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Clinical Article

Benefits of Surgical Treatment for Unruptured Intracranial Aneurysms in Elderly Patients

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Objective : Due to longer life spans, patients newly diagnosed with unruptured intracranial aneurysms (UIAs) are increasing in number. This study aimed to evaluate how management of UIAs in patients age 65 years and older affects the clinical outcomes and post-procedural morbidity rates in these patients.
Methods : We retrospectively reviewed 109 patients harboring 136 aneurysms across 12 years, between 1997 and 2009, at our institute. We obtained the following data from all patients : age, sex, location and size of the aneurysm(s), presence of symptoms, risk factors for stroke, treatment modality, and postoperative 1-year morbidity and mortality. We classified these patients into three groups : Group A (surgical clipping), Group B (coil embolization), and Group C (observation only).
Results : Among the 109 patients, 56 (51.4%) underwent clipping treatment, 25 (23%) patients were treated with coiling, and 28 observation only. The overall morbidity and mortality rates were 2.46% and 0%, respectively. The morbidity rate was 1.78% for clipping and 4% for coiling. Factors such as hypertension, diabetes mellitus, hypercholesterolemia, smoking, and family history of stroke were correlated with unfavorable outcomes. Two in the observation group refused follow-up and died of intracranial ruptured aneurysms. The observation group had a 7% mortality rate.
Conclusion : Our results show acceptable favorable outcome of treatment-related morbidity comparing with the natural history of unruptured cerebral aneurysm. Surgical clipping did not lead to inferior outcomes in our study, although coil embolization is generally more popular for treating elderly patients. In the treatment of patients more than 65 years old, age is not the limiting factor.

Key Words : Unruptured intracranial aneurysms · Elderly patients · Risk factors · Clipping · Coil embolization · Treatment-related morbidity.

INTRODUCTION

The increase in the number of Korea's elderly is growing faster than the elderly population of any other OECD nations. In 1960, the number of Korean citizens aged 65 and older was 726,000, or 2.9% of the whole Korean population. Korea's elderly population increased to 3.37 million, or 7.1% of the total, in the year 2000. Moreover, Korea's elderly citizens are expected to reach the number of 10.1 million, or 19.3% of the total population, by 2030. The life expectancy of Koreans in 1960 was 52.4 years. In 2000, it reached 75 years, and it will likely reach 79 years by the year 2030. Recently, the incidence of unruptured intracranial aneurysms (UIAs) has shown a steady increase owing to advances in neuroimaging modalities, such as computed tomography (CT) angiography and magnetic resonance (MR) angiography, with sensitivities of 76% to 98% and specificities of 85% to 100%[25]. Physicians are performing those tests more frequently during patients' general health check-ups and to evaluate minor symptoms. However, the established guidelines do not exist yet for ideal management of unruptured intracranial aneurysms in elderly patients. Approximately 2% of adults have unruptured aneurysms, and these aneurysms' annual risk of rupture is approximately 0.7%, according to an epidemiologic study by Rinkel, et al.[19]. The number of subarachnoid hemorrhages (SAHs) in the general population is relatively low (6 to 9 cases per 100,000 person-years) in U.S.2 The International Study on Unruptured Intracranial Aneurysms (ISUIA) indicated that the natural progression of unruptured aneurysms might be more benign than physicians previously thought[3].

Considerable discussion among researchers has focused on the natural history of asymptomatic unruptured aneurysms. After the ISUIA reported its results, many institutions felt obliged to manage patients with UIAs in a more conservative fashion. Endovascular morbidity and mortality seem to be less dependent on a patient's age, suggesting that this approach offers ad-

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vantages for older patients[20]. Deciding on the optimal treatment strategy for elderly patients with unruptured intracranial aneurysms requires careful assessment of each individual's treatment-related morbidity and life expectancy and an accurate knowledge of the natural history of this disease process. Unfortunately, physicians have had only limited data regarding elderly patients with unruptured aneurysms. In this single unit series, we report our experience with managing unruptured intracranial aneurysms in elderly patients.

