Long-term outcome after surgical treatment of brain arteriovenous malformations: a 27-year follow-up study

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### Paper included

Manuscript in preparation
Long-term outcome after surgical treatment of brain arteriovenous malformations: a 27-year follow-up study

OBJECTIVE: The purpose of this study was to provide knowledge about long-term outcome for patients with cerebral arteriovenous malformations (AVMs) undergoing surgery.

METHODS: In the period 1970-1992, 208 out of 306 patients diagnosed with AVM underwent surgery. Outcome was assessed postoperatively and at long-term follow up (median 26.6 years) in 2011. Assessment was based on the Glasgow Outcome Scale (GOS), the Modified Rankin Scale (MRS), working ability, and the presence of intracranial hemorrhage (ICH), headache, epilepsy and focal neurological deficits during the follow-up period.

RESULTS: At postoperative control, 25 patients (12.1%) had deteriorated according to the Glasgow Outcome Scale. Adverse outcome correlated significantly with increasing Spetzler-Martin grade and size of the AVM. At long-term follow-up 48 patients (23.3%) were dead and 19 (9.2%) were lost to follow-up. Of the remaining 139 patients, 10 (7.2%) had a disabling neurological deficit (MRS score of ≥ 3). No factors with statistical power to predict adverse outcome were identified. Ten patients experienced an intracranial hemorrhage and 31 developed de novo epilepsy during follow-up. A total of 104 patients reported neurological deficits, and 34% had been forced to leave their jobs.

CONCLUSION: Cerebral AVMs are associated with increased mortality and morbidity. Among long-term survivors after surgical treatment 58.3% were able to return to work. Our findings show that only a small proportion of the respondents (7.2%) had disabling neurological deficits at long-term follow-up. However, many of the patients have focal neurological deficits although not disabling that may have impact on their daily-lives.

INTRODUCTION

Arteriovenous malformations in the brain (AVM) can be defined as abnormal conglomerates of dilated arteries and veins in the brain parenchyma. There is a lack of intervening capillary bed, which results in arteriovenous shunting (1). This shunting takes place in a central nidus, which can be defined as the place where one or more arteries converge and from where one or more veins drain (2). The small arteries that are involved have a defect in the smooth muscle layer. On the venous side, there is fibromuscular thickening and an incompetent elastic lamina (3).

AVMs are regarded as sporadic developmental vascular lesions. The exact embryologic origin is unknown (4). They are thought to arise at the embryonic stage of vessel formation, the fetal stage, or after birth (1). AVMs are more often seen in families with hereditary hemorrhagic telangiectasies or hereditary neurocutaneous angiomatous malformations. An accumulation of AVMs has also been described in families without these hereditary diseases. This suggests that some cases can be attributed to genetic factors. Patients with familial AVMs are diagnosed at a significant earlier age (4).

The prevalence of AVMs is reported to be between 15 and 18 per 100 000 adults, the incidence is 1 per 100 000 per year (5, 6). They are most commonly diagnosed in the third or fourth decade of life (6). AVMs are responsible for between 1 and 2% of all strokes, some studies report 4% in young
patients with the general Finnish population using relative survival ratio (RSR) as a measure, and found an excess mortality of more than 50% compared with the general population (12). The results also suggested that this excess mortality can be reduced by active treatment.

The surgical treatment of AVMs is primarily intended to eliminate the risk of future intracerebral hemorrhage. Control of seizure activity and stabilization of progressing focal neurological deficits can be other treatment goals (13). The different treatment options for AVMs include microsurgery, endovascular embolization and stereotactic radiosurgery, either alone or in combination (1, 8). The use of radiosurgery is limited to AVMs with a nidus of less than 3.5 cm in diameter. There is a latency period of 1 to 3 years with a risk of ICH until the nidus is obliterated. Obliteration may be incomplete, and complications such as radiation edema or necrosis can occur (2, 5). Embolization can be used to obliterate small malformations, or as part of multimodality treatment prior to microsurgery or radiosurgery (1, 2, 5).

