Microsurgery for ARUBA Trial (A Randomized Trial of Unruptured Brain Arteriovenous Malformation)–Eligible Unruptured Brain Arteriovenous Malformations

Johnny Wong, PhD; Alana Slomovic, BSc; George Ibrahim, PhD; Ivan Radovanovic, PhD; Michael Tymianski, MD, PhD

Background and Purpose—The management of unruptured brain arteriovenous malformations (ubAVMs) remains controversial despite ARUBA trial (A Randomized Trial of Unruptured Brain Arteriovenous Malformation), a controlled trial that suggested superiority of conservative management over intervention. However, microsurgery occurred in only 14.9% of ARUBA intervention cases, raising concerns about the study’s generalizability. Our purpose was to evaluate whether, in a larger ARUBA-eligible ubAVM population, microsurgery produces acceptable outcomes.

Methods—Demographic data, AVM characteristics, and treatment outcomes were evaluated in 155 ARUBA-eligible bAVMs treated with microsurgery between 1994 and 2014. Outcomes were rates of early disabling deficits and permanent disabling deficits with modified Rankin Scale score ≥ 2 or any permanent neurological deficits with modified Rankin Scale score ≥ 1. Covariates associated with outcomes were determined by regression analysis.

Results—Of 977 AVM patients, 155 ARUBA-eligible patients had microsurgical resection (71.6% surgery only and 25.2% with preoperative embolization). Mean follow-up was 36.1 months. Complete obliteration was achieved in 94.2% after initial surgery and 98.1% on final angiography. Early disabling deficits and permanent disabling deficits occurred in 12.3% and 4.5%, respectively, whereas any permanent neurological deficit (modified Rankin Scale score ≥ 1) occurred in 16.1%. Among ubAVM of Spetzler–Martin grades 1 and 2, complete obliteration occurred in 99.2%, with early disabling deficits and permanent disabling deficits occurring in 9.3% and 3.4%, respectively. Major bleeding was the only significant predictor of early disabling deficits on multivariate analysis (P < 0.001).

Conclusions—Microsurgery in this cohort produced less disabling deficits than ARUBA with similar morbidity and AVM obliteration as other cohort series. This disparity between our results and ARUBA suggests that future controlled trials should focus on the safety and efficacy of microsurgery with or without adjunctive embolization in carefully selected ubAVM patients. (Stroke. 2017;48:136-144. DOI: 10.1161/STROKEAHA.116.014660.)

Key Words: angiography ■ arteriovenous malformations ■ microsurgery ■ radiosurgery ■ regression analysis
overarching conclusion of ARUBA could, therefore, unnec-
sarily deprive certain ubAVMs patients of a beneficial therapy.
Our purpose was to evaluate whether there exists a subset of
ARUBA-eligible patients selected by clinical judgment and
AVM characteristics that can be safely treated by microsurgi-

cal resection. A secondary goal was to identify any prognostic
factors for outcome in this patient cohort.

Methods

Data Collection
This study was approved by the Research Ethics Board at University
Health Network and was conducted in accordance with the institu-
tional ethics guidelines. The University of Toronto Brain AVM study
group database is a prospectively collected database containing demo-


graphic, clinical, and radiological information. To identify patients
with ubAVMs treated by microsurgical resection at Toronto Western
Hospital between 1994 and 2014, the database was interrogated using
the search terms: arteriovenous malformation and AVM. All patients
with an unruptured intracerebral AVM and treated with microsurgery
were included in the study. Exclusion criteria included evidence of
previous intracranial hemorrhage on computed tomography or mag-
netic resonance imaging, diagnosis of other vascular malformations
(eg, cavernous malformations, facial, or body AVM), or any treatment
without microsurgical resection of AVM. All AVM cases were diag-
nosed based on magnetic resonance imaging, computed tomography
angiogram, or digital subtraction angiography (DSA).

