Population-based analysis of arteriovenous malformation treatment

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Object. The author sought to describe overall management data on cerebral arteriovenous malformations (AVMs) and to focus the actuarial need for different treatment modalities on a population-based scale. Such data would seem important in the planning of regional or national multimodality strategies for the treatment of AVMs. This analysis of a nonselected, consecutive series of patients representing every diagnosed case of cerebral AVM in a population of 1,000,000 over one decade may serve to shed some light on these treatment aspects.

Methods. During the 11-year period from 1989 to 1999, data from every patient harboring a cerebral AVM that was presented clinically or discovered incidentally in a strictly defined population of 986,000 people were collected prospectively. No patient was lost to follow up. There were 12.4 de novo diagnosed AVMs per 1,000,000 population per year (135 AVMs). Large high-grade AVMs (Spetzler–Martin classification) were rare, and Grade 1 to 3 lesions represented 85% of the caseload. Hemorrhage was the initial manifestation of AVM in 69.6% of the cases. Intracerebral hematoma was the most common hemorrhagic manifestation occurring in 78 patients. There were 4.4 cases per 1,000,000 population per year of hematomas needing expedient surgical evacuation. In the remaining patients who did not require hematoma surgery, small, critically located Grade 3 and Grade 4 lesions amounted to 1.6 cases per 1,000,000 population per year. There were 5.8 cases per 1,000,000 population per year of Grade 1 to 2 and larger noncritically located Grade 3 malformations. There were 0.5 cases per 1,000,000 population per year of Grade 5 AVMs. The overall outcome in 135 patients was classified as good according to the Glasgow Outcome Scale (Score 5) in 61% of the cases, and the overall mortality rate was 9%.

Conclusions. In centers with population-based referral, AVM of the brain is predominantly a disease related to intracranial bleeding, and parenchymal clots have a profound impact on overall management outcome. The rupture of an AVM is as devastating as that of an aneurysm. Aneurysm ruptures are more lethal, whereas AVM rupture tends to result in more neurological disability due to the high occurrence of lobar intracerebral hematoma. In an attempt to quantify the need for different modalities of AVM treatment based on a population of 1,000,000 people, figures for surgeries performed range from six to 10 operations per year and embolization as well as gamma knife surgery procedures range from two to seven per year, depending on the strategy at hand. When using nonsurgical approaches to Grade 1 to 3 lesions, the number of patients requiring treatment with more than one method for obliteration increases drastically as does the potential risk for procedure-related complications.

Key Words • cerebral arteriovenous malformation • overall management result • multimodality treatment

Modern technology has greatly expanded possibilities for treatment of cerebral AVMs. The role of surgery has been modified, and today multimodality therapeutic protocols are standard treatment, at least in complex lesions. A wealth of data support various algorithms for selection of one or more treatment modalities in individual cases and, in some patients, the withholding of therapy. The focus is primarily on the technical aspects of AVM treatment, with little attention currently being paid to the actuarial need for different treatment modalities on a population-based scale. Such data would seem important in the planning of regional or national multimodality strategies for treatment of AVMs. This analysis of a nonselected, consecutive series of patients for whom every diagnosed case of cerebral AVM in a population of 1,000,000 people is represented during one decade may serve to shed some light on these matters.

Abbreviations used in this paper: AVM = arteriovenous malformation; GKS = gamma knife surgery; GOS = Glasgow Outcome Scale; ICH = intracerebral hematoma; SAH = subarachnoid hemorrhage.

Clinical Material and Methods

In Sweden neurosurgical care is provided exclusively by six university centers, each serving a defined catchment area. There are no other neurosurgical facilities in the country, and there is very little regional crossflow of patients among these centers. The Linköping University catchment area comprises a population of 986,000 people who are primarily served by 10 local hospitals and the University Hospital. A very liberal, open-door policy for all patients with neurosurgical disorders is practiced. During the 11-year period from 1989 to 1999, data from every case of cerebral AVM presenting clinically or being discovered incidentally were collected prospectively in the neurosurgical center. Additional retrospective tracking of cases in the records of the 10 local hospitals in our area yielded only another three patients not previously known to us during this time span, and these three cases were included in the analysis. No patient was lost to follow-up review.

Patients underwent embolization procedures at one of the other five neurosurgical centers with a well-established interventional radiology department, and all gamma knife
surgeries were performed in the national treatment center. Two patients underwent proton-beam radiation treatment.

The Spetzler and Martin grading system was used to classify the AVMs. We adopted a classification of the Spetzler–Martin Grade 3 that was proposed by de Oliveira and coworkers to facilitate grouping of cases, based on treatment modalities. Malformations in cortical areas classified as Grade 3 because of size were denoted as Grade 3a, whereas smaller AVMs classified as Grade 3 because of their critical location in central areas were denoted as Grade 3b. Based on our protocol, small, critically located Grade 3 lesions (Grade 3b) were most frequently treated using GKS, whereas patients with larger pial Grade 3 lesions (Grade 3a) underwent operation with or without preoperative embolization. Most Grade 4 AVMs were primarily treated with embolization followed by surgery or focused radiation. Most patients with Grade 5 AVMs declined therapy.

