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Clinical Article

Treatment of Unruptured Intracranial Aneurysms in South Korea in 2006 : A Nationwide Multicenter Survey from the Korean Society of Cerebrovascular Surgery

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Objective : There have been no clinical studies regarding the epidemiology and treatment outcome for unruptured intracranial aneurysm (UIA) in South Korea yet. Thus, The Korean Society of Cerebrovascular Surgery (KSCVS) decided to evaluate the clinical and epidemiological characteristics, and outcome of the treatment of UIA in 2006, using the nationwide multicenter survey in South Korea.

Methods : A total of 1,696 cases were enrolled retrospectively over one year at 48 hospitals. The following data were obtained from all patients : age, sex, presence of symptoms, location and size of the aneurysm, treatment modality, presence of risk factors for stroke, and the postoperative 30-day morbidity and mortality.

Results : The demographic data showed female predominance and peak age of seventh and sixth decades. Supraclinoid internal carotid artery was the most common site of aneurysms with a mean size of 5.6 mm. Eight-hundred-forty-six patients (49.9%) were treated with clipping, 824 (48.6%) with coiling, and 26 with combined method. The choice of the treatment modalities was related to hospital (p = 0.000), age (p = 0.000), presence of symptom (p = 0.003), and location of aneurysm (p = 0.000). The overall 30-day morbidity and mortality were 7.4% and 0.3%, respectively. The 30-day mortality was 0.4% for clipping and 0.2% for coiling, and morbidity was 8.4% for clipping and 6.3% for coiling. Age (p = 0.010), presence of symptoms (p = 0.034), size (p = 0.000) of aneurysm, and diabetes mellitus (p = 0.000) were significant prognostic factors, while treatment modality was not.

Conclusion : This first nation-wide multicenter survey on UIAs demonstrates the epidemiological and clinical characteristics, outcome and the prognostic factors of the treatment of UIAs in South Korea. The 30-day postoperative outcome for UIAs seems to be reasonable morbidity and mortality in South Korea.

KEY WORDS : Aneurysm · Intracranial · Unruptured · National survey · Korea · Multicenter study · Treatment outcome.

INTRODUCTION

The prevalence of unruptured intracranial aneurysms (UIAs) has been reported to be between 1 and 6% in general population, depending on the study cited[3,7,13]. Most UIAs remain asymptomatic until they rupture and cause subarachnoid hemorrhage (SAH) with an annual incidence of 6-8/100,000 person years in the most recent studies[8]. The estimated mortality rate in the first 30 days post-SAH is in the range of 40 to 50%, and almost half of the survivors will be left with a neurologic deficit[2], despite the advances of modern medical and surgical management. The natural history of UIA including annual risk of bleeding has been debated and the best management of patients with asymptomatic intracranial aneurysms is also currently

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uncertain. New data from the second part of the International Study of UIA showed rupture rates in the range of 0.5-3% per annum. Any prophylactic treatment to prevent future aneurysm rupture should therefore be very safe.

No reliable nationwide clinical data for the treatment of UIA has been available in South Korea yet. The Korean Society of Cerebrovascular Surgery (KSCVS) was founded in 1986, and the role played by the KSCVS in this area has been increasingly important, because the incidence of UIAs increased steadily owing to the advances of noninvasive imaging of the brain and the increase of the aging population. The first nationwide multicenter survey on the treatment of UIA was performed in 2007 for the patients treated over one year in 2006 by KSCVS.

The purpose of this study was to identify the clinical and epidemiological characteristics of the treatment of UIA in Korea, using this survey data.

We further expect that we could understand UIA treatment outcome in Korea systematically and precisely through this data. This understanding could hopefully make treatment outcome of the UIA better in South Korea.

