Adjuvant Embolization With N-Butyl Cyanoacrylate in the Treatment of Cerebral Arteriovenous Malformations

Outcomes, Complications, and Predictors of Neurologic Deficits

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Background and Purpose—The purpose of this study was to assess the frequency, severity, and predictors of neurological deficits after adjuvant embolization for cerebral arteriovenous malformations.

Methods—From 1997 to 2006, 202 of 275 patients with arteriovenous malformation received embolization before microsurgery (n = 176) or radiosurgery (n = 26). Patients were examined before and after endovascular embolization and at clinical follow-up (mean, 43.4 ± 34.6 months). Outcome was classified according to the modified Rankin Scale. New neurological deficits after embolization were defined as minimal (no change in overall modified Rankin Scale), moderate (modified Rankin Scale = 2), or significant (modified Rankin Scale > 2).

Results—Two hundred two patients were treated in 377 embolization procedures. There were a total of 29 new clinical deficits after embolization (8% of procedures; 14% of patients), of which 19 were moderate or significant. Postembolization deficits resolved in a significant number of patients over time (P < 0.0001). Five patients had persistent neurological deficits due to embolization (1.3% of procedures; 2.5% of patients). In multivariate analysis, the following variables significantly predicted new neurological deficit after embolization: complex arteriovenous malformation with treatment plan specifying more than one embolization procedure (OR, 2.7; 95% CI, 1.4 to 8.6), diameter > 3 cm (OR, 3.2; 95% CI, 1.2 to 9.1), diameter > 6 cm (OR, 6.2; 95% CI, 1.0 to 57.0), deep venous drainage (OR, 2.7; 95% CI, 1.1 to 6.9), or eloquent location (OR, 2.4; 95% CI, 1.0 to 5.7). These variables were weighted and used to compute an arteriovenous malformation Embolization Prognostic Risk Score for each patient. A score of 0 predicted no new deficits, a score of 1 predicted a new deficit rate of 6%, a score of 2 predicted a new deficit rate of 15%, a score of 3 predicted a new deficit rate of 21%, and a score of 4 predicted a new deficit rate of 50% (P < 0.0001).

Conclusions—Small and large size, eloquent location, deep venous drainage, and complex vascular anatomy requiring multiple embolization procedures are risk factors for the development of immediate postembolization neurological deficits. Nevertheless, a significant number of patients with treatment-related neurological deficits improve over time. The low incidence of permanent neurological deficits underscores the usefulness of this technique in carefully selected patients. (Stroke. 2009;40:2783-2790.)

Key Words: arteriovenous malformation • complication • embolization • outcome • surgery

The goal of treatment in cerebral arteriovenous malformations (AVMs) is elimination of intracerebral hemorrhage risk, alleviation of clinical symptoms, and preservation or improvement of neurological function. Microsurgery, radiosurgery, and endovascular embolization have all been used successfully in various combinations. Treatment planning requires selection of a modality or a combination of modalities with the greatest success rate according to patient characteristics and AVM morphology. Embolization-related morbidity and mortality vary greatly in reports. Risks depend on patient selection, treatment modalities, and outcomes measures. Risk is also related to the goals of endovascular embolization therapy. In the past, embolization was commonly used as “primary therapy.” However, more recently, studies demonstrated that AVMs treated only with embolization have low obliteration rates. Therefore, embolization is usually not recommended as single-modality therapy except for palliation of nonsurgical or nonradiosurgical AVMs. Beginning in 1997, the treatment paradigm at our institution changed significantly with the introduction of gamma knife radiosurgery, regular application of intra- and postoper-
reative angiography, and application of the Spetzler-Martin grading system biased against treating high-grade (Spetzler-Martin 4 and 5) AVMs. Moreover, except in uncommon circumstances requiring palliation only, embolization has been generally used only as a preoperative adjuvant before microsurgical resection or radiotherapy. The goals of this study were: (1) to analyze the frequency, severity, and types of neurological deficits after preoperative embolization of cerebral arteriovenous malformations; (2) to determine how these deficits evolve over time; (3) to assess the predictors of new neurological deficits after embolization; and (4) to use multivariate analysis to identify predictors of endovascular treatment outcomes.