All patients treated throughout this period were seen by the same team of neurovascular surgeons and neuroradiologists.

The results of treatment were evaluated angiographically in terms of nidus occlusion and clinically by using the GOS. Therapy was considered unsuccessful if flow through the fistula could be seen on angiograms 2 years after treatment. In cases treated using more than one therapeutic modality, the angiographically documented end point was set at 2 years after the final treatment was given. The patients' clinical conditions were assessed 12 months after treatment.

### Results

In this regional population of 986,000 people cerebral AVMs were diagnosed de novo during an 11-year period (1989–1999) in 135 patients, representing an incidence of 12.4 de novo diagnosed AVMs per 1,000,000 population per year. These cases were evenly distributed over the studied time span. The patients' clinical presentations were diverse (Table 1), although hemorrhage was the initial manifestation of AVM in 69.6% (94 patients), giving a presentation incidence of 8.7 cases per 1,000,000 population per year. Epileptic seizures were the second most common presenting manifestation, whereas incidental findings of AVMs were rare.

An ICH was present in 83% of 94 patients presenting with hemorrhage. In 30 patients with small hematomas, the timing of AVM therapy was based on the angiographic findings, whereas in 48 patients harboring large (most often lobar) ICHs expedient surgical decompression was necessary. In 16 of these latter 48 patients with large ICHs suspected to have resulted from AVM rupture, their clinical condition allowed for the acquisition of preoperative angiography. In 13 patients transtentorial herniation was manifest on arrival in the neurosurgical center, and evacuation of the ICH was performed without preoperative angiography. In 19 mostly elderly patients with large lobar ICHs, the neurosurgeon on call at the time did not suspect an AVM as the source of bleeding, and surgery was performed without obtaining a preoperative angiogram. In total, 32 patients with large ICHs underwent surgery without undergoing preoperative angiography. In the majority of these 32 cases, the AVM revealed at surgery was small to medium sized and was extirpated in the same session. In four patients, large AVMs were found, and simple hematoma evacuation was performed. Only two of these four patients survived, both in poor condition, and follow-up angiography was not performed. Eighteen of the 32 patients who underwent surgery without undergoing preoperative angiography recovered, and in three of these an angiographically demonstrated AVM remnant received adjuvant treatment.

Coexistent arterial aneurysms were found in 19 patients; 11 of these presented with hemorrhage. Three patients suffered both ICH and SAH; eight patients suffered only SAH. In the entire series of 135 patients 27 suffered SAH and the 16 patients who did not harbor an arterial aneurysm all had coexistent ICH. Intraventricular hemorrhage occurred in 16 patients and was an isolated finding in seven of these.

The Spetzler–Martin classification was used to characterize 103 AVMs that were angiographically evaluated prior to therapy (Table 2). Large high-grade AVMs were rare; Grade 1 to 3 lesions comprised 85% of the caseload. Frontal and temporal locations of the AVMs were most common, and 20 large AVMs involved more than one cortical region of the brain. There were 18 cases of cerebellar AVM, and brainstem and/or central structure involvement was present in 16 cases.

Seventeen percent of patients presented during the first two decades of life, and 20% presented in the seventh and eighth decades. Rupture of the AVM was predominately found in children and adolescents (74%) and in patients older than 60 years of age (83%). Patients in their 30s and 40s had the lowest risk of bleeding (54%) when seizures and progressive deficits were most commonly observed. The male/female ratio was 1.33:1. For hemorrhage and seizure presentation the male/female ratio was 1.47 and 1.5, respectively, whereas for headache and progressive deficits the corresponding ratio was 0.6.

Primary therapy administered, selected according to our protocol, is shown in Table 3, together with data for obliteration rates obtained after primary therapy and final obliti-
population-based analysis of arteriovenous malformations

Eighth-seven percent of patients with Grade 1 to 2 AVMs were treated with surgery; the remaining patients preferred to be treated with GKS. Patients with larger pivotal Grade 3 lesions (Grade 3a) underwent surgery with or without preoperative embolization, whereas most of those with small, critically located Grade 3 lesions (Grade 3b) were treated with GKS. Embolization was the first treatment performed for most patients with Grade 4 AVMs, followed by surgery or focused radiation therapy. In most patients with Grade 5 AVMs treatment was deferred. Using the present protocol, the final obliteration rate for Grade 1 to 3 AVMs, representing 85% of the overall caseload was 96%.

The overall management outcome in the 135 patients was classified as good according to the GOS (Score 5) in 61% of the cases, and the overall mortality rate was 9%. Based on population, 4.7 individuals per 1,000,000 population per year suffer death or permanent disability from cerebral AVMs. For patients with AVMs and hemorrhage, a good overall management outcome was obtained in only 48%. Parenchymal hemorrhage caused death and permanent morbidity in 59% of the cases.

