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Lower DWI-ASPECTS Score in Cortical Regions Predicts Unfavorable Outcome after Successful Thrombectomy

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Abstract

Background Mechanical thrombectomy has been established as an effective treatment for acute ischemic stroke (AIS) caused by large vessel occlusion (LVO). However, the factors predicting poor outcomes despite successful reperfusion after thrombectomy remain unclear.

Methods This study included 50 patients who achieved successful reperfusion after mechanical thrombectomy between January 2014 and March 2021. The diffusion-weighted imaging (DWI) Alberta Stroke Program Early Computed Tomography Score (ASPECTS) was stratified into deep (dDWI-ASPECTS) and cortical (cDWI-ASPECTS) components. Baseline clinical characteristics and procedural factors were statistically analyzed to identify variables associated with unfavorable outcomes, defined as a modified Rankin scale score of 3 to 6.

Results Seventeen patients (34%) achieved favorable outcomes, while 33 (66%) had unfavorable outcomes. The cDWI-ASPECTS were significantly higher in the favorable outcome group compared with the unfavorable outcome group ($p = 0.01$), whereas no significant differences were observed in the dDWI-ASPECTS. Multivariate analysis identified older age ($p < 0.01$; odds ratio [OR]: 1.15; 95% confidence interval [CI]: 1.04–1.27), lower baseline cDWI-ASPECTS ($p < 0.01$; OR: 2.71; 95% CI: 1.30–5.56), and higher baseline National Institutes of Health Stroke Scale (NIHSS) scores ($p = 0.03$; OR: 1.21; 95% CI: 1.02–1.44) as independent predictors of unfavorable outcomes.

Conclusion A lower baseline cDWI-ASPECTS score serves as a predictive factor for unfavorable outcomes following successful thrombectomy, particularly in older AIS-LVO patients with higher baseline NIHSS scores.

Keywords
- DWI-ASPECTS
- thrombectomy
- acute ischemic stroke
- large vessel occlusion

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Introduction

Mechanical thrombectomy has been established as an effective treatment for acute ischemic stroke (AIS) caused by large vessel occlusion (LVO).[1–5] Following mechanical thrombectomy, poor prognosis has been reported to be associated with factors such as advanced age, female sex, high National Institutes of Health Stroke Scale (NIHSS) score, extensive infarct area, and specific infarct locations.[6–11] Furthermore, even in the cases where complete recanalization is achieved through mechanical thrombectomy, some patients still experience poor outcomes, with many aspects of the underlying causes remaining unclear.

The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) is a valuable computed tomography (CT) based tool for identifying and assessing early ischemic changes in the brain regions associated with various functions.[12] On the other hand, diffusion-weighted imaging (DWI) in magnetic resonance (MR) sequences provide greater clarity than CT for identifying acute ischemic changes.[13] In clinical practice, the effectiveness of ASPECTS evaluated based on DWI images (DWI-ASPECTS) has also been demonstrated.[14] It has been suggested that specific locations of ischemic lesions detected by DWI-ASPECTS may influence the outcomes of AIS cases.[7,9] However, no detailed studies have been conducted to determine whether specific ischemic lesions can serve as predictive factors for outcomes in the cases where complete recanalization is achieved after mechanical thrombectomy.

This study aimed to investigate whether the location of infarction at the onset of AIS, specifically deep lesions and cortical lesions, as assessed by DWI-ASPECTS, influences the outcomes of AIS patients with LVO who achieved complete reperfusion following thrombectomy.

Methods

Patient Selection

We conducted a retrospective analysis of AIS cases that underwent mechanical thrombectomy at Yokosuka General Hospital Uwamachi between January 2014 and March 2021. The study was approved by the Institutional Review Board (IRB 2021028). According to the *Japan Stroke Society Guideline 2021 for the Treatment of Stroke*,[15] the inclusion criteria were defined as follows: (1) time from ischemic stroke onset to puncture within 24 hours, (2) prestroke modified Rankin scale (mRS) score of 0 to 1, (3) occlusion of the internal carotid artery (ICA) or segment M1 of the middle cerebral artery (MCA), (4) DWI-ASPECTS $\geq$ 6, and (5) successful revascularization, defined as thrombolysis in cerebral infarction (TICI) grade 2b to 3. Mechanical thrombectomy was performed under local anesthesia using a balloon-guiding catheter, with the ICA occluded, employing a combined technique with an aspiration catheter and a stent retriever. Postoperatively, all cases were admitted to the intensive care unit, where standard treatment for cerebral ischemia was administered, and early rehabilitation intervention was initiated.

