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Arterial spin labeling signal ratio between the lesion and contralateral sides for evaluation of acute middle cerebral artery infarct

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Abstract

The purpose of our study was to differentiate arterial transit artifact from post-recanalization luxury perfusion on arterial spin labeling (ASL) image, and obtain the relationship between ASL signal intensity and clinical outcomes in patients with acute ischemic stroke.

Thirty-five subjects with an acute middle cerebral artery (MCA) infarct were enrolled (18 with recanalized and 17 with non-recanalized MCAs). ASL images were obtained using pseudo-continuous ASL technique with 1600 ms (millisecond) of post-label delay within 3 days from symptom onset. Signal intensities on color ASL images were classified as high, intermediate, and poor grade visually. The ratio of maximum ASL signal between the ischemic area and contralateral side was calculated and compared between patients with and without MCA recanalization. Among patients with non-recanalized MCA, ASL signal ratios were compared between patients with and without hyperintense vessel sign on fluid attenuated inversion recovery (FLAIR). Also, correlation between the ASL signal ratio and National Institutes of Health Stroke Scale (NIHSS) score was evaluated.

High or intermediate grade on color ASL images were more frequently found in patients with recanalized MCA ($P < .01$). Patients with non-recanalized MCA had higher ASL signal ratio in overall ASL signal grade ($P = .010$) and intermediate grade ($P = .011$). Among patients with non-recanalized MCA, those with hyperintense vessel sign on FLAIR had higher ASL signal ratios ($P = .049$). ASL signal ratio was negatively correlated with both initial ($P = .023$) and final ($P = .003$) NIHSS scores.

The ASL signal ratio could help to differentiate between the pial collaterals and post-recanalization luxury perfusion. A higher ASL ratio was related with the hyperintense vessel sign on FLAIR and lower NIHSS score.

Abbreviations: ASL = arterial spin labeling, ATA = arterial transit artifact, CT = computed tomography, CTA = CT angiography, DSA = digital subtraction angiography, FLAIR = fluid attenuated inversion recovery, FOV = field of view, MCA = middle cerebral artery, MRA = magnetic resonance angiography, MRI = magnetic resonance imaging, ms = millisecond, NIHSS = National Institutes of Health Stroke Scale, PLD = post-label delay, T1WI = T1-weighted image, TE = echo time, TI = inversion time, TOF = time of flight.

Keywords: acute stroke, arterial spin labeling, collateral, magnetic resonance imaging

Editor: Neeraj Lalwani.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Lee J, Park DW, Kim YS, Kim HY, Lee YJ. Arterial spin labeling signal ratio between the lesion and contralateral sides for evaluation of acute middle cerebral artery infarct. Medicine 2022;101:2(e28569).

Received: 8 February 2021 / Received in final form: 9 December 2021 / Accepted: 22 December 2021

http://dx.doi.org/10.1097/MD.0000000000028569

1. Introduction

The information about the regional perfusion or collateral circulation is important for treatment of patients with acute ischemic stroke. Computed tomography (CT) perfusion, multiphase CT angiography (CTA), or digital subtraction angiography (DSA) are helpful to get these information, however, an imaging method without radiation exposure, contrast agents, or invasive approach would be beneficial for repetitive examination in the early critical period of acute ischemic stroke.

Arterial spin-labeling (ASL) is a quantitative magnetic resonance imaging (MRI) technique that uses arterial water as a freely diffusible tracer to evaluate cerebral blood flow.[1] This technique is noninvasive, easily repeatable, and does not require gadolinium contrast agents.[1] When acquiring images, the time between the end of the labeling pulse and image acquisition is known as the post-label delay (PLD). In the case of proximal arterial occlusion, there is an increase in ASL signal intensity compared with the signal in the contralateral side, which is called arterial transit artifact (ATA).[2,3] Therefore, in patients with acute ischemic stroke, the high signal intensities on ASL images can either be due to ATA or due to increased blood flow by post-recanalization luxury perfusion.[4] ATA and luxury perfusion can be distinguished by clinical history and signal characteristics. ATA is usually accompanied by ipsilateral hypoperfusion. However, if the occluded vessel is a small distal branch, the hypoperfused area may not be prominent enough to be recognized on ASL images. Because the risk of hemorrhagic transformation can increase by luxury perfusion, discrimination of ATA from luxury perfusion would be needed.

Although it is known that ATA is associated with pial collateral in acute ischemic stroke, the interpretation of high signal intensity on ASL is not entirely established. Therefore, the purpose of our study was to determine a method to differentiate ATA from post-recanalization luxury perfusion on ASL and obtain the relationship between ASL signal intensity and clinical outcomes in patients with acute ischemic stroke.

2. Materials and methods

Our institutional review board approved this study, and informed consent was waived in accordance with the requirements of a retrospective study.

