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Clinical Outcome of Surgery for Unruptured Intracranial Aneurysms

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Objective : To determine the rationale for treating pure unruptured intracranial aneurysms(UIAs), it is mandatory to know the risk of each treatment modality. The purpose of this study is to evaluate the surgical risk for treating UIAs.

Methods : Between December 1994 and May 2005, 147 unruptured aneurysms in 135 patients were treated. The majority of these cases (94.6%) were treated with aneurysmal neck clipping. The remainder received aneurysmal wrapping (2.7%), trapping with bypass (2.0%), or proximal occlusion (0.7%). The clinical outcomes were evaluated in each patient by the Glasgow Outcome Scale at one month post-surgery.

Results : The patient pool consisted of 41 males and 94 females. The mean age was 55.9 years (range : 16~82). The aneurysms were located at middle cerebral artery in 63 (42.9%), anterior communicating artery 30 (20.4%), posterior communicating artery in 26 (17.7%), internal carotid artery(ICA) in 14 (9.5%), anterior choroidal artery in 4 (2.7%) and others in 10 (6.9%). One hundred fifteen (78.2%) of aneurysms were small (<10mm). Others were large (10 to 25mm) and giant (>25mm); 29 (19.7%) and 3 (2.1%) respectively. More than ninety percent (91.1%) of all patients recovered well. Mild to severe disability was seen in 8.7% of the patients. One patient succumbed to complications following injury to the ICA.

Conclusion : The mortality and morbidity associated with UIA surgery at our hospital compared very favorably to the previous reported literature and with the previously established natural history of this disease.

KEY WORDS : Unruptured intracranial aneurysm · Surgical treatment · Outcome · Complication.

Introduction

Subarachnoid hemorrhage(SAH) due to rupture of a cerebral aneurysm is a serious disorder that has high mortality and morbidity rates, and this in spite of the recent developments for the management of SAH. Therefore, it seems reasonable to prevent disastrous SAH and treat cerebral aneurysms before they rupture. With the widespread use of non-invasive modalities such as magnetic resonance(MR) angiography to detect cerebral aneurysm, we are experiencing more opportunities to treat patients with asymptomatic unruptured cerebral aneurysms. The prevalence of unruptured intracranial aneurysms (UIAs) is approximately 2.1% with an incidence of approximately 16.1% for the people between 40 and 49 years of age, and the incidence is up to 30.2% for people 60 to 69 years of age[9,30]; the annual UIA rupture rate is 0.05~5.3%[9,22-25,28]. If left untreated, UIAs may be associated with significant complications, including rupture, mass effect, seizures and thromboembolic strokes. There has been controversy during the past few years concerning the recommendations for the treatment of UIAs. The most recent larger meta-analysis involving 1591 patients demonstrated a morbidity rate of 9.9% and a mortality rate of 2.7% at one year after surgery for unruptured aneurysms[22]. While prophylactic surgery is often deferred for small unruptured aneurysms, the literature has consistently reported the increasing risk of rupture as well as the technical difficulties that come about as the aneurysmal size increases and as the patients get older[15,17,27]. We report here on the surgical outcome of 135 patients with UIAs and we review the relevant medical literature on the risk of surgery.

Materials and Methods

We retrospectively reviewed the medical records of 135 patients who were operated on for 147 unruptured aneurysms between December 1995 and May 2005 at our

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Table 1. Preoperative Characteristics of Patients

Patient and Aneurysmal Characteristics	Number
Number of patients	135 (100 %)
Females	94 (69.6%)
Males	41 (30.1%)
Mean age (years)	55.9
Range (years)	16~82
Hypertension	61 (45.2%)
Diabetes	6 (4.4%)
Conditions leading to aneurysm diagnosis	
Headache	60 (44.5%)
Incidental	45 (33.3%)
3rd nerve palsy	15 (11.1%)
Dizziness	11 (8.2%)
Previous cerebral infarction	3 (2.1%)
Diplopia	1 (0.7%)

