Unruptured Intracranial Aneurysms: Current Perspectives on the Origin and Natural Course, and Quest for Standards in the Management Strategy

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Abstract

Unruptured intracranial aneurysms are relatively common, and can cause subarachnoid hemorrhage. Management of unruptured intracranial aneurysms requires knowledge of the natural course and management risks of individual aneurysms. Current knowledge on the natural course and management risks is summarized and our current management strategy presented. Extensive literature review was conducted to identify risk factors influencing the natural course and management outcome of unruptured intracranial aneurysms. Our consecutive surgical series from October 2006 through June 2009 were reviewed retrospectively. The risk factors for rupture were size and location, as well as history of subarachnoid hemorrhage in small aneurysms. Management morbidity was significantly influenced by the size, location, and patient's age. Since 2006, we have monitored motor evoked potentials in all surgeries of cerebral aneurysms and utilized endoscope control, and skull base and bypass techniques in selected cases. In 133 consecutive surgeries, two patients (1.5%) suffered severe neurological morbidity. Unruptured intracranial aneurysms have various clinical characteristics and we need to stratify management strategy according to the aneurysm features such as size, location, shape, and patient's clinical status. In Japan, with national efforts to elevate management standards, morbidity associated with the treatment of the unruptured intracranial aneurysms is relatively low. To improve future care further, we need to continue seeking better and less invasive management modalities and technique.

Key words: unruptured intracranial aneurysm, natural course, rupture, growth, management

Introduction

Unruptured intracranial aneurysms are relatively common, occurring in 2–6% of the adult population, and can have grave consequences after rupture resulting in subarachnoid hemorrhage. Surgical intervention significantly reduces the risk of rupture but the risk of such prophylactic treatment cannot be ignored. To determine management strategy, we need to assess the natural history and management risks of individual aneurysms. Since the majority of the patients with this pathology are asymptomatic, management must minimize the interventional risks as far as possible.

This review summarizes the current knowledge of the origin and the natural course, and standard management strategy of unruptured intracranial aneurysms.

Characteristics of Unruptured Intracranial Aneurysms

I. Origin and rupture

The origin and cause of rupture of cerebral aneurysms remain unclear. The impact of the blood stream may damage the arterial wall, especially at the arterial bifurcation, and cause the aneurysm. However, a recent hemodynamic study has proven that the impact force at the originating site is not significantly different from other sites. On the other hand, the shear stress was relatively high adjacent to the origin of the aneurysm, which is thought to work as the force tearing the vessel wall. The aneurysm then grows with physiological remodeling of the arterial wall caused by the relatively low shear stress at the aneurysm dome. Histological studies of intracranial aneurysms have demonstrated that both symptomatic unruptured and ruptured aneurysms
incorporate degenerative processes of the arterial wall similar to atherosclerosis, and such features are not commonly seen in asymptomatic unruptured intracranial aneurysms.\(^5\) Recently, atherosclerosis has been considered to originate in inflammation of the arterial wall. Such inflammatory processes are considered to be important in the growth and rupture of the aneurysms. A recent experimental study showed statins inhibit the growth of experimental cerebral aneurysms.\(^1\) Development of medical treatments for unruptured intracranial aneurysms are awaited.

II. Natural course of unruptured intracranial aneurysms

Many studies have investigated the natural course (analysis of risk of rupture) of unruptured intracranial aneurysms.\(^8,10,20,30,37,38,41,42,45,46\) Most studies were retrospective and some were prospective, but no randomized clinical trials have been published. In general, higher rupture risks have been reported in retrospective studies than in prospective studies. Also, the independent risk factors are rather difficult to clarify in retrospective series. Table 1 summarizes the natural course of unruptured intracranial aneurysms from retrospective series. The annual rupture risk of all intracranial aneurysms was reported as between 1% to 3% in retrospective studies. However, there is inevitable selection bias in the included patients. Elderly, sicker patients or patients with aneurysms carrying high management risks tend to be observed conservatively.

