The effect of embolization with N-butyl cyanoacrylate prior to surgical resection of cerebral arteriovenous malformations

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Endovascular therapy of cerebral arteriovenous malformations (AVM’s) is an accepted adjunct to surgical therapy. However, the literature has not characterized the benefits or the liabilities of preoperative embolization. This series compares two groups of patients who underwent surgical resection of a cerebral AVM; one group (20 patients) received preoperative transfemoral selective embolization with N-butyl cyanoacrylate (NBCA) and the other group (13 patients) did not. In the group with preoperative embolization, the AVM’s were larger (3.9 vs. 2.3 cm) and of a higher Spetzler-Martin grade (3.2 vs. 2.5) as compared to the nonembolized group. The NBCA embolization facilitated surgical resection. Arteries supplying the vascular malformation were readily distinguished from those supplying the normal brain parenchyma. Embolized vessels were compressible and easily cut with microscissors. No bleeding occurred from transected vessels. Operative time and intraoperative blood loss for the two groups were not statistically different, despite the significant differences in lesion size and grade. Endovascular complications included immediate and delayed hemorrhage (15%) and transient ischemia (5%); there were no embolization-related deaths. Postoperative complications for both groups included hemorrhage (15%), residual AVM (6%), and cerebrospinal fluid leak (3%); the mortality rate was 3%. There was no statistically significant difference in surgical complications between the embolized and nonembolized groups. Most patients (91%) in both groups had an excellent or good late neurological outcome, with no significant difference between the groups. This study concludes that preoperative NBCA embolization of AVM’s makes lesions of larger size and higher grade the surgical equivalent of lesions of smaller size and lower grade by reducing operative time and intraoperative blood loss, with no statistically significant difference in surgical complications or long-term neurological outcome.

**KEY WORDS** • cerebral arteriovenous malformation • endovascular therapy • N-butyl cyanoacrylate • embolization

This study was undertaken to evaluate the usefulness of preoperative embolization in patients undergoing surgical resection of cerebral arteriovenous malformations (AVM’s). The advent of microsurgical techniques has allowed neurosurgeons to undertake the resection of more formidable cerebrovascular malformations and has fostered the evolution of preoperative endovascular therapy. Endovascular embolization of cerebral AVM’s is now an accepted adjunct to surgical therapy. However, the indications for endovascular therapy are still being clarified. The literature has not characterized the benefits or the liabilities of preoperative embolization, and the issue is further complicated by the widely different types of embolic agents available and the different methods of delivery.

Embolization of the AVM proper is considered to be more efficacious than the proximal occlusion of arterial feeders. Materials that consistently and reliably penetrate the AVM are limited to acrylic agents and polyvinyl alcohol mixtures. Acrylic agents may be more advantageous since they permanently occlude the vessel and do not recanalize when a solid column is introduced. Isohbutyl 2-cyanoacrylate (IBCA) has been the predominant acrylic used in endovascular therapy of AVM’s; however, IBCA has been criticized for complicating the surgical resection of vascular malformations. A more accommodating embolization material is required to assist the surgeon intraoperatively. Since 1987, the authors have used N-butyl cyanoacrylate (NBCA) exclusively for the endovascular treatment of AVM’s. It was thought that, because of ad-

Preoperative embolization of cerebral AVM's provides a distinct advantage in preoperative embolization of AVM's decreases the operative time and the amount of blood loss; however, statistical analysis with comparable data from nonembolized patients is lacking. The only study demonstrating a statistically significant reduction in intraoperative bleeding as well as improved postoperative clinical outcome following the use of preoperative embolization utilized selective embolization with polyfilament polyethylene threads. Statistical evidence supporting the benefit of acrylic embolization is not available in the literature.

This study evaluates the effect of preoperative embolization with NBCA on the surgical resection of AVM's. Two concurrent groups of patients underwent surgical resection of purely parenchymal cerebral AVM's. One group received preoperative transfemoral selective embolization with NBCA. The impact of embolization upon the technical aspects of AVM resection, the operative time and blood loss, and the complications and clinical outcome are examined.

Clinical Material and Methods

Patient Population

Between January, 1989, and December, 1990, 34 patients with pial AVM's of the brain were treated surgically by one of the authors (J.J.J.) at the Tisch Hospital of New York University Medical Center. One patient had been embolized 6 years previously with IBCA and was excluded from the study. Thirteen patients were treated with surgery only and had not undergone previous endovascular embolization therapy.

