Pediatric patients with poor neurological status and arteriovenous malformation hemorrhage: an outcome analysis

Clinical article


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Object. In general, patients who present with low Glasgow Coma Scale (GCS) scores and/or fixed and dilated pupils are not expected to do well following arteriovenous malformation (AVM) hemorrhage. However, there is a sense among neurosurgeons that pediatric patients may make a better recovery than adults following such an event. There have been few studies focusing on the outcome of pediatric patients with poor neurological status following AVM hemorrhage. The purpose of this study was to characterize functional outcome in pediatric patients with severe disability after AVM hemorrhage.

Methods. This was a retrospective analysis of clinical presentation and outcome in 15 patients seen at the authors’ pediatric hospital presenting with low GCS scores (defined as GCS ≤ 8) following AVM hemorrhage.

Results. Initial GCS scores ranged from 3 to 6, and 11 of 14 patients had fixed pupils on clinical examination (data were not available in 1 patient). Eight of 15 patients suffered primarily a lobar hemorrhage, 3 suffered primarily infratentorial bleeding, 2 suffered primarily hemorraghes of the basal ganglia, and 2 suffered intraventricular hemorrhage. The overall mortality rate was 20% (3 of 15 patients). The clinical outcome of survivors was defined by the Pediatric Cerebral Performance Category (PCPC) and Pediatric Overall Performance Category (POPC) scores at follow-up. One year after AVM hemorrhage, 7 (58%) of the 12 surviving patients showed normal or mild disability (PCPC Score 1 or 2), whereas 5 (42%) of 12 patients had moderate or severe disability (PCPC Score 3 or 4). No patients were in a coma or vegetative state, and 11 (92%) of the 12 patients were functioning independently (POPC Score 1, 2, or 3) 1 year after AVM hemorrhage. All patients were functionally independent by last follow-up, with 8 patients (67%) in the normal or mild disability PCPC category, and 4 in the moderate category (PCPC Score 3). All 12 survivors made a meaningful recovery and went on to live independent lives.

Conclusions. Pediatric patients suffering AVM hemorrhage have a good outcome and are able to function independently, despite a poor neurological state initially. (DOI: 10.3171/2011.2.PEDS10355)
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Methods

This was a retrospective case series done with formal approval from the research ethics board of the University of British Columbia. Patients with AVMs were ascertained from a prospectively maintained database in the neurosurgery department at BCCH. A search through the charts of these patients was performed to identify those who presented with poor neurological status due to AVM hemorrhage. In the context of this study, poor neurological status was defined as having a GCS score of \( \leq 8 \).

The following information was collected by reviewing the medical records and neuroimaging reports of the identified patients: demographic data, initial clinical presentation, neurological signs at admission, neuroimaging findings, location of hemorrhage, AVM location, surgical intervention(s), clinical outcome on discharge, and clinical outcome status at 1 year and at the most recent follow-up date.

The GOS\(^{23} \) was used to assess clinical outcome at the time of discharge from the BCCH. Although nonspecific, it allows overall patient disability to be assessed without the need for detailed neurological and psychological assessment.\(^{19} \)

Clinical outcome status at follow-up was defined by the PCPC and POPC scales. These scales are validated and reliable clinical measures designed to assess functional morbidity and cognitive impairment after critical illness and injury;\(^{4,5} \) they are summarized in Table 1.

Results

Demographic Data

Between 1982 and 2006, a diagnosis of AVM was made in 128 patients at BCCH, and 15 of them met the criteria for the study (AVM hemorrhage presenting with a GCS score of \( \leq 8 \)). The study group consisted of 9 girls and 6 boys with a mean age of 9.7 years (range 4 months–16.4 years). The clinical information and follow-up data are summarized in Table 2.

Clinical Presentation

Initial symptoms of AVM hemorrhage included impaired consciousness (9 patients), headache (9), focal neurological deficits (7), nausea and vomiting (4), and seizures (3). Those with initially normal consciousness went on to deteriorate in the ensuing hours. Patients presented to BCCH at an average of 4.3 hours after symptom onset (range 0.9–9 hours). Thirteen of the 15 patients initially presented to a different institution in British Columbia prior to transfer to BCCH for further care.

