Predictors of long-term shunt-dependent hydrocephalus in patients with intracerebral hemorrhage requiring emergency cerebrospinal fluid diversion


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Object. Intracerebral hemorrhage (ICH) is frequently complicated by acute hydrocephalus, necessitating emergency CSF diversion with a subset of patients, ultimately requiring long-term treatment via placement of permanent ventricular shunts. It is unclear what factors may predict the need for ventricular shunt placement in this patient population.

Methods. The authors performed a retrospective analysis of a prospective database (ICH Outcomes Project) containing patients with nontraumatic ICH admitted to the neurological ICU at Columbia University Medical Center between January 2009 and September 2011. A multiple logistic regression model was developed to identify independent predictors of shunt-dependent hydrocephalus after ICH. The following variables were included: patient age, admission Glasgow Coma Scale score, temporal horn diameter on admission CT imaging, bicaudate index, admission ICH volume and location, intraventricular hemorrhage volume, Graeb score, LeRoux score, third or fourth ventricle hemorrhage, and intracranial pressure (ICP) and ventriculitis during hospital stay.

Results. Of 210 patients prospectively enrolled in the ICH Outcomes Project, 64 required emergency CSF diversion via placement of an external ventricular drain and were included in the final cohort. Thirteen of these patients underwent permanent ventricular CSF shunting prior to discharge. In univariate analysis, only thalamic hemorrhage and elevated ICP were significantly associated with the requirement for permanent CSF diversion, with p values of 0.008 and 0.033, respectively. Each remained significant in a multiple logistic regression model in which both variables were present.

Conclusions. Of patients with ICH requiring emergency CSF diversion, those with persistently elevated ICP and thalamic location of their hemorrhage are at increased odds of developing persistent hydrocephalus, necessitating permanent ventricular shunt placement. These factors may assist in predicting which patients will require permanent CSF diversion and could ultimately lead to improvements in the management of this disorder and the outcome in patients with ICH.

*Key Words* • intracerebral hemorrhage • hydrocephalus • external ventricular drain • ventriculoperitoneal shunt

**Abbreviations used in this paper:** CUMC = Columbia University Medical Center; EVD = external ventricular drain; GCS = Glasgow Coma Scale; ICH = intracerebral hemorrhage; ICP = intracranial pressure; IVH = intraventricular hemorrhage; NICU = neurological ICU; rtPA = recombinant tissue plasminogen activator; SAH = subarachnoid hemorrhage; VP = ventriculoperitoneal.
care center identified thalamic location and elevated ICP as independent predictors of the need for VP shunt placement in patients with ICH admitted for acute hydrocephalus. We sought to identify early predictors of long-term shunt dependency in a prospectively studied cohort of patients with ICH who had undergone EVD placement for emergency CSF diversion.

Methods

Patient Selection and Data Collection

All patients with primary spontaneous ICH admitted to the NICU within 7 days of ICH onset at CUMC between January 2009 and August 2011 were screened for enrollment in our prospective ICH Outcomes Project. All patients opted to participate and were entered into the database. The protocol was approved by the CUMC institutional review board, and written consent was obtained from the patient or a designated surrogate. Admission head CT imaging was used to establish the diagnosis of ICH. Patients with ICH secondary to trauma or underlying vascular abnormalities such as arteriovenous malformations were excluded from our analysis. Patients were followed throughout their hospital course, and their disorder was managed according to current ICH guidelines set forth by the American Heart Association and the American Stroke Association.

Clinical Variables

Demographic information collected at admission included age, ethnicity, and sex. Neurological and general medical evaluations, including determination of disease severity according to the ICH score, were performed by neurointensive care physicians on admission. Clinical variables were recorded at admission and subsequently examined for potential associations with shunt-dependent hydrocephalus. Treatment modalities and complications were recorded, including placement of an EVD, number of days with an EVD in place, maximum ICP during the index ICU stay, and development of ventriculitis. Ventriculitis was defined as fever with CSF pleocytosis, with or without positive CSF cultures, and without other identifiable sources of fever. Maximum ICP was analyzed as 2 dichotomous variables (any ICP ≥ 25 mm Hg and/or a recorded ICP ≥ 20 mm Hg on ≥ 2 consecutive days) based on criteria used in a previous study by Miller et al.