Table 2. Characteristics of Aneurysms

Aneurysms Characteristics	Number
Total number of aneurysms	147 (100%)
Patients with a single aneurysm	126 (92.6%)
Patients with multiple aneurysms	9 (7.4%)
Two aneurysms	6 patients
Three aneurysms	3 patients
Size of aneurysms	
<10mm	115 (78.2%)
10~24mm	29 (19.7%)
≥25mm	3 (2.1%)
Location of aneurysms	
Middle cerebral artery	63 (42.9%)
Anterior communicating artery	30 (20.4%)
Posterior communication artery	26 (17.7%)
Internal carotid artery	14 (9.5%)
Anterior choroidal artery	4 (2.7%)
Anterior cerebral artery	4 (2.7%)
Ophthalmic artery	3 (2.1%)
Vertebral artery	2 (1.4%)
Basilar artery	1 (0.7%)

hospital (Table 1, 2). The patient pool consisted of 94 females and 41 males. The age of the patients at the initial diagnosis was between 16 and 82 years (mean age : 55.9 years). Forty-five (33.3%) of the patients were asymptomatic, while the remainder (66.7%) had various symptoms, including headache, diplopia, dizziness, gaze disturbance and previous cerebral infarction. One hundred twenty six (92.6%) patients had single aneurysm and 9 (7.4%) patients had multiple aneurysms; 6 patients had two aneurysms and 3 patients had three aneurysms. Regarding the aneurysmal size, 3 were giant aneurysms above 25mm in diameter (2.1%), 29 were large aneurysms from 10 to 24mm in diameter (19.7%) and 129 (78.2%) were small aneurysms less than 10mm in diameter. The location of the aneurysms were as follows : 63 (42.9%) aneurysms were on the MCA, 30 (20.4%) aneurysms were on the anterior communicating artery(AComA), 26 (17.7%) aneurysms were on the posterior communication artery(PComA), 14 (9.7%) aneurysms were on the internal carotid artery(ICA), 4 (2.7%) aneurysms were on the anterior cerebral artery(ACA), 4 (2.7%) aneurysms were on the anterior choroidal artery(AchA), 3 (2.1%) aneurysms were on the ophthalmic artery, 2 (1.4%) aneurysms were on the vertebral artery and 1 (0.7%) aneurysm was on the basilar artery.

Operations for the unruptured aneurysms were performed for the patients who were in an acceptable mental and physical condition before the surgery and after agreement from the patients and their families. Surgery was indicated if the aneurysm size was more than 3mm at the maximum diameter and the patient's age was less than 70 years. However, an operation was performed even though the patient's age was more than 70 years when patients had symptoms like 3rd nerve palsy and severe headache. The majority of the middle cerebral artery(MCA) territory aneurysms were treated by clip ligation.

The clinical characteristics and postoperative courses were

Table 3. Summary of patients with postoperative complications

No.	Sex	Age	An. location	An. size (mm)	Operation	Complication	GOS
1	F	29	Rt. MCA	30	Clipping	Temporal lobe infarction. Weakness	4
2	M	50	AComA	3.3	Clipping	Lt. ACA territory infarction. Dysarthria	4
3	M	45	Lt. MCA	15	Clipping	Lt. MCA stenosis. Weakness	4
4	F	61	AComA	6	Clipping	Lt. ACA territory infarction. Weakness	4
5	F	31	Lt. ICA	20	Saphenous v. Bypass	EDH, SDH. BG and caudate nucleus infarction. weakness	4
6	F	61	Rt. MCA	8.6	Clipping	Cerebellar ICH. Dysarthria, dizziness	4
7	F	64	Lt. PComA	19	Clipping	Lt. BG infarction. Weakness	4
8	F	62	Lt. MCA, AComA	3, 5	Clipping	Corpus callosum infarction. Memory disturbance	4
9	M	59	Rt. VA	20	Clipping	Swallowing difficulty	4
10	F	59	Lt. VA	11	Proximal occlusion	Swallowing difficulty	4
11	F	63	Rt. ACA (A2)	6	Wrapping	ACA territory infarction with hemorrhage. weakness	3
12	F	54	Rt. MCA, BA, PComA	9, 4, 3	Clipping	ICA injury during operation. Death	1

ACA : anterior cerebral artery, AComA : anterior communicating artery, BA : basilar artery, BG : basal ganglia, ICA : internal carotid artery, ICH : intracranial hemorrhage, MCA : middle cerebral artery, PComA : posterior communicating artery, VA : vertebral artery, SDH : subdural hemorrhage

evaluated by reviewing the medical records. The postoperative outcomes were evaluated based on the Glasgow Outcome Scale (GOS) at one month after the surgery.

