

Cerebral infarct volume measurements to improve patient selection for endovascular treatment

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Abstract

Patients who have large cerebral infarctions may not be good candidates for endovascular treatment. Various methods for determining infarct volume have been used in clinical studies. We evaluated the effectiveness of several methods for measuring infarct volume, especially regarding futile outcomes despite endovascular treatment.

Patients with acute ischemic stroke in unilateral anterior circulation territory who were treated with intra-arterial thrombectomy were included. For assessing infarct volume, the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) scoring system was applied to images obtained by noncontrast computed tomography (NCCT), postcontrast CT (PCCT), and diffusion-weighted imaging (DWI). DWI stroke volume was semiquantitatively measured with the manually outlined hyperintense lesion. Infarct core volume was calculated with a threshold apparent diffusion coefficient value of $600 \times 10^{-6} \text{ mm}^2/\text{s}$. Intraclass correlation coefficients (ICC) were estimated to assess inter-reader reliability for ASPECTS scoring and DWI stroke volume. Receiver operating characteristic (ROC) curve analyses, and univariable and multivariable comparative analyses, were performed with each evaluation method to predict futile outcome (modified Rankin Scale score 5–6).

The mean age of the included 79 patients was 65.1 ± 15.7 years. Among them, 55 (69.6%) patients demonstrated successful reperfusion after intra-arterial thrombectomy, but 34 (43.0%) patients had futile outcomes. Inter-reader agreement was excellent for measurement of the DWI stroke volume (ICC, 0.973), DWI ASPECTS (0.940), and PCCT ASPECTS (0.859), but was moderate for NCCT ASPECTS (0.694). Regarding prediction of futile outcomes, area under ROC curve was 0.551 on NCCT ASPECTS and it was significantly smaller than that in PCCT ASPECTS (area under ROC 0.651, $P=0.030$), DWI ASPECTS (0.733, $P=0.003$), DWI stroke volume (0.702, $P=0.022$), and infarct core volume (0.702, $P=0.021$). Besides old age and high National Institutes of Health Stroke Scale score on admission, MRI parameters such as DWI ASPECTS and infarct core volume indicating large volumes were independently associated with futile outcomes in multivariable analyses.

DWI ASPECTS can be a good parameter predicting futility, which is easily measured and has high prediction power.

Abbreviations: ADC = apparent diffusion coefficient, ASPECTS = Alberta Stroke Program Early Computed Tomography Score, CT = computed tomographic, DWI = diffusion-weighted imaging, FLAIR = fluid-attenuated inversion recovery, ICC = intraclass correlation coefficients, MR = magnetic resonance, mRS = modified Rankin Scale, mTICI = modified thrombolysis in cerebral infarction, NCCT = noncontrast CT, NIHSS = National Institutes of Health Stroke Scale, PCCT = postcontrast CT, PWI = perfusion-weighted imaging, ROC = receiver operating characteristic, rt-PA = recombinant tissue plasminogen activator.

Keywords: cerebral infarction, cerebral revascularization, magnetic resonance imaging, stroke volume, x-ray computed tomography

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1. Introduction

Acute ischemic stroke is a devastating condition with a high burden of neurologic disability and death especially when a large intracranial artery is occluded.^[1] Early reperfusion treatment is the best way for reducing the disability.^[2] Endovascular treatments for patients with acute ischemic stroke have evolved over the past few years.^[3] Recently, several randomized control studies have succeeded in showing that endovascular treatment surpasses medical treatment based on intravenous recombinant tissue plasminogen activator (rt-PA) in patients with intracranial artery occlusions, especially in the anterior circulation.^[4–8] Baseline computed tomographic (CT) or magnetic resonance (MR) angiography are the primary tools used for patient selection for endovascular treatment. However, additional imaging protocols varied widely between studies, and therefore, it is not clear which imaging protocols should be used for optimal results.

For further patient selection, some trials have used additional imaging protocols to exclude patients who already had large infarcts prior to initiating endovascular treatment.^[9] Some of

those studies used the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) scoring system with noncontrast CT (NCCT) images.^[10–12] Some studies have alternatively used other modalities: 1 study used ASPECTS with diffusion-weighted imaging (DWI),^[12] another study used infarct core volume on DWI,^[11] and another study used infarct core volume on cerebral blood flow by perfusion CT.^[13] Thus, a variety of imaging protocols were used in these successful trials.

