Treatment of brain arteriovenous malformations with high-flow arteriovenous fistulas: risk and complications associated with endovascular embolization in multimodality treatment

Clinical article

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Object. High-flow fistulas associated with brain arteriovenous malformations (AVMs) pose a significant challenge to both stereotactic radiosurgery (SRS) and surgical treatment. The purpose of this study was to examine the outcomes of multimodality treatment of AVMs in association with a large arteriovenous fistula (AVF), with a special focus on endovascular embolization and its associated complications.

Methods. One hundred ninety-two patients harboring cerebral AVMs underwent endovascular treatment in the authors’ department between 1997 and 2003. Of these, the authors selected 74 patients presenting with an AVM associated with high-flow AVF(s) for a retrospective analysis based on the findings of superselective angiography. After endovascular embolization, 32 patients underwent resection, 33 underwent either SRS or hypofractionated stereotactic radiotherapy (HSRT), and 3 underwent both surgery and SRS. Six patients underwent embolization only. Immediate and midterm treatment outcomes were analyzed.

Results. Fifty-seven (77%) of the 74 patients had AVMs that were Spetzler-Martin Grade III or higher. A complete resection was achieved in all 32 patients. Of patients who underwent SRS/HSRT, 13 patients (39.3%) had either complete or > 90% obliteration of the AVM, and 2 patients (6.1%) had incomplete obliteration. Fourteen patients (42.4%) with residual AVM underwent repeated radiotherapy (and remain under observation). Of the 3 patients who underwent both SRS and resection, resection was complete in 2 and incomplete in one. No follow-up was obtained in 6 patients (8.1%). An endovascular complication was observed in 4 patients (5.4%). Fistula embolization was safely performed in every patient, whereas every endovascular complication was associated with other procedures such as nidus embolization.

Conclusions. Endovascular occlusion of the fistulous component was successfully achieved in every patient; every endovascular complication in this series was related to other procedures such as nidus embolization. The importance of the fistula treatment should be emphasized to minimize the endovascular complications and to maximize the treatment effect when a multimodality therapy is used to treat brain AVMs with large AVF.

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Key Words • brain arteriovenous malformation • high-flow fistula • endovascular complication • multimodality treatment

Abbreviations used in this paper: AVF = arteriovenous fistula; AVM = AV malformation; GDC = Guglielmi detachable coil; GOS = Glasgow Outcome Scale; HSRT = hypofractionated stereotactic radiotherapy; NBCA = N-butyl cyanoacrylate; SRS = stereotactic radiosurgery.
In this series, we reviewed the treatment outcomes of 74 patients with brain AVMs and high-flow AVFs. All patients underwent endovascular embolization followed by resection or SRS. The treatment outcome was analyzed with a special focus on the risk of endovascular treatment.

**Methods**

**Patient Demographics**

One hundred ninety-two patients with cerebral AVMs underwent endovascular treatment in our department between January 1997 and October 2003. Of these individuals, 74 patients presenting with an AVM and an associated high-flow AVF were selected for a retrospective analysis. Thirty-two patients were male and 42 patients were female. Their average age was 40 years. The AVMs were diagnosed by either CT or MR imaging at the time of initial presentation. Preembolization digital subtraction angiography was performed in all cases to obtain a detailed angioarchitecture of the vascular malformation.

**Image Evaluation**

The AVMs were classified using the Spetzler-Martin classification (size of the AVM, eloquence of the adjacent brain, and the presence/absence of deep venous drainage). The AVM size was determined by CT, MR imaging, or digital subtraction angiography. Cerebral digital subtraction angiography was used to determine the patterns of the angioarchitecture and to identify the presence of any intranidal aneurysms, high-flow AVFs, and compromised venous drainage associated with the AVM nidus.