The GCS scores ranged from 3 to 6 for the 15 patients in this series. Documented scores were the lowest scores recorded between presentation and surgery (that is, the lowest GCS score was noted in cases in which the child deteriorated prior to neurosurgical intervention). Intubated patients received a score of 1 on the verbal component of the GCS. Nine patients had a GCS score of 3, 3 patients had a score of 4, 1 patient had a score of 5, and 2 patients had a score of 6 (Fig. 1). Pupil reactivity and size was available for 14 patients at the time of AVM hemorrhage: 7 of these 14 patients had bilateral fixed and dilated pupils, 4 had bilateral midfixed pupils, and 3 had bilateral reactive pupils. Two patients initially presented with a unilateral fixed pupil, and their condition subsequently deteriorated to bilateral fixed pupils prior to surgical intervention. The median time from initial symptom onset to pupil change was 2.5 hours (range 0.5–9.7 hours) in the 9 patients for whom the exact time of pupil change was available.

Location of Hemorrhage

Eight of 15 patients suffered a lobar hemorrhage, 3 of which extended into the ventricles; 3 of 15 patients suf-

<table>
<thead>
<tr>
<th>Score</th>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCPC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>normal</td>
<td>normal child (if school age, normal school grade in a normal program)</td>
</tr>
<tr>
<td>2</td>
<td>mild disability</td>
<td>possible mild neurological deficit; child behaves &amp; interacts appropriately for age (if school age, normal school program, but perhaps delayed a grade)</td>
</tr>
<tr>
<td>3</td>
<td>moderate disability</td>
<td>child attends to ADLs in age-appropriate manner, but development delayed (if school age, modified curriculum)</td>
</tr>
<tr>
<td>4</td>
<td>severe disability</td>
<td>dependent on others for daily support, but conscious &amp; interacts</td>
</tr>
<tr>
<td>5</td>
<td>coma or vegetative state</td>
<td>unaware of or has no meaningful interaction w/ surroundings, not roused by verbal stimuli (but eye-opening &amp; reflex responses possible)</td>
</tr>
<tr>
<td>6</td>
<td>brain death</td>
<td>meets clinical brain death criteria (apnea, EEG silence, brainstem reflexes)</td>
</tr>
<tr>
<td>POPC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>good overall performance</td>
<td>capable of normal ADLs</td>
</tr>
<tr>
<td>2</td>
<td>mild overall disability</td>
<td>independent, normal life, but w/ minor physical problems</td>
</tr>
<tr>
<td>3</td>
<td>moderate overall disability</td>
<td>independent in ADLs, but disabled for competitive performance in school</td>
</tr>
<tr>
<td>4</td>
<td>severe overall disability</td>
<td>conscious but dependent on others for ADLs</td>
</tr>
<tr>
<td>5</td>
<td>coma or vegetative state</td>
<td>as defined by PCPC 5</td>
</tr>
<tr>
<td>6</td>
<td>brain death</td>
<td>as defined by PCPC 6</td>
</tr>
</tbody>
</table>

* ADLs = activities of daily living; EEG = electroencephalographic.
A VM hemorrhage was associated with a high risk of intraventricular hemorrhage (IVH), as 2 of 15 patients suffered IVH, of whom 1 had an IVH, and 2 of 15 patients suffered basal ganglia hemorrhages, of whom 1 had an IVH. Two of 15 patients suffered exclusively IVH (Fig. 2). Axial CT scans obtained in 2 of the patients presenting to BCCH for treatment of A VM hemorrhage are shown in Fig. 3 to demonstrate the size and severity of the bleeding.