Twenty patients were treated with a combined therapy consisting of transfemoral endovascular embolization with NBCA and surgical excision. All charts were reviewed for these 33 patients, and a retrospective analysis was undertaken.

Data Base

Data collected included patient age, sex, clinical presentation, and pertinent physical findings on admission: computerized tomography (CT) and/or magnetic resonance imaging findings and evidence of intracerebral hemorrhage (ICH); the size of the AVM as determined by the largest measurement on angiography to the nearest one-half centimeter: the location, arterial supply, and venous drainage of the AVM; the number of preoperative embolizations performed; the total amount of NBCA used; and the complications of endovascular therapy; the number of days postembolization that surgery was performed; the extent of surgical resection and the operative time and estimated blood loss; the surgical complications and number of reoperations; the results of postsurgical angiography; the histopathological diagnosis; and the clinical outcome as determined at the latest examination. Each AVM was graded according to the Spetzler-Martin classification system utilizing the size of the AVM, the eloquence of the involved parenchyma, and the character of the venous drainage.

Endovascular Therapy

All patients included in this study were reviewed by the authors prior to or at the time of admission to determine the appropriate therapeutic plan. All surgical candidates were considered for preoperative endovascular embolization. Of 33 patients with pial AVM's, 20 were treated with NBCA embolization. Each patient underwent selective catheterization of the feeding arterial vessels via femoral artery percutaneous catheterization under neuroleptic or general endotracheal anesthesia. Catheterization was performed by either of two authors (A.B. or I.S.C.). An attempt was made to penetrate the AVM with NBCA and obliterate as many perforating arteries as possible. Multiple injections of acrylic were performed at each session, and nine of the 20 patients underwent more than one session. Embolization of cerebrovascular malformations was performed exclusively with NBCA. Embolization was contraindicated in 11 patients either because it was the opinion of the treating physicians that the ease of the surgical resection did not warrant the additional risk of embolization or because no angiographically identifiable arterial feeding vessels could be safely catheterized and embolized. In two patients, catheterization and embolization were attempted, but could not be performed. A total of 13 patients were not embolized preoperatively.

Surgical Therapy

Nonembolized patients underwent operation on an elective basis. An attempt was made to operate on embolized patients between 2 and 7 days postembolization. In each case, a one-step total surgical resection procedure was planned. Three of the 20 embolized patients were brought to the operating room on an emergency basis secondary to intra- or postembolization hemorrhage. One of these patients had an inoperable AVM, however, and underwent an emergency craniotomy secondary to postembolization ICH.

Surgery was performed using microvascular techniques and mild hypotensive anesthesia, maintaining the systolic blood pressure at approximately 100 mm Hg. For Grade IV AVM's, barbiturate anesthesia was administered. Postoperative management including pentobarbital-induced coma with intracranial pressure monitoring was performed depending upon the complexity of the AVM and the difficulty of the surgical resection.

Complications of surgery in a patient were defined as postoperative problems not considered to be part of the routine course of convalescence, and included asymptomatic postoperative intracerebral hematomas demonstrated on CT, extra-axial hemorrhages, and infections. Late outcome was determined by the clinical and social status at the latest evaluation (usually at 6 months), and follows the classification system described by Heros, et al. A patient with an excellent outcome is defined as having no neurological deficits other than a partial visual field deficit; a patient with a good outcome is fully independent, working, with a minimal neurological deficit; a patient with a fair outcome is
fully independent, unable to work full-time, with mild to moderate neurological deficits; and a patient with a poor outcome is dependent, incapacitated, with moderate to severe neurological deficits.

All lesions were confirmed by histopathological examination to be AVM's. All patients underwent postoperative angiography to confirm total excision of the vascular malformation.

Results

Clinical and Radiological Characteristics

Patient data are summarized in Table 1. The average age for embolized patients was younger than that for nonembolized patients (32.2 vs. 41.5 years, p < 0.05, Student's t-test). There is a nonsignificant preponderance of females in each group.

The clinical presentation of the two groups differed significantly. Of interest is the larger number of patients in the nonembolized group presenting with symptoms of ICH (p < 0.05, Fisher's exact test). Radiographically, nine (69%) of the 13 nonembolized patients had evidence of ICH as compared with six (30%) of 20 embolized patients, a statistically significant difference (p < 0.05, Fisher's exact test). The embolized patients presented with a greater number of seizures and headaches, but the difference was not statistically significant. The distribution of AVM's within the brain was similar for the two groups. There was no difference in involvement of the dominant hemisphere.