Table 2 shows the three prospective studies published. The international study of unruptured intracranial aneurysms (ISUIA) including 1,692 prospective cases demonstrated the rupture rate is about 0.78% annually, and is strongly related with aneurysm size and anterior or posterior location (Table 3).\(^42\) Small anterior circulation aneurysms rarely ruptured (0% for \(<7\) mm aneurysms located in the anterior circulation without history of subarachnoid hemorrhage). On the other hand, large aneurysms frequently ruptured (8% or more annually). The SUAVE study in Japan included all small aneurysms less than or equal to 5 mm, and demonstrated that even small aneurysms can grow and rupture.\(^46\) The annual rupture rate in the follow-up period of 375 aneurysm-years was 0.8%. An additional 18 aneurysms (4.7%) grew more than 2 mm, and 5 of them underwent repair of the aneurysm before its rupture. Considering the growing aneurysm

### Table 1 Natural history of unruptured intracranial aneurysms from retrospective series

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>No. of cases</th>
<th>Mean age (yrs)</th>
<th>Follow up</th>
<th>Annual rupture rate (%)</th>
<th>Factors affecting rupture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yasui et al. (1997)(^{41})</td>
<td>234 pt, 303 an</td>
<td>59.6</td>
<td>75.1 mos</td>
<td>2.3</td>
<td>multiplicity</td>
</tr>
<tr>
<td>Rinkel et al. (1998)(^{30})</td>
<td>3907 pt·yr</td>
<td></td>
<td></td>
<td>1.9 (1.5–2.4); 0.7: &lt;1 cm, 4.0: &gt;1 cm</td>
<td>symptomatic, sex, size, location</td>
</tr>
<tr>
<td>ISUIA (1998)(^{38})</td>
<td>727 pt, 977 an</td>
<td>56</td>
<td>8.3 yrs, 12,023 pt·yr</td>
<td>0.05: &lt;1 cm, 0.5: &gt;1 cm</td>
<td>size</td>
</tr>
<tr>
<td>Juvela et al. (2000)(^{30})</td>
<td>722 pt, 960 an</td>
<td>49.4</td>
<td></td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Tsutsumi et al. (2000)(^{37})</td>
<td>142 pt, 181 an</td>
<td>41.9</td>
<td>19.7 yrs, 2575 pt·yr</td>
<td>1.3</td>
<td>smoking, older age, size</td>
</tr>
<tr>
<td>Morita et al. (2005)(^{20})</td>
<td>62 pt</td>
<td>70.8</td>
<td>4.8 yrs</td>
<td>2.3</td>
<td>size</td>
</tr>
<tr>
<td>Wermer et al. (2007)(^{41})</td>
<td>4705 pt, 6556 an</td>
<td>59.6</td>
<td>26122 pt·yr</td>
<td>1.2: &lt;5 yrs, 0.6: 5–10 yrs, 1.3: &gt;10 yrs</td>
<td>Japanese or Finnish, size &gt;5 mm, posterior, symptom</td>
</tr>
</tbody>
</table>

an: aneurysms, pt: patients, pt·yr: patient·year.

### Table 2 Natural history of unruptured intracranial aneurysms from prospective series

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>No. of cases</th>
<th>Mean age (yrs)</th>
<th>Follow up</th>
<th>Annual rupture rate (%)</th>
<th>Factors affecting rupture</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISUIA (2003)(^{38})</td>
<td>1692 pt, 2686 an</td>
<td>55.2</td>
<td>4.1 yrs, 6544 pt·yr</td>
<td>0.78</td>
<td>size, posterior location, history of SAH</td>
</tr>
<tr>
<td>Yonekura (2004)(^{46})</td>
<td>329 pt, 380 an, all ≤5 mm</td>
<td>62</td>
<td>375 an*yr</td>
<td>0.8 (0.2–3)</td>
<td>multiple, female, ACom, basilar location, age &gt;70 yrs</td>
</tr>
<tr>
<td>Ishibashi et al. (2009)(^{34})</td>
<td>419 pt, 529 an</td>
<td>2.5 yrs, 1039 pt·yr</td>
<td>1.4</td>
<td>history of SAH, size, posterior location</td>
<td></td>
</tr>
</tbody>
</table>

ACom: anterior communicating artery, an: aneurysms, an*yr: aneurysm-year, pt: patients, pt·yr: patient·year, SAH: subarachnoid hemorrhage.

