Clipping surgery for aneurysmal subarachnoid hemorrhage in patients aged 75 years or older

Tetsuyoshi Horiuchi, M.D. and Kazuhiro Hongo, M.D.

Department of Neurosurgery,

Shinshu University School of Medicine,

Matsumoto, Japan

Correspondence to:

Tetsuyoshi Horiuchi, M.D.

Department of Neurosurgery,

Shinshu University School of Medicine,

3-1-1 Asahi, Matsumoto 390-8621, Japan

Telephone: 81-263-37-2690

Fax: 81-263-37-0480

E-mail: tetuyosi@shinshu-u.ac.jp

Abstract

Object: The incidence rate of aneurysmal subarachnoid hemorrhage (SAH) in the elderly is increasing. Although endovascular coiling has become a major form of treatment for SAH in elderly patients, not all ruptured aneurysms can be managed with an endovascular approach. Conventional surgical clipping still plays an important role in SAH treatment. The present study was performed to assess the outcome in patients older than 75 years of age in whom ruptured aneurysms were treated by clipping surgery.

Methods: This retrospective study included patients 75 years of age or older who underwent clipping surgery for ruptured cerebral aneurysms between 1988 and 2009. Age, gender, preoperative grade, Fisher grade, size, and location of the ruptured aneurysm were compared between cases showing favorable and unfavorable outcomes.

Results: A total of 333 patients were analyzed. There were significant differences in preoperative grade, Fisher grade, and location of the aneurysm between the favorable and unfavorable outcome groups. In multivariate logistic regression analysis, independent predictors of unfavorable outcome were poor grade and ruptured anterior cerebral artery aneurysm, but not age of 80 years or older.

Conclusions: Advanced age did not represent a risk factor for poor outcome of clipping surgery in elderly patients. Although coil embolization has been shown to be a useful form of treatment, direct surgery should also be considered.

Running title: Clipping surgery of ruptured aneurysms in the elderly
Keywords: cerebral aneurysm, elderly, subarachnoid hemorrhage, surgery

Introduction

There are many problems associated with the aging populations in many developed countries. For example, doctors will encounter increasing numbers of elderly aneurysmal subarachnoid hemorrhage (SAH) patients.[1] Elderly SAH patients have more comorbid diseases and are often excluded from surgical treatment. However, the results of conservative treatments are often unsatisfactory. Several studies have suggested that surgical treatment is as effective in the elderly as in younger patients.[1-3] Recently, endovascular coil embolization for the elderly has emerged as a generally better-tolerated alternative to surgical clipping.[4-6] However, coil embolization cannot be performed in all elderly patients, *e.g.*, in those with severely tortuous vessels, kidney insufficiency, or allergic reaction to contrast medium. Clipping surgery is still a candidate for treatment of ruptured aneurysm in some elderly patients.

Here, we present the outcomes in patients aged 75 years and older treated with surgical clipping for ruptured aneurysms at Shinshu University Hospital and its affiliated hospitals. We also present the results of analysis of risk factors associated with unfavorable outcome.

Clinical Material and Methods

The study protocol was approved by the Ethics Committee of the Shinshu University School of Medicine.

From the SAH database of Shinshu University Hospital and its affiliated hospitals, we retrieved the data of patients who underwent the clipping surgery between 1988 and 2009 and were 75 years or older at the onset of SAH. Elderly patients treated with coil embolization were excluded from the present study. Glasgow Outcome Scale[7] evaluation was assigned at discharge, and cases were classified into the favorable outcome (good recovery and moderate disability) or unfavorable outcome (severe disability, vegetative state, and dead) groups. The two groups were compared on the basis of age, sex, preoperative grade, computed tomographic (CT) scan findings, and aneurysm location and size.

Clinical condition was assessed by the World Federation of Neurosurgical Societies (WFNS) Grading Scale for SAH.[8] We dichotomized clinical condition into good (WFNS I-III) and poor (WFNS IV and V). Based on CT scans, the bleeding severity was classified

according to the Fisher classification.[9] The ruptured aneurysm location was divided into internal carotid artery (ICA), anterior cerebral artery (ACA), middle cerebral artery (MCA), and vertebrobasilar artery (VBA) aneurysms. The aneurysm size was categorized into 4 groups: S (< 6 mm in diameter), M (6 – 15 mm), L (16 – 25 mm), and G (> 25 mm).

