Use of Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTS) and Ischemic Core Volume to Determine the Malignant Profile in Acute Stroke

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Background—Malignant profiles were identified by imaging profiles and unfavorable outcomes that have poor response to reperfusion therapy. Many trials have used this profile in their inclusion criteria including large-vessel occlusion acute ischemic stroke trials. We aimed to redefine the cutoff values for malignant profile in acute ischemic stroke patients with large-vessel occlusion regardless of reperfusion therapy.

Methods and Results—Consecutive acute ischemic stroke patients with anterior large-vessel occlusion were prospectively extracted from the National Cerebral and Cardiovascular Center Stroke Registry between March 2014 and December 2017. Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTS) and diffusion-weighted imaging lesion ischemic core volume (Vol_{DWI}) were measured in acute ischemic stroke patients with large-vessel occlusion with or without treatment. Unfavorable outcome was defined as a modified Rankin Scale score 5 to 6 at 3 months, and optimal DWI-ASPECTS and Vol_{DWI} for unfavorable outcome were assessed. In total, 198 patients (111 men, 77±13 years old) were enrolled. Median DWI-ASPECTS was 7 (5-9), and median Vol_{DWI} was 55 (6-134) mL. Among the patients, 72 (36%) patients underwent reperfusion therapy, and 83 (42%) had unfavorable outcomes. The threshold values for a malignant profile on receiver operating characteristic curve analysis for DWI-ASPECTS and Vol_{DWI} were 4 (area under the curve 0.78, $P<0.01$; sensitivity 0.71, specificity 0.75) and 71 mL (area under the curve 0.80, $P<0.01$; sensitivity 0.76, specificity 0.77), respectively.

Conclusions—The cutoff values for our redefined malignant profile were DWI-ASPECTS 4 and Vol_{DWI} 71 mL with no selection bias for reperfusion therapy in the real-world clinical practice.

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Key Words: large-vessel occlusion • malignant profile • stroke

Recently, the efficacy and safety of endovascular treatment (EVT) in acute ischemic stroke (AIS) patients due to anterior large-vessel occlusion (LVO) were established for acute-onset including wake-up stroke.[1,2] Especially in anterior LVO AIS, the volume of the magnetic resonance (MR) diffusion-weighted imaging (DWI) lesion predicts poor outcomes after intravenous thrombolysis (IVT)[3] and symptomatic intracerebral hemorrhage after EVT,[4] and ischemic core volumes between 70 and 100 mL have been suggested to be reliable cutoffs to identify so-called "malignant profiles."[5,6]

The optimal indication for EVT is currently determined by tissue-based evaluation, which is imaging dependent and not time dependent. Thus, acute-phase imaging of AIS has become increasingly important. Volumetrically assessing the ischemic core with an automated image postprocessing system within 5 minutes is extremely useful for deciding whether to perform EVT for LVO AIS patients.

Clinical Perspective

What Is New?

- We found the cutoff values for predicting unfavorable outcome were Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTS) 4 and DWI lesion ischemic core volume 71 mL with no selection bias for reperfusion therapy in the real-world clinical practice.

What Are the Clinical Implications?

- The optimal DWI-ASPECTS and treatable upper limit of core volumes are suggested from patient-selected randomized controlled trials in most idealistic conditions.
- Our results align with the previous highly selective randomized controlled trials, although favorable outcomes were still observed in endovascular treatment patients above this threshold, and DWI-ASPECTS may not be an adequate substitute for DWI lesion ischemic core volume in cases with DWI-ASPECTS ≤4.
- In our study not all patients had attempted reperfusion therapy, and we found a variety of outcomes in large-core patients; therefore, the optimal ischemic core volume threshold for unfavorable outcome may be higher than 71 mL in endovascular treatment patients.

In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining MR imaging (MRI) DWI is recommended to aid in patient selection for EVT in the AHA/ASA (American Heart Association/American Stroke Association) Guideline,[7] and DWI lesion ischemic core volume (Vol_{DWI}) is known to predict a poor outcome.[8] However, because automated volume calculation software is not necessarily available in all facilities, Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTS) has been reported as an alternative index. In addition, recent EVT randomized controlled trials have used imaging profile for inclusion criteria to exclude patients with a large ischemic core.

The aims of the present study were to clarify the correlation between DWI-ASPECTS and Vol_{DWI} measured by automated software in anterior LVO AIS and to redefine the malignant profile for DWI-ASPECTS and Vol_{DWI} regardless of reperfusion therapy in real-world clinical practice.

