# Accuracy of the ABC/2 Score for Intracerebral Hemorrhage Systematic Review and Analysis of MISTIE, CLEAR-IVH, and CLEAR III

Alastair J.S. Webb, DPhil; Natalie L. Ullman, BS; Tim C. Morgan, MPH; John Muschelli, ScM; Joshua Kornbluth, MD; Issam A. Awad, MD; Stephen Mayo, MD; Michael Rosenblum, PhD; Wendy Ziai, MD; Mario Zuccarrello, MD; Francois Aldrich, MD; Sayona John, MD; Sagi Harnof, MD; George Lopez, MD; William C. Broaddus, MD; Christine Wijman, MD†; Paul Vespa, MD; Ross Bullock, MD, PhD; Stephen J. Haines, MD; Salvador Cruz-Flores, MD; Stan Tuhrim, MD; Michael D. Hill, MD; Raj Narayan, MD; Daniel F. Hanley, MD; for the MISTIE and CLEAR Investigators\*

**Background and Purpose**—The ABC/2 score estimates intracerebral hemorrhage (ICH) volume, yet validations have been limited by small samples and inappropriate outcome measures. We determined accuracy of the ABC/2 score calculated at a specialized reading center (RC-ABC) or local site (site-ABC) versus the reference-standard computed tomography—based planimetry (CTP).

Methods—In Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation-II (MISTIE-II), Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage (CLEAR-IVH) and CLEAR-III trials. ICH volume was prospectively calculated by CTP, RC-ABC, and site-ABC. Agreement between CTP and ABC/2 was defined as an absolute difference up to 5 mL and relative difference within 20%. Determinants of ABC/2 accuracy were assessed by logistic regression.

**Results**—In 4369 scans from 507 patients, CTP was more strongly correlated with RC-ABC ( $r^2$ =0.93) than with site-ABC ( $r^2$ =0.87). Although RC-ABC overestimated CTP-based volume on average (RC-ABC, 15.2 cm³; CTP, 12.7 cm³), agreement was reasonable when categorized into mild, moderate, and severe ICH ( $\kappa$ =0.75; P<0.001). This was consistent with overestimation of ICH volume in 6 of 8 previous studies. Agreement with CTP was greater for RC-ABC (84% within 5 mL; 48% of scans within 20%) than for site-ABC (81% within 5 mL; 41% within 20%). RC-ABC had moderate accuracy for detecting ≥5 mL change in CTP volume between consecutive scans (sensitivity, 0.76; specificity, 0.86) and was more accurate with smaller ICH, thalamic hemorrhage, and homogeneous clots.

Conclusions—ABC/2 scores at local or central sites are sufficiently accurate to categorize ICH volume and assess eligibility for the CLEAR-III and MISTIE III studies and moderately accurate for change in ICH volume. However, accuracy decreases with large, irregular, or lobar clots.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: MISTIE-II NCT00224770; CLEAR-III NCT00784134. (Stroke. 2015;46:2470-2476. DOI: 10.1161/STROKEAHA.114.007343.)

**Key Words:** cerebral hemorrhage ■ controlled clinical trials, randomized ■ review, systematic ■ sensitivity and specificity ■ tissue-type plasminogen activator

Spontaneous intracerebral hemorrhage (ICH) is associated with >40%<sup>1</sup> 1-month mortality and >60% dependency<sup>1</sup> but remains the only major stroke subtype without specific

treatment, except potentially acute blood pressure lowering.<sup>2</sup> Morbidity and mortality are associated with age, intraventricular extension, and presenting level of consciousness.<sup>3</sup>

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From the Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom (A.J.S.W.); Division of Brain Injury Outcomes, Johns Hopkins Medical Institutions, Baltimore, MD (N.L.U., T.C.M., J.K., W.Z., D.F.H.); Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (J.M., M.R.); Department of Neurosurgery, University of Chicago, IL (I.A.A.); Emissary International, LLC, Austin, TX (S.M.); Department of Neurosurgery, University of Maryland, Baltimore (F.A.); Department of Neurosurgery, Rush Medical Center, Chicago, IL (S.J., G.L.); Department of Neurosurgery, Sheba Medical Center, Ramat Gan, Israel (S.H.); Department of Neurosurgery, Medical College of Virginia, Richmond (W.C.B., R.B.); Department of Neurology and Neurological Sciences, Stanford Medicine, CA (C.W.); Department of Neurosurgery, University of California, Los Angeles (P.V.); Department of Neurological Surgery, Medical University of South Carolina, Charleston (S.J.H.); St. Louis University, MO (S.C.-F.); Department of Neurology, Mount Sinai School of Medicine, New York, NY (S.T.); Department of Clinical Neurosciences, University of Calgary, Alberta, Canada (M.D.H.); and Department of Neurosurgery, Wayne State University, Detroit, MI (R.N.).

