Comparison of ABC/2 Estimation Technique to Computer-Assisted Planimetric Analysis in Warfarin-Related Intracerebral Parenchymal Hemorrhage

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Background and Purpose—The ABC/2 formula is a reliable estimation technique of intracerebral hematoma volume. However, oral anticoagulant therapy (OAT)–related intracerebral hemorrhage (ICH) compared with primary ICH is based on a different pathophysiological mechanism, and various shapes of hematomas are more likely to occur. Our objective was to validate the ABC/2 technique based on analyses of the hematoma shapes in OAT-related ICH.

Methods—We reviewed the computed tomography scans of 83 patients with OAT-associated intraparenchymal ICH. Location was divided into deep, lobar, cerebellar, and brain stem hemorrhage. Shape of the ICH was divided into (A) round-to-ellipsoid, (B) irregular with frayed margins, and (C) multinodular to separated. The ABC/2 technique was compared with computer-assisted planimetric analyses with regard to hematoma site and shape.

Results—The mean hematoma volume was 40.83 ± 3.9 cm^3 (ABC/2) versus 36.6 ± 3.5 cm^3 (planimetric analysis). Bland–Altman plots suggested equivalence of both estimation techniques, especially for smaller ICH volumes. The most frequent location was a deep hemorrhage (54%), followed by lobar (21%), cerebellar (14%) and brain stem hemorrhage (11%). The most common shape was round-to-ellipsoid (44%), followed by irregular ICH (31%) and separated and multinodular shapes (25%). In the latter, ABC/2 formula significantly overestimated volume by +32.1% (round shapes by +6.7%; irregular shapes by +14.9%; P ANOVA <0.01). Variation of the denominator toward ABC/3 in cases of irregularly and separately shaped hematomas revealed more a precise volume estimation with a deviation of −10.3% in irregular and +5.6% in separately shaped hematomas.

Conclusions—In patients with OAT-related ICH, >50% of bleedings are irregularly shaped. In these cases, hematoma volume is significantly overestimated by the ABC/2 formula. Modification of the denominator to 3 (ie, ABC/3) measured ICH volume more accurately in these patients potentially facilitating treatment decisions. **(*Stroke*. 2006;37:404-408.)**

Key Words: stroke ■ warfarin

The volume of an intracerebral intraparenchymal hematoma (intracerebral hemorrhage [ICH]) is known to be an independent predictor for poor outcome and mortality.[1–6] Therefore, a quick and reliable bedside technique for estimating hematoma volume has been established, the so-called ABC/2 technique, which meanwhile has been validated repeatedly.[7–10] However, the pathophysiological mechanism of ICH related to oral anticoagulant therapy (OAT) is different from that of primary ICH, and the mechanism of hematoma growth is thought to result in various shapes of the hematoma.[11] The ABC/2 technique is derived from an approximation according to the formula for ellipsoids, in which A is the greatest hemorrhage diameter, B is the diameter 90° degrees to A, and C is the approximate number of computed tomography (CT) slices with hemorrhage multiplied by the slice thickness.[9] Therefore, hematoma volume is calculated most precisely in round to ellipsoid shapes of hematomas. However, even in regularly shaped primary ICH, a small overestimation (5% to 10%) of the ABC/2 formula compared with planimetric analyses has been shown previously, which was larger in smaller hematoma volumes because of increasing imprecision of the ABC/2 formula.[9] Irregular bleedings are mathematically not accurately covered by the ABC/2 formula. Taking this into account and expecting irregular lobulated shapes to occur more frequently in OAT-related ICH,[11] we hypothesized a distinct overestimation of hemorrhage volumes by the ABC/2 formula in theses cases. Hence, we aimed to validate the ABC/2 formula in a prospectively

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acquired series of patients with OAT-related ICH by comparison with computer-assisted planimetric analysis.

Methods

Patient Selection

Data of all ICH patients have been prospectively collected in a database. For this study, we included all patients admitted to our neurological stroke and intensive care units between January 1999 and December 2003 with the diagnosis of an OAT-related parenchymal ICH (n=131). The diagnosis was made in agreement of the neurologist and neuroradiologist at duty. ICH patients with an international normalized ratio <1.5 were considered to be not sufficiently anticoagulated and were excluded from analysis (n=8). From the remaining 123 patients, we excluded: (1) 17 patients with evidence of subdural or epidural hematomas, (2) 3 patients because of ICH attributable to vascular malformations, (3) 4 patients with subarachnoid hemorrhage, (4) 9 patients with ICH after head trauma, and (5) 7 patients with ICH related to tumors. Finally, 83 patients remained for analysis.

