Delayed hemorrhage following resection of an arteriovenous malformation in the brain


Department of Radiology, Sydney Aneurysm and AVM Neurosurgical Centre, The University of Sydney, Royal North Shore Hospital, Sydney, Australia

Object. Between 1989 and 2002 the authors treated 416 cases of angiographically confirmed arteriovenous malformations (AVMs) of the brain.

Methods. Three hundred fifty-five patients underwent resection of an AVM; 2% died and 12% experienced a permanent morbidity (1.7% experienced a deterioration of modified Rankin Scale [mRS] score of 3–5). Patient outcomes in this series were based on the Spetzler–Martin grade. For patients with Grade I and II AVMs the rate of permanent morbidity was 1% and the rate of mortality was 0.5%. For patients with Grade III AVMs the morbidity rate was 18.9% (2.7% experienced a deterioration of mRS score of 3–5) and the mortality rate was 2.7%. For patients with Grade IV and V AVMs the morbidity rate was 25.6% (5.1% experienced a deterioration of mRS score of 3–5) and the mortality rate was 7.7%. No patient with a Spetzler–Martin Grade I or II lesion had a worsened outcome due to delayed hemorrhage, whereas 3.6% of patients with a Grade III and 12.8% of patients with Grade IV and V AVMs experienced delayed hemorrhage that led to a permanent downgrade in function.

With the introduction of an aggressive postoperative blood pressure protocol (for AVMs with grades ≥ II and sizes ≥ 3.5 cm in diameter) the incidence of delayed postoperative hemorrhage leading to mortality or permanent morbidity decreased from 4.4 to 1%. This difference was significant. Neither case selection nor complications other than delayed hemorrhage changed between these two periods.

Conclusions. In selected cases an aggressive postoperative blood pressure protocol is likely to reduce delayed hemorrhage following AVM resection.

KEY WORDS • arteriovenous malformation • brain • hemorrhage • complication • surgery

The morbidity and mortality rates that have been reported for surgery to resect AVMs in the brain have varied markedly during the last 20 years, with mortality rates ranging from 0 to 12.5% and morbidity rates from 7.8 to 30%.2,3,6–9,12,15,17,19,22–24 Delayed hemorrhage following the resection of an AVM can be catastrophic and accounts for a significant proportion of deaths in most series dating from 1956. The overall incidence of delayed hemorrhage is approximately 2%.12,13 In reported series delayed hemorrhage is almost entirely confined to AVMs in which the Spetzler–Martin grade is greater than II and the size is larger than 3 cm. This is true for both case reports and for recent series focusing on small low-grade AVMs.6,7,10,17,19,22 Delayed hemorrhage is also more likely to occur from AVMs that are fed by the lenticulostriate arteries.11

The causes of delayed hemorrhage are controversial. A retained AVM nidus with outflow obstruction,2 the rupture of a thin-walled feeding artery in response to an increase in pressure from long-standing low pressure,14 the failure of an autoregulatory mechanism to protect the microcirculation from an increase in arterial pressure,21 the weakened integrity of the microcirculation,18 and a propagated venous occlusion obstructing normal flow6 have all been cited as contributing factors for delayed hemorrhage. These mechanisms may also combine. Regardless of the underlying pathophysiological mechanism, the common pathway is a failure in vascular integrity due to a local increase in transmural pressure. As such, the best umbrella term for this complication might be “arterial-capillary-venous hypertensive” syndrome.13

Two treatment strategies that may be critical to minimize the risk of delayed hemorrhage are complete resection of the AVM and strict postoperative management of blood pressure. The aim of this study was to assess the impact of a strict postoperative blood pressure regimen on the incidence of delayed postoperative hemorrhage from AVMs that were resected in our center between 1989 and 2002.

Clinical Material and Methods

Data Collection and Analysis

Data were collected prospectively in a specifically designed AVM database. The information included demographic characteristics, clinical features before and after...
surgery, mRS score before surgery and at follow-up review, angiographic features (feeding arteries, venous drainage, and the presence of aneurysms), appearance of the lesion on MR imaging (including its size, location, and relationship to eloquent brain), and the Spetzler–Martin grade,10 which was assigned preoperatively.

