ABC/XYZ Estimates Intracerebral Hemorrhage Volume as a Percent of Total Brain Volume in Children

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Background and Purpose—Intracerebral hemorrhage volume (ICHV) as a percentage of total brain volume (TBV) is a strong predictor of outcome in childhood intracerebral hemorrhage with ICHV/TBV >2% associated with functional impairment. We aimed to determine whether easily performed approximations of intracerebral hemorrhage and brain volume can accurately and reliably stratify intracerebral hemorrhage by size.

Methods—CT scans of 18 children with spontaneous intracerebral hemorrhage were independently reviewed by 4 neurologists. ICHV as a proportion of TBV was estimated as ABC/XYZ expressed as a percentage: A = largest axial hemorrhage diameter; B = largest axial diameter perpendicular to A on the same slice; and C = hemorrhage vertical diameter. Similarly, X = largest midline axial diameter of supratentorial brain; Y = largest axial diameter perpendicular to X; and Z = brain vertical diameter. Interrater reliability was measured with intraclass correlation coefficients. ICHV and TBV were measured using computer-assisted manual segmentation tracings to establish criterion validity. Each intracerebral hemorrhage was classified as small (<2% TBV) or large (>2% TBV).

Results—Estimates of ICHV, TBV, and ICHV/TBV using the ABC/XYZ method had outstanding interrater reliability (intraclass correlation coefficient, 0.95 to 0.99). These estimates were highly correlated with volumetric measures ($R^2$ = 0.77 to 0.96). Sensitivity of the ABC/XYZ method for identifying an ICHV >2% TBV was 100% (95% CI, 89% to 100%). Specificity was 95% (95% CI, 83% to 99%).

Conclusions—The ABC/XYZ method accurately and reliably estimates ICHV and TBV in children. These values can be used to approximate quickly and easily ICHV as a percentage of TBV, which has important prognostic implications.

Key Words: hemorrhage volume ■ intracerebral hemorrhage ■ pediatric

The volume of intracerebral hemorrhage (ICH) is well established as a predictor of outcome in adults.1–3 In children, ICH volume (ICHV) also predicts short-term outcome, although it must be adjusted for the total brain volume (TBV) to account for the varying head sizes during development.4,5 For research purposes, ICHV and TBV measurements have used manual segmentation tracing, which can take up to several hours per patient. A more clinically useful technique would allow treating physicians of different training levels to assess rapidly and easily ICHV as a percent of TBV in the acute hospital setting with good reliability and accuracy. The elliptical approximation method ABC/2 has been successfully used to estimate ICHV in adults.6,7 We sought to assess the reliability and validity of a similar formula to estimate both ICHV and TBV in pediatric ICH.
neurologist (S.R.M.), one pediatric stroke fellow (L.A.B.), and one adult neurology resident (M.T.M.). The size of the intraparenchymal ICH was estimated by ABC/2, in which A was defined as the largest axial diameter of the hemorrhage evident on any slice, B was the largest axial diameter perpendicular to A on the same slice, and C was the vertical diameter (slice thickness multiplied by number of slices where hemorrhage was visible) as previously described by Broderick et al. Similarly, TBV was estimated by XYZ/2, in which X was defined as the largest anteroposterior diameter of the supratentorial brain, Y as the largest axial diameter perpendicular to X, and Z as the vertical diameter (slice thickness multiplied by number of slices from foramen magnum to vertex). ICH volume was then expressed as a proportion of TBV by the formula (ABC/2)/XYZ, which reduces to ABC/XYZ and was then expressed as a percentage. A representative example of one patient’s ABC/2 and XYZ/2 measurements is depicted in Figure 1, top panel and bottom panel, respectively.

Manual segmentation tracing to assess ICHV and TBV was performed on all CT images by a single rater (L.A.B.) using a computer program, ITK-SNAP, that is available online (www.itksnap.org). Similar techniques have been used reliably in both childhood ICH and in measurements of pediatric brain structures. On segmentation imaging, TBV included the cerebral hemispheres, cerebellum, and brain stem. Intraventricular hemorrhage volume was not included in the ICH volume measurements, and ventricular volume was not included in the TBV measurements. Values obtained by manual segmentation tracing were considered the reference criterion.

All measurements performed by both ABC/XYZ and manual segmentation were categorized as small if ICH/TBV was <2% or as large if ICH/TBV was >2%. The threshold of 2% was chosen based on the observation that 30 mL in adult ICH is an important and validated ICHV threshold for predicting outcome. An ICHV of 30 mL represents approximately 2% of the TBV of an average adult brain of approximately 1400 mL. In addition, hemorrhages >2% TBV are associated with functional impairment in childhood ICH.

Statistical Analysis
Statistical analysis was performed using STATA Version 10.0 (Stata Corp, College Station, Texas). Interrater reliability was measured with intraclass correlation coefficients (ICCs) with the use of analysis of variance. An ICC of 1 demonstrates perfect reliability, and an ICC >0.8 represents excellent reliability. Criterion validity was established by comparison of estimated values by ABC/XYZ relative to those obtained with computer-assisted manual segmentation volume measurements. Wilcoxon signed rank tests were used to determine whether the estimated and reference measurements differed significantly. Linear regression was performed to determine the correlation of the estimated measures with the volumetric measures clustered by patient because the 4 estimations for each subject were not independent; the parameter $R^2$ was reported as the result. For sensitivity and specificity, hemorrhages were dichotomized as either small (≤2% TBV) or large (>2% TBV). Sensitivity and specificity for detecting large ICHs were calculated along with their 95% binomial CIs.