Radiographic Variables

Admission head CT imaging was used for independent assessment of radiographic characteristics including ICH location, ICH volume, presence of IVH, the IVH volume, presence of third ventricular blood, presence of fourth ventricular blood, temporal horn diameter, and bicaudate index. The LeRoux score was calculated from radiographic measurements. Location was classified into the following categories: thalamic, basal ganglia, cortical, cerebellar, brainstem, or subcortical white matter. Hydrocephalus was dichotomized as present or absent on the admission CT scan, based on temporal horn diameter and bicaudate index. Both the Graeb and LeRoux

scores were calculated for each scan. The volume of ICH and IVH was quantified using MIPAV software (version 4.3, National Institutes of Health).

Placement and Management of the EVD

The neurological status of all patients admitted with spontaneous ICH was assessed at least hourly by qualified staff while the patients remained in the NICU. Any clinical evidence of hydrocephalus (for example, severe headache or decrement of GCS) during this period prompted evaluation for acute CSF diversion via EVD placement. Subsequent radiographic assessment for hydrocephalus was then performed in all cases using head CT imaging, with comparison of temporal horn diameter, bicaudate index, and shape of the third ventricle to any available prior imaging. The presence of clinical and radiographic hydrocephalus was ultimately determined based on the clinical judgment of the NICU team. The EVD insertion was preferentially performed on the right (generally non-dominant) side unless there were relative radiographic contraindications as determined by the attending neurosurgeon, such as hematoma in the planned path of the EVD, difficulty in accessing the right lateral ventricle, a completely blood-filled right lateral ventricle, or a concern for worsened left-to-right midline shift. The site of EVD insertion was at the Kocher point in all cases and was performed in routine fashion. Following placement and confirmation at the bedside of a working drain, an immediate postprocedure CT scan was obtained to document the location of the proximal EVD tip. All patients received a preprocedure dose of prophylactic antibiotics (cefazolin, or vancomycin if the patient was allergic to penicillins or cephalosporins). Appropriate prophylactic antibiotics were continued for the time that the EVD remained in place and were discontinued thereafter.

Random CSF sampling from the EVD collection system was performed routinely 3 times per week and when clinically indicated. If patients were deemed by the NICU team to have ventriculitis, either due to a persistently worrisome CSF profile or to positive CSF cultures, patients were treated with a course of appropriate antibiotics (generally vancomycin and cefepime). The EVDs were not prophylactically exchanged for fresh catheters, nor were prophylactic intraventricular antibiotics routinely administered, given a lack of evidence for these practices. In patients with significant IVH, intraventricular thrombolysis with rtPA was administered per the Clot Lysis: Evaluating Accelerated Resolution of IVH (CLEAR IVH) protocol to facilitate clot resolution.

Intracranial pressure was recorded at least hourly in all patients with EVDs. Drain height was adjusted as needed based on the patient’s neurological status and to maintain a goal ICP between 0 and 20 mm Hg. Any recorded ICP ≥ 25 or ≥ 20 mm Hg for > 10 consecutive minutes was considered to be elevated ICP and was treated with additional CSF drainage and/or standard medical therapy.

Weaning from the EVD was performed based on the patient’s neurological status, radiographic criteria (such as ventricular size and resolution of IVH), and hourly CSF output. When deemed appropriate by the NICU team and

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attending neurosurgeon, daily EVD clamp trials were initiated. During periods when an EVD was clamped, ICP was continuously transduced. Clinical criteria for aborting an EVD clamp trial included the following: 1) decline in neurological status or significant worsening of symptoms, such as persistent severe headache; and 2) sustained ICP ≥ 20 mm Hg for > 10 minutes. When possible, a repeat head CT would be obtained without contrast to assess radiographic appearance of the ventricular system prior to reopening of the EVD. Patients successfully completing a 24-hour clamp trial would have their EVD removed at the bedside. For those patients in whom repeated EVD clamp trials failed, a VP shunt was placed as definitive treatment for persistent hydrocephalus.