Data were extracted from the database and transferred into PASW Statistics 18 (SPSS Japan) for analysis. Continuous variables are expressed as means ± SD and were compared by the unpaired *t* test. Categorical variables were compared by Pearson's χ^2 test. In all analyses, $P < 0.05$ was taken to indicate statistical significance. Logistic regression analysis was also performed to determine the influence of the following factors on the occurrence of unfavorable outcome: advanced age (≥ 80 years), male gender, preoperative poor condition (WFNS grade IV or V), Fisher grade 4, larger aneurysm size (L or G), and ACA aneurysm.

Results

Of the total of 3313 patients in the database, 347 patients (10.5% of total patients) were aged 75 years or older. As there were no data regarding preoperative condition or outcome in 14 patients, the final study population consisted of 333 patients who underwent clipping surgery for ruptured aneurysm. The baseline characteristics of the elderly patients are shown in Table 1. The median age of the patients was 79.5 years (range 75 – 93 years) with a strong female predominance. The most commonly affected site was the ICA. Fisher 3 grade and medium-sized aneurysm were the most frequent in the elderly. One hundred seventy patients (51.1%) had favorable outcome at discharge.

There were significant differences in preoperative grade, CT findings, and aneurysm location between the favorable and unfavorable outcome groups (Table 2). In contrast, unfavorable outcome was not associated with patients' age, sex, or aneurysm size (Table 2). One hundred forty-seven of the 217 (67.7%) patients with good preoperative grade achieved favorable outcome compared to 23 of 116 (19.8%) with poor preoperative grade. Logistic regression analyses demonstrated that preoperative poor condition and ACA aneurysm were significantly related to unfavorable outcome in elderly patients (Table 3). In the subgroup analysis of ACA aneurysm, preoperative grade and CT scan findings were shown to affect the outcome (Table 4).

Discussion

In aneurysmal SAH patients who survive the initial ictus, the ruptured aneurysm is targeted for obliteration by surgical clipping or endovascular coiling to prevent re-rupture. The International Subarachnoid Aneurysm Trial (ISAT) study[10] compared clipping with coiling of ruptured aneurysms, and the results favored coiling at 1 year. This study resulted in an increase in endovascular management[4] and many centers are currently using coil embolization as the first treatment option in the majority of aneurysmal SAH cases. In contrast, Nilsson and colleagues[11] reported that introducing coil embolization did not have significant effects on outcome or complications. They concluded that the best outcome predictor was still the severity of SAH. These conclusions were also the same in elderly patients.[12] In addition, coil embolization was associated with significant increases in the hazard of death or subsequent readmission after aneurysm obliteration.[13]

Recently, in subgroup analysis of elderly patients in the ISAT, coil embolization was shown to achieve more favorable outcome than clipping in patients with internal carotid and posterior communicating artery aneurysm.[5] In contrast, clipping of ruptured MCA aneurysms appeared to excel compared with coiling.[5] In this subgroup analysis, the definition of elderly patients was those 65 years or older at ictus, and there were many patients with good preoperative grade and relatively small-sized aneurysms.[5] As both direct and endovascular treatments are necessary to obliterate various types of aneurysm, the optimal method should be selected based on several factors, including clinical conditions, aneurysm characteristics, and comorbidity conditions.

Although age is certainly a determinant of outcome after aneurysmal SAH,[14-16] surgical treatments often result in favorable outcome in some elderly patients, especially in those with good preoperative grade. [3,17,18] In the present study, advanced age was not associated with unfavorable outcome in elderly patients who underwent clipping surgery. Thus, age alone is not a contraindication to surgery. There is no question that preoperative neurological grade is the most important predictor of outcome. Therefore, in general, elderly patients with poor grade received conservative treatment. However, 23 of 116 (19.8%) patient with poor preoperative grade showed favorable outcome after direct surgery in the present study. This result indicated that surgical treatment may be suitable even in patients with poor grade because conservative treatments resulted in catastrophe.[19-21]

Although the ICA was the most commonly affected site in this study, previous reports[3,5,17,20] indicated that the most frequent site of ruptured aneurysm was the ACA in

elderly patients. Sakaki[22] found that aneurysms in older patients (≥ 65 years old) occur frequently in the vertebral, basilar, and anterior communicating arteries and less often in the ICA. These differences in location may have been due to patient age distribution because there are many definitions of the elderly in the literature.

