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

LA Beslow[1], **RN Ichord**[1], **SE Kasner**[2], **MT Mullen**[2], **DJ Licht**[1], **SE Smith**[1], **PB Storm**[3], **LC Jordan**[4], and **SR Messé**[2]

[1] Division of Neurology, The Children's Hospital of Philadelphia, 34th Street and Civic Center Blvd, Philadelphia, PA 19104

[2] Department of Neurology, The Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, 3400 Spruce Street, Philadelphia, PA 19104

[3] Division of Neurosurgery, The Children's Hospital of Philadelphia, 34th Street and Civic Center Blvd, Philadelphia, PA 19104

[4] Department of Neurology, Division of Pediatric Neurology, Johns Hopkins University School of Medicine, 200N. Wolfe Street, Suite 2158, Baltimore, MD 21287

Abstract

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 (ICH) with ICHV/TBV>2% associated with functional impairment. We aimed to determine whether easily performed approximations of ICH and brain volume can accurately and reliably stratify ICH by size.

Methods—CT scans of 18 children with spontaneous ICH 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. Inter-rater reliability was measured with intraclass correlation coefficients (ICC). ICHV and TBV were measured using computer-assisted manual segmentation tracings to establish criterion validity. Each ICH 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 inter-rater reliability (ICC 0.95–0.99). These estimates were highly correlated with volumetric measures (R^2 0.77–0.96). Sensitivity of the ABC/XYZ method for identifying an ICHV >2% TBV was 100% (95%CI: 89–100%). Specificity was 95% (95%CI: 83–99%).

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

Keywords

intracerebral hemorrhage; hemorrhage volume; pediatric

---

*Communicating author: Lauren A Beslow, MD, Division of Neurology, 6th Floor Wood Building, The Children's Hospital of Philadelphia, 34th Street and Civic Center Blvd, Phone: 1-215-590-1719, Fax: 1-215-590-1771, beslow@email.chop.edu.

Introduction

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 though 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 utilized 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 rapidly and easily assess 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.

Subjects and methods

Case Identification

With institutional review board approval, a prospective consecutive cohort of patients with spontaneous ICH was identified from a single large tertiary care children's hospital stroke registry between January 2006 and March 2009. Inclusion criteria for this study were: age 4 months to 18 years with spontaneous supratentorial ICH confirmed by CT. Exclusion criteria were: infratentorial hemorrhage, isolated subarachnoid hemorrhage, isolated intraventricular hemorrhage, hemorrhage due to brain tumor, and hemorrhage due to hemorrhagic conversion of either arterial ischemic stroke or cerebral venous sinus thrombosis.

Measurements

Head CT scans of 18 pediatric patients with acute spontaneous ICH were independently reviewed by 4 neurologists of varying experience: 1 pediatric stroke neurologist (RI), 1 adult stroke neurologist (SM), 1 pediatric stroke fellow (LB), and 1 adult neurology resident (MM). The size of the intraparenchymal ICH was estimated by ABC/2, wherein 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. [6]. Similarly, TBV was estimated by XYZ/2, where X was defined as the largest anterior-posterior axial 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/2) 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 Figures 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 (LB) using a computer program, ITK-SNAP, that is available online (www.itksnap.org) [8]. Similar techniques have been used reliably in both childhood ICH and in measurements of pediatric brain structures[4, 8]. On segmentation imaging, TBV included the cerebral hemispheres, cerebellum, and brainstem. 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 ICHV/TBV was > 2%. The threshold of 2% was chosen based on the observation that 30cc in adult ICH is an important and validated ICHV

threshold for predicting outcome[1–3, 6]. An ICHV of 30 cc represents approximately 2% of the TBV of an average adult brain of about 1400 cc. In addition, hemorrhages >2% TBV are associated with functional impairment in childhood ICH[5].

Statistical analysis

Statistical analysis was performed using STATA version 10.0 (Stata Corp, College Station, TX). Inter-rater reliability was measured with intraclass correlation coefficients (ICC) with the use of ANOVA. An ICC of 1 demonstrates perfect reliability, and an ICC> 0.8 represents excellent reliability[9]. 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 since the four 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 confidence intervals.