In 35 patients harboring an unruptured Grade 1 to 3 AVM, a good management outcome was achieved in 96%.

Discussion

Only three other comparable population-based studies on cerebral AVMs are reported in the literature.1,3,13,15 Numerous longitudinal studies offer insight into the natural history of the disease, but they do not provide definite data on the overall management perspective, and therapeutic needs because of the inevitable inclusion bias.2,4,10,21 Cerebral AVMs are rare lesions with 12.4 de novo diagnosed cases per 1,000,000 inhabitants per year in Sweden, a figure in close agreement with the findings in previous population-based series. It is clear from our unique epidemiological basis that this prospectively collected material represents every case of clinically manifest as well as incidentally discovered AVM in a population of 986,000 people during an 11-year period. Nonetheless, the calculated incidence most likely underestimates the true number of symptomatic AVMs. Many ICHs, especially those in elderly patients, are not studied angiographically or treated, and AVMs certainly account for some cases of sudden death. Autopsy records from this regional population were not reviewed in this study.

The patient age profile in our study is different from that of the Olmsted County study,3 with more patients being in advanced decades of life. In Sweden, 18% of the population is older than the age 70 years, and treatment is never declined based on age alone. Our data demonstrate that elderly patients with AVMs present almost exclusively with hemorrhage and that AVMs are more commonly a cause of bleeding in this group of patients than is suggested by most researchers.2,4,10,21 Each year, one elderly patient underwent surgery for an ICH, which proved at surgery to be caused by an AVM, suggesting that preoperative angiography in elderly persons with lobar ICHs should be performed more liberally. In pediatric patients, hemorrhage was the dominant form of presenta-

<table>
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* No angiogram.
† Survivors.

TABLE 3

Primary and adjuvant treatments and obliteration rates for AVMs

formation, whereas seizures and progressive deficits were mostly found in the intermediate-age groups. These observations on presenting symptoms are in agreement with observations from longitudinal natural history studies on cerebral AVMs.

Rupture of the AVM was the initial manifestation in 70% of all cases in this consecutive, nonselected series. These figures are higher than in all previously published series and draw attention to the relevance of bleeding from AVMs. Our findings contradict a recent study on morbidity among survivors of AVM rupture25 but are supported by the findings of the population-based Olmsted County study.3 In centers with population-based referral, AVM of the brain is predominantly a disease related to intracranial bleeding, and parenchymal clots have a profound impact on overall management outcome. In every seventh patient in whom an AVM has ruptured, transtentorial herniation from a hematoma became manifest within hours of ictus, and in 68% neurological deficits from hemorrhage were present prior to treatment.

The overall management result was classified as good (GOS Score 5) in 61% of all 135 patients included and in 49% of 94 patients presenting with hemorrhage. The overall mortality rate was 9%. This overall outcome of AVM management should be compared with the results of treatment for ruptured aneurysms. In our recent nationwide study of patients with 435 ruptured aneurysms, good overall management outcome was achieved in 56% of the cases, and the mortality rate was 21% 1 year after treatment.30 Clearly, AVM rupture is as devastating as aneurysm rupture. Aneurysm ruptures are more lethal, whereas AVM rupture tends to result in more disability due to the high occurrence of lobar ICH. Despite the severity of AVM rupture, aneurysms, because of their relative frequency of occurrence, still cause six times as many poor results (26.8 cases/1,000,000 population/year30) as AVMs (4.6 cases/1,000,000 population/year) from a population-based perspective. In rare patients with aneurysms and brainstem compression from large hematomas close to the Sylvian or interhemispheric fissures, salvage surgery involving blind clipping without preoperative angiography can result in a remarkably good outcome.4 In this series of patients with AVMs, salvage surgery for large lobar ICHs in 13 patients with manifest transtentorial herniation resulted in five deaths, seven poor recoveries, and only one good outcome.

In patients with unruptured AVMs, 77% were classified

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635
as Grade 1 to 2, and in this group, management outcome was good (GOS Score 5) in 98%; there were no deaths.

The selection of treatment modalities for different AVM categories in this study is only one of many possible combinations. Primary GKS for surgically accessible, small cortical AVMs is a strong alternative in patients unwilling or unable to undergo surgery, although the obliteration rate at 2 years does not exceed 80%.

Endovascular therapy for small surgically accessible lesions as Grade 1 to 2, and in this group, management outcome was good (GOS Score 5) in 98%; there were no deaths.

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Population-based analysis of arteriovenous malformations

ness than GKS for small AVMs, provided that surgical morbidity and mortality rates are below 12% and 4%, respectively. From a regional perspective, the scarcity of small, critically located Grade 3 or Grade 4 AVMs (1.6 cases/1,000,000 population/year) raises important questions, not only about how these malformations should be treated, but also about who should treat them.

References


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