MATERIALS AND METHODS

All the patients included in this study was newly diagnosed as UIA and treated with clipping, coiling or both during 1 year period from January 1 to December 31, 2006, at hospitals in South Korea. Nationwide, 48 hospitals participated in this project. Forty-one hospitals were university hospitals. The participating hospitals were evenly distributed across the central, southeastern and southwestern part of the Korean peninsula. All data were collected retrospectively from participating hospitals in the form of recorded UIA registration sheets, which included following variables; age, sex, presence of symptoms, location and size of the aneurysm, treatment modality, presence of risk factors for stroke, such as hypertension, diabetes mellitus, smoking, and family history of stroke, and the postoperative 30-day outcome. The numerical continuous variables such as age and size of the aneurysm were categorized into 7 in age, and 6 in size of the aneurysm for statistical analysis. The 30-day clinical outcome was also classified into four categories : good recovery without deficits, mild disability, severe disability, and death. Statistical analysis was performed using SPSS version 15.0 for Windows (SPSS Inc. Chicago, IL, USA). Chi-square test was applied to evaluate the significance of difference in categorical variables in the univariate analysis, and logistic regression in the multivariate analysis. A value of $p < 0.05$ was regarded as statistically significant.

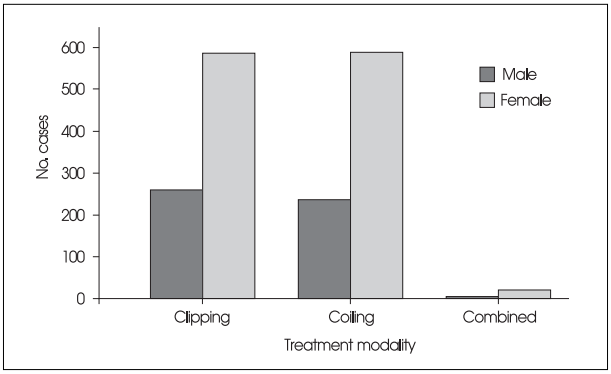

Fig. 1. Gender of patients with unruptured intracranial aneurysm according to treatment modality. Female patients are predominantly included in this survey in each treatment modality.

RESULTS

Patient characteristics

The 1,696 patients were enrolled in this survey. The 1,696 patients included 499 men (29.4%) and 1,197 women (70.6%) (Fig. 1). Most patients were in their seventh (n =

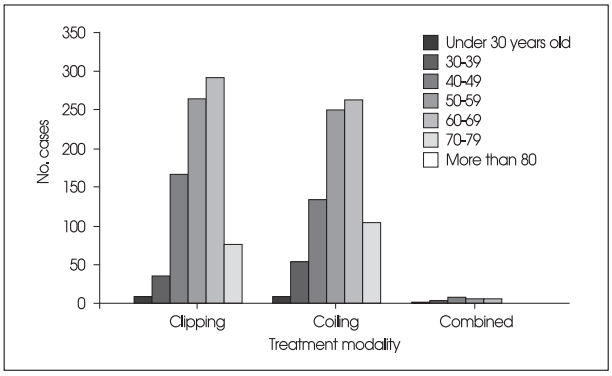

Fig. 2. Age distribution of patients with unruptured intracranial aneurysm according to treatment modality. Regardless of treatment modality, most patients are in their seventh and sixth decades of life.

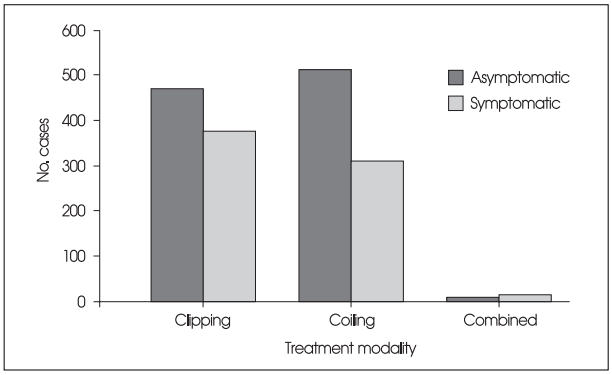

Fig. 3. Clinical presentation of patients with unruptured intracranial aneurysm according to treatment modality. Symptomatic lesions, such as cranial neuropathy due to mass effect, headache, dizziness, and coincidence to other ruptured aneurysms are 41.4%, and asymptomatic lesions, such as detection from the health care exam and incidental findings on MRA or CTA are 58.6%.