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]: 2.3–24 hours). 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: 4–37mL), median TBV was 1286 mL (IQR: 1188–1343mL), and median ICHV/TBV was 1.6% (IQR: 0.3–2.8%). Using the ABC/XYZ estimation, median ICHV was 23 mL (IQR: 5–38mL), median TBV was 1192 mL (IQR: 1030–1296mL), and median ICHV/TBV was 1.8% (IQR: 0.4–3.0%).

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% confidence interval [CI]: 0.99–1.0). The ICC for TBV by XYZ/2 was 0.95 (95% CI: 0.92–0.99). The ICC for the estimation of ICHV expressed as a proportion of TBV by the equation ABC/XYZ was 0.99 (95% CI: 0.99–1.0).

There was no difference in the estimates of ICHV by ABC/2 compared to 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: 0.0–0.3%]; 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% – 4% in 6 patients, and >4% in 2 patients. When ABC/XYZ was dichotomized as ≤2% vs. >2%, 70 of 72 measurements (18 ICHs × 4 raters) were classified correctly compared to the reference criterion. The sensitivity of the ABC/XYZ method for identifying an ICHV that was >2% of TBV was 100% (95% binomial CI: 89–100% and specificity was 95% (95% binomial CI: 83–99%).

Discussion

This study demonstrates that the elliptical approximation method ABC/XYZ may be used to estimate ICH volume in children as a proportion of total brain volume with excellent reliability and validity. The XYZ/2 approach tends to underestimate TBV compared to 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 this method maximizes sensitivity with minimal loss of specificity at this threshold. Nevertheless, despite this potential pitfall, 70/72 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, sub-analyses 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 since 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, primary intraventricular, subarachnoid, or epidural hemorrhage. The ABC/XYZ method may not be valid for these hemorrhages since 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 for both outcome prediction 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.

References

1. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ich score: A simple, reliable grading scale for intracerebral hemorrhage. Stroke 2001;32:891–897. [PubMed: 11283388]

2. Rost NS, Smith EE, Chang Y, Snider RW, Chanderraj R, Schwab K, FitzMaurice E, Wendell L, Goldstein JN, Greenberg SM, Rosand J. Prediction of functional outcome in patients with primary intracerebral hemorrhage: The func score. Stroke 2008;39:2304–2309. [PubMed: 18556582]

3. Ruiz-Sandoval JL, Chiquete E, Romero-Vargas S, Padilla-Martinez JJ, Gonzalez-Cornejo S. Grading scale for prediction of outcome in primary intracerebral hemorrhages. Stroke 2007;38:1641–1644. [PubMed: 17379820]

4. Jordan LC, Kleinman JT, Hillis AE. Intracerebral hemorrhage volume predicts poor neurologic outcome in children. Stroke 2009;40:1666–1671. [PubMed: 19286576]

5. Beslow LA, Storm PB, Licht DJ, Smith SE, Heuer GG, Zimmerman RA, Feiler AM, Ichord RN. Hemorrhage volume is a predictor of short-term outcome in pediatric intracerebral hemorrhage: a prospective consecutive cohort study. Stroke. in press.

6. Broderick JP, Brott TG, Duldner JE, Tomsick T, Huster G. Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality. Stroke 1993;24:987–993. [PubMed: 8322400]

7. Kothari RU, Brott T, Broderick JP, Barsan WG, Sauerbeck LR, Zuccarello M, Khoury J. The abcs of measuring intracerebral hemorrhage volumes. Stroke 1996;27:1304–1305. [PubMed: 8711791]

8. Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, Gerig G. User-guided 3d active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. Neuroimage 2006;31:1116–1128. [PubMed: 16545965]

9. Fleiss, JL. Statistical methods for rates and proportions. New York, NY: John Wiley & Son; 1981.

10. Freeman WD, Barrett KM, Bestic JM, Meschia JF, Broderick DF, Brott TG. Computer-assisted volumetric analysis compared with abc/2 method for assessing warfarin-related intracranial hemorrhage volumes. Neurocrit Care 2008;9:307–312. [PubMed: 18392784]