Materials and Methods
Between 1997 and 2006, a total of 275 patients with AVM were treated by the Department of Neurological Surgery at Columbia University Medical Center. Two hundred two of these patients (74%) underwent catheter cerebral arteriography and endovascular embolization as a part of multimodality therapy. After embolization treatment, 176 patients (87%) underwent microsurgical resection and the remaining 26 (13%) received gamma knife radiosurgery. Outcomes were assessed in this IRB approved study.

Patient Selection
A team of cerebrovascular microsurgeons, endovascular neurosurgeons, and radiosurgeons evaluates each brain AVM to determine the best treatment plan. The goal of combined multimodality intervention was complete elimination of the AVM along with preservation of normal neurological function or alleviation of neurological deficits. Treatment planning was based on selecting a modality or a combination of modalities with the greatest success rate according to patient characteristics and AVM morphology.

Outcome Measures
We retrospectively analyzed the charts of 275 patients from a historical AVM database. All patients were examined immediately before and after each embolization procedure. Long-term outcomes were recorded in 251 patients (91%). Seventeen patients (8%) were lost to long-term follow-up after microsurgery. In these patients, outcome assessment on follow-up was performed (mean time from embolization to discharge after surgery and follow-up assessment was 26 months). All patients were alive after embolization and surgery. Mean follow-up in all patients was 43.4±34.6 months.

Neurological outcomes were stratified according to the modified Rankin Scale (mRS).37 New neurological deficits after embolization were defined as minimal if there was no change in mRS, moderate (mRS 2), or significant (mRS >2). If a patient with significant pre-existing disability (mRS >2) had a new deficit due to treatment that did not change his or her overall function, the deficit was still recorded as a new significant deficit as a result of treatment. If a deficit was made worse due to microsurgery or radiosurgery (ie, occurring in the same distribution), assessment on follow-up was made as to the overall change in mRS.

Embolization Technique
Endovascular embolization was performed using the transfemoral approach with patients under monitored anesthetic care general. Biplane, high-resolution digital subtraction angiography was used for treatment planning in each case. Microcatheter navigation of the cerebral vasculature was performed using subtraction roadmap imaging. Superselective angiography was performed before embolization, and provocative anesthetic testing was performed as needed using amobarbital and lidocaine. N-butyl cyanoacrylate (Trufill NBCA; Cordis Neurovascular, Miami Lakes, Fla) was used to occlude the vascular nidus once the microcatheters were advanced into position.

Table 1. Baseline Characteristics of 202 Patients Treated for Cerebral AVMs*

| Age, years | 35±13 (range, 4–75) |
| Female gender | 118 (58%) |
| Race |  |
| White | 131 (65%) |
| Hispanic | 31 (15%) |
| Black | 9 (5%) |
| Asian | 9 (5%) |
| Other | 22 (10%) |
| Medical history |  |
| Hypertension | 11 (6%) |
| Diabetes mellitus | 5 (3%) |
| Hypercholesterolemia | 6 (3%) |
| Cardiac disease | 3 (2%) |
| Smoking | 30 (15%) |
| Initial presentation |  |
| Hemorrhage | 79 (39%) |
| Seizure | 60 (30%) |
| Headache | 101 (50%) |
| Neurological deficit | 80 (40%) |
| Syncope | 11 (6%) |
| Asymptomatic | 7 (4%) |
| AVM characteristics |  |
| No. of major arterial feeders | 1.5±0.7 |
| Concurrent aneurysm | 86 (43%) |
| Spetzler-Martin criteria |  |
| Deep venous drainage | 89 (44%) |
| Eloquent location | 60 (30%) |
| Small diameter (<3 cm) | 118 (58%) |
| Medium diameter (3–6 cm) | 80 (40%) |
| Large (>6 cm) | 4 (2%) |
| RBGSR |  |
| <0.5 | 7 (4%) |
| 0.5–1.0 | 68 (34%) |
| >1.0 to <1.5 | 65 (32%) |
| >1.5 | 62 (30%) |
| Treatment |  |
| Embolizations | 377 |
| Surgery after endovascular treatment | 176 (87%) |
| Radiosurgery after endovascular treatment | 26 (13%) |