In the emergency room in our institute, concomitant CT imaging such as NCCT, CT angiography, and postcontrast CT (PCCT) is used for selecting patients for endovascular treatment. Multimodal MRI is also performed before entering the angio suite. Considering the variety of protocols successfully used, it is imperative to determine the simplest and most effective one. Therefore, we evaluated the prediction power of these protocols for clinical outcomes in patients with endovascular treatment, especially focusing on imaging protocols to determine infarct volumes.

2. Methods

2.1. Patient enrolment

This retrospective study included 79 patients (45 men; 34 women) selected from a database of 201 consecutive patients with ischemic stroke who had undergone endovascular treatment at Ajou University Hospital, Suwon, Korea and between January 2010 and March 2014. Inclusion criteria were (Fig. 1): an acute ischemic stroke due to intracranial large artery occlusions in the unilateral anterior circulation; pretreatment MRI within 6 hours after symptom onset; intra-arterial mechanical thrombectomy within 8 hours after symptom onset, using the Penumbra system (Penumbra, Alameda, CA), Solitaire stent system (Covidien,

Irvine, CA) or a combination of these as a primary method; and available clinical neurologic data at admission and follow-up at approximately 3 months poststroke.

Exclusion criteria were: primary treatment with an intra-arterial thrombolysis agent such as urokinase, and acute stroke involving bilateral hemisphere or both anterior and posterior circulation. This study was approved by the local institutional review board, and written informed consent was achieved for patients' revascularization treatments.

2.2. Imaging protocols

The CT scans (SOMATOM Sensation 16, Siemens, Erlangen, Germany), including noncontrast and postcontrast axial parenchymal images, were acquired with contiguous 4.5-mm thick axial sections (120 kV, 270 mAs). CT angiography was performed using 1-mm slice thickness, 0.5-mm reconstruction interval, 100 kV, 170 mAs. A maximum of 90 mL (1.2 mL/kg) of iodinated contrast agent (Ioversol; Optiray 320; Mallinckrodt, Hazelwood, MO) was injected at 4 mL/s, immediately followed by a 15 mL saline bolus. The CT source images were postprocessed to create coronal, sagittal, and axial multiplanar reformats in maximum-intensity projection images and volume-rendered 3D images.

MRI was performed with a 3T MR scanner (Intera Achieva; Philips Healthcare, Best, The Netherlands) using a 16-channel neurovascular (NV) head coil. The MRI protocol for acute stroke included the following sequences: localizer, DWI, T2 turbo spin echo, fluid-attenuated inversion recovery (FLAIR), gradient echo (GRE), perfusion-weighted imaging (PWI). Total acquisition time was 9 minutes 35 seconds. The DWI sequences were single-shot echo planar imaging acquired in the axial plane with the following parameters: TR 3000 ms; TE 80 ms; *b* value 1000 s/mm²; field of view 22 cm; matrix size 128 × 128; and 28 slices with 5-mm slice

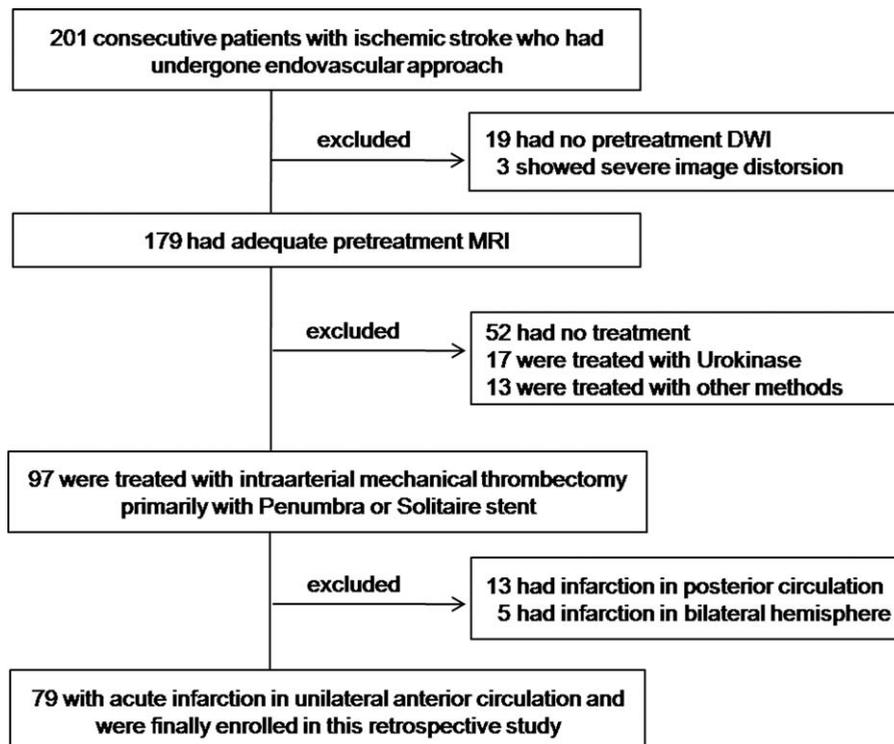


Figure 1. Study flow for patient enrolment.