Results

One hundred thirty nine (94.5%) aneurysms were treated by clipping, four were treated by wrapping (2.7%), three were treated by bypass surgery with clipping (2.1%), and one was treated by proximal occlusion (0.7%). Two of the bypass surgeries were for giant ICAs, and saphenous vein grafts used to treat them. The third employed a superficial temporal artery-middle cerebral artery connection to bypass a thrombosed MCA aneurysm. One case with a vertebral artery aneurysm was treated by proximal occlusion.

One hundred twenty three patients recovered without any complications. Postoperative complications occurred in 12 (8.9%) patients, and one (0.7%) of these patients died (0.7%). Eight patients (5.7%) suffered from postoperative cerebral infarctions. Intracranial hemorrhage(ICH) occurred in two patients. Hemiparesis was recorded in one case following venous infarction. One patient died due to ICA injury during the operation. Two patients with vertebral artery aneurysm complained about difficulties with swallowing after the surgery. The surgical outcomes according to aneurysmal size (p=0.088), location (p=0.784), multiplicity (p=0.11), the procedural method (p=0.629), and age (p=0.799) did not have statistical significances. The clinical outcomes were evaluated according to the GOS, and they were based on the follow-up examinations that took place more than one month after the operation with using the following scale : 5 = good recovery (91.1%), 4 = moderate disability (7.5%), 3 = severe disability (0.7%) and 1 = death (0.7%). The summary of the 12 patients along with their postoperative complications is provided in Table 3.

Illustrative cases

Case 5

A 31-year-old woman had suffered from left tinnitus and hearing difficulty for 3 months before her hospital visit. The MRI that was taken from the local hospital showed a left ICA aneurysm. She was referred to our hospital for further evaluation and treatment on December, 2004. A left distal ICA bifurcation aneurysm 2cm in diameter was found on performing a 4 vessel angiogram (Fig. 1). Direct clipping and endovascular treatment could not be attempted because the ACA (A1) and MCA (M1) vessels were included in the aneurysmal sac. As the first procedure, external carotid artery(ECA) and MCA (M2) anastomosis with using the great saphenous vein was done to maintain the distal blood flow. There was no blood leakage at both anastomosis sites on the operation field. After the anastomosis, clipping was done in the proximal site of the aneurysmal sac. The site of the MCA that emerged from the aneurysmal sac was clipped, and then this was followed by clipping the site just proximal to the ICA. The patency of the ACA was maintained to reduce the risk of decreased blood flow in the anterior perforate substances and the lenticulostriate arteries. The pulsation of the grafted vessel and distal MCA (M2) was good. There were no other brain and vessel injuries during the operation. The patient had no neurologic deficit