Imaging

ICH was diagnosed by CT (Siemens Somatom Volume zoom) according to a standardized institutional protocol including a slice thickness of 4 mm for posterior fossa and 8 mm supratentorially, the slice spacing being equal to slice thickness. The hematoma location was categorized into: (1) deep hematomas, including ganglionic, thalamic, and periventricular supraganglionic hemorrhage; (2) lobar hematomas; (3) cerebellar hemorrhage; and (4) hemorrhage within the brain stem. The shape of the hemorrhage was divided into: (1) round to ellipsoid with smooth margins: (2) irregular with frayed margins; and (3) multinodular to separated (Figure 1).[11] ICH volume was calculated by the ABC/2 technique and by computer-assisted planimetric analysis using the Osiris software package. The categorization of the shape as well as all volume estimations using the ABC formula and planimetric analyses were performed independently and in randomized order by 2 physicians,[12] modeled after the technique of Hier et al.[13] Thus, no measurement could bias the other. With regard to the categorization of the hematoma shape, a joint decision of both reviewers was made in cases of disagreement (n=6). With regard to hematoma volume measurement, disagreement between both reviewers was only noted when differences in the estimated volume exceeded 1 mL. This occurred in 1 case using the planimetric approach and in 13 cases using the ABC formula. The hematoma volume used for analysis in these cases was averaged over both single values. In cases of hematoma extension into the ventricles, the portion of intraventricular blood was not considered for hematoma volume measurement. The hematoma volumes are given in cm^3. The deviation of both techniques concerning the hematoma volume is given as a percentage.

Alternation of the ABC/2 Formula

Expecting the ABC/2 formula to overestimate hematoma volumes in cases of other than round-to-ellipsoid shape (ie, irregular and multinodular or separated hematoma shapes), we a priori decided to change the denominator to decrease the quotient and provide a more precise approximation of the measured volumes. Therefore, we calculated for all 3 hematoma shapes a modified volume using an ABC/3 formula. This simple variation was chosen arbitrarily and was not based on a mathematic approach.

Statistical Analysis

All statistical analyses were performed using the SPSS software package (SPSS 13.0). Equivalence of both techniques was tested with Bland–Altman plots.[14] Comparison of both techniques was performed by calculating the percentual deviations of hematoma volumes estimated by the ABC/2 formula from planimetric analysis. After confirmation of normal distribution of the data by using the Shapiro–Wilk test, data are expressed as mean±SD and were compared using the unpaired *t* test and 1-way ANOVA as appropriate. Post hoc analyses were performed using the Tukey B test and the Scheffé procedure to investigate possible homogeneities between the various subgroups (values are given in percent deviation). χ^2 test was used for comparison of frequencies. A value of $P \leq 0.05$ was considered statistically significant.

Results

The mean calculated hematoma volume was 40.83±3.9 cm^3 using the ABC/2 technique versus 36.6±3.5 cm^3 in the planimetric analysis. The mean deviation in percentage between both techniques was 14.54±2.1%. The most frequent