Ruptured ACA aneurysm was a risk factor of unfavorable outcome in the present study. The majority of ACA aneurysms were anterior communicating artery aneurysms and were treated via the pterional approach (Table 4). Surgical approach was not associated with poor outcome in ruptured ACA aneurysm. In the elderly, internal carotid and posterior communicating artery aneurysm[23] or MCA aneurysm[19] were reported to be predictors of good outcome. ICA and MCA aneurysms may be more easily accessed than ACA aneurysms and clipped with minimal brain retraction because of the wide cistern due to brain atrophy. The brain becomes more fragile and its elasticity is lost due to aging. Memory disturbance and cognitive dysfunction are often observed in patients with ruptured anterior communicating artery aneurysm. These symptoms would be related to unfavorable outcome. These symptoms are most likely due to the initial brain damage, prolonged retraction of the frontal lobe, manipulation of the basal forebrain, and/or the injury of the perforating arteries. Coil embolization may reduce these symptoms without brain retraction and perforation injury. [24,25]

Although the aneurysm size has also been reported to be an important risk factor associated with outcome,[16] the results of the present study indicated no association between aneurysm size and poor outcome. Generally, in direct surgical treatment of large and giant aneurysms, more brain manipulation such as retraction and dissection may be needed to obtain a sufficient operative field, resulting in poor outcome. However, the majority of cases in the present study had small- or medium-sized aneurysms. Therefore, the size was not a risk factor of poor outcome in this study population.

Conclusions

In the present study, we analyzed the outcomes of 333 aneurysmal SAH patients aged 75 years or older. Our data indicated that poor preoperative grade and ACA aneurysm were independent risk factors of unfavorable outcome of clipping surgery.

Acknowledgments

We are grateful to all of the neurosurgeons of the University Hospital and its affiliated hospitals for maintaining the SAH database.

Table 1. Characteristics of the elderly patients.

		Age (years)		
	All	75-79	80-84	85-
No. of patients	333 (100)	192 (57.7)	109 (32.7)	32 (9.6)
Sex				
Female	274 (82.3)	154 (80.2)	93 (85.3)	27 (84.4)
Male	59 (17.7)	38 (19.8)	16 (14.7)	5 (15.6)
Preoperative grade (WFNS)				
Good (I-III)	217 (65.2)	117 (60.9)	75 (68.8)	25 (78.1)
Poor (IV, V)	116 (34.8)	75 (39.1)	34 (31.2)	7 (21.9)
Fisher grade				
1	14 (4.2)	8 (4.2)	6 (5.5)	0
2	56 (16.8)	30 (15.6)	22 (20.2)	4 (12.5)
3	182 (54.7)	109 (56.8)	54 (49.5)	19 (59.4)
4	81 (24.3)	45 (23.4)	27 (24.8)	9 (28.1)
Location of aneurysm				
ICA	130 (39.0)	73 (38.0)	47 (43.1)	10 (31.2)
ACA	93 (27.9)	56 (29.2)	25 (22.9)	12 (37.5)
MCA	89 (26.7)	54 (28.1)	27 (24.8)	8 (25.0)
VBA	21 (6.3)	9 (4.7)	10 (9.2)	2 (6.3)
Size of aneurysm				
Small (<6 mm)	129 (38.7)	74 (38.5)	43 (39.4)	12 (37.5)
Medium (6-15 mm)	170 (51.1)	98 (51.0)	56 (51.4)	16 (50.0)
Large (16-25 mm)	33 (9.9)	20 (10.4)	9 (8.3)	4 (12.5)
Giant (>25 mm)	1 (0.3)	0	1 (0.9)	0
Outcome at discharge				
Favorable (GR, MD)	170 (51.1)	91 (47.4)	63 (57.8)	16 (50.0)
Unfavorable (SD, VS, D)	163 (48.9)	101 (52.6)	46 (42.2)	16 (50.0)

Values are given as in n (%)

WFNS: World Federation of Neurosurgical Societies, ICA: internal carotid artery, ACA: anterior cerebral artery, MCA: middle cerebral artery, VBA: vertebro-basilar artery, GR: good recovery, MD: moderate disability, SD: severe disability, VS: vegetative state, D: dead

Table 2. Clinical relationship between favorable and unfavorable outcome of elderly patients who underwent clipping surgery for ruptured aneurysms.