Image Acquisition

A 1.5-T whole-body MRI scanner (Magnetom Vision; Siemens, Erlangen, Germany) equipped with a standard head coil was used for imaging examinations. The DWI protocol was as follows: slice thickness of 5 mm, repetition time (TR) of 4,000 milliseconds, echo time (TE) of 80 milliseconds, matrix size of 128×128, and a field of view (FOV) of 240 mm.

One of the reported predictors associated with poststroke outcomes is the volume of cortical infarction.[16–18] Given this, it is plausible that outcomes may differ between patients whose infarct core is located in the cortex and those whose infarct core is in the subcortical white matter. Therefore, this study specifically examined the infarct location by focusing on cortical and subcortical regions as follows. DWI-ASPECTS was assessed using MRI at admission, and the regions of interest were classified into two categories: deep DWI-ASPECTS (dDWI-ASPECTS), which includes four structures (the caudate nucleus, lentiform nucleus, internal capsule, and deep white matter), and cortical DWI-ASPECTS (cDWI-ASPECTS), which includes seven structures (the insular ribbon and MCA cortical regions; ►**Fig. 1**). ►**Fig. 2** illustrates representative radiological findings: higher cDWI-ASPECTS (5/7) with lower dDWI-ASPECTS (1/4) and lower cDWI-ASPECTS (3/7) with higher dDWI-ASPECTS (3/4).

Data Collection

Patients were classified into favorable and unfavorable outcome groups, and data were analyzed for each group regarding age, sex, hypertension, dyslipidemia, diabetes mellitus, coronary artery disease, smoking status, alcohol consumption, prestroke antithrombotic therapy, TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification, stroke severity as assessed by the NIHSS, dDWI-ASPECTS, cDWI-ASPECTS, use of intravenous tissue plasminogen activator (tPA), number of procedural attempts, and treatment-related time intervals, including the time from stroke onset to hospital arrival, groin puncture, and recanalization. Procedure-related symptomatic hemorrhagic complications were defined as an increase of $\geq$4 points in the NIHSS score from baseline or hemorrhage-related mortality.[19] Outcomes were assessed using the mRS score at discharge, with favorable outcomes defined as an mRS score of 0 to 2 and unfavorable outcomes as an mRS score 3 to 6.

Statistical Analysis

Continuous data are presented as means $\pm$ standard deviation (SD). Comparisons between patients with favorable and unfavorable outcomes were performed using Student's *t*-test or the Mann–Whitney *U* test, as appropriate. Categorical data were analyzed using the chi-squared test. Multivariate analysis was conducted using logistic regression models, including variables with a *p*-value less than 0.2 in the univariate analysis, as these were considered potential predictors of unfavorable outcomes.