Materials and Methods

Patients, Clinical Assessments, and Outcome Measures

Consecutive AIS patients were prospectively extracted from the National Cerebral and Cardiovascular Center Stroke Registry (ClinicalTrials.gov: NCT02251665),[9] where MRI was implemented as first-line pretreatment imaging. Patients who fulfilled the following eligibility criteria between March 2014 and December 2017 were included: (1) imaging within 24 hours of AIS onset; (2) patients with clinical outcome obtained at 3 months after onset; (3) baseline MR angiography to confirm an internal carotid artery (ICA) or middle cerebral artery (MCA) M1 proximal (horizontal segment of MCA within <5 mm from the terminal bifurcation of the ICA) occlusion; and (4) AIS confirmed by baseline MRI (3 T; DWI: 3 directions; b=0-1000 s/mm^2: 6-mm contiguous slices). Because ASPECTS best indicates MCA M1 proximal occluded territories in scoring, patients with anterior cerebral artery (ACA), MCA M1 distal, M2 or M3, posterior circulation LVO were excluded from this analysis to fully match the area within DWI-ASPECTS.

Clinical characteristics including baseline demographics (sex, age, premorbid modified Rankin Scale score,[10] cerebrovascular risk factors), baseline National Institutes of Health Stroke Scale score,[11] stroke subtype, imaging findings (arterial occlusion site on baseline MR angiography, baseline DWI-ASPECTS,[12] DWI and perfusion MRI, and Vol_{DWI}), treatment details (reperfusion therapy; use of IVT, EVT, and combination therapy of IVT and EVT), time metrics (times from stroke onset to qualifying imaging and times from stroke onset to reperfusion), and outcomes (modified Rankin Scale score 3 months after onset, symptomatic intracranial hemorrhage) were retrospectively collected and examined. Stroke subtype was determined according to the Trial of Org 10172 in Acute Stroke Treatment criteria[13] by board-certified stroke neurologists (K.F., Kanta T). Tandem occlusion was defined as both ICA and MCA occlusion. The time from stroke onset to qualifying imaging was defined as the time from symptom onset to the start of obtaining scout view imaging of baseline MRI. Onset to reperfusion time was defined as the time from symptom onset to successful reperfusion confirmed or procedure terminated with no reperfusion in the patients who underwent EVT. The time of onset was defined as either the time point when the symptom appeared or when "last-known-well" if the symptom onset was unknown.

Patients received IVT (0.6 mg/kg alteplase) according to the Japanese-approved standard care protocol[14] if eligible before EVT. All interventional procedures were performed by the Japanese Society for Neuroendovascular Therapy board-certified neurointerventionalists.

A favorable outcome was defined as modified Rankin Scale score 0 to 2 at 3 months after onset, and an unfavorable outcome was defined as modified Rankin Scale score 5 to 6 at 3 months after onset. A malignant profile was defined as optimal DWI-ASPECTS and Vol_{DWI} for unfavorable outcome. Successful reperfusion after EVT was defined as modified Thrombolysis in Cerebral Infarction scale grade 2b or 3.[15] A

symptomatic intracranial hemorrhage was defined as an increase of 4 points or more in the National Institutes of Health Stroke Scale score or death within 48 hours.[16]

Statistical Analyses

Two stroke neurologists (T.Y., K.F.) independently evaluated baseline DWI and DWI-ASPECTS. When the readers' assessments differed, final consensus was obtained with a third reader (Kanta T). Interobserver agreement for DWI-ASPECTS was assessed using weighted-κ and intraclass correlation coefficients. Vol_{DWI} was measured retrospectively using an automated processing system (RAPID version 4.7, iSchemaView, Menlo Park, CA) by apparent diffusion coefficient index $<620 \times 10^{-6}$ mm^2/s, and unreliable blurry lesions which RAPID could not detect were manually measured (MIPAV, Ver 8.0.2, Bethesda, MA). The correlation between DWI-ASPECTS and Vol_{DWI} was determined using the Spearman rank correlation coefficient. To identify the optimal Vol_{DWI} threshold, receiver operating characteristic curves were assessed. Significance was set at $P<0.05$ for all tests. The statistical analyses were performed by JMP 13.2.1 statistical software (SAS Institute Inc, Cary, NC).

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Institutional Review Board of NCVC (approved number M23-073-4). Written, informed consent for reperfusion therapy, as well as thrombectomy, was obtained from each patient or a relative if the patient had communication problems, and the opt-out method for patient recruitment was used.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

