Intracerebral Hemorrhage Volume Predicts Poor Neurologic Outcome in Children

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Background and Purpose—Although intracerebral hemorrhage (ICH) volume and location are important predictors of outcome in adults, few data exist in children.

Methods—A consecutive cohort of children, including full-term newborns to those younger than 18 years of age with nontraumatic, acute ICH and head CT available for analysis were studied. Clinical information was abstracted via chart review. Hemorrhage volume was expressed as percentage of total brain volume (TBV) with large hemorrhage defined as ≥4% of TBV. Hemorrhages were manually traced on each head CT slice and volumes were calculated by multiplying by slice thickness. Location was classified as supratentorial or infratentorial. Logistic regression was used to identify predictors of poor neurological outcome, defined as a Glasgow outcome scale ≤2 (death or persistent vegetative state).

Results—Thirty children were included, median age 6 years. Median ICH volume was 20.4 cm³ and median ICH size as a percentage of TBV was 1.9%. Only 4 of 22 children with ICH <4% of TBV had poor outcomes, vs 5 of 8 children with ICH ≥4% of TBV (P=0.03). In multivariate analysis, hemorrhage ≥4% of TBV (OR, 22.5; 95% CI, 1.4–354; P=0.03) independently predicted poor outcome 30 days after ICH. In this small sample, infratentorial hemorrhage location and the presence of intraventricular hemorrhage did not predict poor outcome.

Conclusions—ICH volume predicts neurological outcome at 30 days in children, with worst outcome when hemorrhage is ≥4% of TBV. Location and ICH etiology may also be important. These findings identify children with ICH who are candidates for aggressive management and may influence counseling regarding prognosis. (Stroke. 2009;40:1666-1671.)

Key Words: child • intracerebral hemorrhage • stroke

...Stroke is among the top 10 causes of death in children.1 2 In contrast to adults, approximately half of strokes in childhood are hemorrhagic.3 Because there are few studies of hemorrhagic stroke in children, physicians caring for these children struggle to give their families information on prognosis. Outcome after intracerebral (parenchymal) hemorrhage (ICH) in adults is closely tied to hemorrhage size. In a series of adult ICH, 30-day mortality was ≈90% if the size of the hemorrhage exceeded 60 cubic centimeters (cm³) and the Glasgow coma scale (GCS) was <9 at presentation, as compared to a 17% mortality with hemorrhage volume of <30 cm³ and a GCS of ≥9.4 These adult data on hemorrhage size and prognosis are used frequently in clinical decisions involving adult patients with ICH, and scores predicting mortality and good functional outcome have been developed using ICH volumes categorized as <30 cm³, 30 to 60 cm³, and >60 cm³.5 6 No previously published study has evaluated outcome in children as a function of ICH volume or, perhaps more importantly, ICH volume as a percentage of total brain volume. Unlike adult studies, outcome prediction after ICH in children must be tied to both ICH size and brain volume which varies markedly with the age of the child.

Hemorrhage location is presumably also important for prognosis. In adults, posterior fossa hemorrhage is a predictor of poor outcome.5 Small pediatric case series show that posterior fossa hemorrhage has been associated with fatal outcomes, but that overall prognosis, if the child survives, may be better than in adults.7 8 Other hemorrhage locations may be important as well, but to date, there has not been a large study assessing outcome and location of hemorrhage in children.

We hypothesized that neurological outcome would be worse in children with larger ICH and that certain locations of ICH, posterior fossa, and intraventricular hemorrhage would be associated with poor neurological outcome.

Materials and Methods

Study Setting

A convenience sample was collected from a single tertiary care center in Baltimore, Maryland, between 2001 and 2006; consecutive cases meeting inclusion criteria were included. The hospital serves a region with a broad range of socioeconomic and racial groups, but relative to the entire country it has a larger black and smaller Asian population.