\*A list of all MISTIE and CLEAR Investigators is given in the Appendix.

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Correspondence to Daniel F. Hanley, MD, Division of Brain Injury Outcomes, Johns Hopkins Medical Institutions, 1550 Orleans St 3M53-S, Baltimore, MD. E-mail dhanley@jhmi.edu

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However, reference-standard measurement of ICH by sophisticated techniques such as computed tomography-based planimetry (CTP) is not widely available and requires substantial analysis time,<sup>4</sup> limiting its use in clinical practice and large studies.<sup>5,6</sup>

The ABC/2 score is a simple assessment of ICH size, "where A is the greatest hemorrhage diameter by CT, B is the diameter 90° to A, and C is the approximate number of CT slices with hemorrhage multiplied by the slice thickness."7 It has been used in the Surgical Trials in ICH (STICH I+II)6 to define patients most likely to benefit from craniotomy for ICH and is currently being used as 1 element in determining eligibility for randomization in the ongoing Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage III (CLEAR-III)<sup>8</sup> and Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation (MISTIE) III trials.9 However, ABC/2 has primarily been validated in small research cohorts by trained researchers.<sup>7</sup> The ABC/2 score is also commonly used in clinical practice for prognostication and treatment decisions, potentially with increased use with the advent of effective treatments. Therefore, in CLEAR-III, CLEAR-IVH and MISTIE-II, and published studies, we addressed the following hypotheses:

- 1. The ABC/2 score accurately determines ICH volume when compared with reference standard CTP, by experienced scorers (trial reading center) and after limited training (local trial sites).
- The ABC/2 score is a valid tool for determining eligibility and clot resolution within randomized controlled trials of interventions for ICH.

#### Methods

#### Clinical Protocol

Participants were recruited from MISTIE-II,10 CLEAR-IVH,11 and CLEAR-III,7 the details of which have been reported previously. MISTIE-II (R01NS046309) was a prospective randomized controlled trial testing image-guided catheter-based removal of ICH at 27 sites. Eighty-one patients were assigned to minimally invasive surgery and 42 patients to standard medical care. In CLEAR-IVH, patients with intraventricular hemorrhage were randomized to placebo, 0.3 mg, 1 mg, or 3 mg of intraventricular recombinant tissue-type plasminogen activator twice daily or to 1 mg recombinant tissue-type plasminogen activator at different time intervals.11 CLEAR-III is a phase III, placebo-controlled trial randomizing 500 patients to either 1 mg recombinant tissue-type plasminogen activator or placebo 8 hourly via an extraventricular drain in patients with complete obstruction of the third and fourth ventricle(s), small ICH (<30 mL) at the time of enrollment, IVH and ICH clot stability at the time of enrollment, and acquisition of the first CT scan within 24 hours of symptom onset. Patients undergo daily CT scans until 72 hours after study treatment has finished, with a follow-up scan at ≈30 days. Scans included in this analysis had either an RC-ABC/2 or site-ABC/2 prospectively recorded during the trial.

# CT Analysis

The ABC/2 score was prospectively performed by the local site to determine eligibility for enrollment. In CLEAR-III and MISTIE-II, local sites were trained in the ABC/2 score as part of the Radiology Training Course, whereas in CLEAR-IVH no specific training was provided. Subsequently, all scans were reviewed by

the centralized CT Reading Center by trained observers, calculating ABC/2 including all slices with any ICH and estimating ICH volume by CTP.<sup>4,12</sup>

Clot location and the presence and size of IVH by CTP were recorded. In the MISTIE study, the morphology of the ICH was determined by 2 (J.K., N.U.) observers, semiquantitatively scoring ICH from 1 to 5 for regularity and heterogeneity of the clot.<sup>13</sup>

