Utility of Minimum Apparent Diffusion Coefficient Ratios in Alberta Stroke Program Early CT Score Regions for Deciding on Stroke Therapy

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Background and Purpose: Therapeutic indications for recombinant tissue plasminogen activator therapy and endovascular therapy need to be assessed for patients with hyperacute ischemic stroke. We investigated the relationship between the minimum apparent diffusion coefficient ratios in each Alberta Stroke Program Early CT Score region and reversible lesion in patients with hyperacute ischemic stroke receiving recombinant tissue plasminogen activator therapy and/or treated with endovascular therapy. *Materials and Methods*: We retrospectively evaluated 29 patients with first ischemic stroke due to stenosis/occlusion of the internal carotid artery or horizontal portion of the middle cerebral artery that was successfully recanalized by recombinant tissue plasminogen activator therapy and/or treated with endovascular therapy. We measured the minimum apparent diffusion coefficient value in each Alberta Stroke Program Early CT Score region (11 regions) and calculated the ratio. *Results*: There was a significant difference in minimum apparent diffusion coefficient ratios between regions that included and did not include infarction ($P < .0001$), which were distinguishable with a cutoff value of .808 (area under the curve = .80, $P < .001$). A statistical difference in the proportion of infarction with the cutoff value was observed between patients treated with endovascular therapy and receiving recombinant tissue plasminogen activator therapy alone (9.9% versus 24.6%, $P = .0041$) and between patients with affected middle cerebral and internal carotid arteries (7.0% versus 24.2%, $P = .0002$). The lowest apparent diffusion coefficient ratio was associated with the time to recombinant tissue plasminogen activator injection. *Conclusions*: Minimum apparent diffusion coefficient ratios in Alberta Stroke Program Early CT Score regions are useful in predicting therapeutic effect.

Key Words: Apparent diffusion coefficient—ASPECTS—hyperacute ischemic stroke—recombinant tissue plasminogen activator—endovascular therapy

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Introduction

Hyperacute ischemic stroke therapy, including recombinant tissue plasminogen activator (rt-PA) therapy and endovascular therapy (EVT), can rescue larger penumbral lesions and has progressed over recent years. The Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials reported that the proportion of patients with modified Rankin scale score of 0-1 or 0-2 at 90 days who underwent endovascular thrombectomy was higher than that of patients receiving rt-PA therapy alone.[1] Along with the progression of hyperacute ischemic stroke therapy, we need to assess the therapeutic indications for rt-PA therapy and EVT.

Immediate imaging of penumbral lesions is important in order to decide on therapeutic strategy. Recently, advancement in analysis software for the evaluation of penumbra or diffusion-perfusion mismatch has been remarkable.[2] However, in practice, such analysis software has not been available in many institutions. The Alberta Stroke Program Early CT Score (ASPECTS) has been used to assess the extent of early ischemic lesions on computed tomography (CT).[3] Furthermore, diffusion-weighted imaging (DWI) is one of the most favorable magnetic resonance imaging (MRI) methods for the detection of ischemic lesions. The ASPECTS + W (including white matter lesions on DWI) is currently a well-known and broadly used modified scoring method that enables physicians to easier decide on therapy.[4] However, it is often difficult to exactly evaluate the ASPECTS + W score because our judgment is formed based on visual impression. Moreover, some high-intensity lesions on DWI are reversibly rescued. It has been reported that low apparent diffusion coefficient (ADC) is associated with brain infarction.[5-8] However, ADC values vary depending on coil systems, vendors, and field strengths used for MRI.[9] In addition, there is regional difference in the development of absolute ADC values,[10,11] and false elevation in ADC values could occur by partial volume averaging of the cerebrospinal fluid with the parenchyma.[12] Nonetheless, the ADC ratio, which refers to the ratio of the affected side's ADC value to the opposite side's ADC value, is one of the standards associated with infarction. Evaluating ADC ratios can serve as one of the practical and useful methods that may be employed to reduce errors in ADC value measurement.

In this study, we investigated the relationship between minimum ADC ratios in each ASPECTS region and reversible lesions in patients with hyperacute ischemic stroke receiving rt-PA therapy and/or treated with EVT. Moreover, we examined the differences in cutoff minimum ADC ratio for predicting infarction between occluded arteries, therapies, and recanalization time.

Subjects and Methods

Subjects

This was a single-center hospital-based retrospective study. Patients who received rt-PA therapy and/or underwent EVT for hyperacute stroke from February 2012 to June 2016 were identified. Furthermore, patients who had ischemic stroke due to stenosis/occlusion of the internal carotid artery (ICA) or horizontal portion of the middle cerebral artery (M1) that was successfully recanalized by rt-PA therapy and/or EVT and who had a modified Treatment in Cerebral Ischemia scale score of 2b or 3, as determined using magnetic resonance angiography or digital subtraction angiography, were included in the study.[13,14] A previous study reported that ADC value in chronic stroke is different from that in the normal brain[15]; hence, patients with a history of stroke were excluded from the study (Fig 1).

We also investigated the relationship between the ADC ratio and therapeutic time. We recorded the time point of onset, hospital visitation, MRI, rt-PA injection, puncture for EVT, and recanalization and measured the duration between each point.

