Intracranial Hemorrhage in Children
An Evolving Spectrum

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Background: Nontraumatic intracranial hemorrhages (ICHs) are uncommon in children, but are important causes of death and injury.

Objectives: To determine whether the risk factors for ICH have changed compared with those in earlier published series and to estimate the residual deficits in the survivors.

Design, Setting, and Patients: We performed a retrospective review of patients admitted to a single tertiary care, academic pediatric hospital from January 1, 2000, through May 31, 2007. Records were retrieved if the diagnostic codes from the International Classification of Diseases, Ninth Revision, were pertinent to ICHs. We searched reports from computed tomograms and magnetic resonance images of the brain for terms pertaining to ICH.

Main Outcome Measures: Risk factors and functional outcome. Secondary measures were hemorrhage type and clinical presentation.

Results: We identified 85 children who had nontraumatic ICH. There were 10 subarachnoid, 61 intracerebral, and 14 subdural hemorrhages. Intracranial vascular anomalies were the most frequent risk factor, followed by congenital heart disease and brain tumors. Arteriovenous malformations did not account for as large a percentage as in previous studies. Twenty-nine children died. Of the 48 survivors for whom follow-up information was available, 26 had no reported deficits and 22 had deficits ranging from mild to severe.

Conclusions: In this series, brain tumors and congenital heart disease accounted for a greater proportion of ICHs than in previous studies. The mortality due to ICH remains high but may be related as much to the severity of the underlying illnesses as to the hemorrhage itself. We found significant long-term morbidity, but more than half of the survivors for whom follow-up data were available had no detectable deficits. A long-term outcome study of pediatric ICH is needed.

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METHODS

We performed a retrospective analysis of patients who were admitted to the Nationwide Children’s Hospital from January 1, 2000, through May 31, 2007. We selected this interval because magnetic resonance angiography became readily available at this institution in 2000 and because radiology reports could be easily reviewed online to confirm the clinical report of ICH. Hospital records were retrieved according to coding from the International Classification of Diseases, Ninth Revision (ICD-9). We searched records that included the ICD-9 codes 228.02 (hemangioma of intracranial structures), 430 (subarachnoid hemorrhage), 431 (intracerebral hemorrhage), 432.0 (nontraumatic extra-
We performed χ² analysis and post hoc testing using commercially available software (SPSS; SPSS Inc, Chicago, Illinois). This study was approved by the institutional review board for human research.

### BASIC DEMOGRAPHICS

We identified 85 children who had sustained a nontraumatic ICH, including 54 boys and 31 girls (sex ratio, 1.7:1). Among these children, 67 were white; 10, African American; 1, Southeast Asian; 1, Asian Indian; 1, other ethnicity; and 5, unknown ethnicity. The home counties of the children mirrored the referral patterns of the hospital, with 41 children coming from urban or contiguous counties, 42 from rural counties, and 2 from another state. The median age at presentation was 7 years (range, 7 days to 17 years); however, there was a distinct skew toward younger ages, with 27 children 2 years or younger. The median length of hospital stay was 13 days, with a range from 0 (ie, patients who survived <1 day) to 260 days.

### TYPES AND LOCATIONS OF HEMORRHAGES

The cases were classified according to the location of the predominant hemorrhage. There were 10 subarachnoid hemorrhages, 61 intraparenchymal hemorrhages, and 14 subdural hemorrhages. The term intraparenchymal includes hemorrhages within the brain and those that extend into the ventricles. The intraparenchymal hemorrhages varied in location; 50 were supratentorial and 11 were infratentorial. Of the supratentorial hemorrhages, 7 were predominantly intraventricular, 33 were lobar, 4 involved the white matter, and 9 primarily involved the basal ganglia or thalami. (Some of the supratentorial hemorrhages involved more than 1 region.) All 14 subdural hemorrhages were supratentorial, and the origin of all 10 subarachnoid hemorrhages was supratentorial. A mixed pattern of hemorrhage occurred in a number of children. For example, hemorrhage extended into the ventricles or parenchyma in 3 children with subarachnoid hemorrhage. Hemorrhage extended to the subarachnoid or subdural spaces or to the ventricles in 20 children with intraparenchymal hemorrhage.

### CLINICAL PRESENTATION

For each patient, 3 signs and symptoms at presentation were tabulated and then condensed into similar categories. The presentations varied with the age of the child (Table 1); in the 34 children 6 years or younger, the clinical presentations were often nonspecific, such as mental status changes, seizures, and vomiting. In the 51 children 6 years or older, headache, mental status changes, focal neurological deficits, and nausea/vomiting were the most common clinical signs. Blood pressure was elevated above the 90th percentile in 38 children (45%) at presentation.