**Treatment Methods**

In 3 of 12 patients the initial operation was a hematoma evacuation, and in 9 of 12 patients there was an early attempt to resect the A VM. An EVD was inserted in 3 patients as the sole surgical procedure. Four patients underwent multiple operations while in hospital (2–3 separate surgeries), whereas the remaining 11 patients had a single operation.

The timing and sequence of initial interventions varied among the 12 patients who underwent early craniotomy. Three of 12 patients were immediately taken to the operating room following CT imaging for emergency hematoma evacuation. All 3 patients underwent acute resection of A VMs that were discovered intraoperatively, and in 2 of the patients an EVD was inserted (one of these insertions took place during a later procedure). In 5 patients DS angiography or CT angiography was performed prior to acute A VM resection and evacuation of intracranial blood. Two of the 5 patients also had an EVD inserted during the same craniotomy. One patient underwent decompressive craniotomy prior to undergoing angiography, EVD placement, and A VM resection. In 2 of the 12 patients, an early hematoma evacuation and EVD placement were attempted to treat the A VM hemorrhage. Last, 1 patient underwent a frontal EVD placement prior to undergoing cerebral angiography, ventriculoperitoneal shunt insertion, hematoma evacuation, and ligation of A VM feeding vessels. No patient had embolization in the acute phase.

Time from symptom onset to first surgery ranged from 2 to 68.8 hours, with a median of 4.3 hours. It was possible to determine the precise time of pupillary abnormality in 9 of the 11 patients with either unilateral or bilateral fixed pupils.

**TABLE 2: Clinical and follow-up data for AVM hemorrhage in 15 pediatric patients with a GCS score of ≤ 8**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>GCS Score</th>
<th>Neurological Signs at Presentation</th>
<th>Location of Hemorrhage</th>
<th>Treatment</th>
<th>Time to Op (hrs)</th>
<th>Time in Hospital (days)</th>
<th>Clinical Outcome at FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.9, M</td>
<td>6</td>
<td>PERL</td>
<td>basal ganglia</td>
<td>craniotomy</td>
<td>3.83</td>
<td>17</td>
<td>5.8</td>
</tr>
<tr>
<td>2</td>
<td>10.9, M</td>
<td>6</td>
<td>PERL</td>
<td>lobar</td>
<td>craniotomy</td>
<td>6.06</td>
<td>21</td>
<td>2.4</td>
</tr>
<tr>
<td>3</td>
<td>16.4, F</td>
<td>5</td>
<td>fixed</td>
<td>lobar &amp; IVH</td>
<td>craniotomy, EVD</td>
<td>5.08</td>
<td>34</td>
<td>18.1</td>
</tr>
<tr>
<td>4</td>
<td>0.3, M</td>
<td>4</td>
<td>fixed</td>
<td>basal ganglia &amp; IVH</td>
<td>craniotomy, VPS, EVD</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>8.8, M</td>
<td>4</td>
<td>fixed, dilated</td>
<td>IVH</td>
<td>EVD</td>
<td>6.50</td>
<td>34</td>
<td>1.9</td>
</tr>
<tr>
<td>6</td>
<td>12.6, F</td>
<td>4</td>
<td>fixed</td>
<td>lobar &amp; IVH</td>
<td>EVD</td>
<td>4.17</td>
<td>23</td>
<td>5.1</td>
</tr>
<tr>
<td>7</td>
<td>0.4, M</td>
<td>3</td>
<td>fixed, dilated</td>
<td>lobar</td>
<td>craniotomy</td>
<td>68.75</td>
<td>10</td>
<td>11.0</td>
</tr>
<tr>
<td>8</td>
<td>7.1, F</td>
<td>3</td>
<td>fixed</td>
<td>lobar</td>
<td>craniotomy, EVD</td>
<td>2.67</td>
<td>27</td>
<td>4.0</td>
</tr>
<tr>
<td>9</td>
<td>9.0, F</td>
<td>3</td>
<td>fixed (U), dilated</td>
<td>lobar</td>
<td>craniotomy, EVD</td>
<td>13.18</td>
<td>21</td>
<td>2.9</td>
</tr>
<tr>
<td>10</td>
<td>9.5, F</td>
<td>3</td>
<td>fixed, dilated</td>
<td>ITH</td>
<td>craniotomy, EVD</td>
<td>3.50</td>
<td>34</td>
<td>2.8</td>
</tr>
<tr>
<td>11</td>
<td>10.5, F</td>
<td>3</td>
<td>—</td>
<td>ITH</td>
<td>craniotomy, EVD</td>
<td>2.00</td>
<td>14</td>
<td>5.7</td>
</tr>
<tr>
<td>12</td>
<td>14.2, F</td>
<td>3</td>
<td>fixed, dilated</td>
<td>lobar</td>
<td>craniotomy</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>13</td>
<td>12.8, F</td>
<td>3</td>
<td>PERL</td>
<td>lobar &amp; IVH</td>
<td>EVD</td>
<td>4.33</td>
<td>4</td>
<td>NA</td>
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<tr>
<td>14</td>
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<td>IVH</td>
<td>craniotomy, EVD</td>
<td>5.00</td>
<td>3</td>
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<tr>
<td>15</td>
<td>15.6, F</td>
<td>3</td>
<td>fixed (U), dilated</td>
<td>ITH &amp; IVH</td>
<td>craniotomy, EVD</td>
<td>4.25</td>
<td>8</td>
<td>NA</td>
</tr>
</tbody>
</table>

