 24 h after arrival at our hospital (referral or newly visited). In the patients who needed emergency ventriculostomy, the procedure was performed before craniotomy in the same operation. In case that craniotomy could not perform in the same operation due to requirement of further investigations or under resuscitations, ventriculostomy was performed first. For unstable or poor-grade patients who were not eligible for surgery or caregiver refused aggressive treatments, conservative treatments were done.

Direct clipping of aneurysm with preservation of parent artery was attempted in all cases. If failed, other modalities

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Address for correspondence:
Dr. I-sorn Phoominaonin, Department of Surgery, Neurosurgery Unit, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, 681 Samsen Road, Dusit, Bangkok 10300, Thailand.
E-mail: popo.japan@gmail.com

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including proximal parent arterial occlusion, trapping with bypass, wrapping, or coating were done." change to "Clipping of aneurysms were attempted in all cases. If the aneurysm cannot be clipped, other modalities (proximal parent arterial occlusion, trapping of aneurysm with bypass, wrapping of aneurysm or coating of aneurysm) were done. Parent arteries and surrounded perforators were evaluated patency by using intraoperative Doppler ultrasound and indocyanine green video-angiography. Postoperation, patients were treated within the neurosurgical intensive care unit. If delayed ischemic neurological deterioration (DIND) is suspected in case of newly developed of focal neurological deficit, there is a decreased level of consciousness or new-onset seizure. The imaging and laboratory investigations were done to exclude possible causes of DIND. Specific treatments were given to patients with the obvious cause of DIND. If the investigations did not show explainable causes, patients were treated as clinical vasospasm, blood pressure was elevated by using intravenous inotropic drugs until symptoms improved or maximal systolic blood pressure (220 mmHg) was reached." change to "If there were not obvious causes of deterioration, the patient was treated as clinical vasospasm. Blood pressure was elevated by intravenous inotropic drugs until symptoms improved or maximal systolic blood pressure (220 mmHg) was reached.

Finally, 221 patients were included. Clinical data regarding patient and aneurysm characteristics, clinical status at presentation, treatment, and status at discharge and 1 year after discharge were recorded.

Outcome assessment

Outcomes 1 year after surgery were assessed using the Glasgow Outcome Scale (GOS).[5,6] Patients were divided into two groups according to the GOS score: the favorable outcome group (GOS scores 4 and 5) and unfavorable outcome group (GOS scores 1–3). Patient and clinical characteristics were analyzed to assess association with functional outcome.

Statistical analysis

Statistical analyses were conducted using GNU PSPP version 1.2.0 software. Data between groups were compared using the unpaired *t*-test, Fisher's exact test, and Chi-square test as appropriate. $P < 0.05$ was considered significant.

Results

Patient and clinical characteristics are shown in Table 1. Among the 158 patients (71.4%) of the favorable outcome group, 57 were male (36.1%) and 101 were female (63.9%). In this group, the mean age was 49.8 years and the mean Hunt and Hess grade was 2.4. Seventy-five patients (47.7%) were Hunt and Hess Grade 2. Aneurysm distribution [Table 2] was as follows: ophthalmic artery aneurysm: 4 (2.5%); superior hypophyseal artery aneurysm: 1 (0.6%); posterior communicating artery (PcoA) aneurysm: 32 (20.2%); anterior choroidal artery aneurysm: 5 (3.1%); internal carotid artery bifurcation aneurysm: 4 (2.5%); anterior communicating artery (AcoA) aneurysm: 60 (37.9%); anterior cerebral artery (ACA) aneurysm: 10 (6.3%); middle cerebral artery (MCA) aneurysm: 27 (17.2%); posterior–inferior cerebellar artery (PICA) aneurysm, 6 (3.8%); vertebral artery aneurysm (including aneurysm at the vertebrobasilar junction): 4 (2.5%); superior cerebellar artery aneurysm: 2 (1.2%); and basilar tip aneurysm: 3 (1.9%). The superficial temporal artery–MCA bypass with proximal occlusion of MCA was performed in one patient presenting with unclippable MCA aneurysm.

