Role of Surgery in the Management of Brain Arteriovenous Malformations
Prospective Cohort Study

Miikka Korja, MD, PhD; David Bervini, MD, MAdvSurg; Nazih Assaad, MBBS; Michael Kerin Morgan, MD

Background and Purpose—Management of brain arteriovenous malformation (bAVM) is controversial. We have analyzed the largest surgical bAVM cohort for outcome.

Methods—Both operated and nonoperated cases were included for analysis. A total of 779 patients with bAVMs were consecutively enrolled between 1989 and 2014. Initial management recommendations were recorded before commencement of treatment. Surgical outcome was prospectively recorded and outcomes assigned at the last follow-up visit using modified Rankin Scale. First, a sensitivity analyses was performed to select a subset of the entire cohort for which the results of surgery could be generalized. Second, from this subset, variables were analyzed for risk of deficit or near miss (intraoperative hemorrhage requiring blood transfusion of ≥2.5 L, hemorrhage in resection bed requiring reoperation, and hemorrhage associated with either digital subtraction angiography or embolization).

Results—A total of 7.7% of patients with Spetzler–Ponce classes A and B bAVM had an adverse outcome from surgery leading to a modified Rankin Scale >1. Sensitivity analyses that demonstrated outcome results were not subject to selection bias for Spetzler–Ponce classes A and B bAVMs. Risk factors for adverse outcomes from surgery for these bAVMs include size, presence of deep venous drainage, and eloquent location. Preoperative embolization did not affect the risk of perioperative hemorrhage.

Conclusions—Most of the ruptured and unruptured low and middle-grade bAVMs (Spetzler–Ponce A and B) can be surgically treated with a low risk of permanent morbidity and a high likelihood of preventing future hemorrhage. Our results do not apply to Spetzler–Ponce C bAVMs. (Stroke. 2014;45:3549-3555.)

Key Words: arteriovenous malformations ■ brain ■ cohort studies ■ neurosurgery ■ risk factors ■ treatment outcome

Ruptured brain arteriovenous malformation (bAVM) is the most common cause of spontaneous intracerebral hemorrhage (ICH) in people aged <40 years.1 However, more than one third of people with bAVM present without ICH,2 and the decision to intervene in a relatively young and healthy person with an unruptured bAVM can only be made with a clear understanding of the natural history of bAVMs and the outcomes of treatment. The natural history data suggest an annual rate of hemorrhage of 2.2% for unruptured and 4.5% for ruptured bAVMs.3 The cumulative long-term chance of major morbidity or death for ruptured bAVM is reported to be as high as 85%.4 Despite these figures, A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) concluded that conservative management is superior to interventional therapy for the prevention of death or stroke in patients with unruptured bAVMs.5 For ruptured bAVMs, no rigorous treatment trials have been conducted.

Interventional therapy for bAVMs includes surgical resection, endovascular embolization, radiotherapy, or a combination of the aforementioned. ARUBA recruited only a small proportion of cases to surgery;6 and therefore intervention outcomes in this trial reflect outcomes from endovascular embolization and radiotherapy.7 With no randomized trials for surgical treatment of bAVMs, the best available evidence is from cohort studies. Because most of the surgical cohort studies do not include data on initial treatment decisions or cases excluded from surgery, an assessment of how cohort outcomes reflect the general population of cases cannot be made. This selection bias of cohort series can lead to outstanding outcomes for complex cases that are not reflective of the group as a whole (eg, only 5% of patients with Spetzler–Ponce Class (SPC) C bAVM were treated by Han et al8). Therefore, the treatment results of surgical cohort studies cannot be assumed to be generalizable to all patients with bAVMs. Putative surgical risk factors derived from previous cohort studies include: bAVM size; deep venous drainage (DVD); location in critical brain; presentation with hemorrhage; preoperative embolization; experience of the treating surgeon, age of the patient; diffuseness of the bAVM; and lenticulostriate supply.9–12

Received August 25, 2014; final revision received September 19, 2014; accepted September 25, 2014.

From the Australian School of Advanced Medicine, Macquarie University, Sydney, New South Wales, Australia (M.K., N.A., M.K.M.); Department of Neurosurgery, Helsinki University Central Hospital, Helsinki, Finland (M.K.); and Department of Clinical Neurosciences, Lausanne University Hospital, Lausanne, Switzerland (D.B.).