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could have ruptured unless treated, the annual rupture rate is not negligible in such patients. A follow-up study on untreated 419 patients at a single institution found the rupture rate was 1.4% per year and was significantly influenced by history of subarachnoid hemorrhage, posterior location, and size of the aneurysm. Currently, in Japan, two prospective studies (UCAS Japan and UCAS II) have been conducted, and the preliminary results indicate that the natural course is significantly related to size as well as specific locations of the aneurysms. Aneurysms located at the anterior communicating and internal carotid-posterior communicating arteries tended to rupture more frequently than other locations, even if small (unpublished data).

Several studies compared three-dimensional (3D) images between groups of ruptured and unruptured intracranial aneurysms. Aneurysms with large height and high ASPECT (dome height/neck width) ratio, and located on the posterior communicating artery and anterior communicating artery, as well as the posterior circulation are more commonly ruptured. Irregular shape and coexistence of bleb are also found more in ruptured aneurysms. These findings suggest that the aneurysms with such features can rupture easily.

Table 4 summarizes the reports on aneurysm growth. Larger aneurysms often grew more than smaller aneurysms. Posterior location and multiple aneurysms also tended to grow frequently. Rate of growth is exponentially increased along with the follow-up year. Such findings coincide with the risk factors found for aneurysm rupture.

### III. Management outcome and risks

Numerous studies on the management outcome for unruptured intracranial aneurysms are summarized in Table 5. Reported and published clinical outcomes are significantly different between various types of studies. The ISUIA found that mortality was 1.6% and significant morbidity (modified Rankin scale 3 or below or mini-mental state examination (MMSE) score below 25) was 10.9% at the one month follow-up. Decline of cogni-
Table 5  Outcome of management of unruptured intracranial aneurysms

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>No. of cases</th>
<th>Type of study</th>
<th>Risk</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wirth et al. (1983)</td>
<td>107 pt, 119 an</td>
<td>open surgery</td>
<td>mortality: 0%;</td>
<td>size, location</td>
</tr>
<tr>
<td></td>
<td></td>
<td>multicenter</td>
<td>morbidity: 6.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>retrospective cohort,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 centers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>King et al. (1994)</td>
<td>733 pt</td>
<td>open surgery</td>
<td>mortality: 1.0%</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td></td>
<td>meta-analysis,</td>
<td>(0.4–2.0%);</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>28 studies</td>
<td>morbidity: 4.1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.8–5.8%)</td>
<td></td>
</tr>
<tr>
<td>Raaymakers et al. (1998)</td>
<td>2,460 pt</td>
<td>open surgery</td>
<td>mortality: 2.6%</td>
<td>old publication,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>meta-analysis,</td>
<td>(2.0–3.3%);</td>
<td>giant an,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>61 studies</td>
<td>morbidity: 10.9%</td>
<td>posterior circulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(9.6–12.2%)</td>
<td>early series</td>
</tr>
<tr>
<td>Murayama et al. (1999)</td>
<td>115 pt, 120 an</td>
<td>endovascular</td>
<td>morbidity: 4.3%</td>
<td></td>
</tr>
<tr>
<td>Johnston et al. (2001)</td>
<td>2,069 pt</td>
<td>1699: open surgery, 370: endovascular</td>
<td>mortality: 3.5% (open surgery), 0.5% (endovascular); morbidity: 25% (open surgery), 11% (endovascular)</td>
<td>open surgery</td>
</tr>
<tr>
<td>ISUIA (2003)</td>
<td>1917 pt</td>
<td>open surgery</td>
<td>mortality: 1.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>multicenter</td>
<td>morbidity: 11.7%</td>
<td>size, age, location,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>retrospective cohort,</td>
<td>(1 mo)</td>
<td>ischemic disease, symptom</td>
</tr>
<tr>
<td></td>
<td></td>
<td>61 centers</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>451 pt</td>
<td>endovascular</td>
<td>mortality: 1.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>morbidity: 7.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1 mo); complete occlusion: 51%, unsuccessful: 5%</td>
<td></td>
</tr>
</tbody>
</table>

an: aneurysms, pt: patients.