Results
Head CT scans from 18 pediatric patients, median age 9.5 years (range, 4.5 months to 16.6 years), were evaluated. The head CT scans were performed at a median of 9.6 hours (interquartile range [IQR], 2.3 to 24 hours) from symptom onset. Causes of ICH were arteriovenous malformation in 10, cavernoma in 3, aneurysm in 1, hematologic abnormality in 2, and unknown in 2. Hemorrhage locations were frontal in 8, temporal in 3, parietal in 3, frontotemporal in 1, occipital in 1, basal ganglia in 1, and thalamic in 1. Using computer-assisted manual segmentation volumetric measurements, median ICHV was 23 mL (IQR, 4 to 37 mL), median TBV was 1286 mL (IQR, 1188 to 1343 mL), and median ICHV/TBV was 1.6% (IQR, 0.3% to 2.8%). Using the ABC/XYZ estimation, median ICHV was 23 mL (IQR, 5 to 38 mL), median TBV was 1192 mL (IQR, 1030 to 1296 mL), and median ICHV/TBV was 1.8% (IQR, 0.4% to 3.0%).

Reliability of the ABC/2, XYZ/2, and ABC/XYZ measurements was high. The ICC for the estimation of ICH volume by the ABC/2 method was 0.99 (95% CI, 0.99 to 1.0). The ICC for TBV by XYZ/2 was 0.95 (95% CI, 0.92 to 0.99). The ICC for the estimation of ICHV expressed as a proportion of TBV by the equation ABC/XYZ was 0.99 (95% CI, 0.99 to 1.0).
There was no difference in the estimates of ICHV by ABC/2 compared with volumetric measurements (median difference 0 mL [IQR, −1 to 1 mL]; P=0.62 by signed rank test), but the XYZ/2 method underestimated the TBV by a median of 91 mL (IQR, 32 to 145 mL; P<0.001 signed rank test). The net impact was a small but statistically significant difference in the ICHV/TBV (median difference 0.1% [IQR, 0.0 to 0.3%]; P=0.0005). In regression analysis, the $R^2$ for the ABC/2 approximation and volumetric ICHV measurement was 0.97 (P<0.001; Figure 2A). The $R^2$ for XYZ/2 and volumetric TBV analysis was 0.77 (P<0.001; Figure 2B). The $R^2$ for ABC/XYZ and volumetric analysis of ICHV as a proportion of TBV was 0.96 (P<0.001; Figure 2C).

Using the reference criterion, ICHV/TBV was ≤2% in 10 patients, >2% to 4% in 6 patients, and >4% in 2 patients. When ABC/XYZ was dichotomized as ≤2% versus >2%, 70 of 72 measurements (18 ICHs×4 raters) were classified correctly compared with the reference criterion. The sensitivity of the ABC/XYZ method for identifying an ICH that was >2% of TBV was 100% (95% binomial CI, 89% to 100%), and specificity was 95% (95% binomial CI, 83% to 99%).

**Discussion**

This study demonstrates that the elliptical approximation method ABC/XYZ may be used to estimate ICH volume as a proportion of total brain volume in children with excellent reliability and validity. The XYZ/2 approach tends to underestimate TBV compared with volumetric measurements, presumably because the pediatric brain is not truly elliptical. This limitation could result in overestimation and misclassification of some small hemorrhages as large, particularly those just below the 2% ratio. The net effect is that the ABC/XYZ method maximizes sensitivity with minimal loss of specificity at the 2% threshold. Nevertheless, despite this potential pitfall, 70 of 72 categorizations were correct.

Several other limitations of the ABC/XYZ method should be noted. In several adult studies, the ABC/2 method for hemorrhage volume measurement has been shown to overestimate hemorrhage volume for both irregularly shaped hemorrhages and for large hemorrhages.10–12 With 18 subjects, subanalyses of the effect of various hemorrhage shapes or of various hemorrhage sizes could not be performed. Additionally, this method was not tested in patients with ICH due to brain tumors. The ABC/XYZ equation might not work as well in this setting because it can be difficult to differentiate hemorrhage from underlying tumor in some cases. Furthermore, this method was not tested in patients with hemorrhagic transformation of arterial ischemic stroke; hemorrhagic transformation of cerebral sinus venous thrombosis; or primary intraventricular, subarachnoid, or epidural hemorrhage. The ABC/XYZ method may not be valid for these hemorrhages because their shapes are often more irregular and depart from true ellipses.

Despite the potential limitations of this method, the calculation of ABC/XYZ is easily performed in just minutes using measurement tools available in standard image-viewing software and a calculator and can be implemented by raters of different experience with minimal training. Until now, there has been no accurate method to evaluate hemorrhage size as a percent of total brain volume quickly in the acute setting. Therefore, information of critical prognostic value has been unavailable to clinicians and parents. The ABC/XYZ formula will be useful to clinicians both for predicting outcome in the acute setting and for choosing appropriate participants for...
future acute trials. The ABC/XYZ method should be validated in a separate cohort to determine widespread applicability.

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Disclosures
None.

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