Hydrocephalus in children with ruptured cerebral arteriovenous malformation

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OBJECTIVE Hydrocephalus is a strong determinant of poor neurological outcome after intracerebral hemorrhage (ICH). In children, ruptured brain arteriovenous malformations (bAVMs) are the dominant cause of ICH. In a large prospective cohort of pediatric patients with ruptured bAVMs, the authors analyzed the rates and predictive factors of hydrocephalus requiring acute external ventricular drainage (EVD) or ventriculoperitoneal shunt (VPS).

METHODS The authors performed a single-center retrospective analysis of the data from a prospectively maintained database of children admitted for a ruptured bAVM since 2002. Admission clinical and imaging predictors of EVD and VPS placement were analyzed using univariate and multivariate statistical models.

RESULTS Among 114 patients (mean age 9.8 years) with 125 distinct ICHs due to ruptured bAVM, EVD and VPS were placed for 55/125 (44%) hemorrhagic events and 5/114 patients (4.4%), respectively. A multivariate nominal logistic regression model identified low initial Glasgow Coma Scale (iGCS) score, hydrocephalus on initial CT scan, the presence of intraventricular hemorrhage (IVH), and higher modified Graeb Scale (mGS) score as strongly associated with subsequent need for EVD (all $p < 0.001$). All children who needed a VPS had initial hydrocephalus requiring EVD and tended to have higher mGS scores.

CONCLUSIONS In a large cohort of pediatric patients with ruptured bAVM, almost half of the patients required EVD and 4.4% required permanent VPS. Use of a low iGCS score and a semiquantitative mGS score as indicators of the IVH burden may be helpful for decision making in the emergency setting and thus improve treatment.

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KEYWORDS hydrocephalus; ventriculoperitoneal shunt; arteriovenous malformation; intracerebral hemorrhage; external ventricular drain; vascular disorders

Ruptured brain arteriovenous malformations (bAVMs) are the main cause of pediatric intracerebral hemorrhage (ICH).^{1–3} Acute hydrocephalus secondary to intraventricular hemorrhage (IVH) or ventricle compression is a key therapeutic target at the acute phase to improve neurological outcome.⁴ CSF diversion procedures, i.e., acute external ventricular drainage (EVD) and delayed ventriculoperitoneal shunt (VPS) placement, have been studied only in adult cohorts.^{5–11} These proce-

dures are reported in 13%–53% and 1.9%–24.2% of cases, respectively, depending on the setting and underlying ICH etiology.

In pediatric ICH, data are scarce on the need for EVD and VPS, leading to uncertainty in acute decision making for CSF diversion and care stratification. We aimed to assess the rates and predictive factors of hydrocephalus requiring acute EVD and VPS in children with ICH after bAVM rupture.

ABBREVIATIONS AUC = area under the curve; bAVM = brain arteriovenous malformation; EVD = external ventricular drainage; ICH = intracerebral hemorrhage; iGCS = initial Glasgow Coma Scale; IVH = intraventricular hemorrhage; KOSCHI = King's Outcome Scale for Childhood Head Injury; mGS = modified Graeb Scale; VPS = ventriculoperitoneal shunt.

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Methods

STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed.¹² Because the investigation was a noninterventional retrospective study of routinely acquired data, the requirement for written informed consent from all participating patients was waived, and patients and their guardians were informed that they could oppose the use of their health-related data for research purposes. The institutional review board (CPP Ile de France III; 18062012) approved the collection of data into the dedicated database.

Study Design and Data Extraction

Based on the previously described registry of children presenting with ICH at the pediatric hospital of our institution (Necker Enfants Malades, Paris, France),² patients < 18 years old who were treated for ruptured bAVM at our institution since 2002 were identified. Clinical data included age at event, sex, and initial Glasgow Coma Scale (iGCS) score and were retrospectively completed with the help of a data warehouse.¹³ Clinical outcome, assessed 18 months after ICH, was defined as favorable for King's Outcome Scale for Childhood Head Injury (KOSCHI) scores of ≥ 5 and severely disabled for KOSCHI scores of < 4.¹⁴ Six patients with follow-up periods of < 18 months were excluded from outcome analysis.