Among the 63 patients (28.5%) of the unfavorable outcome group, 19 were male (30.1%) and 44 were female (69.9%). The mean age was 59.7 years and the mean Hunt and Hess grade was 3.2. An equal number of patients (19) were Hunt and Hess Grades 3 and 4. Aneurysm distribution was as follows: ophthalmic artery aneurysm: 2 (3.1%); superior hypophyseal artery aneurysm: 1 (1.5%); PcoA aneurysm: 20 (31.7%); anterior choroidal artery aneurysm: 1 (1.5%); internal carotid artery bifurcation aneurysm: 2 (3.1%); AcoA aneurysm: 14 (22.2%); ACA aneurysm: 3 (4.7%); MCA aneurysm: 8 (12.6%); PICA aneurysm: 2 (3.1%); vertebral artery aneurysm (including aneurysm at the vertebrobasilar junction): 4 (6.3%); superior cerebellar artery aneurysm: 2 (3.1%); and basilar tip aneurysm: 4 (6.3%). In case of vertebral artery dissection (one patient) involvement of origin of PICA, the occipital artery–PICA bypass with proximal occlusion of the vertebral artery was performed.

Age at presentation and Hunt and Hess grade were significantly higher in the unfavorable outcome group than the favorable outcome group ($P < 0.05$). The mean aneurysm size was significantly smaller in the favorable outcome group (6.3 mm vs. 7.5 mm; $P = 0.049$). The proportion of patients who developed clinical vasospasm did not significantly differ between the favorable and unfavorable outcome groups (10.1% vs. 14.3%; $P = 0.48$). The mean GOS score at discharge was significantly higher in the favorable outcome group (4.2 vs. 2.4; $P < 0.05$). Seventy-three patients (46.2%) in the favorable outcome group had good recovery status (GOS score 5) at discharge.

Aneurysm locations and characteristics of unfavorable outcome group

As shown in Table 3, aneurysmal characteristics and intraoperative results of unfavorable outcome group based on aneurysm locations were shown as follows: mean age, mean aneurysm size, mean date of operation (SAH date), number of patients with intraoperative rupture of aneurysm, mean intraoperative blood loss, and postoperative

Table 1: Patient and clinical characteristics and outcome groups

	Favourable outcome at 1-year (GOS 4-5)	Unfavourable outcome at 1-year (GOS 1-3)	*P*
Number of patients	158	63	
Sex (male/female)	57/101	19/44	
Mean age (years)	49.8±12.4	59.7±13.7	<0.05**
Hunt and Hess grading, *n* (%)			
1	19 (12)	6 (9.5)	<0.05**
2	75 (47.4)	9 (14.2)	
3	46 (29.1)	19 (30.1)	
4	14 (8.8)	19 (30.1)	
5	4 (2.5)	10 (15.8)	
Mean SAH date of surgical intervention	SAH day 3.8±4.3	SAH day 5.6±7.9	0.095
Number of clinical vasospasm patients, *n* (%)	16 (10.1)	9 (14.3)	0.48**
Number of local Vitamin C irrigation, *n* (%)	108 (68.3)	32 (50.7)	0.02**
Mean GOS at discharge	4.2	2.4	<0.05**
GOS 5 at discharge, *n* (%)	73 (46.2)	-	
GOS at discharge (*n*)			
GOS 5	73		
GOS 4	52	2	
GOS 3	30	36	
GOS 2	1	13	
GOS 1		10	
Shunt dependent patients, *n* (%)	27 (17.1)	23 (36.5)	0.0039**

GOS – Glasgow Outcome Scale, SAH – Subarachnoid hemorrhage, ** — Statistically significant

Table 2: Aneurysm characteristics and outcome groups

	Favorable outcome at 1 year (GOS 4-5) (*n*=158), *n* (%)	Unfavorable outcome at 1 year (GOS 1-3) (*n*=63), *n* (%)	*P*
Aneurysm size (mean, mm)	6.3±4	7.5±3.9	0.049**
Location of aneurysm (%)			
Anterior circulation			
Ophthalmic artery	4 (2.5)	2 (3.1)	
Superior hypophyseal artery	1 (0.6)	1 (1.5)	
PcoA	32 (20.2)	20 (31.7)	
Anterior choroidal artery	5 (3.1)	1 (1.5)	
ICA bifurcation	4 (2.5)	2 (3.1)	
AcoA	60 (37.9)	14 (22.2)	
ACA	10 (6.3)	3 (4.7)	
MCA	27 (17.1)†	8 (12.6)	
Posterior circulation			
PICA	6 (3.8)	2 (3.1)	
VA (included VBJ)	4 (2.5)	4 (6.3)‡	
SCA	2 (1.2)	2 (3.1)	
Basilar tip	3 (1.9)	4 (6.3)	