The average size of the largest AVM dimension as determined by angiography was larger for the embolized group as compared with the nonembolized group (3.9 vs. 2.3 cm, p < 0.001, Student's t-test). The average grade according to the Spetzler-Martin classification was greater for the embolized patients than for the nonembolized patients (3.2 vs. 2.5, p < 0.05, Student's t-test) (Table 1). Venous drainage patterns were similar for both groups. Slightly less than one-half of the patients in each group demonstrated deep venous drainage on angiography.

Endovascular Therapy and Complications

Twenty patients underwent endovascular embolization with NBCA, with nine requiring more than one session. In two cases, a second attempt at embolization could not be accomplished. The average amount of acrylic deposition was 2.05 cc, ranging from 0.25 to 9.1 cc. Not all arterial feeders could be catheterized or safely embolized, and in almost all cases the AVM was only partially obliterated. Occlusion estimates were based upon the subjective impression of the endovascular radiologist as reported in the procedure notes and were often between 50% and 90%.

Four (20%) of the 20 patients suffered postembolization complications. A 37-year-old man with a 3-cm left temporal AVM developed transient receptive aphasia following embolization secondary to cerebral ischemia; he ultimately died from postoperative sepsisemia and meningitis. A 30-year-old woman with a 3-cm left angular gyrus AVM suffered rupture of the middle cerebral artery secondary to balloon inflation during endovascular embolization; this patient required an emergency craniotomy but made an excellent recovery.

Two patients experienced delayed complications. One suffered an intracerebral and intraventricular hemorrhage 24 hours following the embolization of a 3.5-cm right temporal AVM. She required an emergency craniotomy but made an excellent recovery, with a residual left homonymous hemianopsia. The other patient developed ICH 72 hours following an 80% occlusion of a 4-cm right temporal AVM; this patient required emergency surgical evaluation of the hematoma and excision of the AVM with prolonged pentobarbital-induced coma and intracranial pressure monitoring, and ultimately made an excellent recovery. There were no deaths related to the endovascular procedures.

Surgical Therapy and Complications

Of the 33 patients in this series, 13 did not undergo embolization prior to surgery. In the 20 patients who underwent surgery following NBCA embolization, three craniotomies were performed on an emergency basis for hemorrhagic complications secondary to endovascular embolization as described above. Excluding these three patients, 11 patients (65%) underwent surgery within 1 week of embolization, two patients within 2 weeks, one within 3 weeks, and three within 2 to 5 months. The most common period for surgery was 2 to 5 days following embolization.

Intraoperatively, embolization with NBCA was thought to facilitate surgical resection by identifying parent vessels supplying the malformation. The embolized arteries were gray in color, and accompanying vessels supplying normal parenchyma were readily identified and spared. Embolized vessels were easily

### Table 1

<table>
<thead>
<tr>
<th>Factor</th>
<th>Nonembolized Patients</th>
<th>Embolized Patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean ± SEM</td>
<td>41.5 ± 3.3†</td>
<td>32.2 ± 2.2†</td>
<td>—</td>
</tr>
<tr>
<td>range</td>
<td>20–60</td>
<td>19–66</td>
<td>—</td>
</tr>
<tr>
<td>sex (M/F)</td>
<td>6/7</td>
<td>9/11</td>
<td>15/18</td>
</tr>
<tr>
<td>no. of cases</td>
<td>13</td>
<td>20</td>
<td>33</td>
</tr>
<tr>
<td>clinical presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>intracerebral hemorrhage</td>
<td>8 (62)†</td>
<td>4 (30)†</td>
<td>12 (36)</td>
</tr>
<tr>
<td>seizure</td>
<td>1 (8)</td>
<td>8 (40)</td>
<td>9 (27)</td>
</tr>
<tr>
<td>headache</td>
<td>1 (8)</td>
<td>5 (25)</td>
<td>6 (18)</td>
</tr>
<tr>
<td>miscellaneous</td>
<td>3 (23)</td>
<td>3 (15)</td>
<td>6 (18)</td>
</tr>
<tr>
<td>AVM size (cm)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>mean ± SEM</td>
<td>2.3 ± 0.3‡</td>
<td>3.9 ± 0.3‡</td>
<td>—</td>
</tr>
<tr>
<td>range</td>
<td>1.6–4.0</td>
<td>2.5–6.0</td>
<td>—</td>
</tr>
<tr>
<td>AVM grade§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean ± SEM</td>
<td>2.5 ± 0.3†</td>
<td>3.2 ± 0.2†</td>
<td>—</td>
</tr>
<tr>
<td>range</td>
<td>1–4</td>
<td>2–5</td>
<td>—</td>
</tr>
</tbody>
</table>

