Original Article

Reliability of ABC/2 Method in Measuring of Infarct Volume in Magnetic Resonance Diffusion-Weighted Image

Abstract

Aims: Manual planimetry is the current method defining infarct volume on magnetic resonance (MR) diffusion-weighted image. ABC/2 method is an ellipsoid geometric formula with advantage estimation of intraparenchymal hemorrhage volume. Our study aimed to find the reliability and reproducibility of ABC/2 method compared to manual planimetric segmentation method. **Settings and Design:** This was a cross-sectional analytical study with retrospective and prospective data collection. **Subjects and Methods:** A total of 109 patients with acute ischemic stroke and underwent MR images at Ramathibodi Hospital were retrospectively reviewed. Relationship between manual planimetric segmentation and ABC/2 methods (nonadjusted ABC/2 method and adjusted ABC*/2 method) was determined using Wilcoxon signed-rank test, linear regression analysis, and Bland–Altman plot. Subgroup analysis by location, onset, shape, and size of infarct volume was performed. Interobserver reliability was established using intraclass correlation coefficient and Bland–Altman plot. **Statistical Analysis Used:** Wilcoxon signed-rank test, linear regression analysis, and Bland–Altman plot were used for statistical analysis. **Results:** Infarct volume measured with nonadjusted ABC/2 method (23.56, 48.81, 4.25, 0.11, 318.94) (mean, standard deviation, median, minimum, maximum) and adjusted ABC*/2 method (13.37, 28.3, 2.08, 0.06, 170.10) was smaller than manual planimetric method (28.50, 58.64, 5.56, 0.27, 335.49) ($P < 0.001$). Linear regression's slope confirmed underestimation of volume infarct. In round-to-ellipsoid shape and white matter group, the differences found between nonadjusted ABC/2 and manual planimetric methods are not statistically significant. **Conclusions:** ABC/2 method is a simple, rapid, and reproducible method with an excellent positive correlation of both adjusted and nonadjusted ABC/2 methods to manual planimetric segmentation method but tendency to underestimated infarct volume. High interobserver reliability and good agreement between two observers have been established. The utilization of nonadjusted ABC/2 method should be used with caution due to its tendency to underestimate the infarct volume.

Keywords: *ABC/2 infarct volume, adjusted ABC/2, infarct volume estimation, measure infarct volume, reliability ABC/2*

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Introduction

Stroke remains a major global health burden, while the worldwide prevalence in 2013 was 25.7 million people with 10.3 million people having first stroke. In 2010, the incidence of ischemic strokes worldwide is about 11.6 million with 6.5 million deaths in 2013.[1] Due to the narrow window of treatment, a delayed or untreated stroke can lead to long-term neurological disability. As a result, the burden of stroke was estimated to be 118 million disability-adjusted life years lost. However, in Thailand, stroke is the third most common cause of death, with approximately 250,000 patients suffering from both new and recurrent stroke each year.[2]

Reperfusion therapy has proved to be a successful endovascular treatment for patients who have suffered from acute cerebral infarction within a limited time period.[3,4] The so-called "golden hour" is known to be <6 h.[5] A recent endovascular thrombectomy trial (diffusion-weighted image [DWI] or computerized tomography perfusion [CTP] Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo [DAWN] trial) expanded its focus onto patients presented at the extended window of time of between 6 and 24 h after onset of stroke.[5,6] The patients were selected based on a mismatch between the severity of clinical deficit and the infarct volume

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delineated on magnetic resonance imaging (MRI) or CTP, which indicated the presence of ischemic penumbra and was able to be salvaged by means of reperfusion therapy.[7] Infarction volume is one of the factor that is calculated when mismatch is presented. Several studies aimed to determine the accuracy of infarct volume estimation through comparison between manual planimetric segmentation method and automated software.[8,9]

The ABC/2 method used to be considered an effective way of measuring intraparenchymal hemorrhage volume.[10] However, recent studies have proposed a new concept of applying ABC/2 method into the infarct volume measurement technique.[11-14] Due to it being quick, readily available, and feasible, the calculation can be done in an acute setting. The objective of this study is to determine the reliability of ABC/2 in comparison with the planimetric segmentation method, where it can be used to measure the infarct volume in DWI.