#### **Statistical Analysis**

Differences in patient characteristics between trials were assessed by ANOVA and  $\chi^2$  tests for absolute (numeric difference between ABC/2 score and CTP) or relative differences (percentage). Agreement between each 2 of the 3 measures (CTP, RC-ABC/2, and site-ABC/2) was assessed by correlation coefficient  $(r^2)$  and Bland-Altman plots for each study individually and for a pooled data set. The accuracy of the RC-ABC/2 and site-ABC/2 scores was determined by the proportion of scores within 5%, 10% or 20% or within 5 mL (the threshold for stability in MISTIE-III and CLEAR-III), 12.5 mL or 25 mL of the CTP volume. Scans with no blood on any score were excluded from the primary analyses. The null hypothesis of equal accuracy for RC-ABC/2 and site-ABC/2, compared with the reference-standard CTP, was tested with a modified McNemar test, adjusted for clustered data.14 For each of the above accuracy thresholds, agreement between ABC/2 measures and CTP was determined by  $\kappa$  statistics with confidence intervals computed by nonparametric bootstrapping at the individual level. The relevant data set of n individuals was replicated 10000 times, where each replicated data set is constructed by resampling (with replacement) n individuals and including the corresponding scans and k calculated. Confidence intervals were derived as the 2.5 and 97.5 percentiles of the resulting distribution.

Accuracy was also determined for categorizing ICH volume into mild (<15 mL), moderate (15–30 mL), or severe clots (>30 mL), for detecting ≥5 mL change in ICH volume in consecutive scans and for categorizing sequential change in ICH volume in bands of 5 mL. Because hematoma margins are less distinct with time, analyses were performed for all scans, and for each patient's first eligible scan.

Determinants of accuracy of the ABC/2 score were explored using logistic regression, adjusted for repeated measures, for 5 mL or 20% agreement between CTP and the best-available ABC/2 score (preferentially RC-ABC/2). Models were derived including scanspecific factors (clot size, location, and presence of IVH) with further models including age and sex. The impact of clot regularity and heterogeneity on the initial scan was determined in the MISTIE study.

#### **Systematic Review**

To assess consistency between our results and previously published studies, we searched Medline and EMBASE between inception and July 1, 2013 with the terms (Hemorrhage OR Hemorrhage) AND (ABC OR ABC/2), excluding non-English language papers. Reference lists of identified reviews and corresponding supplemental data were searched. After review of potential abstracts, all articles reporting a relationship between ABC/2 score versus a computer-based volumetric method were reviewed in full. Studies were assessed for quality according to the specificity of their population, size of study, method of assessment of ABC/2 score and ICH volume, and relevance of reported outcomes.

# **Results**

There were 4369 scans in 507 patients with ICH on CTP and an ABC/2 score (MISTIE: 1029 scans, 117 patients; CLEAR-IVH: 568 scans, 83 patients; CLEAR-III: 2772 scans, 307 patients), with 3422 scans in 390 patients with both RC-ABC/2 and site-ABC/2 scores (Table 1).

There was good agreement (Figure) between RC-ABC/2 score and CTP, and a strong correlation between these measures on first eligible scans across all 3 trials ( $r^2$ =0.93; Figure I in the online-only Data Supplement), as well as for

Table 1. Characteristics of Included Patients

Characteristic	MISTIE	CLEAR-IVH	CLEAR-III	Combined	P Value
Age (SD), y	61.4 (12)	55.0 (10)	58.6 (11)	58.7 (11.4)	< 0.001
Male (SD)	77 (66)	48 (58)	171 (56)	296 (58)	0.17
Ethnicity (%)					< 0.001
White	66 (56)	18 (22)	147 (48)	231 (46)	
Black	35 (30)	44 (53)	104 (34)	183 (36)	
Hispanic	4 (3)	8 (9.6)	4 (1)	16 (3)	
Asian	12 (10)	8 (9.6)	47 (15)	67 (13)	
Other/unknown	0 (0)	5 (6)	5 (2)	10 (2)	
Hypertension (%)	102 (87)	43 (78)	283 (92)	428 (89)	0.006
Diabetes mellitus (%)	28 (24)	6 (7.5)	36 (12)	70 (14)	0.001
Antiplatelet use (%)	15 (13)	7 (16)	63 (21)	85 (18)	0.18
Baseline GCS (IQR)	12 (8-14)	8 (5-13)	10 (7-14)	10 (7-14)	0.001
Clot volume, mL (SD)	39.0 (20)	10.9 (10)	10.6 (7.9)	17.2	< 0.001
Clot location (%)					< 0.001
Basal ganglia	75 (64.7)	48 (58.5)	77 (25.7)	200 (40.2)	
Thalamus	5 (4.3)	27 (33)	188 (62.6)	220 (44.2)	
Lobar	36 (31)	7 (8.5)	35 (11.7)	78 (15.6)	
Presence of IVH (%)	76 (65)	83 (100)	307 (100)	466 (92)	<0.001

