Surgical Treatment of Spetzler-Martin Grade III to V Cerebral Arteriovenous Malformations: 10 Years Experience in Kyoto University

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Abstract
Cerebral arteriovenous malformations (AVMs) are abnormal connections between arteries and veins leading to arteriovenous shunting with nidus formation. This study reviewed the clinical outcomes of surgical treatment for AVMs of Spetzler-Martin grades III to V in our institute. In addition, we summarized the technical aspects of surgical treatment for cerebral AVMs. Our development of the surgical modality for high-grade AVMs included intraoperative digital subtraction cerebral angiography, non-stick bipolar forceps, magnetic resonance tractography, and indocyanine green videoangiography. Excellent outcomes were obtained, but about 40% of all patients with AVMs could not receive surgical treatment. Multimodality approach including Onyx embolization may extend the surgical indications.

Key words: arteriovenous malformation, surgical treatment, indocyanine green videoangiography, Onyx, bipolar forceps

Introduction
Cerebral arteriovenous malformations (AVMs) are abnormal connections between arteries and veins leading to arteriovenous shunting with nidus formation.7,15,18) Cerebral AVM prevalence varies between 15 and 18 per 100 000 adults. About half of all patients with cerebral AVMs present with intracranial hemorrhage, resulting in a first-ever hemorrhage rate of 0.55 per 100 000 person-years. Little is known about the etiology of brain AVMs, but the etiology is likely to be multifactorial.7,15,18) Cerebral AVMs are commonly classified with the Spetzler-Martin grading scale, which is a composite score of nidus size, adjacent eloquent areas, and presence of deep venous drainage. The risk of subsequent hemorrhage from the cerebral AVM is increased by the presence of hemorrhage or deep venous drainage, association with aneurysms, or deep location. The target of cerebral AVM treatment is typically the prevention of hemorrhage.7,15,18) Microsurgery has a low risk of complications for Spetzler-Martin grade I and II cerebral AVMs and results in immediate cure, but is invasive. Stereotactic radiosurgery can be effective for malformations that are smaller than 3.5 cm, but complete obliteration is only completed approximately 1 to 3 years after treatment and cure is not always obtained. Embolization is used to obliterate small malformations or to make larger malformations amenable for surgery. Cerebral AVMs categorized as Spetzler-Martin grade IV or V generally require multimodality treatment.2,3,7,13,15,18,19)

This study reviews our clinical experience of treatment for AVMs of Spetzler-Martin grades III to V in our institute, and summarizes the technical aspects of surgical treatment of cerebral AVMs based on specific cases.
### Table 1 Grades of cerebral arteriovenous malformations admitted to Kyoto University Hospital (April 2001–June 2012)

<table>
<thead>
<tr>
<th>Spetzler-Martin grade</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>30</td>
</tr>
<tr>
<td>II</td>
<td>54</td>
</tr>
<tr>
<td>III</td>
<td>43</td>
</tr>
<tr>
<td>IV</td>
<td>22</td>
</tr>
<tr>
<td>V</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>156</strong></td>
</tr>
</tbody>
</table>

### Table 2 Summary of surgical cases (Spetzler-Martin grades III–V)

<table>
<thead>
<tr>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>38</td>
</tr>
<tr>
<td>hemorrhagic</td>
<td>25</td>
</tr>
<tr>
<td>non-hemorrhagic</td>
<td>13</td>
</tr>
<tr>
<td>Indication</td>
<td></td>
</tr>
<tr>
<td>hemorrhage</td>
<td>5</td>
</tr>
<tr>
<td>motor weakness</td>
<td>14</td>
</tr>
<tr>
<td>visual pathway</td>
<td>7</td>
</tr>
<tr>
<td>seizure</td>
<td>2</td>
</tr>
<tr>
<td>consciousness disturbance</td>
<td>5</td>
</tr>
<tr>
<td>others</td>
<td>5</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>headache</td>
<td>2</td>
</tr>
<tr>
<td>motor weakness</td>
<td>14</td>
</tr>
<tr>
<td>incidental</td>
<td>8</td>
</tr>
<tr>
<td>consciousness disturbance</td>
<td>7</td>
</tr>
<tr>
<td>others</td>
<td>7</td>
</tr>
</tbody>
</table>