Stroke subtypes were decided by 2 stroke neurologists (Y.M. and M.N.) according to the Trial of Org 10172 in Acute Stroke Treatment classification.[16] Neurological deficit was estimated using the National Institutes of Health Stroke Scale.[17]

Hypertension was defined as a confirmed blood pressure of 140/90 mm Hg or higher at rest at 1 week after stroke onset or the use of antihypertensive medicine before admission. Diabetes mellitus was defined as a hemoglobin A1c level of 6.5% or more, a fasting blood glucose level of 126 mg/dL or higher, or the use of hypoglycemic agents. Dyslipidemia was defined as a total cholesterol level of 220 mg/dL or higher, a low-density lipoprotein cholesterol level of 140 mg/dL or higher, a high-density lipoprotein cholesterol level of 40 mg/dL or lower, or a triglyceride level of 150 mg/dL or higher on admission or during hospitalization or the use of antihyperlipidemic medications. Atrial fibrillation was diagnosed based on electrocardiographic findings on admission or during hospitalization or a history of atrial fibrillation. Antithrombotic drugs included aspirin, clopidogrel, cilostazol, warfarin, and direct oral anticoagulants.

The study protocols were approved by the ethics committee of Suiseikai Kajikawa Hospital and performed in accordance with national government guidelines based on the 1964 Declaration of Helsinki. The requirement for informed consent for this study was waived owing to its retrospective nature; upon admission, the included patients agreed that their data would be used for future study.

Treatment

Intravenous rt-PA injection was performed following the guidelines published by the Japan Stroke Society.[18] The inclusion and exclusion criteria for intravenous tissue-type plasminogen activator therapy were in accordance with the Japan Alteplase Clinical Trial until September 2012[19] and with the new guideline published