thickness and without interslice gap. Apparent diffusion coefficient (ADC) values were calculated at 2 different b values ($b=0$ and $b=1000$ s/mm²). DWI images and ADC maps were generated on the scanner console at the time of imaging. For the PWI sequences, dynamic susceptibility contrast T2*-weighted images were collected using a single-shot gradient echo planar imaging sequence with the following parameters: TR 1874 ms; TE 30 ms; flip angle 40°; field of view 24 cm; matrix size 128 × 128; 5-mm slice thickness without interslice gap. Images were acquired after gadolinium contrast (Gadovist, gadobutrol, Bayer HealthCare) injection (0.1 mmol/kg; flow rate 3 mL/s) using a power injector immediately followed by a 20 mL saline flush.

2.3. Acute stroke treatment

For acute ischemic stroke treatment, a bridging endovascular treatment protocol based on noncontrast CT and CT angiography was used. Patients who met the criteria for IV rt-PA within 3 to 4.5 hours of onset were treated with 0.9 mg/kg IV rt-PA. If an occluded intracranial large artery corresponding to the stroke signs on CT angiography was observed, the patients were brought to the angiography room for endovascular treatment. Patients in whom intracranial large artery occlusion was identified despite IV rt-PA treatment, and those who were ineligible to receive IV rt-PA or who were late for the IV rt-PA time window were considered candidates for endovascular treatment. The time window for endovascular treatment was less than 6 hours of onset-to-puncture time. If the time window was expected to be 6 to 8 hours, the decision to perform endovascular treatment was based on DWI-PWI mismatch. If the onset was unclear (e.g., wake-up stroke), the decision was based on DWI-FLAIR mismatch. The MRI with PWI was achieved before the entering the angio suite. Written consents were achieved from family members for taking CT, MRI, endovascular treatment, respectively. Physicians describe the reason and rationale for taking those imaging and invasive treatments and warn well-known side effects for each protocol in the emergent practices.

The methods of endovascular treatment were determined at the treating physicians' discretion. For mechanical thrombectomy, the clot aspiration method with the Penumbra system was used in the early study period, while the embolus retrieval method with the Solitaire stent system was mostly used after 2011. Reperfusion was graded with a modified Thrombolysis in Cerebral infarction (mTICI) score 2b (>50% reperfusion) or 3 was defined as a successful reperfusion.

2.4. Imaging analysis

Baseline ASPECTS^[14] was independently evaluated on NCCT and PCCT by 1 neurologist (KSL) and 1 neuroradiologist (MH). ASPECTS was also evaluated on baseline DWI (MH, KSL). Infarct volume was semiquantitatively measured using the manually outlined hyperintense lesion on diffusion MRI (defined as DWI stroke volume) by 2 independent readers (KSL, MH) using an institutional picture archiving and communication system. Volume was calculated as total hyperintense area in single slices multiplied by slice thickness.^[15,16] Infarct core volume was quantitatively calculated with the multiple margin thresholds of ADC value as 550×10^{-6} , 600×10^{-6} , 650×10^{-6} , and 700×10^{-6} mm²/s using commercial automatic software (NordicICE, NordicNeuroLab, Bergen, Norway). The area under the receiver operating characteristic (ROC) curve according to

ADC thresholds (550×10^{-6} , 600×10^{-6} , 650×10^{-6} , and 700×10^{-6} mm²/s) for predicting clinical outcome was quite similar (supplement Table and Figure, <http://links.lww.com/MD/B238>). Therefore, we representatively present the data from the threshold 600×10^{-6} mm²/s of ADC, which is mostly used in clinical trials.^[17]

Occurrence of haemorrhagic transformation after endovascular treatment was evaluated on follow-up images within 72 hours after treatment. Parenchymal hematoma was determined according to the European Cooperative Acute Stroke Study.^[18]

2.5. Clinical scoring

The National Institutes of Health Stroke Scale (NIHSS) was used to assess the neurological status of patients with acute stroke on admission. A 3-month poststroke modified Rankin Scale (mRS) was used for assessing the clinical outcome. Good outcomes and futile outcomes were defined as mRS scores ≤ 2 and 5 to 6, respectively.