Surgical Strategy and Case Series in Our Institution

I. Surgical strategy

To accomplish the safest intervention, we need to carefully assess the patient and involve updated surgical technique and assist devices. In our institution, we follow the recommendations of the Japanese Society of Screening of Asymptomatic Cerebral Disorders in deciding on repair of unruptured intracranial aneurysms. Basically, aneurysm repair is indicated in patients with management risks considered lower than the natural risks for rupture or physical factors for the next 10 years. When we decide to treat the aneurysm of specific patients, either open craniotomy and clipping or endovascular coiling is selected individually according to the following strategy.

A: Clipping is the preferred method when the surgical risk in the specific patient is similar or lower to that of coiling. Aneurysm repair in the location of the basilar tip or in patients with very high medical risks is often managed better by endovascular methods. However, wide-based basilar aneurysms are repaired by open clipping after thorough discussion with endovascular specialists.

B: If the patient strongly prefers endovascular management after thorough discussion, endovascular treatment is indicated.

In our institution, surgical managements are as-
sisted by the following advanced techniques to diminish surgical morbidity: Pre-operative thorough evaluation of aneurysm images including 3D angiography, 3D computed tomography (CT) angiography and magnetic resonance (MR) angiography, MR imaging with Fast Imaging Employing STeadystate Acquisition (FIESTA), and Preoperative 3D simulation.

The gold standard for the diagnosis of cerebral aneurysms is digital subtraction angiography. This technique is still essential for assessing cerebral circulation and obtained details of the cerebral vascular anatomy including the venous system. However, recent advances in CT and MR angiography have reduced the needs for catheter angiography. With advanced imaging techniques, we now can visualize and anticipate perforators around the aneurysm, and imagine the space between the aneurysm and the adjacent parent arteries. CT and MR angiography provide the internal shape of the aneurysm and FIESTA images provide the external shape of the aneurysm, and detect adjacent perforator and cranial nerves. More accurate imaging incorporating heart beat influence will provide information on the distortion of the aneurysm by the heart beat and the wall thickness of the aneurysm. Combination of such 3D images can provide very useful virtual reality simulations for surgical procedures. Currently, we can create an actual-sized elastic hollow model of individual aneurysms from the preoperative 3D images. These models were very useful in deciding how to apply clips to occlude the closure line of the aneurysm and combination of aneurysm clips for complex-shaped aneurysms.

Electrophysiological monitoring: Electrophysiological monitoring is essential to reduce operative complications. Motor evoked potential monitoring is very useful for reducing managing morbidity during aneurysm surgery, especially around the perforating branches such as the anterior choroidal, posterior communicating, M1, and vertebro-basilar arteries. Visual evoked response is also very useful in reducing risks to visual acuity during intervention for paraclinoid aneurysms.

Meticulous microsurgical, skull base surgical and bypass technique: For open aneurysm surgery, the basic surgical technique involves meticulous microsurgical procedures preserving all possible venous and arteriolar structures. To accomplish appropriate clipping, we need to fully dissect and expose the aneurysm dome and neck with sharp dissection. Also, with the widespread availability of endovascular technique, open surgeons are now facing more complex cerebral aneurysms, which cannot be simply obliterated using the usual microsurgical techniques. We should be able to utilize skull base and bypass techniques as routine additional microsurgical techniques. The anterior clinoid process including optic canal unroofing and/or posterior clinoid process should be drilled in treating paracrinoid aneurysms or basilar aneurysms to widely expose the adjacent anatomical structures and create extra room for safe access. Such procedures can be safely performed using the SONOPET ultrasonic bone curettage instrument (UST-2001; Stryker Japan, Tokyo) without the fear of causing rolling-up injury to the important structures by the drills. Other cranial base approaches including anterior petrosectomy and combined petrosal approach, and transcondydar approaches are utilized in managing vertebrobasilar complex aneurysms. Bypass technique including superficial temporal artery (STA) to middle cerebral artery, A3-A3 anastomosis or high flow technique, is often required in the management of some wide neck aneurysms to salvage parent arteries, especially aneurysms incorporating wide or thrombosed wall.

