Complications of surgery for arteriovenous malformations of the brain

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 \vee A series of 112 patients undergoing complete surgical resection of arteriovenous malformations (AVM's) of the brain between 1974 and 1990 were analyzed for complications and 12-month outcomes. The cohort consisted of 44 patients with small AVM's (< 2 cm in diameter), 43 patients with medium-sized AVM's (2 to 4 cm in diameter), and 25 patients with large AVM's (> 4 cm in diameter). There was a 3.6% series mortality rate and an 18% morbidity rate. One of the four deaths was caused by normal perfusion pressure breakthrough. Analysis of logistic regression found that the most important factor influencing the occurrence of complications in this series was AVM size (p = 0.005) and that the occurrence of complications (p < 0.001) and the neurological grade at the time of surgery (p < 0.004) both significantly contributed to the outcome at 12 months.

This study stresses the importance of defining complications in terms of rigid criteria when analyzing AVM series in order to allow for a correct evaluation of the risk; benefit ratio of surgery. Furthermore, it emphasizes the need for a separate analysis of the importance of complications upon outcome.

KEY WORDS • cerebral arteriovenous malformation • intracerebral hemorrhage • normal perfusion pressure breakthrough • cerebral hemodynamics

Norder to ascertain the merits of management of any condition, there must be an understanding of both the natural history of the condition and the complications of management. The natural history for cerebral arteriovenous malformations (AVM's) is becoming increasingly understood. There is a risk of clinically significant first hemorrhage of 2% to 4% per year^{4,11,14,28} and a risk of recurrent hemorrhage of 7% to 14% per year initially, which declines to a prehemorrhage level after 5 years. ^{10,11,14} The mortality rate for hemorrhage may be as high as 30%. ^{4,17} In addition, excluding hemorrhagic complications, there is a risk of a decline in functional capacity in 1.5% of patients per year. ⁴

The risks of treatment are less clearly understood. The overall morbidity and mortality rates in large series reported over the last 10 years range from 0% to 12.5% and from 8% to 30%, respectively. 1.7.13.19.30.39.41.46 Causes for morbidity and mortality are as diverse as the overall incidence of complications. This is particularly so for hyperemic complications occurring after cerebral AVM resection. The reported incidence of normal perfusion pressure breakthrough varies from 0% 20.29.30.45 to being the major cause for morbidity and mortality. 3.18.43.44 Indeed, an incidence of 21% of AVM resections result-

ing in hemodynamic complications has been reported.³ In all previous reports, the complication of normal perfusion pressure breakthrough remained hard to prove because of the difficulty in excluding the alternative diagnoses of postretraction edema and hemorrhage, rupture of occult retained AVM, and venous and arterial occlusion to normal parenchyma. The aim of this review of resected cerebral AVM's is to gain some understanding of the morbidity and mortality following the surgical management of this condition.

Clinical Material and Methods

Patient Population

All patients with AVM of the brain undergoing surgical resection at Royal Prince Alfred and Royal Alexandra Hospitals, Sydney, from June, 1974, until August, 1990, were included in this study. Data were obtained from medical records, computerized tomography (CT) scans, angiograms, surgeons' records, and patient review. Data collected included age, sex, mode of presentation, size of AVM, location of AVM, neurological condition at the time of surgery, complications of surgery, and neurological condition at 12 months following surgery. The size of a cerebral AVM was

measured as the largest diameter of the nidus and categorized as being small (< 2 cm), medium (2 to 4 cm), or large (> 4 cm).

A total of 112 patients were included in the study. The patients' ages ranged from 6 months to 67 years (mean 29 ± 16 years). Two patients were less than 1 year old and 13 were less than 10 years of age. There were 63 male and 49 female patients.

The mode of presentation for the patients was cerebral, cerebellar, brain-stem, or subarachnoid hemorrhage in 81 (72%), seizures in 22 (20%), headache unrelated to hemorrhage in six (5%), neurological deficit unrelated to hemorrhage in two (2%), and hydrocephalus in one (1%). There were 44 patients with lesions less than 2 cm in diameter, 43 with lesions of medium size, and 25 cases with lesions greater than 4 cm in diameter. The lesions were located in the cerebrum in 96 patients, the cerebellum in 12, and the brain stem in four. Over 50% of the operations were performed since 1984.