<table>
<thead>
<tr>
<th>Table 1. Clinical Presentations in Children</th>
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<tbody>
<tr>
<td>Presenting Sign</td>
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<td>-----------------</td>
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<tr>
<td><strong>Age &lt;6 y (n=34)</strong></td>
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<tr>
<td>Mental status changes</td>
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<tr>
<td>Convulsions</td>
</tr>
<tr>
<td>Vomiting</td>
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<tr>
<td>Respiratory distress</td>
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<tr>
<td>Decreased movement/weakness</td>
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<tr>
<td><strong>Age ≥6 y (n=51)</strong></td>
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<tr>
<td>Headache</td>
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<tr>
<td>Mental status changes</td>
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<tr>
<td>Focal neurological deficits</td>
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<tr>
<td>Nausea or vomiting</td>
</tr>
<tr>
<td>Convulsions</td>
</tr>
<tr>
<td>Miscellaneousb</td>
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*Some children had more than 1 of these signs. 

b Includes dysphasia, fever, dizziness, stomach, neck or ear pain, bradycardia, respiratory arrest, and abnormal gait.
RISK FACTORS

The most common risk factors for any type of ICH were intracranial vascular anomalies (n = 24), congenital heart disease (n = 14), and brain tumors (n = 13) (Table 2). Of the intracranial vascular anomalies, AVMs accounted for the largest number of hemorrhages. Several children had multiple risk factors. For example, a number of children who had congenital heart disease died of sepsis. Many children who had sepsis, leukemia, or other systemic diseases had thrombocytopenia, and 1 child who had leukemia had undergone thrombolysis with tissue plasminogen activator. In 13 patients, no cause could be identified; some of these children died so soon after presentation that, if they had survived longer, a more complete evaluation might have identified a cause.

When we analyzed risk factors according to the location of the predominant hemorrhage, 2 patterns appeared. Intraparenchymal hemorrhages were predominantly associated with brain tumors, intracranial vascular anomalies, and cases in which no risk factor could be identified. Subdural hemorrhages occurred predominantly in children who had clotting factor deficiencies or who had undergone surgical repair of congenital heart defects. Most of the children who presented after surgery had undergone cardiac bypass or concomitant anticoagulation therapy. Subarachnoid hemorrhages were not linked to any single risk factor.

OUTCOMES

The individuals in this series had significant mortality. Twenty-nine of the 85 patients (34%) died. The median time to death was 1 month (range, 0-47 months after the hemorrhage). In 8 children, the hemorrhage was followed by acute herniation (4 cerebellar and 4 transtentorial or uncal). In 12 children, the hemorrhage occurred with overwhelming systemic disease (ie, sepsis, inborn error of metabolism, or cardiopulmonary arrest). Thirteen died of the underlying disease well after the hemorrhage occurred. Four children with brain tumors, for example, survived the hemorrhage only to die 1 to 3 years later.

Follow-up information was available in 48 of the 56 surviving children. The median time of follow-up was 25 months after the hemorrhage (range, 1-83 months). The median age at the last recorded follow-up visit was 10.5 years (range, 0.1-20.6 years). Of the 48 survivors who had follow-up information, 26 had no documented deficits. The remaining children had a broad range of deficits. Poor outcomes (defined as a PSOM score ≥5) occurred in 5 children, 1 each of whom had an AVM, herpes encephalitis, a brain tumor, Down syndrome, and factor XII deficiency with obstructive hydrocephalus. Follow-up blood pressures were available in 22 children and were elevated in 3. However, hypertension was not believed to be the cause of the hemorrhage in any of these children, and none were treated for hypertension at the time of follow-up.

To analyze the effect of different risk factors on outcome, we pooled cases into the 4 categories of intracranial vascular anomaly, malignancy (systemic and brain), congenital heart disease, and other (including sepsis, coagulopathy, and genetic syndromes). Outcomes were categorized as good or poor (PSOM score ≥5 or death). The groups were significantly different (Table 3), mainly because of the better outcome of the individuals with intracranial vascular anomalies compared with the other 3 categories.

A striking variation was noted between the ICD-9 coding documented in the records and the clinical diagnosis resulting from a review of the actual record. In 211 of 309 records reviewed (68%), the ICD-9 codes were inconsistent with the clinical diagnosis of the case. The most frequent differences occurred in the coding of traumatic hemorrhages as nontraumatic hemorrhages and in the coding of neonatal intraventricular hemorrhage as intracerebral hemorrhage. A small number of cases were clearly miscoded (eg, 1 case of intractable epilepsy was miscoded as intracerebral hemorrhage).
A key finding of this retrospective cohort study is that the relative frequency of risk factors differs from that of earlier reports (Table 4). In the present study, a greater proportion of children had brain tumors, congenital heart disease, or childhood malignancies than in previous reports. One possible explanation is that, as the management of these illnesses improves, we may be observing hemorrhages in a cohort of patients who would not have survived long enough to have been included in earlier series. As more complex procedures are performed such as extracorporeal membrane oxygenation, cardiac transplantation, and infusion of thrombolytic agents to open occluded catheters, there may be more complications in the management of these conditions.

