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ABSTRACT

BACKGROUND AND PURPOSE: Questions remain as to what benefits embolectomy provides to patients presented with considerable early ischemic changes on baseline imaging studies. This study aimed to investigate the impact of the Alberta Stroke Program Early CT Score applied to DWI on treatment outcomes in patients with acute stroke undergoing stent-retriever embolectomy.

MATERIALS AND METHODS: We retrospectively analyzed the clinical and DWI data from 171 patients with acute anterior circulation stroke who were treated with stent-retriever embolectomy within 6 hours of symptom onset. DWI-ASPECTS scores were analyzed with the full scale or were dichotomized (4–6 versus 7–10). Patients with DWI-ASPECTS ≤3 were excluded from the study. Associations between outcome and clinical and radiologic factors were determined with a multivariate logistic regression analysis. A good outcome was defined as a modified Rankin Scale score of 0–2 at 3 months.

RESULTS: The median DWI-ASPECTS was 7 (interquartile range, 6–8). The rates of good outcome, symptomatic hemorrhage, and mortality were not different between high DWI-ASPECTS (scores of 7–10) and intermediate DWI-ASPECTS (scores of 4–6) groups. In patients with an intermediate DWI-ASPECTS, good outcome was achieved in 46.5% (20/43) of patients with successful revascularization, whereas no patients without successful revascularization had a good outcome ($P = .016$). In multivariate logistic regression analysis, independent predictors of good outcome were age and successful revascularization.

CONCLUSIONS: Our study suggested that there were no differences in outcomes between patients with a high DWI-ASPECTS and those with an intermediate DWI-ASPECTS who underwent stent-retriever embolectomy for acute anterior circulation stroke. Thus, patients with an intermediate DWI-ASPECTS otherwise eligible for endovascular therapy may not be excluded from stent-retriever embolectomy or stroke trials.

ABBREVIATION: IQR = interquartile range

Recent randomized controlled trials have shown that stent-retriever embolectomy in addition to standard care was associated with improved functional outcome in patients with acute anterior circulation stroke due to large-vessel occlusion within 6–8 hours of symptom onset.[1-5] For further advancement in treating acute anterior circulation stroke, it is becoming important to more clearly refine the selection criteria for stent-retriever embolectomy. Several clinical and imaging factors are known to be associated with functional outcomes after endovascular treatment for acute anterior circulation stroke.[6-9] However, questions remain as to what benefits embolectomy provides to patients who present at extended time periods or those with considerable early ischemic changes on baseline imaging studies. Furthermore, the imaging technique that best determines candidacy for embolectomy in these patients remains unknown.

ASPECTS is a 10-point semiquantitative scoring system, which was developed to offer the simplicity and reliability of CT to assess early ischemic changes in patients with acute ischemic stroke in the anterior circulation.[10] ASPECTS has recently been applied to DWI, which is much more sensitive and accurate in the detection of acute infarction than noncontrast CT.[11-14] A recent study showed that interrater agreement for DWI-ASPECTS was superior to that for CT-ASPECTS and that DWI-ASPECTS outperformed CT-ASPECTS in predicting functional outcome at 90 days.[9] The DWI-ASPECTS can also provide similar risk assessment far more rapidly than measurement of the infarct volume

on DWI, an independent predictable marker of the clinical outcome, in patients with anterior circulation stroke.[9,15-17] However, few studies have investigated the association between pretreatment DWI-ASPECTS and functional outcome after stent-retriever embolectomy in patients with acute anterior circulation stroke.[9,14,18]

Although several studies showed that a DWI-ASPECTS of 7 was the optimal cutoff value for predicting clinical outcomes in patients undergoing intra-arterial or IV pharmacologic thrombolysis,[19-21] results of recent studies have suggested that some patients with a DWI-ASPECTS of <7 may still benefit from complete recanalization.[14] Successful revascularization can be achieved more frequently by using stent-based embolectomy than by using pharmacologic thrombolysis or other mechanical devices.[1-5] In this context, patients with acute stroke and a DWI-ASPECTS of <7 might have a similar chance of a good outcome compared with those with a higher DWI-ASPECTS if they are treated with stent-retriever embolectomy in a short time window. However, this hypothesis has not been tested. Thus, this study aimed to investigate the impact of DWI-ASPECTS on functional outcome in patients with acute anterior circulation stroke who underwent stent-retriever embolectomy.