Combination of open and endovascular technique in selected cases: If cases present possible difficulty for both open and endovascular techniques, we should combine both techniques. Especially in cases with wide neck aneurysm combined with vessel wall calcification, or adjacent perforator difficult to dissect from the neck, we can intentionally partially occlude the aneurysm neck with clips and obliterate the aneurysm completely with endovascular coils. Endovascular procedure can be achieved safely after the aneurysm neck is narrowed and the clipping can be done without sacrificing the perforators. In Japan, advanced intracranial stent technique is currently under trial and only performed in selected institutions. When such endovascular techniques including the soft flexible stenting method are available widely, we should actively incorporate such techniques. However, we need to carefully assess the long term outcome of such endovascular procedures, since the ISAT showed frequent rebleeding after endovascular procedures. Current endovascular technique is not completely reliable protection against bleeding from aneurysms.

Application of endoscopy and Indocyanine Green (ICG) angiography: Endoscopy and ICG are very useful techniques in assessing the patency of adjacent perforating and parent arteries. In selected cases, clipping can be accomplished under the control of the endoscope to prevent occlusion of the perforating vessels. Recently developed ICG technique is useful in assessing the patency of adjacent arteries.

Cosmetic skin incision and craniotomy repair: To
reduce patient’s burden in social life, we should always consider cosmetic concerns in assessing surgical outcome. We should avoid facial nerve palsy after craniotomy and minimize surgical depression of the temporal area. Muscle atrophy should be avoided by meticulous dissection technique, avoiding injury to the temporal muscle nerves and vasculature, and reduce the bone defect caused by the craniotomy.

II. Our series of open aneurysm surgeries

From October 2006 through June 2009, 133 open aneurysm surgeries for unruptured intracranial aneurysms were performed by the authors utilizing the above mentioned techniques. Bypass surgery was included in 13 procedures and cranial base technique was involved in 18 cases (anterior clinoidectomy in 13, posterior clinoidectomy in 3, anterior petrosal approach in 1, and combined posterior petrosal approach in 1). Endovascular procedures (coiling) were added in 2 cases for planned incomplete occlusion of the aneurysm. The endoscope was used in all cases except for middle cerebral aneurysms. Electrophysiological monitoring was applied in all cases. At discharge, two patients (1.5%) suffered severe morbidity (modified Rankin scale less than or equal to 2, or Mini-mental State Examination Score less than or equal to 25). Both patients had giant thrombosed aneurysms (Table 6).

Postoperative MR imaging, obtained in all open surgical cases, showed unexpected T2 hyperintensity in 6 cases. In addition to the severe morbidity, four patients experienced four subdural hematomas, which required surgical evacuation one to 3 months after surgery. Seizure occurred in 5 patients, which was controlled with antiepileptic medication. Wound complication was found in 2 patients, including one patient who required surgical repair for CSF leak. No other clinical complication was noted.

III. Illustrative cases

Case 1 (Fig. 1): This 63-year-old female presented with a left asymptomatic small posterior communicating artery aneurysm. Left pterional craniotomy was performed and clipping was performed under endoscopic control. After initial clipping, her right upper-extremity motor evoked potential diminished and endoscopic imaging showed the clip had occluded a perforator from the posterior communicating artery. The clip was repositioned to not constrict the perforator circulation. Motor evoked response returned and the patient recovered uneventfully.

Case 2 (Fig. 2): This 72-year-old female presented with a large left basilar superior cerebellar artery aneurysm. Preoperative FIESTA MR imaging demonstrated several perforators on the right back side of the aneurysm. Endovascular intervention was not indicated because the left superior cerebellar artery was at risk of occlusion. Surgery was performed through the left modified pterional-anterior temporal approach involving anterior and posterior clinoid resection using SONOPET. During surgery,
Fig. 2 Illustrative Case 2. A: Preoperative magnetic resonance image using the Fast Imaging Employing STeady-state Acquisition sequence showing several perforators in the right back side of the aneurysm (arrow) and the left P₁ segment attached to the aneurysm dome. B: Three-dimensional angiogram showing the large basilar-superior cerebellar artery aneurysm with a relatively wide neck through the narrowed neck (arrow). C: After partial clipping across the neck, the aneurysm dome was still patent. D: Endovascular coiling was performed to occlude the majority of the dome.