Table 1. Participating hospitals and treatment modality

Hospital no.	Area	No. of patients			Total
		Clipping	Coiling	Combined	
1	C	66	135	2	203
2	C	38	119	4	161
3	C	101	46	0	147
4	C	72	49	0	121
5	C	57	46	1	104
6	SE	10	66	2	78
7	C	42	28	0	70
8	SE	28	32	0	60
9	SE	45	11	0	56
10	C	19	37	0	56
11	C	10	42	1	53
12	SE	26	21	2	49
13	SE	36	8	0	44
14	SW	31	9	0	40
15	C	26	12	0	38
16	C	18	12	4	34
17	C	20	12	1	33
18	SW	22	4	0	26
19	C	4	19	1	24
20	C	1	20	1	22
21	SE	8	11	2	21
22	C	12	8	1	21
23	SW	18	2	0	20
24	C	3	15	2	20
25	C	11	7	0	18
26	C	14	4	0	18
27	C	6	10	0	16
28	C	3	11	0	14
29	SE	11	1	0	12
30	C	10	0	1	11
31	SE	10	0	0	10
32	C	6	4	0	10
33	C	10	0	0	10
34	SE	9	0	0	9
35	SE	9	0	0	9
36	C	7	0	0	7
37	C	0	7	0	7
38	SW	6	0	0	6
39	C	2	4	0	6
40	C	4	0	1	5
41	C	3	2	0	5
42	C	2	2	0	4
43	C	2	2	0	4
44	C	2	2	0	4
45	C	3	0	0	3
46	C	2	1	0	3
47	C	1	1	0	2
48	C	0	2	0	2
Total		846	824	26	1,696

C : central, SE : southeast, SW : southwest

560, 33.0%) and sixth (n = 521, 30.7%) decades of life, followed by the fifth, eighth, fourth decades of life (Fig. 2). Symptomatic lesions, such as cranial neuropathy due to mass effect, headache, dizziness, and coincidence with other ruptured aneurysms were 702 (41.4%) and asymptomatic lesions, such as detection from the health care survey and incidental findings on MRA or CTA were 994 (58.6%) (Fig. 3). The hospitals treating more than100 patients per year were 5, and the mean number of patients treated per hospital was 35.3 with a range from 2 to 203 (Table 1). Many patients had stroke risk factors; history of hypertension in 850 (50.1%), diabetes mellitus in 185 (10.9%), smoking in 238 (14.0%), and family history of stroke in 210 patients (12.4%) (Table 2).

Characteristics of the aneurysms and treatment modalities

The location of the aneurysms were internal carotid artery (ICA) in 647 (38.1%), middle cerebral artery (MCA) in 445 (26.2%), anterior cerebral artery (ACA) in 272 (16.0%), and vertebro-basilar artery (VA-BA) in 153 patients (9.0%) (Fig. 4). Multiple aneurysms were 166 (10.3%). The mean size of the aneurysms was 5.6 mm. One-thousand-twenty-two aneurysms (60.3%) were less than 5 mm in size, 512 were from 6 to 10 mm, and 108 were from 11 to 15 mm (Fig. 5). The number of intracranial aneurysms treated during the same period was 5,229 and the ruptured to unruptured ratio was 68 : 32. The treatment modality was clipping for 846 patients (49.9%), coiling for 824 (48.6%) and combined for 26. The proportion of coiling to clipping was 0.97. For five hospitals treating more than 100 cases, the average proportion of coiling to clipping was 1.18,

which was higher than the overall average. The choice of the treatment modalities in unruptured aneurysm was related to patients' age, symptom, and location with statistical significance. However, sex and size of aneurysm were not significant factors for choosing the treatment modality. Coiling was also preferred for older (p = 0.000) and asymptomatic (p = 0.003) patients. Aneurysm location did influence on the selection of treatment modality. Aneurysms located on the internal carotid artery and vertebrobasilar artery were treated more frequently with coiling, whereas aneurysms on the anterior cerebral artery and middle cerebral artery were treated more frequently with clipping (p = 0.000).