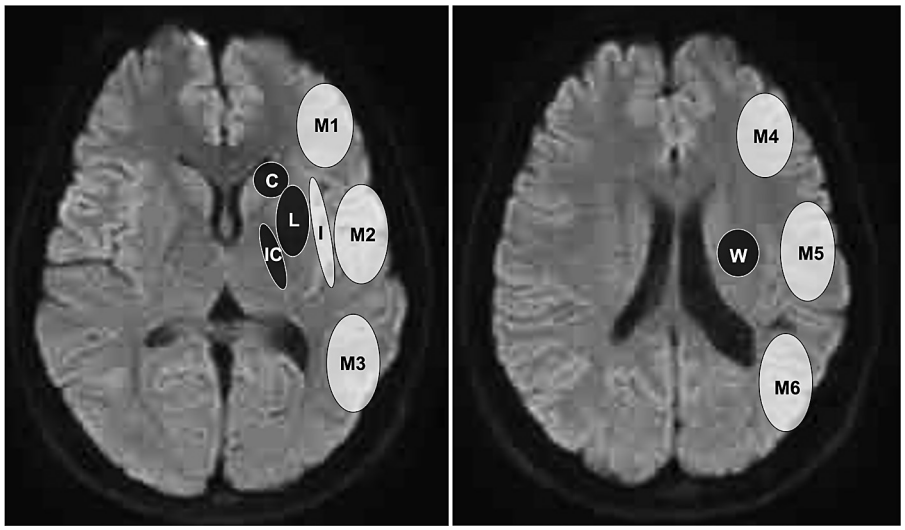

Fig. 1 Diffusion-weighted imaging-Alberta Stroke Program Early CT score (DWI-ASPECTS) is divided into deep DWI-ASPECTS, which includes four structures (C, L, IC, and W), and cortical DWI-ASPECTS, which includes seven structures (I, M1, M2, M3, M4, M5, and M6). C represents the caudate nucleus; L, the lenticular nucleus; IC, the internal capsule; W, the deep white matter; I, the insular ribbon; M1, the anterior middle cerebral artery (MCA) cortex; M2, the MCA cortex lateral to the insular ribbon; M3, the posterior MCA cortex; and M4, M5, and M6, the anterior, lateral, and posterior MCA territories immediately superior to M1, M2, and M3.

Results

This study included 50 patients with ICA or M1 occlusion who achieved reperfusion classified as TICI 2b to 3. Among them, 17 patients (34%) had a favorable outcome (mRS: 0–2), while 33 patients (66%) had an unfavorable outcome (mRS: 3–6). The characteristics of each group are summarized in ►**Table 1**. The mean age of the favorable outcome group was 73.6 ± 8.08 years, with 12 males (70.6%), whereas the mean age of the unfavorable outcome group was 81.1 ± 10.1 years, with 17 males (51.5%). The mean age in the favorable outcome group was significantly lower than that in the unfavorable outcome group ($p = 0.005$). No significant differences were observed between the two groups regarding sex, hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, smoking status, alcohol intake, or prestroke antithrombotic therapy.

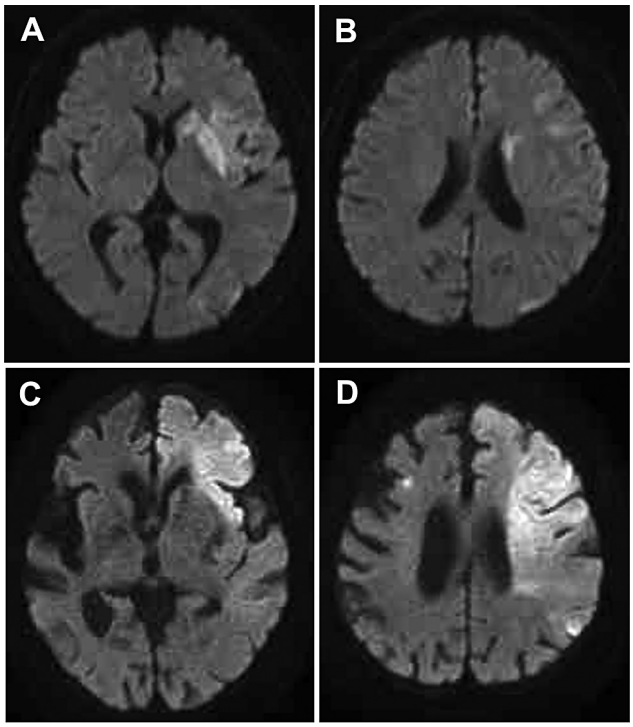

Fig. 2 Representative radiological findings in the (**A, B**) cases with cortical diffusion-weighted imaging-Alberta Stroke Program Early CT score (DWI-ASPECTS) and low deep DWI-ASPECTS and (**C, d**) cases with low cortical DWI-ASPECTS and high deep DWI-ASPECTS.

Intravenous tPA therapy was administered significantly more frequently in the favorable outcome group than in the unfavorable outcome group ($p = 0.016$). The mean number of thrombectomy passes tended to be lower in the favorable outcome group than in the unfavorable outcome group. No significant differences were observed between the two groups regarding stroke etiology, baseline NIHSS score, time from stroke onset to hospital arrival, time to groin puncture, rate of successful recanalization, distal thrombus embolization, or symptomatic hemorrhagic complications related to the procedure.

The median DWI-ASPECTS score was significantly higher in the favorable outcome group (8 [7–9]) compared with the unfavorable outcome group (7 [6–8], $p = 0.006$). While no significant difference was observed in the median dDWI-ASPECTS score between the two groups, the median cDWI-ASPECTS score was significantly higher in the favorable outcome group (6 [4–6]) than in the unfavorable outcome group (4 [3–5], $p = 0.01$).