* FU = follow-up; ITH = infratentorial hemorrhage; NA = not applicable; PERL = pupils equal and reactive to light; (U) = initially unilateral fixed pupil; VPS = ventriculoperitoneal shunt; — = not available.

**Fig. 1.** Bar graph showing the GCS scores at presentation.

**Fig. 2.** Bar graph showing location of the AVM hemorrhages.
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![Fig. 3. Representative nonenhanced axial CT scans obtained in 2 patients with AVM hemorrhage. Left: A 16-year-old patient with a presenting GCS score of 5 and fixed pupils. Right: A 12-year-old patient with a presenting GCS score of 3 and dilated pupils.](image)

...pupils. The median time to surgery in these 9 patients was 80 minutes (range 22–4095 minutes) from the time the pupillary abnormality was first noted. The one outlier, with 4095 minutes (> 68 hours), was a patient in whom unilateral pupillary dilation was noted at another institution; the patient responded promptly to mannitol and Lasix.

The average length of stay at BCCH was 19 days, and the average length of stay in the intensive care unit was 10 days. Eight of the 12 surviving patients were transferred to an in-patient rehabilitation facility following discharge from BCCH.

**Clinical Outcome**

Three (20%) of the 15 patients died in the hospital following AVM hemorrhage. Of these 3 patients, one experienced an infratentorial hemorrhage involving both the cerebellum and brainstem; one suffered a hemorrhage involving much of the cerebrum, basal ganglia, and ventricles; and the other patient had a fourth ventricle hemorrhage with extension into the third and lateral ventricles. Two patients died as a result of the hemorrhage, and 1 died of AVM hemorrhage complicated by surgical site infection. Death occurred 3 to 8 days following symptom onset.

Of the 3 patients who received an EVD as the only surgical treatment in the acute phase, the first was found to have a caudate head AVM, and predominantly IVH. After EVD, there was rapid progression to diabetes insipidus, and ultimately brain death. In a second patient there was an IVH with a small periventricular hemorrhage. An early angiogram was negative, and a 2-month DS angiography study demonstrated a medial parietal AVM, which was subsequently completely resected. In a third patient with predominantly IVH, a small AVM of the trigone was identified initially, but subsequent DS angiography did not visualize the malformation, suggesting that the AVM had spontaneously thrombosed and/or involuted.

One of the 2 patients who had hematoma evacuation and EVD placement as part of the initial intervention died as a result of a fourth ventricle hemorrhage, with blood extending into the third and lateral ventricles.

