

## Risk of Seizures after Operative Treatment of Ruptured Cerebral Aneurysms\*

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= Abstract =

뇌동맥류 파열 환자의 수술 후 경련발작의 위험인자

장인복 · 조병문 · 신동익 · 심영보 · 박세혁 · 오세문

**O**bjective : Postoperative seizure is a well documented complication of aneurysm surgery. The purpose of the present study was to analyze risk factors for postoperative seizure.

**Methods** : Between January 1990 and December 1996, we performed craniotomy for ruptured cerebral aneurysms in 321 patients. Among them 206 patients who could be followed up for more than 1 year (range, 1 to 4.6 years) were enrolled to present study. All patients were treated with anticonvulsants for 3 to 18 months postoperatively. We analyze the incidence of postoperative seizure in different sex and age groups, and risk factors associated with postoperative seizures following aneurysm rupture. For statistical processing chi - square test and Fisher's exact test were used.

**Results** : In the follow - up period of 1 to 4.6 years (mean, 1.8 years) postoperative seizure appeared in 18 out of 206 patients (8.7%). Mean latency between the operation and the first seizure was 6 months (range, 3 weeks to 18 months). The age of the patients has significant influence on the risk of seizure, it occurred more often in younger patients ( $p=0.0014$ ). Aneurysm location in the MCA was associated with a significantly a higher risk of seizure ( $p=0.042$ ). Eight patients (19%) out of 42 patients who suffered delayed ischemic neurologic deficit (DID) developed seizure. Delayed ischemic neurologic deficit was associated with significantly a higher risk of seizure ( $p=0.019$ ). Infarct and hypertension were associated with significantly a higher risk of seizure ( $p<0.05$ ). pre - or postoperative intracranial hematoma (intracerebral or epidural hematoma) was associated with significantly a higher risk of seizure ( $p<0.0001$ ). H - H grade, Fisher grade, Glasgow Outcome Scale of patients and timing of operation after subarachnoid hemorrhage had no significant relation with the risk of seizure.

**Conclusion** : Factors associated with the development of postoperative seizure were middle cerebral artery aneurysm, delayed ischemic neurologic deficit, infarct on late postoperative CT scan, hypertension, pre or postoperative intracranial hematoma (intracerebral or epidural hematoma). Identification of the risk factors may be help to focus the antiepileptic drug therapy in cases prone to develop seizures. Prospective evaluation is indicated.

**KEY WORDS** : Aneurysm surgery · Seizure · Subarachnoid hemorrhage.

### Introduction

Postoperative seizure is a well documented complication

of aneurysm surgery. Despite recent advances in the care of such patients, subarachnoid hemorrhage (SAH) due to ruptured intracerebral aneurysm continues to carry a high

rate of morbidity and mortality.

During the acute phase of SAH various factors can aggravate a patients good neurological state and every effort should thus be made to prevent such occurrences. The incidence of seizure after surgical treatment of ruptured cerebral aneurysms varied from 10 to 27% according to different investigators<sup>1)5)19)21)</sup>. Predisposing factors for seizures occurring at the onset of SAH have not been yet identified. Significant risk factors for seizure after aneurysmal SAH include poor neurological grade, delayed cerebral ischemia, location of the aneurysm in the middle cerebral artery(MCA), and the presence of a large intracerebral hematoma<sup>14)</sup>. Patients are often administered anti convulsants for a year or more after aneurysm surgery. Despite the routine use of various anticonvulsants therapy to decrease seizure frequency<sup>6)</sup>, it is not clear that anticonvulsants therapy prevents the development of postoperative seizure. The purpose of the present study was to analyze risk factors for postoperative seizure.

### Clinical materials and methods

Between January 1990 and December 1996, we performed craniotomy for ruptured cerebral aneurysms in 321 patients. Among them 206 patients who could be followed up for more than 1 year(1 to 4.6 years) were enrolled to present study. The data was collected retrospectively from medical records and radiographic studies. The outcome was established in the Glasgow Outcome Scale(GOS)<sup>13)15)</sup> and specially all events of seizures or equivalents of seizures were carefully noted. All patients underwent surgery as soon as the patients' condition and operating theater facilities allowed through pterional approach using microscope. All patients were treated with anticonvulsants for 3 to 18 months post-operatively. Main anticonvulsant was phenytoin ; however, valproic acids, carbamazepine, phenobarbital and primidone were substituted in patients showing side effects of phenytoin. Serum levels of anticonvulsants were usually but not routinely monitored. Seizure was diagnosed in those patients in whom two or more seizure attacks occurred independently of their clinical pattern. Previous hypertension(defined according to WHO criteria), neurological status, clinical severity quantified by the Hunt and Hess grade<sup>12)</sup> and Fisher's grade<sup>9)</sup> at admission were compared in patients with and without onset seizures. Postoperative vasospasm was treated with aggressive volume expansion, including

dextran, and induced hypertension. Use of nimodipine for three weeks and volume expansion therapy were also done routinely. Information was collected regarding aneurysm location, previous hypertension history, delayed ischemic neurologic deficit and infarct on pre- or post operation CT scan. We analyze the incidence of postoperative seizure in different sex and age groups, and risk factors associated with postoperative seizures following aneurysm rupture. For statistical processing chi-square test and Fisher's exact test were used.