**Definition of “High-Flow AVF” in an AVM**

In most cases, an AVM is a cluster of multiple components with different types of angioarchitecture. Although conventional selective angiography with a guide catheter is useful to ascertain general angiographic information about the AVM, the modality is not sufficient to delineate the angioarchitecture of its structural components. Once the complete picture of an AVM is obtained, superselective injection of every major feeding artery using a microcatheter is mandatory to evaluate detailed angioarchitecture of the vascular malformation.

**Selective catheterization of the artery supplying the AVF** was performed using road-mapping techniques. Superselective angiography of the AVF was performed to locate the junction between the feeding artery and the initial venous component. The primary aim of the procedure was to occlude the lesion at the fistula site. However, not infrequently, it was necessary to occlude the abnormally dilated venous component associated with the fistula. Prior to the embolization, we always confirmed that there were multiple venous outlets in the AVM and that the target fistula component was not the conjoined outlet of a plexiform AVM but an isolated arteriovenous shunt. As an initial step, oftentimes, detachable coil devices were delivered to a target site through a microcatheter that was advanced using an over-the-wire technique. To avoid untoward embolic migration into the venous system, cerebral veins, dural sinus, and pulmonary circulation, the liquid embolic agents were used only after a sufficient flow reduction was obtained by predeployed coil materials. Liquid embolic agents used included NBCA or the Onyx Liquid Embolic System. In most cases, the endovascular procedure was shifted to embolization of the nidus component. In some cases, however, the nidus embolization was postponed for a few days if postembolization angiography showed intense flow stagnation in large cerebral varix/varices. An immediate postembolization head CT scan was obtained in all cases to rule out the development of “silent” intracranial bleeding. On average, a total of 2 to 4 feeders were embolized per session. Multistaged embolizations were performed at intervals of 3–4 weeks.

**Treatment Strategy of Radiation Therapy/Resection**

Surgically approachable lesions were generally indicated for resection. Small-sized AVMs (defined as < 3 cm) and superficial AVMs were generally resected. For those considered to be surgically unapproachable, stereotactic radiotherapy was considered. There were 2 different approaches depending on the radiation method: single-dose SRS or HSRT. If an AVM was < 5 cm in maximal diameter, it was treated with SRS. If the maximal diameter was ≥ 5 cm, it was treated with HSRT. Lesions treated with HSRT had a volume of 12 ml or larger (12–155 ml). Three to 5 years after the radiation therapy, repeated SRS or HSRT was discussed with the patient if any residual AVM was observed on follow-up imaging studies. In individuals with remaining fistulous components or a significant plexiform component, additional endovascular treatment was performed prior to the second SRS/HSRT. Resection was generally performed between 7–10 days after the final embolization. All patients underwent postoperative angiography and MR imaging. For those who underwent SRS, a Radionics BRW or a BrainLAB stereotactic frame was placed during the last endovascular procedure. The patients were then transferred to the SRS treatment room. A custom-fitted thermoplastic mask...
Treatment of brain AVMs with high-flow fistula (U-PLAST, BrainLAB AG) was used for immobilization during HSRT. The Novatis dedicated system (BrainLAB AG) with miniature multileaf collimator capability was used in this series.

**Evaluation of Posttreatment Imaging Studies**

For the purpose of analysis, the patients were subdivided into 4 groups: patients who underwent resection, radiation therapy, both surgery and radiosurgery, and those who only underwent embolization. For those who underwent resection, postoperative angiograms were obtained 1–2 weeks after the procedure. Posttreatment MR images were acquired at 3 and 6 months. For those who underwent radiation therapy, posttreatment MR imaging and MR angiography were performed every 12 months up to 36 months after treatment or until complete occlusion was confirmed. Magnetic resonance angiography was used as the screening tool to evaluate the occlusion rate, but conventional angiography was always performed to make the final confirmation. Regardless of the treatment modality, patients with residual AVM confirmed on follow-up angiograms were reevaluated for repeated radiation therapy or resection on the basis of their age, clinical condition, and the response to the first radiosurgical procedure.

**Evaluation of Clinical Outcome**

The GOS\textsuperscript{4} was used to evaluate clinical results after surgery or SRS/HSRT. Midterm follow-up evaluations were performed in each case with office visits and telephone interviews. Just as we did with the image analysis, the patients were subdivided into 4 groups, and the clinical outcome in each group was independently evaluated.

**Results**

**Patient Demographics**

Seventy-four patients underwent 127 embolizations for an average of 1.7 embolizations per patient. Seven patients (9.5%) had Spetzler-Martin Grade I, 10 (13.5%) had Grade II, 20 (27%) had Grade III, 22 (29.7%) had Grade IV, and 15 (20.3%) had Grade V lesions (Table 1). Thirty-nine percent of patients underwent endovascular embolization followed by resection. Thirty-three patients underwent endovascular embolization followed by SRS/HSRT. In the subgroup of patients treated with SRS/HSRT, there were no Grade I lesions. Two patients (6.1%) had Grade II, 12 patients (36.4%) had Grade III, 12 patients (36.4%) had Grade IV, and 7 patients (21.2%) had Grade V. In the subgroup of patients treated by surgery, 6 patients (18.8%) had Grade I, 7 patients (21.9%) Grade II, 8 patients (25.0%) Grade III, 5 patients (15.6%) Grade IV, and 6 patients (18.8%) had Grade V lesions. Clinical presentations associated with hemorrhagic events included parenchymal hemorrhage in 20 patients (27%), subarachnoid hemorrhage in 3 patients (4%), and intraventricular hemorrhage in 5 patients (6.8%). Other clinical presentations were seizures in 27 patients (36.5%), headaches in 10 patients (13.5%), progressive neurological deficit in 5 patients (6.8%), and an incidental finding in 4 patients (5.4%).

**Angiographic Outcome**

In all 32 patients (100%) who underwent resection after embolization, complete AVM removal was achieved. In 33 patients who underwent postembolization radiation therapy, complete AVM obliteration was achieved in 10 patients (30.3%) and >90% obliteration was achieved in 3 patients (9.1%), whereas in 2 patients (6.1%) obliteration was incomplete. In 14 patients (42.4%) the lesion remained incompletely obliterated and these individuals underwent repeated radiotherapy for a residual nidus component. No follow-up was obtained in 4 patients (12.1%). Of the 3 patients who underwent both SRS and resection, 2 patients had complete resection and 1 had an incomplete resection. In the 6 patients who underwent endovascular embolization alone, complete AVM obliteration was demonstrated in 2 and incomplete obliteration was shown in 2. The remaining 2 patients did not undergo follow-up evaluation (Table 2).

**Immediate Morbidity/Mortality**

Fifty-three patients (71.6%) exhibited a good recovery (GOS Score 5) immediately after the acute treatment.
Fourteen patients (18.9%) exhibited a moderate disability (GOS Score 4) and 5 patients (6.8%) severe disability (GOS Score 3). One patient died of initial bleeding and another died (2.7%) of a complication related to the embolization procedure (GOS Score 1).

Midterm Morbidity/Mortality

The mean follow-up duration after the last treatment was 20.2 months. Fourteen of 33 patients who underwent SRS/HSRT had follow-up of at least 3 years Fifty-four patients (73.0%) exhibited a good recovery (GOS Score 5). Ten patients (13.5%) had a moderate disability (GOS Score 4) and 6 (8.1%) had severe disability (GOS Score 3). Four patients (5.4%) died (GOS Score 1). One patient died due to a technical complication. The other 3 patients died due to hemorrhage of AVMs after treatment.

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Midterm Morbidity Related to Technical Complication: Endovascular Treatment

Technical complications related to the embolization occurred in 4 patients.

Case 1 (Spetzler-Martin Grade II). A cerebral cortical infarction occurred 2 days after the initial embolization. The patient presented with transient hemiparesis that resolved over a month (GOS Score 5).

Case 2 (Spetzler-Martin Grade V). A distal migration of NBCA into the draining vein occurred during the nidus embolization, which resulted in cortical bleeding.

Although we removed the AVM immediately after the endovascular procedure, the patient had mild hemiparesis (GOS 3).

Case 3 (Spetzler-Martin Grade III). A perforation of a parent artery occurred during the procedure. A postembolization CT scan revealed mild subarachnoid hemorrhage, and the patient underwent resection of the AVM immediately. The patient presented with a mild lower-extremity monoplegia (GOS Score 4).

Case 4 (Spetzler-Martin Grade III). A patient with intractable seizure caused by a large AVM in the posterior fossa was treated with 2 sessions of embolization. An arterial perforation occurred in the second procedure, and intraparenchymal bleeding was confirmed on a postoperative CT scan. This patient died in the acute postoperative period.

There was no complication related to the endovascular occlusion of high-flow AVFs.

Midterm Morbidity Related to Technical Complication: Surgical Treatment

Technical complications related to the resections occurred in 2 patients.

Case 1 (Spetzler-Martin Grade III). This patient had a mild short-term memory disturbance after removal of an AVM located at the left temporal lobe (GOS Score 4).

Case 2 (Spetzler-Martin Grade V). A postoperative hemorrhage occurred. A minor oozing from the residual AVM was confirmed during the second operation and hematoma evacuation was performed. The patient had mild cerebellar symptoms (GOS Score 4).

Midterm Morbidity Related to Technical Complication: SRS/HSRT

Case 1 (Spetzler-Martin Grade V). A radiation necrosis caused by SRS occurred in this patient 1 year after the treatment. The patient, who has an AVM located in the right temporal lobe, developed progressive left hemiparesis that exhibited a mild improvement at the last visit (GOS Score 4) (Table 3).

Discussion

High-Flow AVF Associated With AVMs: Anatomical and Hemodynamic Challenge for Radiation Therapy and Surgery

Cerebral AVMs associated with high-flow AVFs present a therapeutic challenge to SRS and frequently result in incomplete AVM obliteration. Histopathological findings observed in animal experiments as well as in clinical data suggest that SRS is more successful in occluding small vessels of plexiform AVMs than in larger high-flow vessels. Meanwhile, AVMs with high-flow AVFs are also associated with increased perioperative hemorrhagic events. Therefore, endovascular embolization of large AVFs is considered to be of utmost importance in the endovascular management before the SRS/HSRT or resection.
Concerns About Postembolization Hyperemic Status and Postoperative Bleeding

In general, acute compromise of the venous drainage of a plexiform AVM or dural sinus in the early phases of embolization does carry a risk of hemorrhage.\(^1\)\(,\)\(^3\)\(^7\) Nevertheless, a fistulous occlusion does not necessarily lead to such hemorrhagic complications as long as the procedure does not compromise venous drainage of the plexiform component or dural sinuses. Moreover, despite the fact that fistula embolization was always the priority during the endovascular procedure and was often done before the occlusion of the plexiform component in this series, there was no perioperative bleeding directly associated with fistula embolization. Figure 1 shows conceptual diagrams of an AVM before and after fistulous occlusion. A high-flow fistula unit, in most cases, is observed as an independent vascular architecture from the nidus component (Fig. 1 upper). Before the treatment, in most cases, intracranial venous pressure is significantly increased because of the high-flow shunting. The resultant venous hypertension would therefore induce a circulation disturbance in the surrounding tissue, including nidus components. In fact, after the occlusion of a large AVF, angiograms often demonstrate a significant reduction of cortical vein reflux as well as remarkable size reduction in the draining veins of a plexiform AVM (Fig. 1 lower). Therefore, it is conceivable that the positive effect from the decreased venous pressure can outweigh the potential negative effect from the relatively increased flow in the plexiform AVM.

Preoperative Embolization and Perioperative Hemorrhagic Event

Spetzler and colleagues\(^2\)\(^8\) have reported their clinical experience of surgically treated AVMs that were pretreated with staged embolization. They emphasized the importance of staged presurgical embolization to facilitate the intraoperative manipulation and to minimize the perioperative complications such as nonperfusion-pressure breakthrough. In every patient in our series who underwent resection, a complete AVM removal was achieved, and there was no postoperative hemorrhagic event associated with the hemodynamic change. This may indicate that the presurgical embolizations indeed played a positive role in this series.

Use of SRS/HSRT for the Treatment of Large AVMs

Thirty-one (93.9%) of 33 patients in the SRS/HSRT group had a Spetzler-Martin Grade III or higher lesion, and 30 (90.1%) of 33 harbored AVMs \(\geq 3\) cm at the time of the first treatment.

Treatment of high-grade AVMs (Grades III–V), or so-called large/giant AVMs, has proven to be a greater challenge for SRS,\(^3\)\(^,\)\(^5\)\(^,\)\(^10\)\(^,\)\(^15\) and treatment in this group of patients remains controversial.\(^7\)\(^,\)\(^22\)\(^,\)\(^35\) However, recent reports indicate that the hemorrhage rate of large AVMs is higher than previously believed.\(^2\)\(^,\)\(^29\) It is also to be noted that this patient group includes many young patients with a high risk of bleeding throughout their lives, and the consequences of a large AVM hemorrhage are usually catastrophic. In this series, the treatment indication in each patient was carefully discussed and determined in individual cases.

In our series, 13 patients (39.3%) in the SRS/HSRT group had a Spetzler-Martin Grade III or higher lesion, and 30 (90.1%) of 33 harbored AVMs \(\geq 3\) cm at the time of the first treatment.

**TABLE 3: Midterm morbidity caused by technical complications**

<table>
<thead>
<tr>
<th>Treatment Method</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>embolization</td>
<td>4 (5.4)</td>
</tr>
<tr>
<td>resection</td>
<td>2 (5.6)*</td>
</tr>
<tr>
<td>radiation therapy</td>
<td>1 (2.8)†</td>
</tr>
</tbody>
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* Denominator is the number of patients (35) who underwent surgery.
† Denominator is the number of patients (36) who underwent radiosurgery.

**Fig. 1.** Conceptual diagrams of pre- and postembolization of a high-flow AVF. **Upper:** A high-flow fistula unit (upper portion) is, in most cases, an independent vascular architecture from the plexiform component (lower portion). Because of the high-flow arteriovenous shunting, the venous pressure is significantly increased (arrows). Resultant venous hypertension induces circulation disturbance in the surrounding tissue including plexiform components. **Lower:** After occlusion of a large AVF, local circulation dramatically improves along with venous hypertension. Postoperative angiograms often demonstrate a reduction of cortical vein reflux as well as the size reduction of draining veins of plexiform AVM. The positive effect from the improved local circulation may outweigh the potential negative effect from the relatively increased flow in the plexiform AVM.
going treatment, we believe that the angiographic result in this group was still comparable to other studies of large AVMs treated by SRS.\textsuperscript{8,20}

**Endovascular Technique for Embolization of AVMs With High-Flow AVF**

Recently, the technology of intracranial catheter navigation has dramatically improved due to rapid advances in microcatheter systems. In the past, flow-guided microcatheters, through which we could not deploy detachable coils, were often the only means of reaching distally located fistula sites. Today, the latest microcatheter systems allow us to use the over-the-wire technique and access distal branches so that we can deploy detachable coil materials into the AVF. Furthermore, the presence of an array of embolic materials such as coils and liquid embolic agents has made the endovascular procedure more controllable and predictable.

Unlike the technically challenging maneuvers involved in occluding a large nidus with multiple feeders and drainers, embolizing a fistulous component is relatively simple. The most important aspect is to avoid uncontrolled migration of embolic material into draining veins or dural sinuses. Therefore, we seldom used liquid embolic agents alone to treat large high-flow AVFs. Instead, GDCs or Liquid Coils were primarily used to achieve the gradual reduction of blood flow by multistep delivery of different embolic materials.