In an attempt to estimate the risk associated with surgery, the Spetzler-Martin grading system was introduced in 1986 (14), see table 1. This system takes into account three important factors: size, deep venous drainage and eloquence. Eloquent brain areas are defined as those with an identifiable neurological function, and include the sensorimotor, language, and visual cortex; the hypothalamus and thalamus; the internal capsule; the brain stem; the cerebellar peduncles; and the deep cerebellar nuclei. Total scores range from 1-5, and high scores are associated with an increased risk of surgical morbidity and mortality (14). Several studies have verified the usefulness of this grading system (11, 15, 16). The results of studies assessing outcome after surgery indicate that low-grade AVMs (grades 1-3) can be managed with a low risk of complications (5, 14, 17). In contrast, many patients with high-grade AVMs (grades 4 and 5) are declined treatment because of high surgical risks and high likelihood of neurological deterioration (18). If treated, these lesions will often require a multimodal approach (5).

True long-term follow-up studies in patients with AVMs have been scarce. The relative rarity of the disease makes it difficult to collect large patient populations in single centers, and specialized referral centers are seldom able to

<table>
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<th>TABLE 1. The Spetzler-Martin scale</th>
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<tr>
<td><strong>Graded Feature</strong></td>
</tr>
<tr>
<td>Size of AVM</td>
</tr>
<tr>
<td>Small (≤ 3 cm)</td>
</tr>
<tr>
<td>Medium (3-6 cm)</td>
</tr>
<tr>
<td>Large (&gt; 6 cm)</td>
</tr>
<tr>
<td>Eloquence of adjacent brain</td>
</tr>
<tr>
<td>Non-eloquent</td>
</tr>
<tr>
<td>Eloquent</td>
</tr>
<tr>
<td>Patterns of venous drainage</td>
</tr>
<tr>
<td>Superficial only</td>
</tr>
<tr>
<td>Deep</td>
</tr>
</tbody>
</table>

adults. AVMs are identified in 9% of all subarachnoid hemorrhages, in 1% of patients with first time unprovoked seizures, and in 0.3% of patients presenting with headache without other neurological signs (7).

Hemorrhage is the most common presenting symptom, and is reported to account for 45-72% of all presentations in ten large AVM series. Other modes of presentation include epileptic seizures (18-35%), chronic headache (6-14%) and focal neurological deficits (3-10%) (6). Due to an increased availability of CT and especially MRI, there has been a progressive increase in the number of incidental AVM findings (6-8).

When facing a patient with an AVM, it is important to consider the risk if left untreated versus the risk of surgery (9). Several studies exist on the natural history of AVMs. One problem, emphasized by many authors, is that many of these studies are subject to selection bias, only showing the course of AVMs if left untreated. A commonly cited article, published by Ondra et al in 1990, described the natural history of 168 patients with a mean follow-up time of 24 years. They reported an annual bleeding rate of 4%, an annual rate of major morbidity or death of 2.7%, and an annual mortality rate of 1% (10). Several studies on the natural history have been published after this, with more extensive statistical analysis. They have found an average annual rate of hemorrhage of 2-4% (6, 7), and several factors associated with an increased risk of rupture have been identified: previous rupture, deep and infratentorial location, deep venous drainage, and possibly flow-related aneurysms, venous stenosis and large size (6, 8, 11). Overall annual mortality rate in untreated patients is 0.7-2.9% (6, 7). Laakso et al published an article in 2008, where 623 AVM patients were followed for a mean of 11.9 years. They did a comparison of the AVM
TABLE 2. The Glasgow Outcome Scale (GOS)

<table>
<thead>
<tr>
<th>SCORE</th>
<th>DESCRIPTION</th>
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<tbody>
<tr>
<td>1</td>
<td>DEATH.</td>
</tr>
<tr>
<td>2</td>
<td>PERSISTENT VEGETATIVE STATE. Patient exhibits no obvious cortical function.</td>
</tr>
<tr>
<td>3</td>
<td>SEVERE DISABILITY. Patient depends upon others for daily support due to mental or physical disability or both.</td>
</tr>
<tr>
<td>4</td>
<td>MODERATE DISABILITY. Patient is independent as far as daily life is concerned. The disabilities found include varying degrees of dysphasia, hemiparesis, or ataxia, as well as intellectual and memory deficits and personality changes.</td>
</tr>
<tr>
<td>5</td>
<td>GOOD RECOVERY. Resumption of normal activities even though there may be minor neurological or psychological deficits.</td>
</tr>
</tbody>
</table>