Neurological Grading System

The neurological grading system was divided into four categories: Grade 1 was normal examination for age; Grade 2 was the presence of a neurological deficit but independence with regard to mobility; Grade 3 was the loss of independent mobility; and Grade 4 was death. The preoperative condition of the 112 patients was Grade 1 in 43, Grade 2 in 32, and Grade 3 in 37. All patients had complete resection of the AVM confirmed by angiography or at autopsy.

Statistical Analysis

Descriptive statistics for age are expressed as mean \pm standard deviation. Analysis of factors that may contribute to the outcome at 12 months was undertaken by logistic regression using the SPIDA computer program. The following variables were studied: age, sex, neurological grade at the time of surgery, AVM size, the occurrence of complications, and the outcome at 12 months.

Results

Neurological Grade

At 12 months following resection, 58 patients were without neurological deficit (Grade 1), three were severely disabled with loss of independence (Grade 3), and four were dead (Grade 4). The remaining 47 patients had neurological deficits of varying severity but continued to be functionally independent (Grade 2). Of the 43 patients with AVM's who were neurologically normal preoperatively and have been followed for 12 months, none had loss of independent mobility, eight had at least one minor neurological deficit, and one died.

Complications

Complications were defined as any untoward result of management that led to further surgery (except for planned staged resection), a hospital admission extending longer than 14 days after the last surgical attempt at AVM resection, an increase in neurological deficit, or new seizure development.

Twenty-four patients (21%) had complications (Table 1). There were four deaths (3.6%); three deaths were operative and one occurred more than 30 days after surgery but was nonetheless due to surgery. Death was thought to be caused by either normal perfusion pressure breakthrough (one case) or intraoperative hemorrhage (three cases). Nonfatal hemodynamic complications were normal pressure hyperperfusion breakthrough (two cases) and intraoperative hemorrhage from the AVM (one case).

Normal perfusion pressure breakthrough was suggested as complicating AVM ablation in cases where occlusion of the AVM was associated with edema and hemorrhage of the brain not readily explained by brain retraction, rupture of occult retained AVM, or premature occlusion of the venous drainage. In no case was regional cerebral blood flow obtained. Therefore, no direct evidence for a redistribution of the cerebral circulation can be provided to support this diagnosis.

Neurological complications thought not to be based on hemodynamics were seen in 11 cases (10%). Two of these patients suffered the expected occurrence of visual field loss following occipital lobe resection, six were known preoperatively to have a high risk for the development of neurological deficits due to the location of the planned resection, one developed a facial weakness during preoperative embolization, and two experienced a new onset of seizures. Other complications included bone-flap infection in two, human immunodeficiency virus following a blood transfusion in one, pulmonary embolus in two (one of whom developed an intracerebral hemorrhage after commencing heparin therapy), and a prolonged hospital stay recovering from a severe hemorrhage.

Logistic Regression Analysis

Logistic regression analysis was performed with the independent variables age, sex, AVM size, and neurological grade at the time of surgery, and the dependent variable of no complications. Only the size of the AVM was significant (p = 0.005) and, in fact, the size factor could be reduced to a two-category predictor: those AVM's less than 4 cm and those greater than 4 cm.