Table 2. Risk factors for stroke according to the treatment modalities

Risk factors	No. of patients (%)			Overall
	Clipping	Coiling	Combined	
Hypertension	427 (50.5)	358 (43.4)	12 (46.2)	797 (47.7)
Diabetes mellitus	86 (10.2)	96 (11.7)	3 (11.5)	185 (10.4)
Smoking	105 (12.4)	126 (15.2)	7 (26.9)	238 (15.0)
Family history of stroke	112 (13.1)	96 (11.7)	2 (7.7)	210 (12.8)

Table 3. Clinical outcome according to the treatment modalities

Clinical outcome	No. of patients (%)			Overall
	Clipping	Coiling	Combined	
Good recovery	775 (91.6)	772 (93.7)	24 (92.3)	1,571 (92.6)
Mild disability	57 (6.7)	42 (5.1)	2 (7.7)	101 (6.0)
Severe disability	11 (1.3)	8 (1.0)	0	19 (1.1)
Death	3 (0.4)	2 (0.2)	0	5 (0.3)
Total	846	824	26	1,696

Postoperative 30-day outcome and prognostic factors

The overall 30-day morbidity and mortality were 7.4% and 0.3%, respectively. The 30-day mortality was 0.4% for clipping and 0.2% for coiling, and overall morbidity including mortality was 8.4% for clipping and 6.3% for coiling (Table 3). While patient's age (p = 0.016), symptomatic lesion (p = 0.008), size of the aneurysm (p = 0.000), and smoking (p = 0.043) were the significant prognostic factors for postoperative 30-day outcome in univariate analysis, age (p = 0.012), symptomatic lesion (p = 0.008), size (p = 0.001) of the aneurysm and diabetes mellitus (p = 0.004) were the significant prognostic factors in multivariate analysis along with treatment modality (p = 0.021). The different results were shown in the analysis of the prognostic factors for postoperative 30-day outcome after separation into clipping and coiling groups. For clipping group, patients' age (p = 0.022), the location (p = 0.000) and the size (0.000) of aneurysms were the significant prognostic factors in both univariate and multivariate analyses, and diabetes mellitus (p = 0.005) was added in multivariate analysis. For coiling group, diabetes mellitus (p = 0.047) was the single significant factors in multivariate analysis (Table 4).

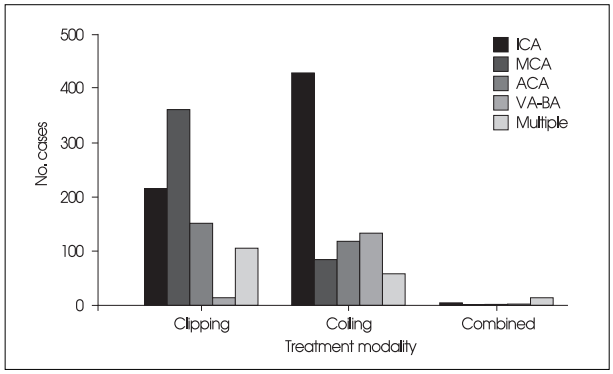

Fig. 4. Location of aneurysms according to treatment modality. Internal carotid artery before the bifurcation is the most common site of aneurysm. Multiple aneurysms are 10.6%. ACA : anterior cerebral artery, ICA : internal carotid artery, MCA : middle cerebral artery, VA-BA : vertebral artery-basilar artery.