Received October 29, 2008; final revision received December 5, 2008; accepted January 6, 2009.
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Stroke is available at http://stroke.ahajournals.org

DOI: 10.1161/STROKEAHA.108.541383
Case Identification
Cases were identified from a hospital discharge database by International Classification of Disease, 9th revision (ICD-9) code. Records were searched that included ICD-9 codes 431 (intracerebral hemorrhage) and 432.9 (unspecified intracranial hemorrhage). Charts were reviewed and abstracted by a single pediatric neurologist (L.C.J.). Inclusion criteria were: age younger than 18 years, acute spontaneous parenchymal hemorrhage with or without intraventricular hemorrhage (IVH), and head CT available for review. Exclusion criteria were: hemorrhage attributable to trauma, hemorrhagic conversion of ischemic stroke (ICH conforming to an arterial vascular distribution), epidural or subdural hematoma, and primary subarachnoid hemorrhage. Preterm infants younger than 37 weeks gestation and term infants with pure IVH were excluded because IVH in newborns is typically regarded as a distinct entity with a different pathophysiology, related to immaturity of the germinal matrix. Therefore, we excluded all preterm infants as well as cases of neonatal IVH (pure IVH, without ICH, occurring within the first 28 days of life).

Neurological status at presentation to the hospital was recorded. GCS at initial presentation for medical care was abstracted from the chart or, when not available, was assigned retrospectively if medical documentation of initial neurological status was present.9 Neurological outcome at 30 days and at the longest point of follow-up was recorded. The Glasgow outcome scale (GOS) was used, because more refined measures were not possible based on retrospective chart review.10 This study was approved by the institutional review board.

Data Analysis
All comparisons of proportions were analyzed using χ² tests, or Fisher exact tests when any expected frequency was <5. Absolute hemorrhage volume and hemorrhage as a percentage of total brain volume (TBV) were analyzed as both continuous and categorical variables. Descriptive statistics were used to look for nonlinear associations. In our primary analysis, multivariate logistic regression was used to determine independent predictors of poor neurological outcome in children with ICH; “poor outcome” was defined as a GOS of ≤2 (death or vegetative state). We chose to include GOS of 2 but not GOS of 3 (severe disability) as poor outcome because vegetative state at 30 days is more likely to be associated with poor long-term outcome; a child classified with severe disability still has the potential for significant recovery. In 1 study, the initial GOS, scored with 3 months of brain injury, was a reliable predictor of long-term outcome when initial GOS was 4 or 5, but not in patients with an initial GOS of 3.11 We selected covariates for the model through univariate screening including those with P≤0.10. A forward stepwise logistic regression model was constructed. We addressed potential confounders by first determining whether they were associated with both the predictor and outcome of interest, and then adjusting for them through both stratification and inclusion in multivariate models. As a posthoc analysis, we repeated these analyses after excluding children who had brain tumors as an underlying etiology. P<0.05 was considered statistically significant. STATA (version 9.0) was used to perform all statistical calculations.

Imaging Analysis for Hemorrhage and Brain Volume
Because radiology studies may be purged after 5 years at our institution, imaging data were only available from 2001 to 2006. Initial CT scans were analyzed via volumetric analysis using ImageJ software (http://rsb.info.nih.gov/ij/download.html). Hemorrhages were traced on each head CT slice and volumes were calculated by multiplying by slice thickness.4,12 Hemorrhage volumes were also expressed as a percentage of total brain volume (cerebral hemispheres, cerebellum, brain stem, and ventricles), as has been previously reported in pediatric ischemic stroke,5,14 to allow a better comparison between younger children and older children given the tripling of brain volume in this time period.13 Presence or absence of IVH was recorded. Hemorrhage size as a percentage of brain volume was categorized into 2 groups: large, ≥4% of TBV, which is approximately ≥75th percentile in this sample, and small, <4% of TBV. This value of 4% of brain volume is comparable to the 60-cm³ ICH volume in adults, assuming an average adult brain volume of 1500 cm³.