MATERIALS AND METHODS

Patient characteristics

We retrospectively analyzed all patients, aged 65 years and older, diagnosed with unruptured intracranial aneurysms (UIAs) at the Cerebrovascular Center from 1997 to 2009. We reviewed 109 patients harboring 136 unruptured aneurysms. All data was in the form of registered data, which provided specifics on the following variables : age, sex, treatment modality, location and size of aneurysm(s), symptoms, 1-year outcome, and risk factors, such as cardiovascular disease, hypercholesterolemia, smoking, and family history of stroke. Cardiovascular diseases included angina, atherosclerosis, stroke, congestive heart failure, coronary artery disease, myocardial infarction, and peripheral vascular disease. We categorized the numerically -continuous variables, such as age and aneurysm size, into three categories, for statistical analyses. Also, we classified the one-year clinical outcomes into four categories: full recovery without deficits, transient disability, permanent disability, and death. We classified treatments into three groups : surgical clipping group (Group A), coil embolization group (Group B), and untreated group (Group C). Of the 109 patients, 56 patients underwent surgical clipping and 25 patients were treated by coil embolization. The remaining 28 patients were untreated but observed. The follow-up period in the outpatient department is 1 to 10 years until loss to follow up. Long-term follow-up methods included charts and telephone calls. We classified the aneurysms' locations as follows : 1) internal carotid artery, 2) anterior cerebral artery, 3) middle cerebral artery, 4) vertebral artery-basilar artery, and 5) multiple lesions in Fig. 1. The use of digital subtraction angiography made accurate estimation of aneurysmal sizes possible. For the size of an aneurysm, we measured the necks and heights of the aneurysms based on vivid angiographic projections reflecting the dome to neck ratio (Dmax/Nmax)[5], using the equation described by Ujiie et al.[7,23]. We excluded patients with the following conditions from this study : comorbid diseases, such as terminal cancer; medical errors; chronic lower respiratory disease; heart attack; septicemia; fat embolism caused by osteoporotic fracture; chronic liver cirrhosis; and death due to aging. In addition, we excluded some patients who moved to other hospitals, and also excluded those who did not agree to voluntary consent regarding content and method.

Decisions of the treatment groups were made by opinions of patients and caretakers. However, some patients with irregular shape of dome and growing size during one year were advised strongly. Selection of treatment modalities followed a decision of patients who received a satisfactory explanation about morbidity, mortality rate, and doctor's opinions that aneurysms on the middle cerebral artery were more frequently treated by clipping and aneurysms on the vertebral artery-basilar artery by coiling. The observation group visited outpatient clinic annually to observe the change of shape of dome and size of aneurysms with computed tomography angiography until loss to follow up.

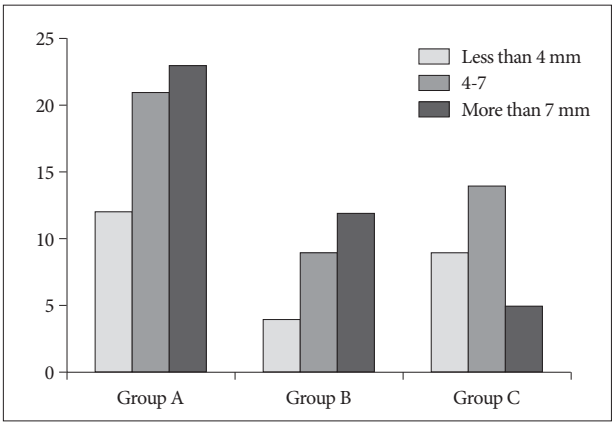

Fig. 1. Size distribution of aneurysms according to treatment modality. The mean size of the aneurysm is 7.19 mm in maximum diameter. Group A (surgical clipping), Group B (coil embolization) and Group C (observation)

Statistical analysis

We analyzed the data using SPSS 15.0 for Windows. We present the outcome scores using mean values and 95% confidence intervals. To compare differences in means of continuous data, we used independent-samples t-tests. *p*-values less than 0.05 were considered statistically significant. We carried out univariate logistic regression analyses to identify predictors of morbidity and mortality.