Management of each individual ubAVM was discussed at mul-

tidisciplinary conference, in which multimodality treatment strate-
gies, including microsurgery, embolization or radiosurgery alone, or
in combination, were considered. Suitability for microsurgery and
need for preoperative embolization were determined by multidiscis-
plinary consensus, based on Spetzler–Martin (SM) grade, AVM
location, angiography, including the presence of high-risk features,
high-flow shunting, or associated aneurysms. Operations were performed by 4 neurosurgeons. Postoperative DSA was per-


formed within the first week of resection to verify bAVM resection.
Clinical follow-up was performed at 6 weeks and 3 to 6 months post
hospital discharge and at annual intervals thereafter. The database
and clinical records were retrieved and analyzed retrospectively
by 2 individuals who were not directly involved in the care of the
patients (J.W. and A.S.).

Study Variables
Study variables included patient demographic data, clinical presenta-
tion (seizures, headaches, neurological deficits, bruits, or asymptom-
atic if not relevant to the AVM), AVM characteristics (SM grading
based on size, eloquence, deep venous drainage, as well as location,
and associated aneurysms), pre- and post-treatment functional out-
comes (modified Rankin Scale scores [mRS]), and treatment outcomes
(�V M obliteration rates and new neurological deficits). AVM obliti-
eration was confirmed by DSA. Neurological deficits were defined as
early disabling deficit (EDD) if mRS ≥2 within 7 days of surgery and
permanent disabling deficit (PDD) if mRS ≥3 at the last clinical fol-


low-up. Other complications were recorded, including major bleeding
(defined as >1000 mL intraoperative blood loss, or transfusion require-
ment for ≥2 U of whole or packed red cells), postoperative hematoma
requiring evacuation, and wound infection. bAVM were dichotomized
into low grade (SM grades 1 and 2) and high grade (SM grades 3–5).

Statistical Analysis
Where stated, Fisher exact tests were used for categorical variables,
and 2-sided t tests for continuous variables. A univariate logistic
regression analysis was performed using the dichotomized outcome
variable as the dependent variable to determine whether covariates
were associated with the primary outcomes (permanent neurological
deficit, EDD, and PDD). Significant covariates on univariate analysis
(P<0.05) were entered into a multivariate logistic regression. Two-
and three-way interactions were tested. Analyses were performed
using R statistics software (version 3.2.1).

Results

Patient Demographics and AVM Characteristics
From 1994 to 2014, 977 bAVM patients were treated of which
528 were ubAVMs. Surgery occurred in 168 patients, but 10
patients were excluded because of inadequate data because the
surgeries were performed before their referral to our institu-
tion, whereas in 3 patients the surgery consisted only of a
decompressive craniectomy to treat complications of AVM
embolization, leaving 155 patients (Figure 1). Mean follow-
up was 36.1 months (range 1–238 months).

Baseline demographics, clinical presentation, and AVM
characteristics are presented in Tables 1 and 2. There were
88 females (57%) and 67 males (43%); mean age at presenta-


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was 4 days. By comparison, in SM3 and SM4 patients, EDD rates were 20% and 28.6%, respectively, whereas PDD rates were 10% and 0%, respectively. In summary, a greater proportion of SM3 and SM4 patients had preoperative embolization, longer length of stay, and higher EDD and PDD when compared with SM1 and SM2.

Univariate and multivariate analyses were performed to identify predictive factors for poor outcome. On univariate analysis (Table 4), several covariates were significantly associated with permanent neurological deficits ($P<0.05$): high-grade AVM, eloquence, deep venous drainage, AVM-associated aneurysms, surgery alone, and major bleeding. On multivariate analysis, a significant interaction was seen between surgery alone and major bleeding, indicating that an adjunct procedure (embolization) in addition to surgical intervention significantly reduced the effect of major bleeding. In patients who underwent surgery alone, major bleeding was the only significant independent predictor ($P<0.001$) of permanent neurological deficit. For EDD, both high-grade AVM and major bleeding reached significance on univariate analysis, but only major bleeding was significant on multivariate ($P<0.001$). Similarly, major bleeding was the only significant factor on univariate analysis for PDD.