* Numbers in parentheses indicate percent of total. AVM = arteriovenous malformation; SEM = standard error of the mean.
† Statistically significant difference: p < 0.05.
‡ Statistically significant difference: p < 0.001.
§ Grade classified according to Spetzler and Martin.21
Preoperative embolization of cerebral AVM's

TABLE 2
Operative characteristics and postoperative complications*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Nonembolized Patients</th>
<th>Embolized Patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>operative time (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean ± SEM</td>
<td>446 ± 61</td>
<td>515 ± 55</td>
<td>—</td>
</tr>
<tr>
<td>range</td>
<td>160–955</td>
<td>240–1100</td>
<td>—</td>
</tr>
<tr>
<td>estimated blood loss (cc)</td>
<td>923 ± 257</td>
<td>1446 ± 395</td>
<td>—</td>
</tr>
<tr>
<td>mean ± SEM</td>
<td>200–3500</td>
<td>200–8000</td>
<td>—</td>
</tr>
<tr>
<td>no. of cases</td>
<td>13</td>
<td>20</td>
<td>33</td>
</tr>
<tr>
<td>complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hemorrhage</td>
<td>1 (8)†</td>
<td>4 (20)§</td>
<td>5 (15)</td>
</tr>
<tr>
<td>residual AVM</td>
<td>1 (8)</td>
<td>1 (5)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>CSF leak</td>
<td>0</td>
<td>1 (5)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>death</td>
<td>0</td>
<td>1 (5)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses indicate percent of total. AVM = arteriovenous malformation; SEM = standard error of the mean; CSF = cerebrospinal fluid.
† Patients may be included in more than one category of complications.
§ This patient had an intracerebral hemorrhage.
¶ In this category two patients had intraventricular hemorrhage, one an intraventricular hemorrhage, and one a subdural hematoma.

Operative settings were compressed and were spongy in character, making them amenable to cutting with microscissors. There was no bleeding from either the transected embolized vessels or around the core of glue deposition. Once transected, no embolized vessels required coagulation or ligation. Deep and small feeding arteries were not embolized preoperatively and were problematic, as is usually the case. All of the vascular malformations were found to be partially thrombosed at the time of surgery.

In spite of the larger size and higher Spetzler-Martin grade for the AVM's in the embolized patients, there was no statistical difference between the embolized and nonembolized groups with regard to total operative time or intraoperative estimated blood loss (Table 2).

There were five patients among the 33 included in this series with serious postsurgical hemorrhagic complications (Table 2), one (7.7%) in the nonembolized group and four (20%) in the embolized group. This difference was not significant (Fisher’s exact test). The patient in the nonembolized group experienced an ICH 48 hours postoperatively in the region of the superior cerebellar artery following excision of a right paraventricular cerebellar AVM; immediate surgical evacuation was performed and the patient ultimately made a good neurological recovery. In the embolized group, two patients experienced a postoperative ICH, both requiring reoperation for hematoma evacuation. One of these patients died from sepsis and Klebsiella meningitis; the other made an excellent recovery. Another patient required reoperation for a postoperative subdural hematoma and a persistent cerebrospinal fluid leak, but ultimately achieved an excellent outcome. The fourth patient suffered a postoperative intraventricular hemorrhage that required a temporary ventriculostomy, but no operative therapy, and made an excellent recovery. The one death (3%) among the 33 patients occurred in the embolized group.

There were two patients with a residual vascular malformation identified by postoperative angiography, one in each group. The nonembolized patient refused reoperation and was referred for focused beam radiation therapy; the embolized patient underwent reoperation for a complete resection of the residual malformation 8 days after the first surgery. One patient in the embolized group with a known residual AVM that was not considered to be a surgical complication underwent an emergency craniotomy for the evacuation of an ICH caused by an arterial rupture during embolization. The location of this large AVM within the dominant angular gyrus precluded the possibility of complete surgical resection, and it was elected at the time of operation to leave the remaining vascular malformation to prevent further neurological deficit. The patient made an excellent recovery.

Late Outcome

Late outcome for all patients is presented in Table 3. In the nonembolized group, nine of 13 patients had an excellent outcome. Of the two patients with a good outcome, one was hemiplegic preoperatively and had no change in her overall neurological grade. Of the two patients with a poor outcome, one was hemiplegic and the other dysphasic and hemiplegic prior to surgery.

