Long-term Outcome of Unruptured Giant Cerebral Aneurysms

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Abstract

The long-term outcome of 39 patients with unruptured giant aneurysm (>2.5 cm) treated during the last 12 years was retrospectively reviewed. The 7 male and 32 female patients, aged 32 to 81 years, presented with symptoms related to compression of the surrounding structures by the aneurysm in 28 cases, cerebral infarction in one, and asymptomatic in 10. The locations were the internal carotid artery (ICA) in 27 cases, middle cerebral artery in three, anterior cerebral artery in one, and basilar artery in eight. Therapeutic modalities were direct clipping in 11 patients, ICA occlusion combined with extracranial-intracranial bypass in 15, and conservative treatment in 13. The follow-up period ranged from 16 to 128 months (mean 54.0 months). The mortality was 9% (1/11), 0% (0/15), and 31% (4/13), and morbidity was 18% (2/11), 20% (3/15), and 8% (1/13), respectively. Surgery reduced the mortality (from 31% to 4%) but increased the morbidity (from 8% to 19%) as compared with conservatively treated patients (p < 0.05).

Giant intracranial aneurysm has a poor prognosis if left untreated, but these lesions are difficult to treat with the present management options.

Key words: unruptured cerebral aneurysm, giant aneurysm, outcome, operation

Introduction

Unruptured aneurysms are detected more frequently by modern neuroradiological techniques. The aneurysm treatment strategy depends on the patient’s age, and neurological and medical conditions. The most important risk factors associated with a poor outcome are giant aneurysm (>2.5 cm diameter) and location in the posterior circulation.3,15,16) Unruptured giant intracranial aneurysm is a serious threat because of the high mortality and morbidity. Giant aneurysm ruptures in more than 50% of cases, and the mortality is >60% within 2 years.3) The International Study of Unruptured Intracranial Aneurysms (ISUIA) part 2 found that the annual rupture rates for giant aneurysms were 8% in the anterior circulation and 10% in the posterior circulation aneurysm.20)

The poor prognosis associated with untreated giant aneurysm mandates some treatment intended to improve the natural history of the untreated lesion. The complication rate for treatment of giant aneurysm is much higher than that for smaller aneurysms. Meta-analysis of studies on the clipping of unruptured aneurysms between 1966 and 199616) found mortality and morbidity of 0.8% and 1.9%, respectively. In contrast, mortality was 7.4% and morbidity was 26.9% in patients with giant aneurysm of the anterior circulation, and 9.6% and 37.9% for patients with giant aneurysm of the posterior circulation. Therefore, the treatment of giant intracranial aneurysm is still one of the greatest neurosurgical challenges and the management remains controversial. The management strategy is individually selected, and the clinical outcome varies considerably even in neurovascular centers with experienced neurosurgeons.10,16)

The present study retrospectively reviewed the long-term outcome of 39 cases of unruptured giant intracranial aneurysm that were treated during the last 12 years at our clinic.

Materials and Methods

This study included seven male and 32 female
Table 1  Clinical summary of each group

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (yrs)</th>
<th>Sex</th>
<th>Location</th>
<th>Main symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clipping (n=11)</td>
<td>57.2</td>
<td>M 1, F 10</td>
<td>ICA 7, MCA 3, ACA 1</td>
<td>cranial nerve palsy 8, cerebral ischemia 1, akinetic mutism 1, asymptomatic 1</td>
</tr>
<tr>
<td>Bypass + ICA occlusion (n=15)</td>
<td>52.5</td>
<td>M 2, F 13</td>
<td>ICA 15</td>
<td>cranial nerve palsy 10, visual disturbance 5 asymptomatic 9, cranial nerve palsy 3, visual disturbance 1</td>
</tr>
<tr>
<td>Conservative (n=13)</td>
<td>69.4</td>
<td>M 4, F 9</td>
<td>ICA 5, BA 8 (apex 6, trunk 2)</td>
<td>asymptomatic 9, cranial nerve palsy 3, visual disturbance 1</td>
</tr>
</tbody>
</table>