Multivariate analysis identified independent predictors of unfavorable outcomes at discharge. Older age ($p < 0.01$; odds ratio [OR]: 1.15; 95% confidence interval [CI]: 1.04–1.27), lower baseline cDWI-ASPECTS ($p < 0.01$; OR 2.71; 95% CI 1.30–5.56), and higher baseline NIHSS scores ($p = 0.03$; OR 1.21; 95% CI

Table 1 Comparisons of the clinical characteristics between the patients with favorable outcome and unfavorable outcome

	Favorable outcome ($n = 17$)	Unfavorable outcome ($n = 33$)	*p*-value
Mean age (y)	73.6 ± 8.1	81.1 ± 10.1	0.005
Male, *n* (%)	12 (70.6)	17 (51.5)	0.24
Hypertension, *n* (%)	11 (64.7)	24 (72.7)	0.56
Diabetes mellitus, *n* (%)	6 (35.3)	10 (30.3)	0.72
Hyperlipidemia, *n* (%)	7 (41.2)	14 (42.4)	0.93
Coronary artery disease, *n* (%)	1 (5.9)	4 (12.1)	0.49
Smoking status, *n* (%)	1 (5.9)	4 (12.1)	0.49
Alcohol intake, *n* (%)	2 (11.8)	2 (6.1)	0.48
Antithrombotic therapy on arrival, *n* (%)	7 (41.2)	17 (51.5)	0.49
Baseline NIHSS, median (IQR)	17 (9–22)	19 (14–23)	0.17
Etiology			
Cardiac embolism, *n* (%)	13 (76.5)	21 (63.6)	0.36
ATBI, *n* (%)	3 (17.6)	5 (21.2)	0.77
ESUS, *n* (%)	1 (5.9)	5 (21.2)	0.34
IV tPA, *n* (%)	10 (58.8)	8 (24.2)	0.016
DWI-ASPECTS, median (IQR)	8 (7–9)	7 (6–8)	0.006
cDWI-ASPECTS, median (IQR)	6 (4–6)	4 (3–5)	0.01
dDWI-ASPECTS, median (IQR)	3 (2–3)	3 (2–3)	0.91
O to A time (min), median (IQR)	70 (39–156)	80 (46–240)	0.27
O to P time (min), median (IQR)	150 (100–200)	194 (120–300)	0.2
O to R time (min), median (IQR)	220 (167–291)	266 (185–400)	0.14
Mean number thrombectomy passes	1.2 ± 0.51	1.6 ± 1.07	0.05
Distal thrombus embolization, *n* (%)	1 (5.9)	3 (9.1)	0.75
Symptomatic hemorrhagic complications, *n* (%)	1 (5.9)	6 (18.2)	0.24

Abbreviations: ATBI, atherothrombotic brain infarction; cDWI-ASPECTS, cortical diffusion-weighted imaging-Alberta Stroke Program Early CT score; ESUS, embolic stroke of undetermined source; IQR, interquartile range; IV tPA, intravenous tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; O to R, onset to successful recanalization.

1.02–1.44) were significant predictors of unfavorable outcomes, after adjustment for tPA administration, time from stroke onset to successful recanalization, and the number of thrombectomy passes (►**Table 2**).

Discussion

In contemporary practice, the rate of successful recanalization following thrombectomy in AIS patients has been reported to reach 58 to 88%.[1,2,5] However, it has also been reported that approximately 45% of cases with successful recanalization still experience unfavorable outcomes.[20] In this study, despite achieving successful recanalization through thrombectomy, the group with unfavorable outcomes was associated with older age, higher baseline NIHSS scores, and lower baseline cDWI-ASPECTS. The first two factors are consistent with previous studies[3,10]; however, the finding that lower baseline cDWI-ASPECTS serves as a predictor of unfavorable outcomes even after successful recanalization represents a novel insight.

ASPECTS encompasses various brain functional areas and is thought to reflect the status of collateral circulation. Recent studies have reported that the infarct regions indicated by ASPECTS may serve as predictors of postischemic stroke outcomes. Specifically, the caudate nucleus, internal capsule, and cortical M5 region in left-sided strokes, as well as the cortical M3 and M6 regions in right-sided strokes, have been identified as independent predictors of outcomes following endovascular treatment for ischemic stroke.[7,9] Additionally, a higher baseline score in cortical regions of ASPECTS has been significantly associated with favorable outcomes in AIS cases with ASPECTS less than 6 following endovascular therapy.[19] Our findings align with the latter report; however, our study introduces novelty by using DWI-ASPECTS as the primary assessment scale and focusing on AIS cases with DWI-ASPECTS $\geq$6, further categorizing ischemic lesions into cortical and deep regions. Given that DWI is superior to noncontrast CT for detecting acute ischemic lesions,[21] DWI-ASPECTS is considered a more precise method for evaluating infarct