Objectives

- To access reliability and reproducibility of ABC/2 method measuring infarct volume in MR DWI
- To identify factors influences outcome by comparing measured volume in different infarct location, size, shape, and onset of infarction.

Subjects and Methods

Patient

The medical records of 109 patients who have been diagnosed with acute ischemic stroke and underwent 1.5-T or 3.0-T MRI at Ramathibodi Hospital between July 2012 and September 2018 available on picture archiving and communication system (PACS) were retrospectively reviewed. The study was approved by the Ethic Committee, Faculty of Medicine, Ramathibodi Hospital, Mahidol University. Patient informed consent did not require due to its retrospective nature. Nine patients were excluded from analysis; seven with too discrete multiple small lesions or too small lesion and two with poor image qualities. The inclusion and exclusion criteria are described below.

Inclusion criteria

- Patient diagnosed with acute ischemic stroke and underwent MRI within 7 days after the onset time of last been known to be well
- Age >18 years.

Exclusion criteria

- No available imaging and demographic data to review
- Too small discrete data or poor image qualities
- Evidence of intracranial tumor or cerebral vasculitis on MRI.

Demographic data

Each patient's demographic data were collected in terms of sex, date of birth, date of MRI, and time interval between onset and MRI.

Image acquisition

MRIs were performed on a 1.5-T system (Signa HDxT, GE healthcare, Milwaukee, Wisconsin, USA) or a 3.0-T system (Philips Ingenia) using stroke protocol that included axial T2W, axial FLAIR, DWI with ADC mapping, axial GRE T2*, or SWI, and TOF MR angiography of the brain and neck. DWI was obtained with a single-shot spin-echo echo-planar pulse with a diffusion gradient b vale of 1000 s/mm^2 in axial axis.

Imaging analysis and measurements

Infarct volume (cm^3) was defined as a hyperintense area visible from the b = 1000 mm/s^2 images and produced apparent diffusion coefficient maps. The measurement using two methods: the manual planimetric segmentation method and the ABC/2 method in both adjusted and nonadjusted slices calculation.

In the manual planimetric segmentation method, the perimeter of infarct volume was delineated with freehand technique. Then, volumetric software GE advantage workstation 4.4 (software release 7.6, GE healthcare, Milwaukee, Wisconsin, USA) was used to calculate the total volume of infarction. Software analyses are based on area delineated and thickness of each slice. The window level and window width were set to acquire the best contrast between the lesion and the surrounding normal tissue.

In ABC/2 method, the measurement was done using Synapse version 3.2.0, FUJIFILM Medical System USA's Synapse PACS System, USA. As a nonadjusted slice calculation, the largest diameter of the selected slice by eye with largest infarct area was measured (A), the largest diameter perpendicular to the line above (B), and the total number of slices of infarct seen multiplying with slice thickness (C). To justify the formula to be more precisely, adjusted slice calculation of total number of slices has been utilized (C*). If the infarct area in particular slice is less than 25% of the largest infarct area, it will be counted as 0 slice. If the infarct area was approximately 25%–75% of the largest infarct area, it will be counted as 0.5 slice. If the infarct area was greater than 75% of the largest infarct area, it will be counted as 1 slice. Summations of the slices described above then multiply with slice thickness in which the lesion was visible (C*). Finally, calculation was done using the formula $0.5 \times A \times B \times C$ in nonadjusted slice method or $0.5 \times A \times B \times C*$ in adjusted slice method [Figure 1]. In some patients, the infarct appeared as a combination of multiple small discrete lesions. In these cases, the volume then was determined in the largest lesion visible.
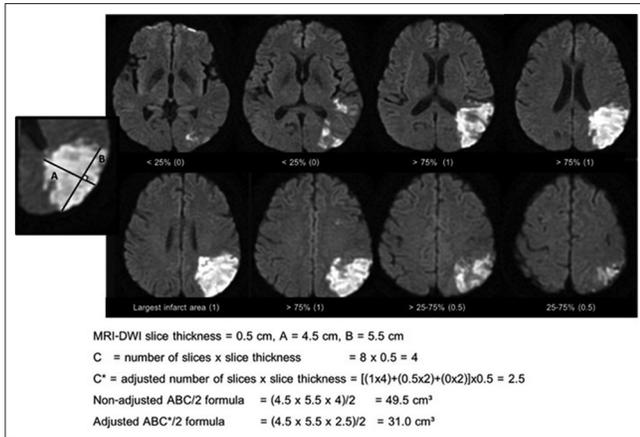
MRI-DWI slice thickness = 0.5 cm, A = 4.5 cm, B = 5.5 cm