	Outcome (%)		
	Favorable	Unfavorable	p Value (test)
No. of patients	170 (51.1)	163 (48.9)	
Mean age ± SD (years)	79.7 ± 3.7	79.3 ± 3.7	0.346*
Sex			0.543†
Female	142 (83.5)	132 (81.0)	
Male	28 (16.5)	31 (19.0)	
Preoperative grade (WFNS)			<0.001†
Good (I-III)	147 (86.5)	70 (42.9)	
Poor (IV, V)	23 (13.5)	93 (57.1)	
Fisher grade			<0.001†
1	12 (7.1)	2 (1.2)	
2	44 (25.9)	12 (7.4)	
3	91 (53.5)	91 (55.8)	
4	23 (13.5)	58 (35.6)	
Location of aneurysm			0.036†
ICA	74 (43.5)	56 (34.4)	
ACA	37 (21.8)	56 (34.4)	
MCA	45 (26.5)	44 (27.0)	
VBA	14 (8.2)	7 (4.3)	
Size of aneurysm			0.481†
Small (<6 mm)	65 (38.2)	64 (39.3)	
Medium (6-15 mm)	91 (53.5)	79 (48.5)	
Large (16-25 mm)	14 (8.2)	19 (11.7)	
Giant (>25 mm)	0	1 (0.6)	

* Unpaired t test.
† Pearson chi-square test.

Table 3. Odds Ratios for unfavorable outcome.

	Odds Ratio	P value	95% CI
Advanced age (80 years or older)	0.827	0.459	0.500-1.368
Male gender (versus female)	0.872	0.682	0.451-1.683
WFNS grade IV or V (versus grade I-III)	8.040	<0.001	4.434-14.579
Fisher grade 4 (versus grade 1-3)	1.478	0.238	0.772-2.828
Size L or G (versus S or M)	1.651	0.238	0.718-3.798
ACA aneurysm (versus other locations)	2.463	0.002	1.392-4.359

CI: confidence interval

Table 4. Clinical relationship between favorable and unfavorable outcome of elderly patients underwent clipping surgery for ruptured ACA aneurysms.

	Outcome (%)		
	Favorable	Unfavorable	p Value (test)
No. of patients	37 (39.8)	56 (60.2)	
Mean age ± SD (years)	78.9 ± 3.5	79.5 ± 3.7	0.692*
Sex			0.557†
Female	25 (67.6)	41 (73.2)	
Male	12 (32.4)	15 (26.8)	
Preoperative grade (WFNS)			0.025†
Good (I-III)	30 (81.1)	33 (58.9)	
Poor (IV, V)	7 (18.9)	23 (41.1)	
Fisher grade			0.039†
1	2 (5.4)	0	
2	8 (21.6)	6 (10.7)	
3	21 (56.8)	29 (51.8)	
4	6 (16.2)	21 (37.5)	
Size of aneurysm			0.499†
Small (<6 mm)	21 (56.8)	25 (44.6)	
Medium (6-15 mm)	14 (37.8)	28 (50.0)	
Large (16-25 mm)	2 (5.4)	3 (5.4)	
Location of ACA aneurysm			0.791†
ACD	7 (18.9)	9 (16.1)	
ACoA	29 (78.4)	44 (78.6)	
Others	1 (2.7)	3 (5.4)	
Surgical appraoch			0.755†
Interhemispheric approach	10 (27.0)	13 (23.2)	
Right pterional approach	13 (35.1)	24 (42.9)	
Left pterional approach	14 (37.8)	19 (33.9)	

ACD: distal anterior cerebral artery aneurysm, ACoA: anterior communicating artery aneurysm
* Unpaired t test.
† Pearson chi-square test.

References

1. Horiuchi T, Tanaka Y, Hongo K. Surgical treatment for aneurysmal subarachnoid hemorrhage in the 8th and 9th decades of life. Neurosurgery 2005;56:469-75.

2. Inagawa T. Management outcome in the elderly patient following subarachnoid hemorrhage. J Neurosurg 1993;78:554-61.

3. Inagawa T, Yamamoto M, Kamiya K, Ogasawara H. Management of elderly patients with aneurysmal subarachnoid hemorrhage. J Neurosurg 1988;69(3):332-339.

4. Gonzalez NR, Dusick JR, Duckwiler G, Tateshima S, Jahan R, Martin NA et al. Endovascular coiling of intracranial aneurysms in elderly patients: report of 205 treated aneurysms. Neurosurgery 2010;66:714-20.

5. Ryttlefors M, Enblad P, Kerr RS, Molyneux AJ. International subarachnoid aneurysm trial of neurosurgical clipping versus endovascular coiling: subgroup analysis of 278 elderly patients. Stroke 2008;39:2720-26.