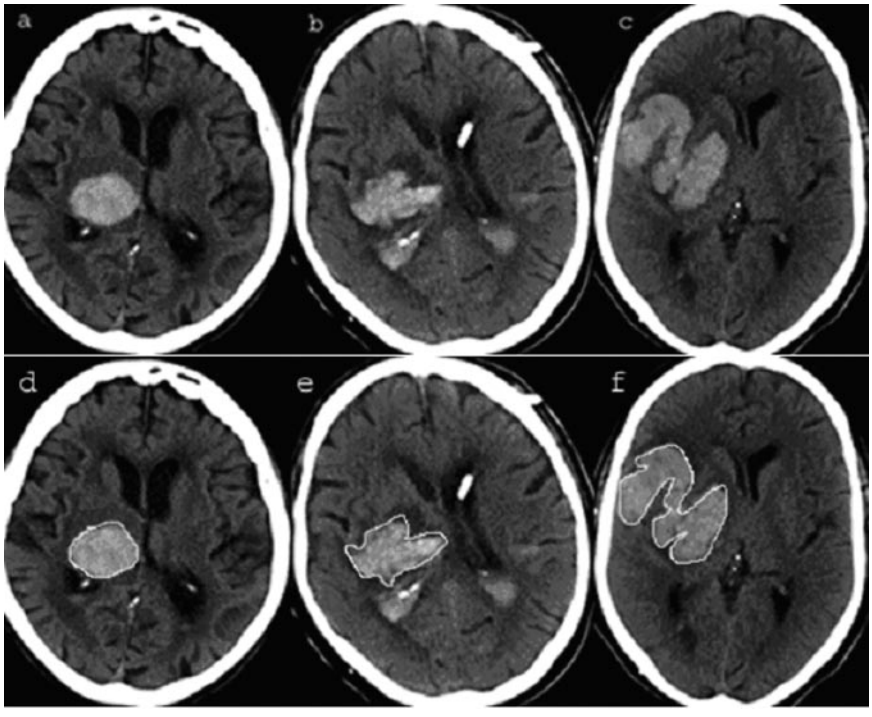

Figure 1. Various shapes of the OAT-related ICH. Examples of the various shapes of the hematomas: a, round-to-ellipsoid; b, irregular; and c, separated. d through f, Examples of the planimetric approach.

TABLE 1. Neuroradiologic Characteristics of All Patients (n=83)

Volume	Mean±SE
Volume–planimetric	36.6±3.5 cm^3
Volume–ABC/2	40.83±3.9 cm^3
Mean % deviation (ABC/2–planimetric analysis)	14.54±2.1%
Localization	**No. of patients (%)**
Deep	45 (54)
lObar	17 (21)
Cerebellar	12 (14)
Brain stem	9 (11)
Shape	**No. of patients (%)**
Round-to-ellipsoid	37 (44)
Irregular	26 (31)
Separated	20 (25)

location was a deep hemorrhage, and the most common shape was round-to-ellipsoid (Table 1). Table 2 shows the measured hematoma volumes for both techniques with respect to hematoma location. The ABC/2 technique generally overestimated hematoma volume, but there was no significant difference to the planimetric analyses. However, when comparing the deviations in percentage (ABC/2 planimetric analysis), the volume overestimation of the ABC/2 was significant in cases of brain stem hemorrhage compared with deep hemorrhages (Table 2; Mann–Whitney *U* test and variance F test $P<0.05$).

To analyze the variance of the volume measurements of both techniques with regard to the hematoma shape, we calculated the mean percentage deviation between both techniques using the ABC/2 and the ABC/3 formulas. The Shapiro–Wilk test confirmed a normal distribution of these percentage deviations. The ABC/2 formula overestimated hematoma volume by 6.69±3.01% in round-to-ellipsoid ICH by 14.85±4.95% in irregular shaped hematomas and by 32.11±10.28% in cases of multinodular and separated ICH (Figure 2A). The ABC/3 formula revealed an underestimation of −20.26±7.09% for round-to-ellipsoid ICH, of −10.25±4.97% in irregular hematomas, and a slight overestimation of +5.6±4.92% in cases of multinodular and separated hematomas (Figure 2B). Whereas round-to-ellipsoid hematomas were better expressed by the ABC/2 formula, the

TABLE 2. Hematoma Volume for Various Locations and Shapes

	Hematoma Volume (cm^3)			
Location	Planimetric	ABC/2	R^2	% Deviation
Deep	46.3±5.3	49.2±5.6	0.97	6.42%
Lobar	43.9±8.3	51.5±9.6	0.73	14.80%
Cerebellar	15.6±2.2	18.8±6.0	0.83	17.16%
Brain stem	5.6±1.4	7.6±4.8	0.77	27.04%
Shape				
Round	39.9±4.8	42.5±6.6	0.81	6.69%
Irregular	34.3±6.6	38.9±8.2	0.83	14.25%
Separated	32.9±7.9	43.3±9.7	0.77	32.11%