11. Huttner HB, Steiner T, Hartmann M, Kohrmann M, Juettler E, Mueller S, Wikner J, Meyding-Lamade U, Schramm P, Schwab S, Schellinger PD. Comparison of abc/2 estimation technique to computer-assisted planimetric analysis in warfarin-related intracerebral parenchymal hemorrhage. Stroke 2006;37:404–408. [PubMed: 16373654]

12. Wang CW, Juan CJ, Liu YJ, Hsu HH, Liu HS, Chen CY, Hsueh CJ, Lo CP, Kao HW, Huang GS. Volume-dependent overestimation of spontaneous intracerebral hematoma volume by the abc/2 formula. Acta Radiol 2009;50:306–311. [PubMed: 19173095]
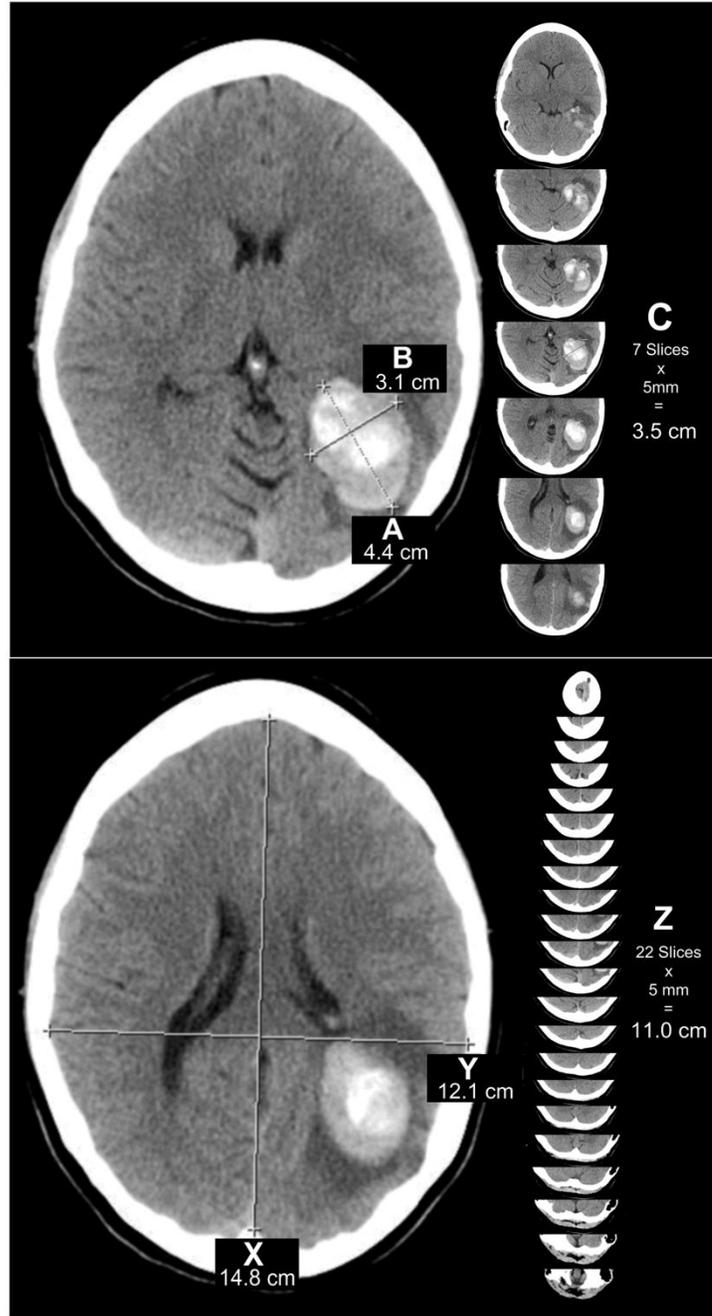
Figure 1. Example ABC/XYZ measurement

Top panel. Intracerebral hemorrhage volume measurement: A – largest hemorrhage axial diameter, B – largest axial diameter perpendicular to A on same slice, C – vertical hemorrhage diameter (number of slices with hemorrhage multiplied by slice thickness). For this example, $ABC/2 = (4.4 \text{ cm} \times 3.1 \text{ cm} \times 3.5 \text{ cm})/2 = 23.9 \text{ cm}^3$.