Correspondence to Michael Kerin Morgan, MD, Macquarie University, 2 Technology Place, Macquarie University, Sydney, New South Wales 2109, Australia. E-mail michael.morgan@mq.edu.au

© 2014 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.114.007206

3549
The combination of some of these variables has led to the development of the Spetzler–Martin grading (SMG) system, its simplification (the 3-tier SPC), and the Lawton–Young scale. To provide evidence for surgical treatment of bAVMs, we report the surgical results and the effect of these variables (excluding diffuseness) for the largest consecutive prospective cohort that includes data on both surgically and nonsurgically managed cases. This data incorporate the reasons for excluding patients from surgery. Patients were stratified by surgical risks according to the widely used 5-tier SMG and 3-tier SPC systems. The 5-tier Spetzler–Martin grades were established by allocating points for size (1 for <3 cm, 2 for size between 3 and 6 cm, and 3 for size >6 cm), the presence of DVD (1), and location in eloquent brain (1 if located in primary sensory cortex, motor cortex, language cortex, internal capsule, diencephalon, brain stem, deep cerebellar nuclei, or cerebellar peduncle). The SPC categories are derived from combining SMG 1 and 2 for SPC A, SMG 3 for SPC B, and combining SMG 4 and 5 for SPC C. We first investigated combining SMG 1 and 2 for SPC A, SMG 3 for SPC B, and SMG 4 and 5 for SPC C. The combination of some of these variables has led to the development of the Spetzler–Martin grading (SMG) system, its simplification (the 3-tier SPC), and the Lawton–Young scale. To provide evidence for surgical treatment of bAVMs, we report the surgical results and the effect of these variables (excluding diffuseness) for the largest consecutive prospective cohort that includes data on both surgically and nonsurgically managed cases. This data incorporate the reasons for excluding patients from surgery. Patients were stratified by surgical risks according to the widely used 5-tier SMG and 3-tier SPC systems. The 5-tier Spetzler–Martin grades were established by allocating points for size (1 for <3 cm, 2 for size between 3 and 6 cm, and 3 for size >6 cm), the presence of DVD (1), and location in eloquent brain (1 if located in primary sensory cortex, motor cortex, language cortex, internal capsule, diencephalon, brain stem, deep cerebellar nuclei, or cerebellar peduncle). The SPC categories are derived from combining SMG 1 and 2 for SPC A, SMG 3 for SPC B, and combining SMG 4 and 5 for SPC C. We first investigated combining SMG 1 and 2 for SPC A, SMG 3 for SPC B, and SMG 4 and 5 for SPC C.

Methods

Ethical Statement

This study was approved by the Macquarie University Human Ethics Committee and was performed in accordance with institutional ethics committee guidelines.

Data Collection and Study Cohort

Data collection protocol has been described previously. Briefly, the senior author (M.K.M.) has prospectively collected a bAVM database including consecutively enrolled patients with bAVM and, for example, demographic, clinical, radiological, and treatment-related information since 1989. There were 779 consecutively enrolled patients between January 1989 and May 2014. The database included prospective decisions on the reasons for the recommended treatment if surgery was not undertaken. Follow-up data include all referred and reviewed patients (ie, including patients who did not undergo surgery because of perceived greater risk, patients who declined the recommended treatment, and patients unsuitable for surgery because of comorbidities, age, or poor neurological condition). The flowchart for exclusion and inclusion of cases for analysis is illustrated in Figure 1. Of the 779 patients, 641 (82%) underwent surgery (Table 1; Figure 1), 39 (5%) were not recommended for surgery because of perceived risk of surgery, 25 (3%) did not undergo surgery because of other clinical grounds (ie, comorbidity [eg, end-stage liver failure, heart failure, and malignancy]), poor neurological state, or age >70 years), and 74 (9%) were treated elsewhere.

Outcome Assessments

Outcome assessment protocol has also been described previously. Briefly, outcome assessment was performed using the modified Rankin Scale (mRS) score administered preoperatively and at follow-up visits. An adverse outcome was considered a new permanent neurological deficit assigned within 6 weeks of surgery, and the mRS score was assigned at the last review of the patient. Surgical outcome assessments included patients who had preoperative embolization, and adverse outcome attributed to embolization was included as a surgical adverse event (surgeon’s decision to proceed with preoperative embolization). Patients were also included in surgery if they had an adverse outcome from embolization that precluded progression to surgery. Surgical treatment was considered effective when a postoperative digital subtraction angiography study showed no residual or new arteriovenous shunting within the brain.