TABLE 3. The Modified Rankin Scale (MRS)

<table>
<thead>
<tr>
<th>SCORE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms at all.</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms, able to carry out all usual duties and activities.</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring some help, but able to walk without assistance.</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent and requiring constant nursing care and attention.</td>
</tr>
<tr>
<td>6</td>
<td>Dead.</td>
</tr>
</tbody>
</table>

provide follow-up on patients for decades. Norway is well suited for population-based epidemiological studies because of its stable population and public health care system. The aim of this study was therefore to provide knowledge about the long-term outcome of patients with AVMs undergoing surgery. The time period was chosen before the treatment of AVMs became multimodal so only a few patients have received other treatment in addition to surgery. The purpose was furthermore to identify morphological, clinical and demographic variables with effect on presentation and prognosis.

PATIENTS AND METHODS

Between 1970 and 1992, 306 patients were diagnosed with an AVM at The National Hospital (Rikshospitalet) in Oslo, Norway. The hospital was responsible for treatment of patients with AVMs from the entire country. Of the 306 patients, 208 were treated with microsurgery. Among these only eight patients were embolized and two patients received stereotactic radiosurgery prior to surgery, as part of multi-modality treatment. Diagnosis of AVM was based on angiographic results. Other intracranial vascular malformations (cavernous malformations, developmental venous anomalies, vein of Galen malformations and dural arteriovenous fistulae) were not included. Data concerning size, location and angioarchitecture were gathered from angiography or CT. AVM location was divided into three main groups: lobar (frontal, temporal, parietal and occipital), central (includes the basal ganglia, thalamus, hypothalamus, corpus callosum and the ventricles) and infratentorial (includes the cerebellum and the brain stem). The AVMs were graded according to four grading systems: ShihChen, Luessenhop, Pelletieri and Spetzler-Martin (introduced in 1986, so patients treated before 1986 were retrospectively graded). Patient data and mode of presentation, including the Glasgow outcome scale (see table 2 for definition(19)), were retrospectively collected in 1986. From this point, data were collected prospectively. Postoperative angiography was performed in 156 patients. Surgical outcome was evaluated postoperatively in hospital or by telephone interview. Long-term follow-up was performed in 2011 through telephone interview and a written questionnaire. Outcome was assessed based on the modified Rankin scale (see table 3), working ability, and the presence of ICH, headache, epilepsy and focal neurological deficits during the follow-up period. At postoperative control, all GOS scores ≤ 3 were defined as adverse outcomes. Good long-term outcomes were defined as a MRS score of 0 to 2, and disabling neurological deficits were defined as a MRS score greater than 2.

Statistics

Statistical analysis was performed using SPSS, version 17.0 (SPSS Inc., Chicago, IL). Cases were analyzed using the chi-squared method. Statistical significance was defined as p<0.05.

Patient characteristics at baseline

Of the 208 patients who were treated with microsurgery, two were eliminated from further analysis because of lack of data regarding their baseline characteristics. Baseline data for the remaining 206 patients are summarized in table 4. There were 113 men and 93 women, which gives a
male/female ratio of 1.22. Median age at initial presentation was 32 years, ranging from 4 to 69 years, see figure 1 for age distribution at time of diagnosis. The majority of the patients (64%) presented with hemorrhage. These cases were confirmed by either CSF analysis or brain imaging. Included in this group are 18 patients (8.7%) who had epilepsy prior to bleeding, without their symptoms leading to diagnosis. A total of 51 patients (25%) presented with epilepsy without ICH, 11 (5%) with headache and 4 (2%) with focal neurologic deficits. In the group other/asymptomatic (4%), one patient was diagnosed based on incidental findings on brain imaging. The majority of the patients (76.7%) underwent elective surgery. The rest (23.3%) were managed in an acute setting, ICH constituted the majority of initial presentations in this group.

**RESULTS**

The median follow-up was 26.6 years (range 0–41 years). We were able to get in contact with 139 patients, whereas 48 were dead and 19 were lost to follow-up (9.2%).