In the embolized group, 19 of 20 patients had an excellent outcome at the last clinical examination. One patient described above died from septic complications. All other patients have returned to work, with only visual field deficits and no other appreciable focal neurological findings. There was no statistically significant difference in late outcome between nonembolized and embolized groups (Fisher’s exact test).

Statistical Analysis

Further analysis of the data was performed to specifically examine the effect of embolization on the relationship between the size and the Spetzler-Martin grade of an AVM and the resulting intraoperative blood loss and operative time.

Statistical analysis of nonembolized patients dem-
Determined a moderate to strong correlation between both the size and grade of an AVM and the operative time and estimated blood loss (Figs. 1 and 2). Similar data for the embolized patients were then compared with the nonembolized group. Multivariate analysis of the embolized patients demonstrated that preoperative NBCA embolization does not significantly change the slope of the regression line or the correlation between the size and the Spetzler-Martin classification of an AVM and the operative time (Fig. 1). However, with regard to the size and grade of an AVM and the intraoperative blood loss, multivariate analysis suggested \( p < 0.07 \), but did not reach, a significant difference in the slope of the regression line, as well as the correlation between the embolized and nonembolized groups (Fig. 2). The lack of statistical significance may have been secondary to the small sample size. These findings indicate that when an AVM is embolized, the operative time is not only reduced but still correlates with the size and grade of a lesion. However, while operative blood loss is reduced for a given AVM following embolization, there may no longer be a direct correlation with the lesion size or grade.

A second analysis was performed to ensure that other patient variables were not responsible for the results obtained in this study. Since the nonembolized and embolized groups differed according to age and incidence of ICH, these variables were examined for their possible effect upon the important dependent variables used to compare the two groups (amount of intraoperative blood loss, duration of operation, and outcome at 6 months postoperatively). Multiple bivariate analyses demonstrated no significant relationship between either age or incidence of ICH and these dependent variables for either the embolized or the nonembolized group.

Hence, any beneficial effect on intraoperative blood loss, operative time, and late outcome attributed to embolization is not secondary to the differences between these groups on the basis of age or incidence of ICH.

**Discussion**

The role of endovascular therapy in the treatment of AVM's is still being clarified. Endovascular therapy for the primary treatment of AVM's is contentious and still in the initial stages of investigation.\(^5\) It may have a role in certain cases, but the long-term results of this therapy are unknown. Most neurosurgeons and interventional neuroradiologists accept the idea that preoperative embolization benefits the surgical resection of AVM's, but are unsure of the nature of this benefit. No clinical or radiographic criteria have been developed regarding the indications for preoperative embolization. Many surgeons prefer to use embolization therapy to make inoperable AVM's operable or to make surgically treacherous lesions more manageable.\(^5,7,14,19,21,23,24\)

Whether preoperative embolization aids the surgical resection of more easily accessible lesions is unknown.

The results of this study demonstrate that preoperative embolization with NBCA enables the surgeon to safely resect AVM's of a larger size and higher Spetzler-Martin grade achieving the same results as with smaller-sized, lower-grade lesions.

**AVM Size and Grade vs. Operative Time and Blood Loss**

Several studies suggested that preoperative embolization with IBCA reduced operative time and blood loss.\(^5,7,19\) Others noted no difference after embolization...
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Fig. 2. Graphs showing data for nonembolized (triangles) and embolized (squares) patients for the intraoperative estimated blood loss (EBL) as related to the size (A) and grade (B) of the arteriovenous malformation (AVM). The regression line for the nonembolized patients is indicated by diamonds and for the embolized patients by circles. The data point for one patient with embolization is not shown, being beyond the abscissa scale. In A, note that following embolization, the correlation coefficient (r) is reduced. In B, the EBL correlates with the AVM grade. Note the striking change in the slope of the regression line and the lack of any correlation (r = 0.01) between EBL and AVM grade. While multivariate analysis only approaches statistical significance for these two graphs, the marked deviation in regression line slope and correlation suggests that the EBL may no longer have a linear relationship with the size or grade of a lesion following embolization.

utilizing acrylic, polyvinyl alcohol, or Gelfoam.\textsuperscript{17,23} No statistical data supporting either claim have been published. Early multimodality therapy of AVM's using embolization with cyanoacrylate included patients receiving transfemoral and/or intraoperative embolization, making it difficult to interpret the results.\textsuperscript{5,24} Only one recent study,\textsuperscript{16} utilizing preoperative selective transfemoral embolization of AVM's with polyfilament polyethylene threads, demonstrated a statistically significant reduction in the incidence of both intraoperative paraventricular bleeding and postoperative transient and major permanent neurological deficits. However, the degree of paraventricular blood loss was not quantified and the incidence of severe intraoperative blood loss (> 2000 ml) was not reduced.