Outcome variables were defined as overall adverse outcome from surgery (including embolization; mRS>1), major adverse outcome (mRS>2), perioperative hemorrhage (a perioperative transfusion of ≥2.5 L, perioperative death from hemorrhage, delayed ICH in the resection bed leading to a neurological deterioration or reoperation, ICH during angiography or ICH during embolization), or deficit or near miss (adverse outcome leading to mRS>1 or perioperative hemorrhage).

Sensitivity Analyses

The principle of the sensitivity analyses used has been described previously. In brief, sensitivity analyses were performed to examine treatment bias. Sensitivity analyses incorporated the 2 possible hypothetical outcomes for nonoperated patients (ie, adverse outcome or no adverse outcome) and adding these cases to the actual outcomes of the cases that underwent surgery. This produced optimistic and pessimistic scenarios. Patients who were not operated because of comorbidity, poor neurological state, age >70 years or who were treated elsewhere were excluded from the analysis because it was considered that these exclusions are less likely to bias those considered suitable for surgery. The analysis for each SPC subgroup was performed comparing adverse outcomes calculated for the 2 hypothetical scenarios (Table 1).

Figure 1. The flowchart for exclusion and inclusion of cases for analysis. bAVM indicates brain arteriovenous malformation; and SPC, Spetzler–Ponce Class.
Having selected the SPC groups in which there was minimal influence of cases not undergoing surgery, multiple logistic regression analyses were performed to identify variables influencing outcomes. Studied risk factors for adverse outcome included age at surgery (continuous variable), preoperative hemorrhage, preoperative embolization (including those that failed to progress to surgery because of complications), largest diameter of bAVM nidus (continuous variable), presence of DVD, eloquent location (as defined by SMG), lenticulostriate feeders, and days since the first bAVM surgery performed by the senior author (M.K.M.; ie, a measure of surgical experience). This analysis does not apply to SPC C because the number of cases excluded from surgery, because of perceived risk, created too much uncertainty as to whether the results could be generalized to all SPC C.

Analysis of Variables Influencing Outcome of Surgery
Having selected the SPC groups in which there was minimal influence of cases not undergoing surgery, multiple logistic regression analyses were performed to identify variables influencing outcomes. Studied risk factors for adverse outcome included age at surgery (continuous variable), preoperative hemorrhage, preoperative embolization (including those that failed to progress to surgery because of complications), largest diameter of bAVM nidus (continuous variable), presence of DVD, eloquent location (as defined by SMG), lenticulostriate feeders, and days since the first bAVM surgery performed by the senior author (M.K.M.; ie, a measure of surgical experience). This analysis does not apply to SPC C because the number of cases excluded from surgery, because of perceived risk, created too much uncertainty as to whether the results could be generalized to all SPC C.

Statistical Analyses
Morbidity and mortality comparisons between groups were performed using a χ², Fisher exact test, and t test, when appropriate. From the SPC subgroups in which no difference could be detected between optimistic and pessimistic scenario (SPC A and B) in the sensitivity analyses (thus assuming that the surgical results obtained were applicable to all eligible patients), multiple logistic regression analyses (forward step-wise) were performed. A statistical significance level of P<0.01 was used throughout as multiple comparisons were made. Statistical analysis was performed using Prism (version 6; GraphPad Software Inc) and IBM SPSS Statistics (version 21; IBM Corporation) software.