**Discussion**

ARUBA is the only prospective randomized trial comparing medical management with interventional treatment for unruptured bAVMs with a statistically significant morbidity associated with interventional treatment.\(^5\,^7\) It reflects the current management of ubAVMs internationally as 39 active centers across 9 countries were involved. ARUBA provided prospective information on the natural history of ubAVMs, confirming that it is not benign because 10.1% of patients suffered a symptomatic stroke or death within 33 months. However, ARUBA was criticized because of its low enrollment rate, small sample size, short follow-up, high rate of adverse outcomes, under-representation of surgical treatment, and lack of treatment stratification.\(^8\,-\,^{22}\) Its primary outcome after interventional treatment was higher than in previous cohorts treated with microsurgery or radiosurgery\(^23\,-\,^{29}\) without a clear explanation. It combined 3 different interventions into a single amorphous category and did not discriminate which modality was harmful.\(^21\) ARUBA also assumed equipoise among all ubAVMs between medical and interventional treatments,\(^30\) an assumption not shared by many physicians, which may explain the small proportion of patients enrolled (226/1740).\(^10\,-\,^{15}\) By not enrolling patients, physicians have potentially introduced bias, leading to the current quandary that ARUBA tried to avoid. It raises questions about the generalizability of ARUBA data to individual ubAVM treatment. AVMs are heterogeneous, with varying angioarchitecture, anatomic locations, and natural history.\(^13\) UbAVMs considered low grade for treatment are not associated with a more benign natural history. The risks of treatment are not homogeneous where treatment strategies depend on characteristics of
the lesion, availability of individual treatment modalities, and institutional expertise. 10,12,17,31–34

Several retrospective series have recently been published on ubAVMs. The SIVMS (Scottish Intracranial Vascular Malformation Study) reported on ubAVMs comparing conservative management with intervention, which also found superiority in the conservative group for death or handicap at 4 years and focal neurological deficit or death at 12 years. 1

Both SIVMS and ARUBA cohorts had predominantly nonsurgical interventions and bAVM obliteration rates of 63% to 71% were observed in SIVMS.35 In contrast, Bervini et al35 presented a 25-year microsurgical series from Sydney, Australia, of 427 unruptured bA VM patients, who were stratified according to the Spetzler–Ponce class4: for class A (n=190), the rate of permanent neurological deficit with mRS increase >1 was 1.6% (95% confidence interval, 0.3–4.8%); class B (n=107), 14.0% (95% confidence interval, 8.6–22.0%); and class C (n=44), 38.6% (95% confidence interval, 25.7–53.4%).35,36 Subsequent sensitivity analyses on the same database by Korja et al37 showed no statistical difference to the combined classes A and B adverse outcome rate of 7.7% when nonoperated patients were assumed to have adverse outcomes. Outcomes in ARUBA-eligible patients at University of California, San Francisco (UCSF) have also been reported.15

Table 1. Baseline Patient Characteristics for 155 Unruptured Brain Arteriovenous Malformation Patients Treated With Microsurgery, Including Mean Follow-Up, Clinical Presentation, Past History, and Preoperative mRS

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>155</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>38.5</td>
</tr>
<tr>
<td>Female (%)</td>
<td>88 (56.8)</td>
</tr>
<tr>
<td>Follow-up, mean, mo</td>
<td>36.1</td>
</tr>
<tr>
<td>Clinical presentation (%)</td>
<td></td>
</tr>
<tr>
<td>Seizure</td>
<td>74 (47.7)</td>
</tr>
<tr>
<td>Neurological deficit</td>
<td>13 (8.4)</td>
</tr>
<tr>
<td>Bruit</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Headache</td>
<td>45 (29)</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>68 (43.9)</td>
</tr>
<tr>
<td>Past history (%)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>85 (54.8)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>13 (8.4)</td>
</tr>
<tr>
<td>Mild head injury</td>
<td>4 (2.6)</td>
</tr>
<tr>
<td>HHT</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Preoperative mRS (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>1</td>
<td>68 (43.9)</td>
</tr>
<tr>
<td>2</td>
<td>77 (49.7)</td>
</tr>
<tr>
<td>3</td>
<td>3 (1.9)</td>
</tr>
</tbody>
</table>

HHT indicates hereditary hemorrhagic telangiectasia; mRS, modified Rankin Scale (score); and TIA, transient ischemic attack.