**Mortality**

Of the 206 patients eligible for analysis, 48 patients (23.3%) died during the follow-up period. The death rate in the group treated in an acute setting was 13 out of 50 (26%), compared to 35 out of 156 (22.4%) among the electively treated patients. Median survival after surgery was 18 years, ranging from three
days to 35 years. Three of the patients died within few weeks after surgical treatment. Two of these arrived in hospital in a comatose condition with large ICH, and one patient operated for ICH suffered a re-bleed three weeks after surgery. For the rest of the patients, the cause of death has not been identified. Median age at death was 65 years, ranging from 12 to 90 years (see fig. 2 for age distribution).

**Early neurological outcome**

GOS score was registered pre- and postoperatively (see table 5). Mean preoperative GOS score among the patients who were treated in an acute setting due to ICH was 2.98 (SD 1.12), compared to a mean score of 4.83 (SD 0.55) among the patients treated electively. A total of 25 patients (12.1%) had a reduction in GOS score relative to their preoperative status, see table 6. The majority of the patients (92%) who deteriorated were treated electively (p=0.13). Two of the patients had a postoperative GOS score of 1 and died after a few days. These are the two patients previously mentioned who came to hospital in a comatose condition after ICH.

We have identified two factors significantly associated with a relative reduction in postoperative GOS-score. These factors are increasing Spetzler-Martin grade (p<0.05) and increasing size of the malformation (p=0.05). Spetzler-Martin grade 1 and 2 lesions were resected with a low incidence of postoperative deterioration (3.2% and 4.7% respectively). Grade 3, 4 and 5 AVMs were associated with higher numbers of adverse outcomes (grade 3: 19%; grade 4: 16%; grade 5: 25%).

**Late neurological outcome**

At follow-up in 2011, MRS scores were registered. Disabling neurological deficits were defined as a MRS score greater than 2. According to this definition, 10 (7.2%) of the 139 respondents had disabling deficits. Of these ten patients, three had a postoperative GOS score of 4, and seven had a postoperative GOS score of 5, indicating good early treatment results. This further indicates that all of the patients with disabling deficits at follow-up in 2011 had worsened relative to their postoperative status. Deterioration was caused by ICH during follow-up in four patients, and two patients had worsened due to other causes unrelated to their AVMs. In contrast, all of the patients with a postoperative GOS score defined as disabling (GOS score ≤ 3, 2 of the respondents) had improved at follow-up (MRS score ≤ 2).

Distribution of MRS scores at follow-up in relation to Spetzler-Martin grade is shown in table 7. Among patients with grade 1 lesions, only one had disabling deficits, caused by severe memory problems. Among patients

| TABLE 7, MRS-scores in relation to Spetzler-Martin grade (SpM), n=139 |
|------------------|------------------|------------------|------------------|------------------|------------------|
|                  | NON-DISABLING DEFICITS (n=129) | DISABLING DEFICITS (n=10) | TOTAL (%)       |
| SpM 1            | MRS 0 | MRS 1 | MRS 2 | MRS 3 | MRS 4 | MRS 5 |                  |
|                  | 10    | 6     | 3     | 0     | 0     | 0     | 20 (14.5) |
| SpM 2            | 15    | 18    | 5     | 5     | 0     | 0     | 43 (31)  |
| SpM 3            | 7     | 23    | 9     | 1     | 1     | 1     | 42 (30)  |
| SpM 4            | 8     | 14    | 3     | 0     | 0     | 0     | 25 (18)  |
| SpM 5            | 4     | 2     | 0     | 1     | 0     | 0     | 7 (5)    |
| Unknown          | 0     | 1     | 1     | 0     | 0     | 0     | 2 (1.5)  |
| TOTAL (%)        | 44 (32)| 64 (46)| 21 (15)| 8 (6)| 1 (0.5)| 1 (0.5)| 139 (100) |
with grade 2 AVMs, five patients reported a MRS score greater than 2. The neurological disabilities in these patients were caused by hemiparesis or cognitive/memory impairments. Two of the five patients had suffered an ICH during the follow-up period, and had deteriorated afterwards. Three patients with grade 3 AVMs had disabling deficits. One had suffered major injuries after a car accident unrelated to the AVM, and two had their disabilities considerably worsened after re-bleed. None of the patients with grade 4 lesions had disabling disabilities. One patient with a grade 5 AVM had disabling deficits due to hemiparesis.