Table 2  Long-term outcome of all patients with unruptured giant aneurysm

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mortality</th>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>14</td>
<td>5/26 (19%)^*</td>
</tr>
<tr>
<td>No improvement</td>
<td>6</td>
<td>5/26 (19%)^*</td>
</tr>
<tr>
<td>Deterioration</td>
<td>5</td>
<td>0/15 (0%)</td>
</tr>
<tr>
<td>Dead</td>
<td>1</td>
<td>3/15 (20%)</td>
</tr>
<tr>
<td>Surgery (n=26)</td>
<td>1/26 (4%)^*</td>
<td>5/26 (19%)^*</td>
</tr>
<tr>
<td>Clipping (n=11)</td>
<td>1/11 (9%)</td>
<td>2/11 (18%)</td>
</tr>
<tr>
<td>Bypass + ICA occlusion (n=15)</td>
<td>0/15 (0%)</td>
<td>3/15 (20%)</td>
</tr>
<tr>
<td>Conservative (n=13)</td>
<td>4/13 (31%)</td>
<td>1/13 (8%)</td>
</tr>
<tr>
<td>Total (n=39)</td>
<td>5/39 (13%)</td>
<td>6/39 (15%)</td>
</tr>
</tbody>
</table>

^*p<0.05 compared with conservative group.  ICA: internal carotid artery.

patients, aged 32 to 81 years (mean 59.5 years). The locations of the aneurysms were the internal carotid artery (ICA) in 27 cases, middle cerebral artery (MCA) in three, anterior cerebral artery (ACA) in one, and basilar artery (6 basilar apex and 2 basilar trunk aneurysms) in eight. No patient had suffered previous subarachnoid hemorrhage (SAH). Twenty-eight patients presented with symptoms related to compression of the surrounding structures by the aneurysm, one with cerebral ischemia, and 10 were asymptomatic.

The therapeutic modalities chosen were direct clipping in 11 cases, ICA occlusion combined with extracranial-intracranial (EC-IC) bypass in 15, and conservative treatment in 13 (Table 1). Follow-up examinations were performed at the outpatient clinic or by telephone interview. Various techniques used during the direct clipping operation included flow control by cervical exposure, suction decompression, brain protection, hypothermia, multiple clipping, intraoperative Doppler ultrasonography, angiography, and others. Postoperative angiography was performed to confirm obliteration of the lesions.

High-flow EC-IC bypass using radial artery or saphenous vein, or superficial temporal artery (STA)-MCA bypass was performed with monitoring by clinical evaluation, electroencephalography, and cerebral blood flow measurements. Hemodynamic stroke risk was examined and vascular reconstruction was determined based on the flowchart from the balloon occlusion test.

Thirteen patients could not be treated surgically due to symptom absence, advanced age, wishes or rejection of the operation, and the high risk involved in the surgery. These patients were followed up with lifestyle modification and strict systemic blood pressure control (below 140/90 mmHg) in the outpatient department, and the aneurysm was monitored by magnetic resonance (MR) angiography or computed tomography (CT) angiography every 6 months.

The chi-square test was used to identify any correlations in the mortality and morbidity between the treated and untreated groups. Statistical significance was set at the 5% level (p<0.05).

Results

Table 2 summarizes the outcomes of all patients with unruptured giant aneurysm. The follow-up duration was 16 to 128 months (mean 54.0 months). The overall mortality and morbidity were 13% (5/39) and 15% (6/39), respectively.
One of the 11 patients treated by clipping had persistent nerve paresis or minor neurological disorders, two patients with cerebral infarction due to the occlusion of the perforating artery had major neurological deficits and required further treatment, and death occurred in one patient. Postoperative angiography confirmed obliteration of the lesions in nine cases and residual aneurysm in two. The latter two patients were followed up in the outpatient department, and no enlarging residual lesion or rupture was observed during 36 and 48 months.

High-flow bypass was performed in seven patients and STA-MCA bypass in eight. Postoperative angiography confirmed obliteration of the lesion and patency of the bypass in all patients. Five patients had persistent cranial nerve paresis or minor neurological disorders. One patient suffered early ischemic complication, and two had late ischemic complications.

All 13 patients treated conservatively were examined by CT or MR angiography every 6 months to detect signs of aneurysm growth. The mean follow-up duration was 52.8 months (Fig. 1). No growth was observed in any patient. Despite such careful follow up under conditions of lifestyle modification and blood pressure control, four patients died of aneurysm rupture. One patient suffered deteriorated visual disturbance.