In the 9 patients who underwent a craniotomy for hemorrhage evacuation and AVM excision, 7 had preoperative CT angiography (3 patients) or conventional angiography (4). The anatomy and location of the AVM were delineated in all 3 patients with CT angiography, and in 3 of 4 patients with conventional angiography. One of the 9 patients who underwent an early attempt to resect the AVM died of surgical site infection following an emergency evacuation of a cerebellar hematoma and partial resection of a brainstem AVM. Two of the patients had early imaging showing AVM “cure,” but no late imaging (both moved out of our practice area). Four patients had AVM “cure” on both early and late imaging (> 1 year). Two patients had late recurrence of AVM (1 at approximately 2 years posthemorrhage, and 1 at approximately 5 years posthemorrhage), despite apparently normal results on early imaging (DS angiography within 2 weeks of AVM and hemorrhage removal).

For the 12 surviving patients (80%), clinical outcome at discharge was assessed using the GOS. Five (42%) of the 12 survivors had a good recovery or moderate disability, with the ability to function independently (POPC Score 1, 2, or 3); 6 patients (50%) had a severe disability and were dependent for daily support; and 1 patient (8%) was in a vegetative state.

Clinical outcome was assessed 1 year after AVM hemorrhage and at the most recent follow-up by using the PCPC and the POPC scales. The PCPC can be divided into 3 categories based on cerebral functioning: normal or mild disability (PCPC Score 1 or 2); moderate or severe disability (PCPC Score 3 or 4); and coma or vegetative state (PCPC Score 5). The POPC can be divided into 2 categories: independent overall function (POPC Score 1, 2, or 3) or dependent on others (POPC Score 4 or 5).

At the 1-year follow-up, 7 (58%) of the 12 surviving patients were in the normal or mild disability PCPC category, whereas 5 (42%) of 12 patients were in the moderate or severe disability PCPC category. No patients were in a coma or vegetative state. Eleven (92%) of the 12 patients were functioning independently (POPC Score 1, 2, or 3) 1 year after AVM hemorrhage.

The average follow-up time for the 12 surviving patients was 5.4 years, ranging from 1.9 to 18.1 years. At follow-up, 8 (67%) of 12 patients were in the normal or mild disability PCPC category, whereas 4 were in the moderate category (PCPC Score 3). No patients were in a coma or vegetative state. All 12 patients were functioning independently at the most recent follow-up date.

**Discussion**

The initial status following neurological injury is often used as a predictor of death and outcome in adult patients. Studies have found that patients with a low GCS score on admission have a tendency toward worse outcomes following intracerebral hemorrhage. This relationship between initial neurological state and outcome may therefore influence the treatment and management of the disorder in patients presenting with poor neurological status. However, in the pediatric population, few studies have focused on the outcome following AVM hemorrhage in children presenting with a low GCS score and/or fixed and dilated pupils. Our study was designed to investigate whether a similar relationship between neurological state and outcome exists in the pediatric age group.
The present study consisted of 15 pediatric patients presenting with symptomatic AVM hemorrhage and low neurological status, defined as a GCS score of ≤ 8. This GCS score was chosen to indicate severe brain injury and neurological state. The patients presented to BCCH between 1982 and 2006. The mean age of our patients was 9.7 years, with a female/male sex ratio of 1.5:1. This ratio differs from that in the literature; there tends to be a slight prevalence of AVM hemorrhage in males.1,15 This inconsistency may be due to the small number of patients in this series. The reason for the sex difference seen in other series remains unclear.

At presentation, the GCS scores in the 15 patients ranged from 3 to 6, with a median score of 3. Eleven (79%) of 14 patients had bilateral fixed pupils (some of whom initially presented with a single fixed pupil and subsequently deteriorated to bilateral fixed pupils). Patients presenting in such a state are generally not expected to do well, and studies have shown the GCS score to be a good indicator for outcome following brain injury.1,12,17,18,21 However, use of the GCS score as an indicator for outcome in pediatric patients with an AVM hemorrhage has been less studied.