Results

Total of 649 patients had AIS due to LVO, and of these, 198 patients met our study criteria. Patients were excluded based on missing cases for outcome at 3 months after onset (n=5), different occluded vessels (anterior cerebral artery, n=14; MCA M1 distal, n=152; M2 or M3, n=156; basilar artery, n=34; vertebral artery, n=20; posterior cerebral artery, n=50) or MRI contraindications (for example pacemaker implantation, n=20) (Figure 1). Of these, 198 patients (111 [56%] men; mean±standard deviation age, 77±13 years) were included. The baseline clinical characteristics of these patients are

presented in Table 1. The median (interquartile range [IQR]) baseline National Institutes of Health Stroke Scale score was 21 (14-27). Median (IQR) values for DWI-ASPECTS and Vol_{DWI} were 5 (3-8) and 55 (6-134) mL, respectively. The median (IQR) time from stroke onset to qualifying imaging was 247 (64-634) minutes. Reperfusion therapy was performed in 72 (36%), IVT in 39 (20%), EVT in 54 (27%), and combination therapy of IVT and EVT in 21 (11%) patients. A favorable outcome was observed in 48 (24%) patients, and unfavorable outcome was seen in 83 (42%), death at 3 months in 34 (17%), and symptomatic intracranial hemorrhage was seen in 12 (6%).

The interobserver intraclass correlation coefficient of DWI-ASPECTS between readers was 0.766 (95% CI 0.693-0.786), and the weighted-κ statistic of DWI-ASPECTS was 0.985 (95% CI, 0.981-0.989), which showed excellent agreement. Figure 2 shows the box-and-whisker plot of baseline DWI-ASPECTS and Vol_{DWI}. There was a strong negative correlation between DWI-ASPECTS and Vol_{DWI} (ρ=−0.901; $P<0.001$). Although 3 stroke neurologists evaluated the DWI-ASPECTS with an extremely high correlation, complete agreement was not obtained. The threshold values of DWI-ASPECTS and Vol_{DWI} by receiver operating characteristic curve analysis for predicting unfavorable outcome were 4 (area under the curve [AUC] 0.78; sensitivity 0.71, specificity 0.75) and 71 mL (AUC 0.80; sensitivity 0.76, specificity 0.77), respectively (Figures 3 and 4). In total, there were 89 patients (45%) with Vol_{DWI} >71 mL and 88 patients (44%) with DWI-ASPECTS ≤4.

According to these results, we identified 2 groups with and without divergence between DWI-ASPECTS and Vol_{DWI}. In the first group with DWI-ASPECTS ≥7 (76 cases), the median Vol_{DWI} was 4 mL and the range was intermediate (0–83 mL), which suggested that DWI-ASPECTS can substitute for Vol_{DWI} in these cases. In the second group with DWI-ASPECTS <7 (122 cases), the median Vol_{DWI} was 114 mL, but the range was wide (40–450 mL) (Table 2). Examining the 39 AIS patients who underwent EVT in the second group, 56% (22/39) had favorable outcomes, and 13% (5/39) had unfavorable outcomes.