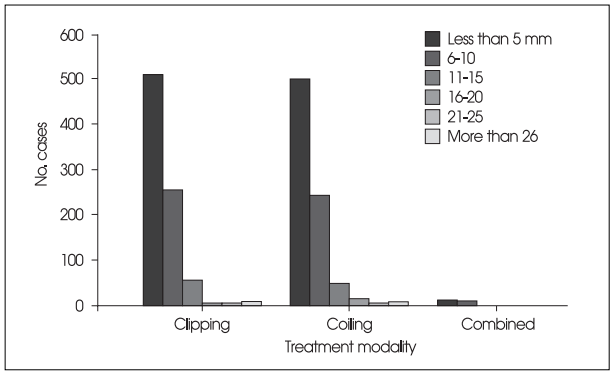

Fig. 5. Size distribution of aneurysms according to treatment modality. The mean size of the aneurysms is 5.6 mm in maximum diameter.

DISCUSSION

The KCVS is the only society representing the Korean vascular neurosurgeons and privileged by the Korean Medical Association. This is the first nationwide survey to assess the clinical characteristics and the efficacy of the treatment for UIAs for one year in Korea. Data from forty-eight participating hospital in this survey would represent those of the whole series of unruptured aneurysm in Korea, because we excluded hospitals that were recently built, or had few new cases or problematic data collection. The total volume of the treatment of the cerebral aneurysm in these hospitals might be estimated almost of all treated UIAs in Korea

Table 4. Prognostic factors for 30-day surgical outcome

	Univariate analysis			Multivariate analysis		
	Total	Clipping only	Coiling only	Total	Clipping only	Coiling only
Sex	0.277	0.734	0.294	0.171	0.308	0.102
Age	0.016*	0.022*	0.508	0.012*	0.007*	0.504
Presence of symptoms	0.008*	0.052	0.147	0.008*	0.099	0.139
Location of aneurysm	0.172	0.000*	0.187	0.104	0.000*	0.460
Size of aneurysm	0.000*	0.000*	0.210	0.001*	0.000*	0.364
Treatment modality	0.212	-	-	0.021*	-	-
Hypertension	0.557	0.871	0.074	0.277	0.556	0.060
Diabetes mellitus	0.133	0.206	0.410	0.004*	0.005*	0.047*
Smoking	0.043*	0.143	0.128	0.099	0.277	0.234
Family history of stroke	0.680	0.356	0.629	0.475	0.258	0.259

*statistically significant

because this study has been designed and cooperated with large hospitals participating in the cerebrovascular surgery and the neurosurgery resident training program in Korea.

A recent systematic review regarding UIAs from many countries reported a prevalence of 0.4% and 3.6% in retrospective and prospective autopsy studies, respectively, and 3.7% and 6.0% in retrospective and prospective angiographic studies, respectively[12]. Number of new patients with treated UIA during recent five years has continuously increased during the 5-year period between 2002 and 2006 (data from the KCVS registry). The proportion of UIA to ruptured intracranial aneurysm has also increased to 32% in 2006, from 20% in 2002 (data from the KCVS registry). The increasing tendency for the UIA to be treated over recent years reflects the advances of the neuroimaging modality, such as CT angiography and MR angiography with sensitivity of 76 to 98% and specificity of 85 to 100%.[14] In Korea, the KCVS has made propaganda for the early detection of the UIA to a nation since 2003, which may contribute to this increasing tendency.

Like the other nationwide survey on the treatment of UIAs[6], there were female and 6th and 7th decades predominance in our study. In their metaanaysis of ruptured intracranial aneurysm from 21 countries, De Rooij et al.[4] reported that the incidence in women was 1.24 times higher than in men and that incidence ratios increased from 0.10 for the younger than 25 years to 1.61 for the older than 85 years. In this study the number of treated UIAs also increased with age except for the 8th decade, probably because many neurosurgeons had a tendency to left untreated the UIAs in this extreme old age.