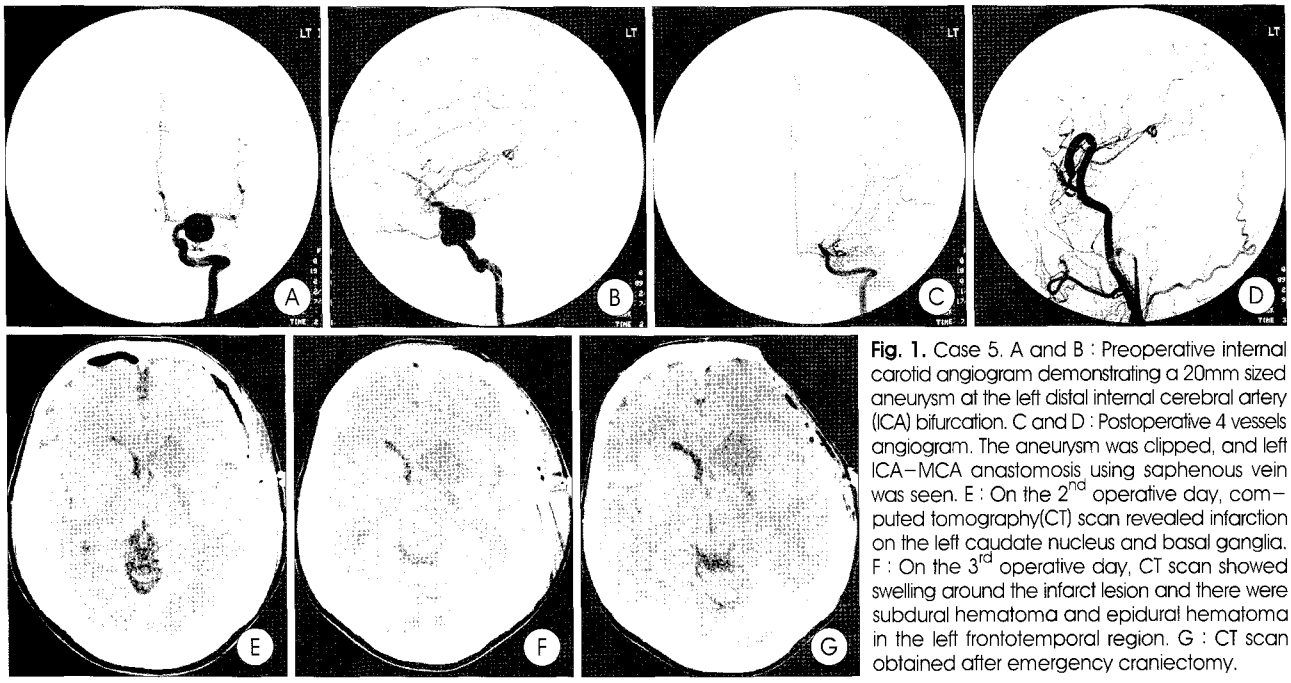

Fig. 1. Case 5. A and B : Preoperative internal carotid angiogram demonstrating a 20mm sized aneurysm at the left distal internal cerebral artery (ICA) bifurcation. C and D : Postoperative 4 vessels angiogram. The aneurysm was clipped, and left ICA–MCA anastomosis using saphenous vein was seen. E : On the 2nd operative day, computed tomography(CT) scan revealed infarction on the left caudate nucleus and basal ganglia. F : On the 3rd operative day, CT scan showed swelling around the infarct lesion and there were subdural hematoma and epidural hematoma in the left frontotemporal region. G : CT scan obtained after emergency craniectomy.

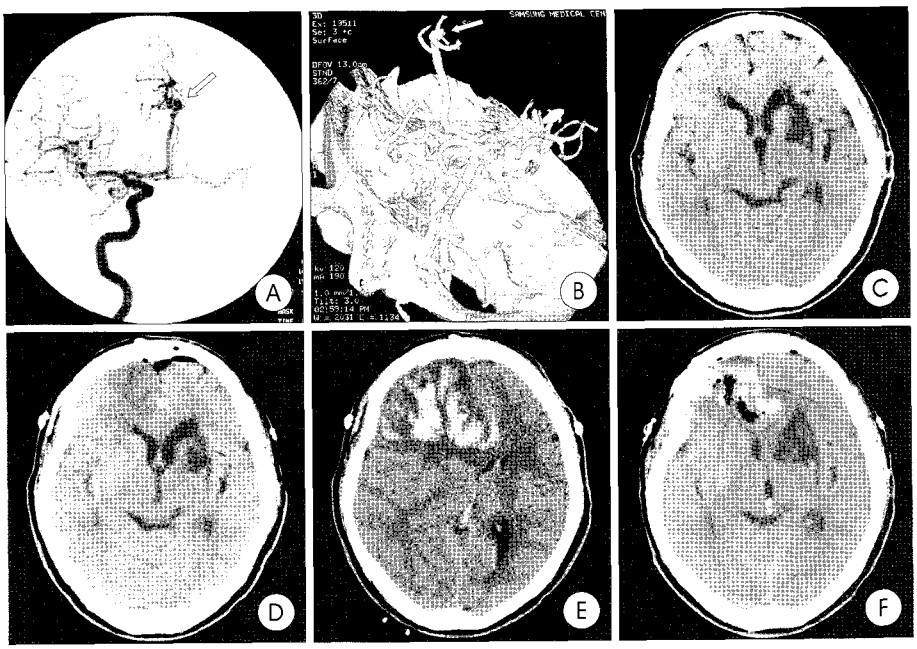

Fig. 2. Case 11. A and B : Preoperative internal carotid angiogram and computed tomography(CT) angiogram demonstrating unruptured A2 aneurysm. C : Preoperative CT scan showing encephalomalasia on the left basal ganglia due to previous basal ganglia intracerebral hemorrhage. D : On the 2nd postoperative day, CT scan revealed a right ACA territory infarction. E : CT scan obtained after 12 hours later and it showed massive hemorrhage at same lesion. F : Postoperative CT scan. The hematoma was removed.

on her 1st post-operative day.