Comparison of the surgical and conservative groups showed that surgery significantly (p < 0.05) reduced the mortality (from 31% to 4%) but increased the morbidity (from 8% to 19%) during the follow-up period.

Illustrative Cases

Case 1 (clipping group, reported previously9): A 77-year-old female presented with a giant aneurysm of the azygos ACA manifesting as acute onset of akinetic mutism caused by enlargement of the aneurysm resulting from rapid thrombus formation within the aneurysm sac. CT showed a well-demarcated, 5 cm-diameter mixed density lesion with slight rim-like enhancement in the frontal interhemispheric fissure, and surrounded by severe edema. MR imaging demonstrated a large globoid lesion comprising a dorsal part appearing hyperintense on both T1- and T2-weighted images, and a ventral part appearing inhomogeneously hyperintense on T1- and inhomogeneously hypointense on T2-weighted images (Fig. 2A). Left carotid angiography revealed partial filling of the giant aneurysm, which arose at the azygos ACA. Surgery was performed using a bifrontal craniotomy approach. Thrombus was removed for decompression of the aneurysm bulk and tension before parent artery occlusion to prevent thromboembolic events. The aneurysm neck was completely clipped but the parent artery and all branches were preserved. Postoperatively the mutism completely disappeared, and angiography revealed complete disappearance of the aneurysm (Fig. 2B). The patient was discharged in excellent condition. Fifty-two months after the operation, the patient was in good health without complaints.

Case 19 (bypass group): A 60-year-old female had a 3-month history of progressive double vision in the left eye. MR imaging revealed a left medial temporal mass, and angiography revealed a giant cavernous ICA aneurysm (Fig. 3A). She tolerated the left ICA
balloon occlusion test for 20 minutes under clinical evaluation and electroencephalography monitoring. A left STA-MCA bypass was performed, and good patency was confirmed using intraoperative Doppler ultrasonography. Subsequently, ICA ligation was performed. The postoperative course was uneventful. Angiography revealed complete occlusion of the left ICA, and left external carotid artery injection demonstrated excellent filling of the distal MCA branches through the bypass graft (Fig. 3B). The symptoms improved gradually, and the patient was in good health without complaints 60 months after the operation.

**Case 39** (conservative group): A 70-year-old male presented with a 3-month history of right oculomotor nerve paresis. MR imaging revealed a medial temporal mass compressing the brain stem (Fig. 4A). The diagnosis was thrombosed giant basilar apex aneurysm (Fig. 4B). Bilateral vertebral artery occlusion and STA-posterior cerebellar artery bypass was planned, but he could not tolerate the balloon occlusion test of the bilateral vertebral arteries. The patient and his family rejected further examination for surgical management, and he was treated conservatively. He was followed up in the outpatient department under strict control of systemic blood pressure. Serial MR angiography every 6 months found no signs of aneurysm growth. However, he died of rupture of the aneurysm after 39 months (Fig. 4C).

**Discussion**

The current consensus on the management of unruptured cerebral aneurysms includes microsurgical clipping, endovascular treatment, and observation.\(^2,4\) Treatment of unruptured aneurysm is recommended for patients with lower risk of management-related morbidity. If the risk outweighs that of observation, careful follow up should be considered on an outpatient basis. The treatment risk is much higher for giant aneurysm than in nongiant aneurysm.\(^1\) Observation is more often selected than surgical or endovascular treatment for giant aneurysm, particularly in aged patients. The untreated patients are followed up in the outpatient department.