Imaging characteristics included bAVM angioarchitecture, i.e., Spetzler-Martin grade, associated aneurysms, deep venous drainage, deep AVM localization, and ICH volume (ml). IVH extent was assessed using the modified Graeb Scale (mGS) score, which ranges from 0 to 32 and is based on the distribution and amount of IVH and associated ventricular dilatation.¹⁵ Temporal horn dilatation was

defined as a diameter larger than 5 mm. According to the institution's practice, which remained unchanged during the study period, the placement of an EVD was indicated to control intracranial pressure in case of either IVH or signs of elevated intracranial pressure on initial imaging, such as shift of midline structures, herniation, or cerebral edema. The EVD was leveled at 15 or 20 mm H₂O and was removed when the drained CSF was free of blood and IVH was cleared on follow-up CT.

Statistical Analysis

Statistical analyses were performed using JMP Pro version 14.0 (SAS Institute Inc., 2019). Differences in bleeding events with and without the need for EVD placement were studied in univariate analyses performed using appropriate tests for each variable category. Those variables associated with EVD placement ($p < 0.1$) were entered in a multivariate nominal logistic regression model, while non-significant variables were backward eliminated. Before performance of the univariable tests, it was prespecified that in the multivariable model age and mGS score would be adjusted independently of their association with EVD placement found in the univariable tests. Two-sided p values < 0.05 were considered statistically significant.

Results

Patient Characteristics

Clinical and radiological characteristics of 114 included patients with 125 ICHs are summarized in Table 1. The distribution of Spetzler-Martin grades was as follows: 21% grade I, 42% grade II, 23% grade III, 10% grade IV, and 4% grade V. At the acute phase, a surgical evacuation of

TABLE 1. Clinical and radiological characteristics of 114 patients with ruptured bAVM

Variable	Patients (n = 114)*	Hemorrhagic Events (n = 125)		p Value
		EVD (n = 55)	No EVD (n = 70)	
Male sex	64 (56%)	32 (58.2%)	36 (51.4%)	0.47
Age in yrs	9.6 (3.7)	10.7 (3.6)	9.1 (3.9)	0.009
iGCS score	11.4 (4.0)	9.7 (4.0)	13.2 (3.0)	<0.0001
iGCS score <9	34 (30%)	26 (47.3%)	9 (12.9%)	<0.0001
IVH	68 (60%)	52 (95%)	22 (32%)	<0.0001
IVH only	10 (9%)	4 (7.3%)	9 (12.9%)	0.38
mGS score	10.7 (11.3)	18.5 (10.2)	4.4 (7.6)	<0.0001
bAVM aneurysm	37 (32%)	25 (45.5%)	15 (21.7%)	0.007
Superficial bAVM	47 (41%)	16 (29.1%)	37 (52.9%)	0.008
Any deep drainage	57 (50.4%)	34 (61.8%)	30 (43.5%)	0.032
ICH volume, ml	20.0 (16.4)	20.2 (17.4)	19 (15.9)	0.68
Temporal horn dilatation	44 (38.6%)	41 (74.5%)	8 (11%)	<0.0001
Outcome†				
Favorable outcome	65/108 (60%)	26/50 (52%)	39/58 (67%)	0.12
Severe disability or worse	15/108 (14%)	10/50 (20%)	5/58 (5%)	0.03

Values are expressed as number (%) or mean (SD) unless otherwise indicated. Boldface type indicates statistical significance.

* For 114 patients at first hemorrhagic event.

† For 108 of 114 patients with follow-up of > 18 months.

TABLE 2. Multivariable model analysis of predictive factors for EVD placement after ruptured bAVM

Variable	Adjusted OR	95% CI	p Value
Age at event (per yr)	1.16	0.98–1.37	0.07
iGCS score (per point)	0.74	0.63–0.88	0.0018
Dilated temporal horn(s)	7.45	2.03–27.38	0.002
mGS score (per point)	1.16	1.08–1.25	<0.0001
Aneurysm (yes)	3.42	0.85–13.85	0.07
bAVM location (superficial vs deep)	0.75	0.19–2.89	0.67
Any deep drainage (yes)	0.63	0.16–2.38	0.49

Boldface type indicates statistical significance.

the parenchymal hematoma and a targeted endovascular embolization was performed in, respectively, 53 and 42 patients, and 4 patients died during initial hospitalization.

Acute Hydrocephalus and Predictive Factors for EVD Placement

EVD was required in 55/125 (44%) of the hemorrhagic events and placed after a median of 0 days (IQR 0–1) following initial imaging, for an average duration of 5.5 ± 7.6 days. Five of the 114 patients (4.4%) required VPS, all of whom had an acute EVD placement.