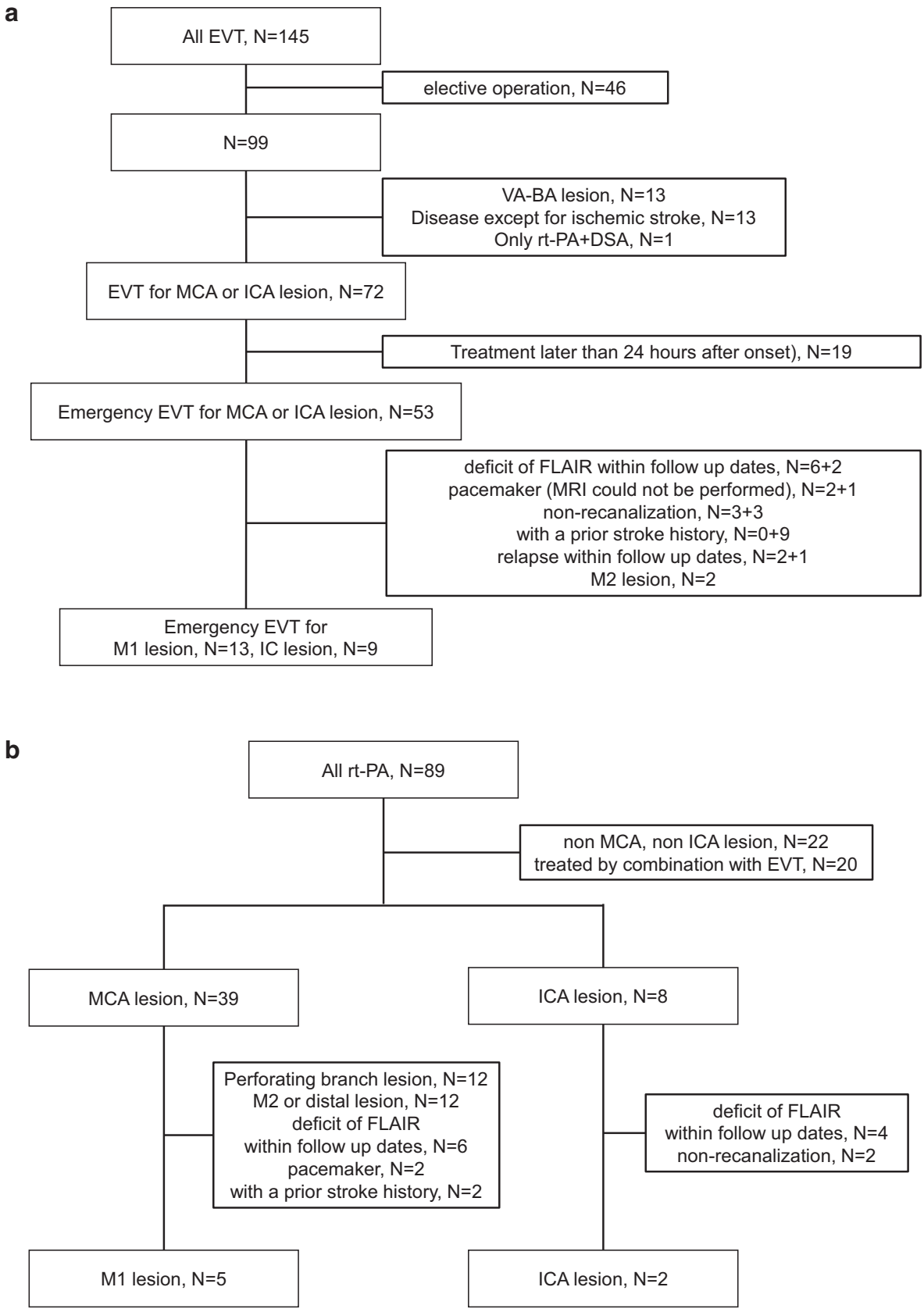


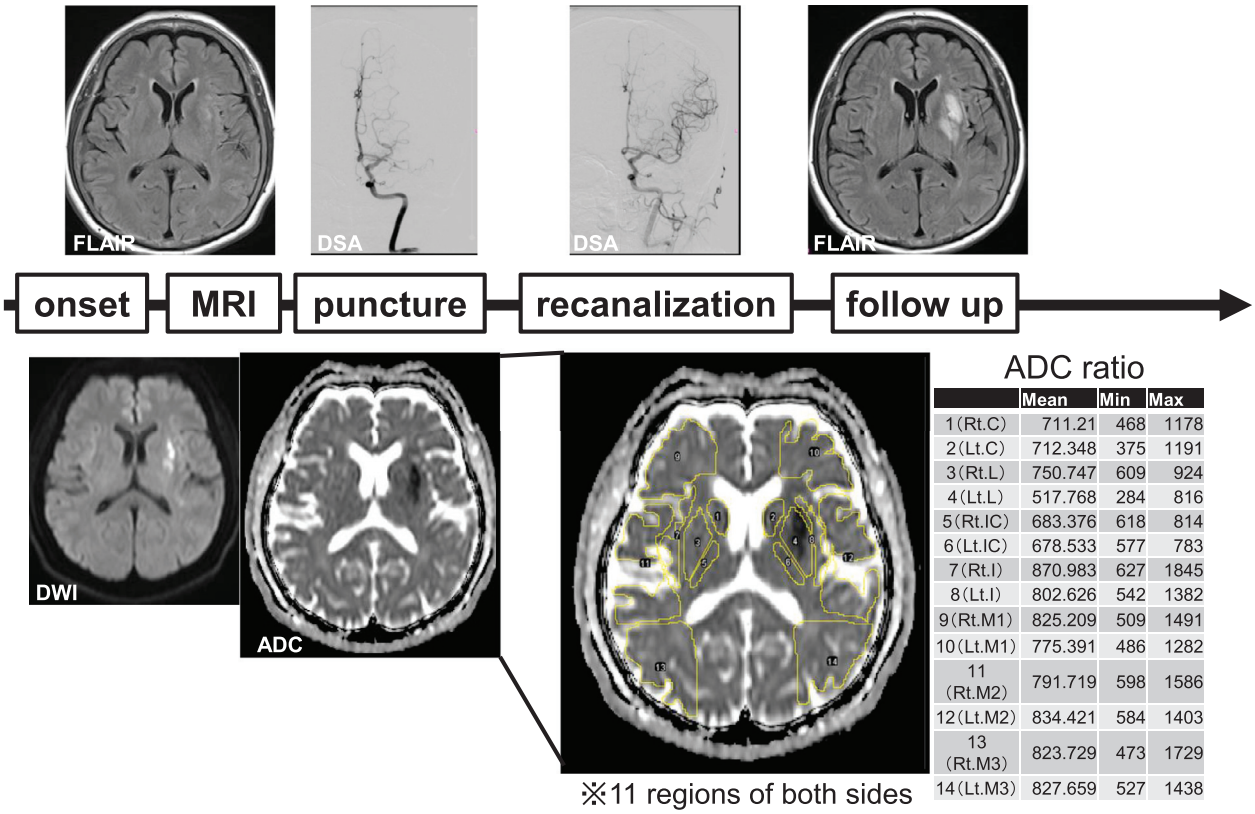
Figure 1. *Flowchart of inclusion and exclusion criteria. Flowchart for EVT (a) and rt-PA (b). Abbreviations: BA, basilar artery; EVT, endovascular therapy; ICA, internal carotid artery; MCA, middle cerebral artery; rt-PA, recombinant tissue plasminogen; VA, vertebral artery.*

in October 2012 because the guideline was revised at that time.[18] EVT was performed by certified neurointerventionalists (Y.I., Y.S., and S.W.) and included thrombectomy using devices, percutaneous transluminal angioplasty, carotid artery stenting, stent implantation (ICA or MCA), and intra-arterial urokinase therapy. Devices for thrombectomy were selected by each neurointerventionalist, such as the MERCI Retriever (Concentric Medical, Inc., Mountain View, CA), Penumbra System (Penumbra Inc., Alameda, CA), Solitaire (Medtronic, Minneapolis, MN), and Trevo Retriever (Stryker Neurovascular, Fremont, CA), and were used as appropriate. Before EVT, rt-PA was injected in patients for therapeutic indications when applicable.

Magnetic Resonance Imaging

MRI was performed using a 1.5-T scanner (Avanto, Siemens Healthineers, Erlangen, Germany) or 3.0-T scanner (Spectra, Siemens Healthineers, Erlangen, Germany). The imaging protocol consisted of ADC (repetition time (TR) = 7000 ms and echo time (TE) = 75 ms for spin echo, field of view (FOV) = 22 cm, matrix size = 98 × 140, slice thickness = 5.0 mm, interslice spacing = 1.5 mm), fluid-attenuated inversion recovery (FLAIR) imaging (TR = 12,000 ms and TE = 87 ms for turbo spin echo, inversion time = 2800 ms, FOV = 22 cm, matrix size = 226 × 384, slice thickness = 5.0 mm, interslice spacing = 1.5 mm), three-dimensional time-of-flight magnetic resonance angiography (TR = 22 ms, TE = 3.69 ms, FOV = 200 cm, matrix size = 215 × 320, slice thickness = .50 mm, interslice spacing = −6.0 mm), T2*-weighted imaging (TR = 617 ms and TE = 14 ms for gradient echo, FOV = 22 cm, matrix size = 224 × 320, slice thickness = 5.0 mm, interslice spacing = 1.5 mm), and DWI (TR = 7000 ms and TE = 75 ms for spin echo, FOV = 22 cm, matrix size = 98 × 140, slice thickness = 5.0 mm, interslice spacing = 1.5 mm).