C = number of slices x slice thickness = 8 x 0.5 = 4

C* = adjusted number of slices x slice thickness = [(1x4)+(0.5x2)+(0x2)]x0.5 = 2.5

Non-adjusted ABC/2 formula = (4.5 x 5.5 x 4)/2 = 49.5 cm³

Adjusted ABC*/2 formula = (4.5 x 5.5 x 2.5)/2 = 31.0 cm³

Figure 1: Example of infarct volume calculations by nonadjusted ABC/2 and adjusted ABC*/2 methods

A neuroradiologist and a 3rd-year diagnostic radiology trainee were blinded to the clinical information and infarct volume estimated by manual planimetric segmentation method. They had a practicing session before measurement session to prevent learning effect during the study. Both observers interpreted the images using ABC/2 method in both adjusted and nonadjusted slice calculation independently. After at least 4 weeks interval, the 3rd-year diagnostic radiology trainee measured volume of DWI lesions by manual planimetric segmentation method. Interobserver reliability in ABC/2 method was determined by comparing the calculated infarct volume between two observers.

Subgroup analysis was done to identify factors influences outcome by comparing volume, onset, shape, and locations of infarct [Table 1]. Location of infarct was then later divided into four categories as cortex, white matter, deep gray nuclei, and combined group. There were two groups of onset <24 h and >24 h and two groups of shape as round-to-ellipsoid and irregular shape. The size of infarct was divided into two categories as <70 and >70 cm³.

Statistical analysis

All statistical analyses were performed using the SPSS software package version 18.0 (IBM Corp. Released 2009. IBM SPSS Stastistics for Windows, Version 18.0, IBM Corp., Armonk, NY, USA). After confirm distribution of data, data were expressed as mean ± standard deviation (SD), median, and range (minimum [min], maximum [max]).

Wilcoxon signed-rank test was used to determine whether the ABC/2 volumes between both nonadjusted ABC/2 and adjusted ABC*/2 methods with manual planimetric segmentation volumes differed significantly. Statistical significance is defined as $P \leq 0.05$. The linear regression analysis was used to predict the relationship between nonadjusted ABC/2 method–manual planimetric segmentation method and adjusted ABC*/2 method–manual

Table 1: Demographic data

Parameters	*n*
Male	46
Age (years), mean±SD	64.42±13.80
Median onset (hr), (range)	48.90 (3.00-180.50)
Onset groups	
≤24 h	15
>24 h-7 days	85
Site of infarct	
Cortex	10
Deep gray nuclei	16
White matter	10
Combined	64
Shape	
Round-ellipsoid	13
Irregular	87

SD – Standard deviation

Table 2: Infarct volume measured by two independent observers with both nonadjusted ABC/2 and adjusted ABC*/2 methods (cm³)

	Observer	Mean±SD	Median	Range
Nonadjusted ABC/2 volume	A	22.80±47.71	3.80	0.11-326.40
	B	23.56±48.81	4.25	0.11-318.94
Adjusted ABC*/2 volume	A	13.14±27.99	2.17	0.08-184.96
	B	13.37±28.30	2.08	0.06-170.10

SD – Standard deviation

planimetric segmentation method. The data were shown in scatter plot of simple linear equation; the slope of the line represents regression coefficient. The strength of relationship between each ABC/2 method and manual planimetric segmentation method was measured by Pearson's correlation. The agreement between nonadjusted ABC/2 method and manual planimetric segmentation method was measured by the Bland–Altman plots. Intraclass correlation coefficient (ICC) and the Bland–Altman plots were used to identify interobserver reliability of the nonadjusted ABC/2 and adjusted ABC*/2 methods between two observers.