Results
Outcomes for Cases Not Treated Because of Perceived Surgical Risk
No SPC A was classified as no surgery because of perceived surgical risk. For the 6 SPC B and 33 SPC C patients, who were recommended not to have surgery because of perceived surgical risk, the median mRS at referral was 0 and 1 (range, 0–4), respectively (Table 1). The median mRS for SPC B and C at last follow-up was 2.5 and 1 (range, 0–4 and 0–6),
Table 2. Descriptive Statistics of Analyzed Cases for SPC A and SPC B bAVM Undergoing Treatment by Surgery (Including Those Who Failed to Proceed to Surgery After Complications of Preoperative Embolization)

<table>
<thead>
<tr>
<th>Characteristic*</th>
<th>Total</th>
<th>Deficit or Near Miss</th>
<th>No Deficit or Near Miss</th>
<th>Deficit or Near Miss. Characteristic* Absent</th>
<th>Deficit or Near Miss. Characteristic* Present</th>
<th>P Value of χ², Fisher Exact, or t Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>All surgery for SPC A and SPC B [95% confidence interval]</td>
<td>562</td>
<td>12.5% (70 of 562)</td>
<td>87.5% (492 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Women [95% confidence interval]</td>
<td>48% (270 of 562)</td>
<td>...</td>
<td>...</td>
<td>11.6% (34 of 292)</td>
<td>13.3% (36 of 270)</td>
<td>0.63</td>
</tr>
<tr>
<td>Age, y±SD (median: range)</td>
<td>37±16 (36: 5: 2–80)</td>
<td>37±15 (37: 11–73)</td>
<td>37±16 (36: 2–80)</td>
<td>...</td>
<td>...</td>
<td>0.90</td>
</tr>
<tr>
<td>&lt;20</td>
<td>14% (78 of 562)</td>
<td>10.3% (8 of 78)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>20–40</td>
<td>45% (252 of 562)</td>
<td>13.5% (34 of 252)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>&gt;40</td>
<td>41% (232 of 562)</td>
<td>12.1% (28 of 232)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Hemorrhage before surgery (95% confidence interval)</td>
<td>47% (263 of 562)</td>
<td>...</td>
<td>...</td>
<td>16.4% (49 of 299)</td>
<td>8.0% (21 of 263)</td>
<td>0.0039*</td>
</tr>
<tr>
<td>mRS&lt;2 before surgery</td>
<td>64.6% (363 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>mRS=2 before surgery</td>
<td>12.6% (71 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>mRS&gt;2 before surgery</td>
<td>2.3% (128 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Infratentorial [95% confidence interval]</td>
<td>14% (78 of 562)</td>
<td>...</td>
<td>...</td>
<td>12.6% (61 of 484)</td>
<td>11.5% (9 of 78)</td>
<td>0.94</td>
</tr>
<tr>
<td>Maximum diameter, cm±SD (median: range)</td>
<td>3.0±1.4 (3: 0.3–12.0)</td>
<td>4.0±1.8 (4: 1–12.0)</td>
<td>2.8±1.3 (2.8: 0.3–7.0)</td>
<td>...</td>
<td>...</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>&lt;3 cm</td>
<td>49.6% (279 of 562)</td>
<td>5.0% (14 of 279)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>3–6 cm</td>
<td>48.2% (271 of 562)</td>
<td>18.8% (51 of 271)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>&gt;6 cm</td>
<td>2.1% (12 of 562)</td>
<td>41.7% (5 of 12)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Eloquent [95% confidence interval]</td>
<td>34.7% (195 of 562)</td>
<td>...</td>
<td>...</td>
<td>9.5% (35 of 367)</td>
<td>17.9% (35 of 195)</td>
<td>0.0061*</td>
</tr>
<tr>
<td>Deep venous drainage [95% confidence interval]</td>
<td>29.0% (163 of 562)</td>
<td>...</td>
<td>...</td>
<td>10.5% (42 of 399)</td>
<td>17.2% (28 of 163)</td>
<td>0.043</td>
</tr>
<tr>
<td>Lenticulostriate supply</td>
<td>4.6% (26 of 562)</td>
<td>...</td>
<td>...</td>
<td>11.8% (63 of 536)</td>
<td>27% (7 of 26)</td>
<td>0.0322</td>
</tr>
<tr>
<td>Preoperative embolization [95% confidence interval]</td>
<td>9.3% (52 of 562)</td>
<td>...</td>
<td>...</td>
<td>11.0% (56 of 510)</td>
<td>26.9% (14 of 52)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Days between surgery and first surgery performed (d±SD) (median: range)</td>
<td>4426±2,169 (4324: 0–8,941)</td>
<td>4731±2134 (4666: 425–8865)</td>
<td>4382±2173 (4324: 0–8941)</td>
<td>...</td>
<td>...</td>
<td>0.21</td>
</tr>
<tr>
<td>Failure to proceed to surgery because of embolization complication</td>
<td>0.2% (1 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Adverse outcome of surgery (or embolization) leading to last mRS&gt;1 [95% confidence interval]</td>
<td>7.7% (43 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Adverse outcome of surgery leading to last mRS&gt;2 [95% confidence interval]</td>
<td>2.3% (13 of 562)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

(Continued)
respective (Table 1). There was no statistically significant difference between referral and last follow-up outcomes for each of the SPC grades.