Table 2 Multivariate analysis for predictors of unfavorable clinical outcome in the patients with successful thrombectomy

	p-value	OR	95% CI
Age	<0.01	1.15	1.04–1.27
Lower baseline cDWI-ASPECTS	<0.01	2.71	1.30–5.56
Higher baseline NIHSS score	0.03	1.21	1.02–1.44
IV tPA	0.07	0.17	0.02–1.15
O to R time	0.27	1.00	0.99–1.01
Number thrombectomy passes	0.35	2.19	0.42–11.4

Abbreviations: cDWI-ASPECTS, cortical diffusion-weighted imaging-Alberta Stroke Program Early CT score; CI, confidence interval; IV tPA, intravenous tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; O to R, onset to successful recanalization; OR, odds ratio.

regions than CT-based ASPECTS. This methodological advantage strengthens the validity and significance of our findings compared with previous studies.

The development of collateral circulation is expected to maximize the preservation of the penumbra from the onset of LVO to reperfusion therapy, thereby mitigating ischemic damage to the brain.[18,22–27] Collateral circulation primarily supplies blood flow to the cortical regions of the anterior circulation; however, its contribution to deep brain regions is limited, with perforating arteries playing the predominant role in blood supply to these areas.[28] Furthermore, a positive correlation has been reported between poor postischemic stroke outcomes and infarct volume in cortical regions.[16–18] Based on these findings, well-developed collateral circulation may play a crucial role in preventing large cortical infarctions and facilitating favorable outcomes. Therefore, a lower baseline cDWI-ASPECTS score is considered indicative of poor collateral circulation. In conjunction with our study findings, the presence of a lower baseline cDWI-ASPECTS score prior to thrombectomy may serve as a predictor of poor outcomes, even in the cases where successful reperfusion is achieved. This association is expected to be particularly pronounced in elderly patients with AIS-LVO who also present with higher baseline NIHSS scores.

In recent years, reports have indicated that strategies involving the direct transfer of AIS patients to the angiography suite for immediate assessment upon hospital arrival have contributed to improved outcomes by reducing the time from AIS onset to thrombectomy.[29] In contrast, MRI generally requires more time, making an initial MRI-based assessment after AIS patient arrival a disadvantage in terms of performing thrombectomy as quickly as possible. However, to prevent severe hemorrhagic complications following thrombectomy, it is crucial to assess the extent of the ischemic core using the DWI–fluid-attenuated inversion recovery (FLAIR) mismatch. Therefore, we recommend MRI evaluation with a minimal protocol before performing thrombectomy to ensure optimal patient selection and minimize risks.

The present study has several limitations. This study is a retrospective analysis conducted at a single institution with a small sample size. Furthermore, no comparative trial was performed with a control group that received medical treatment alone. Therefore, there is a potential for inherent bias arising from multiple factors associated with the limited study population. Since this study did not directly assess infarct volume or perfusion imaging, we were unable to definitively demonstrate whether the baseline cDWI-ASPECTS score is significantly associated with the final infarct volume or the extent of collateral circulation development. Several studies have emphasized the importance of collateral scoring using CT angiography as a predictor of outcomes after thrombectomy,[18,30] highlighting the need to consider its significance. However, we believe that an MRI-based assessment offers advantages as a noninvasive approach, given that it does not require contrast agents and avoids radiation exposure. Since we do not routinely perform noncontrast CT for all AIS cases, we have not conducted a comparative analysis between our study results and those obtained using CT-based ASPECTS. Additionally, in this study, outcomes were evaluated at the time of discharge, which does not necessarily reflect long-term prognosis. Therefore, to validate the reliability of our findings, further research with extended follow-up is required. Finally, a recent randomized clinical trial demonstrating the benefits of thrombectomy in patients with large cerebral infarctions has further supported the use of endovascular intervention.[31] Therefore, we propose that the correlation between cDWI-ASPECTS and clinical outcomes may be particularly relevant in patients with a DWI-ASPECTS score of ≥6 under specific conditions.

Conclusion

A lower baseline cDWI-ASPECTS score serves as a predictive factor for unfavorable outcomes following successful thrombectomy, particularly in older AIS-LVO patients with higher baseline NIHSS scores.

Conflict of Interest
None declared.

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