6. Cai Y, Spelle L, Wang H, Piotin M, Mounayer C, Vanzin JR et al. Endovascular treatment of intracranial aneurysms in the elderly: single-center experience in 63 consecutive patients. Neurosurgery 2005;57:1096-102.

7. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1:480-484.

8. Beck DW, Adams HP, Flamm ES, Godersky JC, Loftus CM. Combination of aminocaproic acid and nicardipine in treatment of aneurysmal subarachnoid hemorrhage. Stroke 1988;19:63-67.

9. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery 1980;6:1-9.

10. Molyneux AJ, Kerr RS, Yu LM, Clarke M, Sneade M, Yarnold JA et al. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet 2005;366:809-17.

11. Nilsson OG, Saveland H, Ramgren B, Cronqvist M, Brandt L. Impact of coil embolization on overall management and outcome of patients with aneurysmal subarachnoid hemorrhage. Neurosurgery 2005;57:216-24.

12. Karamanakos PN, Koivisto T, Vanninen R, Khallaf M, Ronkainen A, Parviainen I et al. The impact of endovascular management on the outcome of aneurysmal subarachnoid hemorrhage in the elderly in Eastern Finland. Acta Neurochir (Wien) 2010;152:1493-502.

13. O'Kelly CJ, Kulkarni AV, Austin PC, Wallace MC, Urbach D. The impact of therapeutic modality on outcomes following repair of ruptured intracranial aneurysms: an administrative data analysis. Clinical article. J Neurosurg 2010;113:795-801.

14. Kassell NF, Torner JC, Haley EC, Jr., Jane JA, Adams HP, Kongable GL. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: Overall management results. J Neurosurg 1990;73:18-36.

15. Lanzino G, Kassell NF, Germanson TP, Kongable GL, Truskowski LL, Torner JC et al. Age and outcome after aneurysmal subarachnoid hemorrhage: why do older patients fare worse? J Neurosurg 1996;85:410-18.

16. Osawa M, Hongo K, Tanaka Y, Nakamura Y, Kitazawa K, Kobayashi S. Results of direct surgery for aneurysmal subarachnoid haemorrhage: outcome of 2055 patients who underwent direct aneurysm surgery and profile of ruptured intracranial aneurysms. Acta Neurochir (Wien) 2001;143:655-63.

17. Ferch R, Pasqualin A, Barone G, Pinna G, Bricolo A. Surgical management of ruptured aneurysms in the eighth and ninth decades. Acta Neurochir (Wien) 2003;145:439-45.

18. Hamada J, Hasegawa S, Kai Y, Morioka M, Fujioka S, Ushio Y. Surgery and long-term outcome for ruptured anterior circulation aneurysms in patients in their ninth decade of life. Surg Neurol 1999;52:123-26.

19. Hamada J, Morioka M, Miura M, Fujioka S, Marubayashi T, Ushio Y. Management outcome for ruptured anterior circulation aneurysms with a Hunt and Hess clinical grade of III in patients in the 9th decade of life. Surg Neurol 2001;56:294-300.

20. Fridriksson SM, Hillman J, Saveland H, Brandt L. Intracranial aneurysm surgery in the 8th and 9th decades of life: impact on population-based management outcome. Neurosurgery 1995;37:627-31.

21. Qu F, Aiyagari V, Cross DT, III, Dacey RG, Jr., Diringer MN. Untreated subarachnoid hemorrhage: who, why, and when? J Neurosurg 2004;100:244-49.

22. Sakaki S, Ohta S, Ohue S, Kohno K, Matsuoka K. Outcome in elderly patients with ruptured intracranial aneurysm. Clin Neurol Neurosurg 1989;91:21-27.

23. Yano S, Hamada J, Kai Y, Todaka T, Hara T, Mizuno T et al. Surgical indications to maintain quality of life in elderly patients with ruptured intracranial aneurysms. Neurosurgery 2003;52:1010-15.

24. Proust F, Martinaud O, Gerardin E, Derrey S, Leveque S, Bioux S et al. Quality of life and brain damage after microsurgical clip occlusion or endovascular coil embolization for ruptured anterior communicating artery aneurysms: neuropsychological assessment. J Neurosurg 2009;110:19-29.

25. Scott RB, Eccles F, Molyneux AJ, Kerr RS, Rothwell PM, Carpenter K. Improved cognitive outcomes with endovascular coiling of ruptured intracranial aneurysms: neuropsychological outcomes from the International Subarachnoid Aneurysm Trial (ISAT). Stroke 2010;41:1743-47.