MATERIALS AND METHODS

Patients
From December 2010 to December 2013, 190 consecutive patients presenting with acute ischemic stroke due to internal carotid artery or middle cerebral artery occlusions were treated with stent-retriever embolectomy at a comprehensive regional stroke center. Patients underwent a nonenhanced CT scan and multimodal MR imaging before endovascular embolectomy procedures. Of these patients, those who had DWI of insufficient quality for reliable evaluation ($n = 3$) or a DWI-ASPECTS of ≤ 3 ($n = 6$) or a previous modified Rankin Scale score of ≥ 2 ($n = 4$) or concomitant anterior and posterior circulation infarction ($n = 6$) were excluded; thus, 171 patients were left in this study. We prospectively collected the following clinical and radiologic data of these 171 patients: demographic features, cerebrovascular risk factors, NIHSS scores on admission, use of IV thrombolysis, time to endovascular treatment, procedure time, time to reperfusion, revascularization status, and clinical outcome. The institutional ethics committee approved this study. For each patient, written informed consent for endovascular therapy was obtained from a family member.

MR Imaging Analysis
MR imaging examinations were performed by using a 1.5T unit (Signa HDxt; GE Healthcare, Milwaukee, Wisconsin). Before the endovascular procedure, patients underwent MR imaging, including DWI, gradient-echo imaging, a FLAIR sequence, 3D TOF-MRA, and perfusion imaging. DWI sequences were obtained in the axial plane by using a single-shot, spin-echo echo-planar technique with the following parameters: TR of 9000 ms, TE of 80 ms, section thickness of 4 mm, intersection gap of 0 mm, FOV of 260 × 260 mm, and b-values of 0 and 1000 s/mm^2. DWI-ASPECTS was assessed by 2 neuroradiologists (with 2 and 4 years of experience, respectively) who were

blinded to any clinical information. Conclusions were reached by consensus.

Endovascular Treatment
On admission, a stroke neurologist performed a neurologic assessment based on the NIHSS. The inclusion criteria for stent-retriever embolectomy were as follows: presentation within 6 hours of stroke onset, baseline NIHSS score of ≥ 4, no intracranial hemorrhage detected on cranial CT or MR imaging, a target mismatch pattern on multimodal MR imaging based on visual estimation (time-to-peak map of perfusion imaging showing a lesion volume $\geq 30\%$ larger than that detected with diffusion imaging), and infarct volume on diffusion imaging or nonenhanced CT of less than one-third of the MCA territory.

Cerebral angiography and endovascular therapy were performed with the patient under conscious sedation. In cases of agitation, an intravenous bolus of midazolam was given and repeated if necessary. Stent-based embolectomy with a Solitaire stent (Covidien, Irvine, California) was performed as the first-line endovascular treatment. When stent-based embolectomy was unsuccessful, additional mechanical approaches were performed, including manual aspiration embolectomy with a Penumbra System reperfusion catheter (Penumbra, Alameda, California). The details of the techniques used for mechanical embolectomy were previously described.[22,23] Revascularization status was assessed on the final angiogram and was classified according to the modified TICI scale,[24] and successful revascularization was defined as a modified TICI grade of 2b or 3. Clinical outcome was assessed by a stroke neurologist by using the mRS during an outpatient visit 3 months after treatment. If patients were unable to attend the outpatient clinic, outcomes were obtained via telephone interview. A good clinical outcome was defined as an mRS score of ≤ 2.