Bottom panel. Total brain volume measurement: X – largest anterior-posterior midline axial diameter, Y – largest axial diameter perpendicular to X on same slice, Z – vertical brain diameter (number of slices from foramen magnum to vertex multiplied by slice thickness). For this example, $XYZ/2 = (14.8 \text{ cm} \times 12.1 \text{ cm} \times 11.0 \text{ cm})/2 = 984.9 \text{ cm}^3$, and $ABC/XYZ \times 100 = 2.4\%$. $1 \text{ cm}^3 = 1 \text{ mL}$
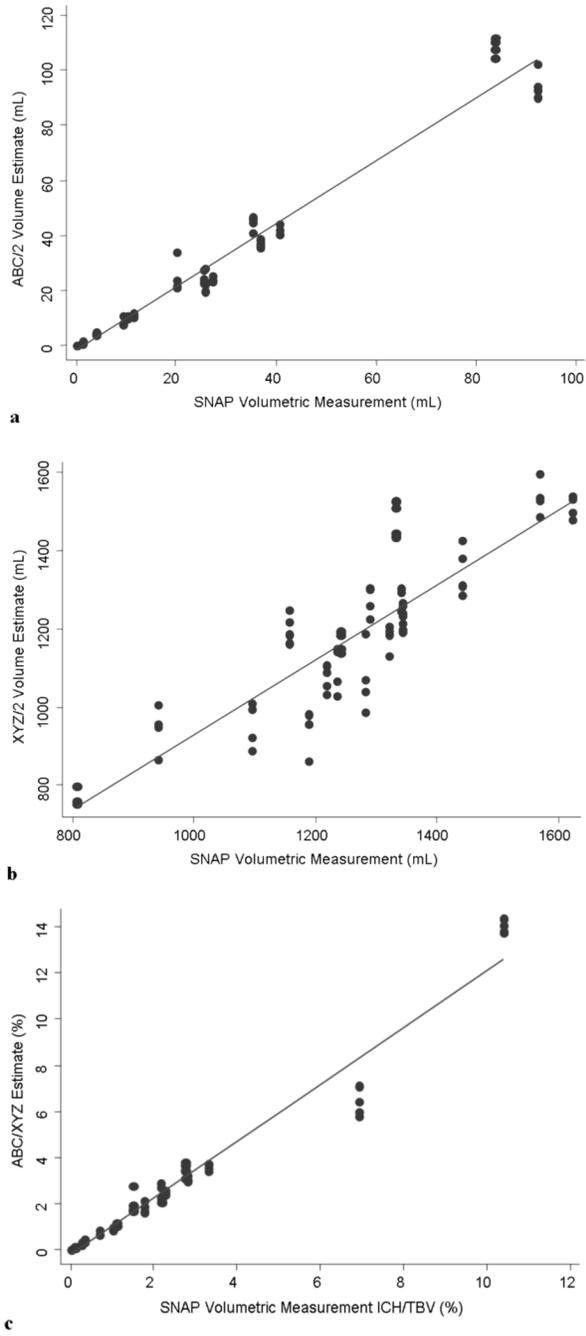
Figure 2. Regression analysis
(a.) Regression line between ABC/2 hemorrhage volume estimation and ITK-SNAP volumetric ICH analysis [slope 1.14, intercept −1.7], (b.) Regression line between XYZ/2 total brain volume (TBV) estimation and ITK-SNAP volumetric TBV analysis [slope 0.96, intercept −30.3], (c.) Regression line between ABC/XYZ (%) and ITK-SNAP volumetric analysis of ICH volume as a % of TBV [slope 1.23, intercept −0.2].