Earlier studies suggested that patients with larger-sized, higher-grade AVM's have a worse surgical outcome.\textsuperscript{10,14-16,22} Data for the nonembolized patients in this study support this concept. Graphs for nonembolized patients (Figs. 1 and 2) demonstrate a moderate to strong correlation between lesion characteristics and operative data. This confirms the clinical impression commonly held by surgeons that larger-sized, higher-grade AVM's take longer to resect and patients have a greater intraoperative blood loss.

The embolized group in this study was characterized by lesions of a larger size and a higher Spetzler-Martin grade as compared with the nonembolized group, but there was no significant difference in operative time or intraoperative blood loss between the two groups. The improved result was attributed to preoperative embolization with NBCA.

Regression analysis gave insight into the mechanism by which embolization with NBCA improved our operative results. The influence of AVM size and grade upon operative time is presented in Fig. 1. There is a strong correlation between AVM size and grade and the operative time in the nonembolized patients, reflecting the commonly accepted relationship between complexity of a lesion and the required time for operative resection. After embolization, the regression line for embolized patients is shifted slightly to the right as compared with the regression line of the nonembolized patients, but maintains a similar slope. This indicates that while embolization does decrease the operative time for a given lesion, the overall relationship between complexity of an AVM and resulting operative time is still maintained (more difficult lesions take longer to resect, but that time is reduced with preoperative embolization).

An unexpected result was obtained when this same analysis was applied to intraoperative blood loss (Fig. 2). A reduced correlation between AVM size and grade and the estimated blood loss was determined for the embolized patients compared to the nonembolized patients. The slopes of the regression lines were also reduced. However, multivariate analysis demonstrated these findings to be marginally nonsignificant, which may be secondary to the sample size. These results suggest that, for a given vascular malformation following preoperative embolization, the expected relationship between AVM size and grade and intraoperative blood loss may be eliminated (that is, vascular malformations overall will have a decreased intraoperative blood loss following embolization, but the complexity of the lesion as defined by size and grade may no longer predict intraoperative blood loss).

Effect of Embolization on AVM Resectability

Preoperative embolization profoundly changes the hemodynamics of an AVM.\textsuperscript{19,23,25} and this study indicates that surgical blood loss may not be predicted by
FIG. 3. Case 1. A 24-year-old man with a history of seizures and memory difficulties. A: An axial T2-weighted magnetic resonance image revealing a right holofrontal arteriovenous malformation (AVM) involving the basal ganglia. B: Right internal carotid artery angiogram, anteroposterior view, demonstrating the extensive vascular supply to the lesion. C: Right internal carotid artery angiogram, anteroposterior view, obtained after embolization with NBCA revealing a significant reduction in the AVM size. D: Postoperative angiography confirming total excision of the AVM. This patient had an excellent outcome.

traditional criteria after embolization. The factors that determine intraoperative blood loss after embolization are speculative, although the authors believe, as do other surgeons,\(^{8,14}\) that the recruitment of deep, collateral arterial feeding vessels after endovascular occlusion of superficial feeding vessels may significantly complicate the resection of some AVM's. A change in arterial supply toward deep inaccessible perforators represents a major disadvantage of adjunct endovascular therapy and must be considered prior to undertaking the final surgical resection. Deep perforators lie on the far side of the lesion, are difficult or impossible to control until the mass of the AVM is retracted or resected, and may produce extreme operative difficulties (Figs. 3 and 4).

Embolization of AVM's with NBCA has been criticized for complicating the resection of these lesions.\(^{1,15,21,23}\) The malformation has been described as a brittle, solid mass that is difficult to manipulate.