Eleven ASPECTS regions were defined according to a previous report.[4] Infarction was defined as a new hyperdense area on follow-up FLAIR imaging. Follow-up MRI was performed from day 4 to day 20 from onset of illness, and FLAIR imaging was performed on admission and during follow-up in all cases. We examined whether these regions included hemorrhagic change using CT or T2*WI. ADC values were measured on admission using ImageJ software version 1.51j8 (National Institutes of



ADC ratio

	Mean	Min	Max
1(Rt.C)	711.21	468	1178
2(Lt.C)	712.348	375	1191
3(Rt.L)	750.747	609	924
4(Lt.L)	517.768	284	816
5(Rt.IC)	683.376	618	814
6(Lt.IC)	678.533	577	783
7(Rt.I)	870.983	627	1845
8(Lt.I)	802.626	542	1382
9(Rt.M1)	825.209	509	1491
10(Lt.M1)	775.391	486	1282
11 (Rt.M2)	791.719	598	1586
12(Lt.M2)	834.421	584	1403
13 (Rt.M3)	823.729	473	1729
14(Lt.M3)	827.659	527	1438

Figure 2. *Timeline and methods for the evaluation of ADC ratio. The ADC value was measured in each Alberta Stroke Program Early CT Score (ASPECTS) region (11 regions at both sides). After treatment, new high-intensity area was defined as infarction. An example is shown. The left lenticular nucleus includes infarction in this figure. The minimum ADC value in the left lenticular nucleus ASPECTS region is 284. The minimum ADC ratio in the lenticular nucleus refers to the ratio of the minimum ADC value for the left lenticular nucleus to that for the right lenticular nucleus (284/609). Abbreviations: ADC, apparent diffusion coefficient; DSA, digital subtraction angiography; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging.*

Health, Bethesda, MD). We measured the minimum ADC value and calculated the minimum ADC ratio in each ASPECTS region. The minimum ADC ratio referred to the ratio of the affected side's minimum ADC value to the opposite side's minimum ADC value in each region (Fig 2). We defined ADC ratio outliers as lower than .50 in normal area and higher than 2.0 in infarcted area and excluded them. Regarding the relationship between ADC ratio and therapeutic time, we used the lowest ADC ratio among the minimum ADC ratios for all ASPECTS regions in each patient. Two stroke neurologists (Y.M. and M.N.) who were unaware of the clinical details of patients determined whether each ASPECTS region included infarction.

Statistical Analysis

Statistical analyses were performed using JMP statistical software version 13.0 (SAS Institute Inc., Cary, NC). Data are expressed as means ± standard deviations or medians (interquartile ranges) for continuous variables and as frequencies and percentages for discrete variables. Statistical significance of intergroup differences was assessed using χ^2 test, unpaired t test, and Mann-Whitney U test, as appropriate. Receiver operating characteristic (ROC) curves were constructed to determine the cutoff minimum ADC ratio for predicting infarction in each ASPECTS region. Moreover, patients were grouped according to therapies and affected arteries, and the same analysis was performed in each group. Statistical significance was set at $P < .05$.

Results

A total of 29 patients (14 females [48.3%]; mean age, 69.7 ± 12.8 years) were enrolled in the study. Of these patients, 22 underwent EVT with or without rt-PA injection, whereas 7 received rt-PA therapy alone. The characteristics of enrolled patients are summarized in Table 1. EVTs are shown in Supplemental table. Overall, 26 patients (89.7%) were diagnosed with atherosclerotic or cardioembolic stroke. Three cases were of unknown or unclassified etiology.

Table 1. *Patient characteristics*

		EVT (N = 22)	rt-PA (N = 7)	*P* value
Age, years†		67.6 ± 13.0	76.4 ± 10.0	.17
Female*		8 (36.4%)	6 (85.7%)	.02
Left side*		11 (50.0%)	4 (57.1%)	.74
3-T/1.5-T MRI*		10 (45.5%)	2 (28.6%)	.43
NIHSS on admission‡		11 [1-31]	8 [1-17]	.09
Hemorrhagic infarction*		8 (36.4%)	3 (42.9%)	.76
Previous history				
Any stroke*		0 (0%)	0 (0%)	1
Af*		6 (27.3%)	3 (42.9%)	.44
Antithrombotic drug*		2 (9.1%)	1 (14.3%)	.69
HT*		13 (59.1%)	4 (57.1%)	.93
DM*		8 (36.4%)	3 (42.9%)	.76
DL*		12 (54.6%)	2 (28.6%)	.23
Stroke subtypes				
Atherosclerotic*		13 (59.1%)	3 (42.9%)	.28
Cardioembolic*		6 (27.2%)	4 (57.1%)	
Others*		3 (13.6%)	0 (0%)	
Time, min				
From onset	To hospital‡	86.5 [30-822]	95 [42-130]	.63
	To MRI‡	106 [40-869]	120 [60-174]	.82
	To rt-PA injection‡	135 [74-186]**	164 [125-236]	.16
	To puncture‡	232 [90-1002]	-	
	To recanalization‡	365 [138-1153]***	-	
From hospital	To MRI‡	20 [6-69]	25 [18-44]	.12
	To rt-PA injection‡	66 [43-91]**	83 [48-112]	.11
	To puncture‡	114 [59-653]	-	
	To recanalization‡	260 [107-738]***	-	

Abbreviations: Af, atrial fibrillation; DL, dyslipidemia; DM, diabetes mellitus; EVT, endovascular therapy; HT, hypertension; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue plasminogen.