### Patients and Clinical Intervention

A total of 156 patients with cerebral AVM were admitted to the Department of Neurosurgery, Kyoto University Hospital from April 2001 to June 2012 (Table 1). During this period, 72 cases of AVM were categorized as Spetzler-Martin grades III to V. Among them, we assessed 62 cases of which 37 cases were treated by microsurgery and one case by radiosurgery, which were treated before September 2011. Twenty-five of these AVMs were hemorrhagic and 13 AVMs were non-hemorrhagic. We analyzed the surgical indications as shown in Table 2. Severe preoperative neurological deficit was present in 19 patients, motor weakness in 14, and consciousness disturbance in 5. Seven non-hemorrhagic AVMs were located on the visual pathway. Mean modified Rankin scale was 2.2 ± 1.5 on admission and 2.3 ± 1.2 on discharge among patients treated surgically. One of these patients suffered over 2 grades worsening. Twenty-four patients were not treated surgically. One AVM was located in the brain stem, 15 in the basal ganglia, and eight in the motor cortex.

### Policy of Surgical Treatment

We have regularly reviewed the surgical policy of our department for AVMs since 1990. High-grade AVMs were aggressively challenged with intravascular surgery in the 1990s. This policy was ended by our previous study that indicated palliative treatment increased hemorrhage of cerebral AVMs.12) Strict surgical indications were applied in the 2000s. We principally avoided surgical treatment for patients who are expected to suffer worsening of neurological findings postoperatively. Usually, we did not perform surgical treatment against AVMs located in the brain stem, basal ganglia, thalamus, and motor cortex. Multimodality approach was introduced from 2009 with the revival of nidus embolization using Onyx.

### Technical Considerations

Our surgical procedures have developed over the last 10 years. We have introduced intraoperative digital subtraction angiography (DSA), magnetic resonance (MR) tractography, non-stick bipolar forceps, intraoperative neuronavigation, and indocyanine green (ICG) videoangiography.7,16) The usefulness of these modalities is discussed based on illustrative cases.

#### I. Intraoperative DSA

Management of the feeding artery is the most important consideration during nidus resection. Intraoperative angiography can detect untreated feeders and the flow pattern in the nidus.6,7,17) Usually a catheter inserted via the right femoral artery was continuously irrigated with saline including heparin throughout surgery. Intraoperative angiography allows assessment of the surgical result and, possibly, correction or completion of removal prior to wound closure. This confirmation reduces the necessity for re-operation and the risk of postoperative complications. Moreover, intraoperative angiography has revealed that perfusion changes in the course of AVM extirpation may alter its configuration. The illustrative case occurred in a 37-year-old male. The AVM was fed by the anterior cerebral artery (ACA) and middle cerebral artery (MCA). At first, major
feeders from the ACA and MCA were clipped. Intraoperative DSA showed reduced and slowed flow in the nidus (Fig. 1A, B). Finally feeders from the lenticulostriate artery were occluded and the nidus was removed (Fig. 1C, D). Figure 1E and F show the C-arm equipment (OEC 9900 Elite; GE Healthcare Japan, Tokyo).