*Mean follow-up 43.4±34.6 months.
†Radiosurgery Based Grading Scale (RBGS)=0.1(volume)+(0.02(patient age)+(0.3)(location).
The purpose of preoperative embolization was staged reduction of blood flow in an AVM by stepwise occlusion of the AVM nidus over several weeks, elimination of deep-feeding arteries such as lenticulostriates that could require extension of the resection plane beyond the margin of the nidus, occlusion of any other feeding arteries not readily accessible during surgery such as skull base dural collaterals, and coil occlusion of feeding artery aneurysms distant from the operative exposure of the AVM itself. Occlusion was performed according to the goals of treatment: (1) nidal occlusion to reduce AVM size and for flow reduction through the fistula; (2) provocative anesthetic testing and occlusion of deep feeding arteries or arteries not readily accessible to surgery; and (3) endovascular occlusion for feeding artery aneurysms without impairment of the parent artery lumen. Standard microsurgical techniques were carried out as previously described. All patients received intraoperative or postoperative catheter angiography to confirm complete obliteration.

Statistical Analysis

Univariate analysis was used to test the ability of patient and AVM characteristics to predict new postembolization neurological deficits. Factors predictive in univariate analysis (P < 0.15) were entered into a stepwise backward multivariate logistic regression analysis to ascertain the effects of patient and AVM characteristics on immediate postembolization neurological complications while controlling for patient gender and age. These variables were weighted and used to compute an AVM Embolization Prognostic Risk Score for each patient. The Mantel-Haenszel test for linear association was used to assess the significance between ascending AVM Embolization Prognostic Risk Score and incidence of deficits.

Results

After 1997, more narrow selection criteria for surgery were adopted; intraoperative or immediate postoperative angiography was routinely performed; the institution’s gamma knife center was opened, and endovascular treatment was regularly used for preoperative treatment. Two hundred two patients received a total of 377 embolizations. One hundred ten (55%) were defined as minimal, 94 (5%) as moderate, and 10 (5%) as significant (mRS ≥ 2). On long-term follow-up, minimal postembolization deficits remained in no patients; 4 had persistent moderate deficits (11% of procedures) and one had a significant deficit (0.3% of procedures). Postembolization deficits resolved in a significant number of patients on long-term follow-up (mean, 43.4 ± 34.6 months; P = 0.0001).

Technical complications of the embolization procedures are shown in Table 4. Intracranial hemorrhage (10 patients) and infarction (6 patients) were the most common peri- or postprocedural complications. Two patients (2.5%) with medium-diameter AVMs had hemorrhage versus 7 patients (6%) with small-diameter AVMs (univariate logistic regression: OR, 5.3; P = 0.13) or one patient (25%) with a large-diameter AVM (OR, 13; P = 0.018; Figure). There were no peri- or postprocedural infarctions in medium-sized AVMs, but there was a trend toward increased risk of infarction in large AVMs versus small AVMs (univariate logistic regression; Figure).

Factors predictive of new deficit due to embolization in univariate analysis (P < 0.15) were staged embolization using more than one procedure (OR, 2.6; 95% CI, 1.1 to 5.9), deep venous drainage (OR, 2.3; 95% CI, 1.0 to 5.5), and eloquent location (OR, 1.8; 95% CI, 0.8 to 4.1; Table 5). Additionally, patients with medium-diameter AVMs (3 to 6 cm) were less likely to experience a neurological deficit due to embolization (OR, 0.3; 95% CI, 0.1 to 1.0), whereas patients with large-diameter AVMs (>6 cm) were more likely (OR, 7.4; 95% CI, 1.0 to 57.0). As might be expected, patients with peri- or postembolization complications were more likely to have postembolization deficits: hemorrhage (OR, 32.5; 95% CI, 6.5 to 163.7) and 5 of 5 patients with infarction.