2.6. Statistical analyses

Intraclass correlation coefficients (ICC) were estimated to assess inter-reader reliability for ASPECTS scoring and semiquantitative infarct volume measurement. ICC value <0.6 indicated poor reliability, 0.6 to 0.79 indicated substantial reliability, and 0.8 to 0.99 indicated excellent agreement. Discordance of ASPECTS scoring between 2 readers was resolved by consensus, and mean value of DWI stroke volume measured by 2 readers was used for further evaluation.

ROC curve analyses were performed for determining the proper threshold of each imaging protocol to predict good outcome, futile outcome, mortality, and occurrence of parenchymal hematoma (types 1–2), respectively. The predicting power of each imaging protocol was also compared.

Patients were classified into 2 groups comparing those with and without futile outcomes. For univariate comparison, χ^2 test (or Fisher exact test if appropriate) for categorical variables and t test (or Mann–Whitney U test if appropriate) for continuous variables were used. Multivariable logistic regression analyses were performed to identify independent factors associated with a futile outcome after major confounding variables including age, sex, initial NIHSS score, location of occlusion, unsuccessful revascularization (mTICI grade 0–2a), and time from stroke onset to final angiography were adjusted. The goodness of fit of the multivariable logistic regression model was tested using the Hosmer–Lemeshow test. Statistical significance was defined as $P < 0.05$. Statistical analyses were performed using MedCalc software (version 15.4, MedCalc) and SPSS software (version 22, IBM Company, Chicago, IL).

3. Results

3.1. Inter-reader reliability for evaluating the infarction area

Baseline characteristics of the 79 study patients are described in Table 1. Intraclass correlation coefficients (ICC) for ASPECTS scoring and quantitative infarct volume measurement are presented in Table 2. Inter-reader agreement for scoring NCCT ASPECTS was 0.694 ($P < 0.001$); however, it was 0.859 ($P < 0.001$) for PCCT ASPECTS. Inter-reader agreement was 0.940 ($P < 0.001$) and 0.973 ($P < 0.001$) for measuring the DWI ASPECTS and DWI stroke volume, respectively.

Table 1**Patient demographics and clinical characteristics.**

Characteristics	N
Patients	79
Sex	
Male	45 (57.0%)
Female	34 (43.0%)
Age (y, mean ± SD)	65.1 ± 15.7
Baseline NIHSS (median, IQR)	17 (14–19)
Intravenous rt-PA	57 (72.2%)
Site of intracranial artery occlusion	
Internal carotid artery, T	30 (38.0%)
Middle cerebral artery, M1	44 (55.7%)
Middle cerebral artery, M2	5 (6.3%)
Time from stroke onset to CT (h, median, IQR)	1.9 (1.1–2.4)
Time from stroke onset to MRI (h, median, IQR)	2.8 (2.2–3.4)
Time from stroke onset to groin puncture (h, median, IQR)	3.7 (3.1–4.4)
Time from stroke onset to final angiography (h, median, IQR)	5.4 (4.5–6.5)
Intra-arterial thrombectomy device	
Solitaire	52 (65.8%)
Solitaire+Penumbra	14 (17.7%)
Penumbra	13 (16.5%)
Successful revascularization (mTICI 2b-3)	55 (69.6%)
Parenchymal hematoma type 1 and 2 on follow-up imaging	12 (15.2%)
Good outcome (mRS score 0–2) after 3 mo	20 (25.3%)
Futile outcome (mRS score 5–6) after 3 mo	34 (43.0%)

IQR = interquartile range, mRS = modified Rankin Scale, mTICI = modified thrombolysis in cerebral infarction, rt-PA = recombinant tissue plasminogen activator.

3.2. ROC curve analyses for each imaging measurement

Table 3 and Fig. 2 show ROC curve analyses of imaging protocols for predicting good outcome, futile outcome, mortality, and subsequent parenchymal hematoma formation (PH1, PH2),

respectively. There were no statistically significant differences among NCCT, PCCT and DWI ASPECTS, infarct core volume, and DWI stroke volume for predicting good outcome and subsequent hematoma formation after endovascular treatment, respectively. However, for predicting futile prognosis and mortality, NCCT ASPECTS scoring showed statistically significant smaller area under the curve ($P < 0.05$). Except for NCCT ASPECTS, other imaging measurements showed similar performance for predicting clinical outcome, but MRI parameters appeared to perform better than CT parameters. Table 4 shows each cut-off level and their sensitivity and specificity for predicting futile outcomes. Noticeably, the cut-off level of DWI ASPECTS was much lower than that of NCCT or PCCT ASPECTS. On the other hand, the cut-off level of DWI stroke volume was about 1.7 times that of the infarct core volume.