Data are mean (SD), median (IQR), or frequency (%). P values from ANOVA or  $\chi^2$  tests comparing the 3 studies. CLEAR-III indicates Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage III; GCS, Glasgow Coma Score; IQR, interquartile range; IVH, intraventricular hemorrhage; and MISTIE, Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation.

all scans from each trial (Figures II–VII in the online-only Data Supplement and Tables I–IV in the online-only Data Supplement). The correlation between site ABC/2 score and CTP on first eligible scans across all 3 trials was only slightly weaker ( $r^2$ =0.87). Despite the stronger correlation, RC-ABC/2 overestimated mean ICH size for all 3 trials combined (CTP 12.7 mL, SD 13.3; RC-ABC/2 15.2 mL, SD 16.6; site-ABC/2 13.1 mL, SD 14.4), particularly in MISTIE which had larger ICH volumes (Figure IV in the online-only Data Supplement; CTP 33.1 mL, SD 18.6; RC-ABC/2 40.2 mL, SD 24.6; site-ABC/2 35.4 mL, SD 20.9). Furthermore, there was greater variance in RC-ABC/2 versus CTP (variance ratio, 1.67; 95% confidence interval, 1.57–1.77). Although the RC-ABC/2 score overestimated ICH size on average, there were a small number of scans with particularly large

differences between RC-ABC/2 scores and CTP with larger CTP volumes (Figure).

The RC-ABC/2 score was accurate for estimating absolute CTP ICH volume with  $\approx 50\%$  of RC-ABC/2 scores within 20% of CTP, >80% of RC-ABC/2 scores within 5 mL of CTP (Table 2), and >95% of RC-ABC/2 scores within 12.5 mL of CTP. In particular, there was good agreement between RC-ABC/2 and CTP in defining ICH volume as mild, moderate, or severe ( $\kappa$ : all scans, 0.74; P < 0.001; first scans, 0.74; P < 0.001). Although site ABC/2 was less accurate than RC-ABC/2, there was no statistically significant association between the number of scans previously performed at a center and the accuracy of the ABC/2 score (as the absolute difference between CTP and ABC/2 score); providing no evidence of a time-dependent learning effect in the accuracy of site-ABC/2.

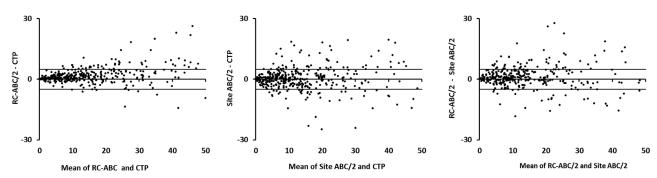


Figure. Bland–Altman plots comparing intracerebral hemorrhage (ICH) volume measured by computed tomography–based volumetrics (CTP) with ABC/2 score at the reading center (RC-ABC/2) or local site. Data includes the first eligible scan for each patient in the Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation-II, Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage (CLEAR-IVH) and CLEAR-III. Error lines indicating 5-mL difference between ABC/2 score and ICH volume are also presented. IVH indicates intraventricular hemorrhage.

Agreement Between CT-Based Volumetrics With ABC/2 Score Measured at the Reading Center or the Local Site

		Percent Within 5 mL of CTP					Percent Within 12.5 mL of CTP			
Study	n	Center	Site	κ	Diff <i>P</i> Value	Center	Site	κ	Diff <i>P</i> Value	
MISTIE										
First scans	83	49.4	39.8	0.23 (0.02 to 0.43)	0.15	80.7	78.3	0.48 (0.23 to 0.70)	0.59	
All scan	535	47.9	44.9	0.19 (0.10 to 0.29)	0.41	81.3	85.4	0.28 (0.18 to 0.40)	0.23	
CLEAR-IVH										
First scans	32	93.8	87.5	0.22 (-0.10 to 0.78)	0.32	96.9	90.6	0.48 (0.00 to 1.00)	0.15	
All scans	175	97.7	84.6	0.10 (-0.03 to 0.35)	0.003*	99.4	96.6	0.28 (0.00 to 0.66)	0.049*	
CLEAR-III										
First scans	275	89.0	82.9	0.23 (0.09 to 0.38)	0.01*	99.3	98.9	†	0.66	
All scans	2712	87.8	84.4	0.23 (0.16 to 0.31)	0.03*	98.6	98.8	-0.01 (0.10 to 0.24)	0.71	
Combined										
First scans	390	81.0	74.1	0.36 (0.25 to 0.46)	0.003*	95.1	93.8	0.48 (0.27 to 0.66)	0.28	
All scans	3422	82.1	78.3	0.32 (0.26 to 0.39)	0.005*	96.0	96.6	0.29 (0.20 to 0.38)	0.34	