Demographic, morphologic and clinical factors were tested statistically to determine whether there was an association with long-term outcome. None of the factors were found statistically significant. There was a higher proportion of disabling deficits at follow-up among patients who had a relative reduction in their GOS score after surgery (p=0.28). Among those who had experienced an ICH at presentation, 8.3% had disabling deficits versus 5.5% of those who had presented with other symptoms.

Focal neurological deficits
A large proportion of the patients have had focal neurological deficits during the follow-up period. Although many report that their impairments have progressively improved since surgery, 104 patients had remaining deficits at long-term follow-up. The most common deficits include varying degrees of paresis (26%), sensory deficits (9%), visual field defects (34%), memory impairment (35%), dysphasia (22%) and reading and writing difficulties (6%).

Working ability
The patients were also asked about their working situation after surgery. More than half of the respondents (52.5%) reported that they had been working full-time jobs, and 5.8% had worked in reduced positions. The rest had been forced to leave their jobs at some point, either because of deficits related to their AVMs (33.8%) or due to other causes (7.9%). Mean MRS score among the patients who had been working full-time jobs was 0.58, compared to 1.55 among those who had been forced to quit their jobs (p<0.001).

Intracranial hemorrhage
A total of 132 patients (64%) had experienced intracranial hemorrhage prior to surgery. Patients with small-sized AVMs (<3 cm) were significantly more likely to have bled compared to patients with medium- and large-sized AVMs (p<0.001). We also found that patients with infratentorial AVMs had a significantly greater risk of hemorrhagic presentation (p<0.05) compared to other locations – 24 (89%) of the 27 patients with AVMs localized infratentorially had suffered from preoperative hemorrhage while 62% of the patients with centrally or cortically located AVMs had undergone hemorrhage.

Postoperative cerebral angiography was performed in 156 of the 206 surgically treated patients. In 149 patients the AVM was totally removed, whereas 7 patients had a remnant AVM.

Of the 139 patients we have been able to establish contact with, 10 patients (7.2%) reported that they had experienced ICH after surgery, and two of these had bled twice. Five of the patients had bled at the time of diagnosis, and three were treated in an acute setting. Two were treated with embolization prior to microsurgery. Postoperative angiography was performed in nine of the ten patients suffering from hemorrhage during follow-up, showing a remnant AVM in only one. Median time from surgery to ICH was 16 years (range 1.1 to 27.6 years). At follow-up, four of the ten patients (40%) had a MRS score greater than 2, compared to only 4.7% among patients without ICH after surgery (p<0.001). All had focal neurological deficits, and six had been forced to leave their jobs. No factors with statistical power to predict postoperative hemorrhage have been identified.

Epilepsy
Preoperative seizures
Overall, 70 patients had experienced seizures prior to surgery. According to the definition of size by the Spetzler-Martin grading system, 18% of patients with small (<3 cm), 51% with medium (3-6 cm), and 42% with large (>6 cm) AVMs had preoperative seizures. Patients with small-sized AVMs were significantly less likely (p<0.001) to have experienced preoperative seizures compared to the two other groups. As one could expect, the patients with cortically located AVMs (79%) had an increased risk (p<0.001) of seizures prior to surgery compared with other locations (central
and infratentorial). Of the 135 patients who had experienced an intracranial hemorrhage at time of diagnosis, 17 (13%) had also experienced seizures, compared to 53 (75%) of the 71 patients with no preoperative hemorrhage (p<0.001).

Postoperative seizures

At follow-up, 57 (41%) of the 139 patients we have maintained contact with reported to have had seizures after surgery. Of the 70 patients (34%) who had experienced one or more seizures at the time of diagnosis, we have been able to reach 51, 19 are either dead or lost to follow-up. Of these, 26 patients (37%) have had seizures after surgery, whereas 25 (36%) have been seizure-free (Fig. 3). Twenty patients (28.6%) use anticonvulsant medications and only two (2.9%) have had seizures the last year.

Of the 136 patients (66%) with no prior seizure history, 31 (22.8%) have had new-onset seizures during the follow-up period. The rest (41%) have remained seizure-free (Fig. 4). Twenty-one patients (15.4%) require anticonvulsant medications and five (3.7%) have had seizures the last year.