3.3. Prediction of futile outcome after endovascular treatment

Table 5 shows comparisons of various parameters including quantified infarct volume after classification of the study population into mRS score 5 to 6 (futile outcome) and mRS score 0 to 4 groups. Patients who showed a futile outcome at 3 months poststroke were older and male, had lower baseline NIHSS scores, differed by location of occlusion, had more postprocedure haemorrhage, and had larger initial infarct volumes. Initial infarct volume based on MRI, MRI ASPECTS, and infarct core volume were significantly different between the 2 different outcome populations, but infarct volumes based on CT, NCCT ASPECTS, and PCCT ASPECTS were not. After adjusting other variables, MRI-based volume parameters were shown to be the strongest independent predictors for futile outcome. The

Table 2**Median score or volume from each measurement and the inter-reader agreement for parameters by manual measurement.**

	Median (IQR)	ICC (95% CI)	P value
NCCT ASPECTS	7 (5–9.5)	0.694 (0.523–0.804)	<0.001
PCCT ASPECTS	6 (3–8.5)	0.859 (0.756–0.915)	<0.001
DWI ASPECTS	4 (2.5–6)	0.940 (0.906–0.961)	<0.001
Infarct core volume ^{*†}	31.7 mL (9.2–81.1)	—	—
DWI stroke volume	64.4 mL (25.2–134.4)	0.973 (0.958–0.983)	<0.001

ASPECTS = Alberta Stroke Program Early Computed Tomography Score, CI = confidence interval, DWI = diffusion-weighted imaging, ICC = intraclass correlation coefficient, IQR = interquartile range, NCCT = noncontrast CT, PCCT = postcontrast CT.

^{*} A threshold of ADC value as $600 \times 10^{-6} \text{ mm}^2/\text{s}$.

[†] The parameter was automatically measured so inter-reader agreement was not evaluated.

Table 3**The area under the ROC curve analysis for predicting clinical outcomes of endovascular treatment.**

Imaging protocol	Good outcome		Futile outcome		Mortality		Parenchymal hematoma	
	AUC	95% CI	AUC	95% CI	AUC	95% CI	AUC	95% CI
NCCT ASPECTS	0.617	0.501–0.724	0.551 [*]	0.435–0.663	0.548 [†]	0.432–0.661	0.647	0.531–0.751
PCCT ASPECTS	0.646	0.531–0.751	0.651	0.536–0.755	0.683	0.568–0.783	0.712	0.599–0.808
DWI ASPECTS	0.672	0.557–0.774	0.733	0.622–0.826	0.786	0.679–0.870	0.726	0.614–0.820
Infarct core volume [‡]	0.686	0.571–0.785	0.702	0.588–0.799	0.785	0.678–0.869	0.763	0.654–0.852
DWI stroke volume	0.692	0.578–0.791	0.702	0.598–0.800	0.783	0.676–0.868	0.751	0.641–0.842

ASPECTS = Alberta Stroke Program Early Computed Tomography Score, AUC = area under the receiver operating characteristic (ROC) curve, CI = confidence interval, DWI = diffusion-weighted imaging, NCCT = noncontrast CT, PCCT = postcontrast CT.

^{*} AUC of NCCT ASPECTS is significantly smaller than that of PCCT ASPECTS ($P = 0.030$), DWI ASPECTS ($P = 0.003$), infarction core volume ($P = 0.021$), and DWI stroke volume ($P = 0.022$) for predicting futile outcome.

[†] AUC of NCCT ASPECTS is significantly smaller than that of DWI ASPECTS ($P = 0.001$), infarction core volume ($P = 0.006$), and DWI stroke volume ($P = 0.004$) for predicting mortality.

[‡] A threshold of ADC value as $600 \times 10^{-6} \text{ mm}^2/\text{s}$.