### Results

In the follow-up period of 1 to 4.6 years(mean, 1.8 years) postoperative seizure appeared in 18 out of 206 patients, that is 8.7%. The seizures were classified as generalized in 14 patients(78%) and focal in 4 patients(22%). Serum levels of anticonvulsants of 15 patients(83%) out of 18 patients with postoperative seizure were checked at the time of first seizure attack and 11(73%) of them did not show effective therapeutic serum level. Mean latency between the operation and the first seizure was 6 months(range, 3 weeks to 18 months). There were nine females with seizure(7.4%) and nine males with seizure(10.6%). There was no statistical difference in sex ; however, age of the patients has significant influence on the risk of seizure, it occurred more often in younger patients( $p=0.0014$ , Table 1). Loca-

**Table 1.** Age of patients and seizure

Age(year)	No. of patients	No. of seizure patient
41 >	32	8
41 - 50	72	2
51 - 60	53	8
61 - 70	36	0
>70	14	0

$p=0.0014$

**Table 2.** Location of aneurysm and seizure

Location	No. of patients	No. of seizure patients(%)*
ICA	64	6( 9)
MCA	94	13(14)
ACoA	73	2( 3)
Distal ACA	9	-
VA	2	-
Multiple	32	2( 6)

\* : Number of the aneurysm is counted in each location  
 $p=0.042$

**Table 3.** Delayed ischemic neurologic deficit and seizure

DID	Seizure		Total
	Yes	No	
Yes	8	34	42
No	10	154	164
Total	18	188	206

p=0.019

**Table 4.** Infarct on postoperative CTscan and seizure

Infarct	Seizure		Total
	Yes	No	
Yes	13	68	81
No	5	120	125
Total	18	188	206

p=0.006

**Table 5.** Hypertension and seizure

Hypertension	Seizure		Total
	Yes	No	
Yes	8	37	45
No	10	151	161
Total	18	188	206

p=0.033

**Table 6.** Various clinical parameters and seizure

	No. of patients	No. of seizure patients(%)
H-H Grade	18	2(11)
	101	8( 8)
	63	6(10)
	21	1( 5)
	3	1(33)
Fisher Grade	11	0( 0)
	95	8( 8)
	73	8(11)
	27	2( 7)
Glasgow outcome scale	138	12(9)
	35	2( 8)
	25	2( 8)
	6	1(17)
	2	1(50)

p>0.05

tion of aneurysm and the risk of seizure is shown in Table 2 Aneurysm location in the MCA was associated with significantly a higher risk of seizure(p=0.042).

Eight patients(19%) out of 42 patients who suffered

**Table 7.** Pre- or postoperative intracranial hematoma(EDH or IDH) and seizure

Hematoma	Seizure		Total
	Yes	No	
Yes	7	4	11
No	11	184	195
Total	18	188	206

p<0.0001

**Table 8.** Timing of the operation and seizure

Days after SAH	Seizure	
	Yes	No
0 - 3	55	5(9)
4 - 7	6	0(0)
> 8	145	13(9)
Total	206	18(9)

p=0.019

delayed ischemic neurologic deficit(DID) developed seizure. Delayed ischemic neurologic deficit was associated with significantly a higher risk of seizure(p =0.019, Table 3). Infarct on follow-up postoperative CT scan was associated with significantly a higher risk of seizure(p=0.006, Table 4). Hypertension was associated with significantly a higher risk of seizure(p=0.033, Table 5). Table 6 illustrates the risk of seizure in each grade of H-H grade, Fisher grade and Glasgow Outcome Scale of patients respectively. No significant differences were found between each grade in these parameters.

Table 7 reveals that pre- or postoperative intracranial hematoma (intracerebral or epidural hematoma) was associated with significantly a higher risk of seizure(p<0.0001). Timing of operation after subarachnoid hemorrhage had no significant relation with the risk of seizure(Table 8).

## Discussion

The problem of prophylactic anticonvulsant treatment after aneurysmal surgery is still controversial. Several reports dealing with this problem give in many cases different conclusions and, moreover, usually can not be compared due to many factors. Older series report the incidence of seizure after the surgical treatment of ruptured aneurysms to be 10 to 27%<sup>1)5)19)21)</sup>. Advances in aneurysm surgery over the last 20 years have greatly reduced the risk of parenchymal injury during aneurysm clipping. North et al.<sup>17)18)</sup> and Matthew et al.<sup>16)</sup> independently concluded that phenytoin decreased seizure incidence from 15 to 10% over placebo

in a group of patients who underwent craniotomies. In our series, the incidence of seizure was 8.7%(Table 6), comparable with studies previous reported<sup>14</sup>. This may be a result of improvement in surgical and anesthetic techniques including the use of the microscope, better medication against spasm, and the routinely given prophylactic anticonvulsant medications. Risk factors have been identified for postoperative epilepsy after aneurysm clipping. Not unexpectedly, factors indicative of parenchymal brain damage are most important, including the presence of intracerebral hematoma<sup>5)10</sup>, resection of gyrus<sup>5</sup>, medial temporal retraction<sup>22</sup>, and persistent major postoperative neurologic deficit<sup>19</sup>. MCA aneurysm are reported to have a much higher risk of postoperative epilepsy than other aneurysm<sup>3)14</sup>, particularly if a postoperative deficit indicating parenchymal brain damage persist. In our series, 13 out of the 94 patients (14%) who developed seizure had an MCA aneurysm as compare with 10 patients who developed seizure in the non-MCA aneurysm group : 6 out of 64(9%), 2 out of 73(3%) and 2 out of 32(6%) ( $p=0.042$ ) (Table 2). The Hunt-Hess grade in the study reported here was not a significant factor in relation to risk of seizure. This finding is in accordance with that reported by Foy et al.<sup>10</sup>. Even in patients with poor grades(grade to ), no significant increase in the frequency of postoperative seizure was evident. Delayed cerebral ischemia has been documented as a risk factor for seizure after an SAH<sup>10)14)24</sup>. The greater incidence of infarcts seen in the follow-up CT scans of the seizure patients as compared with those of the non-seizure group ( $p=0.006$ ) demonstrates the effect of delayed cerebral ischemia in relation to the development of seizure (Table 4). Systemic hypertension is well-known risk factor for increased mortality and morbidity after aneurysmal SAH. Patients with raised systemic blood pressure on admission to a hospital after an SAH are less likely to have good outcomes than normotensive patients<sup>2)7)24</sup>, but a mere history of hypertension does not significantly affect the outcome<sup>7</sup>. In our series, a history of hypertension was clearly associated with the development of seizures after the aneurysmal surgery (Table 5). The correlation between hypertension and cerebral infarction can be reasonably explained but was not overtly predicted in this study, and therefore requires independent confirmation from further studies. The risk of seizure was higher in younger patients of our series and in the group of patients observed by Fabinyi et al.<sup>8</sup>) (Table 1). In Öhman's series<sup>24</sup>) a significant

severe disability at discharge was also found in SAH subjects who sustained seizure, while in the series of Hart et al.<sup>11</sup>) no correlation was found either with severe disability at discharge or death. The problem of prophylaxis is additionally complicated, as in many reports patients received prophylactic anticonvulsant treatment, sometimes started before operation<sup>4)6</sup>. The treatment was continued for various period, from 2 - 3 months to several years and with different antiepileptic drugs<sup>23</sup>). Our study does not specifically address the issue of prophylaxis ; however, given in the relatively high rate of seizures, the data support the contention that antiepileptic drugs following surgery for ruptured aneurysms are indicated at least in the patients with any of these risk factors identified. The long-term use of anticonvulsant medication to prevents postoperative seizure in these individuals has been accepted medical practice<sup>20</sup>). Despite the routine use of these medication to decrease seizure frequency, it is not clear that anticonvulsant therapy prevents the development of postoperative epilepsy.

## Conclusion

The risk of seizure after aneurysmal surgery probably tends to decrease with improvement in surgical technique and perioperative medication. Factors associated with the development of postoperative seizure were middle cerebral artery aneurysm, delayed ischemic neurologic deficit, infarct on late postoperative CT scan, hypertension, pre or postoperative intracranial hematoma (intracerebral or epidural hematoma). Identification of the risk factors may be help to focus the antiepileptic drug therapy in cases prone to develop seizures. Prospective evaluation is indicated.

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### 뇌동맥류 파열 환자의 수술후 경련발작의 위험인자

장인복 · 조병문 · 신동익 · 심영보 · 박세혁 · 오세문

= 국문초록 =

목적 : 본 연구의 목적은 뇌동맥류 파열 환자의 수술 후 경련발작의 위험인자를 규명하는 것이다.

방법 : 1990년 1월 1일부터 1996년 12월 31일까지 321명의 뇌동맥류 파열 환자를 대상으로 하였다. (1990년 4.6명, 1991년 206명, 1992년 31명, 1993년 18명, 1994년 13명, 1995년 10명, 1996년 16명)

결과 : Hunt-Hess grade, Fisher grade, Glasgow Outcome Scale, Seizure Scale, Chi-square test, Fisher's exact test

결과 : 본 연구에서 Hunt-Hess grade 1.8, Fisher grade 2.06, Glasgow Outcome Scale 18, Seizure Scale 8.7%로 나타났다. (19%)

결론 : 본 연구에서 Hunt-Hess grade, Fisher grade, Glasgow Outcome Scale, Seizure Scale의 위험인자를 규명하였다.

중심 단어 : 뇌동맥류 파열, 수술 후 경련발작, 위험인자