II. Bipolar forceps
Management of perinidus small feeders was very important. These tiny vessels easily rupture and are very fragile, so are very difficult to adequately coagulate. Thermal injury to the surrounding tissue causes stickiness on the tips of the forceps. Bipolar forceps with heat-pipe technology (IsoCool; Codman & Shurtleff, Inc., Raynham, Massachusetts, USA) (Fig. 2A) can manage tissue temperature and cause less injury compared with conventional antistick forceps.4,5 Thermography shows less heat elevation in the heat-pipe bipolar forceps (Fig. 2B) compared with the conventional type (Fig. 2C). This type of forceps allowed us to perform AVM removal with less coagulation (Fig. 2D, E).7,8 The surgeons could securely stop bleeding from tiny fragile vessels in and around the nidus. In addition, they could easily confirm the margin of the nidus and normal brain tissue.

III. MR tractography
Diffusion tensor imaging and fiber tractography can visualize the three-dimensional macroscopic fiber tract architectures and offer information about eloquent white matter tracts. We applied this technique to AVM surgery. Preoperatively, the location of corticospinal tract or visual pathways was analyzed. In addition, postoperative connection of these tracts was also assessed.9,14 The illustrative case occurred in a 6-year-old girl. Preoperatively she had mild hemiparesis. Preoperative fiber tractography indicated that the corticospinal tract was located near the dorsomedial part of the nidus (Fig. 3A–D). Preoperative cerebral angiography showed Spetzler-
IV. Intraoperative neuronavigation

Our neuronavigation system provided combined high-resolution MR images including tract images and MR angiograms both pre- and postoperatively. The location of dissection was confirmed intraoperatively. The illustrative case occurred in a 37-year-old male with left frontal Spetzler-Martin grade II AVM. Intraoperative neuronavigation (VectorVision® Compact; Brainlab, Feldkirchen, Germany) indicated the location of the dissection (Fig. 4).16)

V. ICG videoangiography

ICG videoangiography is useful for the intraoperative assessment of cerebral vascular flow, so providing a useful adjunct for the intraoperative control of vessel patency and aneurysm occlusion during aneurysm surgery. ICG videoangiography is available within several minutes and can easily be repeated as previously described.17) Consequently, ICG videoangiography may be a simple tool for intraoperative monitoring and documentation of surgical outcomes. In addition, compared with intraoperative DSA, ICG videoangiography provides the same image as the surgical view, which is a great advantage. Furthermore, ICG videoangiography can monitor dynamic flow changes under surgical view and confirm stopped flow in the nidus.17) The illustrative case occurred in a 47-year-old male. Preoperative angiography indicated right occipital Spetzler-Martin grade III AVM. The captured movie
obtained by intraoperative ICG videoangiography was analyzed with Flow® 800 software (Carl Zeiss Meditec, Jena, Germany) using a OPMI® Pentero® surgical microscope (Carl Zeiss Meditec). Delayed images disclosed reduced and slowed flow of the nidus after clipping of the feeders (Fig. 5A, B). Maximum intensity images indicated that maximum flow volume was not different (Fig. 5C, D). The diagram also showed that the region of interest (ROI) was slowly gained and decreased (especially the green and red ROI) compared with the predissection diagram (Fig. 5E, F). Based on these results, the surgeons could confirm the flow within the AVMs and safely remove the nidus.

VI. Onyx embolization

The introduction of the non-adhesive ethylene vinyl-alcohol copolymer Onyx (ev3, Irvine, California, USA) has largely replaced the use of acrylic glue for the obliteration of the nidus in many centers. Advanced biplane imaging with rapid subtraction fluoroscopy, and refinements of technique in the use of Onyx, now allow a considerable proportion of small and intermediate-sized brain AVMs to be completely obliterated with a low complication rate, on the condition that the nidus is accessible by the microcatheter with feeders suitable for injection with Onyx, allowing 2–3 cm of reflux. In our institute, after the introduction of Onyx, we employed preoperative embolization. Eight of the 12 high-grade AVM patients after 2009 were treated by the multimodality approach. Seven patients received pre-surgical Onyx embolization. One patient received pre-radiosurgical embolization. The illustrative case occurred in a 20-year-old female. Preoperative angiography showed frontal AVM (Fig. 6A). After injection, most of the nidus was embolized with Onyx (Fig. 6B, C). Intraoperative inspection found that the occluded nidus looked black, together with the intranidus necrotic tissue and removed nidus (Fig. 6D–F).