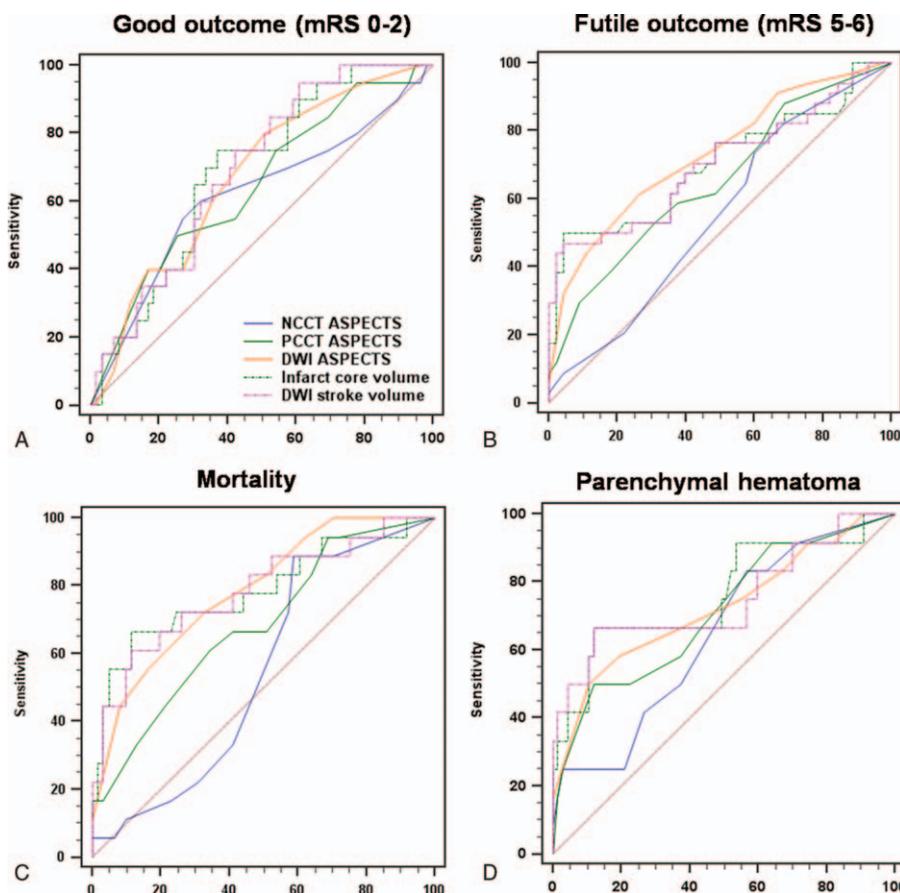


Figure 2. ROC curve analysis for predicting outcome of endovascular treatment according to the imaging protocol. A, Good outcome. B, Futile outcome. C, Mortality. D, Parenchymal hematoma. ROC = receiver operating characteristic.

Hosmer–Lemeshow test showed good fitness ($P=0.352$ for DWI ASPECTS and $P=0.243$ for infarct core volume).

4. Discussion

In the present study, we found that MRI parameters have high inter-reader reliability in assessing cerebral infarct volume and high predictive power for futile outcome following endovascular treatment compared with CT parameters. The commonly used NCCT ASPECTS predicted good outcomes, but not futile outcomes, well. However, despite the 10-minute MRI protocol, the time from onset to puncture was longer than it should ideally be.

An estimation of cerebral infarct volume based on CT has been widely used since NCCT ASPECTS has shown good prediction

power for outcomes in various clinical trials including those for recent endovascular treatment methods.^[4–7,19] The ASPECTS has many advantages since baseline NCCT is performed for most ischemic stroke patients, and since this scoring system can be easily applied. Moreover, this system has been widely validated in various prospective clinical trials.^[19,20] However, our results indicate that ASPECTS is limited by low inter-reader reliability, which is consistent with previous reports.^[21,22] In addition, the ASPECTS system did not have good predictive power especially for good outcomes. This limitation may necessitate the use of additional imaging protocols to ensure optimal patient selection for endovascular treatment. Indeed, a collateral protocol was added to the ASPECTS system in the ESCAPE study,^[10] which resulted in significant improvements in mortality rates.^[5] Because of its success, the additional collateral protocol is expected to be adopted by more institutes, but it may not be acceptable in some institutes due to low-grade CT systems and a high radiation dose. In our hospital, MRI has been performed after baseline CT series and before endovascular treatment since 2010. Therefore, we investigated the potential role of MRI, especially in terms of determining infarct volume, for proper selection of patients who need endovascular treatment based on primary newer thrombectomy devices.

Among the MRI grading systems, prediction power for good and poor outcomes was similarly high in ROC curve analyses of our data. Before discussing this, it is important to differentiate several similar terms: DWI stroke volume, infarct core volume,

Table 4
Cut-off values for futile prognosis after endovascular thrombectomy from ROC curve analyses.