†Data are presented as mean ± standard deviation.

‡Data are presented as median [minimum-maximum].

*Data are presented as number (%).

**N = 10.

***N = 21.

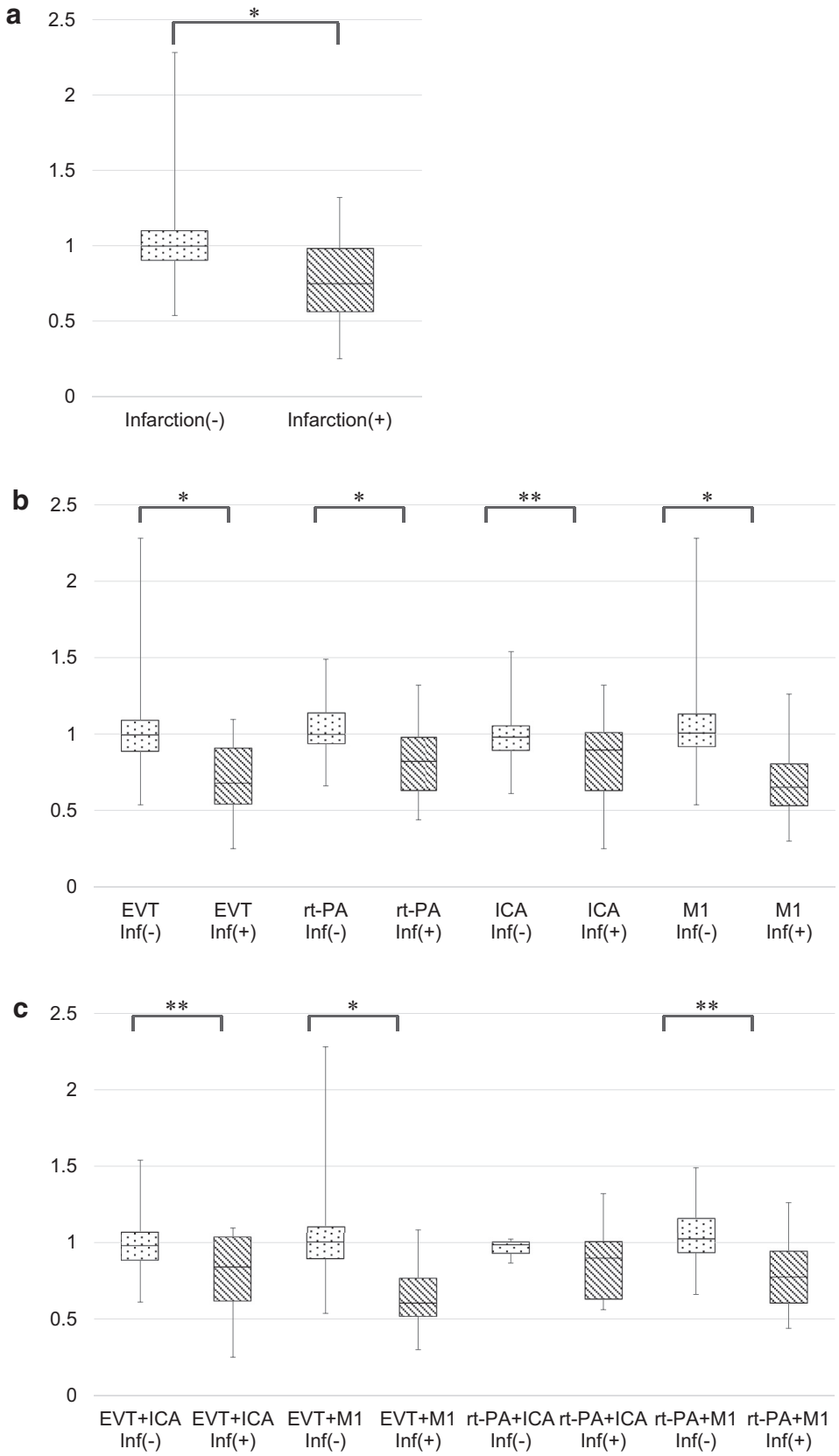


Figure 3. *Minimum apparent diffusion coefficient ratio in regions that included infarction and not in each group. In all patients (a). Comparison between treatments and affected arteries (b). Comparison among combinations of therapies and affected arteries (c). Abbreviations: EVT, endovascular therapy; ICA, internal carotid artery; Inf, infarction; M1, horizontal portion of the middle cerebral artery; rt-PA, recombinant tissue plasminogen.* *P < .0001, **P < .01.