Patients were stratified by Spetzler–Martin grade into lower than Grade III, Grade III, and higher than Grade III. Statistical comparisons were made using this breakdown because prior to this date the longest delay in hemorrhage leading to a downgrade in outcome occurred on postoperative Day 6 and no hemorrhage had occurred in patients with Grade I, Grade II, or small Grade III AVMs.13 Intracranial pressure measurements were obtained using either a subdural or ventricular catheter following surgery and this was only discontinued when the intracranial pressure was normal in the presence of Glasgow Coma Scale score 15. Blood pressure control was initiated with emphasis on prevention of hypertension, which was defined as a systolic blood pressure greater than 140 mm Hg. All patients were treated with preoperative and postoperative dexamethasone and anticonvulsant medications. Occasionally large AVMs were managed with aggressive antihypertensive therapy following surgery, but this was not done with the rigor of the protocol introduced on June 12, 1997.

After June 12, 1997 we followed a new protocol for postoperative management. The new protocol ensured that all patients harboring an AVM that was Spetzler–Martin Grade III or greater and also had a diameter 3.5 cm or larger were treated in the ICU for a minimum of 7 days, during which arterial blood pressure was strictly controlled. These criteria were established because prior to this date the longest delay in hemorrhage leading to a downgrade in outcome occurred on postoperative Day 6 and no hemorrhage had occurred in patients with Grade I, Grade II, or small Grade III AVMs.13 Intracranial pressure measurements were obtained using either a subdural or ventricular catheter following surgery and this was only discontinued when the intracranial pressure was normal in the presence of Glasgow Coma Scale score 15. Blood pressure control was initiated with preoperative loading with a β-adrenoceptor blocker, the administration of which was continued in the postoperative period. Commencing with surgery, each patient’s MABP was limited to a maximum of 70 mm Hg.

Following surgery, a decrease in the patient’s CPP to lower than 60 mm Hg, at the MABP maximum limit of 70 mm Hg, prompted the performance of computerized tomography scanning to exclude the presence of a space-occupying lesion. If a hemorrhage was identified, surgery was...
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**Results**

Four hundred sixteen angiographically confirmed AVMs of the brain were treated between 1989 and 2002. Of these, 355 were surgically resected. Complete obliteration of the lesions was confirmed by angiography in all 353 patients who survived surgery. In 12 (3.4%) of these patients further intervention was required to achieve this goal. This was achieved by surgery (eight cases), focused irradiation for deep small residual lesions (three cases), and obliteration with embolization (one case). No patient with a residual AVM experienced hemorrhagic complications. In all patients who underwent surgery or embolization for a residual nidus, successful obliteration was achieved within 7 days after the initial surgery. Eleven of the 12 patients in whom a residual AVM occurred were treated after June 12, 1997.

The profiles of cases and results are illustrated in Table 1. Among the 355 patients 58% harbored Spetzler–Martin Grade I or II AVMs, 31% had Grade III AVMs, and 11% had Grade IV or V AVMs. The results for each grade are presented in Table 2. One percent of patients with Spetzler–Martin Grade I and II AVMs experienced a deterioration in their mRS score to no worse than 2, and one patient (0.5%) died of myocardial infarction, which occurred before the dura mater was opened. Of the patients with Spetzler–Martin Grade III AVMs 16.2% experienced a deterioration no worse than mRS Score 2, 2.7% of patients deteriorated to an mRS score between 3 and 5, and 2.7% of patients died. Patients with Grade IV and V AVMs had a 25.6% chance of some deterioration, of whom 5.1% worsened to an mRS score between 3 and 5 and 7.7% died.

No patient with a Spetzler–Martin Grade I or II AVM suffered morbidity due to delayed hemorrhage (Table 2). Four (3.6%) of 111 patients with Grade III and five (12.8%) of 39 patients with Grade IV or V AVMs experienced a delayed hemorrhage that resulted in a functional impairment. These cases are reported in Table 3. Generally the onset was sudden and catastrophic and required an immediate return to the operating room. All patients experienced an increase in blood pressure before the hemorrhage occurred. All patients were in the ICU undergoing careful blood pressure surveillance at the time of hemorrhage. With the exception of Case 8 (in which the patient’s blood pressure remained within the desired parameters), an increase in blood pressure—from less than 120 mm Hg systolic to between 130 and 160 mm Hg—was documented to have preceded the clinical deterioration. The MABP in each case exceeded 100 mm Hg. An increase in arterial blood pressure was associated with precipitating events in three cases. These included: insertion of a central venous catheter (Case 5); seizures (Case 3); and an instance in which it was thought desirable not to be as aggressive with blood pressure management because of concerns regarding coronary perfusion (Case 9). Of the cases of delayed hemorrhage the first seven occurred before June 12, 1997. In a comparison of case profiles before and after June 1997, we found that the second period had a slightly higher (nonsignificant) percentage of more complex cases (as judged by the Spetzler–Martin grade and the lenticulostriate blood supply) (Table 1).