The most fragile point of the aneurysm wall is likely to be the site of rupture.\(^1\) Accordingly, enlargement or newly developed thin-wall sac (tiny de novo bleb formation) identified by CT or MR angiography may be a sign of impending rupture.\(^1\) CT and MR angiography are less invasive and safer than digital subtraction angiography, and can provide detailed anatomical information of the selected cerebral aneurysm.\(^6,11\) The accuracy for the detection of intracranial aneurysms by noninvasive imaging techniques is 89% by CT angiography and 90% by MR angiography.\(^19\) In our series, growth-related changes of a known unruptured giant aneurysm was not detected by screening in the conservative group. Nevertheless, four patients died of rupture of the aneurysm.
In recent years, a considerable amount of data describing the natural history of unruptured intracranial aneurysms has been obtained. The current results from the ISUIA part 2 study, which includes a prospective analysis of the natural history, demonstrate a higher rupture rate compared to part 1 of the same study. Part 2 has categorized aneurysms into four groups based on size (7, 7–12, 13–24, and 25 mm). The 5-year cumulative rupture rates were 0%, 2.6%, 14.5%, and 40%, respectively, for aneurysms located in the anterior circulation, and 2.5%, 14%, 18.4%, and 50%, respectively, for aneurysms in the posterior circulation in patients who had no history of aneurysmal SAH. Therefore, the annual rupture rate for giant aneurysms were 8% in the anterior circulation and 10% in the posterior circulation. SAH carries a bleak prognosis, with high mortality and morbidity. The mortality in the 1st month postrupture is estimated to be 40% to 50%, and almost half of the survivors have neurological deficits. In our series, the annual rupture rate in the nonsurgical group (n = 13) was 7% (4/13 cases in 52.8 months), and the mortality and morbidity were 31% (4/13) and 8% (1/13), respectively. The mortality and morbidity in the nontreated group will continue to increase despite strict control of systemic blood pressure (below 140/90 mmHg).

The results of treatment for giant aneurysm are also unsatisfactory. A large series of 1386 patients included 72 with giant aneurysm (5%). Twenty-two patients presented with SAH and 50 patients with cranial nerve paresis or nonspecific symptoms caused by the unruptured giant aneurysm. Treatment modalities included surgical clipping in 35 patients, balloon occlusion of the ICA in 12, endovascular coiling in seven, and combined balloon occlusion, surgical clipping, and EC-IC bypass in eight. Ten patients, seven patients with SAH and three patients without SAH, could not be treated because of advanced age or minor clinical status. Forty-seven patients with unruptured giant aneurysm were treated, the overall mortality was 6% (3/47) and morbidity was 38% (18/47). Surgical clipping was the first choice of treatment, allowing temporary clipping and reconstruction of the normal anatomy by shrinking or/and reconstructive clipping, and reducing the compression of surrounding structures by the aneurysm. Only endovascular coiling was less favorable due to the packing of the coils. Therefore, the combined endovascular and surgical approach has to be considered in selected cases. The meta-analysis study of surgical outcome found patients with giant anterior circulation aneurysm have a 7.4% mortality and 26.9% morbidity.

In our series, the total surgical mortality and morbidity were 4% (1/26) and 19% (5/26), respectively; 9% (1/11) and 18% (2/11) in the direct clipping group, and 0% (0/15) and 20% (3/15) in the indirect bypass group. Therefore, our surgical treatment could significantly reduce the mortality (from 31% to 4%) but unfortunately increased the morbidity (from 8% to 19%) as compared with conservatively treated cases (Table 2). Based on our experience, direct surgical clip occlusion may be indicated for giant aneurysm with perforating arteries which can be preserved, whereas surgical or endovascular ICA occlusion together with EC-IC bypass is indicated for giant ICA aneurysm, particularly symptomatic cavernous ICA aneurysm.

Our data is heterogeneous because of clinical differences between the patients and treatment modalities, and bias such as selection of the therapeutic modalities and aneurysm location. We actually did not surgically treat all giant aneurysms of the posterior circulation in this series. However, this study is fairly large clinical series with carefully collected follow-up data, so we can conclude that giant intracranial aneurysms do have a poor prognosis if left untreated, and these lesions are difficult to treat with our present management options.

Currently there is a great need for alternative or novel treatment strategies for the management of such difficult lesions. One approach involves the combination of surgical and endovascular techniques performed by a team of neurosurgeons and neuroendovascular surgeons. Aneurysms can be treated with combined EC-IC bypass procedures and parent vessel occlusion, flow redirection, or arterial transposition. Combined management of 21 unruptured giant and complex aneurysms achieved occlusion in 20 patients, and the mortality and morbidity were 14% (3/21) and 14% (3/21), respectively. Therefore, treatment of anterior circulation aneurysm is associated with low complication rates, whereas treatment of posterior circulation aneurysm has a higher incidence of complications, although this possibly reflects the more complex nature of these lesions. Presently, aggressive treatment involving considerable risks may still be unavoidable for such lesions. In the future, endovascular embolization or covered stents may be an effective therapeutic alternative to direct surgery in selected cases.