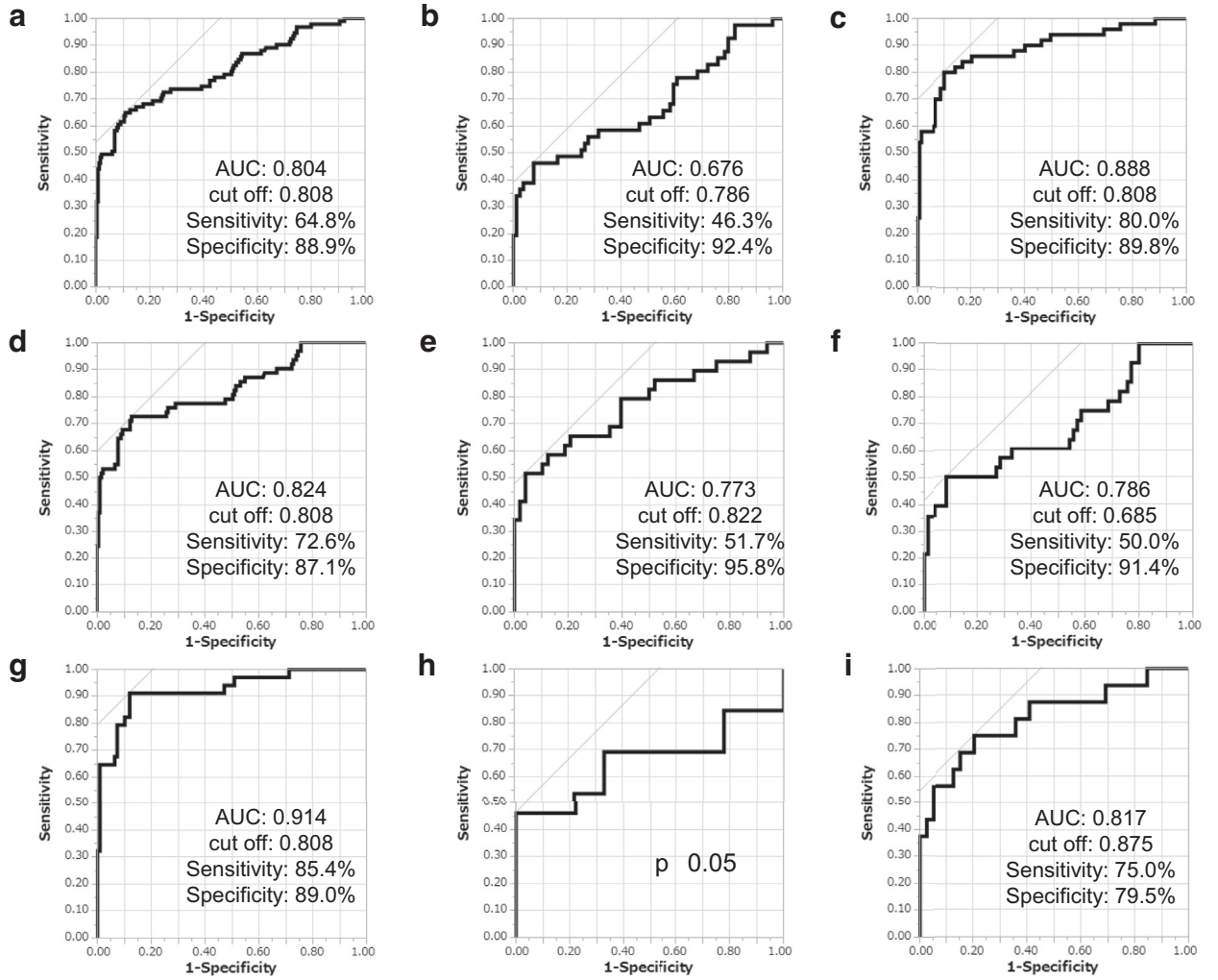


Figure 4. *Receiver operating characteristic curve of minimum apparent diffusion coefficient ratio for predicting infarction in Alberta Stroke Program Early CT Score regions in each group. All patients (a), ICA group (b), M1 group (c), EVT group (d), rt-PA therapy alone group (e), EVT + ICA group (f), EVT + M1 group (g), rt-PA + ICA group (h), and rt-PA + M1 group (i). Abbreviations: AUC, area under the curve; EVT, endovascular therapy; ICA, internal carotid artery; M1, horizontal portion of the middle cerebral artery; rt-PA, recombinant tissue plasminogen.*

Cutoff Minimum ADC Ratio for Predicting Infarction in ASPECTS Regions

Acute ischemic infarctions were included in 91 ASPECTS regions in 29 patients, excluding 2 regions because of obvious outliers. Overall, there was a significant difference in minimum ADC ratios between regions that included and did not include infarction (median, .74 versus .99; $P < .0001$; Fig 3a). The ROC analysis showed that the optimal cutoff minimum ADC ratio for predicting infarction was .808 (sensitivity, 64.8%; specificity, 88.9%; area under the curve = .804; $P < .001$; Fig 4a).

We subsequently divided the patients according to therapies (EVT group and rt-PA therapy alone group) and affected arteries (ICA group and M1 group). The same analyses were performed in each group. Significant differences in minimum ADC ratios between regions that included and did not include infarction were observed in all groups, except for the rt-PA + ICA group (Fig 3b,c). In the rt-PA+ICA group, we could not discuss the association between regions that included and did not include infarction owing to a lack of power (Fig. 1b and 3c). The cutoff minimum ADC ratios for predicting infarction in the ROC analysis are shown in Figure 4. In the EVT + M1 group, ADC ratios could most accurately distinguish the region that included infarction from the normal region (sensitivity, 85.4%; specificity, 89.0%; area under the curve = .914; $P < .001$; Fig 4g).