The tables of results present odds ratios for the various predictor variables. In the analysis of a favorable outcome, such as no complications, an odds ratio greater than 1 represents an increased chance of that outcome if the factor is present, whereas an odds ratio less than 1 represents a decreased chance (Table 2). In addition, logistic regression analysis was performed with the predictor variables age, sex, AVM size, neurological grade at the time of surgery, and the occurrence of complications with the dependent variable "neurologically normal at 12 months (Grade 1)." Only the neurological condition at the time of surgery (p < 0.004) and the presence of complications (p < 0.001) were significant (Table 3). A similar logistic regression analysis using the dichotomous dependent variable of "independent, but some neurological deficit (Grade 2) at 12 months" gave the same variables as significant pre-

TABLE 1
Complications of AVM resection in 112 surgical cases*

Age, Sex Y	Year of AVM Site,		Complication	Operative	Neurological Grade†	
Age, Sex Surger		Size Complication		Death	At Surgery	At 12 Month
25 yrs, M	1976	cerebrum, large	neurological deficit	no	1	2
68 yrs, M	1977	cerebrum, large	normal perfusion pressure breakthrough	yes	3	4
7 mos, M	1978	cerebrum, large	operative hemorrhage	yes	1	4
44 yrs, M	1979	cerebrum, large	normal perfusion pressure breakthrough	no	1	1
21 yrs, M	1980	cerebrum, large	neurological deficit	no	1	2
25 yrs, F	1981	cerebrum, large	operative hemorrhage	yes	3	4
28 yrs, F	1981	cerebrum, large	pulmonary embolus‡§	no	1	2
55 yrs, M	1983	cerebrum, medium	neurological deficit	no	1	1
17 yrs, F	1984	cerebrum, medium	human immunodeficiency virus from transfusion	no	2	2
26 yrs, M	1985	cerebrum, large	operative hemorrhage	yes	3	4
40 yrs, M	1985	cerebrum, medium	neurological deficit	no	1	2
33 yrs, F	1985	cerebrum, small	neurological deficit	no	1	2
21 yrs, F	1986	cerebrum, medium	operative hemorrhage§	no	1	2
31 yrs, M	1987	cerebrum, large	extradural hematoma	no	1	2
21 yrs, F	1987	cerebrum, large	neurological deficit	no	1	2
28 yrs, F	1988	cerebrum, medium	neurological deficit	no	2	2
11 yrs, M	1988	cerebrum, small	prolonged admission	no	3	2
21 yrs, M	1988	cerebrum, large	seizures	no	2	1
32 yrs, M	1988	cerebrum, large	pulmonary embolus	no	3	2
32 yrs, F	1988	cerebrum, small	seizures	no	3	2
33 yrs, F	1989	cerebrum, large	normal perfusion pressure breakthrough	no	2	2
39 yrs, M	1989	cerebrum, large	neurological deficit	no	2	2
35 yrs, M	1990	cerebrum, large	extradural hematoma	no	2	2
55 yrs, M	1990	cerebrum, small	neurological deficit	no	1	1

^{*} Abbreviation: AVM = arteriovenous malformation.

dictors (Table 4). The remaining two grades of "neurological condition at 12 months" were observed in three and four instances, respectively, and as expected, no significant associations were found. However, all four patients who died (Grade 4) had complications, and the three patients who had lost independence at 12 months (Grade 3) were in that grade at the time of surgery. Thus, condition at the time of surgery and the occurrence of complications are the best predictors of the neurological condition at 12 months.

Discussion

Literature Review

Management outcome statistics should include both the morbidity due to complications arising from the AVM itself and the morbidity complicating the surgical removal of AVM's in order to provide guidance when considering the surgical management of these lesions. Variables that have been considered to influence the management outcome for AVM's include size, ^{13,16,19,32,36,41,46} grade of neurological deficit at the time of surgery, ^{13,16,32,35,39,41,46} location in the eloquent cortex, ^{13,32,36,39,41,47} angiographic evidence of steal, ³ supply from deep perforators, ^{3,7} deep venous drainage, ^{13,36,39,47} and vein of Galen aneurysms. ^{15,46} It is not likely that all of these variables contribute significantly to complications of surgery (for example, grade of neurological deficit). Furthermore, while each of these variables might carry

an additional risk, they are not necessarily independent of each other; for example, a large AVM is more likely to have angiographic evidence of steal, derive supply from deep perforators, and have deep venous drainage. In addition, in order to compare series, it is important to include the epidemiology and clinical profile at presentation. If differences occur in comparing these data, they need to be discussed in the interpretation of the results.