†One patient with unclippable MCA aneurysm, STA-MCA bypass with proximal occlusion of MCA was done; ‡One patient with vertebral artery dissection, OA-PICA bypass with proximal occlusion of VA was done. ACA – Anterior cerebral artery; AcoA – Anterior communicating artery; GOS – Glasgow Outcome Scale; ICA – Internal carotid artery; MCA – Middle cerebral artery; OA – Occipital artery; PcoA – Posterior communicating artery; PICA – Posterior inferior cerebellar artery; SCA – Superior cerebellar artery; STA – Superficial temporal artery; VA – Vertebral artery; VBJ – Vertebrobasilar junction, ** — Statistically significant

complications. The mean age in each aneurysm location was as follows: internal carotid artery aneurysm: 59 years; PcoA aneurysm: 67 years; AcoA aneurysm: 52 years; ACA aneurysm: 60 years; MCA aneurysm: 60 years; and posterior circulation: 57 years. Aneurysm size in mean was as follows: internal carotid artery aneurysm: 7.5 mm; PcoA aneurysm: 8.7 mm; AcoA aneurysm: 6 mm; ACA aneurysm: 9 mm; MCA aneurysm: 5.8 mm; and posterior circulation: 8.0 mm. The mean operative date after SAH was highest in ACA aneurysm as date 13, equally in

Table 3: Aneurysm characteristics of unfavorable outcome group

Aneurysm location (*n*)	Age (mean, years)	Aneurysm size (mean, mm)	Operation date (mean, SAH date)	Number of patient with intraoperative rupture of aneurysm, *n* (%)	Intraoperative blood loss (mean, ml)	Number of postoperative complications, *n* (%)
ICA (6); ophthalmic artery, superior hypophyseal artery, anterior choroidal artery, and ICA bifurcation aneurysm	59	7.5	6	2 (33.3)	716	1 clinical vasospasm (16.6) 3 infection† (50) 2 other‡ (33.2)
PcoA (20)	67	8.7	4.5	5 (25.0)	392	2 clinical vasospasm (10) 9 infection† (45) 5 meningitis (25) 5 other‡ (25)
AcoA (14)	52	6.0	6	8 (57.1)	300	1 clinical vasospasm (7.1) 7 infection† (50) 1 meningitis (7.1) 2 other‡ (14.2)
ACA (3)	60	9.0	13	0	533	1 clinical vasospasm (33.3)
MCA (8)	60	5.8	3	2 (25.0)	300	1 clinical vasospasm (12.5) 2 infection† (25) 4 meningitis (50)
Posterior circulation (12)	57	8.0	6.7	3 (25.0)	595	3 clinical vasospasm (25) 6 infection† (50) 1 meningitis (8.3) 1 other‡ (8.3)

†Infection included hospital-acquired infection with or without septicemia except bacterial meningitis; ‡Other complications included peripheral limb arterial occlusion, lung atelectasis, congestive heart failure and seizure. ACA – Anterior cerebral artery; AcoA – Anterior communicating artery; ICA – Internal carotid artery; MCA – Middle cerebral artery; PcoA – Posterior communicating artery; SAH – Subarachnoid hemorrhage

ICA aneurysm and AcoA aneurysm as date 6, and date 6.7, 4.5, and 3 in posterior circulation aneurysm, PcoA aneurysm, and MCA aneurysm, respectively. The results of intraoperative rupture of aneurysm during surgery were highest in AcoA aneurysm, followed by PcoA aneurysm, posterior circulation aneurysm, MCA aneurysm, and ICA aneurysm. None occurred in ACA aneurysm. Furthermore, Table 3 also shows the mean intraoperative blood loss and postoperative complications in each aneurysm location.