In multivariate analysis controlling for patient gender, the following pre-embolization variables were predictive of new neurological deficit: staged embolization using more than one procedure (OR, 2.7; 95% CI, 1.4 to 8.6), deep venous drainage (OR, 2.7; 95% CI, 1.1 to 6.9), eloquent location (OR, 2.4; 95% CI 1.0 to 5.7), and small diameter (<3 cm; OR, 3.2; 95% CI, 1.2 to 9.1; Table 6). Although there were only 4 patients with large-diameter AVMs, size >6 cm also significantly predicted new deficit after embolization. (OR, 6.2; 95% CI, 1.0 to 57.0). The relationship between AVM

Table 2. Overall Outcome Over Time

<table>
<thead>
<tr>
<th>Overall mRS</th>
<th>Before First Embolization</th>
<th>After Last Embolization</th>
<th>Long-Term Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2</td>
<td>184 (91%)</td>
<td>174 (86%)</td>
<td>173 (94%)</td>
</tr>
<tr>
<td>3</td>
<td>15 (7%)</td>
<td>20 (10%)</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>4</td>
<td>3 (2%)</td>
<td>8 (4%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3. New Neurological Deficits Due to Embolization Over Time

<table>
<thead>
<tr>
<th></th>
<th>Any Deficits</th>
<th>Moderate or Significant Deficit</th>
<th>Significant Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate deficits</td>
<td>29 (14%; 8%)</td>
<td>19 (9%; 5%)</td>
<td>10 (5%; 3%)</td>
</tr>
<tr>
<td>Long-term deficits</td>
<td>5 (2.5%; 1.3%)</td>
<td>4 (2%; 1%)</td>
<td>1 (0.5%; 0.3%)</td>
</tr>
</tbody>
</table>

Note. Presented as n (% per patients; % per embolization treatment). Outcome was classified according to the mRS. New neurological deficits after embolization were defined as minimal (no change in overall mRS), moderate (mRS = 2), or significant (mRS > 2).

Table 4. Complications in 377 Embolizations

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri- or postprocedural hemorrhage</td>
<td>10 (2.6%)</td>
</tr>
<tr>
<td>Infarction</td>
<td>6 (1.6%)</td>
</tr>
<tr>
<td>Dissection</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Femoral/retroperitoneal hematoma</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Retrograde arterial thrombosis</td>
<td>1 (0.3%)</td>
</tr>
</tbody>
</table>
Size and neurological deficit after embolization is demonstrated in the Figure.

Variables predictive of embolization-related deficits in multivariate analysis were weighted and used to compute an AVM Embolization Prognostic Risk Score for each patient (Table 7). Patients receive 1 point if their treatment plan requires more than one embolization procedure, 1 point for small-diameter (<3 cm) AVM, 1 point for eloquent location, 1 point for deep venous drainage, and 2 points for large size (>6 cm). Summation of each patient’s points yields a score ranging from 0 to 5. A score of 0 predicted no new deficits, a score of 1 predicted a new deficit rate of 6% (100% moderate/significant), a score of 2 predicted a new deficit rate of 15% (40% moderate/significant), a score of 3 predicted a new deficit rate of 21% (71% moderate/significant), and a score of 4 predicted a new deficit rate of 50% (100% moderate/significant; Mantel-Haenszel test for linear association, \( P < 0.0001 \)). Based on selection criteria, no treated patients had a score of 5. Although the AVM Embolization Prognostic Risk Score predicted immediate deficits due to embolization, it did not predict long-term deficits because a significant number of patients had improvement over time.

**Discussion**

In general, endovascular embolization is performed before surgical resection of AVMs to reduce the size of the active nidus and establish more normal blood flow patterns for brain tissue surrounding the AVM. Embolization is used for Spetzler-Martin Grade II through III lesions before microsurgery or radiosurgery but only used in Grade IV or V lesions in multimodality care in which the goal of treatment is complete occlusion or resection. Identifying factors that predict complications and poor outcome after embolization would improve patient selection and AVM treatment outcomes. Predictors of complications and outcome may also help guide patient management.