In the group with DWI-ASPECTS ≤4 (88 cases), 3.4% (3/88) had favorable outcomes, and 67% (59/88) had unfavorable outcomes overall. Examining the 10 patients who underwent EVT in this group, we found 20% (2/10) had favorable outcomes, and 30% (3/10) had unfavorable outcomes. In the group with DWI-ASPECTS ≤4 and Vol_{DWI} ≥71 mL (73 cases), only 1% (1/73) had favorable outcomes, and 78% (57/73) had unfavorable outcomes overall. Examining the 5 patients who underwent EVT in this group, we found 20% (1/5) had favorable outcomes, and 60% (3/5) had unfavorable outcomes. One patient who had a favorable outcome was 57 years old, and the lesion intensity was faint in the cortex with DWI-ASPECTS 4 and Vol_{DWI} 102 mL.
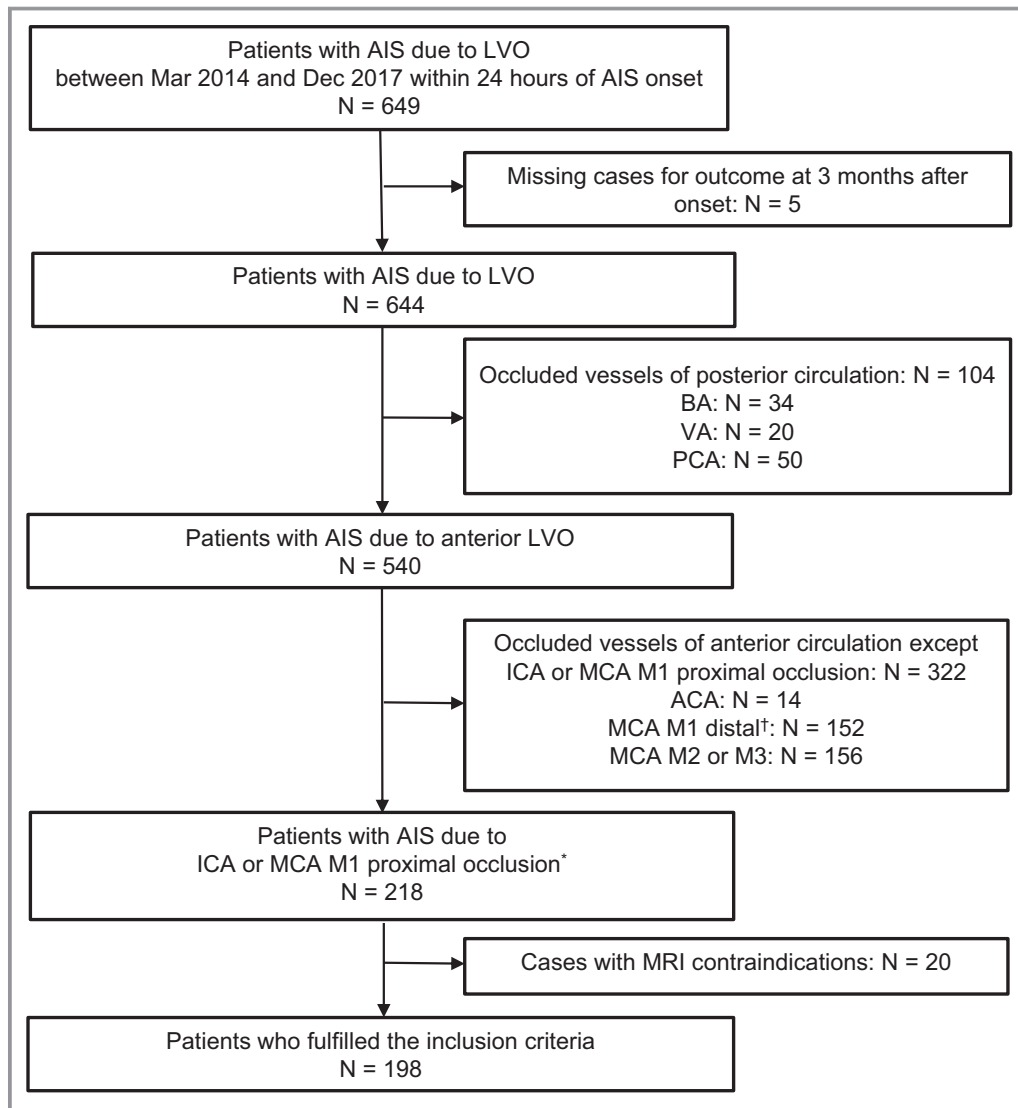
Figure 1. Flow diagram of patient selection. ACA indicates anterior cerebral artery; AIS, acute ischemic stroke; BA, basilar artery; ICA, internal carotid artery; LVO, large vessel occlusion; MCA, middle cerebral artery; MRI, magnetic resonance imaging; PCA, posterior cerebral artery; VA, vertebral artery. *MCA M1 proximal indicates horizontal segment of MCA within <5 mm from the terminal bifurcation of the ICA <5 mm. †MCA M1 distal indicates horizontal segment of MCA except M1 proximal.

The baseline clinical characteristics of patients who underwent EVT are presented in Table 3. There were 54 EVT eligible patients, and of these, the median (IQR) of DWI-ASPECTS was 7 (5-9), the median value of Vol_{DWI} (IQR) 17 (0-58) mL, and the median time from stroke onset to qualifying imaging (IQR) 153 (71-407) minutes. The rate of successful reperfusion after EVT was 93%. Threshold values by receiver operating characteristic curve analysis for DWI-ASPECTS and Vol_{DWI} for unfavorable outcome in these patients were 5 (AUC 0.51; sensitivity 0.33, specificity 0.85) and 58 mL (AUC 0.65; sensitivity 0.56, specificity 0.80), respectively.

Table 2 shows each DWI-ASPECTS cutoff point and corresponding volumes. The highest Vol_{DWI} in the 76 patients with DWI-ASPECTS ≥7 was 83 mL, whereas the lowest Vol_{DWI}

in the 72 patients with DWI-ASPECTS <7 was 40 mL. And, the highest Vol_{DWI} in the 110 patients with DWI-ASPECTS ≥5 was 150 mL, whereas the lowest Vol_{DWI} in the 88 patients with DWI-ASPECTS <5 was 31 mL.

In 93 AIS patients with DWI-ASPECTS >4 and Vol_{DWI} <71 mL, 31% (29/93) had favorable outcomes, and 19% (18/93) had unfavorable outcomes overall.