In univariate analysis, older age, lower iGCS score, IVH, higher mGS score, temporal horn dilatation, bAVM-related aneurysms, and deeply located bAVMs were associated with EVD (Table 1). After adjustment in the multivariable analysis (Table 2), mGS and iGCS were the most powerful predictors for EVD placement (Fig. 1), and bAVM-related aneurysms tended toward significance. The AUC for EVD placement in the fully adjusted multivariate model was 0.95 (95% CI [1000 bootstraps] 0.91–0.98), indicating excellent predictive ability (Fig. 2). The results were similar after further adjustment for bleed recurrence. No relationship between the Spetzler-Martin grading and the need for EVD was found (chi square 4.497, $p = 0.34$). All children requiring VPS required an EVD

and had higher mGS scores (mGS scores with vs those without VPS 19.6 vs 10.2, $p = 0.06$). On follow-up, there was no detectable difference in favorable outcome among children with and those without EVD treatment (52% vs 67% with KOSCHI ≥ 5 , $p = 0.25$), but those with EVD were more frequently severely disabled or worse (KOSCHI score < 4 in 19% with EVD vs 8% without, $p = 0.04$).

Discussion

Our study provides a data-driven framework aimed at guiding acute decision making with regard to the need for EVD placement and long-term shunt dependence in the setting of ruptured bAVM in pediatric patients.

In the present study of children with bAVM-related ICH, EVD placement was required in 44% and VPS placement in 4.4% of patients, rates comparable to those found in studies of adult patients.^{5,8,9,11} Significant risk factors for EVD placement were iGCS score and the presence of IVH and hydrocephalus on initial brain imaging. In addition, we found that the main determinant for EVD placement was the IVH burden assessed by mGS. This was true independently of baseline hydrocephalus. However, because this was a retrospective study without predetermined criteria for EVD placement, the independence of the predictive factors can only be assumed. Also, the establishment of a predictive score was impossible due to the limited statistical power of the study owing to the rarity of pediatric bAVM. As a representative example, in a 10-year-old child with an iGCS score of 13, the probabilities for EVD placement with mGS scores of 0, 10, 20, and 30 would be 6.5%, 23%, 57%, and 86%, respectively. As the median delay between initial CT and EVD placement was < 24 hours, our results suggest the importance of prompt transfer to a neurosurgical ICU for these patients. In the management of children without symptomatic hydrocephalus, no beneficial effect of EVD was found; nevertheless, we advocate close observation of these patients, especially in cases with very extensive IVH and uncertainty regarding low-threshold EVD placement. The study results highlight the important findings that EVD placement in the emergency setting does not increase the risk associated with

FIG. 1. Probability of EVD, in the fully adjusted model, plotted against the mGS score (GS; **A**) and the iGCS score (GCS; **B**). Figure is available in color online only.

FIG. 2. AUC for EVD placement in the model adjusted for male sex, age at event, iGCS score, dilated temporal horn(s), mGS score, AVM-related aneurysm, AVM location, and any deep drainage. Figure is available in color online only.

VPS insertion or the risk of infection. Thus indications for EVD placement after rupture of pediatric bAVM can be kept wide, thereby helping to optimize the management of intracranial pressure.

Baseline ICH volume, although not predictive of acute EVD placement, was among the angioarchitectural characteristics of the bAVM-associated aneurysms that tended to increase the probability of EVD placement. This finding has already been demonstrated in an adult population.⁵ Aneurysms may have been responsible for subsequent worsening of ICH volume and IVH load, likely explaining their higher prevalence in children requiring EVD. Hence, identification of an associated aneurysm responsible for the ICH may have therapeutic implications because these aneurysms may be associated with higher morbidity through a higher incidence of hydrocephalus requiring EVD placement.

Our data also reinforced the finding that children who needed EVD placement were more frequently severely disabled, which has significant clinical implications for hydrocephalus and EVD placement after pediatric bAVM rupture. Hydrocephalus and the resulting elevated intracranial pressure in the setting of ICH are considerable sources of neurological morbidity.¹⁶ Further research is needed on the impact of hydrocephalus, including the influence of methods used for treatment on long-term cognitive development in pediatric patients with ruptured bAVMs.

Conclusions

After bAVM rupture in children, nearly half will require an acute EVD placement. Significant risk factors for EVD placement were high mGS score and low iGCS

score. As EVD placement does not increase the risk for VPS, the indications for EVD placement after rupture of bAVM can be kept wide, which helps to optimize the available options for intracranial pressure management.

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Disclosures

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

Conception and design: Blauwblomme, Stricker, Boulouis, Benichi, Naggara. Acquisition of data: Blauwblomme, Stricker, Boulouis, Gariel, Garzelli, Beccaria, Chivet, de Saint Denis, James, Paternoster, Zerah, Bourgeois, Boddaert, Brunelle,

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