Imaging protocol	Cut-off level	Sensitivity	Specificity
NCCT ASPECTS	≤7	64.7%	42.2%
PCCT ASPECTS	≤6	52.9%	68.9%
DWI ASPECTS	≤3	61.8%	73.3%
Infarct core volume*	>86.2 cm ³	50.0%	95.6%
DWI stroke volume	>149.5 cm ³	47.1%	95.6%

ASPECTS=Alberta Stroke Program Early Computed Tomography Score, DWI=diffusion-weighted imaging, NCCT=noncontrast CT, PCCT=postcontrast CT, ROC=receiver operating characteristic.
* A threshold of ADC value as $600 \times 10^{-6} \text{mm}^2/\text{s}$.

Table 5**Predictors of futile outcomes (mRS scores 5–6).**

Imaging	Univariable analysis			Multivariable logistic regression models			
	mRS score 5–6 (n=34)	mRS score 0–4 (n=45)	P	For DWI ASPECTS		For infarct core volume	
				Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Age, mean ± SD	72 ± 12	60 ± 16	<0.001	1.075 (1.022–1.130)	0.005	1.110 (1.038–1.186)	0.002
Male	15 (44.1%)	30 (66.7%)	0.045	0.637 (0.172–2.366)	0.501	1.458 (0.337–6.312)	0.614
Hypertension	23 (67.6%)	25 (55.6%)	0.276				
Diabetes	13 (38.2%)	9 (20.0%)	0.073				
Atrial fibrillation	21 (61.8%)	20 (44.4%)	0.127				
Initial NIHSS score, median [IQR]	19 [15.5–20.5]	16 [13.5–18]	0.002	1.187 (1.011–1.393)	0.036	1.206 (1.014–1.436)	0.035
Occlusion location			0.048		0.924		0.728
Intracranial ICA	18 (52.9%)	12 (26.7%)		Ref		Ref	
MCA M1	14 (41.2%)	30 (66.7%)		0.793 (0.222–2.826)	0.720	1.720 (0.396–7.470)	0.469
MCA M2	2 (5.9%)	3 (6.7%)		1.051 (0.070–15.752)	0.971	0.965 (0.064–14.572)	0.979
Time from onset to final angiography, median [IQR]	5.5 [4.7–6.6]	5.2 [4.4–6.2]	0.718	1.096 (0.703–1.711)	0.685	1.121 (0.693–1.814)	0.642
mTICI 0–2a	13 (38.2%)	11 (24.4%)	0.187	1.201 (0.306–4.176)	0.793	1.560 (0.339–7.174)	0.568
Parenchymal hematoma	11 (32.4%)	1 (2.2%)	<0.001				
NCCT ASPECTS			0.532				
8–10	12 (35.3%)	19 (42.2%)					
0–7	22 (64.7%)	26 (57.8%)					
PCCT ASPECTS			0.255				
7–10	13 (36.1%)	23 (51.1%)					
0–6	21 (61.8%)	22 (48.9%)					
DWI ASPECTS			0.002		0.025		
4–10	13 (38.2%)	33 (73.3%)					
0–3	21 (61.8%)	12 (26.7%)		4.252 (1.199–15.078)			
Infarct core volume*			<0.001				0.001
0–85 cc	17 (50.0%)	42 (93.3%)					
>85 cc	17 (50.0%)	3 (6.7%)				26.480 (3.669–191.101)	

ASPECTS = Alberta Stroke Program Early Computed Tomography Score, CI = confidence interval, DWI = diffusion-weighted imaging, ICA = internal carotid artery, MCA = middle cerebral artery, mRS = modified Rankin Scale, mTICI = modified thrombolysis in cerebral infarction, NCCT = noncontrast CT, NIHSS = National Institutes of Health Stroke Scale.

* A threshold of ADC value as $600 \times 10^{-6} \text{ mm}^2/\text{s}$.

and DWI ASPECTS. DWI stroke volume has been widely used in previous studies since it can be easily ascertained by outlining abnormally high signal intensity areas on DWI by manipulating the Picture Archiving and Communication System. Considering thickness, the total volume can be calculated using a semiquantitative method.^[15,16] Infarct core volume has been used to analyze mismatches with ischemic penumbras.^[17] The abnormal signal is based on the threshold of the ADC map, and an ADC threshold of $600 \times 10^{-6} \text{ mm}^2/\text{s}$ has been shown to correlate well with clinical outcomes.^[23] In the current study, we analyzed the final volumes and inter-reader reliability, and prediction power for clinical outcomes among infarct core volumes with various thresholds of ADC and DWI stroke volume. We found that there was little difference in these parameters among those protocols. All of them had good inter-reader reliability and high prediction power for both good and poor clinical outcomes. However, the size of the infarction volume was larger in semiquantitative DWI stroke volume than in infarct core volume. The cut-off value for the futile outcomes was 85 cm^3 for infarct core volume with an ADC threshold of $600 \times 10^{-6} \text{ mm}^2/\text{s}$ whereas it was 150 cm^3 for semiquantitative DWI stroke volume in our results. Finally, DWI ASPECTS is a system that applies the ASPECTS scoring system to DWI image. A previous study showed that a DWI ASPECTS score of ≥ 7 corresponded to semiquantitative DWI stroke volume less than 70 cm^3 and a score of ≤ 3 corresponded to a volume of more than 100 cm^3 .^[24] This system has been reported to have