Definition of Outcome

Shunt-dependent hydrocephalus was defined as symptoms of hydrocephalus (decreased mental status) with persistent elevated ICP as measured via a transduced EVD, or radiographic evidence of enlarged ventricles, necessitating the placement of a VP shunt for permanent CSF diversion prior to hospital discharge. No patients with ventriculotrial shunts were included in this analysis, because these types of shunts have not been placed as a first-line permanent diversion system for any patients with ICH at our center.

Statistical Analysis

Univariate analyses were performed using the Student t-test for continuous variables, the Wilcoxon rank-sum test for ordinal variables, and the Fisher exact and Pearson chi-square tests for categorical variables. Location was assessed by comparing each group individually to the remaining locations as an aggregate. A multiple logistic regression model was constructed with significant variables from the univariate analyses to identify predictors of VP shunt placement. All statistical analyses were performed using the R environment for statistical computing (R Development Core Team, 2008).

Results

During the study period, 66 of 210 patients enrolled in our ICH Outcomes Project required emergency CSF diversion via EVD placement on admission. We excluded 2 of these 66 patients from our analysis due to incomplete data, resulting in a final cohort of 64 patients. Of these, 13 patients (20%) developed shunt-dependent hydrocephalus, necessitating VP shunt placement prior to discharge. The mean age was similar, 60.1 versus 61.5 years for those without and with VP shunt placement, respectively, and the admission GCS score was identical in both groups. There was a greater proportion of patients diagnosed with ventriculitis in the VP shunt group, although the difference was not statistically significant. Demographic data and baseline characteristics of the patients included in our analysis are provided in Table 1.

The admission characteristics and radiographic variables significantly associated with shunt dependency in the univariate analysis included maximum ICP (p = 0.013), ICP ≥ 25 mm Hg (p = 0.030), ICP ≥ 20 mm Hg on ≥ 2 consecutive days (p = 0.033), thalamic location (p = 0.008), and number of days with EVD in place (p < 0.001). Of the 23 patients with a thalamic lesion who required placement of an EVD, only 3 also had persistently elevated ICP; 1 of these patients ultimately required VP shunt placement.

Two multiple logistic regression models were then constructed, the first including thalamic location and ICP ≥ 25 mm Hg and the second with thalamic location and ICP ≥ 20 mm Hg on ≥ 2 consecutive days (Table 2). The number of days that an EVD was in place was not included as a variable in our final models because it is probably an index of disease severity rather than a predictive factor for persistent hydrocephalus. Because age, admission neurological status, and IVH volume were not associated with VP shunt placement in our univariate analysis, nor have they been shown to be significant in prior studies of shunt-dependent hydrocephalus after ICH and SAH, they were not included in our multiple logistic regression models.14,23

Discussion

In a cohort of 210 patients admitted to the NICU at CUMC with spontaneous ICH, 64 patients required placement of an EVD for the management of acute hydrocephalus. Within this group, we identified 2 independent predictors of shunt-dependent hydrocephalus: 1) patients with a thalamic ICH, and 2) those demonstrating persistently elevated ICP during their ICU stay. The effect of these factors on the odds of requiring permanent CSF diversion was independent of age, admission neurological status, or IVH volume. Miller and colleagues14 previously identified similar predictors in a comparable cohort of patients following ICH. The results of our analysis confirm the results of this prior study, suggesting that these factors are robust predictors of shunt dependency in patients with acute hydrocephalus from ICH. Furthermore, the rates of emergency CSF diversion via EVD placement and eventual VP shunt placement in these 2 series may serve as a reliable benchmark for future investigations into the clinical course of hydrocephalus.

Interestingly, development of shunt-dependent hydrocephalus was more likely in those patients with a thalamic hemorrhage, but independent of other hemorrhage locations or IVH volume, despite the fact that IVH is known to predict worse outcomes in patients with ICH in a volume-dependent manner.16,25 Given the anatomical relationship of thalamic hemorrhages to the third ventricle and the foramen of Monro, it is intuitive that hematoma formation in this location more easily results in obstruction of CSF flow independent of IVH volume than in hemorrhages occurring in other locations. Reports of thalamic cavernomas and hemorrhages without intraventricular extension have documented the development of
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Hydrocephalus.4,16,19,26,27 The pathophysiological mechanisms predisposing thalamic lesions to hydrocephalus remain unclear and are worthy of further investigation.