FIG. 4. Case 2. Angiograms of a 19-year-old woman with a history of seizures. A: Left internal carotid artery angiogram, anteroposterior view, revealing anterior cerebral, middle cerebral, and lenticulostriate artery supply to the lesion. B: Angiogram obtained after embolization of the anterior cerebral artery with NBCA demonstrating an increase in the deep perforator vascular supply (arrow) from the lenticulostriate arteries. C: Selective injection into the lenticulostriate arterial feeder demonstrating branches to the normal brain parenchyma (large arrow). The catheter tip (small arrow) could not be advanced beyond the normal vessel branching point, and embolization was not attempted. Surgical resection was difficult, secondary to copious bleeding from the inaccessible deep perforating vessels lying on the far side of the lesion, and intraoperative blood loss was estimated at 8000 cc. Reoperation was required to treat a postoperative intracerebral hemorrhage. D: Postoperative angiogram confirming total excision of the AVM. The patient made an excellent recovery.
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without damaging the surrounding softer brain parenchyma. The IBCA-embolized vessels are difficult to cut with microscissors. Continuous bleeding from transected embolized vessels that cannot easily be controlled with bipolar coagulation has been described. The use of NBCA for preoperative embolization precludes these problems. The material properties of NBCA make it superior to IBCA for endovascular therapy. The NBCA produces a more uniform, higher integrity acrylic column with less fragmentation than IBCA. It is less brittle, less rigid, and more elastic than IBCA. The lower bond strength decreases the chance of accidental catheter gluing.

At surgery, NBCA-embolized vessels were found to be spongy in character and easily compressible. They were easily cut with microscissors and no bleeding from around the acrylic column was encountered. The embolized vessels were easily distinguished from arteries supplying adjacent normal parenchyma which were then readily spared. Overall, NBCA embolization was felt to facilitate the technical aspects of surgical resection. These findings are supported by another study, which reported that vessels embolized with NBCA are softer, more pliable, and easier to cut than those embolized with IBCA.

Complications of Endovascular Therapy

The complication rate for endovascular therapy of vascular malformations has decreased significantly with improvements in both equipment and technique and with greater experience among endovascular radiologists. Newer methods utilizing superselective catheterization permit the delivery of embolic agents directly into the interstices of the vascular malformation. Balloon catheters are less frequently used, reducing the risk of arterial rupture. The only arterial rupture in this series occurred during the use of a calibrated-peak balloon. This method is no longer used by our endovascular team.

Recent studies of serious or permanent complication rates following endovascular therapy of AVM's with IBCA and polyvinyl alcohol were reported to be between 4.9% and 27%, 1,7,9,13,19,20,24,25 Immediate and delayed intracerebral/subarachnoid hemorrhage, cerebral ischemia, and inadvertent catheter gluing were the most commonly cited complications. A 0% to 4% mortality rate, 9,13,20,25 directly related to embolization therapy was reported in series utilizing acrylic materials or polyvinyl alcohol. Viñuela, et al., 25 in a series of 228 patients treated with IBCA and/or polyvinyl alcohol embolization, reported that the advent of microcatheter technology, which no longer required a latex calibrated-peak balloon, reduced hemorrhagic and ischemic complications by one-third. In a study of their 100 most recently treated embolized patients, they reported no arterial ruptures and only one embolization-related death. In a recent series of 49 patients treated with superselective catheterization and either IBCA or NBCA embolization, the permanent neurological morbidity rate following embolization was 8%; there was one immediate (3 hours) and one delayed (1 month) ICH following embolization. There were no deaths directly related to the embolization procedures, but the one patient with a delayed hemorrhage ultimately died from perioperative bleeding and cerebral edema.

In our study, immediate complications secondary to endovascular procedures in 20 patients included a transient cerebral ischemic event in one patient (5%) and hemorrhagic complications in three (15%). All three patients with hemorrhagic complications ultimately made an excellent recovery following surgery. There were no deaths related to the endovascular therapy. However, these results are not indicative of the true complication rate of endovascular therapy of AVM's in the authors' experience. One of the embolized patients was entered into this study only because hemorrhagic complications necessitated surgical therapy. Hence, the complication rate for endovascular treatment in this series included those patients originally designated for combined therapy and any additional patients who suffered a serious hemorrhage requiring surgery but who would otherwise have not been included in this study. A review of the most recent experience with acrylic embolization of AVM's revealed a 1.5% incidence of serious morbidity and a 0.3% mortality rate in 188 patients undergoing either IBCA or NBCA embolization between 1985 and 1990. Mild deficits that do not affect lifestyle were noted in 9% of the patients. There were a total of five hemorrhagic complications (5%) among the 101 patients most recently embolized with NBCA (unpublished data), three of whom are included in the 20 embolized patients in this study. Hence, it can be seen that the overall endovascular complication rate in this study was skewed toward a poorer result.