When analyzing risk factors for postoperative seizures regardless of the patients' preoperative seizure status, only cortical location was found statistically significant (p<0.05). Size of the AVM did not reach significance, although there were a larger proportion of seizure-free patients with small- and medium-sized AVMs (58% and 61% respectively) compared to the group with large AVMs (50%).

Among the patients without preoperative seizures, ICH at time of diagnosis was found statistically significant for development of postoperative new-onset epilepsy (p<0.05). As AVMs with a diameter of less than 3 cm are more likely to present with hemorrhage, small size has also been found significant for the development of new seizures after surgery (p<0.05).

Headache

A total of 29 patients (14.1%) suffered from headache prior to surgery, and 30 at the time of follow-up. Of these, 19 were new-onset. We used the VAS-scale (grade 1 to 10) to assess the severity. Mean score was 5.5 (range 2-10).

DISCUSSION

The median age and the age range at time of diagnosis in our material are comparable to other studies (20-23). So is the proportion of male and female patients, of central and infratentorial location (22), and the distribution regarding the Spetzler-Martin scale, including its components (eloquence, deep venous drainage and size). With regard to the mode of presentation, the proportion of hemorrhage, seizures, focal neurological deficits and headaches are the same as found elsewhere in the literature (1, 10, 22, 24). The percentage of incidental findings (0.5%) is similar to some older studies (25) but lower than the numbers published recently (1, 24). The lower number of incidental findings can be explained by the fact the majority of the patients in our study were diagnosed before MRI was introduced.
Our median follow-up time of 26.6 years is the longest compared with similar studies. Outcome after surgery has been assessed at two occasions, first within weeks after treatment, and then at long-term follow-up in 2011. 48 patients (23.3%) have died. No factors were identified to have predictive value with regard to death. Causes of death have not been identified, except for the three patients mentioned earlier who died within weeks after surgery. Mean age at death was 64 years, compared to 82.3 years for women and 78.9 years for men in the Norwegian population (26). About a quarter (23 %) of the patients died at the age of 80 years or above, and we may assume that a large proportion of these died from natural causes, unrelated to their AVMs. A later analysis of the patients who died during follow-up is planned.

The overall early treatment results were classified as good (GOS scores 4 and 5) in 190 patients (92.2%) at the postoperative evaluation. In our statistical analysis, we found that early deterioration relative to the preoperative status (12.1% of the patients, measured by Glasgow outcome scale) was significantly associated with increasing Spetzler-Martin grade and size of the AVM. Other studies support these findings (16, 21, 27). As one could expect, we also found that the majority of patients who had a relative reduction in GOS score were treated electively. In the patient population that the Spetzler-Martin scale is based upon, grade 1 and 2 AVMs were resected with a very low incidence of surgically induced neurological deficits. Surgery for grade 4 and 5 AVMs was accompanied by a greater number of adverse outcomes (9). Although our findings show slightly higher numbers of postoperative deterioration for lower grade lesions (grade 1: 3.2%, grade 2: 4.7%) we have found a significant increase of early adverse outcomes for grade 3 to 5 (grade 3: 19%, grade 4: 16%, grade 5: 25%). Thus, we can support the recommendations citing that grade 1 and 2 AVMs can be treated with microsurgery with a low rate of short-term complications (9, 11, 16).

At long-term follow-up, 10 patients (7.2% of the respondents) had a MRS score greater than 2, defined as disabling neurological deficits. Of these, four had deficits caused by ICH during follow-up, and two had worsened due to other causes unrelated to their AVM. The total proportion of disabling deficits corroborates with those found in other studies (15, 21, 27). However, 104 patients reported to have focal neurological deficits at follow-up in 2011, indicating that a large proportion suffer from non-disabling deficits after surgery or initial hemorrhage. In addition, 34 % of the surviving patients (with a mean MRS score of 1.6) had been forced to leave their jobs at some point during the follow-up period due to deficits related to their AVMs. This indicates that although not defined as disabling, many patients have deficits with impact on their daily-lives.