Percentage of ABC/2 scores calculated within 5 mL or 12.5 mL of the volume measured on CT-based volumetrics are reported.  $\kappa$  statistics assess agreement between site and RC-ABC/2 being within each threshold of the CT-based planimetry volume. P values are given for the null hypothesis of equal accuracy of RC-ABC/2 and site-ABC/2, based on McNemar test among scans with all 3 measures. CLEAR-III indicates Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage III; CT, computed tomography; CTP, CT-based planimetry; MISTIE, Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation; and RC-ABC, reading center-ABC.

 $\pm\kappa$  not computable as only 2 of 275 RC-ABC/2 scans exceeded 12.5 mL of the CTP volume.

Fewer site-ABC/2 scores were within 20% or 5 mL of CTP volume than RC-ABC/2 scores (Table 2). However, >95% of site-ABC/2 scans were within 12.5 mL of the CTP and virtually all scans were within 25 mL of the CTP (Figures I-III in the online-only Data Supplement). Both site-ABC/2 and RC-ABC/2 scores were accurate in defining eligibility for inclusion in the CLEAR-III study (<30 mL ICH), including all scans from all studies (RC-ABC/2: κ=0.79; 95% confidence interval, 0.72–0.85; P<0.001 and site:  $\kappa$ =0.85; 0.79–0.90; P<0.001), first scans from all studies (RC-ABC/2:  $\kappa=0.89$ ; 0.82-0.95; P<0.001 and site:  $\kappa=0.83$ ; 0.74-0.90; P<0.001) or in MISTIE alone (RC-ABC/2:  $\kappa$ =0.79; 0.71–0.86; P<0.001 and site:  $\kappa$ =0.79; 0.71–0.86; P<0.001). For the first scan in each study, 2.1% of site-ABC/2 scores incorrectly classified ICH volume <30 mL when compared with only 0.5% of RC-ABC/2 scores. The maximum error was 24 mL for site-ABC/2 scores and 33 mL for RC-ABC/2 scores.

A change in RC-ABC/2 score ≥5 mL between consecutive scans was moderately accurate for detecting ≥5 mL change in CTP (sensitivity, 0.76; specificity, 0.86, Table 3), with a positive correlation between greater absolute error and increasing CTP volume ( $r^2$ =0.16; P<0.001). There was a moderately strong association between change in ICH volume measured between consecutive scans on CTP and ABC/2 ( $r^2$ =0.56; P<0.0001), with stronger associations for smaller CTP volumes (mild,  $r^2$ =0.70; moderate,  $r^2$ =0.58; and severe,  $r^2$ =0.38). There was moderate agreement in categorizing ICH into 5 mL categories ( $\kappa$ , 0.38; P<0.001) but reasonable agreement when categorizing as small or large changes.

The accuracy of the ABC/2 score varied with CTP clot volume, with reduced accuracy for absolute clot volume but increased accuracy for relative clot volume (Table 4). Lobar hemorrhages were less accurately estimated than thalamic hemorrhages, with no effect of IVH. These factors were similar

Table 3. Agreement in Change in Best Available ABC/2 Score Between Consecutive Scans With a **Change in CTP-Based ICH Volume** 

ABC/2 Category	ICH Volume Category by CT-Based Planimetry, %							
	<5 mL (n=3277)	5–10 mL (n=304)	10–15 mL (n=135)	15–20 mL (n=57)	>20 mL (n=80)			
<5 mL	86.6	38.2	15.6	11.1	1.7			
5–10 mL	10.2	36.1	14.4	8.9	1.7			
10-15 mL	2.1	16.6	32.2	13.3	10			
15-20 mL	0.5	6.6	23.3	17.8	5			
>20 mL	0.5	2.5	14.4	48.9	81.7			
Total	100	100	100	100	100			

Results are given as the percentage of scans within each absolute volume band on CTP-based ICH volume that were found to be in each band of ICH volume on ABC/2 score. CT indicates computed tomography; CTP, CT-based planimetry; and ICH, intracerebral hemorrhage.