RESULTS

Patient characteristics

The 109 patients with at least 1 year of follow-up had a total of 136 aneurysms : numbers of one aneurysm are in 88 patients, two aneurysms in 16 patients, had three aneurysms in four patients, and four aneurysms in one patient. Twenty-nine patients were male, and 80 were female. Their mean age was 72 years. These cases included a variety of UIA clinical manifestations : chronic non-specific headaches; dizziness, with or without nausea; cranial nerve palsy (ptosis, visual dimness, and diplopia); tingling sensations; and seizures.

Chronic headache was not only the most common presenting symptom but also the most frequent symptom accompanied by other neurologic deficits. We defined "chronic headache" using the International Headache Society (HIS) classification[3], requiring that the headache last for at least 3 months, have a fre-

quency of more than 15 days per month, and have a non-catastrophic, recurring character. The preoperative chronic headache group that also received treatment numbered 22 patients. Using Waters's Headache Questionnaire[26], we found 11 patients presented with mild headache, 8 patients with moderate headache, and 3 patients with severe headache. Treatment outcomes included marked relief of headaches in majority of patients complaining of chronic headaches before treatment. In addition, they recovered from preoperative depression and anxiety. However, we didn't find any reason why they recovered from headache after treatment. This is not simply correlated with size effects of aneurysms.

The health check survey and/or routine neuroimaging evaluations incidentally detected seventy-six patients (69.7%). Many elderly patients had risk factors for stroke, as follows : 63 (57.8%) had cardiovascular disease, 45 (41.3%) had diabetes mellitus, 29 (26.6%) smoked, 27 (24.8 %) had hypercholesterolemia, and 18 (16.5%) had a family history of stroke.

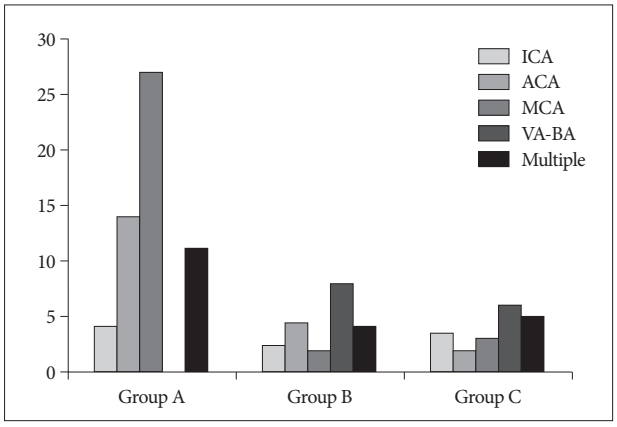

Fig. 2. Location of aneurysms according to treatment modality. Middle cerebral artery including the bifurcation is the most common site of aneurysm. Multiple aneurysms are 18.3%. ACA : anterior cerebral artery, ICA : internal carotid artery, MCA : middle cerebral artery, VA-BA : vertebral artery-basilar artery. Group A (surgical clipping), Group B (coil embolization) and Group C (observation)

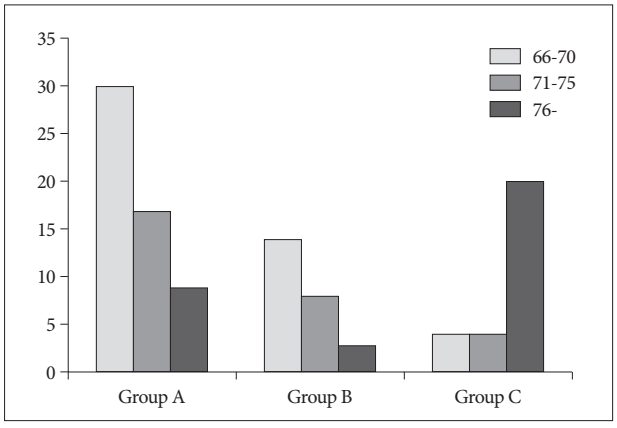

Fig. 3. Age distribution of patients with unruptured intracranial aneurysm according to treatment modality. Regardless of treatment modality, most patients are in their seventh decades of life. Group A (surgical clipping), Group B (coil embolization) and Group C (observation).