She gradually developed motor weakness on her right side, and especially in the upper extremity, on the morning of the 2nd post-operative day. The CT scan was obtained immediately and it revealed infarction within the left basal ganglia and caudate nucleus. She was treated with conservative management for her weakness. On the 3rd post-operative day, the motor weakness was severe and a drowsy mentality appeared. The follow-up CT scan showed swelling around the infarct lesion and there were SDH and EDH in the left frontotemporal region. Emergency craniectomy and evacuation of the EDH was performed, and a small amount of SDH was removed. There was no blood leakage at the anastomosis site during the operation. Duroplasty was done to reduce the brain swelling. Her mentality recovered right after the operation but her right side weakness remained at the time of discharge.

Case 11

This 63-year-old woman suffered from sudden onset left hemiplegia on September, 1998. A CT scan and cerebral angiography were performed immediately at another hospital. The CT scan revealed left basal ganglia ICH and the angiography demonstrated an unruptured A2 aneurysm. First, stereotactic hematoma removal was performed at the left basal ganglia at that time. After hematoma removal, her symptom of right side weakness was much improved (motor grade IV). Three months later, she was transferred to our hospital and a right frontal paramedian craniotomy via the interhemispheric approach and aneurysmal wrapping with small sized cottons were performed for the unruptured A2 aneurysm (Fig. 2). There was not vessel injury during operation. At the immediate postoperative period, she was slightly drowsy and had no motor weakness. On the 2nd postoperative day morning, a routine postoperative CT scan was obtained and it revealed a right ACA territory infarction. 12 hours after the 1st CT scan was obtained, she suffered a generalized tonic clonic seizure. Emergency CT scan was performed and it revealed massive hemorrhage within the previous right frontal postoperative infarct lesion. The patient was immediately transferred to the operating room and we performed extended right frontotemporal craniotomy and right frontal lobectomy with hematoma removal. She was stuporous after surgery, and then rehabilitation therapy was started several weeks later. She was discharged to another hospital 3 months after surgery. At the time of discharge, she had a stuporous mentality and severe disability.

Discussion

The meta-analyses and studies that have been published in the recent years, and especially the International Study of Unruptured Intracranial Aneurysms(ISUIA) that encompassed more than 2600 patients have led to new recommendations for the management of patients suffering with unruptured intracranial aneurysms[19,21,22]. The ISUIA study revealed that the natural course of unruptured aneurysms was substantially different between the patients with previous SAH and those patients who did not experience previous SAH.

The important aspect in the natural history of unruptured aneurysms is the aneurysm size. In the ISUIA study, the risk of rupture of an intact aneurysm less than 10mm in diameter in the patients with no history of SAH (Group 1) was as low as 0.05% per year. The risk of rupture for similar aneurysms in the patients with a history of treated ruptured aneurysm (Group 2) was also quite low (0.5% per year). The risk of rupture of larger aneurysms was approximately 1% per year in both groups[9,21]. Based on the result of the ISUIA, the impact

on life expectancy for repairing unruptured intracranial aneurysms varies from a substantial benefit to a modest detriment. The outcome of small aneurysm surgery was deemed "good" in 93.0% of all cases, whereas the large (10~25mm) and giant (>25mm) aneurysms were associated with a 10.4% and 33.3% chance of morbidity, respectively[15,17,19]. The current studies highlight the prognostic significance of the size of aneurysm and its independent influence on the outcome, in addition to the significance of the probability of incurring technical difficulties that result from intraoperative rupture[13,15].

It was found in our study that 10 out of 132 patients (7.6%) with anterior circulation aneurysms experienced an unfavorable recovery, and this was regardless of the aneurysm size. In contrast, 2 out of the 3 patients (66.7%) with posterior circulation aneurysms (cases 9 and 10) had slightly unfavorable outcomes and these 2 patients suffered from postoperative swallowing difficulties. It is conceivable that these symptoms were associated with the lateral suboccipital approach of the surgery. Khanna et al.[10] have found that the aneurysm location was an independent factor that influenced the surgical outcome, and that the location of an aneurysm on the posterior circulation was associated with an increased incidence of a poor outcome.