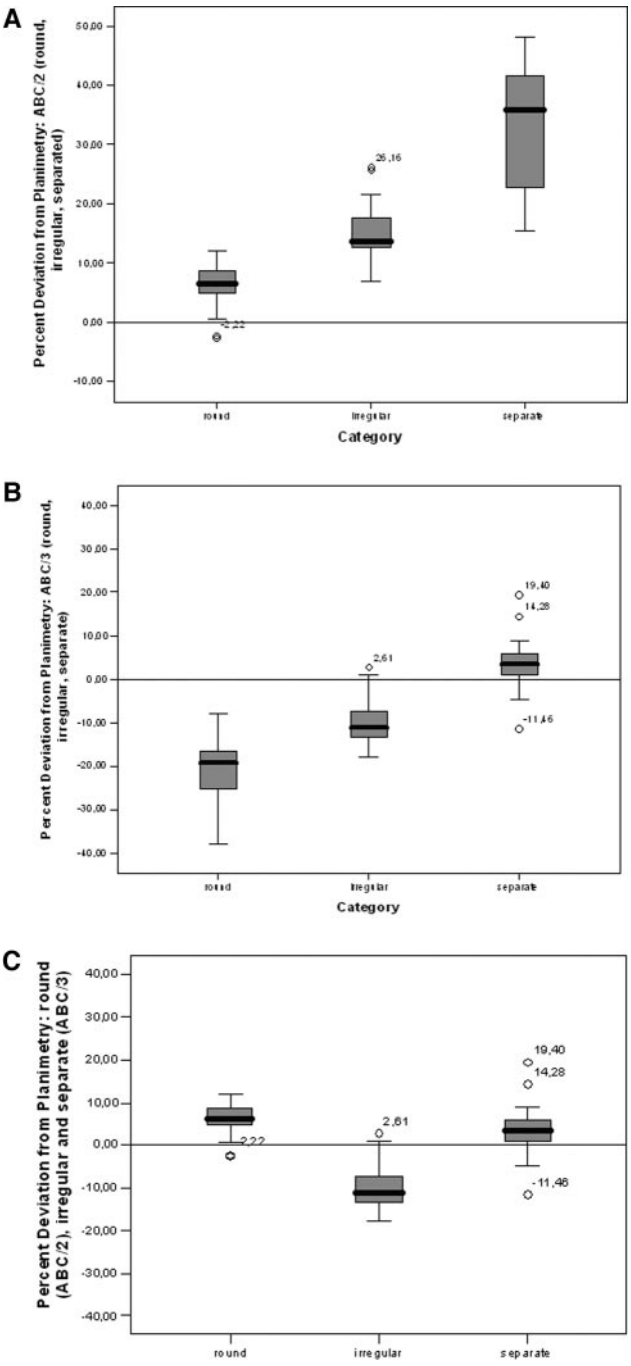

Figure 2. Percent deviation of the hematoma volume estimated by the ABC/2 technique from the hematoma volume measured by planimetric analysis for the different shapes of the ICH (A). Note that for the separated/multinodular shape of ICH, the ABC/2 formula overestimates hematoma volume by +32.11%. B demonstrates the percent deviation of hematoma volume assessed by the ABC/3 formula for all 3 ICH shapes. Note that for irregular and separated ICH, the percent deviations are less than with the ABC/2 formula, whereas in round-to-ellipsoid ICH, a clear underestimation of −20.26% results. C shows a combination of A and B.

