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Risk Factors of Seizures Associated with the Management of Ruptured Cerebral Aneurysms

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ABSTRACT

Objective : This study was designed to to analyze the associated risk factors of seizure after aneurysmal subarachnoid hemorrhage (SAH) for providing guidelines of prophylactic antiepileptic drug administration. **Method** : We retrospectively reviewed the programmed clinical database and radiographic findings of the patients with aneurysmal SAH who were treated from March 1996 to August 2004 and followed up for more than one year. **Result** : A total of 512 patients were enrolled. 20 patients (3.9%) presented with seizures. Aneurysm location and size were not associated with seizures. The incidence of seizure was significantly different in the Hunt & Hess Grade IV patients (8.6%) and V patients (23.1%). Fisher Grade IV was associated with a significantly higher risk of the seizure (12.2%). The incidence of seizure was higher in patients with hydrocephalus (6.7%), intracerebral hematoma (8.8%), and decompressive lobectomy (14.3%). **Conclusion** : The overall incidence of seizures was 3.9%. Risk factors of seizures were poor clinical grade (Hunt &Hess Grade IV and V), higher Fisher Grade (IV), hydrocephalus, intracerebral hematoma, and decompressive lobectomy. **(Kor J Cerebrovascular Surgery 8:10-4, 2006)**

KEY WORDS : Seizure · Subarachnoid hemorrhage · Cerebral aneurysm

Introduction

Post-operative seizures are well-known complications of ruptured cerebral aneurysm, but incidence and risk factors have differed among reports.[11) 15) 16) 22) 25) 27-31) 33) 36)] The reported risk of seizure after surgery for ruptured cerebral aneurysms has varied between 3% and 27.5%.[1-6)8-16)19-26)29-36)] Such inconsistency may be due to different criteria for patient selection, variable follow-up periods, and different timing and methods of surgery.

Post-operative seizure after ruptured cerebral aneurysm is well-established. The effect of craniotomy, however, has not been well evaluated.[1)5)8)15)16)18)19)26)30)] Additionally, there are few reports of seizures after coil embolization for ruptured cerebral aneurysm.[4)]

The use of anti-epileptic drug (AED) after aneurysmal surgery is common, but treatment duration, efficacy, and scientific support for AED usage are not well-established.[2)7)30)31)35)]

This study was designed to find the risk factors of seizures after aneurysmal surgery, and to provide guideline for prophylactic AED administration.

Materials and Methods

Aneurysmal SAH patients, treated from March 1996 to August 2004, were reviewed retrospectively. Patients who were not followed for at least one year or who had a previous history of seizure or epilepsy were excluded. Variables included age, sex, Hunt-Hess grade, Fisher grade, aneurysm location, delayed ischemic neurological deficit (DIND), hydrocephalus, intracerebral hemorrhage (ICH), cerebral infarct, and decompressive lobectomy. The Chi-Square test was used for univariate analyses, and Fisher's Exact Test was used when the population is too small so that

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Chi-Square Test is not appropriate. The parameters proved to be statistically significant in univariate analyses were re-analyzed by multivariate logistic regression analysis. Statistical significance was defined as a p-value less than 0.05.

Results

A total of 512 patients were enrolled. 189 patients were male, and the male to female ratio was 1:1.8. The mean age was 48.2 years, and the mean follow-up period was 50.1 months. The mean duration of AED usage was 12 months. 451 patients were treated with aneurysmal neck clipping and 61 patients with coil embolization of the aneurysm. Among the 512 patients, 20 patients (3.9%) presented with seizures.