Raaymakers et al.[1,19] conducted a meta-analysis on the results of surgical treatment for unruptured aneurysm, and they concluded that the size and location of aneurysms were the two significant prognostic indicators. In Raaymakers's study, non-giant anterior circulation aneurysms had a mortality rate of 0.8% and a morbidity rate of 1.9%, while giant posterior circulation aneurysms had a 9.6% mortality rate and a 37.9% morbidity rate after surgery. For all the patients with additional aneurysm and for those patients with incidentally discovered aneurysms 7mm or more in diameter or aneurysms of the posterior circulation, repairing the aneurysm brought about a slight gain in life expectancy at all ages[2,14,22,25,29]. Another report[31] showed that an unruptured aneurysm can be treated safely, especially in the cases of middle cerebral artery aneurysms and small aneurysms less than 10mm diameter at all locations.

A previous study showed that the overall surgical results for patients with multiple aneurysms were approximately the same as for the patients with a single intracranial aneurysm[18]. Nevertheless, in our study, although the patients with single and multiple unruptured intracranial aneurysms generally had good results, the patients with single aneurysms (118 of 126 patients, 93.6%) fared better than did the patients with multiple aneurysms (6 of 9 patients, 77.8%), but the difference was not statistically significant (p=0.11).

The influence of the patient's age on the surgical outcome of unruptured aneurysms is somewhat controversial. Khanna et al. showed that older patients who underwent surgery for unruptured aneurysms were at a higher risk for a poor outcome[10,17]. In our study, the patients' ages did not significantly affect the surgical outcome. The mean age of the cases for which complications occurred was 53.2 years (age range : 29~64 years).

Currently, the majority of MCA aneurysms are better treated with performing direct surgical clipping. Such aneurysms can be clipped with minimal brain retraction and they are relatively superficial, and unless they are giant sized, they can be completely exposed to allow visualization and control of the entire parent vessel-aneurysm complex. On the other hand, we believe that endovascular embolization still has several drawbacks when it is applied to this subset of aneurysms due to their broad complex necks that partially incorporate the origin of the M2 branches. This characteristic increases the risk of periprocedural thromboembolic complications. Small PCoA aneurysms can be reached with minimal brain retraction and they can be permanently secured by applying clips with very low rates of surgical morbidity and death. We believe that endovascular treatment, with its associated 5% to 8% incidence of hemorrhagic and ischemic complications, still carries an increased risk compared with that for surgical therapy for treating this subset of aneurysms. Therefore, for a patient with a PCoA aneurysm, we consider surgery as the first-line treatment except for the elderly patients (>70 years) who show a poor baseline neurological function, and also for those patients with large aneurysms for which significant manipulation of the AChoA artery can be anticipated. Anterior communicating artery aneurysms represent a complex problem because neuropsychological deficits are common after the application of surgical clips, whereas endovascular embolization is associated with a better functional outcome for these type aneurysms. Yet the risk of aneurysm perforation during embolization is greater for the smaller aneurysms and the risk of perforation during embolization may be even greater for the very small ACoA aneurysms. Given the course of the A1 segment with its acute angle from the ICA bifurcation, it can be difficult to achieve a stable catheter position within a very small aneurysm. We tend to favor applying surgical clips for aneurysms smaller than 4mm and also for those ACoA aneurysms that are pointing posteroinferiorly. We believe that endovascular treatment is definitively superior to surgical clipping for treating BA bifurcation aneurysms and aneurysms of the posterior circulation. These lesions pose significant technical challenges from a surgical point of view, and they are very easy to catheterize given their orientation in the same direction as the blood flow. In the majority of cases, BA caput aneurysms can be safely treated with coil embolization[11,12,26].

In this study, the decisions on how to treat an aneurysm were determined on a case-by-case basis depending on the angiographic findings (aneurysm location, size and shape, and the

tortuosity of the proximal vessels) and the clinical data (patient age, symptoms, the baseline neurological condition and the systemic comorbidities). Especially, the patients who had symptoms of headache, diplopia and 3rd nerve palsy were recommended for treatment. In no instance was the decision to perform surgical clipping or endovascular occlusion based on the preferences of the referring physician, the patient or the patient's family. All the patients and their family members were informed of the treatment options and a final recommendation was provided by the neurosurgeons. Another important consideration was the patient's personal opinion as to whether she or he can bear the knowledge of harboring a potentially dangerous intracranial aneurysm[3,4,7].