Statistical Analysis
Continuous variables are presented as medians and interquartile ranges (IQRs). Discrete variables are presented as counts and percentages. First, the area under the receiver operating characteristic curve was applied to evaluate the prognostic performance of DWI-ASPECTS and the optimal cutoff value for discriminating a good outcome (defined as mRS 0–2 at 3 months). Second, the differences in baseline characteristics and treatment outcomes between DWI-ASPECTS subgroups were determined. Patients were divided into 2 groups according to baseline DWI-ASPECTS for analysis of the prognostic impact on functional outcome; namely, a high DWI-ASPECTS group (scores of 7–10) and an intermediate DWI-ASPECTS group (scores of 4–6). The χ^2 or Fisher exact test was used for comparing categoric variables, and the Mann-Whitney U test was used for comparing continuous variables. Third, independent associations between functional outcome and clinical and radiologic factors were determined with a multivariate logistic regression analysis. The variables tested in the multivariate logistic regression models were those with $P < .2$ in the univariate analysis and time to treatment. Fourth, we further compared functional outcome between patients with or without successful revascularization (modified TICI, $\geq 2b$) according to the DWI-ASPECTS subgroups to evaluate the impact of DWI-ASPECTS on the success of endovascular therapy. The χ^2 or

Table 1: Baseline clinical characteristics of the study population

		DWI-ASPECTS		
	Total (*N* = 171)	7–10 (*n* = 120)	4–6 (*n* = 51)	*P* Value
Age (yr) (median) (IQR)	72 (63.5–78)	73 (65–78)	68 (60–74)	.014
Male sex	88 (51.5%)	58 (48.3%)	30 (58.8%)	.209
Risk factors				
Hypertension	95 (55.6%)	69 (57.5%)	26 (51%)	.432
Diabetes mellitus	32 (18.7%)	22 (18.3%)	10 (19.6%)	.845
Coronary artery disease	20 (11.7%)	14 (11.7%)	6 (11.8%)	.985
Dyslipidemia	42 (24.6%)	35 (29.2%)	7 (13.7%)	.034[a]
Smoking	46 (26.9%)	27 (22.5%)	19 (37.3%)	.059[a]
Atrial fibrillation	87 (50.9%)	64 (53.3%)	23 (45.1%)	.324
Congestive heart failure	6 (3.5%)	5 (4.2%)	1 (1.9%)	.670[a]
History of stroke or TIA	22 (12.9%)	18 (15%)	4 (7.8%)	.317[a]
Intravenous thrombolysis	104 (60.8%)	71 (59.2%)	33 (64.7%)	.497
Time to treatment (min) (median) (IQR)	245 (190–310)	257.5 (190–315)	220 (190–281)	.155
Procedure time (min) (median) (IQR)	33 (20–50)	34 (20.5–50)	30 (20–43.5)	.444
Time to revascularization (min) (median) (IQR)	280 (223.5–352)	297.5 (228.5–355)	252 (221.5–326)	.136
Baseline NIHSS score (median) (IQR)	13 (10–16)	12 (9–15)	15 (12–18)	<.001
Stroke etiology				
Large-artery atherosclerosis	43 (25.1%)	32 (26.7%)	11 (21.6%)	.482
Cardioembolism	99 (57.9%)	70 (58.3%)	29 (56.9%)	.859
Undetermined	28 (16.4%)	17 (14.2%)	11 (21.6%)	.231

[a] Comparisons were performed using the Fisher exact test. Comparisons of categoric variables were performed using χ^2 tests unless otherwise indicated.