Of 74 ARUBA-eligible patients, 61 patients had received intervention, which included surgical resection in 70.5% of patients (with and without preoperative embolization), and radiosurgery in the remainder. The risk of stroke or death was 14.7% in the entire intervention group when compared with 7.7% in the conservative group, though surgery still had a lower risk of stroke or death (11.6%) than the overall intervention group. Functional outcomes demonstrated no significant differences and complete obliteration of AVMs was achieved in 93% of treated patients. Similarly, Nerva et al38 reviewed outcomes of 105 unruptured bAVMs, including a subgroup analysis of 61 ARUBA-eligible patients, on whom microsurgery was used in 61% of low-grade bAVM (SM1 and SM2) and 40% of high-grade AVM. Complete obliteration was achieved in

Table 2. Baseline AVM Characteristics of the Surgical Cohort, Including AVM Laterality, Location, Associated Aneurysms, Overall, and Individual Components of SM Grading

<table>
<thead>
<tr>
<th>AVM Characteristics</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single/multiple lesions (%)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>152 (98.1)</td>
</tr>
<tr>
<td>Multiple</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>AVM side (% of total lesions=159)</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>84 (52.8)</td>
</tr>
<tr>
<td>Left</td>
<td>75 (47.2)</td>
</tr>
<tr>
<td>AVM location (% of total lesions=159)</td>
<td></td>
</tr>
<tr>
<td>Frontal</td>
<td>47 (29.6)</td>
</tr>
<tr>
<td>Parietal</td>
<td>44 (27.7)</td>
</tr>
<tr>
<td>Temporal</td>
<td>40 (25.2)</td>
</tr>
<tr>
<td>Occipital</td>
<td>16 (10.1)</td>
</tr>
<tr>
<td>Insular</td>
<td>6 (3.8)</td>
</tr>
<tr>
<td>Cerebellum/posterior fossa</td>
<td>5 (3.2)</td>
</tr>
<tr>
<td>Periventricular</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Aneurysms (%)</td>
<td></td>
</tr>
<tr>
<td>AVM associated</td>
<td>14 (9.0)</td>
</tr>
<tr>
<td>Non-AVM associated</td>
<td>10 (6.5)</td>
</tr>
<tr>
<td>SM grade (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>52 (33.5)</td>
</tr>
<tr>
<td>2</td>
<td>66 (42.6)</td>
</tr>
<tr>
<td>3</td>
<td>30 (19.4)</td>
</tr>
<tr>
<td>4</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>5</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Size (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;3 cm</td>
<td>112 (72.3)</td>
</tr>
<tr>
<td>3–6 cm</td>
<td>43 (27.7)</td>
</tr>
<tr>
<td>&gt;6 cm</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Eloquent location (%)</td>
<td>62 (40)</td>
</tr>
<tr>
<td>Deep venous drainage (%)</td>
<td>42 (27.1)</td>
</tr>
</tbody>
</table>

AVM indicates arteriovenous malformation; and SM, Spetzler–Martin.
all patients. Persistent neurological deficits and mRS ≥3 were found in 16% and 7%, respectively, of the ARUBA-eligible cohort. In SM1 and SM2 patients, lower rates of persistent deficits and mRS ≥3 (7% and 0%, respectively) were reported.

Interestingly, a recent multicenter retrospective radiosurgical series from 7 international institutions in 509 ARUBA-eligible patients (mean follow-up 86 months) showed an AVM obliteration rate of 75%, with a postradiosurgery latency hemorrhage rate of 0.9% per year. The adverse neurological outcome, permanent neurological morbidity, and mortality rates were 13%, 5%, and 4%, respectively, which were more favorable than the primary outcome in ARUBA interventional group.