Hemorrhagic Complications Following Surgery

The incidence of hemorrhagic complications following the surgical resection of AVM's is not well documented in the literature. When the patient is asymptomatic, hemorrhage within the surgical cavity is often not included within the statistical data of a patient series or retrospective study. When the patient is symptomatic, hemorrhage is often included within the broader category of "morbidity" and listed along with other etiologies. Postoperative edema, ischemia, hemorrhage, and hemorrhagic infarction are occasionally consolidated under the heading "normal pressure perfusion breakthrough" or "hyperemic" complication, further obfuscating the true incidence of these complications. Papers specifically addressing the issue have reported a 0.6% to 10% incidence of symptomatic postoperative hemorrhagic complications; most were closer to the latter figure.

The overall immediate postoperative hemorrhagic complication rate for this study was 15%. When only those patients requiring reoperation for a symptomatic postoperative ICH were included the incidence was reduced to 9%. This is well within the expected results for a group of patients with an average AVM grade of 2.9. Most significantly, there was no statistical difference in immediate postoperative complications between the nonembolized and embolized groups, despite a difference of 0.7 in the average Spetzler-Martin grade.

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and a 70% larger size of the embolized AVM’s. It appears that preoperative embolization does not adversely affect immediate postoperative surgical complications, and may even be beneficial.

Early and Late Outcome

Early postoperative results for patients with surgically excised AVM’s vary widely, but pooled averages of the largest series since the advent of microsurgical techniques indicated a 9% morbidity rate and a 6% mortality rate. Early surgical results are dependent upon the grade of the vascular malformation. Spetzler and Martin demonstrated that as the AVM grade increases from II to III, the morbidity rate increases from 5% to 16%.

Late outcome is perhaps the most important indicator of the results of any therapy for AVM’s. Heros, et al. demonstrated that neurological outcome improves steadily from the early postoperative results over the course of long-term observation. They also noted that late outcome is dependent upon the preoperative grade of the AVM. In this study, there was no statistical difference in late outcome between the embolized and nonembolized patients. The late outcome for both groups combined was 84.8% (28 patients) with an excellent outcome, 6% with a good outcome, and 6% with a poor outcome. The mortality rate was 3%. This is comparable to the results of Heros, et al., for a group of patients with an average AVM grade of 2.9. While the embolized group appears to have a greater number of patients with an excellent outcome compared to the nonembolized group (95% vs. 69%), the difference is not statistically significant. Several patients in the nonembolized group had significant deficits prior to surgical therapy and in actuality had little change in their overall neurological status compared with their preoperative status. Most importantly, the late outcome was excellent for 95% of patients undergoing preoperative NBCA embolization, despite an average AVM grade of 3.2. This result is superior to the previously quoted surgical studies and strongly suggests that endovascular embolization improves surgical outcome.

Statistical Analysis

This paper is a case study and compares data retrospectively. It is faulted with the bias that nonrandomized nonprospective studies inherently possess. Succinctly, the embolized group can be thought of as a slightly younger group of patients with larger-sized, higher Spetzler-Martin grade AVM’s who presented less often with clinical or radiographic evidence of hemorrhage compared to the nonembolized group. As stated earlier, multiple bivariate analyses demonstrated that the difference in patient age and incidence of ICH between the groups does not account for the apparent beneficial effect of embolization.

The differences in patient age, incidence of ICH, and lesion characteristics were not apparent prior to the analysis undertaken in this study, but in retrospect are not surprising. Only those patients without accessible arterial feeders for catheterization or those with small superficial lesions thought to be most easily treated by surgery were not subjected to endovascular therapy. A natural selection bias is immediately apparent. Conversely, one must consider the embolized group to harbor more difficult surgical lesions. Since patients with larger-sized, higher-grade malformations have been shown to have a worse outcome, one would expect the outcome for the embolized group, if treated with surgery alone, to be worse than the nonembolized group regardless of selection bias. The lack of a difference in operative time and blood loss between the two groups and the excellent long-term outcome in the embolized group strongly argues for the benefit of preoperative embolization.

Conclusions

The following may be concluded regarding the preoperative embolization of AVM’s with NBCA.

1. Embolization does not interfere with the technical aspects of the surgical resection of AVM’s and aids in the identification of feeding arteries and the ease of dissection.

2. Embolization makes larger-sized, higher-grade AVM’s surgically equivalent to smaller-sized, lower-grade lesions by reducing operative time and blood loss.

3. The results of surgery and the long-term outcome in patients with larger-sized, higher-grade AVM’s who underwent preoperative NBCA embolization are equivalent to those for nonembolized patients with smaller-sized, lower-grade lesions.

4. Preoperative transfemoral embolization with NBCA is a safe and significantly beneficial adjunct therapy to the surgical resection of AVM’s.

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References


Preoperative embolization of cerebral AVM’s


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