The average size of the treated UIA at this survey was 5.6 mm and 60.3% of them were less than 5 mm. The treatment policy of UIAs is related to the natural history, or rupture rate Data from the second part of the International Study of Unruptured Intracranial Aneurysms (ISUIA) in 2003 showed rupture rates in the range of 0.5-3.0% per year, and stratified the risk according to the lesions' location and size[16]. They also showed 5-year cumulative rupture rates for patients with UIA located in internal carotid artery, anterior communicating artery, anterior cerebral artery or middle cerebral artery which were the major location in our survey were 0% for aneurysms less than 7 mm in size[16]. According to this randomized controlled study, most of the aneurysm we have treated did not need to be treated. However, possible drawbacks of the ISUIA have been well known. They had the potential bias in the patient enrollment and did not explain why the great majority of ruptured aneurysms seen were less than 7 mm[2].

Our survey showed that the determining factors for choosing the treatment modalities were different hospitals, patients' age, presence of symptoms and the location of the aneurysm. Because the treatment of UIAs is so prophylactic that the treatment modalities should have a very low complication rate, the tendency to coiling is acceptable for treating older patients, and the UIAs in the posterior circulation. However, there have been no definite reports on lower complication rate of coiling for symptomatic aneurysms.

Barker et al.[1], comparing the outcome of UIAs for 3,498 clipping and 421 coiling in a retrospective cohort study using Nationwide Inpatient Sample data from 1996 to 2000, showed that when only death and discharge to long-term care were taken as poor outcomes, there was no significant difference between clipping and coiling, but that on the basis of a four-level discharge status outcome scale, coiled patients had a significantly better outcome. In 2003, Ogilvy and Carter[10] at Massachusetts General Hospital retrospectively reviewed their series of 604 UIAs to identify risk factors. The authors found patient age, aneurysm size, and location within the posterior circulation to be independently associated with poor outcome or death. In our survey, older age, symptomatic lesion, larger size of the aneurysm, and diabetes mellitus were related to poor outcome, but the treatment modality of clipping versus coiling was not a prognostic factor. Moreover, for the coiling treated group, patient factors such as age, sex, and the aneurysmal factors, such as location, size, and symptomatic lesion were not included to the prognostic factors. Regardless of treatment modalities, the common prognostic factors for 30-day outcome were only different hospitals and diabetes mellitus in this survey. It is remarkable for diabetes mellitus to be the

only prognostic factor for treated UIAs among the other stroke risk factors, such as hypertension, smoking, and family history of stroke. The Feigin et al.[5] showed a relative risk of SAH for diabetics compared to non-diabetics of 0.3 (95% CI 0.0 to 2.2) reviewing the relationship between diabetes and SAH. In this survey, diabetes mellitus was shown to be also a strong prognostic factor for treated UIAs as well as for SAH, regardless of the treatment modalities.

The assessment of 1,591 patients in the follow-up ISUIA study in 2003 showed that 1.8 and 12.0% mortality and morbidity at 30 days and 2.7 and 10.1% mortality and morbidity at 1 year[15]. In 2005, Moroi et al.[9] presented 0.3% mortality and 2.2% morbidity overall after treating 549 UIAs. Another single center study by Ogilvy and Carter[10] reported that the overall rates of morbidity and mortality for the treated UIAs were 15.9 and 0.8%. A metaanalysis of 2,460 UIAs in 61 publications between January 1996 and June 1996 reported mortality at 2.1% and morbidity rate of 10.9% for clipping[11]. A more recent study of 3,498 UIAs treated with clipping over five years reported mortality at 2.1% and death or discharge other than home at 18.3%[1]. In our survey, 30-day mortality and morbidity were 0.3% and 7.4% for overall. These figures are closer to the better ones in the literature. Taken the smaller average diameter of the treated UIAs, the non-randomized retrospective nature of the study, and the short term of 30 days outcome into account, the outcome in our survey is comparable to those in the other studies.

This study has some limitations. Retrospective studies, without the benefit of randomization, are subject to several biases, including selection bias. Only 30-day clinical outcome after each respective treatment was analyzed, and longer term data including durability of each treatment modality, were not available. Prospective, randomized trials comparing the two treatment modalities are mandatory to evaluate clinical factors related to UIAs outcome that cannot be addressed in short-term database analyses.