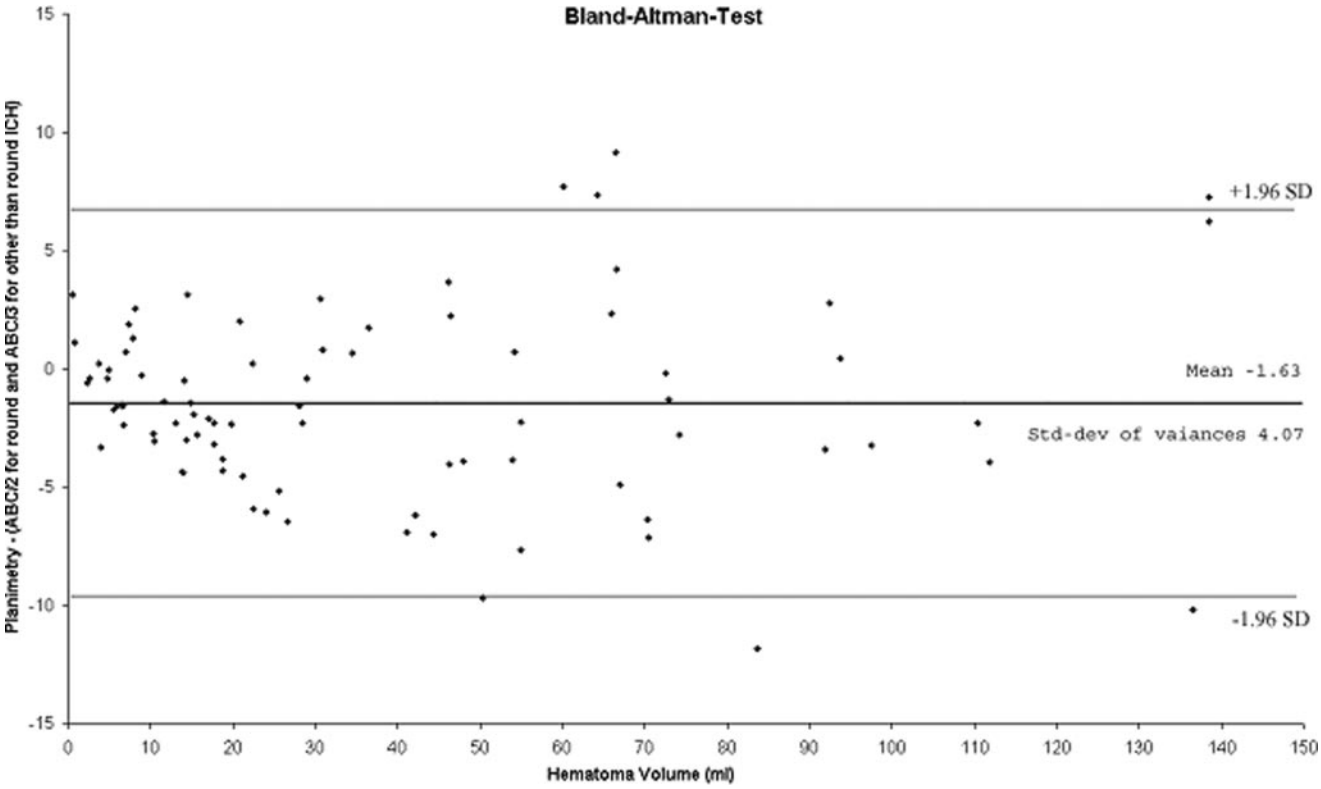

Figure 3. Bland–Altman plots demonstrate no significant difference in the estimated hematoma volume when comparing the ABC/2 formula for round-to-ellipsoid ICH and ABC/3 formula for irregular and separated ICH with computer-assisted planimetric analysis.

ABC/3 formula estimated hematoma volume more precisely for irregular and multinodular and separated hematomas (Figure 2C). Analogous Bland–Altman plots were calculated using ABC2 for round-to-ellipsoid and ABC/3 formula for irregular and multinodular and separated hematomas, which confirmed the equivalence of both techniques (Figure 3).

Three 1-way between-groups ANOVAs were conducted. The first ANOVA compared the ABC/2 formula for all 3 shapes, the second compared the ABC/3 formula for all 3 shapes, and the third compared the ABC/2 formula for round-to-ellipsoid and the ABC/3 formula for other than round-to-ellipsoid ICH shapes. There were statistically significant differences for all 3 ANOVAs: $F_{(2,80)}=114.6$, $P<0.001$; $F_{(2,80)}=85.3$, $P<0.001$; $F_{(2,80)}=83.8$, $P<0.001$. At this level of significance and also when taking the means of deviation into account, this difference is valid despite of violation of homogeneity of variances for the first and third test (Levene statistic $P<0.001$; $P=0.582$; $P=0.04$; data not shown), and therefore no power transformations were performed. Post hoc comparisons (Tukey B, Tukey HSD, and Scheffé tests) showed homogenous subgroups only for the third ANOVA, in which the deviation of volumes in round ICH measured by ABC/2 and separated ICH measured by ABC/3 did not differ. Only volumes of irregularly shaped ICH were underestimated by −10.25%, which differed significantly from round (ABC/2) and separated ICH (ABC/3) but was less imprecise than the +14.85% overestimation by the ABC/2 formula. In the first 2 ANOVAs, post hoc comparisons did not identify any homogenous subgroups.