Case 3 (Fig. 3): This 50-year-old male presented with a left giant vertebral artery aneurysm with progressive brainstem signs after coil embolization in another hospital. He initially presented with subarachnoid hemorrhage 10 years ago. He was found to have left vertebral artery dissecting aneurysm and was conservatively managed. In 2005, he developed progressive right heaviness and giant vertebral aneurysm was diagnosed. Aneurysm obliteration was performed using detachable platinum coils in another hospital. However, even after the occlusion, the aneurysm continued to grow by blood back flow from the distal vertebral artery and his neurological function deteriorated including dysphagia, dizziness, and right hemiparesis. Endovascular trial to occlude the left distal vertebral artery was unsuccessful. We planned to occlude the distal vertebral artery by clipping and decompression of the aneurysm at the second stage surgery. Left anterior petrosectomy was chosen and the clip was placed on the left distal vertebral artery just above the aneurysm. There were several perforators from the vertebral artery, which were spared. Three weeks later, the aneurysm mass with coils compressing the medulla was removed after proximal left vertebral artery clipping. Postoperative course was complicated with hydrocephalus, pneumonia, and persistent orthostatic hypotension. He was transferred to a rehabilitation facility and resumed his job 7 months after surgery. At the last follow-up examination, he was ambulatory and dysphagia was improved. At the last clinical visit, his modified Rankin scale was 1. (This case was managed in collaboration with the Endovascular Unit at Jikei Medical School.)
Current knowledge on the origin and growth of the cerebral aneurysms suggests three types of origin and natural course of unruptured intracranial aneurysms (Fig. 4[66]). Type 1 is an aneurysm which ruptures immediately after formation. Type 2 is an aneurysm which stops enlarging sometime after formation, but grows due to some inflammatory process and ruptures. Type 3 is an aneurysm which stops growing after formation, but still may start regrowth due to some unknown biological cues. Type 1 should present as ruptured aneurysm, so unruptured intracranial aneurysms are likely to be type 2 or 3. To determine whether an aneurysm should be treated, we need to know the type of the individual aneurysm and the process that induces the growth of the aneurysm.

The risk factors influencing the growth and rupture of intracranial aneurysms can be summarized as follows: Group 1 risk factors (evidenced by high level prospective studies), size ($\geq 7$ mm), location (posterior circulation $>$ anterior circulation), specific locations such as anterior communicating, posterior communicating and basilar artery aneurysms, and history of subarachnoid hemorrhage; Group 2 risk factors (evidenced by retrospective case series and studies), history of smoking, multiplicity of aneurysms, higher age, symptomatic aneurysm, Japanese or Finnish population, and shape of aneurysm (irregular or high dome/neck ratio). Such evidence leads us to believe that unruptured intracranial aneurysms should not be considered as a single disease entity. We should stratify unruptured aneurysms according to the specific features such as location, size or shape, and patient factors.

Risk factors that influence management outcomes can be summarized as follows: Group 1 management risk factors (evidenced by high level prospective studies), size, location (vertebro-basilar $>$ anterior circulation), history of subarachnoid hemorrhage, and age; Group 2 management risk factors (evidenced by retrospective case series, studies), history of ischemia, and type of management. The management of unruptured intracranial aneurysms is not risk free and the published outcomes vary according to the study design and the measurement of outcome. We should not apply published outcomes to our own decision making. Before discussing risk communication, we should clarify our own clinical outcome. Thereafter, we need to carefully decide the indications for management by assessing the natural course and institutional outcome in managing individual aneurysms.