Table 2: Outcomes after stent-retriever embolectomy in 171 patients

		DWI-ASPECTS		
	Total (*N* = 171)	7–10 (*n* = 120)	4–6 (*n* = 51)	*P* Value
Modified TICI 2b or 3	144 (84.2%)	101 (84.2%)	43 (84.3%)	.981
Good outcome	81 (47.4%)	61 (50.8%)	20 (39.2%)	.164
Symptomatic hemorrhage	6 (3.5%)	4 (3.3%)	2 (3.9%)	1.000[a]
Mortality	16 (9.4%)	9 (7.5%)	7 (13.7%)	.201

[a] Comparisons were performed using the Fisher exact test. Comparisons of categoric variables were performed using χ^2 tests unless otherwise indicated.
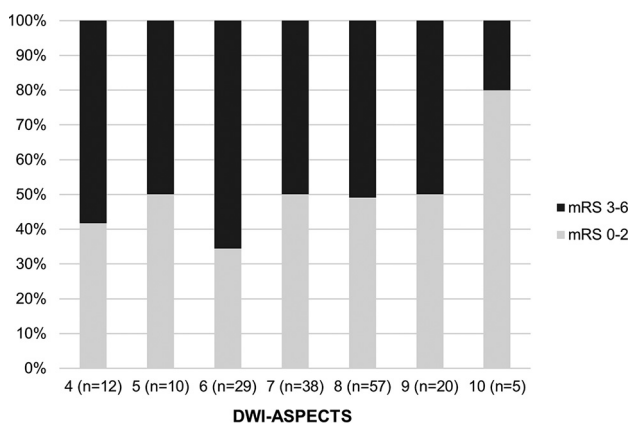

FIG 1. Functional outcome (mRS 0–6) of 171 patients with acute anterior circulation stroke according to pretreatment DWI-ASPECTS. The proportion of outcomes (mRS 0–2 versus mRS 3–6) within each DWI-ASPECTS is shown.

Fisher exact test was used for comparison. All statistical analyses were performed with SPSS software (Version 21.0; IBM, Armonk, New York). A *P* value < .05 was significant.

RESULTS

One hundred seventy-one eligible patients (88 men and 83 women; mean age, 69.9 years; age range, 23–92 years) were identified. Clinical characteristics of the patients are shown in Table 1.

Of the 171 patients, 127 had occlusions in the middle cerebral artery and 44 had occlusions in the internal carotid artery. Overall, the median NIHSS score on admission was 13 (IQR, 10–16). The median time from symptom onset to endovascular therapy was 245 minutes (IQR, 190–310 minutes), and the median procedure time was 33 minutes (IQR, 20–50 minutes). The median time from symptom onset to revascularization was 280 minutes (IQR, 223.5–352 minutes).

In the entire cohort, the median DWI-ASPECTS was 7 (IQR, 6–8); 120 patients had a DWI-ASPECTS of ≥7, and 51 patients had a DWI ASPECTS of 4–6. The median NIHSS score was significantly higher in patients with a DWI-ASPECTS of 4–6 than in those with a DWI-ASPECTS of ≥7 (15 versus 12, *P* < .001). There was a significant correlation between DWI-ASPECTS and admission NIHSS score (*P* < .001). Age and dyslipidemia were also associated with DWI-ASPECTS (Table 1). Patients with an intermediate DWI-ASPECTS were significantly younger than those with a high DWI-ASPECTS (*P* = .014).

Treatment outcomes of patients are summarized in Table 2. Overall, successful revascularization (modified TICI 2b or 3) was achieved in 84.2% (144/171). In the entire cohort, 47.4% (81/171) had a good outcome and 3.5% (6/171) had a symptomatic hemorrhage. Mortality was 9.4% (16/171) at 3 months.

Impact of DWI-ASPECTS on Outcomes

Three-month outcomes according to pretreatment DWI-ASPECTS are shown in the Fig 1. Receiver operating characteristic curve analysis showed that a DWI-ASPECTS of ≥7 was the optimal cutoff to predict a good outcome at 3 months with an area under the curve of 0.57 (95% CI, 0.483–0.656), a sensitivity of 75.3%, and a specificity of 34.4% (Fig 2). Overall, 50.8% (61/120) of patients with a DWI-ASPECTS of ≥7 and 39.2% (20/51) of patients with a DWI-ASPECTS of 4–6 had a good outcome; this difference was not statistically significant (*P* = .164) (Table 2).