It remains unclear precisely how IVH contributes to the development of persistent hydrocephalus, although one hypothesis is that obstruction of the arachnoid villi by blood, a known factor in the development of acute hydrocephalus after IVH, may also contribute to the development of chronic hydrocephalus.5 In our cohort, however, we found no association between IVH volume and the development of shunt-dependent hydrocephalus. It is interesting to note the very high percentage of patients (> 90% for both those requiring VP shunt placement and those who did not) who had any amount of IVH on admission CT imaging. This tends to argue that, although IVH may be important in the development of acute hydrocephalus, continued obstruction of the arachnoid villi by blood products or subsequent scarring may be rare phenomena.

Persistently elevated ICP was also associated with an increased risk of shunt-dependent hydrocephalus in our cohort. Although increased ICP is generally accepted to be a predictor of poor outcome following ICH, controlling ICP via medical and surgical means may not necessarily improve outcomes or reduce the risk for chronic hydrocephalus.1,21 More specifically, our final model supports an association between elevated ICP, despite continued CSF diversion with an EVD, and an increased risk of progressing to shunt-dependent hydrocephalus. One explanation may be that following the onset of acute hydrocephalus, a subset of patients are prone to developing decreased ventricular compliance, poor CSF flow dynamics and reabsorption, or both, resulting in a continued need for CSF diversion. Given that the age range of our cohort is limited, the pathophysiological implications of age-related cerebral volume loss on the development of elevated ICP and shunt dependency are unclear. However, within the typical age range of most patients with ICH, there appears to be no association between age and the development of shunt-dependent hydrocephalus, as evidenced by our results.

Although our study includes a reasonably large co-

TABLE 1: Demographic, clinical, and radiographic characteristics in 64 patients with ICH treated with and without VP shunts*