The Spetzler-Martin scale is generally believed to predict the risk of persistent neurological deterioration after surgery (1, 15, 28). Several factors in addition to the before mentioned grading system have been found significant in other studies. We have not been able to statistically show the connection of any of these factors with long-term adverse outcome. There was a slight increase in long-term disabling deficits among patients who had presented with hemorrhage (8.3% vs. 5.5%), although not statistically significant. What is noticeable is the low number of adverse outcomes in patients with higher-grade lesions (grade 3: 7 %, grade 4: 0 %, grade 5: 14 %), and the seemingly equal distribution of such outcomes across the Spetzler-Martin scale. The grading system’s low predictive value for persistent disabling deficits in our study may be explained by the extremely long follow-up of 26 years. Our findings might suggest that during such a long follow-up time, the patients’ deficits may progressively improve from disabling to non-disabling. Others have found a similar trend towards progressive postoperative improvement in neurological status (20). However, we have been able to maintain contact with only two of the 16 patients with a postoperative GOS score defined as disabling (GOS score ≤ 3). Although these two patients have improved during follow-up, too many patients have died or have been lost to follow-up to draw any clear conclusions. Comorbidity may also occur among the patients, and confound the reported rate of disabling deficits, thereby influencing the statistical analyses. We have tried to adjust for this confounding factor in our questionnaire, but there will always be difficulties assessing the patients’ neurological status based on the chosen methods of this study, with the inevitable risk of detection bias.

We have found that patients with small-sized and infratentorially located AVMs have a
greater risk of hemorrhagic presentation. These factors have also been proven significant in other series (1, 7). Crawford et al. have suggested that small AVMs are more likely to present with ICH because they rarely present with epilepsy or focal neurological deficits (29). Ten of the surviving patients in our study have had seizures the last year, indicating a low likelihood of ongoing postoperative seizures. Among these, 31 patients had developed de novo epilepsy, but only seven had seizures last year. Ten patients (7.2%) had disabling neurological deficits at follow-up. Four of these had deteriorated following an ICH during the follow-up period and two had worsened due to other causes unrelated to the AVM. No factors associated with increased rupture risk have been identified.

In an attempt to determine factors associated with preoperative seizures, increasing size and cortical location of the AVM were found statistically significant. These findings are in corroboration with the results from other series (7, 20). We also found that patients with a preoperative seizure history were significantly less likely to have experienced an ICH at time of diagnosis. However, as shown by others (29, 30), we found that ICH prior to surgery was a risk factor for the development of de novo epilepsy. When reviewing the literature, there are mixed opinions with regard to the effect of AVM surgery on seizure outcome. Some have argued that a medically intractable seizure disorder in itself is an indication for interventional treatment of an AVM (31). Others have a more pessimistic view (25, 32). Forster, et al. found that only 14% of the patients with preoperative seizures had an improvement in their seizure status after surgery, and that 22% of the patients without a preoperative seizure history developed de novo epilepsy (25). Our results are similar for the latter group (23%), but show a relatively better prognosis for the patients who had suffered from preoperative seizures. More than one third of these patients have been seizure-free after surgery, while about the same number have experienced seizures. Only seven patients have had seizures the last year, indicating a low likelihood of ongoing postoperative seizures.

CONCLUSIONS

The present study represents to our knowledge the longest reported follow-up (median 26.6 years) of functional outcome in patients treated for AVMs. Early neurological deterioration was associated with increasing Spetzler-Martin grade (p<0.05) and size of the AVM (p<0.05). At follow-up, 57 (41%) of the 139 patients we obtained follow-up data from reported seizures after surgery. Among these, 31 patients had developed de novo epilepsy, but only seven had seizures last year. Ten patients (7.2%) had disabling neurological deficits at follow-up. Four of these had deteriorated following an ICH during the follow-up period and two had worsened due to other causes unrelated to the AVM. No factors with statistical power to predict an adverse outcome were identified. However, 104 patients reported focal neurological deficits at follow-up, and 34% of the surviving patients had been forced to leave their jobs because of deficits related to their AVMs. This indicates that although not defined as disabling, the deficits may have impact on the patients’ daily-lives.

REFERENCES

ATTACHMENTS:

Questionnaire in Norwegian

Du ble i _______ behandlet for et blodårenøste (arteriovenøs malformasjon) i hjernen på Rikshospitalet. Vi vil gjerne vite hvordan det har gått med deg etter dette.