Relationship of shunt dependency to 1-year functional outcome

The proportion of patients who underwent shunt placement was significantly higher in the unfavorable outcome group than the favorable outcome group (36.5% vs. 17.1%; $P = 0.0039$).

Discussion

In this study of 221 patients who underwent surgical treatment of ruptured intracranial aneurysms, multiple factors were associated with 1-year outcome. Previous studies and meta-analyses have shown that neurological status is the strongest predictor of outcome after aSAH; other predictors include age, aneurysm repair modality, Fisher grade, hypertension, and aneurysm size and location.[7-10] Cognitive decline and memory deficit persist in patients with aSAH, even in those with good functional outcomes.[11-14] Clinical vasospasm is more frequent in poor-grade SAH patients; however, some studies could not demonstrate a significant relationship with outcome up to the individualized collateral flow of patients.[15,16]

Our analysis of patient and clinical characteristics according to the outcome group showed significant group differences in age, neurological status (Hunt and Hess grade), and aneurysm size. Patients in the favorable outcome group were younger, had smaller aneurysms, and lower Hunt and Hess grade. Patients in the favorable outcome group were predominantly Grades 2 and 3, whereas those in the unfavorable outcome group were predominantly Grades 3 and 4.

Aneurysm location also differed between the groups. The AcoA was the most common location in the favorable outcome group, whereas the PcoA was the most common in the unfavorable outcome group. Moreover, the proportion of patients with posterior circulation aneurysms, which may be associated with worse long-term outcome, was higher in the latter.

Furthermore, the unfavorable outcome group was analyzed, as shown in Table 3. The PcoA aneurysms were highest in this group, also carry the highest patients'

mean age. The mean aneurysm size was highest in ACA aneurysm, followed by PcoA aneurysm, but the difference in each group showed no statistically significant. Other factors (operation date after symptomatic SAH, number of aneurysms with intraoperative rupture, intraoperative blood loss, and postoperative complications) were also analyzed but did not show any statistically significant difference.

The proportion of patients who developed clinical vasospasm and shunt dependency was lower in the favorable outcome group. Previous studies have found that poor neurological status is associated with a higher amount of blood on CT at presentation and development of chronic hydrocephalus. In our institution, one of the neurosurgeons uses irrigation of Vitamin C solution (1000 mg in 0.5 L of normal saline) into the subarachnoid space intraoperatively; the proportion of patients who received Vitamin C irrigation was significantly higher in the favorable outcome group. The literature has shown mixed results of usage of Vitamin C in aSAH patients. *In vitro* studies found ascorbic acid (Vitamin C) suppressed the ability of Oxy-Hb to constrict cerebral arteries by conversion of oxyhemoglobin (Oxy-Hb) to verdoheme-like products.[17] However, some study shown significant reduction of clinical vasospasm in high grade subarachnoid hemorrhage (Fisher grading 3 and more) by using continuous irrigation of urokinase and ascorbic acid into subarachnoid space.[18,19] Our study used intraoperative irrigation of Vitamin C into subarachnoid space without thrombolytic agents. A better study design should be further evaluated the significance of Vitamin C irrigation to the outcome of aSAH patients.

Limitations

Several limitations of this study should be noted. First, the study was retrospective in design. Second, we did not evaluate cognitive and memory function, only GOS score. Although ruptured AcoA aneurysms are associated with worse functional outcome, particularly decreased cognitive and memory function, we found that these aneurysms were more common in the favorable outcome group. Third, we did not record data regarding vasospasm treatment and treatment outcome, which is associated with overall outcome and morbidity. However, the proportion of patients who developed clinical vasospasm did not significantly differ between the favorable and unfavorable outcome groups. Finally, subarachnoid space irrigation with Vitamin C solution was only performed by a single surgeon. Further study of Vitamin C irrigation is warranted.

Conclusions

Numerous factors analyzed in this study were significantly associated with 1-year outcome in surgically treated aSAH patients. Most are similar to those found in previous studies. Subarachnoid space irrigation with Vitamin C solution was significantly associated with favorable outcomes. However, due to the design limitations of this study, future prospective studies including various treatment interventions are required.

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Conflicts of interest

There are no conflicts of interest.

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