References

Commentary

The authors have to be congratulated for dealing with the very important subject of treatment of unruptured giant cerebral intracranial aneurysms. The series is rather small and very heterogeneous, and that’s why dealing with the necessary technical details of each group is difficult due to the limited numbers. However, in general, the authors have presented their treatment of giant aneurysms from the microsurgical and endovascular treatment, as well as the combination of both, and also the inclusion of the bypass technique(s). An important fact has been shown repeatedly in the series of patients with this difficult pathology, and that is that the surgical (active) approach does significantly reduce the mortality rate, but on the contrary does significantly increase the morbidity. Taking into consideration the well-known data from technical aspects, it reflects the

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Outcome of Unruptured Giant Cerebral Aneurysms

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I appreciate this effort to delineate the long-term outcome of patients with unruptured giant aneurysms. In recent years, several articles describing the natural history of unruptured intracranial aneurysms (UIAs) have been published. International Study of Unruptured Intracranial Aneurysms (ISUIA) part 2 study detailed that aneurysm size and location have a significant role in determining the risk of future ruptures. The 5-year cumulative rupture rate of giant aneurysm was 40% in the anterior circulation and 50% in the posterior circulation. Generally speaking, the outcomes of giant intracranial aneurysms are very grave. These results suggested that active treatment modality should be adopted instead of conservative management in the treatment of unruptured giant aneurysm.

In this series, the authors suggested that surgery reduced the mortality but increased the morbidity as compared with conservatively treated patients. As the authors mentioned, however, there could be selection bias between the surgically managed group and conservatively treated group. It could be irrational to compare the surgically treated group with conservatively treated group unless they are divided into two groups prospectively and with randomization.

Although there is a limitation of this study, I think that the present study could give valuable information in that it delineates the long-term outcome of unruptured giant cerebral aneurysms. Surgical management of giant aneurysm is troublesome and could leave inevitable complications to patients. Considering, however, the devastating effect of the giant aneurysm if untreated, appropriate management should be adopted, none the less. As the authors have mentioned, the appropriate combination of cerebral revascularization and endovascular treatment could diminish the morbidity and mortality rate of patients who were managed actively rather than conservatively. I believe that with the advancement of microneurosurgical and endovascular technique, the long-term outcome of unruptured giant aneurysm will be improved, eventually.

References


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The authors have performed a very detailed analysis of the long-term outcome of unruptured giant cerebral aneurysms. The results suggest that surgery may reduce mortality but increase morbidity as compared with conservative treatment. They also pointed out the poor prognosis of untreated giant aneurysms, difficulty of treatment with present management options, and expected future endovascular treatment with the covered stent. The morbidity was 18% in the direct clipping group, and 20% in the bypass + ICA occlusion group, suggesting their skillful surgical technique.

However, this statement seems to be influenced by the bias of a significantly different distribution of
aneurysms, in that all patients with surgical treatment had only aneurysms of the anterior circulation, whereas 8 of 13 patients treated conservatively had aneurysms of the posterior circulation. Unruptured giant posterior circulation aneurysms are notorious for their high incidence of bleeding, so any difference in outcome between the surgical and conservative groups may be overemphasized in this article.

Although selection of the bypass type as STA-MCA or high flow has been controversial, the authors selected either according to the result of the balloon occlusion test. Of course, we agree with this strategy. However, we feel somewhat anxious about the long-term outcome of EC-IC bypass, especially in the aspect of de novo aneurysm formation at the anastomotic site. Recently, we experienced two cases with de novo true aneurysm formation on the distal MCA adjacent to the anastomotic site following STA-MCA bypass surgery. Hemodynamic stress, indicated by the observation that whole branches of the MCA were perfused through the anastomosis, and intrinsic risk factors such as hypertension and presence of other aneurysms, are considered to be risk factors for aneurysms in the two patients. Now, we schedule meticulous follow up for this type of patient after EC-IC bypass surgery. Therefore, EC-IC bypass performed in patients with giant aneurysms may require long-term follow up. Further, establishment of a new endovascular option for these patients is awaited.

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