Discussion

This study reports the correlation between DWI-ASPECTS and Vol_{DWI} measured by automated software for LVO AIS with no treatment bias. Baseline DWI-ASPECTS and Vol_{DWI} measured by automated software showed a strong correlation in our

Table 1. Baseline Characteristics

	Total (n=198)
Age, y	79±13
Male	111 (56)
Premorbid modified Rankin scale score	0 (0-3)
Hypertension	139 (70)
Diabetes mellitus	39 (20)
Dyslipidemia	84 (43)
Current smoking	50 (25)
Atrial fibrillation	129 (66)
Baseline NIH Stroke Scale score	21 (14-27)
Stroke subtype	
Large-artery athrosclerosis	29 (14)
Cardioembolism	139 (70)
Others	30 (16)
Imaging findings	
DWI-ASPECTS	5 (3-8)
DWI-ASPECTS ≤4	88 (44)
Diffusion and perfusion MRI	7 (4)
DWI lesion ischemic core volume, mL	55 (6-134)
DWI lesion ischemic core volume >71 mL	89 (45)
Arterial occlusion site on baseline MR angiography	
Internal carotid artery	117 (59)
Middle cerebral artery M1 proximal	73 (37)
Tandem	8 (4)
Treatment details	
Reperfusion therapy	72 (36)
Intravenous thrombolysis	39 (20)
Endovascular treatment	54 (27)
Combination therapy	21 (11)
Time metrics	
Process measures, min	
Time from stroke onset to qualifying imaging	247 (64-634)
Outcomes	
Modified Rankin scale score 3 mo after onset	4 (3-5)
Favorable outcome	48 (24)
Unfavorable outcome	83 (42)
Symptomatic intracranial hemorrhage	12 (6)

Data are mean±SD for age; median (interquartile range) for premorbid modified Rankin scale score, baseline NIH Stroke Scale score, DWI-ASPECTS, DWI ischemic core volume, time from stroke onset to qualifying imaging, and modified Rankin scale score at 3 mo after onset; and number of patients (%) for others. ASPECTS indicates Alberta Stroke Programme Early CT Score; CT, computed tomography; DWI-ASPECTS, Diffusion-Weighted Imaging-Alberta Stroke Program Early CT Score; MR, magnetic resonance; MRI, magnetic resonance imaging.

study. The cutoff value for predicting an unfavorable outcome was 4 for DWI-ASPECTS and 71 mL for Vol_{DWI}.

Interestingly, there were cases with low DWI-ASPECTS scores despite the small Vol_{DWI}. In DWI-ASPECTS ≥7 cases, DWI-ASPECTS was useful to substitute for Vol_{DWI}, but when it turned to <7 (especially in DWI-ASPECTS ≤4 cases), there was a significant divergence between DWI-ASPECTS and Vol_{DWI}. In our results, 1 patient had DWI ASPECTS ≥7, and the Vol_{DWI} was ≥71 mL. The reason why divergence occurred in this case may be characterized by the category and assessment of DWI-ASPECTS. DWI-ASPECTS was derived from computed tomography (CT)-ASPECTS as a tool to semiquantify the early ischemic changes. It was not originally devised as a substitute for Vol_{DWI}, and there are several problems with this quantification method as an evaluation of ischemic core volume. General limitations of DWI-ASPECTS include overestimations in the penetrating branch territory of the MCA. Several of the ASPECT regions (caudate/internal capsule/lentiform/insular ribbon) involve small-volume brain structures; therefore, a small-volume lesion involving these regions can lead to a low score. In contrast, the fact that anterior cerebral artery and posterior cerebral artery territory are not included in ASPECTS may be 1 reason why large-volume lesions have high ASPECT scores. Additionally, because DWI-ASPECTS is a semiquantitative visually assessed measurement, differences in display output and brightness may also cause differences in the result. Especially in the present study, the following 2 limitations in scoring DWI-ASPECTS were (1) punctate DWI high-intensity signals and diffuse DWI high-intensity signals are evaluated equally, and (2) DWI-ASPECTS depends on the reader's impression. The current case was an acute onset ICA occlusion the core of which was too blurry in the ACA/parietal lobe area so that automated software could not detect and had DWI-ASPECTS 8 with Vol_{DWI} as 83 mL.

The group with divergence between DWI-ASPECTS and Vol_{DWI} included 88 patients with DWI-ASPECTS scores ≤4. Of these, 17% (15/88) had Vol_{DWI} <71 mL, and unfavorable outcomes were seen in only 13% (2/15); 33% (5/15) were treated with EVT and had no unfavorable outcomes. From these results, it appears that DWI-APECTS may not be an adequate substitute for Vol_{DWI} in cases with DWI-ASPECTS ≤4. If the patients with DWI-ASPECTS ≤4 were excluded from reperfusion therapy, nearly 20% of patients were erroneously excluded.