In this study, we found that: (1) adjuvant embolization in the treatment of cerebral AVMs results in a low rate of neurological deficits; (2) small and large size, eloquent location, deep venous drainage, and the number of planned embolization procedures predict postembolization neurological deficits; (3) these variables may be weighted in the AVM Embolization Prognostic Risk Score to predict new neurological deficits after embolization; (4) a significant number of patients with deficits will improve over time; and (5) the low incidence of permanent neurological deficits underscores the usefulness of this technique in carefully selected patients.

Studies have demonstrated that preoperative embolization leads to decreased operative time, blood loss, and morbidity and mortality in cerebral AVM surgery. Embolization may be used as: (1) primary therapy, ie, without surgical resection or radiotherapy; (2) adjuvant embolization before microsurgery or radiosurgery; or (3) for palliation of inoperable or otherwise incurable AVMs. Prior studies suggest that primary embolization results in a low obliteration rate; therefore, embolization as a single modality is not generally recommended. In “palliative care” of inoperable AVMs, embolization may be used to treat or reverse a specific symptom due to high-flow cardiovascular impairment, venous hypertension, or arterial steal phenomenon. Staged preoperative embolization was used to decrease flow as a strategy to normalize cerebral blood flow, eliminate deep-feeding arteries, occlude feeding vessels not readily accessible
during microsurgery, reduce volume of the active nidus, and coil occlude feeding artery aneurysms outside the operative field at the time of AVM resection.

There were 29 new postembolization clinical deficits (8% of procedures; 14% of patients), of which 9 were moderate and 10 were significant. After a mean follow-up of 43.4 ± 34.6 months, there were 5 persistent neurological deficits due to embolization (1% of procedures; 2% of patients) of which 4 were moderate and one was significant. This is the first series to demonstrate that the majority of deficits after embolization are transient with a significant number of moderate and severe deficits improving over time. In the literature, there has been a wide range of reported morbidity (1% to 50%) and mortality (1% to 4%) after embolization of AVMs.6–35 Recent and large studies have found a permanent morbidity rate of 3% to 14% and a mortality rate of 0% to 4%.9,10,14,15,18,23,35,42–44 Rates are dependent on many factors: patient selection, embolic agents, means of delivering the occlusive agent, goals of embolization, ie, primary curative