Subgroup analysis by the location (cortex, deep gray nuclei, white matter, and combined), volume (<70 and >70 cm³), onset (<24 and >24 h), and shape (round-to-ellipsoid and irregular) of cerebral infarction was done using Wilcoxon signed-rank tests. The agreement of each group between nonadjusted ABC/2 method and manual planimetric segmentation method was measured by the Bland–Altman plots. The results were reported as limit of agreement and mean differences.

Results

Infarct volume measured with nonadjusted ABC/2 method [Table 2] (23.56, 48.81, 4.25, 0.11, 318.94) (mean, SD, median, min, max) and adjusted ABC*/2 method

(13.37, 28.3, 2.08, 0.06, 170.10) obtained significantly smaller values than manual planimetric segmentation method ($P < 0.001$) (28.50, 58.64, 5.56, 0.27, 335.49). These numbers reflect the superior performance of nonadjusted ABC/2 method as mean and median values were closer to the values obtained from manual planimetric segmentation method.

A strong positive correlation ($R = 0.98$) was observed between nonadjusted ABC/2 and manual planimetric segmentation methods, and the same positive correlation ($R = 0.97$) was also found between adjusted ABC*/2 and manual planimetric segmentation methods [Table 3]. Of 100 cases, 83 cases measured with nonadjusted ABC/2 method underestimated infarct volume by 23.6% median false decrease value under manual planimetric segmentation method, and of 100 cases, 99 cases measured with adjusted ABC*/2 volume underestimated infarct volume by 62.6% median false decrease value under manual planimetric segmentation method, respectively [Table 3].

Linear regression slope confirmed (1) the underestimation of infarct volume compared to manual planimetric segmentation method; (2) the superior performance of nonadjusted ABC/2 method result in a correlated slope of 1.17; and (3) coefficient of determination (R^2) = 95% [Table 3 and Figure 2]. Adjusted ABC*/2 method performed poorly with a correlated slope of 2.01 with a coefficient of determination (R^2) = 93% [Table 3 and Figure 3]. A correlated slope close to 1 implied that there is a strong linear relationship between these sets of data. Both regression analyses were statistically significant with $P < 0.001$. Our results found that the larger the infarct volume presented, the larger the false volume differences were seen [Figure 4].

Interobserver agreement

There was a substantial agreement for both nonadjusted ABC/2 and adjusted ABC*/2 methods between two observers; the ICC was excellent at approximately 0.997 for nonadjusted ABC/2 method and 0.996 for adjusted ABC*/2 method. Pearson's correlation coefficient was
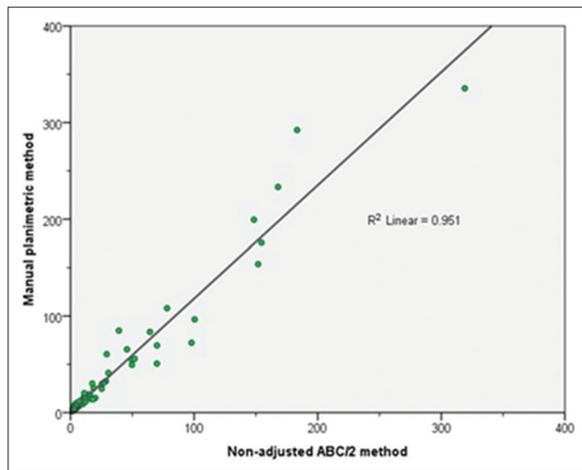