There were also no significant differences in the rates of successful revascularization, symptomatic hemorrhage, and mortality between patients with DWI-ASPECTS of 7–10 and those with scores of 4–6.

When each year of age, each point of the NIHSS, time to treatment, symptomatic hemorrhage, DWI-ASPECTS (each score or dichotomized into 7–10 versus 4–6), and successful revascularization were selected into the multivariate logistic regression analysis, independent predictors of good outcome were age (OR, 0.941; 95% CI, 0.909–0.974; P = .001) and successful revascularization (OR, 8.511; 95% CI, 2.298–31.525; P = .001) (Table 3).

Impact of Revascularization on Outcomes among DWI-ASPECTS Subgroups

There was no significant difference in the rate of successful revascularization between patients with a DWI-ASPECTS of 7–10 and those with a DWI-ASPECTS of 4–6 (84.2% versus 84.3%). In the high DWI-ASPECTS group, a good outcome was achieved more frequently in patients with successful revascularization than in those without (58.4% versus 10.5%, P < .001). In this group, the OR for good outcome with successful revascularization was 11.94 (95% CI, 2.62–54.47; P < .001). A similar relationship was found for the intermediate DWI-ASPECTS group. In this group, a good outcome was achieved in 46.5% (20/43) of patients with successful revascularization, whereas no patients without successful revascularization had a good outcome (P = .016) (Fig 3).
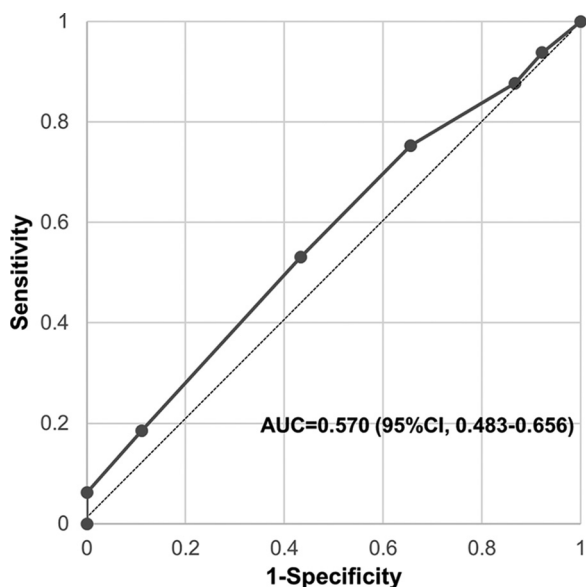

FIG 2. Receiver operating characteristic curve of DWI-ASPECTS for prediction of a good outcome (mRS 0–2 at 3 months). AUC indicates area under the curve.

DISCUSSION

The present study showed that treatment outcomes are not significantly different between patients with a high DWI-ASPECTS of 7–10 and those with an intermediate DWI-ASPECTS of 4–6 who underwent stent-retriever embolectomy for acute anterior circulation stroke. There were no significant differences in the rates of successful revascularization, good outcome, symptomatic hemorrhage, and mortality between the 2 groups in our study.

Several factors might explain the finding that patients with an intermediate DWI-ASPECTS benefited from stent-retriever embolectomy in our study. First, stent-retriever embolectomy can achieve a dramatically increased rate of successful recanalization of up to 80%–90% without an increased risk of symptomatic hemorrhage, compared with intra-arterial pharmacologic thrombolysis or previous mechanical approaches.[23] Recanalization is one of the most powerful independent predictors of good outcome in patients with acute stroke undergoing endovascular treatment.[16,25-27] In our study, the overall rate of successful revascularization was 84%, and it was identical among high and intermediate DWI-ASPECTS groups. The rate of symptomatic hemorrhage was quite low (3.5%) in our study. Among the intermediate DWI-ASPECTS group, almost half of patients with recanalization had a good outcome in the present study. In addition, recanalization was one of the independent predictors of good outcome (OR = 8.512), while DWI-ASPECTS was not. This finding is consistent with the results of a previous study by Inoue et al.[14] In their study, patients with anterior circulation stroke were treated with various endovascular therapies, including IV/intra-arterial thrombolysis and mechanical embolectomy with a snare or Solitaire stent, and 50% of patients with complete recanalization (Thrombolysis in Myocardial Infarction score of 3) in the subgroup with DWI-ASPECTS of <5 had a good outcome.[14] Thus, the results of our study and the study of Inoue et al[14] suggest that recanalization is far more important than pretreatment DWI-ASPECTS to predict good outcome in patients with anterior circulation stroke after endovascular therapy.