Characteristics of the aneurysms and treatment modalities

The aneurysms were located in the internal carotid artery (ICA) in 49 instances (35.5%), in the middle cerebral artery (MCA) in 42 (30.5%), the anterior cerebral artery (ACA) in 28 (20.2%), and the vertebro-basilar artery (VA-BA) in 19 (13.8%) (Fig. 2). The mean size of the aneurysms was 7.19 mm. The size of aneurysms were less than 4 mm in 25 patients, from 4 mm to 7 mm in 44 patients, and larger than 7 mm in 40 patients, mean size of 7.19 mm (Fig. 1). Fifty-six patients (55%) underwent clipping, 25 underwent coiling (22.9%), and 28 patients (25.7%) received no treatment but, rather, close monitoring of their clinical conditions, with neuroimaging follow-up periodically. The mean age of patients receiving clipping was 70.6 years. The patients undergoing coil embolization had a mean age of 71 years. The mean age in the untreated group was 75.6 years (Fig. 3).

Patients with certain conditions showed poor clinical outcomes, as compared with who did not have these factors, as follows: hypertension (p=0.009), diabetes mellitus (p=0.000), hypercholesterolemia (p=0.000), smoking (p=0.000), a family history of stroke (p=0.001), and cardiovascular risk factors (hypercholesterolemia, p=0.008; diabetes mellitus, p=0.008). Patients age 75 years or older did not receive treatment but were observed.

Postoperative 1-year outcome and prognostic factors

The overall 1-year morbidity and mortality rates were 2.46% and 0%. The morbidity was 1.78% for clipping treatment and 4% for coiling treatment (Table 1). In univariate analysis, which considered only the treatment groups, multiple aneurysms (p=0.021), hypertension (p=0.012), diabetes mellitus (p=0.000), hypercholesterolemia (p=0.000), smoking (p=0.000), and family history of stroke (p=0.000) correlated significantly with poor recovery at 1-year post-operative. Observation group was not evaluated because only one variable could be processed in univariate group with the outcome of treatment groups not the treatment availability. However, in multivariate analysis with diverse variables of outcome, which included the observation group, symptomatic lesion (p=0.000), multiple aneurysms (p=0.004), hypertension (p=0.009), diabetes mellitus (p=0.000), hypercholesterolemia (p=0.000), smoking (p=0.000), and family history of stroke (p=0.001) had a strong influence on poor clinical outcomes. When we excluded the untreated group, we found a difference between clipping and coiling. For the clipping group, symptomatic lesion (p=0.002), multiple aneurysms (p=0.013), diabetes mellitus (p=0.027), hypercholesterolemia (p=0.000), and smoking (p=0.021) were significant prognostic factors, in both univariate and multivariate analyses, and age (p=0.039) was significant in the univariate analysis. For the coiling group, smoking (p=0.016) and family history of stroke (p=0.004) were the significant factors in the univariate analysis, and hyper cholelesterolemia (p=0.01) was significant in the multivariate analysis (Table 2).

Aneurysm size in elderly patients did not correlate with poor

outcome, even though former studies noted that aneurysms <5 mm had a higher risk of rupture than did aneurysms of a larger size[13]. Complications after the treatment procedures were perforator ischemia in the clipping group and thromboembolism in the coiling group. In the clipping group, four patients suffered from perforator ischemia, and three of them recovered fully. One patient suffered from postoperative infections. In the coiling group, three patients experienced thromboembolism, and one of them developed permanent disability but there was no recanalization. In the observation group, patients older than 75 years also suffered from terminal cancer, heart attack, and infectious respiratory disease but did not experience hemorrhage. Only two patients with symptomatic lesions, hypertension, and/or family history of stroke refused treatment against recommendation of treatment, despite repeated advice from the neurosurgeons because of irregular shape of domes, and died of ruptured subarachnoid hemorrhages within one year of diagnosis. One patient had irregular shape of multiple aneurysms with multi-lobulated domes.