Overall Surgical Outcome

Length of time of follow-up is provided in Table 1. For those undergoing surgery, adverse outcome rates increased with increasing SPC grades from SPC A to SPC C (Table 1). Of the 641 operated patients with bAVMs, 74 (11.5%) had overall adverse outcome (mRS>1) from surgery (including embolization; Table 1). The combined adverse outcome rates leading to a mRS>1 were 1.4%, 19%, and 39% for SPC A, B, and C, respectively. The adverse outcome rates leading to an mRS>2 were 0.6%, 6%, and 19% for SPC A, B and C, respectively (Table 1).

Sensitivity Analyses

The sensitivity analyses demonstrated no significant difference between the optimistic and pessimistic scenarios for SPC A and SPC B bAVMs (Table 1). Sensitivity analysis for SPC C demonstrated a significant difference between the optimistic and the pessimistic scenarios (Table 1). Therefore, it was assumed that the results were not subject to presurgical decisions (selection bias) for SPC A (SMG 1 and 2) and SPC B (SMG 3) bAVMs. This was not the case for SPC C (SMG 4 and 5) bAVMs, and therefore these bAVMs were excluded from further analyses.

Analysis of SPC A and B Subgroups for Risks of Surgery

For SPC A and B bAVMs, analyses of outcomes were performed (Tables 1 and 2). The detailed descriptive statistics are provided in Table 2. In brief, 7.7% (43 of 562 cases) developed an adverse outcome from surgery or preoperative embolization leading to an mRS>1 and 2.3% (13 cases) developed an adverse outcome from surgery or preoperative embolization leading to an mRS>2. Perioperative hemorrhage occurred in 8.0% (45 of 562 patients; 95% confidence interval, 6.0–10.6) of patients with SPC A and B bAVMs, and 70 (12.5%; 95% confidence interval, 10.0–15.5) of the same subgroup had deficits or near miss events (adverse events leading to an mRS>1 or perioperative hemorrhage; Table 1; Figure 2). When ignoring neurological status at presentation, 79.0% (444 of 562 patients) of SPC A and B had an mRS<2 (with or without complication) after treatment, 14.6% had an mRS 2, 5.0% had an mRS 3 to 5, and 1.4% were dead. Complete bAVM resection (effective surgical treatment) was achieved in 99.1% (557 of 562 patients; 95% confidence interval, 97.9–99.7) of patients with SPC A and B bAVMs.

Preoperative Embolization and Outcome

A significant change in embolization practice was observed during the 25 years of the study (Figure 2). Preoperative embolization declined during the 25 years for each of the SPC subgroups. For example, during the first 5 operative years, the embolization rate was 20%, 60%, and 65% for SPC A, SPC B, and SPC C, respectively. During the past 5 operative years, no embolization procedures were performed. However,
during the 25-year period, adverse outcome rate or perioperative hemorrhage rate did not change with the decline in the use of preoperative embolization.

**Discussion**

Our results suggest that ≈90% of SPC A and B bAVMs can be treated effectively by surgery. In our cohort of 797 reviewed patients with bAVM, 628 (79%) were SPC A or B bAVM. Of these patients, 562 were operated on with a morbidity (mRS>1) of 7.7% including a 1.4% mortality. The morbidity (mRS>1) was much higher in the SPC B subgroup (18.9%) in comparison with patients with SPC A bAVMs (1.4%). A modern era population-based inception cohort study suggests that >90% of unruptured bAVMs, which are brought to medical attention, consist of low- and middle-grade bAVMs, to our cohort. Therefore, it is reasonable to conclude that most bAVMs can be treated effectively by surgery. In contrast to the results for low- and middle-grade bAVMs, sensitivity analyses suggest that the results for high-grade bAVMs were not generalizable for all our SPC C cases. In other words, a significant number of cases of high-grade bAVMs were recommended for nonsurgical management because of perceived risk of surgery, and therefore outcome rates do not reflect the rates for all high-grade bAVMs. Our results of the sensitivity analyses together with the knowledge that a minority of high-grade bAVMs undergo surgical treatment suggest that the SMG and SPC surgical risk for high-grade bAVMs is likely understated in the literature and not comparable between institutions. However, the presented results validate the reliability of the SPC system for unruptured and for ruptured low- and middle-grade bAVMs.