Our analysis of 155 consecutive ubAVM patients who were generally eligible for ARUBA and treated with microsurgery at a single multidisciplinary institution represents 29.3% of the entire ubAVM cohort (528 patients) treated during the same period. The analyzed cohort had similar patient characteristics to ARUBA except for 8 patients aged <18 years and 3 patients with initial mRS >2. The SM grade distribution was also similar with no SM grade 5 patients and the majority (76%) were SM1 and SM2. Within this subset, microsurgical resection alone was performed in 78% of cases, when compared with 14% in SM4. In high-grade ubAVMs, preoperative embolization and neurological deficits were more common, median length of stay and follow-up were longer, and AVM obliteration rates were also lower.

Outcomes from our series demonstrated a similar result to the aforementioned surgical series. In our series, the overall EDD and PDD (mRS ≥3) rates were 12.3% and 4.5%, respectively. Postoperative DSA confirmed complete resection in 98.1% of cases, accounting for the refusal of 1 patient to undergo DSA and thus assuming persistence of AVM in that individual. In contrast, the low-grade ubAVMs (SM1 and SM2) in our series were associated with higher obliteration rates (99.2%) and lower PDD (3.4%), which compares favorably to the overall morbidity (2.2%) and complete obliteration rates (98.5%) presented in a recent systematic review of microsurgery on low-grade AVMs by Potts et al. The mean
and median duration of follow-up in our series were 36.1 and 18 months, respectively, which is comparable to the mean follow-up in ARUBA (33 months). The short duration of follow-up in this series can be explained by our institutional practice to discharge patients from further clinical follow-up beyond 12 months postoperatively once curative resection is confirmed by DSA.

In summary, the current series and other retrospective surgical cohorts have demonstrated that microsurgical resection can be performed safely and effectively in a subset of predominantly low-grade ubAVMs (SM1 and SM2). By definition, one can infer that such ubAVMs would not have >1 high-risk feature: eloquence, size >3 cm, or deep venous drainage. To identify specific prognostic factors and AVM features associated with treatment risk, univariate and multivariate analyses were performed in this study. On the basis of logistic regression, the most consistent significant predictors of permanent neurological deficit, EDD, and PDD on univariate analysis were high-grade AVM and major bleeding. Individual components of the SM grading, such as eloquence and deep drainage, were also significant predictors of permanent deficit on univariate analysis but did not reach significance in multivariate modeling. Major bleeding was the most significant predictive factor for permanent neurological deficit, EDD, and PDD on multivariate analysis. Although the threshold defined herein for major bleeding in surgical patients (>1000 mL of blood loss, or transfusion requirement of ≥2 U of whole blood or packed red cells) is arbitrary, this may be a surrogate measure of either high-risk features in bAVM specified or unspecified by the SM grade or the surgeon’s technical expertise. The relevance of major bleeding as a significant predictor for poor outcome may be applicable to the role of preoperative embolization. Embolization may be used as an adjunct to reduce intraoperative bleeding by addressing high-risk features, such as an intranidal aneurysm, or to generally reduce flow through the nidus preoperatively, or to control deep arterial feeders which may be difficult to access surgically. However, risks of embolization will vary depending on the treatment strategy. Occasionally, embolization has been used for definitive cure, with reported cure rates of 15% to 50% and higher morbidity rates. In ARUBA, embolization alone constituted 26% of cases, but the treatment strategy or specific agents were not mentioned. Within the subset of low-grade AVMs, a review of endovascular series using Onyx embolization demonstrated morbidity and cure rates of 6.2% and 29.5%, respectively. Although there is no established treatment algorithm or paradigm at our institution, consensus decision at the multidisciplinary conference would determine the most appropriate modality of treatment for individual bAVMs. In general, microsurgery would be recommended if the bAVM is accessible and can be resected with minimal acceptable morbidity, usually in the setting of SM1 and SM2 and possibly SM3.