<sup>\*</sup>P<0.05.

for all 3 studies except clot location was less predictive in the CLEAR-III study. In MISTIE, the initial irregularity and homogeneity of the clot reduced accuracy of the ABC/2 score across all scans, but there were too few patients to demonstrate this on initial scans alone (Table V in the online-only Data Supplement).

## **Systematic Review**

Ten studies<sup>9,15-23</sup> from 201 abstracts reported valid comparisons between the ABC/2 score and CT-based, computerassisted volumetric assessments. Two of these studies were in children, 15,16 whereas 3 studies only included patients on oral anticoagulants.<sup>17–19</sup> The studies varied from 8<sup>17</sup> to 244<sup>20</sup> patients and the majority of studies only reported summary estimates of association, or mean agreement (Table VI in the online-only Data Supplement), with only 1 study reporting percentage agreement within clinically applicable limits.<sup>23</sup> Six of 8 studies demonstrated that ABC/2 score overestimated ICH size with greater errors at larger ICH sizes in 2 studies and greater errors with clot irregularity in 2 studies. However analysis methods varied considerably such that a quantitative synthesis was not possible.

#### Discussion

RC-ABC/2 was strongly correlated with CTP, with good accuracy within 5 mL or 20% of CTP volume and when categorizing ICH volume as mild, moderate, or severe. However, the RC-ABC/2 score was only moderately accurate at detecting change in CTP volume. RC-ABC/2 scores were more accurate than site-ABC/2 scores for individual scans. Errors in estimating CTP volume increased with larger ICHs, lobar location, clot irregularity, and clot heterogeneity.

This is the largest study validating the ABC/2 score in a clinical trial setting. Previous validations have provided unreliable assessments because of small sample sizes, and limited applicability because of reporting solely of measures of association or mean error rather than frequency of agreement. Our study confirms that ABC/2 overestimates larger ICHs, either through inflation of errors with nonspheroidal hemorrhages or differences in methods of calculating ABC/2, 20 although there was good agreement for ICH <60 mL, and ICH irregularity and heterogeneity also reduced accuracy. 19 The strength of this study is the large number of patients and measures of agreement within clinically applicable limits.

ABC/2 score at local sites was also reasonably accurate, justifying its use for randomization in clinical trials and probably in clinical practice. This is in contrast to the Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) study,<sup>23</sup> but this report included only 56 scans from one trial. This discrepancy may also reflect the greater experience of local sites in our studies. Nonetheless, with lesser experience in routine clinical practice or new centers in trials, the accuracy of the ABC/2 score may be reduced, especially with larger, irregular clots. Furthermore, the ABC/2 score was accurate for small or large changes in CTP volume and differences between change in ICH estimated by CTP and ABC/2 were usually less than the absolute change in ICH volume.

This study suggests that the ABC/2 score is sufficiently accurate to be used as a rapid tool for randomization in trials. In particular, the high accuracy with CTP volumes <30 mL

Table 4. Associations With Agreement Between ABC/2 Score and Planimetric CT-Based Measures of ICH Volume

	Predictors of 20% Agreement				Predictors of 5-mL Agreement			
Model	Predictor	OR	95% CI	P Value	Predictor	OR	95% CI	<i>P</i> Value
All scans	Study			0.18	Study			0.08
	CLEAR-III vs MISTIE	1.03	(0.70-1.49)	0.89	CLEAR-III vs MISTIE	1.13	(0.66-1.95)	0.66
	CLEAR-III vs CLEAR IVH	1.39	(0.98-1.99)	0.07	CLEAR-III vs CLEAR IVH	1.64	(1.06-2.55)	0.027
	Clot location			< 0.001	Clot location			0.08
	Thalamus vs lobar	2.11	(1.49-3.01)	< 0.001	Thalamus vs lobar	1.49	(0.91-2.45)	0.12
	Basal ganglia vs lobar	1.19	(0.86-1.66)	0.29	Basal ganglia vs lobar	0.97	(0.63-1.50)	0.91
	ICH volume	1.02	(1.01-1.03)	0.001	ICH volume	0.92	(0.91-0.94)	< 0.001
	IVH present	1.03	(0.70-1.52)	0.88	IVH present	1.37	(0.85-2.22)	0.20
First scans	Study			0.06	Study			0.06
	CLEAR-III vs MISTIE	1.23	(0.54-2.81)	0.63	CLEAR-III vs MISTIE	2.34	(0.91-6.00)	0.08
	CLEAR-III vs CLEAR IVH	1.87	(1.12-3.15)	0.018	CLEAR-III vs CLEAR IVH	1.92	(1.03-3.60)	0.04
	Clot location			0.008	Clot location			0.88
	Thalamus vs lobar	2.07	(1.16-3.68)	0.014	Thalamus vs lobar	1.16	(0.55-2.47)	0.70
	Basal ganglia vs lobar	1.09	(0.62-1.91)	0.76	Basal ganglia vs lobar	1.00	(0.50-2.00)	0.99
	ICH volume	1.02	(1.00-1.04)	0.055	ICH volume	0.95	(0.93-0.97)	< 0.001
	Age	1.00	(0.98-1.01)	0.70	Age	1.01	(0.99-1.03)	0.39
	Sex	1.29	(0.88-1.89)	0.18	Sex	1.04	(0.63-1.73)	0.85

Associations identified by logistic regression for within 20% or 5 mL for measures across all scans (study, clot location, ICH volume, and the presence of IVH) and for each subject's initial scan (scan-specific measures+age, sex, and admission GCS). Where available, reading center-ABC/2 score used; otherwise, site-ABC was used. OR >1 indicates greater agreement. Cl indicates confidence interval; CLEAR-III, Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage III; CT, computed tomography; GCS, Glasgow Coma Score; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; MISTIE, Minimally Invasive Surgery Plus Recombinant Tissue-Type Plasminogen Activator for Intracerebral Hemorrhage Evacuation-II; and OR, odds ratio.

supports its use in the CLEAR-III study, with the lack of interaction with IVH volume implying that clinicians could accurately distinguish IVH and ICH, and also supports its use for inclusion in MISTIE-III which requires an ICH volume >30 mL. However, potential inaccuracies in determining change in ICH volume at moderate ICH volumes need to be assessed in future studies.

There were differences between MISTIE-II, CLEAR-IVH, and CLEAR-III. This is expected given differences in the inclusion criteria for these trials, with smaller ICH volumes, fewer lobar hemorrhages, and more IVH in CLEAR-IVH and CLEAR-III when compared with MISTIE-III. Despite these differences, the ABC/2 score was accurate within each study, and the same predictors of accuracy were present across the 3 studies.

This analysis was limited by significant heterogeneity between studies. However, this reflected inclusion of a broad range of patients, and the analysis was particularly appropriate to CLEAR-III and MISTIE-III. Second, the effect of ICH irregularity and heterogeneity was only prospectively assessed in the MISTIE study, but the results were in agreement with previous studies. 17-19 Third, the experience of local sites in trials is likely to be greater than in routine clinical practice. This analysis is therefore most applicable to randomized trials where repeat assessments are perhaps more common. However, this suggests that with relatively brief training, the ABC/2 score is sufficiently accurate to guide treatment decisions. Fourth, heterogeneity in the systematic review was too great to allow for a quantitative synthesis of studies. However, our study was the largest and consistent with most other reported trials, supporting the overall conclusions.

#### **Conclusions**

ABC/2 scores at local or central sites can be performed rapidly in a variety of settings. They are sufficiently accurate to categorize ICH volume and assess eligibility for the CLEAR-III and MISTIE III studies, and moderately accurate for change in ICH volume. However, accuracy decreases with large, irregular, or lobar clots. Attempts to improve the accuracy of volume measurements could provide additional clinical value.

# **Appendix**

# Members of the MISTIE, CLEAR-IVH, and CLEAR-III Study Groups

Allegheny General Hospital, Pittsburgh, PA: Ashis H. Tayal, MD, PI; Bellvitge Hospital, Barcelona, Spain: Alberto Torres Diaz, MD, PI; Case-Western Reserve Hospital, Cleveland, OH: Alan Hoffer, MD, PI; Cedars-Sinai Medical Center, Los Angeles, CA: Asma Moheet, MD, PI; Chaim Sheba Medical Center, Ramat-Gan, Israel: Sagi Harnof, MD, PI; Columbia University, New York, NY: Sachin Agarwal, MD, PI; Georgetown University, Washington, DC: Mason Markowski, MD, PI; Hadassah Hebrew University Hospital, Jerusalem, Israel: Guy Rosenthal, MD, PI; Hartford Hospital, Hartford, CT: Inam Kureshi, MD, PI; Henry Ford Health System, Detroit, MI: Panayiotis Varelas, MD, PI; Hospital de Clinicas de Ribeirao Preto, Sao Paulo, Brazil: Pedro Telles Cougo Pinto, MD, PI; Hospital de la Santa Creu i Sant