Similar situations were reported in previous studies, in which the cutoff value of DWI-ASPECTS and Vol_{DWI} did not match. According to the study done by Terasawa et al, the cutoff value of DWI-ASPECTS >7 detects DWI lesion volume ≤25 mL in anterior circulation AIS treated with IVT for manually outlined volumetric calculation.[17] When these values, DWI-ASPECTS >7 and Vol_{DWI} ≤25 mL, were applied to the condition reported in this study, a high correlation was
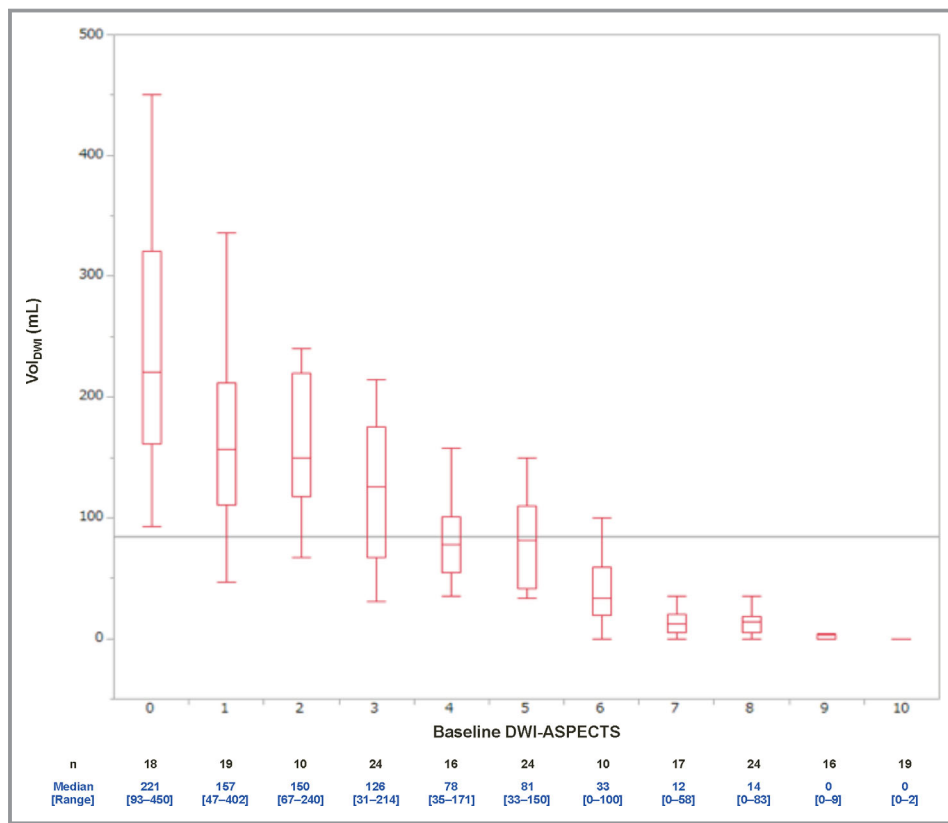
Figure 2. Box-and-whisker plot of baseline DWI-ASPECTS and Vol_{DWI}. Boxes indicate interquartile range; whiskers, extreme values; horizontal lines in each box, median; and horizontal gray line, mean. CT indicates computed tomography; DWI, Diffusion-Weighted Imaging; DWI-ASPECTS, Diffusion-Weighted Imaging-Alberta Stroke Program Early CT Score; Vol_{DWI}, DWI lesion ischemic core volume.

observed in our data set (sensitivity 0.93, specificity 0.98). de Margerie-Melon et al reported that DWI-ASPECTS <4 or ≥7 may be used as reliable surrogates of Vol_{DWI} >100 or <70 mL, respectively, in AIS due to MCA occlusion in patients treated by IVT and/or EVT using a workstation (Advantage Workstation, GE Healthcare, Chalfont, UK) with an application for functional mapping calculation (READY View, GE Healthcare, Chalfont, UK),[18] but they also concluded that DWI-ASPECTS has limitations when lesion location is not considered. Our data set confirmed selection bias as reported in similar trials. Another problem seems to lie in the fact that most studies targeted their population as IVT- and/or EVT-eligible AIS patients and excluded the medical treatment group. When the threshold values derived from favorable outcomes in the previous volumetric study[17] (optimal Vol_{DWI} 25 mL) were applied, the sensitivity was 0.77, and the specificity was 0.73 (AUC 0.81). This result also confirms that our data-set population was not different from those of previous volumetric studies.