A single investigator performed image analysis on all 30 head CT (J.T.K.). A second blinded investigator repeated the analysis on a 20% sample of head CT (L.C.J.). Hemorrhage volumes and TBV varied little between investigators; the intraclass correlation coefficient for absolute hemorrhage volume was r=0.996, r=0.978 for brain volume, and r=0.996 for hemorrhage volume as a percentage of TBV.

Assessment of Hemorrhage Location
All head CT were reviewed and the location of hemorrhage was recorded. Presence or absence of IVH was also recorded. For the purposes of analysis, ICH location was classified as infratentorial (cerebellum and brain stem) or supratentorial.

Results
The ICD-9 code search identified 69 potential cases. After review of medical records 34 cases were excluded that were not spontaneous ICH (Figure 1), including 3 cases that were felt to represent hemorrhagic conversion of an infarct based on the arterial-distribution of the ICH. Of the remaining 35 cases, there was no head CT available for review in 5. No children were excluded because they were lost to follow-up before 30 days after ICH. Therefore, from 2001 to 2006, 30 children with spontaneous ICH met inclusion criteria (see supplemental Table 1 for information on individual cases, available online at http://stroke.ahajournals.org). Median age at the time of ICH was 6 years (range, 0–16 years; Table 1). The study population was 60% boys. The racial distribution was 67% white, 30% black, and 3% Hispanic. Median length of follow-up was 8.9 months (range, 1 day–3.7 years). An initial GCS was available for 70% of patients, 40% were scored prospectively, and 30% were scored retrospectively. Time-to-presentation data could be inferred from the medical records in 47% of children. Neurosurgical evacuation of the hemorrhage was performed in 8 children. A retrospective GOS could be determined at 30 days for 100% of patients, at 3 months for 90% of patients, and at 12 months for 53% of patients.
Median brain volume was 1189 cm³ (range, 457-1952 cm³).

CM³ (SD, 30.5), compared with children who survived, 21.9
median, 52.5
0.004% to 11.56% (median, 1.92%). The mean hemorrhage
19.8;

Race, N

Male, N 18 60%

Asian 1 3%

Time to presentation* 8.25 hr 1–96 hr

GCS at presentation* 14 3–15

ICH volume 20.4 cm³ 0.05–88.8 cm³

Total brain volume 1189 cm³ 457–1952 cm³

ICH volume as % of TBV 1.92% 0.004%–11.56%

Length of follow-up care 8.9 mo 1 day–3.7 yr

*Data not available for all 30 children; time-to-presentation, N = 14; GCS, N = 22.

Predisposing conditions for ICH were known for 14 of 30 children (Table 2). Evaluation for ICH etiology typically included a head CT, MRI, and MRA of the brain, and conventional cerebral angiography if a vascular malformation was suspected based on CT or MRI, or if there was no clear etiology for the hemorrhage. Blood tests for platelet count, prothrombin time, international normalized ratio, and partial thromboplastin time were performed on all children. Final risk factors or etiology for ICH are presented in Table 2. Hemorrhagic brain tumor, idiopathic ICH, and arteriovenous malformation were the most common reasons for parenchymal hemorrhage in this series of children. Seven children (23%) had idiopathic ICH; only 2 of these 7 children did not undergo both brain MRI/MRA and catheter cerebral angiography to carefully evaluate for ICH etiology. One of these children experienced tonsillar herniation and died within hours of presentation, so only CT was performed. The other child was 2 months old and had MRI/MRA only. Repeat catheter angiography was not performed in any of the children with idiopathic ICH.

**Hemorrhage Volume**

Median ICH volume was 20.4 cm³ (range, 0.05–88.8 cm³). Median brain volume was 1189 cm³ (range, 457–1952 cm³). Hemorrhage size as a percentage of TBV ranged from 0.004% to 11.56% (median, 1.92%). The mean hemorrhage volume was significantly larger in children who died, 52.5 cm³ (SD, 30.5), compared with children who survived, 21.9 cm³ (SD, 19.8; t = −2.89; P = 0.007). When hemorrhage as a percentage of TBV was analyzed categorically, in the small hemorrhage group 4 of 22 (18%) had poor outcomes (death or vegetative state) at 30 days. In the large hemorrhage group, 5 of 8 (62.5%) had poor outcomes (Fisher exact test, P = 0.03).