Table 3. **Logistic Regression Analysis for Combined Spetzler–Ponce Class A and B (Forward Step Conditional) for Deficit or Near Miss and Adverse Outcome From Surgery or Embolization Leading to mRS>1 and mRS>2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adverse Outcome With mRS&gt;1 or Near Miss</th>
<th>Adverse Outcome With mRS&gt;1</th>
<th>Adverse Outcome With mRS&gt;2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$P \text{ Value}$</td>
<td>Adjusted Odds Ratio (95% CI) Included</td>
<td>$P \text{ Value}$</td>
</tr>
<tr>
<td>Deep venous drainage</td>
<td>&lt;0.001</td>
<td>4.0 (2.1–7.6) Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum diameter, cm</td>
<td>&lt;0.001</td>
<td>1.8 (1.5–2.2) Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eloquent location</td>
<td>&lt;0.001</td>
<td>3.2 (1.8–5.7) Yes</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hemorrhage before surgery</td>
<td>0.017</td>
<td>0.5 (0.3–0.9) Yes</td>
<td>0.39</td>
</tr>
<tr>
<td>Age</td>
<td>0.090</td>
<td>… No</td>
<td>NA</td>
</tr>
<tr>
<td>Preoperative embolization</td>
<td>0.207</td>
<td>… No</td>
<td>NA</td>
</tr>
<tr>
<td>Days between first surgery</td>
<td>0.474</td>
<td>… No</td>
<td>NA</td>
</tr>
</tbody>
</table>

bAVM indicates brain arteriovenous malformation; CI, confidence interval; mRS, modified Rankin Scale; and NA, not applicable.
Because treatment options for bA VMs are difficult to study through retrospective observational studies, and prospective cohort studies are faced with the challenges of recruitment and follow-up, most of these studies have been small and of limited generalizability. As the results are based on sensitivity analyses with data on excluded patients, despite the more generalizable and informative than many previous studies, as the results are based on sensitivity analyses with data on excluded patients. Despite the more generalizable results and study design, and large number of cases (our cohort is 4× larger than the ARUBA cohort), our cohort study does have drawbacks. Patients were most likely recruited to the cohort with a referral bias. However, the cohort is likely to include more surgically complex than simple bAVMs, reflecting referral bias to a center with expertise in bAVM surgery. A possible grading bias, where bAVMs may have been graded differently, cannot be ruled out. Unfortunately, similar to ARUBA and most of the bAVM studies, we did not study the inter-rater variability. Finally, these results are not applicable to all cerebrovascular neurosurgeons who operate bAVMs. However, these results are not meant to be applicable to all surgical centers. The treatment results that we report are likely to be similar to the other high-volume bAVM surgical centers.

The recent randomized trial, ARUBA, concluded that unruptured bAVMs should be left untreated, at least until the first bleed. However, the results of our comprehensive cohort study provide evidence that most of the low- and middle-grade bAVMs, whether ruptured or unruptured, can be relatively treated safely by surgery. On the contrary, high-grade bAVMs have a high risk of surgery and should only be considered for treatment by surgery in highly nuanced situations.

**Sources of Funding**

This study was supported in part by grants from the Sigrid Juselius (M.K.), Biomedicum Helsinki (M.K.), Orion-Farmos Research (M.K.), Instrumentarium Research (M.K.), and from the Finnish Medical Association (M.K.).

**Disclosures**

None.

**References**

Role of Surgery in the Management of Brain Arteriovenous Malformations: Prospective Cohort Study
Miikka Korja, David Bervini, Nazih Assaad and Michael Kerin Morgan

Stroke. 2014;45:3549-3555; originally published online October 16, 2014;
doi: 10.1161/STROKEAHA.114.007206
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
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/45/12/3549

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/