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
<th>OR</th>
<th>95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>35±13 (range, 4–75)</td>
<td>1.02</td>
<td>0.99–1.05</td>
<td>0.180</td>
</tr>
<tr>
<td>Female gender</td>
<td>118 (58)</td>
<td>0.98</td>
<td>0.38–2.54</td>
<td>0.961</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>131 (65)</td>
<td>0.97</td>
<td>0.11–8.27</td>
<td>0.975</td>
</tr>
<tr>
<td>Hispanic</td>
<td>31 (15)</td>
<td>0.97</td>
<td>0.11–8.27</td>
<td>0.975</td>
</tr>
<tr>
<td>Black</td>
<td>9 (5)</td>
<td>0.26</td>
<td>0.32–2.02</td>
<td>0.198</td>
</tr>
<tr>
<td>Asian</td>
<td>9 (5)</td>
<td>0.36</td>
<td>0.05–2.94</td>
<td>0.346</td>
</tr>
<tr>
<td>Other</td>
<td>22 (10)</td>
<td>0.96</td>
<td>0.11–7.94</td>
<td>0.971</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td>1.61</td>
<td>0.59–5.23</td>
<td>0.428</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (6)</td>
<td>1.06</td>
<td>0.41–1.74</td>
<td>0.658</td>
</tr>
<tr>
<td>Smoking</td>
<td>30 (15)</td>
<td>1.02</td>
<td>0.37–2.55</td>
<td>0.965</td>
</tr>
<tr>
<td>Initial presentation</td>
<td></td>
<td>1.07</td>
<td>0.38–2.75</td>
<td>0.947</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>79 (39)</td>
<td>1.79</td>
<td>0.69–4.63</td>
<td>0.227</td>
</tr>
<tr>
<td>Seizure</td>
<td>60 (30)</td>
<td>1.71</td>
<td>0.66–4.56</td>
<td>0.262</td>
</tr>
<tr>
<td>Headache</td>
<td>101 (50)</td>
<td>0.84</td>
<td>0.35–2.04</td>
<td>0.704</td>
</tr>
<tr>
<td>Neurological deficit</td>
<td>80 (40)</td>
<td>1.79</td>
<td>0.69–4.63</td>
<td>0.227</td>
</tr>
<tr>
<td>Syncope</td>
<td>11 (6)</td>
<td>1.96</td>
<td>0.11–7.94</td>
<td>0.971</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>7 (4)</td>
<td>1.02</td>
<td>0.22–4.74</td>
<td>0.984</td>
</tr>
<tr>
<td>No neurological deficit at baseline</td>
<td>184 (91%)</td>
<td>1.53</td>
<td>0.70–3.39</td>
<td>0.295</td>
</tr>
<tr>
<td>AVM characteristics</td>
<td></td>
<td>1.58</td>
<td>0.41–1.74</td>
<td>0.658</td>
</tr>
<tr>
<td>No. of arterial feeders</td>
<td>86 (43)</td>
<td>0.98</td>
<td>0.37–2.55</td>
<td>0.965</td>
</tr>
<tr>
<td>Concurrent aneurysm</td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small diameter (&lt;3 cm)</td>
<td>118 (58)</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Medium diameter (3–6 cm)</td>
<td>80 (40)</td>
<td>0.29</td>
<td>0.08–1.04</td>
<td>0.058</td>
</tr>
<tr>
<td>Large (&gt;6 cm)</td>
<td>4 (2)</td>
<td>7.43</td>
<td>0.97–57.00</td>
<td>0.054</td>
</tr>
<tr>
<td>Deep venous drainage</td>
<td>89 (44)</td>
<td>2.31</td>
<td>0.97–5.51</td>
<td>0.058</td>
</tr>
<tr>
<td>Eloquent location</td>
<td>60 (30)</td>
<td>1.83</td>
<td>0.82–4.13</td>
<td>0.141</td>
</tr>
<tr>
<td>Spetzler-Martin score</td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>49 (24)</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>78 (39)</td>
<td>1.85</td>
<td>0.55–6.16</td>
<td>0.318</td>
</tr>
<tr>
<td>3 or 4</td>
<td>75 (37)</td>
<td>1.58</td>
<td>0.38–6.63</td>
<td>0.533</td>
</tr>
<tr>
<td>RBGS location*†</td>
<td>202 (100%)</td>
<td>1.25</td>
<td>0.52–3.02</td>
<td>0.023</td>
</tr>
<tr>
<td>RBGS</td>
<td>202 (100%)</td>
<td>1.10</td>
<td>0.77–1.56</td>
<td>0.608</td>
</tr>
<tr>
<td>&gt;1 embolization procedure planned</td>
<td>92 (46%)</td>
<td>2.60</td>
<td>1.1–5.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peri-/postprocedural hemorrhage</td>
<td>10 (2.7%)</td>
<td>32.50</td>
<td>6.5–163.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peri-/postprocedural infarction‡</td>
<td>5 (1.32)</td>
<td>5 of 5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Radiosurgery Based Grading Scale (RBGS) = (0.1)(volume) + (0.02)(patient age) + (0.3)(location).
†RBGS location: frontal, temporal = 0; parietal, occipital, intraventricular, corpus callosum, cerebellar = 1; basal ganglia, thalamic, brainstem = 2. When an AVM involves multiple sites, fractional values are used according to the no. of sites (0.5 for 2 sites, 0.33 for 3 sites).
‡Infarction predicts any new neurological deficit in 5 of 5 patients.
or adjuvant therapy, time of outcome assessment, and pre-existing neurological morbidity.6,8–13,27,28,31,35,36

It is important to note inherent limitations of our outcome data. The mRS does not measure higher cortical function and postoperative cognitive decline. This must be taken into account when considering operative morbidity.45,46 Moreover, neuropsychological testing after surgical AVM excision is critical to accurate outcome assessment and should be integrated into future clinical trials.