**Predictors of Poor Outcome**

Univariate logistic regression was performed to assess predictors of poor outcome (death or vegetative state) at 30 days after ICH (Table 3). Age younger than 1 year, gender, and presenting signs and symptoms, such as headache, emesis, seizure, focal deficit, altered mental status, and GCS <9, were not significant predictors. Imaging characteristics such as presence of hydrocephalus, IVH, infratentorial location, and bilateral hemorrhage also were not significant. Significant univariate predictors of poor outcome included black race (OR, 7.1; 95% CI, 1.2–42.8; P = 0.03), hemorrhage ≥4% of TBV (OR, 7.5; 95% CI, 1.2–45.1; P = 0.02), and ICH volume (per 10 cm³; OR, 1.6; 95% CI, 1.1–2.5; P = 0.02).

We used multivariate logistic regression to identify independent predictors of poor neurological outcome. We selected covariates for the model through univariate screening, including those with alpha ≥0.10. The variables included in the model were the significant univariate predictors mentioned plus presence of brain tumor as ICH etiology and age (as potential confounders). Our final model included race, ICH ≥4% of TBV, presence of brain tumor, and age. Age was analyzed as a continuous and dichotomous variable (age younger than 1 year compared with older children). Interactions were sought between age and race, age as a dichotomous variable (younger than 1 year) and hemorrhage category, and race and brain tumor. These interactions could not be assessed statistically given the small sample size. Among white infants, 0 of 4 had poor outcome; among non-white infants, 1 of 3 had poor outcome. Looking at age and hemorrhage category, 1 of 2 infants with large hemorrhage had poor outcome, whereas 4 of 6 older children with large hemorrhage had poor outcome.

Hemorrhage ≥4% of TBV was an independent predictor of poor neurological outcome (OR, 22.5; 95% CI, 1.4–354; P = 0.03). Black race was also associated with poor outcome (OR, 30.1; 95% CI, 1.7–504; P = 0.02). In our primary analysis, the independent variable, hemorrhage size as a percentage of TBV, was dichotomized to mirror adult studies in which ICH volume has been treated categorically. To confirm the association, we also looked at ICH volume as a continuous variable. Again, ICH volume significantly inde-
independently predicted poor outcome at 30 days (OR, 1.6; 95% CI, 1.1–2.4; P = 0.02) for every additional 10 cm$^3$ of hemorrhage volume, when adjusted for age.

**Mortality**

Thirty-day mortality was 16.7% (5/30 children). Extremely poor neurological outcome (GOS = 2) was seen in an additional 14%. In total, 9 of 30 children (30%) in our cohort had a poor outcome. There was not a significant difference in mortality for children with infratentorial vs supratentorial ICH, nor was there a gender difference in 30-day mortality. Black children had a higher mortality than white children (33% vs 5%; P = 0.01). On further investigation, 2 of 3 black children who died had hemorrhagic brain tumors; the other had sickle cell disease and cerebral sinovenous thrombosis.

In the entire group of children, cause of death was most often related to massive ICH (Table 4). One of the 5 children who died had a respiratory arrest related to aspiration pneumonia contracted after ICH and had a do-not-resuscitate order. One child died after ICH into a high-grade brain tumor; a cerebral herniation syndrome led to brain death from a combination of tumor edema and ICH. The other 3 children died from cerebral herniation after massive ICH. There were 5 children with recurrent ICH. Two had high-grade brain tumors that rebled; the other 3 had vascular lesions (1 child with untreated cavernoma, 1 child awaiting treatment for his arteriovenous malformation, and 1 child with a massive partially treated dural AV fistula, a few weeks after the first stage of embolization).

**Hemorrhage Location and Characteristics**

Twenty-six children (87%) had supratentorial hemorrhage, whereas 4 children (13%) had infratentorial hemorrhage. Twelve children (33%) had some intraventricular blood, whereas only 9 had hydrocephalus visible on head CT. Infratentorial location was not a significant predictor of poor outcome.