1. Har du i årene etter inngrepet hatt noen av følgende plager ? (kryss av)

   - Hjerneblødning □
   - Epileptisk anfall □
   - Hodepine □
   - Nedsatt følelse, lammelse, språkproblem, sviktende hukommelse, syn, hørsel eller liknende □
   - Ingen slike plager □

Skriv eventuelt mer utfyllende dersom ingen av svaralternativene over passer:
2. Dersom du har hatt hjerneblødning i årene etter operasjonen:
   a. Hvor mange ganger har du hatt det?
      ________________________________
   b. Angi etter beste evne årstall for hjerneblødningen(e)
      ________________________________

3. Dersom du har hatt epileptisk anfall etter operasjonen:
   a. Har du hatt anfall det siste året?
      Ja [ ] Nei [ ]
   b. Hvis ja, omtrent hvor mange har du hatt (det siste året)?
      ________________________________
   d. Bruker du i dag medikamenter mot epilepsi?
      Ja [ ] Nei [ ]
   e. Hva slags type epileptiske anfall har du hatt?
      Lette uten bevissthetstap [ ]
      Med bevissthetstap, men uten kramper [ ]
      Med bevissthetstap og kramper [ ]
      Vet ikke [ ]

4. Dersom du er plaget av hodepine:
   a. Hvor lenge har du vært plaget av hodepine?
      Helt siden jeg fikk diagnosen [ ]
      Startet senere [ ]
      | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
      |---|---|---|---|---|---|---|---|---|---|
      Ingen plager | Svært plaget |
5. Dersom du er / har vært plaget av nedsatt følelse, lammelse, språkproblem, sviktende hukommelse, syn, hørsel eller liknende etter operasjonen:

a. Beskriv hvordan disse plagene arter seg:


b. Har du disse plagene i dag?

Ja ☐ Nei ☐

d. Når oppsto disse plagene?

- Plagene har vært til stede siden jeg fikk diagnosen ☐
- Plagene oppsto etter at jeg fikk diagnosen, i forbindelse med hjerneblødning ☐
- Plagene oppsto etter at jeg fikk diagnosen, og skyldes helt andre forhold ☐

Dersom ingen av svaralternativene over passer, vennligst beskriv:
6. a. Synes du at du i dag har normalt funksjonsnivå?

Ja, jeg greier alle dagliglivets aktiviteter (påkledning, vasking, handling, matlagning osv.) □

Nei, jeg greier ikke alle dagliglivets aktiviteter □

b. Dersom du ikke har normalt funksjonsnivå, hva skyldes dette?

Karnøstet du ble operert for / operasjonen □

Andre ting □

c. Dersom du det siste året har hatt nedsatt funksjonsnivå av andre årsaker enn karnøstet / operasjonen, vennligst beskriv årsaken til dette:

7. Har du det siste året vært påvirket av karnøstet som ble fjernet, operasjonen eller den blødning du eventuelt hadde før du ble innlagt hos oss (hjerneblødning)? Kryss av på ett av alternativene nedenfor:

Jeg har ikke hatt spesielle plager som følge av karnøstet/operasjonen det siste året □

Jeg har hatt noe plager som følge av karnøstet/operasjonen det siste året, men jeg har greid vanlige aktiviteter (påkledning, vasking, handling, matlagning osv.) □

Som følge av karnøstet/operasjonen er det en del vanlige aktiviteter jeg ikke har greid det siste året, men jeg har klart meg uten hjelp fra andre. □

Som følge av karnøstet/operasjonen har jeg vært avhengig av noe hjelp i dagliglivet det siste året, men jeg kan gå uten hjelpemidler □

Som følge av karnøstet/operasjonen må jeg ha hjelp på toalettet og er ikke i stand til å gå uten hjelpemidler □

Som følge av karnøstet/operasjonen er jeg sengeliggende og trenger pleie. □
8. Har du vært i arbeid etter operasjonen?

   Ja, jeg har stort sett arbeidet full tid  
   (gjelder også om du senere ble pensjonert)  ☐

   Ja, men jeg er/ble delvis uføretrygd etter  
   operasjonen (angi %:______)  ☐

   Ja, men jeg er/ble delvis uføretrygd av  
   andre årsaker (angi %:______)  ☐

   Nei, jeg ble uføretrygd etter operasjonen  ☐

   Nei, jeg ble uføretrygd av andre årsaker  ☐

Eventuelt beskriv dersom ingen av alternativene passer: