Morbidity of Intracranial Hemorrhage in Patients With Cerebral Arteriovenous Malformation

Andreas Hartmann, MD; Henning Mast, MD; J.P. Mohr, MD; Hans-Christian Koennecke, MD; Andrei Osipov, MD; John Pile-Spellman, MD; D. Hoang Duong, MD; William L. Young, MD

Background and Purpose—Decisions on invasive arteriovenous malformation (AVM) treatment are currently based on natural-course risk estimates of AVM bleeding and assumptions on morbidity from cerebral hemorrhage in general. However, morbidity of AVM hemorrhage has rarely been reported. We sought to assess the morbidity of intracranial hemorrhage in patients with cerebral AVMs.

Methods—From a prospective AVM database, 119 patients were analyzed: 115 had a hemorrhage as the diagnostic event, and 27 of them suffered a second hemorrhage during follow-up; an additional 4 patients had other diagnostic symptoms but bled during follow-up. The type (parenchymal, subarachnoid, intraventricular) and location of AVM hemorrhage were determined by CT/MR brain imaging. Disability and neurological impairment were assessed with the Barthel Index, the Rankin Scale, and the National Institutes of Health Stroke Scale, with a mean follow-up time of 16.2 months.

Results—Of the 115 incident hemorrhages, 34 (30%) were subarachnoid, 27 (23%) parenchymal, 18 (16%) intraventricular, and 36 (31%) in combined locations. In 54 patients (47%; 95% confidence interval [CI], 38% to 56%) the incident hemorrhage resulted in no neurological deficit, and an additional 43 patients (37%; 95% CI, 28% to 46%) were independent in their daily activities (Rankin 1). Fifteen patients (13%; 95% CI, 7% to 19%) were moderately disabled (Rankin 2 or 3), and 3 (3%; 95% CI, 0% to 6%) were severely disabled (Rankin ≥4). Parenchymal hemorrhages were most likely to result in a neurological deficit (52%). Type and morbidity of hemorrhage during follow-up were similar to incident events. Twenty (74%) of 27 patients with both incident and follow-up hemorrhages were normal or independent (Rankin 0 or 1). None of the patients with a hemorrhage during follow-up died during the observation period.

Conclusions—Hemorrhage from cerebral AVMs appears to have a lower morbidity than currently assumed. This finding encourages a reevaluation of the risks and benefits of invasive AVM treatment. (Stroke. 1998;29:931-934.)

Key Words: cerebral arteriovenous malformations • hemorrhage • morbidity

The primary reason to treat cerebral AVMs is the prophylaxis against new or recurrent intracranial hemorrhage. Currently, decisions on surgical, endovascular, or radiation treatment are based on natural-course risk estimates of AVM bleeding. Assumptions on hemorrhage-related morbidity are largely derived from a small number of previously published studies,1-4 which contain mostly retrospective analyses of hospital charts, as well as from information on intracranial hemorrhage from other causes, such as non–AVM-associated ruptured intracranial aneurysms or arterial hypertensive bleeds.5 However, the specific morbidity of intracranial hemorrhages in patients with AVMs has rarely been reported. Given the potential risk of invasive AVM treatment,7 such data are needed for the development of rational treatment strategies.

Using data from the prospective Columbia-Presbyterian AVM Study Project, we assessed the impact of intracranial hemorrhage in patients with AVM on neurological impairment and disability.

Subjects and Methods

The Columbia-Presbyterian Medical Center AVM Study Project prospectively collects information from consecutive patients with cerebral AVMs since 1987. As a tertiary referral center, patients are recruited from the greater New York area as well as from distant sites.

A total of 300 patients were enrolled in the database between January 1987 and August 1996, of whom 151 (50%) had presented with an intracranial AVM hemorrhage. Of these, we analyzed the 119 consecutive patients who had the hemorrhage confirmed by brain imaging: 115 had experienced a cerebral hemorrhage as the diagnostic event, and 27 of them suffered a second hemorrhage during subsequent follow-up. The initial presentations of an additional 4 patients who bled during follow-up were seizures (n=2) and nonspecific headaches (n=2) with no signs of hemorrhage on brain imaging at the time of presentation. Patients were excluded from the analysis if their follow-up time was shorter than 1 month or if the hemorrhage was not confirmed by brain imaging (n=32).

The mean age at the time of hemorrhage was 37.5 years (SD, 14.7; range, 6 to 70); 56 patients (49%) were female. Race-ethnicity was white in 93 (81%) patients, black in 7 (6%), Hispanic in 9 (8%), and Asian in 4 (4%). Hemorrhage location (supratentorial/infratentorial)

Received February 2, 1998; accepted February 11, 1998.

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and type (parenchymal, subarachnoid, intraventricular, or combined) were defined by CT or MRI.

Neurological deficit, impairment, and disability were assessed with the NIHSS,9 Rankin Scale,10 and Barthel Index11 before any treatment or further hemorrhage resulting in a change of neurological status. Patients with a Rankin score of 0 or 1 were considered independent in their daily activities, mild to moderately disabled with a score of 2 or 3, and severely disabled with a score of 4 or 5. Patients with a Rankin score of 2 could still have a Barthel score of 100 if their minor disability did not interfere with their capacity to look after themselves.

The mean observation time following incident hemorrhage was 16.2 months (SD, 31.7; range, 1 to 214 months) and was 11.6 months (SD, 20.7; range, 1 to 108 months) for the 31 patients who had suffered a bleed during follow-up. In the 27 patients with hemorrhages both as initial and follow-up event, the mean time interval between first and second hemorrhage was 44.7 months (SD, 47.1; range, 1 to 276 months).

Outcome was compared between patients with incident and with follow-up hemorrhages by calculating mean Rankin scores with standard deviations and the difference between the two means with the 95% CI.

From the Northern Manhattan Stroke Study (NOMASS), a prospective, community-based stroke databank,2 the 59 consecutive patients (mean age, 65 years) with mainly hypertensive or supposed amyloid angiopathy, non-AVM intracranial hemorrhages, and no neurological impairment before hemorrhage were used as a comparison group. Their mean Barthel scores at 1 year after hemorrhage were compared with those of the group with incident AVM bleeds.

Results

AVM hemorrhage types for incident (n=115) and follow-up hemorrhages (n=31) are given in Table 1. The location of the incident bleeds was supratentorial in 99 patients (86%). Of the 16 cases (14%) with infratentorial lesions, 4 (4%) were located in the brain stem and 12 (10%) in the cerebellum. The types of initial and follow-up hemorrhages were identical in 23 of 27 patients (85%). Follow-up hemorrhages were similarly distributed: 29 (94%) supratentorial and 2 (7%) infratentorial.

In 54 patients (47%; 95% CI, 38% to 56%) the incident hemorrhage resulted in no neurological deficit, and an additional 43 patients (37%; 95% CI, 28% to 46%) were independent in their daily activities (Rankin 1). Fifteen patients (13%; 95% CI, 7% to 19%) were moderately disabled (Rankin 2 or 3), and 3 (3%; 95% CI, 0% to 6%) were severely disabled (Rankin ≥4), adding to a total of 18 patients (16%; 95% CI, 9% to 23%) with an at least moderately disabling deficit. Of the 27 patients with both incident and recurrent hemorrhages, 20 (74%; 95% CI, 57% to 91%) were neurologically normal or independent, 6 (22%; 95% CI, 6% to 38%) were moderately disabled, and 1 patient (4%; 95% CI, 0% to 11%) was severely disabled. Rankin Scale, Barthel Index, and NIHSS scores for patients with incident and with both incident and recurrent hemorrhages are shown in Tables 2, 3, and 4. The mean Rankin score for the cases with incident hemorrhage was 0.76 (±0.91); for the cases with incident and follow-up hemorrhage the mean was 0.89 (±1.09). The difference between the means of the two groups was not significant (0.13; 95% CI, −0.31 to 0.57). No patient had died during the observation period.

Parenchymal hemorrhages showed the highest rate of associated focal deficits (51.9%), followed by subarachnoid (41.2%) and exclusively intraventricular bleeds (27.8%).

### TABLE 1. Distribution of AVM Hemorrhage Types

<table>
<thead>
<tr>
<th>Type</th>
<th>Incident Hemorrhages (n=115)</th>
<th>Follow-up Hemorrhages (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subarachnoid</td>
<td>34 (30%)</td>
<td>10 (32%)</td>
</tr>
<tr>
<td>Parenchymal</td>
<td>27 (23%)</td>
<td>7 (23%)</td>
</tr>
<tr>
<td>Intraventricular</td>
<td>18 (16%)</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Combined</td>
<td>36 (31%)*</td>
<td>8 (26%)†</td>
</tr>
</tbody>
</table>

*Including 35 cases with parenchymatous hemorrhage.
†All with parenchymatous component.

### TABLE 2. Rankin Scale Scores of Patients With Incident (n=115) and Both Incident and Recurrent (n=27) Hemorrhages

<table>
<thead>
<tr>
<th>Rankin Scale Score</th>
<th>Incident Hemorrhage</th>
<th>Incident and Recurrent Hemorrhages</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>54 (47%)</td>
<td>13 (48%)</td>
</tr>
<tr>
<td>1</td>
<td>43 (37%)</td>
<td>7 (26%)</td>
</tr>
<tr>
<td>2</td>
<td>13 (11%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>3</td>
<td>2 (2%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>4</td>
<td>3 (3%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>5</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>6</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

### TABLE 3. Barthel Index Scores of Patients With Incident (n=115) and Both Incident and Recurrent (n=27) Hemorrhages

<table>
<thead>
<tr>
<th>Barthel Index Score</th>
<th>Incident Hemorrhage</th>
<th>Incident and Recurrent Hemorrhages</th>
</tr>
</thead>
<tbody>
<tr>
<td>100*</td>
<td>107 (93%)</td>
<td>25 (93%)</td>
</tr>
<tr>
<td>95</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>90</td>
<td>3 (3%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>85</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>80</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>75</td>
<td>1 (1%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>70</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>65</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>60</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>55</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>50</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>45</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>40</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>35</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>30</td>
<td>0 (0%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Patients with a Rankin score of 2 could still have a Barthel score of 100 if their minor disability did not interfere with their capacity to look after themselves.
Approximately half of all cerebral AVMs present with a hemorrhage. Current practice assumes an associated morbidity comparable to the one reported for ruptured arterial aneurysms and other causes. Schütz et al. analyzed in a hospital-based study the 2-month outcome of 100 surgically or conservatively treated patients with aneurysmal and presumed aneurysmal bleeding. Among the 77 survivors, 43% made a good recovery (GOS 5), 30% suffered a moderate to severe disability (GOS 3 and 4), and 4% were left in a persistent vegetative state (GOS 2). Drake reported a morbidity of 25% among survivors of aneurysmal bleeding. Proportions of “good outcome” after aneurysmal hemorrhage were reported between 13% and 56% and were shown to be dependent on age and the initial Hunt and Hess grade.

A similar clinical impact is observed after intracranial hemorrhages from other causes. Franke et al. studied 157 patients with supratentorial hemorrhages and found a 1-year death or dependency rate of 57%. In the patients from the NOMASS, who served as a comparison group in our study, 58% were at least moderately disabled.

The morbidity from AVM-associated hemorrhages has rarely been addressed. Graf et al. described the outcome of 191 patients between 1946 and 1980 and found a deficit in 81% of patients immediately after the hemorrhage but provided no follow-up data. Perret and Nishioka found that 58% of patients with an AVM-related hemorrhage had neurological deficits. Ondra et al. reported a long-term combined follow-up mortality and major morbidity of 34% in patients who had not been treated surgically but noted that a selection bias may have led to the disproportional high morbidity in his study. Crawford et al. in a retrospective chart review, found that 62% of patients with AVM hemorrhages had no handicap at the time of discharge from the hospital, 25% had a minor handicap, and only 6% suffered a major deficit. Svien and McRae found a “good survival quality” in 85% of patients with incident hemorrhages and 86% of patients with subsequent hemorrhages, and Brown et al. described functional independence in at least 86%.

Most of these investigations, although they provided valuable insights into the natural-course risk of AVMs, are based on retrospective analyses of hospital charts; some were conducted before the widespread availability of modern brain imaging or do not specify the degree of impairment or the time interval between hemorrhage and follow-up assessment. Our study of patients with CT- and MRI-defined hemorrhages demonstrates a lower morbidity of AVM-associated hemorrhage than currently assumed; the majority of our patients (84%) did not have a neurological deficit or were independent (Rankin 0 or 1) after their first hemorrhage. The functional outcome of patients with both incident and subsequent hemorrhages was similar to the outcome of patients with only one bleed, denying evidence for an important cumulative effect of recurrent hemorrhages.

Several factors may play a role in the difference in outcome: (1) Spontaneous hypertensive parenchymal hemorrhages and subarachnoid hemorrhages from ruptured aneurysms may be more extensive because they are driven by full systemic arterial pressures. Similar hemodynamic conditions may prevail in small AVMs, but especially in large AVMs the low-resistance arteriovenous shunts result in reduction of pressure in the feeding arteries and can thus limit
the size of the hemorrhage. In addition, complications such as vasospasm frequently observed after aneurysmal ruptures are rarely associated with a ruptured AVM.24 (2) The mechanism involved in AVM hemorrhage may not be the same in all cases. Arteries with varying transmural pressures or associated aneurysms may be the site of hemorrhage, but venous hemorrhages, particularly from deep draining veins with a high probability of causing predominantly intraventricular hemorrhages, may also account for the rather low clinical impact. (3) Since parenchymal AVM hemorrhages can be limited to the AVM nidus, the amount of intact neuronal structures damaged could be smaller than in intracranial hemorrhages from other causes, which usually affect otherwise healthy brain tissue. (4) Age may also account for the good recovery. In particular, patients with hypertensive bleeds tend to be older (the mean age in the NOMASS cohort was 65 years), and age has been shown to be an independent predictor of good clinical outcome in patients with intracranial hemorrhage.6

Some limitations of our study should be considered. As in most hospital-based investigations, a referral bias may have had an ameliorating effect on the findings. In addition, the assessment of mortality was not possible from our data because only hemorrhage survivors were assessed for further treatment options. Even though no patient followed in our data set died from the subsequent hemorrhage, which may hint at a lower mortality rate than the estimated rate of 10%,7 the rather small sample size does not allow definite conclusions. To determine the AVM-associated mortality accurately, a population-based study or a large multicenter study is needed.

Aneurysms were found in 26% of our patients (associated with AVMs in 21%, not associated with AVMs in 5%). Aneurysms in patients with AVMs are reported with a frequency of up to 60%, and their association with a clinical presentation of hemorrhage has been suggested.25 However, determination of the source of hemorrhage is often difficult, and the question of how often AVM-associated aneurysm rupture is the cause of hemorrhage remains unsettled. If we assume that subarachnoid bleeding is a leading feature of aneurysm rupture, uncertainty as to the origin of subarachnoid hemorrhage remained in a small number of our patients with aneurysms.

Given the estimated overall morbidity and mortality of 8% from surgical, endovascular, and/or radiosurgical therapy of AVMs2 and our evidence of a limited number of disabling deficits from incident or recurrent intracranial hemorrhages in patients with AVMs, a reevaluation of the risk and benefit of invasive AVM treatment seems warranted.

Acknowledgments

The Columbia-Presbyterian AVM Study Project is supported by the National Institute of Neurological Disorders and Stroke (NS 27517 and NS 29993). The NOMASS is supported by the National Institute of Neurological Disorders and Stroke (NS 27713 and NS 34949). The authors thank Ralph L. Sacco, MD, and Bernadette Boden-Albala, MPH, for supplying data from the NOMASS.

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Stroke. 1998;29:931-934
doi: 10.1161/01.STR.29.5.931

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