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**Table 3. Univariate Analysis of Predictors of Poor Outcome After Spontaneous ICH in Children**

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Good Outcome (N=21, n (%))</th>
<th>Poor Outcome (N=9, n (%))</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;1 yr</td>
<td>6 (86)</td>
<td>1 (14)</td>
<td>0.3</td>
<td>0.1–3.1</td>
<td>0.31</td>
</tr>
<tr>
<td>Male</td>
<td>8 (38)</td>
<td>4 (44)</td>
<td>1.3</td>
<td>0.3–6.3</td>
<td>0.75</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>17 (81)</td>
<td>3 (33)</td>
<td>7.1</td>
<td>1.2–42.8</td>
<td>0.03*</td>
</tr>
<tr>
<td>Black</td>
<td>4 (19)</td>
<td>5 (56)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0)</td>
<td>1 (11)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>6 (29)</td>
<td>3 (33)</td>
<td>1.5</td>
<td>0.2–6.7</td>
<td>0.79</td>
</tr>
<tr>
<td>Emesis</td>
<td>9 (42)</td>
<td>2 (22)</td>
<td>0.4</td>
<td>0.1–2.7</td>
<td>0.38</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>12 (57)</td>
<td>5 (55)</td>
<td>1.3</td>
<td>0.2–6.7</td>
<td>0.79</td>
</tr>
<tr>
<td>Focal deficit</td>
<td>11 (52)</td>
<td>1 (11)</td>
<td>0.1</td>
<td>0.1–1.1</td>
<td>0.06</td>
</tr>
<tr>
<td>Seizure</td>
<td>7 (44)</td>
<td>3 (33)</td>
<td>0.8</td>
<td>0.2–3.7</td>
<td>0.82</td>
</tr>
<tr>
<td>GCS &lt;9</td>
<td>2 (10)</td>
<td>2 (22)</td>
<td>0.4</td>
<td>0.1–3.1</td>
<td>0.36</td>
</tr>
<tr>
<td>Hemorrhage characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICH volume (per 10 cm$^3$)</td>
<td>NA</td>
<td>NA</td>
<td>1.6</td>
<td>1.1–2.5</td>
<td>0.02</td>
</tr>
<tr>
<td>ICH volume ≥4% TBV</td>
<td>3 (14)</td>
<td>5 (62)</td>
<td>7.5</td>
<td>1.2–45.1</td>
<td>0.03</td>
</tr>
<tr>
<td>IVH</td>
<td>7 (33)</td>
<td>5 (55)</td>
<td>2.5</td>
<td>0.5–12.3</td>
<td>0.26</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>5 (24)</td>
<td>4 (44)</td>
<td>2.6</td>
<td>0.4–12.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Infratentorial ICH</td>
<td>3 (14)</td>
<td>1 (11)</td>
<td>0.8</td>
<td>0.1–8.4</td>
<td>0.82</td>
</tr>
<tr>
<td>Bilateral ICH</td>
<td>4 (19)</td>
<td>3 (33)</td>
<td>2.1</td>
<td>0.4–12.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Surgical evacuation of ICH</td>
<td>4 (19)</td>
<td>4 (44)</td>
<td>3.4</td>
<td>0.6–18.7</td>
<td>0.16</td>
</tr>
<tr>
<td>Abnormal coagulation</td>
<td>4 (19)</td>
<td>2 (22)</td>
<td>1.1</td>
<td>0.2–7.7</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*Overall P for race categories.