The incidence of seizure was 4.2% in the group of age younger than 40 year old, 4.8% in the age of fifties, 3.6% in the sixties, and 4.1% in the seventies. There was no significant difference of seizure incidence between different age groups (Table 1). Table 2 shows the locations of the ruptured cerebral aneurysms. The incidence of seizure was 3.5% in the group of internal carotid artery (ICA) aneurysm, 5.0% in the group of middle cerebral artery (MCA) aneurysm, 4.2% in the group of anterior communicating artery (AComA) aneurysm, and 2.8% in the vertebrobasilar artery aneurysm. In case of the ruptured aneurysms in the MCA and AComA, the incidence of seizure was slightly higher than others but statistically not significant. The incidence of seizure was 3.7% in the group of small aneurysm (smaller than 5 mm in diameter), 3.8% in the group of the aneurysm size from 6 mm to 10 mm, and 5.6% in those with large aneurysm (larger than 10 mm). Aneurysm size was not related to seizure occurrence (Table 3). None of patients in the Hunt-Hess Grade I showed seizure. 1.2% of the patients In Grade II, 3.8% in Grade III, 8.6% in Grade IV, and 23.1% in Grade V had seizures. Higher Hunt & Hess Grade had higher incidence of seizures significantly (Table 4). The Amount of SAH affected the incidence of seizures; 2.5% in Fisher Group I, 1.3% in Group II, 3.3% in Group III. Fisher Group was significantly associated with the risk of seizure (9 of 74 patients in Group IV, 12.2%) (Table 5). Table 6 reveals the relationship between the various clinical parameters and seizures. Six of 85 patients (7.1%) with DIND had seizures, however, it was not statistically significant. Among 194 patients with hydrocephalus, 13 patients (6.7%) developed seizures. Hydrocephalus was

Table 1. Age distribution and seizure

Age (years)	No. of seizure patients / No. of total patients (%)
<39	3 /71 (4.2)
40~49	6 /124 (4.8)
50~59	7 /193 (3.6)
60~69	4 /98 (4.1)
>70	0 /26 (0)

*Univariate analysis by Fisher's Exact Test ; p-value=0.9233

Table 2. Aneurysm location and seizure

Location	No. of seizure patients / No. of total patients (%)
ICA	5 / 142 (3.5)
MCA	7 / 139 (5.0)
Acom	7 / 168 (4.2)
Distal ACA	0 / 17 (0)
VA-BA	1 / 36 (2.8)
PCA	0 / 10 (0)

*Univariate analysis by Fisher's Exact Test ; p-value=0.9773

Table 3. Aneurysm size and seizure

Size (mm)	No. of seizure patients / No. of total patients (%)
≤5	5 / 135 (3.7)
6~10	13 / 341 (3.8)
>10	2 / 36 (5.6)

*Univariate analysis by Chi-Square Test ; p-value=0.8678

Table 4. Hunt-Hess grades and seizure

H-H grade	No. of seizure patients / No. of total patients (%)
I	0 / 37 (0)
II	2 / 169 (1.2)
III	8 / 212 (3.8)
IV	7 / 81 (8.6)
V	3 / 13 (23.1)

*Univariate analysis by Fisher's Exact Test ; p-value=0.0026

Table 5. Fisher grades and seizure incidence

Fisher grade	No. of seizure patients / No. of total patients (%)
1	1 / 40 (2.5)
2	2 / 154 (1.3)
3	8 / 244 (3.3)
4	9 / 74 (12.2)

*Univariate analysis by Fisher's Exact Test ; p-value=0.0032

related to a significantly higher risk of seizure. In patients with ICH, the incidence of seizure was also significantly higher (8.7%). Patients with cerebral infarct present high incidence of seizure (3 of 23, 13.0%). Although the difference was proved to be not statistical significant due to small population (p-value;0.0206 in Chi-Square Test versus 0.0547 in Fisher's Exact Test), it was thought to be associated with seizures. Among 451 patients treated surgically, 34 patients received decompressive cerebral lobectomy. In these patients, 5 (14.7%) presented with seizures, and lobectomy was associated with a significantly higher seizure risk. Interestingly, none of the 61 patients treated with endovascular coil embolization had any seizures. But, the endovascular procedures was not associated with seizure risk regardless of age-sex matched correction. With significant factors in univariate analyses (Hunt-Hess grade, Fisher grade, Hydrocephalus, ICH, decompressive lobectomy), multivariate logistic regression analysis was performed, and Hunt-Hess grade was only statistically significant risk factor (Table 7).

Discussion

Seizures after aneurysmal SAH are a well-known complication, but the incidence and risk factors of seizures vary among previous reports.[11)15)16)22)25)27-31)33)36)] These inconsistencies may be associated with differences in the definition of seizure or epilepsy, follow-up period, or patient population. Nonetheless, the incidence of seizures has declined from 10~27%[5)29)32)] before 1976, to 3~10% more recently.[2)11)15)22)28)30)33)34)35)] This change may be due to more advanced microsurgical techniques, AEDs, anesthetic methods, and the evolution of management programs.

Seizure risk factors also vary among reports. The following have all been reported as risk factors: younger age, middle cerebral artery aneurysms, intracerebral hematoma, poor initial clinical grade, postoperative focal neurological deficit due to cortical infarction, rebleeding, intra-operative damage including medial temporal lobe retraction, resection of the gyrus, history of seizures, persistent post-operative deficit, shunt-dependent hydrocephalus, EEG abnormality, multiple lesions, duration of coma, hypertension, amount of subarachnoid hemorrhage, wrapping technique, and onset seizure.[1-6)8-16)19-26)29-36)] A number of factors are mentioned in many reports, but some are reported in only one.

In this study, seizures were associated with Hunt-Hess grade, Fisher grade, hydrocephalus, intracerebral hematoma, and decompressive lobectomy. Patients with cerebral infarct were so few that it did not show statistical significance, but it is thought to be correlated with seizures. These showed that

Table 6. Various parameters and seizure incidence

Parameters	No. of seizure patients / No. of total patients (%)	P-value
DIND	6 / 85 (7.1)	0.1206*
Hydrocephalus	13 / 195 (6.7)	0.0115**
ICH	6 / 69 (8.7)	0.0399*
Infarct	3 / 23 (13.0)	0.0547*
Lobectomy	5 / 34 (14.7)	0.0072*
Endovascular Tx.	0 / 61 (0)	0.2357*

DIND : delayed ischemic neurological deficit, ICH : Intracerebral hemorrhage, Tx. : Treatment *Univariate analysis by Fisher's Exact Test, **Univariate analysis by Chi-Square Test

Table 7. Multivariate logistic regression analysis of risk factors associated with seizures

Parameters	Estimate	Standard Error	Odds Ratio	95% CI	p-value
Hunt-Hess Grade	-0.5333	0.2339	0.587	0.371-0.928	0.0226
Fisher Grade	-0.6609	0.4370	0.516	0.219-1.216	0.1304
Hydrocephalus	-0.7609	0.5039	0.468	0.174-1.255	0.1313
ICH	0.3361	0.7137	1.399	0.346-5.668	0.6377
Lobectomy	-1.0345	0.6107	0.355	0.107-1.176	0.0903

CI : Confidence Interval, ICH : Intracerebral hemorrhage

seizures after aneurysmal SAH seemed to be closely related to secondary cortical damage. Patients with middle cerebral artery aneurysms had a relatively higher incidence of seizure, although the difference was not statistically significant. Age was not associated with seizure.

Although, Byrne et al, reported that endovascular procedure seemed to have relatively low risk of seizure due to low risk of cortical injury,[4] there are many obstacles and biases that complicate the comparison of patients treated with endovascular coil embolization or surgery. In this study, despite of no seizure with patients treated by endovascular procedures, endovascular procedures is proved not to be associated with seizure risk. Age-sex matched correction did not affect the result. A larger, randomized, well-planned study is needed to conclude whether endovascular procedures are associated with low seizure risk, compared that associated with surgery.

There are many controversies surrounding the prophylactic use of AEDs in cases of aneurysmal SAH, and regimens vary in different centers.[2)7)30)31)35)] Many authors argue that long-term prophylaxis should be restricted. Byrne et al. discourage prophylactic AED prescription and argue that it is unnecessary, especially in patients treated solely with coil embolization.[1)2)4)12)] Such restrictions seem well advised, given the lower incidence of seizures in recent reports. Our study also supports reducing AED prophylaxis, although not decisively.

Conclusions

The significant risk factors associated with seizures following aneurysmal SAH were poor initial Hunt-Hess grade (IV and V), poor Fisher grade (IV), hydrocephalus, intracerebral hematoma, and decompressive lobectomy. Among these, Hunt-Hess grade was the only high risk factor proven by multivariate regression logistic analyses. Long-term prescription of prophylactic AED was restricted to the high-risk patients, as characterized in this study.

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