Endovascular treatment of multiple intracranial aneurysms by using Guglielmi detachable coils

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Object. The purpose of this paper is to present the authors’ experience with Guglielmi detachable coil (GDC) embolization of multiple intracranial aneurysms and to evaluate the results of this therapy in single-stage procedures.

Methods. Clinical and angiographic evaluations were performed in 38 consecutive patients with multiple intracranial aneurysms treated by GDC embolization between March 1990 and October 1997. Twenty-nine patients presented with subarachnoid hemorrhage (SAH), four with mass effect, and five were asymptomatic. These 38 patients harbored 101 aneurysms, 79 of which were treated with GDCs, 14 by surgical clipping, and eight were left untreated. Of the GDC-treated lesions, a complete endovascular occlusion was achieved in 55 aneurysms (70%), and 24 (30%) presented neck remnants. Twenty-five patients (66%) underwent GDC embolization of more than one aneurysm in the first session. Eighteen (86%) of 21 patients with acute SAH underwent treatment for all aneurysms within 3 days after admission (15 of 21 in one session). Follow-up angiographic studies in 30 patients demonstrated an unchanged or improved result in 94% of the aneurysms (59 lesions) and coil compaction in 6% (four lesions). The overall clinical outcome was excellent in 34 patients (89%), good in one (3%), fair in one (3%), and death in two (5%).

Conclusions. Endovascular treatment of multiple intracranial aneurysms, regardless of their location, with GDCs was performed safely in one session, even during the acute phase of SAH. Treatment of all aneurysms in one session protected the patient from rebleeding and eliminated the risk of mistakenly treating only the unruptured aneurysms.

KEY WORDS • multiple aneurysms • Guglielmi detachable coil • endovascular therapy

Intracranial aneurysms present in multiples in up to 34% of patients. The natural history of the disease has led to a consensus that, when technically possible, all aneurysms should be treated. The type of surgical approach as well as the timing of surgery have been extensively discussed in the neurosurgical literature. The patient’s clinical condition as well as the size and location of the aneurysms are important factors that must be evaluated before surgery. The introduction of Guglielmi detachable coils (GDCs) has made it possible to treat aneurysms safely by endovascular means. In patients in poor clinical condition and in aneurysms less suitable for surgical clipping, GDCs have been shown to be a feasible alternative modality to clipping, even in the acute phase of subarachnoid hemorrhage (SAH). The shape and size of the aneurysm, more than its topography, may present technical difficulties for treatment with GDCs. The purpose of this paper is to describe the results of endovascular management of multiple intracranial aneurysms at our institution.

Clinical Material and Methods

Patient Population

Between March 1990 and October 1997, 395 patients with intracranial aneurysms were treated with GDC embolization at our institution. Thirty-eight of these patients were treated for multiple intracranial aneurysms. There was a female predominance (32 females and six males), with patient ages ranging from 14 to 77 years (mean 49 years). This group only comprises patients in whom at least two aneurysms were treated with GDCs or in whom GDC embolization of one aneurysm was completed, followed by attempts to treat additional aneurysm(s) with GDCs. Patients treated with initial surgical clipping of one or more aneurysms followed by GDC treatment of an additional single aneurysm are not included in this study.

The 38 patients harbored a total of 101 aneurysms. Twenty-seven patients (71%) harbored two aneurysms each, six patients had three aneurysms each, and two had four aneurysms each. One patient had a total of five aneurysms, one had seven, and one had as many as nine.

Clinical Presentation

Twenty-nine patients (76%) presented with SAH, four (11%) with mass effect, and five patients (14%) were asymptomatic. Twenty-one of the 29 patients presenting with SAH were admitted during the acute phase with respect to the risk of vasospasm (within 2 weeks post-SAH). These patients were evaluated according to Hunt and Hess clinical grading. Two patients (10%) were admitted with...
Grade I, nine (43%) with Grade II, and 10 (48%) with Grade III SAH. The remaining eight patients presenting with SAH were admitted between 16 days and 5 months after recovery from the hemorrhage, and their SAH was not graded clinically.

All patients presenting with acute SAH were closely monitored in the intensive care unit for signs of vasospasm. Repeated neurological examinations, transcranial Doppler ultrasonography, monitoring of intracranial pressure and electroencephalograms, and xenon computerized tomography (CT) scanning were used for detection of vasospasm. Albumin and vasopressors were used to maximize the cardiac output and mean arterial blood pressure if vasospasm was detected. A 15 to 20% increase in the systolic blood pressure was initially induced, up to a maximum of 200 mm Hg.

Aneurysm Size/Neck Size

Of the 84 aneurysms that were treated using GDCs (including the five treatment failures) 71 (85%) were less than 15 mm in size, eight (10%) were 15 to 25 mm, and five (6%) were larger than 25 mm. Fifty-two aneurysms (62%) had necks measuring 4 mm or less, 30 (36%) had necks measuring 4 to 15 mm, eight (10%) were 15 to 25 mm, and two aneurysms (2%) were fusiform.

Aneurysm Location

Twenty-five (30%) of the 84 aneurysms that were treated using GDCs (including the five treatment failures) were located in the posterior circulation, 21 (25%) at the ophthalmic segment of the internal carotid artery (ICA), 13 (15%) at the anterior communicating artery (ACoA), and 10 (12%) at the ICA–posterior communicating artery (PCoA) junction. The remaining locations are shown in Table 1. In 17 (45%) of the 38 patients, all aneurysms were located in the anterior circulation, and in 21 patients (55%) at least one aneurysm was in the posterior circulation.

The patients were assigned to groups based on the location of their aneurysms (Table 2). In 11 patients (29%) all aneurysms were located unilaterally in the anterior circulation including the ACoA (Group 1); in six patients (16%) aneurysms were located bilaterally in the anterior circulation (Group 2); in five patients (13%) all aneurysms were located in the posterior circulation (Group 3); in 13 patients (34%) aneurysms were located in the anterior and the posterior circulations (Group 4); and in three patients (8%) the aneurysms were located bilaterally in the anterior circulation as well as in the posterior circulation (Group 5). The outcomes were assessed according to the Glasgow Outcome Scale. 15

The indications for endovascular treatment included: anticipated surgical difficulty in 26 cases (68%), failed clipping in five (13%), poor neurological grade in five (13%), and poor medical condition in two (5%). A patient was placed in the category of anticipated surgical difficulties if at least one aneurysm was considered to be surgically complex.

Technical Considerations

The endovascular technique of GDC embolization of intracranial aneurysms has been described previously. 7,9 Complete anterior and posterior circulation cerebral angiography was performed via a transfemoral route before embolization. The morphological aspects of the multiple intracranial aneurysms were evaluated. In patients with SAH the location of blood on the CT scans, the size and shape of the aneurysms, the presence of a nipple, and the presence of local vasospasm were used for identification of the ruptured aneurysm. 28 The aneurysms presumed to be ruptured were always treated first.

A Tracker No. 10 or 18 microcatheter was navigated coaxially to enter the aneurysm. Embolization was then performed using GDCs and was considered complete when a dense packing of the aneurysm with coils was achieved without compromising the lumen of the parent artery. In patients with giant or fusiform aneurysms of the intracavernous ICA or distal vertebral artery, an angiographic and functional evaluation was conducted to assess a possible endovascular treatment with parent artery occlusion. The therapeutic alternatives were always discussed with the neurosurgical team before treatment.

Timing of GDC Embolization

As a general principle, we attempted to treat all aneurysms in one session (Fig. 1). If this was not possible, a second session was scheduled soon after the first. All patients presenting with acute SAH were treated within 9 hours after admission.

Twenty-five (66%) of the 38 patients had more than one aneurysm treated using GDCs in the first session. Three patients (8%) did not return for a second session of embolization because of failed attempts in the first session (two cases) or death due to vasospasm (one case). Ten patients (26%) returned for a subsequent session of embolization.

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of Lesions</th>
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<tr>
<td>ophthalmic ICA</td>
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<tr>
<td>ACoA</td>
<td>13</td>
</tr>
<tr>
<td>BA</td>
<td>13</td>
</tr>
<tr>
<td>vertebrobasilar junction except BA tip</td>
<td>12</td>
</tr>
<tr>
<td>PCoA</td>
<td>10</td>
</tr>
<tr>
<td>MCA</td>
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<tr>
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<tr>
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<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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<td>34</td>
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<td></td>
<td></td>
<td></td>
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<td>1</td>
</tr>
<tr>
<td>BA</td>
<td>fair</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<td>1</td>
</tr>
<tr>
<td>vertebrobasilar junction except BA tip</td>
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<td>1</td>
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<td>6</td>
<td>5</td>
<td>13</td>
<td>3</td>
<td>38</td>
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</table>

* For definitions of groups see Aneurysm Location.
of additional aneurysm(s). Two of these patients, who presented with SAH, returned within 3 days to complete the treatment of the ruptured aneurysms, followed by treatment of the incidental aneurysms. Another patient returned the following day for treatment of the incidental aneurysm. The reasons for a second session in the remaining seven patients were as follows (two patients apiece): treatment with parent artery occlusion; large number of aneurysms; large or giant aneurysms; or (one patient) inexperienced treatment during the early phase of GDC development.

Of the 29 patients presenting with SAH, 10 (34%) were treated fewer than 4 days post-SAH, 11 (38%) between 4 and 14 days post-SAH, and eight (28%) more than 14 days post-SAH. Fifteen (71%) of the 21 patients presenting with acute SAH (Days 1–14) underwent treatment of all aneurysms in one session. Fourteen of these patients underwent GDC treatment for all aneurysms, and one patient with three aneurysms underwent initial surgical clipping of one, followed immediately by GDC embolization of the remaining two aneurysms (Fig. 2). Three patients with acute SAH who have been described previously had incidental aneurysms that were left untreated during the first session, and they returned for a second session within 3 days. Thus, 18 (86%) of 21 patients with acute SAH underwent treatment for all of their aneurysms during the acute phase. Two of the three remaining patients with acute SAH had incidental aneurysms that were untreated because of their very small size (≤ 2 mm), and one patient died of vasospasm before a second embolization could be attempted.

Results

Seventy-nine (78%) of 101 aneurysms were actually treated using GDCs. Twelve aneurysms (12%) in five pa-
Patients were initially treated with surgical clipping with no attempt at endovascular treatment, and two incidental aneurysms (2%) were treated with surgical clipping after failed attempts at GDC embolization. Eight aneurysms (8%), all incidental, were left untreated. In two of these untreated aneurysms (in one patient) GDC embolization was attempted but failed because of the very small size of the aneurysm. A neurosurgical evaluation was made and no additional treatment was recommended because of the patient’s age. This patient will undergo follow-up angiographic studies.

Two small incidental aneurysms were left untreated in a patient with severe vasospasm after attempts had been made to treat one of the lesions. This patient died of severe vasospasm before a second embolization session could be performed. The remaining four aneurysms were left untreated because of their small size ($\leq$ 2 mm; Table 3).

Twenty-nine patients harboring a total of 72 aneurysms presented with SAH. Presuming that only one aneurysm was ruptured in each of these patients, 43 incidental aneurysms were found in patients presenting with SAH.

In two patients the ruptured aneurysms were treated with surgical clipping followed by GDC embolization of four incidental lesions. Three additional patients were referred from other institutions for GDC embolization after incomplete clipping of a ruptured aneurysm. In two of these partially clipped aneurysms, a complete occlusion was achieved using GDCs. One partially clipped, wide-necked middle cerebral artery (MCA) aneurysm was surgically clipped after GDC embolization attempts failed. In the remaining 24 patients presenting with SAH, the ruptured aneurysm was successfully treated using GDCs as the only treatment modality. Thirty-four incidental aneurysms in the 29 patients with SAH were treated with GDCs, four with surgical clipping, and five were left untreated because the patient died (two aneurysms) or the lesions were very small ($\leq$ 2 mm).

In 29 patients (76%) all aneurysms were initially treated using GDCs alone. Four patients (11%) underwent GDC embolization of at least one aneurysm and had additional lesions that were left untreated. Five patients (13%) were initially treated with a combination of surgical clipping and GDCs embolization, and two of them had aneurysms that were left untreated. Two of the patients whose aneurysms were all initially treated with GDCs underwent
Multiple intracranial aneurysms and GDCs

TABLE 3
Treatment modality used in 38 patients with 101 aneurysms

<table>
<thead>
<tr>
<th>Presentation</th>
<th>GDCs</th>
<th>Surgery</th>
<th>No Treatment</th>
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<td>SAH</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ruptured</td>
<td>26</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>non-SAH</td>
<td>19</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>total</td>
<td>79</td>
<td>14</td>
<td>8</td>
</tr>
</tbody>
</table>

Technical Complications

Technical complications related to the GDC procedure occurred in five patients (13%), none of which led to a permanent deficit identified at clinical follow-up review. Three of the technical complications were related to thromboembolism, one to increased mass effect, and one to aneurysm rupture during the procedure. One additional patient required thrombolysis due to thrombosis of the popliteal artery after a diagnostic follow-up angiogram, also with excellent outcome.

One of the patients with thromboembolic complications experienced transient ischemic attacks from the vascular territory corresponding to the ruptured aneurysm. These symptoms resolved completely with no further treatment. Another thromboembolic event occurred in a patient treated 2 months post-SAH. This patient experienced symptoms of ischemia in the right parietal region 6 hours after GDC treatment of an anterior inferior cerebellar artery aneurysm and an aneurysm of the right PCoA. Angiographic studies demonstrated slowing of the flow in the right temporoparietal region but no branch occlusion. This indicated spontaneous recanalization after thrombembolism from the PCoA aneurysm. This patient recovered completely after 12 hours. Another thromboembolic complication occurred during treatment of an unruptured basilar artery (BA) tip aneurysm in the nonacute phase after SAH. This patient was treated with superselective urokinase infusion resulting in complete recanalization of the posterior circulation and excellent clinical recovery. The case of aneurysm rupture occurred during GDC treatment of a second aneurysm 2 days post-SAH. This rupture caused a massive SAH that led to immediate deterioration and a comatose state. The massive SAH also led to severe vasospasm that was treated with angioplasty. This patient made a remarkable recovery and was discharged in excellent condition. One patient experienced symptoms of increased mass effect from a large aneurysm in the verteobasilar junction after GDC treatment. These symptoms resolved within 2 weeks. Again, none of these complications led to clinical sequelae.

Angiographic Follow-Up Studies

As seen in Table 4, follow-up angiography was performed in 30 patients (76%) with 63 aneurysms. The follow-up period for this group varied between 2 days and 4 years, with an average of 10.7 months. These 63 aneurysms included 43 that were initially completely occluded. Forty-two (98%) of the completely occluded aneurysms remained unchanged, and one (2%) showed coil compaction and was subsequently reembolized with GDCs, achieving a complete occlusion.

Nine (45%) of the initially incompletely occluded aneurysms remained unchanged, with neck remnants; eight (40%) demonstrated complete occlusion; and three (15%) showed coil compaction. One of the three aneurysms was reembolized and complete occlusion was achieved. The other two were surgically clipped after failed retreatment with GDCs. In one of these two cases complete surgical clipping was not possible, but surgical reconstruction of the aneurysm neck allowed subsequent complete occlusion with GDCs.

Clinical Outcome

The overall clinical outcome was excellent in 34 (89%), good in one (3%), fair in one (3%), and death in two (5%). The longest follow-up time was more than 5 years, with an average follow up of 15 months (Table 4). One patient with a Hunt and Hess Grade III SAH, previously described, died of an intraparenchymal hemorrhage remote from the aneurysms after treatment with angioplasty. Another patient with a Hunt and Hess Grade II SAH, also previously described, died of vasospasm refractory to therapy. The patient who had a fair outcome was a 77-year-old woman who presented with a Hunt and Hess Grade III SAH and who was disoriented when discharged, with no other neurological deficit, despite uneventful GDC treatment. No patient has presented with a new hemorrhage or rehemorrhage.
Discussion

The initial severity of the primary intracranial hemorrhage, aneurysm rerupture, and symptomatic vasospasm are the major causes of morbidity and mortality related to a ruptured intracranial aneurysm. Early treatment of the ruptured aneurysm by surgery or embolization eliminates the risk of rebleeding. A maximum effort can then be focused on postoperative care and the treatment of vasospasm.

Patients harboring multiple intracranial aneurysms and presenting with SAH have at least one additional incidental aneurysm. The annual bleeding risk of an unruptured aneurysm has been described as 1 to 2.3% regardless of previous occurrence of SAH from other aneurysms. The frequency of rupture has been reported to be even higher in patients with multiple aneurysms. The risk of rupture of an incidental aneurysm during the aggressive treatment of vasospasm is not known.

Surgery for multiple intracranial aneurysms can be performed in a single or multiple session(s). The surgical technique depends on the size and location of the multiple intracranial aneurysms and the neurological condition of the patient and varies among different institutions. Surgical clipping of all aneurysms can be performed in one session in 70 to 80% of patients with multiple intracranial aneurysms. A unilateral location of multiple intracranial aneurysms in the anterior circulation is more favorable for a one-stage procedure than one involving the bilateral anterior circulation or a combination of anterior and posterior circulation. The one-stage procedure can be performed using a unilateral, a contralateral, or a bilateral surgical approach. A unilateral approach can be used when all aneurysms are located unilaterally in the anterior circulation. The contralateral approach favors a single craniotomy with surgical access to aneurysms located in the ipsilateral as well as the contralateral vasculature. In the bilateral approach, surgery is performed via two sequential craniotomies. However, in an acute setting after SAH the surgical access to multiple aneurysms is more difficult because of brain swelling and hydrocephalus, which reduce the surgical space.

The clinical presentation is a major factor contributing to the overall clinical outcome in patients with multiple intracranial aneurysms. Misdagnosis of the ruptured aneurysm, the necessity of multiple surgical approaches during the acute phase post-SAH, age, and large aneurysms are other factors contributing to poor outcome in patients with multiple intracranial aneurysms. Delayed neurological deficits have been reported to cause a worse outcome in patients with multiple intracranial aneurysms than in those with single intracranial aneurysms.

Aggressive HHH therapy increases the intracranial arterial pressure to ensure brain perfusion in patients with symptomatic vasospasm. This pressure regimen carries the potential risk of rupturing an unprotected incidental aneurysm. Postoperative volume expansion has been used without complications, but the rupture of an incidental unprotected aneurysm during the early phase after surgery has also been described.

Mizoi, et al., reported four ruptures of untreated lesions in 14 patients, which occurred within 16 days after surgical clipping of aneurysms presumed to be ruptured. Operative findings, CT scans, and angiograms obtained in three of these patients indicated that these bleeds came from previously unruptured aneurysms. The risk of bleeding of an unprotected aneurysm favors a single-stage procedure in patients with multiple intracranial aneurysms. However, the use of multiple surgical approaches during the acute stage after SAH has been reported to be one of the factors leading to poor outcome.

Elective surgery of unruptured intracranial aneurysms in patients with a single lesion results in low rates of morbidity (4.1%) and mortality (1%). A multistage procedure in patients with multiple intracranial aneurysms involves a cumulative risk of complications. Multiple intracranial aneurysms in the bilateral anterior circulation or in the posterior circulation in patients with SAH create additional surgical difficulties with increased morbidity and mortality rates.

In a series of 136 patients with multiple intracranial aneurysms and SAH, Inagawa reported no difference in surgical outcome when comparing multiple and single intracranial aneurysms. However, in his series 30 patients (22%) with multiple intracranial aneurysms received no surgical treatment, with an 83% mortality rate after 1 year. A similar result when comparing single and multiple aneurysms has been described for bilateral craniotomies performed in a single session by Edner. In his series, 17 (24%) of 70 patients with acute SAH did not undergo treatment of all aneurysms in one session because of severe brain edema, extended operative time, or other anticipated surgical difficulties.

In a series of 221 patients with multiple intracranial aneurysms treated by surgical clipping, Orz, et al., reported an excellent or good overall outcome in 67.9% of patients presenting with SAH, compared with 86.5% in patients with unruptured aneurysms. This was comparable to the results in single intracranial aneurysms treated during the same period. In his series, treatment of all aneurysms in one session was achieved in 132 (90%) of 147 patients harboring multiple intracranial aneurysms unilaterally in the anterior circulation, compared with only four (9%) of 44 with lesions located bilaterally in the anterior circulation and 18 (60%) of 30 with lesions in the anterior and posterior circulation. Furthermore, 64% of patients with aneurysms located bilaterally in the anterior circulation and 30% of patients with aneurysms in the anterior and posterior circulation did not receive treatment for all lesions. Older patient age, poor neurological grade, and relatively small or intracavernous lesions were the main reasons for not treating all aneurysms.

Mizoi, et al., reported an overall morbidity rate of 14 to 19% and a mortality rate of 6 to 8% in 372 patients who underwent surgery for unilateral or bilateral multiple intracranial aneurysms after SAH, which were comparable to rates seen in surgery of single aneurysms in the anterior circulation. The mortality rate in patients harboring multiple intracranial aneurysms involving the posterior circulation was as high as 27%. In his study, 78% of the patients received complete treatment of all aneurysms in one session, 7% underwent complete treatment in two sessions, and 15% did not receive treatment of all aneurysms. Ninety-one percent of the patients with aneurysms located unilaterally in the anterior circulation underwent treatment of all aneurysms in one session, compared with 62%...
with lesions located bilaterally in the anterior circulation and 42% with aneurysms in the anterior and posterior circulation. Six (11%) of 55 patients left with untreated aneurysms died when these lesions ruptured.

In GDC embolizations, difficulties may be created by the size of the aneurysm and its neck rather than its location. An incomplete GDC embolization with loose coil packing may lead to coil compaction and aneurysm recanalization. This is particularly true in small aneurysms with wide necks or in large or giant lesions. In cases of aneurysm recanalization, attempts should be made to occlude the aneurysm completely by reembolization or by surgical clipping.

Endovascular occlusion of unruptured aneurysms can be performed in one session immediately after treatment of the ruptured aneurysm, with no need for an extended craniotomy and brain retraction. In case of technical difficulties, a second session can be performed soon after, even during the acute phase post-SAH.

In our series, in 15 patients (71%) treated during the acute phase after SAH all aneurysms were treated in one session, regardless of lesion location, and 18 (86%) had undergone treatment of all aneurysms within 3 days after the initial treatment. The remaining three patients treated during the acute phase after SAH were left with untreated aneurysms because of size (2 mm; two patients) or death from severe vasospasm (one patient).

Even if all aneurysms are embolized in one session, the ruptured lesion should always be treated first. This eliminates the risk of early rebleeding and provides the option of treating additional aneurysms in a second session either by embolization or surgery in case of technical difficulties.

The risk of rupturing an unprotected incidental aneurysm during the early phase after SAH has been described. In our series, there were no episodes of rebleeding or new hemorrhage from aneurysms treated with either GDCs or by surgical clipping, even during HHF treatment for vasospasm.

Clinical deterioration caused by vasospasm can be reversed adjunctively by endovascular treatment with papaverine and/or balloon angioplasty. Angioplasty and papaverine infusion can be performed in the same session.

The number of patients in our study does not allow a complete statistical analysis of the clinical outcome in relation to the location of the aneurysms (Table 3). However, technical difficulties were never related to the location of the aneurysms, and no patient underwent a second session of GDC embolization or had aneurysms that were left untreated because of their location.

The long-term results of GDC treatment are not yet known. The numbers of patients and aneurysms in this study do not provide enough information for a statistical analysis of the long-term results of multiple intracranial aneurysms treated with GDCs. One would expect, however, that the long-term result on angiographic studies in one GDC-treated aneurysm should be unaffected by the presence of other lesions.

Conclusions

Embolization of multiple intracranial aneurysms by using GDCs is a viable therapeutic alternative with low morbidity and mortality rates. With the endovascular technique, all multiple intracranial aneurysms can be treated in one session regardless of their location. The single-stage procedure eliminates the risk of mistakenly treating only the unruptured aneurysms and minimizes the potential risk of hemorrhage from an unprotected incidental aneurysm during treatment of vasospasm.

References


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