<table>
<thead>
<tr>
<th>Variable</th>
<th>No VP Shunt</th>
<th>VP Shunt</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>51</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>age in yrs</td>
<td>60.1 ± 16.1</td>
<td>61.46 ± 10.1</td>
<td>0.707</td>
</tr>
<tr>
<td>admission GCS score</td>
<td>7 (IQR 5–13)</td>
<td>7 (IQR 5–9)</td>
<td>0.663</td>
</tr>
<tr>
<td>ventriculitis</td>
<td>7 (13.7%)</td>
<td>3 (23.1%)</td>
<td>0.411</td>
</tr>
<tr>
<td>lat ventricular blood</td>
<td>46 (90.2%)</td>
<td>12 (92.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>3rd ventricle &gt;50%†</td>
<td>33 (64.7%)</td>
<td>7 (53.8%)</td>
<td>0.688</td>
</tr>
<tr>
<td>4th ventricle &gt;50%†</td>
<td>31 (60.8%)</td>
<td>8 (61.5%)</td>
<td>0.788</td>
</tr>
<tr>
<td>multiple ventricles &gt;50%</td>
<td>32 (62.7%)</td>
<td>7 (53.8%)</td>
<td>0.788</td>
</tr>
<tr>
<td>max ICP</td>
<td>22 (IQR 18–28)</td>
<td>30 (IQR 27–33)</td>
<td>0.013</td>
</tr>
<tr>
<td>max ICP ≥25 mm Hg</td>
<td>21 (41.2%)</td>
<td>10 (76.9%)</td>
<td>0.030</td>
</tr>
<tr>
<td>ICP ≥20 mm Hg on ≥2 days</td>
<td>26 (51.0%)</td>
<td>11 (84.6%)</td>
<td>0.033</td>
</tr>
<tr>
<td>ICH location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>thalamic</td>
<td>14 (27.5%)</td>
<td>9 (69.2%)</td>
<td>0.008</td>
</tr>
<tr>
<td>basal ganglia</td>
<td>11 (21.6%)</td>
<td>2 (15.4%)</td>
<td>1.000</td>
</tr>
<tr>
<td>cortical</td>
<td>15 (29.4%)</td>
<td>1 (7.7%)</td>
<td>0.157</td>
</tr>
<tr>
<td>cerebellum</td>
<td>9 (17.6%)</td>
<td>1 (7.7%)</td>
<td>0.672</td>
</tr>
<tr>
<td>brainstem</td>
<td>1 (2.0%)</td>
<td>0 (0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>subcortical white matter</td>
<td>1 (2.0%)</td>
<td>0 (0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>ICH score</td>
<td>3 (IQR 2–3)</td>
<td>2 (IQR 2–3)</td>
<td>0.302</td>
</tr>
<tr>
<td>Graeb score</td>
<td>7 (IQR 4–8.5)</td>
<td>6 (IQR 5–7)</td>
<td>0.769</td>
</tr>
<tr>
<td>LeRoux score</td>
<td>10 (IQR 5–11)</td>
<td>9 (IQR 6–10)</td>
<td>0.688</td>
</tr>
<tr>
<td>hydrocephalus</td>
<td>37 (72.5%)</td>
<td>11 (84.6%)</td>
<td>0.489</td>
</tr>
<tr>
<td>bicaudate index</td>
<td>0.18 ± 0.07</td>
<td>0.21 ± 0.06</td>
<td>0.290</td>
</tr>
<tr>
<td>ICH vol in cm³</td>
<td>11.6 (IQR 3.4–30.5)</td>
<td>13.7 (IQR 6.2–17.0)</td>
<td>0.854</td>
</tr>
<tr>
<td>rtPA</td>
<td>9 (17.6%)</td>
<td>1 (7.7%)</td>
<td>0.672</td>
</tr>
<tr>
<td>days w/ EVD</td>
<td>8 (IQR 5–11)</td>
<td>14 (IQR 12–15)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Data are presented as the mean ± SD; median (IQR); or number (%). Abbreviations: IQR = interquartile range; max = maximum.
† The entries “3rd ventricle >50%” and “4th ventricle >50%” refer to hemorrhage obstructing > 50% of the volume of the respective ventricles on admission CT scans.
short of patients with primary ICH in whom adjudicated prospectively collected data were available, it has several limitations. First, there were relatively few patients (13 [20.3%] of 64) who reached the study end point of long-term shunt dependency requiring permanent CSF diversion. Second, our study is also potentially subject to survivor bias, in that within our cohort there was a subset of patients in whom care was ultimately withdrawn due to the patient’s or family’s wishes following EVD placement, but prior to establishing a requirement for permanent CSF diversion. It is possible that several of these patients may have eventually required VP shunt placement. Ultimately, additional tertiary care center studies may strengthen our benchmark data and elucidate other risk factors for persistent posthemorrhagic hydrocephalus. Future investigations using data from multimodality intracranial monitoring may provide greater insight into the pathophysiological mechanisms that underlie the development of shunt dependency.

Conclusions

The development of shunt-dependent hydrocephalus after ICH was associated in our cohort with thalamic location of the hemorrhage and persistently elevated ICP. This is in agreement with a prior study, and our results include the following. Conception and design: Zacharia, Vaughan. Acquisition of data: Vaughan, Carpenter. Analysis and interpretation of data: Zacharia, Vaughan, Bruce, Petersen, Deiner. Drafting the article: Vaughan. Critically revising the article: Zacharia, Hickman, Petersen, Deiner, Badjatia, Connolly. Reviewed submitted version of manuscript: Zacharia, Badjatia, Connolly. Approved the final version of the manuscript on behalf of all authors: Zacharia. Statistical analysis: Bruce, Petersen, Deiner. Administrative/technical/material support: Carpenter, Badjatia, Connolly. Study supervision: Zacharia, Hickman, Carpenter, Connolly.

References


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Author contributions to the study and manuscript preparation include the following. Conception and design: Zacharia, Vaughan. Acquisition of data: Vaughan, Carpenter. Analysis and interpretation of data: Zacharia, Vaughan, Bruce, Petersen, Deiner. Drafting the article: Vaughan. Critically revising the article: Zacharia, Hickman, Petersen, Deiner, Badjatia, Connolly. Reviewed submitted version of manuscript: Zacharia, Badjatia, Connolly. Approved the final version of the manuscript on behalf of all authors: Zacharia. Statistical analysis: Bruce, Petersen, Deiner. Administrative/technical/material support: Carpenter, Badjatia, Connolly. Study supervision: Zacharia, Hickman, Carpenter, Connolly.
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