potential predictive power for clinical outcomes of stroke endovascular treatment, but age-related stratification is necessary to improve the predictive accuracy.^[25] In our study, consistent with previous reports, DWI ASPECTS had good inter-reader reliability and high prediction power for clinical outcomes similar to DWI infarct volume protocols.^[26,27]

Recently, many randomized clinical trials have successfully used shift analysis of mRS scores as a primary endpoint for endovascular treatment.^[4–8] Based on this, the aim of the endovascular treatment should be, more importantly, to avoid futile outcomes like mRS scores 5 to 6. In some reports, patients with ADC infarct core volumes over 70 cm^3 or even 50 cm^3 have been excluded from trials of endovascular treatment.^[11,17] DWI ASPECTS less than 6 has also been considered an exclusion criterion.^[7] In the current study, we found that the cut-off volume for futile outcome was larger than that used for exclusion criteria of previous trials. Patients included in the current study used newer thrombectomy devices as the primary device for endovascular treatment. As shown by recent successful clinical trials based on stent retrievers or aspiration devices, revascularization performance and clinical outcomes have improved, and it is expected that patients with bigger infarct volumes can now be included for endovascular treatment.

Despite the high performance of MRI protocols, a significant delay from time of stroke onset to groin puncture was observed in our study. A crucial component of recent successful clinical trials

for endovascular treatment was the reduction of the stroke onset-to-puncture time, and some studies set their CT-to-puncture time to less than 1 hour.^[5,6] Theoretically, our protocol requires less than 15 minutes including contrast injection for PWI; however, the CT-to-puncture time can be up to 2 hours in total. The long CT-to-puncture time was attributed to several factors. Our MRI rooms are not located between the emergency room and angio suite, whereas the CT machine is in the emergency room. In addition, other delays prior to imaging such as screening and preparation of patients for the MRI environment were inevitable. Otherwise, intravenous rt-PA is infused, a Foley catheter is inserted, and other larger-bore needles should be inserted for delivery of the bolus of contrast agent for PWI after CT. Our next step would be to develop protocols that take lesser time to prepare all the above processes. Recently, a 6-minute MRI protocol was introduced that uses echo-planar imaging and a parallel acquisition technique.^[28] Nevertheless, all efforts are necessary to reduce onset to puncture time for using the more accurate protocol, MRI. Close monitoring of institutional time frames is also needed.

MRI can be also effective in some other unusual situations. In Asian countries, underlying intracranial atherosclerotic diseases are often hidden in the large artery occlusions.^[29] Difference in infarct pattern on the DWI may be useful to differentiate in situ thrombosis of intracranial atherosclerotic disease from cardioembolism.^[30,31] In addition, multimodal MRI can be useful for proper patient selection for endovascular treatment beyond usual time window (> 6 hours).

There were some limitations in the current study. First, the current study was performed in only 1 hospital and the sample size was relatively small. Additionally, this study was performed retrospectively and only included patients who received the endovascular treatment. This represents a potential inherent selection bias. Secondly, CT perfusion has been used for additional imaging protocol in many institutes. We could not incorporate CT perfusion into our evaluation because we do not take this protocol. PWI is included in our MRI protocol but it was also not evaluated because DWI is more representative for measuring infarct core volume than PWI. Finally, interpretation should be cautious about our institutional protocols. We have taken CT, CTA, and MRI together; however, we do not want to suggest that our protocol is a best option. In the current study, we want to show the advantages and disadvantages regarding imaging protocols so that physicians can choose their best option for their hospital settlement.

5. Conclusion

In summary, MRI protocols such as DWI stroke volume, infarct core volume, and DWI ASPECTS system that measure the infarct volume in acute ischemic stroke showed high inter-reader reliability and good prediction power for clinical outcomes. The performance of these MRI protocols appeared to be superior to CT ASPECTS systems; however, time delay from taking MRI is one of major concerns for acute ischemic stroke treatment so that reducing the time required to perform these MRI protocols is a challenging issue that will need to be addressed in future studies.

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