Some of our results were also supported by recent studies. Compared with the HERMES (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) collaboration, 46% of all subjects had favorable outcomes, and 22% had unfavorable outcomes,[19] and these clinical outcomes were almost equivalent to those in our study. In addition, according to our data, the cutoff value for the malignant profile was Vol_{DWI} 71 mL in 89 patients. Of these, 11% (10/89) underwent EVT, and 20% (2/10) of these achieved favorable outcomes; while 30% (3/10) had unfavorable outcomes. Similarly, in the HERMES collaboration's meta-analysis, favorable outcomes occurred in 19% (9/48), and unfavorable outcomes occurred in 44% (21/48), of AIS patients who underwent EVT with ischemic core volume ≥70 mL. Compared with the HERMES collaboration meta-analysis, our study included a higher proportion of AIS patients with ischemic core volume ≥70 mL (43% versus 12%) but a lower proportion treated with EVT.[20] Although these results support our findings, there is a strong difference of backgrounds between HERMES collaboration's meta-analysis and ours. Sixty-six percent of the cores estimated in HERMES collaboration's meta-analysis[20] were done by CT perfusion regardless of its ischemic core size, whereas MR DWI was 100% used to measure the core in our study. MR DWI is known to have better detection than CT perfusion from its sensitivity and specificity, and even though CT perfusion cerebral blood flow has reasonable correlation with DWI,[21] it still has some
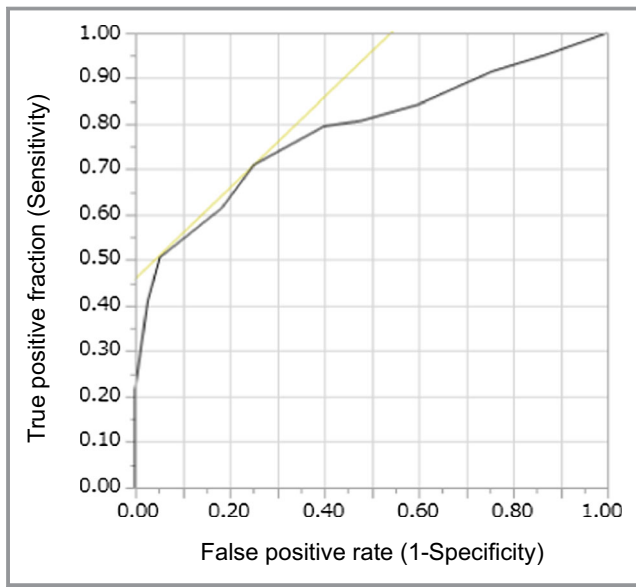
Figure 3. Receiver operating characteristic curves of DWI-ASPECTS for predicting the malignant profile for the unfavorable outcomes. CT indicates computed tomography; DWI, diffusion-weighted imaging; DWI-ASPECTS, Diffusion-Weighted Imaging-Alberta Stroke Program Early CT Score.

Table 2. DWI-ASPECTS Cutoff Points and Corresponding DWI Lesion Ischemic Core Volume

DWI-ASPECTS	DWI Lesion Ischemic Core Volume, mL			
	n	Median	IQR	Range
<4	72	152	114 to 215	31 to 450
≥4	126	17	0 to 56	0 to 171
<5	88	137	90 to 207	31 to 450
≥5	110	11	0 to 85	0 to 150
<6	112	124	75 to 183	31 to 450
≥6	86	5	0 to 18	0 to 100
<7	122	114	67 to 180	40 to 450
≥7	76	4	0 to 15	0 to 83
<7	139	100	47 to 163	0 to 450
≥8	59	0	0 to 9	0 to 83

CT indicates computed tomography; DWI, diffusion-weighted imaging; DWI-ASPECTS, Diffusion-Weighted Imaging-Alberta Stroke Program Early CT Score; IQR, interquartile range.

under/overcalls in certain cutoffs between cerebral blood flow <38% and cerebral blood flow <30%.[22]

Our study reflected real-world clinical practice without selection bias and suggested that Vol_{DWI} ≥71 mL can still be a valuable indicator of the malignant profile regardless of EVT, but we also found a variety of outcomes in large ischemic core
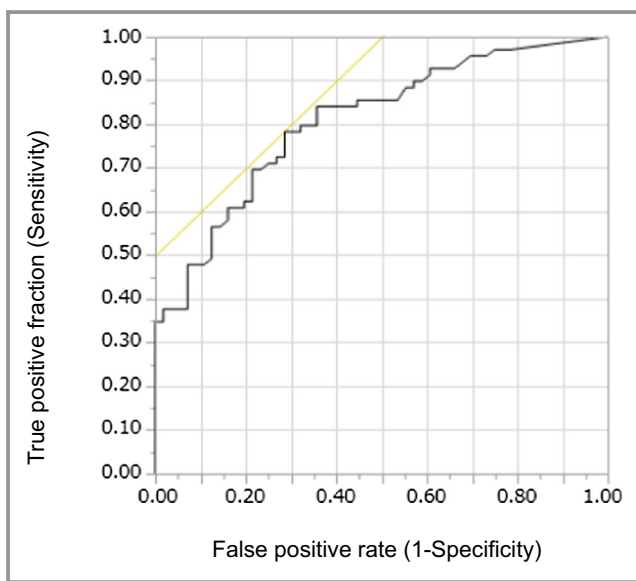