Considerable variation in morbidity and mortality rates has been reported in the literature. A review

TABLE 2
Logistic regression analysis of patients with complications

Variable*	p Value	Odds Ratio	90% Confidence Interval	
age	0.758	0.995	0.969-1.022	
male	0.688	0.815	0.352-1.885	
AVM size (2-4 cm)	0.988	1.010	0.357-2.857	
AVM size (> 4 cm) condition at surgery	0.005	0.186	0.069-0.501	
some deficit	0.571	1.412	0.518-3.845	
loss of independence	0.328	1.793	0.672-4.779	
final logistic regression o	dds ratio			
AVM size (> 4 cm)	0	0.173	0.075-0.399	

^{*} AVM = arteriovenous malformation.

[†] For explanation of neurological grades, see text.

[‡] Pulmonary embolus treated with heparin administration complicated by intracerebral hemorrhage.

[§] Subsequent bone-flap infection.

TABLE 3
Logistic regression analysis of patients with no deficit at 12 months (Grade 1)

Variable*	p Value	Odds Ratio	90% Confidence Interval	
age	0.221	1.021	0.993-1.049	
AVM size (2 to 4 cm)	0.308	0.550	0.210 - 1.441	
AVM size (> 4 cm)	0.415	0.549	0.164 - 1.842	
male	0.653	0.788	0.329 - 1.887	
condition at surgery				
some deficit	0.003	0.040	0.007-0.240	
loss of independence	0.000	0.011	0.002-0.064	
complications	0.000	0.015	0.002-0.103	
final logistic regression o condition at surgery	dds ratio			
some deficit	0.002	0.038	0.007-0.226	
loss of independence	0.000	0.010	0.002-0.060	
complications	0.000	0.014	0.002 - 0.089	

^{*} AVM = arteriovenous malformation.

demonstrated a 0% to 12.5% series mortality rate and a 3% to 30% series morbidity rate (Table 5). 1.7-9.13. 16,19,26,30-35,41-43,46 There is little doubt that there is variation in the results because of selection criteria. An example of how methodology influences the results is seen in the series presented by Davis and Symon. They reported a 1.5% mortality rate; however, seven patients who died postoperatively with a poor neurological grade on admission were excluded. If these patients had been included, the management mortality rate would have been 10%. Therefore, the mortality rate as reported in the literature may be as much a reflection of case selection as surgical expertise.

Epidemiology and Clinical Profile at Presentation

This series included a greater number of males than females, which is consistent with other reports, 1,4-6.9. 12.16.21,22.26.27.31.33.34.46 and 12% of the 112 patients were less than 10 years of age, which is in contrast to the two

TABLE 4
Logistic regression analysis of patients with some deficit at 12 months (Grade 2)

Variable*	p Value	Odds Ratio	90% Confidence Interval
age	0.340	0.986	0.963-1.010
AVM size (2 to 4 cm)	0.110	2.296	0.976-5.401
AVM size (> 4 cm)	0.488	1.561	0.544-4.481
male	0.672	1.218	0,566-2.625
condition at surgery			
some deficit	0.001	8.661	2.917-25.715
loss of independence	0.000	13.118	4.531-37.979
complications	0.002	8.251	2.722-25.010
final logistic regression o condition at surgery	dds ratio		
some deficit	0.000	8.616	3.010-24.664
loss of independence	0.000	13.528	4.743-38.583
complications	0.001	8.200	2.836-23.708

^{*} AVM = arteriovenous malformation.

TABLE 5
Literature review of morbidity and mortality rates for AVM resection*

Authors & Year	No. of Cases Resected	Mortality (%)	Morbidity (%)	
Paterson & McKissock, 1956	36	8.0	_	
Perret & Nishioka, 1966	119	12.0	_	
Forster, et al., 1972	95	4.0	_	
Drake, 1979	140	11.0	_	
Nornes, et al., 1979	63	1.6	3.0	
Pellettieri, 1979	112	8.0	16.0	
Pertuiset, et al., 1979	162	11.0	-	
Suzuki & Onuma, 1979	147	3.0	3.0	
Wilson, et al., 1979	65	6.0	28.0	
Parkinson & Bacher, 1980	90	4.0	_	
Albert, 1982	124	12.0	_	
Luessenhop & Rosa, 1984	90	2.0	11.0	
Davis & Symon, 1985	69	1.5	8.7	
Jomin, et al., 1985	119	12.5	30.0	
Yaşargil, 1988	414	2.0	_	
Steinmeier, et al., 1989	48	0.0	10.0	
Heros, et al., 1990	153	0.6	7.8	
Sundt, et al., 1990	279	2.5	_	
Morgan, et al., 1993	112	3.6	18.0	

^{*} AVM = arteriovenous malformation; - = data not reported.

largest series (all ages included) where this incidence was no more than 8%. 33,34 The high incidence of children in our series is likely to reflect peculiarities of referral patterns. The presentation symptoms in this series included hemorrhage in 72% of patients, seizures in 20%, headaches unrelated to hemorrhage in 5%, and either neurological deficits unrelated to hemorrhage or hydrocephalus in 3%. This is comparable to the distribution reported in the literature (Table 6).

Normal Perfusion Pressure Breakthrough

The major causes for mortality and morbidity in our series of 24 patients with complications were an in-

TABLE 6
Incidence of common modes of presentation in larger series

Authors & Year	Hemor- rhage (%)	Seizure (%)	Nonhemor- rhagic Neurological Deficit (%)*	
Paterson & McKissock, 1956	46	26	7	
Perrett & Nishioka, 1966	68	28	_	
Moody & Poppen, 1970	41	50	_	
Morello & Borghi, 1973	70	35	-	
Drake, 1979	79	10	-	
Pertuiset, et al., 1979	64	38	4	
Wilson, et al., 1979	66	16	16	
Parkinson & Bacher, 1980	53	67	_	
Albert, 1982	65	15	_	
Davis & Symon, 1985	67	16	9	
Jomin, et al., 1985	55	31	_	
Yaşargil, 1988	51	33	_	
Heros, et al., 1990	58	23	_	
Morgan, et al., 1993	72	20	3	

^{* - =} data not reported.

crease in neurological deficit unrelated to hemorrhage or edema (nine cases), normal perfusion pressure breakthrough (three cases), and intraoperative hemorrhage unrelated to normal perfusion pressure breakthrough (four cases). The cause of death was either normal perfusion pressure breakthrough (one case) or intraoperative hemorrhage (three cases). This latter complication has not occurred since the introduction of highly selective preoperative embolization with graded-stiffness microcatheters.* However, the contribution to the management of AVM's by embolization techniques is still controversial as there may be a risk of enlarging and attenuating the smaller deep-feeding vessels, which increases the difficulty of their ablation at surgery. The frequency of these complications is comparable with that in other series (Table 7).

In the three cases (3% of all AVM's and 12% of all large AVM's) in which normal perfusion pressure breakthrough was said to complicate surgery in this series, the diagnosis was derived by a process of excluding reasonable alternative explanations for the hemorrhage or edema. No direct evidence for the existence or mechanism of normal perfusion pressure breakthrough was derived from these cases. Despite the significance of normal perfusion pressure breakthrough being in question 20,29,43 and its pathophysiological basis yet to be substantiated.^{23–25} there are several reported series in which this complication constitutes the major cause for morbidity and mortality unrelated to technical error or poor preoperative neurological condition. 3,18,34,35,43,44 The highest incidence is that of Batjer, et al.,3 who defined hyperemic complications as "unexpected or abnormal degrees of intraoperative brain swelling or hemorrhage unrelated to technical error or concealed ventricular hemorrhage . . . and CT evidence of edema associated with neurological deficit not related to inadvertent proximal vascular occlusion or intraoperative brain retraction as well as hemorrhage after angiographically proven complete AVM resection;" they reported these complications in 13 (21%) of 62 patients undergoing AVM resection. Of these 13 patients, seven were either dead or not capable of independence. Spetzler, et al.,37 and Andrews and Wilson2 considered the complication to be sufficiently frequent in larger AVM's that they advocated a staged surgical resection for these larger lesions in order to avoid the development of normal perfusion pressure breakthrough. However, this strategy has been questioned.25

While the cases from our series fit well with the clinical criteria for normal perfusion pressure breakthrough as described in literature,³⁸ there are no blood flow data to support these clinical and radiological observations. Therefore, although the unproven mechanism of normal perfusion pressure breakthrough may be responsible for the observed complications, alternative explanations, such as normal venous outflow obstruction and occult technical error, cannot be entirely excluded.⁴⁰

Nonhyperemic Causes for Morbidity and Mortality

The nonhyperemic causes of morbidity and mortality are more straightforward and can be readily understood in terms of complications to be anticipated with resection of any vascular cerebral lesion. In our experience, the majority of complications can be broadly grouped into either hemorrhage from the AVM (poor neurological condition preoperatively, intraoperative hemorrhage — which occurred only in our first 40 cases — and blood product replacement complications) or resection of eloquent brain. Pulmonary embolus and its sequelae, extradural hematoma, infection, and post-operative seizures are all general complications of craniotomy and occur as isolated complications in this series.

Size of Arteriovenous Malformation

The major risk factor for the prediction of complications was AVM size. It must be borne in mind that patients with AVM's located in eloquent cortex as well as some with very large AVM's may have been rejected from surgical consideration. Therefore, the results do not negate the possibility that other factors may also be influential in predicting complications. However, it is understandable how size of AVM can influence surgical results when considering the complications of surgery leading to death (normal perfusion pressure breakthrough and intraoperative hemorrhage). It is likely that the common underlying physiological factor in most of the anatomical variables is high flow through the AVM. The one anatomical variable that is likely to be independent of high flow is the location of the lesion adjacent to eloquent cortex. The reasons for risks of surgically managing lesions in these locations are selfevident. Neurological deficit at the time of surgery is a predictor of outcome at 12 months but it was not seen to be a factor influencing complications in this series.

TABLE 7

Major causes for morbidity and mortality

A sidh a sa	No. With	Causes of Morbidity and Mortality				
Authors & Year	Mor- bidity & Mor- tality	Preop Neuro- logical Status	Intraop Hemor- rhage	Postop Hemor- rhage	NPPB*	
Paterson & Mc-	3	1	_	2	-	
Kissock, 1956						
Drake, 1979	16	_	-	2	2	
Wilson, et al., 1979	4	-	1	1	2	
Pertuiset, et al., 1979	18	8	_	4	4	
Pellettieri, 1979	9	3	3	3	_	
Parkinson & Bacher, 1980	4	-	-	3	_	
Albert, 1982	15	_	2	1	_	
Luessenhop, et al., 1982	12	-	-	6	3	
Davis & Symon, 1985	1	_	_	1	_	
Yaşargil, 1988	10	-	1	6	-	
Morgan, et al., 1993	24	-	3	-	1	

^{*} NPPB = normal perfusion pressure breakthrough.

^{*} Tracker microcatheters manufactured by Target Therapeutics, Inc., Fremont, California.

Conclusions

The 3.6% mortality rate and 18% morbidity rate in this series can be compared with those of other reported series. The occurrence of complications strongly influenced an adverse outcome in our patients as did a young age and the neurological condition at the time of surgery. A strong influence on the occurrence of complications is the size of the lesion. This is likely to manifest its effect by the flow of blood through the AVM.

The results of this study suggest that management outcome forecasting should be divided into factors that may result in complications of management and factors that are complications of the AVM itself. Furthermore, it is anticipated that, as a physiological phenomenon appears to underlie many of the risk factors, physiological imaging modalities may prove to be of importance in contributing to our predictions of surgical complications. It is important that strict definitions of complications are employed and stated in the methodology of AVM series in order to properly compare series.

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