Figure 2: Linear regression of infarct volume measured with nonadjusted ABC/2 method and manual planimetric segmentation method (cm³)
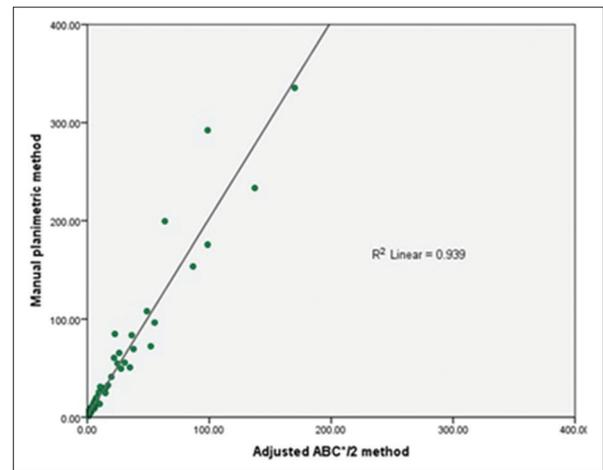

Figure 3: Linear regression of infarct volume measured with adjusted ABC*/2 method and manual planimetric segmentation method (cm³)

Table 3: Regression analysis between infarct volume measured with nonadjusted ABC/2, adjusted ABC*/2 methods, and manual planimetric segmentation method

	Volume (cm³), (median, range)	Correlation	Slope	R^2	P
Manual planimetric volume	5.56 (0.27, 335.49)				
Nonadjusted ABC/2 volume	4.25 (0.11, 318.94)	0.98	1.17	0.95	<0.001
Adjusted ABC*/2 volume	2.08 (0.06, 170.10)	0.97	2.01	0.93	<0.001

Table 4: Correlation (R) between each method and observers

	Manual planimetric	A: Nonadjusted ABC/2	A: Adjusted ABC*/2	B: Nonadjusted ABC/2	B: Adjusted ABC*/2
Manual planimetric	1.00				
A: Nonadjusted ABC/2	0.96	1.00			
A: Adjusted ABC*/2	0.96	0.98	1.00		
B: Nonadjusted ABC/2	0.98	0.99	0.99	1.00	
B: Adjusted ABC*/2	0.97	0.97	0.99	0.98	1.00

0.99 for both methods [Table 4]. The Bland–Altman plots [Figure 5] of two independent infarct volumes demonstrated an acceptable agreement (the mean difference was 0.76 [confidence interval (CI) −0.29–1.81] for the nonadjusted ABC/2 method and mean difference was 0.23 [CI − 4.67–0.93] for the adjusted ABC*/2 method respectively), within thresholds defined by mean ± 1.96 SD from the mean difference. The Bland–Altman plots confirmed interobserver reliability.

Subgroup analysis

Subgroup analysis by location was conducted in nonadjusted method due to the superior performance over adjusted method. A comparison was made between manual planimetric method and nonadjusted ABC/2 method measuring cerebral infarction in the different locations, including cortex, deep gray nuclei, and combined group,
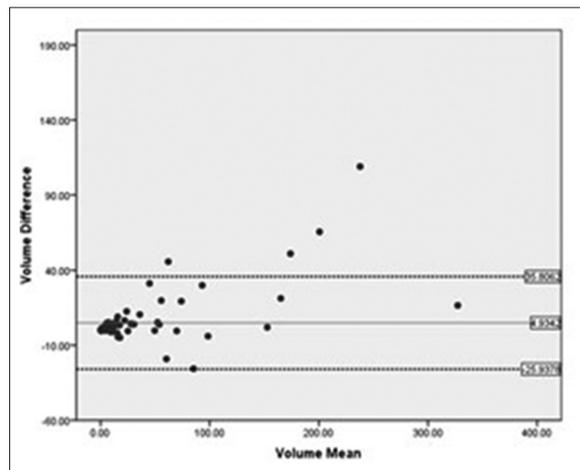