**Table 4. Cause of Death After Spontaneous ICH in Children (N=5)**

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>ICH Location</th>
<th>ICH Volume, cm$^3$</th>
<th>ICH % of Brain Volume, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH, herniation syndrome</td>
<td>Left frontal, parietal</td>
<td>88.8</td>
<td>7.6</td>
</tr>
<tr>
<td>ICH, herniation syndrome</td>
<td>Bilfrontal</td>
<td>64.8</td>
<td>4.5</td>
</tr>
<tr>
<td>ICH, herniation syndrome</td>
<td>Right temporal, parietal</td>
<td>64.1</td>
<td>4.5</td>
</tr>
<tr>
<td>Respiratory arrest*</td>
<td>Right cerebellum</td>
<td>35.1</td>
<td>2.4</td>
</tr>
<tr>
<td>Tumor, ICH, herniation syndrome</td>
<td>Left frontal</td>
<td>9.8</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Do-not-resuscitate order after ICH.
outcome (OR, 0.75; 95% CI, 0.1–8.4; \( P=0.82 \)), perhaps because 2 of the 4 infratentorial ICH were attributable to small volume hemorrhage from cavernous hemangiomas. IVH was also not a significant predictor of poor outcome (OR, 2.5; 95% CI, 0.5–12.3; \( P=0.26 \)).

**Excluding Children With Brain Tumor**

Our goal was to study all children with spontaneous nontraumatic ICH; however, we recognize that children with a hemorrhagic brain tumor may be considered a special population in terms of outcome. We repeated our analysis excluding the 8 children with brain tumor. Of the 22 remaining children, results were very similar to the larger group. Median age was 7.5 years, median ICH volume was 22.7 cm\(^3\) (range, 0.05–88.8 cm\(^3\)), and median hemorrhage volume as a percentage of brain volume was 2.26% (range, 0.004%–11.56%). Mortality was 3 of 22 children (13.6%). No child with a hemorrhage volume <4% of brain volume died (0/16) and half of children with hemorrhage volume ≥4% of brain volume (3/6) died (Fisher exact test, \( P=0.01 \)). Children who died had a mean ICH volume of 72.6 cm\(^3\) (SD, 14.0), whereas children who survived had a mean ICH volume of 20.8 cm\(^3\) (SD, 19.4; \( P=0.0003; t = -4.93 \)). Using multivariate logistic regression, only hemorrhage volume ≥4% of brain volume independently predicted poor outcome (OR, 35.8; 95% CI, 1.4–891), adjusted for age. Black race was not a significant predictor of poor outcome.

**Discussion**

Volume of ICH, as well as ICH expressed as a percentage of TBV, are strong predictors of 30-day poor outcome, defined as death or vegetative state, in children. These data echo the findings of a classic adult study\(^4\) of ICH that reported that mortality was >90% if ICH volume was ≥60 cm\(^3\) and initial GCS was <9. Because a 60-cm\(^3\) hemorrhage is approximately equivalent to 4% of brain volume in an adult, a hemorrhage volume ≥4% of intracranial volume is a logical predictor of poor neurological outcome in children.

Black children have been found to be at higher risk for all stroke subtypes, including intracerebral hemorrhage; however, race did not predict case fatality or stroke severity.\(^5\) In our study, black race was associated with poor neurological outcome; however, because of small sample size, we were unable to adjust well for a number of potential confounders and interactions could not be well-evaluated statistically. When children with brain tumors were excluded, however, race was no longer associated with poor outcome. There may be other unmeasured confounders of the relationship between race and outcome. Time to presentation for medical care after ICH was only available for 47% of our sample, but the median time to presentation was 4 hours (range, 1–96 hours) in white children and 61 hours (range, 4–96 hours) in black children, suggesting difficulties with access to care. The relationship between race and neurological outcome after ICH deserves further study.

Infants seemed to do well after ICH (Table 3), with only 1 of 7 children younger than 1 year of age classified as having a poor outcome, compared with 8 of 23 older children with poor outcome; this was not statistically significant. Although our study did not have the sample size to adequately assess interaction between age and hemorrhage size on neurological outcome, the fact that 1 of 2 infants with large hemorrhage had poor outcome compared with 4 of 6 older children with large hemorrhage is suggestive of an interaction. One reason for such an interaction is the presence of an open fontanel may be protective, particularly for very large ICH volume, because it may minimize the consequences of elevated intracranial pressure. For example, the infant shown in Figure 2 had a good outcome, despite an ICH that was >10% of brain volume. Another infant had a cerebellar hemorrhage that was ∼6% of brain volume and had a good outcome. Because duration of follow-up in this cohort is limited and retrospective, long-term outcomes in infants may be worse than reported.