In the current study, location of hemorrhage following AVM rupture was consistent with the literature.1,3,7,15 The majority of our patients (10 of 15) suffered a supratentorial hemorrhage (lobar or basal ganglia), 3 (20%) of 15 suffered an infratentorial hemorrhage, and 2 (13%) of 15 had an IVH.

Effects of hemorrhage tend to be worse in patients younger than 15 years of age, with a mortality rate ranging from 7.1% to 25% after a first hemorrhage, compared with 6%–10% in adults.1,14,15 Consistent with the literature, the mortality rate in the current study was 20% (3 patients). In these 3 patients, hemorraghes were massive or included hemorrhage in the brainstem. The location and size of these hemorrhages therefore seemed to play a role in patient mortality rates. In a study by Kondziolka et al.11 of clinical data and management in 132 patients with AVMs, death from an AVM hemorrhage was found to be dependent on location. Other studies have confirmed this finding showing the increased mortality rate in patients with infratentorial AVMs, specifically lesions found in the brainstem.2,6,9,22 Hemodynamic and compressive effects of infratentorial hemorrhage can lead to life-threatening symptoms earlier than in cases of supratentorial hemorrhage.2,3

For the 12 patients in the current series who survived AVM hemorrhage, the clinical outcome was defined by the GOS, PCPC, and POPC scales. At discharge from BCCH, 5 patients (42%) had a good recovery or moderate disability, with the ability to function independently, 6 (50%) were severely disabled and dependent on others for support, and 1 (8%) was in a vegetative state. At the 1-year follow-up, 7 patients (58%) were in the normal or mild disability PCPC category, whereas 5 (42%) were in the moderate or severe disability PCPC category. Despite low neurological status on presentation, no patients were in a coma or vegetative state. In addition, nearly all patients (11 of 12) were functioning independently. Therefore, 1 year after discharge from hospital, the ability to function independently increased from 5 (42%) to 11 (92%), which is quite a remarkable difference. At the most recent follow-up, which averaged 5.4 years following hemorrhage, 8 of 12 patients were in the normal to mild disability PCPC category, and 4 of 12 were in the moderate to severe disability PCPC category. Eleven of the 12 patients remained in the same PCPC category from 1 year after AVM hemorrhage to the most recent follow-up, indicating that much of the recovery after AVM hemorrhage occurs during the 1st year. This is consistent with a study done by Malik et al.,13 who found that neurological deficits from AVM hemorrhage or the surgery to treat it tend to improve dramatically within the first 3 months. All 12 patients in this series were functioning independently at the most recent follow-up date.

Therefore, despite studies that have found low GCS scores to be associated with poor outcomes following AVM hemorrhage,2,3 the current study indicates that in the pediatric population, those who survive can make a meaningful recovery and go on to live independent lives. This supports the idea that the child's brain may better compensate following hemorrhage, because it is a developing organ with preserved cerebral plasticity.1,3-3,8 As emphasized by Humphreys et al.,1 “the child's biologic plasticity is such that the degree of postoperative recovery can be as complete and gratifying as the preoperative deterioration was rapid and dramatic.”

Conclusions

The current study suggests a better recovery than might be expected of pediatric patients with AVM hemorrhage presenting with poor neurological status. Rapid neurological deterioration, even with the development of bilaterally fixed, dilated pupils, is not a contraindication to surgical decompression, because the majority of patients survive and have a high probability of making a meaningful recovery and living an independent life. This is promising both to the treating physicians and to the family who anxiously awaits the prognosis of their child. It is hoped that this understanding will help guide the decision-making process and the management of this disorder in these patients in the future, and better inform families of the chances of survival and functioning in the years to come.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: Singhal, Adirim. Analysis and interpretation of data: Singhal, Adirim, Steinbok. Drafting the article: all authors. Critically revising the article: all authors. Reviewed final version of the manuscript and approved it for submission: all authors. Administrative/technical/material support: Cochrane, Steinbok. Study supervision: Singhal, Cochrane, Steinbok.

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