Figure 4: Bland–Altman plots compare nonadjusted ABC/2 and manual planimetric segmentation volume measured. Solid line indicates the mean difference between two methods, dashed lines indicate the limits of the agreements (1.96 standard deviations of the mean difference)

and this showed volume underestimation by nonadjusted ABC/2 method with a statistically significant difference, using Wilcoxon-signed rank test ($P < 0.001$). There was no statistically significant difference in the measured volume in the white matter group ($P = 0.075$) (the mean difference was 0.23 [CI − 3.60–4.07]). The round-to-ellipsoid-shaped group was also found to have no statistically significant differences in the measured volume ($P = 0.249$) (the mean difference was − 0.32 [CI − 0.87–0.24]), which was in contrast with the irregular-shaped group ($P < 0.001$). In terms of size of infarct volume measured between manual planimetric segmentation and nonadjusted ABC/2 methods, there was a statistically significant difference in infarct volume measured in both the <70 cm³ group ($P < 0.001$) (the mean difference was 1.83 [CI −7.97–11.63]) and the >70 cm³ group ($P = 0.026$) (the mean difference was 30.03 [CI − 42.18–102.30]). Both onset time groups of <24 and >24 h were found to have a statistically significant difference in volume measured ($P < 0.001$) [Table 5].

Discussion

Gold standard

Our study aimed to find the reliability and reproducibility of ABC/2 method compared to the gold standard of manual planimetric segmentation method. van der Worp *et al*. tested five different methods to measure infarct volume and found that the manual tracing of the perimeter was reliable and thought to be accurate.[11] Austein *et al*. studied the accuracy of three automated software applications to find the best final infarct volume approximation in comparison to perimeter tracing method. Thus, we used the manual planimetric segmentation method as the appropriated gold standard.

Table 5: Subgroup analysis of infarct volume measured with nonadjusted ABC/2 and manual planimetric segmentation method (cm³)

| Type (*n*)	Median (range)		*P*
	Manual planimetric volume	**Nonadjusted ABC/2 volume**	
Site of infarct			
Cortex (10)	8.70 (2.49, 30.12)	5.84 (1.52, 17.55)	<0.001
Deep gray nuclei (16)	1.50 (0.27, 9.70)	0.96 (0.11, 4.88)	<0.001
White matter (10)	1.64 (0.64, 15.17)	0.663 (0.448, 20.06)	0.075
Combined (64)	11.18 (0.70, 335.49)	9.55 (0.42, 318.94)	<0.001
Shape			
Round-to-ellipsoid (13)	1.14 (0.27, 4.39)	2.00 (1.00, 3.50)	0.249
Irregular (87)	7.86 (0.64, 335.49)	5.78 (0.18, 318.94)	<0.001
Volume			
<70 cm³ (91)	4.40 (0.27, 69.53)	3.36 (0.11, 69.98)	<0.001
>70 cm³ (9)	153.69 (84.85, 335.49)	148.40 (39.10, 318.94)	0.026
Onset			
<24 h (14)	15.92 (0.92, 175.70)	13.87 (0.12, 154.44)	<0.001
>24 h (86)	4.69 (0.27, 335.49)	3.43 (0.11, 318.94)	<0.001
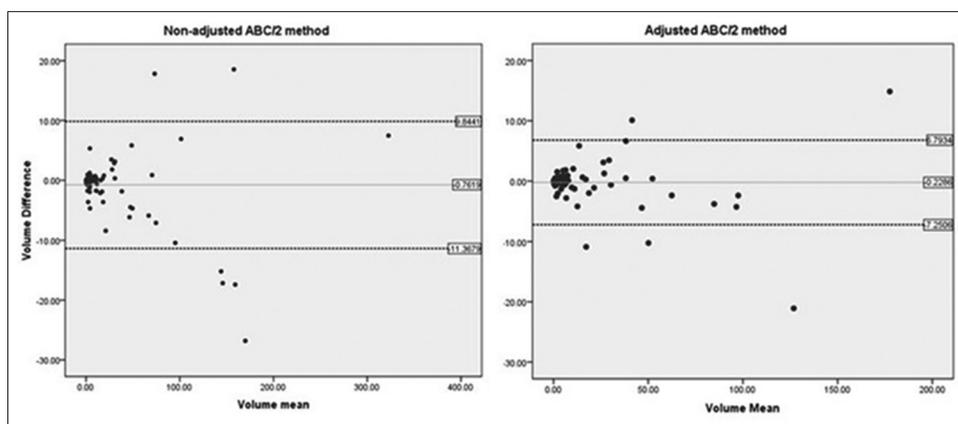
Figure 5: Bland-Altman plots compare volume measured between two observers in nonadjusted ABC/2 and adjusted ABC*/2 methods. Solid line indicates the mean difference between two observers in each method, dashed lines indicate the limits of the agreements (1.96 standard deviations of the mean difference)