After achieving sufficient reduction of flow rate, total occlusion was completed by injecting liquid materials such as NBCA or Onyx (Fig. 2). Occasionally, if the feeders were extremely tortuous and coil deployment was considered to be difficult, a microballoon system was placed proximal to the tip of the microcatheter to control the flow rate while delivering liquid embolic agents via the microcatheter (Fig. 3).

**Risk of Endovascular Procedure as a Part of Multimodality Treatment for AVMs**

A discussion of the anticipated benefit of preoperative embolization compared with the risks needs to take place before treatment. Intracranial embolization still

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**Fig. 2.** A: An internal carotid artery (ICA) angiogram, lateral projection, demonstrating a right frontal AVM (Spetzler-Martin Grade II). A dilated venous component of AVF is observed. B: A superselective angiogram, lateral projection, showing a large high-flow fistula. A microcatheter navigated through abnormally dilated single feeder (small arrows) goes directly into the dilated venous component (arrow). C: A postembolization ICA angiogram, lateral view, demonstrating an embolized fistulous component with GDC coils followed by NBCA (arrow). A partial embolization of the nidus component was also performed. D: A postoperative ICA angiogram, lateral view, revealing complete removal of the AVM.

**Fig. 3.** A: An ICA angiogram, lateral view, demonstrating a left occipital AVM (Spetzler-Martin Grade III). B: A superselective angiogram, lateral view, obtained through the advanced microcatheter. C: A balloon system (Hyperglide 4 × 10) (arrowhead) was used to control the blood flow rate at the proximal side of the feeding artery (arrow; tip of the microcatheter). Onyx-34 was injected to embolize this fistulous component. D: A postembolization ICA angiogram, lateral view, revealing an obliterated fistulous component and significantly reduced arteriovenous shunting.
Treatment of brain AVMs with high-flow fistula

carries a risk of morbidity and death. Risks of complications leading to long-term morbidity range from 2 to 20%.11,21,34 Taylor et al.10 have reported their series of 201 patients treated with embolization prior to resection: death occurred in 2% and permanent neurological deficits developed in 9%. They emphasized that the complication rate of the endovascular procedure itself should be carefully evaluated prior to the treatment because the number is not negligible.

In our series, 3 patients (4.1%) had endovascular complications leading to morbidity, and 1 patient (2.5%) died. Although most of the patients (3 of 4) with technical morbidity experienced a relatively mild neurological deficit, the incidence of the complication is far from negligible and should be carefully considered.

Of particular note is the fact that there was no technical complication directly related to the fistula embolization, whereas all the endovascular complications were related to other procedures such as nidus embolization. Given the benefit from the procedure and its relatively safe technique, the importance of the fistula treatment should be emphasized to minimize the endovascular complication and to maximize the treatment effect when a multimodality therapy is used to treat brain AVMs.

Conclusions

Seventy-four patients with AVMs and associated high-flow AVFs underwent endovascular embolization followed by radiation therapy or surgical treatment. Most patients (77%) had lesions classified as Spetzler and Martin Grade III or higher. In the resection group, a total resection was achieved in each patient without a major perioperative hemorrhagic event. In the SRS/HSRT group, 39.3% of the patients had a complete or > 90% occlusion, and 6.1% had an incomplete obliteration. Patients undergoing SRS/HSRT tended to have larger lesions than individuals in the surgical group.

Fistula occlusion was prioritized in every endovascular procedure and nidus occlusion was also undertaken as a supportive therapy in light of the subsequent surgical or radiosurgical treatment. There was no technical complication directly related to the AVF embolization, whereas all the endovascular complications associated with long-term morbidity were related to other procedures such as nidus embolization. The importance of the fistula treatment should be emphasized to minimize endovascular complications and to maximize the treatment effect when a multimodality therapy is used to treat brain AVMs.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References