Differences in the Proportion of Infarction with a Cutoff Minimum ADC Ratio of ≥.808 between Occluded Arteries or Therapies

We investigated the difference between therapies and affected arteries. The fate of each ASPECTS region was evaluated using the cutoff minimum ADC ratio of .808. With respect to therapies, there was a statistical difference in the proportion of infarction with a minimum ADC ratio of ≥.808

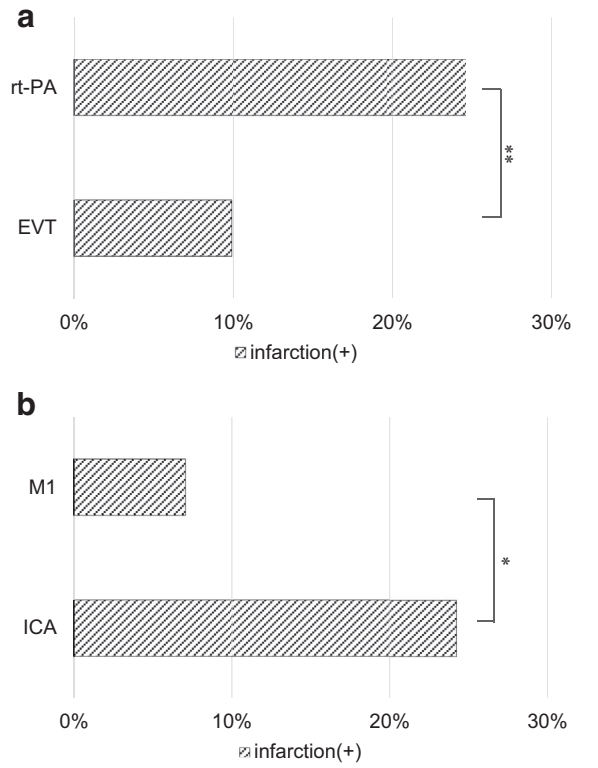


Figure 5. *Proportion of infarction in each group with minimum apparent diffusion coefficient ratio of .808 or more. Comparison between therapies (a) and affected arteries (b). Abbreviations: EVT, endovascular therapy; ICA, internal carotid artery; M1, horizontal portion of the middle cerebral artery; rt-PA, recombinant tissue plasminogen.*

between the EVT group (EVT + ICA and EVT + M1 groups) and rt-PA therapy alone group (rt-PA + ICA and rt-PA + M1 groups; 9.9% versus 24.6%, $P = .0041$). With respect to affected arteries, there was also a statistical difference in the proportion of infarction (7.0% versus 24.2%, $P = .0002$; Fig 5).

Associations between the Lowest ADC Ratio and Therapeutic Times

With respect to the associations between the lowest ADC ratio and therapeutic times, the lowest ADC ratio was significantly associated with the time from hospital visitation to rt-PA injection ($r = .629$, $P = .007$). In addition, it tended to be associated with the time from onset to rt-PA injection ($r = .462$, $P = .062$). However, in our study, no significant correlations between the lowest ADC ratio and other therapeutic times, such as the time to MRI, puncture, and recanalization, were observed.

Discussion

In this study, we used minimum ADC ratios in ASPECTS regions and determined the optimal cutoff value for predicting infarction. It is generally recommended that the ASPECTS score and diffusion-perfusion mismatch imaging should be used in the course of hyperacute ischemic stroke therapy. However, it is often difficult to exactly evaluate the ASPECTS score because our judgment is formed based on visual impression. Diffusion-perfusion mismatch imaging is very useful to show the penumbra area, but it is also qualitative analysis. In addition, it requires renal function evaluation and takes more time. The Rapid Processing of Perfusion and Diffusion system could provide more accurate perfusion images,[2] which was used in EXTEND-IA,[20] SWIFT-PRIME,[21] DAWN,[22] and DEFFUSE3.[23] However, in practice, these methods are not yet available in many institutions. Because the software for measuring ischemic core volume or hypoperfusion lesion is not popular, we have to consider the therapeutic indications carefully on a case-by-case. The method in this study (minimum ADC ratios in each ASPECTS region) is meaningful in the point of quantitative analysis. The quantitative evaluation might make us easier to decide the treatment. Moreover, it takes within a few minutes to measure ADC ratios. Radiology technicians only have to set regions of interest, and the mirror point of the regions of interest. They could measure ADC ratios immediately subsequently to MRI images.

This study showed that infarcted regions had significantly reduced minimum ADC ratios and that the optimal cutoff minimum ADC ratio for predicting infarction was .808. A previous study has reported statistically significant difference in ADC values among the normal brain, penumbra, and infarcted region with no overlap in 95% confidence intervals for the means (847 ± 103, 764 ± 110, 533 ± 157, respectively; $P < .05$).[24] There have been several reports on the cutoff ADC ratio for predicting infarction. Desmond et al reported that an ADC ratio of .75-.90 was associated with penumbral regions that later progressed to infarction.[5] Relative ADC values were higher in regions with DWI reversal ($.81 \pm .07$) than in the acute DWI region that infarcted ($.74 \pm .07$, $P = .02$).[7] Shinoda et al reported that in patients with acute ICA or M1 occlusion who underwent endovascular revascularization, a relative ADC ratio $<.70$ (control) resulted in infarction despite treatment, whereas a relative ADC ratio $>.80$ did not.[25] These findings supported our results.