According to the ISUIA study, recent management recommendations for unruptured intracranial aneurysm did not advocate surgical management for incidental small intracranial aneurysms unless the patient is young or has other specific hemodynamic features. However, a recent study of the long-term outcome of ISUIA cases with mean follow-up of 9.2 years reported that the overall outcome was better in treated than untreated patients. Relatively risk-matched patient groups were extracted from the prospective patient cohort of ISUIA using propensity analysis score and compared untreated and treated patients (ISUIA report at the AANS 2010, unpublished data). Although the case risks in both groups matched relatively well, there might be hidden bias as sicker patients may not be indicated for treatment. Nevertheless, we need to realize the importance of long term assessment to evaluate the real outcome and benefit of treatment of unruptured in-
tracranial aneurysms.

In Japan, even carefully designed prospective studies showed relatively low overall morbidity and mortality in managing unruptured intracranial aneurysms.\textsuperscript{19) To achieve low-risk intervention, meticulous care in preoperative assessments and involvement of advanced surgical and interventional techniques are mandatory, including high resolution MR imaging, preoperative 3D simulation, meticulous surgical technique, skull base technique, bypass surgery, advanced neuro-physiological and neuro-imaging monitoring, and collaboration with neuro-interventional techniques. In illustrative Case 1, the authors demonstrated the need for electrophysiological monitoring and endoscopic control in managing simple small aneurysms. In Cases 2 and 3, we illustrated the need for cranial base approaches as well as combination of surgery and endovascular techniques in managing difficult cases. Brain stem compression caused by the mass effect of the aneurysm and endovascular material must be decompressed to alleviate clinical signs, and can be effective even after months of progressive symptoms. Well organized and dedicated rehabilitation efforts and physical care is mandatory to obtain good recovery.

In 2008, the revised guidelines of the Society of Screening of Asymptomatic Cerebral Disorders in Japan were published. Recommendations were made according to the published series of natural course and management outcome. The Japanese experiences were stressed rather than reports from western countries since the natural course of UIA might be slightly different between Japan and other western countries.\textsuperscript{41) The management outcomes in our prospective series are also relatively better than those reported by ISUIA.

The recommendations for managing unruptured intracranial aneurysms are as follows (http://www.snh.or.jp/jsbd/pdf/guideline2008.pdf).

i) Interventions for unruptured cerebral aneurysms should be determined by the age and health status of the patient, size, location and nature (shape and other characteristics) of the aneurysm, the expected natural course of the aneurysm, and the institutional or surgeon's management outcome. Full detailed informed consents should be obtained and good risk communication between caregivers and patients should be created before deciding on intervention or careful follow up.

ii) Surgical or endovascular management is recommended for patients with the following aneurysms with life expectancy of more than 10–15 years.

ii-i) Aneurysms more than or equal to 5 to 7 mm

ii-ii) Smaller than above but

ii-ii-i) Symptomatic

ii-ii-ii) Located at anterior communicating, internal carotid-posterior communicating arteries or posterior circulation.

ii-ii-iii) Aneurysm with daughter sac, irregular shape, or large dome-neck aspect ratio.

iii) Risk benefit analysis based on large previously published cohort studies can be a useful indicator in deciding the management of unruptured cerebral aneurysms in general. However, the natural course, quality of life, mental status of each patient and aneurysm, and institutional surgical outcome should be carefully assessed.

iv) If the unruptured cerebral aneurysm is to be followed up without surgical intervention, smoking and excessive alcohol intake should be avoided and hypertension needs to be treated. Aneurysm should be carefully followed every half or one year by high quality imaging devices.

v) If any change of shape or increasing size is detected by the follow-up imaging, management of aneurysms should be re-assessed.

vi) Long-term follow up is mandatory after endovascular and surgical clipping of aneurysms.

Conclusions

Unruptured intracranial aneurysms show various clinical characteristics and risk analysis should be based on their features. Indication and decision of management should be decided carefully based on the aneurysm features and updated institutional management risks. All possible measures to achieve safe surgery for this disease, which is mostly asymptomatic, should be deployed. To advance future care of the unruptured intracranial aneurysms, we need continue to obtain more accurate data on the natural course by well designed prospective studies and develop less invasive management measures with minimal morbidity including medical treatment.

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