### Table 3. Distribution of Treatment Modalities, Outcomes, and Complications When Stratified According to SM Grade

<table>
<thead>
<tr>
<th>Treatment modalities (%)</th>
<th>Overall, n=155</th>
<th>SM1, n=52</th>
<th>SM2, n=66</th>
<th>SM3, n=30</th>
<th>SM4, n=7</th>
<th>SM1 and SM2, n=118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery only: single operation</td>
<td>107 (69.0)</td>
<td>47 (90.4)</td>
<td>45 (68.2)</td>
<td>14 (46.7)</td>
<td>1 (14.3)</td>
<td>92 (78.0)</td>
</tr>
<tr>
<td>Surgery only: multiple operations</td>
<td>4 (2.6)</td>
<td>0 (0)</td>
<td>4 (6.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (3.4)</td>
</tr>
<tr>
<td>Preoperative embolization+surgery</td>
<td>39 (25.2)</td>
<td>5 (9.6)</td>
<td>15 (22.7)</td>
<td>14 (46.7)</td>
<td>5 (71.4)</td>
<td>20 (16.9)</td>
</tr>
<tr>
<td>Preoperative radiosurgery+surgery</td>
<td>2 (1.3)</td>
<td>0 (0)</td>
<td>1 (1.5)</td>
<td>1 (3.3)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Surgery+postoperative radiosurgery</td>
<td>2 (1.3)</td>
<td>0 (0)</td>
<td>1 (1.5)</td>
<td>1 (3.3)</td>
<td>0 (0)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Embolization+surgery+radiosurgery</td>
<td>1 (0.6)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (14.3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

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<tr>
<th>Outcomes (%)</th>
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<th>SM2, n=66</th>
<th>SM3, n=30</th>
<th>SM4, n=7</th>
<th>SM1 and SM2, n=118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure on initial postoperative DSA*</td>
<td>146 (94.2)</td>
<td>51 (98.1)</td>
<td>63 (95.5)</td>
<td>27 (90.0)</td>
<td>5 (71.4)</td>
<td>114 (96.6)</td>
</tr>
<tr>
<td>Cure on final postoperative DSA*</td>
<td>152 (98.1)</td>
<td>52 (100)</td>
<td>65 (98.5)</td>
<td>29 (96.7)</td>
<td>6 (85.7)</td>
<td>117 (99.2)</td>
</tr>
<tr>
<td>Length of admission, mean, d</td>
<td>7.1</td>
<td>4.3</td>
<td>8.2</td>
<td>7.1</td>
<td>17.9</td>
<td>6.4</td>
</tr>
<tr>
<td>Length of admission, median, d</td>
<td>5.0</td>
<td>3.5</td>
<td>5.0</td>
<td>5.5</td>
<td>13.0</td>
<td>4.0</td>
</tr>
<tr>
<td>mRS same or better at last FU</td>
<td>123 (79.4)</td>
<td>45 (86.5)</td>
<td>48 (72.7)</td>
<td>26 (86.7)</td>
<td>3 (43.9)</td>
<td>93 (78.8)</td>
</tr>
<tr>
<td>mRS worse at last FU</td>
<td>32 (20.6)</td>
<td>7 (13.5)</td>
<td>18 (27.3)</td>
<td>4 (13.3)</td>
<td>4 (57.1)</td>
<td>25 (21.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications (%)</th>
<th>Overall, n=155</th>
<th>SM1, n=52</th>
<th>SM2, n=66</th>
<th>SM3, n=30</th>
<th>SM4, n=7</th>
<th>SM1 and SM2, n=118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early neurological deficit, within 7 d</td>
<td>47 (30.3)</td>
<td>11 (21.2)</td>
<td>18 (27.3)</td>
<td>13 (43.3)</td>
<td>5 (71.4)</td>
<td>29 (24.6)</td>
</tr>
<tr>
<td>Early disabling deficit, mRS≥3 within 7 d</td>
<td>19 (12.3)</td>
<td>5 (9.6)</td>
<td>6 (9.1)</td>
<td>6 (20.0)</td>
<td>2 (28.6)</td>
<td>11 (9.3)</td>
</tr>
<tr>
<td>Permanent neurological deficit, at last FU</td>
<td>25 (16.1)</td>
<td>2 (3.8)</td>
<td>10 (15.2)</td>
<td>9 (30.0)</td>
<td>4 (57.1)</td>
<td>12 (10.2)</td>
</tr>
<tr>
<td>Permanent disabling deficit, mRS≥3 at last FU</td>
<td>7 (4.5)</td>
<td>0 (0)</td>
<td>4 (6.1)</td>
<td>3 (10.0)</td>
<td>0 (0)</td>
<td>4 (3.4)</td>
</tr>
<tr>
<td>Postoperative hemorrhage</td>
<td>6 (3.9)</td>
<td>2 (3.8)</td>
<td>0 (0)</td>
<td>2 (6.7)</td>
<td>2 (28.6)</td>
<td>2 (1.7)</td>
</tr>
</tbody>
</table>