All patients had undergone postoperative angiography before the onset of hemorrhage; none of the studies had demonstrated evidence of an AVM. In addition, following evacuation of the hemorrhage, a second postoperative angiogram also confirmed the absence of an AVM.

In a comparison of outcomes between the two periods, 12.6% of patients experienced a worsening of their conditions during the first period and 8.7% during the second (Table 1). This difference was not significant. During the first time period 3.8% of patients had an outcome worse than mRS Score 2 and during the second period 3.5% had a worse outcome. When patients with a delayed postopera-
tive hemorrhage were excluded, the percentage of patients with a worsening of outcome during the first period was 8.2% compared with 7.7% during the second period. This difference was not significant. When patients who suffered a downgrade in function due to delayed postoperative hemorrhage were considered in isolation, a deterioration in function occurred in seven (4.4%) of 159 cases during the first period and in two (1%) of 196 cases during the second period. This difference was significant (p < 0.03).

Strict blood pressure control was generally well tolerated. In the first 7 postoperative days no patient died, experienced acute myocardial infarction, was found to have a borderline cerebral infarction, or required dialysis as a result of the strict blood pressure control.

### Discussion

The outcomes for the 355 surgically treated patients show the strong relationship between outcome and Spetzler–Martin grade. An mRS score greater than 2 occurred in 0.5% of patients whose original AVM grade was less than III, 5.4% of those whose AVM grade was III, and 12.8% of those whose AVM grade was greater than III. The contribution of changes in case selection, surgical expertise, and postoperative management to outcome can be inferred from both the surgical profiles and the results. With the introduction of the strict blood pressure protocol there was a reduction in the incidence of delayed postoperative hemorrhage from 4.4% before application of the protocol to 1% afterward. Furthermore, in one of the two cases in which delayed hemorrhage occurred in the latter period, the protocol was disregarded because of the possible potential compromise of coronary perfusion.

Because the comparison involves temporally different groups, another possible explanation for the reduced complication rate with time might be the increased experience of the single surgeon performing the operations (either changing case selection or improved surgery). Evidence for this hypothesis, however, is not supported by either a change in the distribution of cases (reflecting a change in case selection) or a change in morbidity due to causes other than delayed hemorrhage over time (reflecting, in part, a change in surgical skill). The only changes that were apparent during the second time period were a significant reduction in preoperative embolization and an increased number of patients requiring additional intervention to achieve complete AVM ablation.

The mechanism for delayed postoperative hemorrhage has been the topic of a long history of debate. A year prior to the first successful removal of a cerebral AVM in 1889 by Pean (cited by Yaşargil)24, Gowers1 described a condition called “congestive apoplexy” as the most severe complication of cerebral congestion and defined “partial active congestion” as that occurring “when an artery is obstructed, and the adjacent branches of the main vessel receive too much blood.” This is the central argument applied today in the controversy of a hemorrhage complicating surgery for large AVMs. The underlying pathophysiological disturbance responsible for delayed hemorrhage is thought to be a loss of autoregulation and has been termed the “normal perfusion pressure breakthrough” theory.21 Nevertheless, several mechanisms are likely to contribute to delayed hemorrhage and these can be summarized as a retained AVM nidus, the rupture of feeding arteries, normal perfusion pressure breakthrough, a weakened capillary wall (microcirculatory weakness), and occlusive venous hyperemia.1,4

### Conclusions

A rigidly applied aggressive blood pressure management protocol may be effective in reducing the incidence of delayed postoperative hemorrhage following resection of AVMs of the brain.

### References

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Address reprint requests to: Michael K. Morgan, M.D., Sydney Aneurysm and AVM Neurosurgical Centre, Level 8, 193 Macquarie Street, Sydney, NSW 2000, Australia. email: morgan@med.usyd.edu.au.