Figure 4. Receiver operating characteristic curves of Vol_{DWI} for predicting the malignant profile for the unfavorable outcomes. Vol_{DWI} indicates diffusion-weighted imaging lesion ischemic core volume.

patients, and this deviation needs to be clarified. One reason is the difficulty of prediction in transition of brain edema after the ischemia. Minimum cytotoxic edema occurs after ischemia and is characterized by failure of ATP-dependent ion transportation, cellular depolarization, and increased cell swelling. Despite the consequences of the recanalization, brain edema is complex to control, and its progress is difficult to predict. From our data set we came across cases that had large cores but did not have unfavorable outcomes. This might be explained by the inadequate lowering of apparent diffusion coefficient values and early renormalization, which produced no cell damage in the brain tissue even with slight edema. To elucidate these issues several randomized ongoing trials might clarify these varieties in large-core patients such as the CHARM (Severe Cerebral Edema Following Large Hemispheric Infarction) trial (ClinicalTrials.gov: NCT02864953) for brain edema and SELECT (Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke) study (ClinicalTrials.gov: NCT02446587) for large cores.

Our study has some limitations. It was a single-center, retrospective, nonrandomized, observational study. Nevertheless, it is a valuable study to explore alternative methods of automated software for AIS to evaluate ischemic core volume; our study may also be valuable as evidence for using EVT in facilities where automated software is unaffordable. In our present result, not all patients had attempted reperfusion therapy, and therefore, the optimal ischemic core volume threshold for unfavorable outcome may be higher than 71 mL in EVT patients. We excluded MCA M1 distal occlusion and other vessel occlusion cases that might be eligible for EVT in order to match the DWI-ASPECTS evaluable territory. The limitation of RAPID software is that it cannot assess the very

Table 3. Baseline Characteristics of Patients Who Underwent Endovascular Treatment

	Total (n=54)
Age, y	73±13
Male	24 (44)
Premorbid modified Rankin scale score	0 (0-1)
Hypertension	35 (66)
Diabetes mellitus	11 (21)
Dyslipidemia	20 (38)
Current smoking	17 (32)
Atrial fibrillation	35 (67)
Baseline NIH Stroke Scale score	20 (13-24)
Stroke subtype	
Large-artery athrosclerosis	5 (9)
Cardioembolism	41 (76)
Others	8 (15)
Imaging findings	
DWI-ASPECTS	7 (5-9)
Diffusion and perfusion MRI	4 (7)
DWI lesion ischemic core volume, mL	17 (0-58)
Arterial occlusion site on baseline MR angiography	
Internal carotid artery	44 (81)
Middle cerebral artery M1 proximal	4 (7)
Tandem	6 (11)
Treatment details	
Intravenous thrombolysis	21 (39)
Time metrics	
Process measures, min	
Time from stroke onset to qualifying imaging	153 (71-407)
Time from qualifying imaging to femoral puncture	51 (37-66)
Time from femoral puncture to reperfusion	59 (37-86)
Outcomes	
Modified Rankin scale score 3 mo after onset	3 (1-4)
Favorable outcome	22 (45)
Unfavorable outcome	45 (83)
Successful reperfusion	50 (94)
Symptomatic intracranial haemorrhage	2 (4)

Data are mean±SD for age; median (interquartile range) for premorbid modified Rankin scale score, baseline NIH Stroke Scale score, DWI-ASPECTS, DWI ischemic core volume, time from stroke onset to qualifying imaging, time from qualifying imaging to femoral puncture, time from femoral puncture to reperfusion, and modified Rankin scale score at 3 mo after onset; and number of patients (%) for others. ASPECTS indicates Alberta Stroke Programme Early CT Score; CT, computed tomography; DWI-ASPECTS, Diffusion-Weighted Imaging-Alberta Stroke Program Early CT Score; MR, magnetic resonance; MRI, magnetic resonance imaging.

subtle DWI high intensity which the apparent diffusion coefficient index has not decreased enough, and manually outlined volumetric estimation may be beneficial in these cases. Further studies are required to include any kind of vessel-occluded LVO to assess the ASPECTS and volumes.

Conclusions

In AIS due to ICA or MCA M1 proximal occlusion, a significant correlation was found between DWI-ASPECTS and Vol_{DWI}. The cut-off values for poor clinical outcomes were DWI-ASPECTS 4 and Vol_{DWI} 71 mL. These results align with the previous highly selective randomized controlled trials, although favorable outcomes were still observed in EVT patients above this threshold. DWI-ASPECTS may not be an adequate substitute for Vol_{DWI} in cases with DWI-ASPECTS ≤ 4.

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Disclosures

None.

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