In our study, there were 10 periprocedural or early hemorrhages after embolization (2.6% of procedures; 4% of patients), which is similar to bleeding complication rates reported in the literature (1% to 2% of procedures; 3% to 15% of patients).20,47,48 Hemorrhage was more likely to occur in small and large AVMs. Hemorrhage during or after embolization may be due to vessel perforation during catheterization, AVM rupture, intranidal aneurysm rupture, or hemodynamic changes due to alterations in feeder pressures, normal perfusion breakthrough, or venous outflow obstruction.48–52 Further studies are necessary to elucidate the etiology of these bleeds, the factors predictive of peri- or postembolization bleeds, and their relevance toward long-term outcome.

In multivariate analysis, greater than one embolization procedure planned, small- and large-diameter nidus, deep venous drainage, and eloquent location predicted new neurological deficit after embolization. The Spetzler-Martin grading scale was designed and validated to predict surgical treatment outcome, and its applicability to endovascular embolization is unclear.5,53 Previous studies have found that not all elements of the Spetzler-Martin grading scale are predictive in outcomes after embolization.9,10,42 This may in part be due to the assumption that AVM size in the Spetzler-Martin grading scale has a linear relationship with outcome as it does in microsurgery. In our series, however, patients with small AVMs and larger AVMs were significantly more likely to develop deficits after embolization. One explanation is that we have demonstrated that small and large AVMs are more likely to hemorrhage after embolization. Small AVMs may be technically more difficult to embolize than medium-sized AVMs. The increased propensity of small, untreated AVMs to bleed has been demonstrated in many studies and may be due to increased pressure within small AVMs.54–56 Although there are relatively few patients with large AVMs in this study, size >6 cm is predictive in univariate and multivariate analysis. These results should be confirmed in studies of patients with large AVMs, but we expect that deficits are more likely to occur after embolization of larger AVMs because it is more difficult to achieve complete embolization resulting in an increased risk of hemorrhage versus medium-sized AVMs.

These variables were weighted based on their ORs to create the AVM Embolization Prognostic Risk Score to facilitate the prediction of outcome. One point is assigned for each variable and 2 points are assigned for large AVM size. A prognostic score of 0 predicted neurological deficits in 0% of patients, a prognosis score of 1 predicted deficits in 6% of patients, a score of 2 predicted deficits in 15% of patients, a score of 3 predicted any deficit in 21%, and a prognosis score of 4 predicted deficits in 50% of patients. The AVM prognostic score is predictive of immediate deficits, but as a significant number of patients improved, it was not predictive of long-term persistent deficits. This may be a Type II error due to the small number of patients with long-term deficits. The AVM prognostic score is also shaped by selection bias. We have moved toward more conservative management of patients with large (Spetzler-Martin 4 to 5) AVMs.6,9,10 Validation in large clinical trials is necessary.

### Table 6. Multivariate Logistic Regression Analysis of the Predictive Value of Pre-Embolization Patient AVM Characteristics on New Neurological Deficit

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spetzler Martin components</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium diameter (3–6 cm)</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small diameter (&lt;3 cm)</td>
<td>3.20</td>
<td>1.2–9.1</td>
<td>0.025</td>
</tr>
<tr>
<td>Large (&gt;6 cm)</td>
<td>6.23</td>
<td>1.0–57.0</td>
<td>0.048</td>
</tr>
<tr>
<td>Deep venous drainage</td>
<td>2.73</td>
<td>1.1–6.9</td>
<td>0.034</td>
</tr>
<tr>
<td>Eloquent location</td>
<td>2.38</td>
<td>1.0–5.7</td>
<td>0.050</td>
</tr>
<tr>
<td>&gt;1 embolization planned</td>
<td>2.70</td>
<td>1.4–8.6</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*Age and gender were not significant predictors of outcome. When adjusting for age and gender, significance was unchanged. Peri-embolization complications such as periprocedural hemorrhage or infarction were not included in this analysis.