It is possible that the risk factor profile of this series is unique to the institution and simply reflects referral bias. A recent population-based study used a similar strategy to identify ICHs in children who were covered by a health maintenance organization from 1993 to 2003. That study reported a distribution of risk factors that was similar to those of previous reports in that most of the nontraumatic ICHs were caused by structural vascular lesions, whereas hemorrhages associated with brain tumors and congenital heart disease were uncommon. However, referral bias seems an unlikely explanation for our findings. There is no other pediatric hospital in the immediate service region of this hospital; thus, most children 16 years or younger who have an ICH will receive care at this institution. Furthermore, the hospital provides care for children from all socioeconomic levels, so there is less likely to be the selection bias of a population covered by a health maintenance organization.

Hypertension did not appear to be a common risk factor in this series. At initial evaluation, 49% of the patients were hypertensive; however, on follow-up examination, only 3 of 22 patients (14%) had elevated blood pressures, and none of these children needed treatment for their blood pressure. Although there is evidence that hypertension in children and adolescents is more common than generally thought, there was not a clear association between hypertension and ICH in this series, consistent with previous observations.

The mortality rate of this series is higher than that of most previous reports (Table 5). The higher mortality rate in our series appears to be owing to the presence of associated risk factors rather than to the hemorrhage itself. A larger proportion of patients in this series had conditions such as sepsis, malignancy, complex congenital heart disease, and other severe medical disorders. Furthermore, a number of patients had multiple risk factors. For example, of patients who died soon after the hemorrhage occurred, 6 had congenital heart defects complicated by sepsis, arrest, or multiple organ failure. Most of the subjects who died months after the hemorrhage occurred died of recurrent brain tumors or complications of congenital heart disease. In contrast, most of the children who had intracranial vascular anomalies survived.

Surviving children had a broad range of outcomes, but most of the survivors had no or relatively mild deficits, similar to the findings of previous reports. This finding should be interpreted cautiously because cognitive and behavior outcomes were extracted from clinic records. In the 1 report that examined cognitive or behavior outcomes in detail, almost half of the survivors had some degree of cognitive deficit, and 77% reported a decreased quality of life. It is possible that if cognition and behavior were assessed prospectively the outcomes in the present study might be poorer.

An important finding of this study was that the ICD-9 coding of discharge records differed substantially from the clinical interpretation of the same records. This difference is important for clinical researchers who use administrative databases to study pediatric stroke. Previous studies have identified inaccuracies in ICD-9 coding of arterial ischemic stroke and cerebral sinus venous thrombosis in children. The present study extends these observations to pediatric hemorrhagic stroke. Clinical researchers must be aware of these discrepancies in coding.
This study has limitations. Because the series of patients was collected at a single tertiary care, academic pediatric hospital, the findings may not be completely representative of the general population. Referral bias could have resulted in a disproportionately high number of children with brain tumors and congenital heart disease treated at this institution. Validation of these findings will require a larger, likely multicenter, study to determine the prevalence of pediatric ICH and associated risk factors. The outcome measures are also limited. We used a modified version of the PSOM to estimate the severity of deficits. The PSOM was developed to assess outcomes after ischemic stroke; however, no tools have been developed to measure outcomes after pediatric hemorrhagic stroke; therefore, we used the best available tool. As noted, cognitive and behavior deficits may be underestimated because they were not assessed systematically. A more comprehensive assessment of cognition and behavior might yield different results. Therefore, the proportion of children with a favorable outcome in this study may represent an overly optimistic estimate.

**CONCLUSIONS**

We report a higher frequency of complex chronic illnesses as risk factors for pediatric ICH than what was previously reported.1-12,28 The mortality due to pediatric ICH remains high, but the risk of death may reflect the underlying risk factors for ICH and not just the risk from the hemorrhage itself. More complete information about outcomes is needed if we are to develop effective treatments for hemorrhagic stroke and to better understand the abnormal behavior, cognition, and social function that often remain after a hemorrhagic stroke. As has been noted in a recent review of pediatric hemorrhagic stroke,32 a prospective study is warranted to determine the prevalence of risk factors and the functional outcomes of pediatric ICH. Finally, investigators who use ICD-9 codes to study pediatric stroke should be aware of the limitations regarding the coding of ICHs in children.

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Author Contributions: Study concept and design: Lo and Roach. Acquisition of data: Lee, Rusin, and Perkins. Analysis and interpretation of data: Lo and Roach. Drafting of the manuscript: Lo and Lee. Critical revision of the manuscript for important intellectual content: Lo, Rusin, Perkins, and Roach. Administrative, technical, and material support: Lee, Perkins, and Roach. Study supervision: Lo.

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