Accuracy of ABC/2 and manual planimetric methods and subgroup analysis

The previous study by Pedraza *et al*.[12] showed less accuracy with overestimation of ABC/2 method measuring the irregular-shaped infarct volume, which is discordant to our results that underestimated the infarct volume. The explanation for the discordant result with Pedraza *et al*. might be due to longer time of onset-to-imaging in our study, which may result in better delineation of the infarct area. However, we still observed the inferior accuracy of ABC/2 method measuring the irregular-shaped infarct volume, which was found in the majority of our cases, as well as in other published data.

Statistical significant differences in volume measured were found in all regions (cortex, deep grey, nuclei, and combined), onset times (<24 h, and >24 h), volumes (<70 cm^3, and >70 cm^3) and irregular shape group. Except in round-to-ellipsoid shape and white matter group, the differences found between nonadjusted ABC/2 and manual planimetric segmentation methods are not statistically significant. Sims *et al*. found that ellipsoid-shaped infarct volume had better accuracy for measuring with ABC/2 method, which corresponds with our results.[13] Furthermore, our results showed better accuracy for measuring white matter infarct than the other location.

In our study, nonadjusted ABC/2 and adjusted ABC*/2 method found median false decreased values under manual planimetric segmentation of 23.6% and 62.6%, respectively. The nonadjusted ABC/2 method performed better with an R^2 value of 95% compared to adjusted ABC*/2 method with a value of 93%. Inferior outcome of adjusted ABC*/2 method might result from the exclusion of slices seen with infarction >75% of the largest infarct area, which decreased the total volume calculation.

According to our study, we also found a strong positive correlation between nonadjusted/adjusted ABC/2 methods and manual planimetry method, with high interobserver

reliability. The results of our study are supported by Gómez-Mariño *et al*., who also found a high correlation between linear planimetry and ABC/2 method.[14] However, there was a statistically significant difference in infarct volume measured between ABC/2 method and manual planimetric segmentation method. Our results suggested that the larger infarct volume presented, the larger the false volume differences were found.

In summary, our study supports the use of ABC/2 method in the acute or emergency setting and under caution, because both nonadjusted ABC/2 and adjusted ABC*/2 methods underestimated infarct volume. However, it took only a few minutes to measure infarct volume using ABC/2 method in all of the cases. According to the DAWNs trial, the value of clinical deficit-infarct volume mismatch in selection of stroke patient to receive thrombectomy is emphasized. The importance of this biomarker makes nonadjusted ABC/2 method becomes more appealing if the manual planimetric segmentation method is not available.

Limitations of the study

Our study was lack of normal distribution of data, and the sample size was not sufficient, i.e., the majority of our study cases were in the group of small infarct volume (5.56 cm^3 [0.27, 335.49]) (median, [range]) with combined location. Since the extended golden period of ischemic stroke was proposed to be 24 h from onset of stroke, our study included an MRI study of stroke patients presented from the time between the onsets up to 7 days. The results of this study can only be applied to MRI with DWI sequences, which will not be available in all clinical settings; the most frequent being performed in acute cerebral infarction is noncontrast-enhanced CT investigation. Future trials are needed to for an improved guide in relation to therapeutic utilization or clinical outcome.

Conclusions

The nonadjusted ABC/2 and adjusted ABC*/2 method has a strong positive correlation with manual planimetric

segmentation method and high interobserver reliability but underestimated infarct volume. Superior performance was found in nonadjusted method over adjusted method. Our study supports the utilization of nonadjusted ABC/2 providing caution is given to the tendency infarct volume underestimation. In a clinical setting without manual tracing or RAPID software, the ABC/2 method is clearly a simple, rapid, reproducible, and accurate measurement of infarct volume in ellipsoid shape and in white matter location. However, our study shows that this method cannot be applied for very large infarct volumes.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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