Second, the DWI-ASPECTS cannot substitute for DWI lesion volume in patients with anterior circulation stroke and an intermediate ASPECTS of 4–6 because an intermediate DWI-ASPECTS corresponds to a wide range of lesion volumes.[28] It has been reported that DWI lesion volume is a strong predictor of clinical outcome after endovascular treatment.[16,29] Recently, Ribo et al[29] suggested the concept of the maximal admission lesion volume compatible with favorable outcome, which was defined as the admission core volume above which the possibility of favorable outcome (mRS 0–2) was <10% in patients with acute anterior circulation stroke. In their study, maximal admission lesion volume compatible with favorable outcome was found to

Table 3: Logistic regression analysis of predictors of good outcome

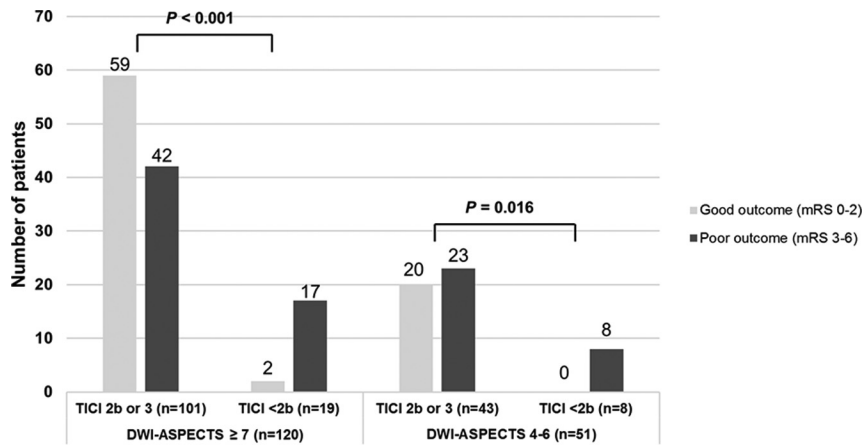|	Unadjusted OR	95% CI	P Value	Adjusted OR	95% CI	P Value
Age per 1-yr increase	0.947	0.918–0.976	<.001	0.941	0.909–0.974	.001
Baseline NIHSS, per 1-point increase	0.900	0.834–0.971	.006	–	–	–
Time to treatment	1	0.996–1.004	.999	–	–	–
Modified TICI 2b or 3	9.455	2.725–32.808	<.001	8.511	2.298–31.525	.001
Symptomatic hemorrhage	0.213	0.240–1.859	.125	–	–	–
DWI-ASPECTS, per 1-point increase	1.150	0.930–1.421	.196	–	–	–
DWI-ASPECTS ≥7 vs <7	1.603	0.823–3.120	.165	–	–	–

FIG 3. Impact of successful revascularization on functional outcome according to DWI-ASPECTS.

be 39 mL and was shown to be a potent predictor of favorable outcome (OR, 9.3; $P = .01$), independent of recanalization and age.[29]

DWI-ASPECTS is commonly used as surrogate for lesion volume to save time in an acute setting. However, a previous study showed that DWI lesion volume in patients with a DWI-ASPECTS 4–6 ranged from 10 to 197 mL (median, 66 mL; IQR, 41–97 mL).[28] An explanation for this variability is that ASPECTS regions are weighed unequally and in favor of the striatocapsular region.[30] Another recent study showed that there is a striking disparity of DWI ASPECTS–DWI lesion volume correlations between the superficial (cortical) and the deep (striatocapsular) MCA regions.[31] DWI-ASPECTS showed only a poor correlation to DWI lesion volume for stroke lesions in the striatocapsular region in that study. In this regard, patients with a DWI-ASPECTS of 4–6 but small ischemic lesion volume are likely to have a chance of a good outcome after stent-retriever embolectomy, especially when successful revascularization occurs.