*DSA indicates digital subtraction angiography; FU, follow-up; mRS, modified Rankin Scale (score); and SM, Spetzler–Martin.

**Table 3. Distribution of Treatment Modalities, Outcomes, and Complications When Stratified According to SM Grade**
This can be observed in the distribution of SM grading in our cohort, with few SM4 or SM5 patients treated. Adjunctive preoperative embolization may be used to aid microsurgical resection by addressing high-risk features, such as intranidal aneurysms, or major arteriovenous shunts, or the deep nidal component of a multicompartment AVM, and is more commonly used in higher SM grades. For deeply located bAVM, stereotactic radiosurgery may be recommended. In summary, not all bAVM should be considered homogeneously for intervention, and intervention should be individualized according to the AVM characteristics and the expertise of the treating institution.

The current series highlights the need for continuing investigation into identifying prognostic factors to appropriately select ubAVM patients for treatment. Potts et al recently proposed a new randomized trial for low-grade bAVM to ultimately address concerns raised by ARUBA, BARBADOS trial (Beyond ARUBA: Randomized Low-Grade Brain AVM Study: Observation Versus Surgery). It is hoped that this would inspire greater participation from neurosurgeons in high-volume centers to produce a positive result against ARUBA. However, similar issues with funding and duration of follow-up may also apply to BARBADOS, as has plagued ARUBA previously. Given the scarcity of AVMs and the complexity of their treatments, the cumulative experience from high-volume surgical centers on bAVM, with this study included, will supply data to refine future prospective intervention trials for all ubAVMs, such that an evidence-based treatment algorithm may be formulated.

### Limitations of Current Study

Although our data were collected prospectively, it remains a retrospective review from a single institution. Surgical patients were selected mainly based on the SM grade, angioarchitecture, and location of bAVM, and thus, low-grade lesions were heavily represented. Outcomes were assessed by clinicians who were not blinded or independent of the care of the patients.
patients. Adjuvant endovascular techniques have evolved in the past 20 years, the results, therefore, reflect past treatment trends, rather than the latest techniques.  

Conclusions

Although ARUBA remains the only level 1 evidence for management of ubAVMs, our study demonstrates the safety of microsurgical resection in a carefully selected population of ubAVM patients based on SM grade, AVM angioarchitecture, and judicious use of preoperative embolization. It adds weight to the emerging evidence from other microsurgical series consisting of predominantly low-grade ubA VMs (SM1 and SM2) that microsurgery can be efficacious and challenges the conclusion that medical management is superior to all interventions. Data from retrospective surgical series, such as this study, may be used to develop future prospective trials and a potential treatment algorithm for ubAVMs.

Acknowledgments

All authors contributed to the data collection, writing, statistical analysis, and illustration of the article. Dr Tymianski is a Canada Research Chair (tier 1) in translational stroke research.

Sources of Funding

This work was funded by the aneurysm research fund, Neurovascular Therapeutics Program, University Health Network. Dr Wong was supported by the Royal Australasian College of Surgeons for the Stuart-Morson Travel Scholarship.

Disclosures

None.

References


Microsurgery for ARUBA Trial (A Randomized Trial of Unruptured Brain Arteriovenous Malformation) – Eligible Unruptured Brain Arteriovenous Malformations

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Stroke. 2017;48:136-144; originally published online November 17, 2016; doi: 10.1161/STROKEAHA.116.014660

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

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