### Table 7. AVM Embolization Prognostic Score

<table>
<thead>
<tr>
<th>AVM Embolization Prognostic Score*</th>
<th>No. of Patients</th>
<th>Any Deficit (n=29)†</th>
<th>Moderate or Significant Deficit (n=19)‡</th>
<th>Significant Deficit (n=10)§</th>
<th>Long-Term Moderate or Significant Deficit (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>52</td>
<td>6%</td>
<td>6%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>2</td>
<td>83</td>
<td>15%</td>
<td>6%</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>3</td>
<td>47</td>
<td>21%</td>
<td>15%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>50%</td>
<td>50%</td>
<td>25%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Greater than 1 embolization treatment planned, deep venous drainage, eloquent location, and small AVM size (0–3 cm) are all assigned 1 point and AVM large size is assigned 2 points.

†Any deficit includes transient/minimal, moderate, and significant deficits. There is a significant association between increasing AVM embolization prognostic score and risk of deficit after embolization (Mantel-Haenszel test for linear association, P<0.0001).

‡There is a significant association between increasing AVM embolization prognostic score and risk of moderate or significant deficit after embolization (Mantel-Haenszel test for linear association, P<0.006).

§There is not a significant association between AVM embolization prognostic score and risk of significant deficit after embolization (Mantel-Haenszel test for linear association, P<0.095).
Although the AVM Embolization Prognostic Risk Score predicts deficits due to embolization, a significant number of patients had improvement over time. Further studies are needed to determine how complications from embolization affect overall long-term outcome. The true risk and benefit profile for embolization of brain AVMs in multimodality therapy is not clearly defined. Considered beneficial by some authors, AVM embolization has reportedly resulted in excess complications, which may outweigh its benefits. Case-control studies have demonstrated a beneficial effect of embolization before surgery, but not before radiosurgery.

Our results are limited to patient treated with NBCA. Recent studies of patients treated with Onyx demonstrate similar obliteration rates as those case series using NBCA, but assessment of recanalization and long-term effects are currently being assessed. Additionally, many centers are using Onyx as a primary modality of therapy and microsurgery and radiosurgery as a secondary modality in patients with incomplete obliteration. This partially accounts for the higher complication rates observed in some studies. Preliminary studies with Onyx are promising, but further studies necessary. Our results would be beneficial in treatment planning of patients treated with Onyx if confirmed in this cohort.

This study demonstrates that significant neurological complications occur in 2.7% of patients immediately after embolization, yet a majority of deficits improve or resolve over time. The combined experience and overwhelming bias of 3 microsurgeons and 2 neurointerventionalists support preoperative embolization in nearly all cases whereby definitive treatment with microsurgery is deemed beneficial. Selective cases to be treated with stereotactic radiosurgery might also benefit from preoperative embolization. Our surgical experience over the last 25 years has shown a progressive decrease in operative complications and significantly decreased operative time and blood loss as endovascular techniques have improved, resulting in more complete, staged preoperative AVM occlusion.

Conclusions
Adjuvant embolization in the treatment of cerebral AVMs results in a low rate of neurological deficits. Eloquent location, deep venous drainage, large size, and multiple embolization procedures are risk factors for the development of postembolization neurological deficits. Although the AVM Embolization Prognostic Risk Score predicts complication rates in this patient population, a significant number of patients improve over time. The low incidence of permanent neurological deficits underscores the usefulness of this technique in carefully selected patients. Larger, multicenter trials are necessary to determine how deficits from embolization affect overall long-term outcome.

Sources of Funding
R.M.S.’s efforts were partially supported the CTSA Grant UL1 RR025750 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the NCRR or NIH.

Disclosures
None.

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Robert M. Starke, Ricardo J. Komotar, Marc L. Otten, David K. Hahn, Laura E. Fischer, Brian Y. Hwang, Matthew C. Garrett, Robert R. Sciacca, Michael B. Sisti, Robert A. Solomon, Sean D. Lavine, E. Sander Connolly and Philip M. Meyers

Stroke. 2009;40:2783-2790; originally published online May 28, 2009;
doi: 10.1161/STROKEAHA.108.539775
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/40/8/2783

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