Discussion

Most cerebral AVMs of Spetzler-Martin grades I and II can be surgically removed with acceptably low morbidity and mortality by experienced neurosurgeons, whereas most cerebral AVMs of grades IV and V are not indicated for surgery. The reported annual bleeding rates of palliatively treated AVMs are over 10%. Although some beneficial roles of palliative treatment have been proposed, such as partial embolization to reduce shunt flow in patients with progressive neurological deficits caused by the steal phenomenon, or embolization of intranidal aneurysms, palliative treatment should be avoided general-
ly or considered as a possible and significant increase in bleeding risk.7,15,18 There is a diverse treatment spectrum of grade III AVMs, and treatment options or combinations vary between surgeons, depending on experience or preference and the applicability of other treatment modalities. In general, small, deep-seated AVMs are good candidates for radiosurgery. Embolization should be performed after considering the potential risks and benefits, and feeder occlusion by embolization behind the nidus is effective as a preoperative treatment. Nidus embolization is effective for increasing the chance of curing large AVMs by radiosurgery. Staged operations are also recommended for large AVMs to reduce the risk of intra- and postoperative hemorrhage. Recently, the multimodality approaches were tested for the treatment of Spetzler-Martin grade III to V AVMs.7,15,18 The clinical results were reported for one AVM in Spetzler-Martin grade III, 9 in Spetzler-Martin grade IV, and 43 in Spetzler-Martin grade V.21 Nineteen patients (36%) were completely cured of giant AVMs, 90% obliteration was achieved in 4 patients (8%), and less than 90% obliteration was achieved in 29 patients (55%) who had residual AVMs even after multimodality therapy. In another series including 5 grade III, 21 grade IV, and 14 grade V lesions, 31 (77.5%) demonstrated excellent or good outcome, but this report included palliative treatment.19 Staged radiosurgery has also been performed for large AVM, but satisfactory clinical results have not been obtained. In our study, only one case (2.6%) showed worsened clinical outcome among 38 patients. This result depended on the selection bias of the patients. Our study included 24 untreated patients.

The natural history of high-grade AVMs was recently investigated in a series of 63 patients with grade IV and V AVMs with a mean follow-up time of 11.0 years.10 The mean annual rate of rupture was 3.3%, but was 6.0% in patients with hemorrhagic presentation compared to 1.1% in patients with unruptured AVMs.10 Therefore, it is important to consider the expected natural course of the AVM when the surgeons plan treatment options.

We have introduced intraoperative DSA,5 bipolar forceps,4,5 MR tractography,9,13 and ICG videoangiography.17 Intraoperative DSA enabled us to exclude the possibility of residual nidus. Recently, various types of bipolar forceps and generator have become available. Use of non-stick bipolar forceps is very important in the dissection of the nidal vessels buried in the white matter. MR tractography helped us to assess the likely neurological deficit after nidus removal. We selected the patients to receive surgical treatment based on the findings of neural tract imaging. Finally, we developed intraoperative ICG videoangiography to visualize nidus flow directly and reduce the frequency of intraoperative DSA.17

The usefulness of Onyx embolization in the treatment of AVMs was recently discussed.1,11,13 In our institute, aggressive embolization using Onyx was employed to treat high-grade AVMs. Preoperative Onyx embolization reduces intraoperative bleeding and occludes deep feeders which cannot be seen from the surface of the brain. However, the complication rate is reported to be relatively high, so careful management and planning are advisable.

The present study of the clinical outcome and development of surgical modality for high-grade AVMs in our institute showed excellent outcome of the treatment. However, despite recent surgical advances, about 40% of the patients did not receive surgical treatment. Multimodality approach including Onyx embolization may extend the surgical indications.

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