Pau, Barcelona, Spain: Joan Marti-Fabregas, MD, PhD, PI; Johns Hopkins Hospital, Baltimore, MD: Wendy Ziai, MD, PI; Kansas University Medical Center, Kansas City, KS: Paul Camarata, MD, PI; Maine Medical Center, Portland, ME: David B. Seder, MD, PI; Mayo Clinic Jacksonville, Jacksonville, FL: William Freeman, MD, PI; Medical College of Wisconsin, Milwaukee, WI: Ann Helms, MD, PI; Medical University of South Carolina, Charleston, SC: Christos Lazaridis, MD, PI; Mercy General Sacremento, Roseville, CA: Kavian Shahi, MD, PI; Montreal Neurological Institute at McGill University, QC, Canada: David Sinclair, MD, PI; Mount Sinai Medical Center, New York, NY: Stanley Tuhrim, MD, PI; New Jersey Neuroscience Institute at JFK, Edison, NJ: Martin Gizzi, MD, PI; NorthShore Chicago, Evanston, IL: Issam Awad, MD, PI; NorthShore Long Island, Manhasset, NY: David LeDoux, MD, PI; Ohio State University Medical Center, Columbus, OH: Michel Torbey, MD, PI; Penn State Hershey Medical Center, Hershey, PA: Kevin Cockroft, MD, MSC, PI; Providence Stroke Center, Portland, OR: David Antezana, MD, PI; Rush University, Chicago, IL: Sayona John, MD, PI; SUNY Upstate Medical Center, Syracuse, NY: Julius Gene Latorre, MD, MPH, PI; Saint Louis University, St. Louis, MO: Salvador Cruz-Flores, MD, PI; Sourasky Medical Center, Tel Aviv, Israel: Nevo Margalit, MD, PI; Springfield Neurological and Spine Institute, Springfield, MO: H. Mark Crabtree, MD, PI; St. Luke's Brain and Stroke Institute, Kansas City, MO: Darren Lovick, MD, PI; Stanford University, Stanford, CA: Christine Wijman, MD, Chitra Venkatasubramanian, MD, PI; Temple University, Philadelphia, PA: Michael Weaver, MD, PI; Thomas Jefferson University Hospital, Philadelphia, PA: Jack Jallo, MD, PI; University Hospital Inselspital, Bern, Germany: Michael Reinert, MD, PI; University of California, Los Angeles, Los Angeles, CA: Paul Vespa, MD, PI; University of Alberta, Edmonton, Alberta, Canada: Ken Butcher, MD, PI; University of Buffalo, Buffalo, NY: Jody Leonardo, MD, PI; University of Chicago, Chicago, IL: Agnieszka Ardelt, MD, PhD, PI; University of Cincinnati, Cincinnati, OH: Opeolu Adeoye, MD, PI; University of Debrecen, Debrecen, Germany: Laszlo Csiba, MD, PI; University of Halle, Halle, Germany: Katja Wartenberg, MD, PI; University of Heidelberg, Heidelberg, Germany: Julian Bosel, MD, PI; University of Illinois at Chicago, Chicago, IL: Fernando Testai, MD, PhD, PI; University of Iowa, Iowa City, IA: Harold Adams, MD, PI; University of Leipzig, Leipzig, Germany: Carsten Hobohm, MD, PI; University of Mainz, Mainz, Germany: Thomas Kerz, MD, PI; University of Maryland, Baltimore, MD: E. Francois Aldrich, MD, PI; University of Pittsburgh Medical Center, Pittsburgh, PA: Lawrence Wechsler, MD, Paul Gardner, MD, PI; University of South Florida, Tampa, FL: David Decker, MD, PI; University of South Hampton Hospital, Southampton, Hampshire, Great Britain: Diederik Bulters, MBchB, PI; University of Texas, Houston, Houston, TX: Nicole Gonzales, MD, PI; University of Texas, San Antonio, San Antonio, TX: Jean-Louis Caron, MD, PI; University of Texas, Southwestern, Dallas, TX, Dallas, TX: Christiana Hall, MD, PI; University of Utah, Salt Lake City, UT: Safdar Ansari, MD, PI; University of Zurich, Zurich, Switzerland: Andreas Luft, MD, PI; Vall d'Hebron University Hospital, Barcelona, Spain: Fuat Arikan, MD, PI; Virginia Commonwealth University, Richmond, VA: R. Scott Graham, MD, PI; Wake Forest University, Winston-Salem, NC: Kristi Tucker, MD, PI.

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