Discussion

We reviewed the images of 83 OAT-related ICH patients and found that: (1) overall, hematoma volumes estimated by the ABC/2 technique do not significantly differ from those measured by planimetric analyses; (2) in OAT-related ICH, separated and multinodular shapes occur more frequently than in previously reported studies on primary ICH;[11] (3) the ABC/2 technique accurately estimates volume in cases of round-to-ellipsoid shape of the hematoma but significantly overestimates volume in irregular and separated shapes; and (4) increasing the denominator to 3 (ie, ABC/3) for irregular and separated ICH revealed a more accurate calculation of hematoma volume than with the ABC/2 formula.

Other studies have shown the accuracy of the ABC/2 technique for estimation of hematoma volumes in intraparenchymal and even subdural hematomas.[9,10] Furthermore, overestimation of hematoma volumes by the ABC/2 technique in relation to hematoma site has been shown, especially in cases of lobar and cerebellar ICH.[9] In this regard, we found an increasing overestimation in ascending order for lobar, cerebellar, and brain stem hemorrhage. Because the ABC/2 formula represents a rapid bedside technique, overestimation is the more likely to occur the smaller the hematoma size is attributable to increasing imprecision (eg, overestimation for A by 1 mm makes a greater difference in smaller hematoma sizes than in larger).

In previous reports, only 29% of non–OAT-related ICH are of irregular and multinodular or separated shape.[11] This number is nearly twice as high in our series of OAT-associated ICH (56%). Although in non–OAT-associated

ICH, the ABC/2 formula for oval-shaped lesions is fairly accurate (<8% deviation[9,10]), this only holds true for the subset of roundly shaped ICH in OAT-associated hemorrhage (6.69% deviation in our set). For irregularly or separated shaped ICH, the ABC/2 formula substantially overestimated ICH volumes by nearly 15% in the former and >32% in the latter group. In these bleedings, which account for more than half of OAT-associated ICH, the alternative formula ABC/3 renders a more accurate assessment of hematoma volume (10% underestimation for irregular and 5.6% overestimation for separated ICH).

The frequent occurrence of irregular and separated shapes of OAT-related ICH is an interesting finding because it may reflect a different pathomechanism compared with primary ICH. It has been suggested that OAT merely unmasks pre-existing subclinical intracerebral bleeding, especially in patients with underlying hypertension and cerebrovascular disease.[15] However, previous studies revealed the presence of white matter lesions, so-called "leukoaraiosis" on CT scans, which was an independent predictor of ICH.[16] It is also possible that OAT directly causes ICH because adequate levels and functional forms of the antagonized clotting factors are essential to counteract the burden placed on blood vessels as part of normal daily activities. Together, various possible causes of OAT-associated ICH are likely to be responsible for a more frequent occurrence of irregular and separately shaped ICH than found in primary ICH.

Why is this "fifth-grade arithmetic problem" worth thinking about? Because hematoma volume is one of the most important predictors for poor outcome,[1–3,6] and a falsely large estimated hematoma volume might influence initial treatment decisions, such as "do not resuscitate" orders, and therefore lead to undesirable self-fulfilling prophecies with regard to outcome.[17] Accurate hematoma measurements are also of importance for clinical trials, in which ICH volume change may be a surrogate end point.[18,19] Further studies should focus on potential differences in the long-term outcome of patients with separated compared with more regularly shaped hematomas with regard to similar hematoma volumes and locations.

We conclude that OAT-related ICH vary from primary ICH in the shape of the hematoma showing twice as often irregular, multinodular, and separated forms. The ABC/2 formula for estimating hematoma volume falls short in these cases, whereas a modification toward a ABC/3 formula leads to a significantly more accurate volume estimation. We suggest that in any OAT-associated ICH, bleeding volumes with shapes other than round-to-ellipsoid may be assessed with the formula ABC/3, albeit this approach needs to be prospectively validated in another study.

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