Table 1. Clinical outcome according to the treatment modalities

Clinical outcome	Number of patients (%)		Overall
	Clipping	Coiling	
Good recovery	51 (91)	22 (88)	73 (90)
Transient disability	4 (7)	2 (8)	6 (7)
Permanent disability	1 (2)	1 (4)	2 (3)
Death	0	0	0
Total	56	25	81

Good recovery : immediately after surgery, Transient disability : recovered within 1 month

Table 2. Variables related to unfavorable clinical outcome (within 1 year)

	Univariate analysis			Multivariate analysis		
	Total	Clipping	Coiling	Total	Clipping	Coiling
Sex	0.942	0.519	0.118	0.909	0.598	0.383
Age (more than 70 years)	0.473	0.039*	0.176	0.897	0.079	0.135
Presence of symptom	0.000*	0.002*	0.418	0.000*	0.023*	0.112
Location of aneurysm	0.116	0.056	0.633	0.057	0.103	0.302
Size of aneurysm (anterior and posterior circulation)	0.859	0.900	0.349	0.768	0.917	0.740
Dome to neck ratio (more than 2 ratio)	0.961	0.186	0.127	0.279	0.192	0.469
Multiplicity of aneurysm	0.021*	0.013*	0.310	0.004*	0.036*	0.079
Hypertension	0.012*	0.078	0.211	0.009*	0.059	0.166
Diabetes mellitus	0.000*	0.027*	0.077	0.000*	0.019*	0.055
Hypercholesterolemia	0.000*	0.000*	0.087	0.000*	0.000*	0.010*
Smoking	0.000*	0.021*	0.016*	0.000*	0.023*	0.031*
Family history of stroke	0.000*	0.455	0.004*	0.001*	0.230	0.011*
Treatment modality	0.373	-	-	0.482	-	-

*statistically significant. Univariate analysis was considered only in the treatment group but multivariate analysis included the observation group

The other patients showed growing size during one year. Also, 26 observed but untreated patients with few risk factors constantly worried that they carried a risk of rupture from unruptured intracranial aneurysms.

DISCUSSION

In younger patients, surgical treatment, as opposed to the natural progression of the disease, is more effective in terms of both prolonging lives and improving the quality of life[9]. Surgical treatment is probably of less relevance to elderly persons, because the initial concern is usually their risk of perioperative complications with advancing age. In contrast to the risk of rupture, we expect surgical treatment to shorten such a patient's remaining lifespan. However, we must recognize that the risk of rupture also increases with age. Lawrence et al.[16] reported that the annual incidence of SAH in the Framingham study was 2.8 per 100,000 for the total population, but for the elderly population, the rate was 7.8 per 100,000. Other groups noted incidence rates three times higher in the elderly population[6,27]. One autopsy study demonstrated the increased prevalence of aneurysms with age[23]. Atherosclerotic vessel degeneration due to prolonged exposure to hypertension might affect the risk of aneurysm formation or rupture[21]. Carter et al.[1] noticed a 1.1 mm increase in diameter per decade in UIAs. As aneurysm rupture remains a deadly and devastating event in this age group, the elderly should still merit serious consideration for treatment of unruptured aneurysms. Krisht et al.[11] suggested considering patients with unruptured aneurysms and a 5-year life expectancy for surgical intervention, to improve their outcomes with regard to the mortality and severe morbidity of their expected natural history.

In this study, two patients aged 72 and 73 years old ignored symptoms and multiple risk factors such as cardiovascular diseases, high cholesterol levels, and symptomatic lesions. When asked on the phone with regards to their health, they were already died from rupture of aneurysms. The treatment modalities for UIAs in the elderly focus on low complications in the prophylaxis of ruptures. Therefore, physicians have a certain tendency to prefer coiling for older, asymptomatic aneurysms and aneurysms located on the internal carotid artery and vertebrobasilar artery. At this point it appears that the risks associated with surgical clipping and endovascular coiling, in terms of stroke or death from the procedure, are the same[18]. A critical point in endovascular treatment is that the morphological result

may be incomplete or may worsen after time. Given the potential life spans of elderly patients (man; 76 years old, woman; 82 years old by Statistics Korea), partial treatments (if they protect against early rebleeding and recanalization), may be preferential to the complete treatments appropriate for younger patients. This study's results suggest coil packing can be the better choice for elderly patients who have short life expectancy.