CONCLUSION

This first nation-wide multicenter survey on UIAs demonstrates the epidemiological and clinical characteristics, outcome and the prognostic factors of the treatment of UIAs in South Korea. The 30-day postoperative outcome for UIAs seems to be reasonable morbidity and mortality in South Korea.

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References

1. Barker FG 2nd, Amin-Hanjani S, Butler WE, Hoh BL, Rabinov JD, Pryor JC, et al. : Age-dependent differences in short-term outcome after surgical or endovascular treatment of unruptured intracranial aneurysms in the United States, 1996-2000. **Neurosurgery 54** : 18-28; discussion 28-30, 2004
2. da Costa LB, Gunnarsson T, Wallace MC : Unruptured intracranial aneurysms : Natural history and management decisions. **Neurosurg Focus 17** : E6, 2004
3. de la Monte SM, Moore GW, Monk MA, Hutchins GM : Risk factors for the development and rupture of intracranial berry aneurysms. **Am J Med 78** : 957-964, 1985
4. de Rooij NK, Linn FH, van der Plas JA, Algra A, Rinkel GJ : Incidence of subarachnoid haemorrhage : a systematic review with empha-sis on region, age, gender and time trends. **J Neurol Neurosurg Psychiatry 78** : 1365-1372, 2007
5. Feigin VL, Rinkel GJ, Lawes CM, Algra A, Bennett DA, van Gijn J, et al. : Risk factors for subarachnoid hemorrhage : an updated systematic review of epidemiological studies. **Stroke 36** : 2773-2780, 2005
6. Higashida RT, Lahue BJ, Torbey MT, Hopkins LN, Leip E, Hanley DF : Treatment of unruptured intracranial aneurysms : a nationwide assessment of effectiveness. **AJNR Am J Neuroradiol 28** : 146-151, 2007
7. Inagawa T, Takahashi M, Aoki H, Ishikawa S, Yoshimoto H : Aneu-

rysmal subarachnoid hemorrhage in izumo City and Shimane Prefecture of Japan. **Outcome. Stroke 19** : 176-180, 1988
8. Linn FH, Rinkel GJ, Algra A, van Gijn J : Incidence of subarachnoid hemorrhage : role of region, year, and rate of computed tomography : a meta-analysis. **Stroke 27** : 625-629, 1996
9. Moroi J, Hadeishi H, Suzuki A, Yasui N : Morbidity and mortality from surgical treatment of unruptured cerebral aneurysms at Research Institute for Brain and Blood Vessels-Akita. **Neurosurgery 56** : 224-231; discussion 224-231, 2005
10. Ogilvy CS, Carter BS : Stratification of outcome for surgically treated unruptured intracranial aneurysms. **Neurosurgery 52** : 82-87; discussion 87-88, 2003
11. Raaymakers TW, Rinkel GJ, Limburg M, Algra A : Mortality and morbidity of surgery for unruptured intracranial aneurysms : a meta-analysis. **Stroke 29** : 1531-1538, 1998
12. Rinkel GJ, Djibuti M, Algra A, van Gijn J : Prevalence and risk of rupture of intracranial aneurysms : a systematic review. **Stroke 29** : 251-256, 1998
13. Stehbens WE : Aneurysms and anatomical variation of cerebral arteries. **Arch Pathol 75** : 45-64, 1963
14. Wardlaw JM, White PM: The detection and management of unruptured intracranial aneurysms. **Brain 123** : 205-221, 2000
15. Wiebers DO : Unruptured intracranial aneurysms : natural history and clinical management. Update on the international study of unruptured intracranial aneurysms. **Neuroimaging Clin N Am 16** : 383-390, 2006
16. Wiebers DO, Whisnant JP, Huston J 3rd, Meissner I, Brown RD Jr, Piepgras DG, et al. : Unruptured intracranial aneurysms : natural history, clinical outcome, and risks of surgical and endovascular treatment. **Lancet 362** : 103-110, 2003