In our study, a statistical difference in the proportion of infarction with a minimum ADC ratio $\geq .808$ was observed between the EVT and rt-PA therapy groups (9.9% versus 24.6%, $P = .0041$), suggesting that EVT could rescue regions with lower ADC ratio compared with rt-PA therapy alone. It has been reported that lesions with lower ADC ratio could be treated if patients would undergo treatment.[26] According to the Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials, the proportion of patients with an modified Rankin scale score of 0-1 or 0-2 at 90 days who underwent endovascular thrombectomy was higher than that of patients treated with alteplase alone (+13.8%, +19.4%).[1] Both rt-PA

therapy and EVT can rescue more patients with hyperacute ischemic stroke, indicating that they could rescue lesions with lower ADC ratio.

In addition, we showed that the proportion of infarction was significantly lower in patients with M1 occlusion/stenosis than in patients with ICA occlusion/stenosis (7.0% versus 24.2%, P = .0002). The difference might be due to collateral circulation or greater thrombosis. The recanalization rate has been reported to be lower in ICA occlusion than in M1 occlusion by rt-PA injection, with patients with ICA occlusion having worse prognosis than patients with M1 occlusion.[27] Tandem cervical ICA/middle cerebral artery occlusion had poor recanalization and outcome rates compared with terminal ICA occlusion.[28-30] ICA occlusion might progress earlier than M1 occlusion, and EVT and/or rt-PA therapy could prevent the region with lower ADC ratio from developing into infarction in patients with M1 occlusion/stenosis compared with those with ICA occlusion/stenosis.

This study showed that the time from hospital visitation—but not onset—to rt-PA injection was more likely to be associated with a lower minimum ADC ratio, which may be attributed to the fact that onset time is not always exactly accurate. In this study, the affected arteries in all enrolled patients were recanalized. The proportional positive correlation between the lowest ADC ratio and time to rt-PA indicated that the penumbra could be rescued if the ADC value might slowly decrease. To the best of our knowledge, it remains unclear whether the acceleration of decline in ADC values in the penumbra could suggest progression to infarction. Relative ADC values in stroke rat models had been shown to already decrease at 3 hours after reperfusion despite 30-60 minutes M1 occlusion and to decrease until 24 hours.[31] According to Loubinoux et al, there seems to be little difference in the spreading rate of ADC value reduction in the affected region with cerebral infarction.[11]

Improvement in ADC value (ΔADC) is an important broadly studied factor to avoid infarction and is strongly associated with reperfusion in acute ischemic stroke within 6 hours from onset, but not with initial ADC value reduction.[32] The ΔADC is statistically greater in the region in which reperfusion has been achieved than in the region with no reperfusion.[32]

The present study possesses the following impressive points that are worthy of mention: First, we confirmed the association between ADC ratios and infarctions; although numerous studies have already reported this, no investigation has evaluated ADC values or ratios in each ASPECTS region. Second, we compared the ADC ratios according to affected arteries, treatments, and times. Several previous reports have indicated the association between ADC values (or ratios) and infarction only; nonetheless, few studies have examined the associations among ADC values (or ratios), infarction, affected arteries, treatments, and times. Third, our method is comparable to previous methods and is more readily available in several institutions than high-performance analysis methods, such as the Rapid Processing of Perfusion and Diffusion system. Nevertheless, this study has several limitations. First, it was a single-center hospital-based retrospective study. Although we showed that the optimal cutoff minimum ADC ratio was .808, this ratio might vary among other institutions. Nevertheless, this ratio was almost equal to that in previous reports.[5,7,25] In addition, our institution specializes in stroke care, and the usual therapy protocol was implemented. Second, the number of patients enrolled in this study was inadequate. A multivariate analysis for the relationship between minimum ADC ratio and therapeutic time could not be performed owing to the insufficient number of enrolled subjects. Third, we could not adequately discuss the association between hemorrhagic change and ADC ratio because of the lack of power. Large-scale studies could clarify this association.

Conclusions

Minimum ADC ratios in ASPECTS regions are useful in predicting reversible lesions and therapeutic effect. This method, which is available in more institutions and is comparable to previous methods, can enable us to more accurately evaluate the ASPECTS score so as not to miss infarction. The performance of EVT could rescue regions with lower ADC ratio compared with rt-PA therapy alone. In addition, we could rescue the ischemic penumbra with lower ADC ratio in M1 occlusion/stenosis than in ICA occlusion/stenosis. Although advancement in hyperacute ischemic stroke therapy and imaging technique is expected to rescue more severe ischemic penumbra, practical and simple techniques are nonetheless required.

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Authors' Contributions

Y.M. examined and evaluated the patients. Y.M. and M.N. designed the study and wrote the manuscript draft. Y.M. and M.N. contributed to the acquisition, analysis, and interpretation of clinical data. E.I., Y.I., H.A., Y.S., and S.W. participated in the design of the study and helped in drafting the manuscript. H.M. and S.W. supervised the finalization of the manuscript. All authors have read and approved the final version of the manuscript.

Ethical Approval and Consent to Participate

All procedures performed in our study, which involved human participants, were approved by the ethics committee of Suiseikai Kajikawa Hospital and were in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.02.003.

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