However, we found different results in the long-term follow-up that ranged from 1 to 10 years. During this time, some patients were offered the option of observations without endovascular therapy or microsurgical clip ligation. As in another survey[4], unruptured aneurysms found in the elderly were predominantly in females. Moreover, elderly females also showed a higher frequency of multiple aneurysms and a lower frequency of anterior communicating artery aneurysms when compared to younger female patients[22]. Nevertheless, the one year clinical outcome did not correlate to treatment modality in either univariate analysis (p=0.373) or multivariate analysis (p=0.482). The recent review by the Korean Society of Cerebrovascular Surgery (KSCVS) showed the same results in a retrospective study of 1,696 cases enrolled over one year at 48 hospitals in South Korea[10]. Oglivy et al.[15] investigated the risk factors in 604 UIAs. The authors noticed age, aneurysm size, and location of the posterior circulation was independently associated with morbidity and with mortality. In our study, we could find six strong risk factors: multiple aneurysms, hypertension, diabetes mellitus, hypercholesterolemia, smoking, and family history of stroke. Probably these risk factors might influence on the growing of aneurysms, perforator ischemia after clipping and thromboembolism after coiling.

We propose that preoperative routine chemistry must include monitoring patient cholesterol levels, which have frequently been neglected. In addition, we found headache, the most common symptom, was treatable after management. Among the 22 patients who presented with preoperative, chronic headache, only one complained of worsened headache after receiving surgical clipping. Two patients stated that they experienced no changes in their headaches. Twenty patients (90.9%) reported their headaches improved. All of these patients reported their headaches improved during the first week after treatment. This is not simply correlated with size effects of aneurysms. Further evaluation for this result should be analyzed.

The ISUIA study in 2003 assessed 1,591 patients during follow-up and found 10.1% morbidity and 2.7% mortality rates[3]. In 2005, Moroi et al. reported 0.3% mortality and 2.2% morbidity rates.[14] Another study, by Raaymakers, found 2.1% mortality and 10.9 % morbidity rates in a meta-analysis of 2,460 UIAs treated by clipping and reported in 61 publications between January and June 1996[17]. In our survey, the overall one morbidity and mortality rates were 2.46% and 0%, respectively. The one year morbidity rate was 1.78% for clipping and 4% for coiling procedures. These figures are lower than the ones in the literature. Furthermore, we need to consider cost-effectiveness. Of South Korea's 49-million population, 7% is over age 65, and half of South Korea's elderly households live in a state of "relative poverty," having incomes below 50% of the nation's average household income. The major health-care problems of the Korean elderly are difficulties in paying for health care services and in providing long-term care when they become frail. The treatment costs for elderly patients with cerebral aneurysms increase as the patients get older. For this reason, physicians should make greater efforts, via a screening system, to treat unruptured cerebral aneurysms as early in each patient's life as possible. Then, physicians need to determine the approach that is most cost-effective for each patient.

This study has some limitations. This study does not address the influence of endovascular therapy, which should feature prominently in any decision-making process[8,12]. Without randomization, a management protocol where neurosurgeons and interventional neuroradiologists decide, on a case-by-case basis, about the preferred individual treatment causes selection bias. For example, a primary physician with unjustifiable optimism and unreasonable risk aversion might insist that unruptured aneurysms in old and sick patients with cerebrovascular diseases should be left untreated. Endovascular repair of aneurysms can be inferior in broad-based aneurysms, and surgery is superior to endovascular treatment for MCA aneurysms with an unfavorable geometry, even if the patient has many risk factors for general anesthesia. Finally, we derived the data from a single institute with a relatively low number of patients. We may have methodologically overlooked some potential, confounding variables of statistical significance.

CONCLUSION

We found patients with certain conditions showed poor clinical outcomes as compared with those who did not have these factors, which were as follows: hypertension, diabetes mellitus, hypercholesterolemia, smoking, and a family history of stroke. Treatment modality in these elderly patients did not correlate with poor outcomes. Both clipping and coiling treatments had favorable results in elderly patients. Surgical clipping did not lead to inferior outcomes in our study, although coil embolization is generally more popular for treating elderly patients. We emphasize that there is no mortality case and rupture of aneurysms in the treatment groups. In the treatment of patients more than 65 years old, treatment of unruptured intracranial aneurysms should be considered positively.

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