In a recent multicenter study[16,17,19-22,32], rupture of the UIA during surgery was reported to occur in 6% of the patients, with the incidence of intracranial hemorrhage and cerebral infarction being 4% and 11%, respectively. The combined morbidity and mortality rate for the patients with open surgical repair was 4~17.5%, and the overall mortality associated with the surgical treatment of UIA was 0% to 4%. Postoperative ischemic events, as a complication of aneurysmal surgery, happened in many cases (cases 1~5, 7, 8 and 11). The reasons might be that small vessels or adjacent vessels were clipped together, or vascular spasm happened during or after the operations (case 11), or the severe brain retraction promoted brain edema or infarction. So, we think that performing careful procedure during clipping and also during the other related procedures is required. Especially in the case 5, we created an anastomosis between the ECA and the MCA, and we maintained the patency of the ACA to reduce the risk of decreased blood flow in the anterior perforators and lenticulostriate arteries. However, the infarctions on the left basal ganglia and the caudate nucleus happened at the 2nd postoperative day. We thought the reason for the infarctions was that thromboocclusions occurred in the left anterior perforate substances and in the lenticulostriate arteries. In case 11, during the dural opening, a cortical vein was sacrificed because the vein was firmly attached to the dura. We thought that it might have caused the venous hemorrhage infarction. The remote cerebellar hemorrhage (case 6) that occurred as a complication of supratentorial aneurysmal surgery arose not as an intraoperative event, but as a postoperative event. This zebra-pattern hemorrhage seems to be typical for a postoperative loss of CSF. Close postoperative monitoring is essential for the patients who have suction drains implanted and also for those patients who have undergone an operation that's associated with an increased risk of remote cerebellar hemorrhage[6].

Our outcomes were usually assessed one month after treatment, but another study[5] showed that improvement continued to occur until at least 1 year after treatment; further improvement may also occur thereafter. Yet in the short term, surgical treatment for the patients having an unruptured aneurysm has a considerable impact on their functional heath and quality of life.

Conclusion

Our data are consistent with previous studies, i.e., that there is an overall low risk of surgical treatment for unruptured intracranial aneurysms. The outcome was favorable in 91.1% of all cases and death was exceedingly rare (0.7%). The mortality and morbidity rates were comparable to those of the previously reported studies. These results should be taken into account when making a balanced decision on whether or not to proceed with surgery for an individual patient having an unruptured aneurysm.

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Commentary

UIAs are diagnosed with a greater frequency as advanced imaging techniques are improving. There exists some reports that the risk of rupture in patients with unruptured intracranial aneurysms of small size is very low (about 0.1% per year) but the cumulative hemorrhage rate reported by Juvela et al. was 10.5% at 10 years, 23% at 20 years, and 30.3% at 30 years. In those patients who had their aneurysms discovered at a younger age or in whom the aneurysm was large and especially in those patients who are smoking, the incidence of SAH rate was known to be high. Therefore, considering the devastating effect of subarachnoid hemorrhage (50% or greater mortality up to 83% for each episode of bleeding), the psychological effects of having a known but untreated UIA and the benefits of surgery, the aggressive treatment of UIAs is justified.

The investigators are reporting their experiences of surgical treatment for the UIAs. Their surgical results of excellent outcome in 91.1% and mild to severe disability in 8.7% are comparable with previous reported data. The primary importance of this publication is that it could be a very excellent paper for those neurosurgeons to treat the UIAs.

However, there are some controversies about the treatment policy of UIAs. The most important aspects in the treatment of UIAs is not whether UIAs should be treated or not, but which treatment modality should be selected. The authors treated UIAs surgically but did not mention about the possibility of endovascular treatment of UIAs. Recently, with the remarkable technical advancement of endovascular surgery, some aneurysms are more feasible for coil embolization. The appropriate selection of treatment modality in the treatment of UIAs could reduce the complications and improve the clinical outcomes.

The authors reported poor surgical outcomes in the treatment of posterior circulation UIAs. Accumulated data demonstrated that posterior circulation aneurysms are more amenable to endovascular surgery due to the difficulty in surgical approach, the intricately entangled neurovascular structures, and the relative feasibility of endovascular access. Of course, it couldn't be denied that there remains many things to be solved even in endovascular coil embolization, such as a steep learning curve, compaction and recanalization, lack of long-term follow-up and need for repeated angiography.

The most important thing in the treatment of UIAs is that the serious considerations between the benefits and risks of surgical or endovascular intervention and the natural history.

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