More than half of children in this study had no known risk factors for ICH at the time of presentation. Together, brain vascular malformations and brain tumors accounted for ∼50% of ICH in children in this series from a tertiary center. Arteriovenous malformations were all new diagnoses at the time of ICH, whereas most brain tumors were known. Despite a thorough medical evaluation including vascular imaging, ∼25% of pediatric ICH remained idiopathic; this finding is in line with previous studies: 2 conducted at pediatric referral centers\(^6,16\) and 1 that was population-based.\(^17\) The heterogeneous nature of pediatric ICH is emphasized by the diverse list of etiologies and risk factors in Table 2.

Children with ICH and brain tumor were included in our primary analysis, because child neurologists are often asked to comment on the morbidity related to ICH, even in children with known brain tumor. There are few data regarding the incidence of ICH in children with cancer. In 1 case series, brain tumors accounted for as many as 13% of ICH in children.\(^15\) In our secondary analysis, when children with
brain tumor where excluded, hemorrhage as a percentage of TBV was a strong predictor of outcome.

The major limitations of this study are the retrospective single-center design and the fact that it included only a small number of patients. A study population that is not population-based, but rather a convenience sample, has the potential for referral bias. ICD-9 code searches have been shown to miss cases in pediatric arterial ischemic stroke and cerebral sinovenous thrombosis.18,19 It is likely that some cases of pediatric ICH were missed via ICD-9 code search in this study.

The study depended on chart review for the measurement of most predictors and outcome. The fact that presenting signs and symptoms including focal deficit, altered mental status, and GCS <9 were not significant predictors of poor clinical outcome may be attributable to study limitations, particularly small sample size. Additionally, the retrospective design and the inclusion of children with brain tumor may affect the predictive value of signs and symptoms in our study.

A limiting factor at our institution was the fact that radiology images were available retrospectively for relatively only a few years, reducing the number of cases available for review. Strengths of this study, however, are the careful review and analysis of all head CT.

The retrospective nature of the study necessarily limited the duration of follow-up and outcome measures that could be used. The GOS is a validated scale in adults and has been used to study outcome after ICH.6 The GOS has also been used in pediatric studies of brain injury.20 In a prospective study, we would use a more detailed, well-validated instrument such as the pediatric stroke outcome measure21 and follow-up children for a longer period of time. Despite the short duration of follow-up, recurrent hemorrhages were seen in 5 of 30 children, this finding is in keeping with published literature17; the risk of recurrent hemorrhage in children is highest in those with structural lesions, and children with idiopathic ICH did not recur.

It is unlikely that these limitations affected the measurement of our primary predictor of outcome, ICH volume. Likewise, chart review should not significantly impact the ascertainment of our primary outcome, death, or vegetative state at 30 days. This category of extremely poor outcome is clear. Therefore, our major conclusion is minimally affected by study limitations.

Summary

ICH volume predicts neurological outcome at 30 days post- hemorrhage in children. The odds of poor outcome increase significantly for every 10 cm$^3$ of additional hemorrhage volume and for hemorrhage ≥4% of brain volume. In this small series, infratentorial location of ICH and the presence of IVH did not predict poor outcome. Our results show which children are at the highest risk for serious morbidity and mortality after nontraumatic ICH. These findings identify children who are candidates for aggressive management and may influence counseling provided to families regarding prognosis. Further study in a larger, prospective cohort is indicated.

Disclosures

None.

Source of Funding

L.C.J. received funding from K12 NCCR017627 and K23NS062110.

References

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Lori C. Jordan, Jonathan T. Kleinman and Argye E. Hillis

Stroke. 2009;40:1666-1671; originally published online March 12, 2009;
doi: 10.1161/STROKEAHA.108.541383
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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