Third, patients with a high DWI-ASPECTS were significantly older than those with an intermediate ASPECTS, and age was one of the independent predictors of good outcome in the present study. This might attenuate the positive effect of DWI-ASPECTS on outcome in the high DWI-ASPECTS group and thus contribute to the statistical insignificance of the DWI-ASPECTS.

Our study result has an important clinical implication, in that patients with an intermediate DWI-ASPECTS otherwise eligible for endovascular therapy, especially with scores of 4 and 5, may not be excluded from stent-retriever embolectomy or stroke trials on the basis of the DWI-ASPECTS alone. Our study suggested that the DWI-ASPECTS may not be a relevant imaging predictor of outcome in patients with anterior circulation stroke presenting within 6 hours. The DWI-ASPECTS was not significantly associated with outcomes in univariate and multivariate analysis in the present study. The results of our study are consistent with a recent study by Danière et al.[18] Among 26 patients with a DWI-ASPECTS of <5 in their study, 60% of patients younger than 70 years of age had a good outcome, whereas 10% of those 70 years of age and older had a good outcome after stent-retriever embolectomy. The authors suggested that younger patients may still benefit from recanalization despite a DWI-ASPECTS of <5. In the present study, the absence of statistical significance of

DWI-ASPECTS on outcome may be partly because patients with a low DWI-ASPECTS of ≤3 were not included. Previous studies showing a positive correlation between DWI-ASPECTS and outcome after endovascular therapy mostly included patients with an ASPECTS of 0–3, and most of these patients had an mRS of 5–6, which might explain any statistically significant relationship between DWI-ASPECTS and outcome in their analyses.[9,14]

Although the DWI-ASPECTS may not be suitable for prediction of infarction volume and outcome in patients with intermediate-to-high ASPECTS, it can still be used to predict a lesion volume cut-point of >100 mL, which corresponds to a traditional concept of greater than one-third of the middle cerebral artery territory and serves as an exclusion criterion for endovascular therapy in ongoing trials. In a study by de Margerie-Mellon et al,[28] 94% of patients (32/34) with a DWI-ASPECTS of ≤3 had a lesion volume of >100 mL and the lowest lesion volume in those patients was 93 mL. While DWI-ASPECTS may not predict outcome in patients with acute anterior circulation stroke, it may be useful for defining the presence of a benign imaging pattern to establish candidacy in the new embolectomy era.

Our study has several limitations, including a retrospective and monocentric study design. We did not measure DWI lesion volume and thus did not examine the relationship between lesion volume and ASPECTS. However, that relationship has been well documented in previous studies,[28,31] and the aim of our study was to investigate whether the DWI-ASPECTS can be used as an imaging predictor of clinical outcome after stent-retriever embolectomy in anterior circulation stroke. The patients were selected for endovascular therapy by using perfusion imaging and a target mismatch profile. The results of the study might be different if patients with a nontarget mismatch profile were included. Finally, the patient number in the high DWI-ASPECTS group was larger than that of the intermediate group.

CONCLUSIONS

Our study suggested that treatment outcomes were not different between patients with a high DWI-ASPECTS of 7–10 and those with an intermediate DWI-ASPECTS of 4–6 who underwent stent-retriever embolectomy for acute anterior circulation stroke. Thus, patients with intermediate DWI-ASPECTS otherwise eligible for endovascular therapy may not be excluded from stent-retriever embolectomy or stroke trials.

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