2.1. Study participants

From October 2017 to June 2019, 35 consecutive patients with an acute MCA infarct were enrolled (20 men and 15 women, mean age: 70.7 years [age range: 43–93 years]). Eight of them underwent mechanical thrombectomy. Six patients underwent intravenous t-PA injection only. Twenty-one patients who had contraindications for mechanical thrombectomy or intravenous t-PA injection underwent conservative treatment. The follow-up MRI was performed within 3 days from initial CTA. Recanalized MCA was defined as recanalization of previously occluded vessel on magnetic resonance angiography (MRA). Non-recanalized MCA was defined as the persistent occlusion on MRA. Eighteen patients had recanalized MCA comprising 13 post-treatment and 5 spontaneous recanalizations. Non-recanalized MCA was in 17 patients (Table 1).

2.2. Image protocol

MRI was performed with a 3-T scanner (Achieva, or Ingenia, Philips, The Netherlands). The MRI protocol included T1-weighted image (T1WI), T2-weighted image, T2-fluid attenuated inversion recovery (FLAIR), susceptibility weighted image, diffusion weighted image, 3D time-of-flight (TOF)-MRA, gadolinium enhanced T1WI, and ASL. Images were acquired using the following parameters: T1WI with inversion recovery (TR 2000 millisecond [ms]; echo time [TE] 10 ms; inversion time (TI) 800 ms; flip angle 90°; field of view (FOV) 220 × 220; section thickness 5 mm; intersection gap 1.5 mm; number of sections 23; scanning time 3 min 54 s), T2-weighted image with turbo spin-echo (TR 3000 ms; TE 100 ms; flip angle 90°; FOV 220 × 220; section thickness 5 mm; intersection gap 1.5 mm; number of sections 23; scanning time 1 minute 42 seconds), T2-FLAIR with fat saturation (TR 9000 ms; TE 120 ms; TI 2500 ms; flip angle 90°; FOV 220 × 220; section thickness 5 mm; intersection gap 1.5 mm; number of sections 23; scanning time 3 minutes 18 seconds), susceptibility-weighted image 3D multi-echo gradient-echo sequence (TR 31 ms; TE 17 ms; ΔTE 6.2 ms; number of echo times 4; flip angle 17°; matrix 368 × 368; section thickness 2 mm; intersection gap 0 mm; number of sections 71; scanning time 3 minutes 38 seconds), diffusion-weighted image (TR 3240.54 ms; TE 82.08 ms; section thickness 5 mm; matrix 148 × 145), 3D TOF-MRA (multiple overlapping thin slab acquisition [MOTSA] technique; repetition time 23 ms; TE 3.5 ms; flip angle 18°; FOV 200 × 200; matrix size 512 × 322; 5 slabs; slice thickness 0.6 mm; voxel size 0.39 × 0.39 × 0.6; scanning time 7 minutes 21 seconds) and ASL (pseudo-continuous ASL technique, repetition time 4550 ms, TE 14 ms, post-label delay 1600 ms, FOV 220 × 220 mm, slice thickness 6 mm, matrix 80 × 80).

Table 1

Demographic and clinical data and ASL signal grades.

	Non-recanalization (n = 17)	Recanalization (n = 18)
Age (mean ± SD)	72.0 ± 11.1	69.4 ± 12.1
Sex (M:F)	6:11	14:4
Location (M1:M2)	8:9	N/A
NIHSS score		
Initial	8.6 ± 6.9	12.3 ± 6.5
Final	5.5 ± 4.4	2.9 ± 2.9
Hospital days	19.4 ± 15.3	16.3 ± 15.0
Mechanical thrombectomy*	0	8
t-PA injection only	1	5
ASL signal grade (n)		
High	0	8
Intermediate	11	10
Low	6	0

ASL = arterial spin labeling, N/A = not applicable.
* All patients who underwent mechanical thrombectomy also had intravenous t-PA injection by the protocol.

2.3. Imaging analysis

All images obtained from each patient were interpreted by 2 neuroradiologists. Both neuroradiologists were blinded to subjects' clinical information and reached a diagnostic consensus. For patients with non-recanalized MCA, hyperintense vessel sign on FLAIR was evaluated. Hyperintense vessel sign on FLAIR imaging, represents sluggish leptomeningeal collaterals and suggests less ischemic injury to tissue.[5,6] The presence of hyperintense vessel sign is widely known as a good prognostic factor.

The grade of ASL signal intensity on color ASL images was assessed on picture archiving and communication system (PACS). Color ASL signal intensity was classified as high- (full gyriform high signal intensity), intermediate- (area of low signal intensity with partial gyriform high signal intensity), and low- (area of low signal intensity with or without peripheral spotty high signal intensity) grade (Fig. 1).

Measurement of the ASL signal intensity on gray scale images was performed by drawing a region of interest (ROI) at the axial section including both the infarct core and MRI vessel signs on PACS (Figs. 2 and 3). Another ROI was drawn at the contralateral side symmetrically. The ratio of the maximum ASL signal intensity was calculated between the ischemic area and contralateral side.

2.4. Data analysis

The ASL signal ratios were compared between patients with and without MCA recanalization and also among subgroups according to the grading of color ASL images. Within the non-recanalization group, the ASL signal ratios were compared between patients with and those without hyperintense vessel sign

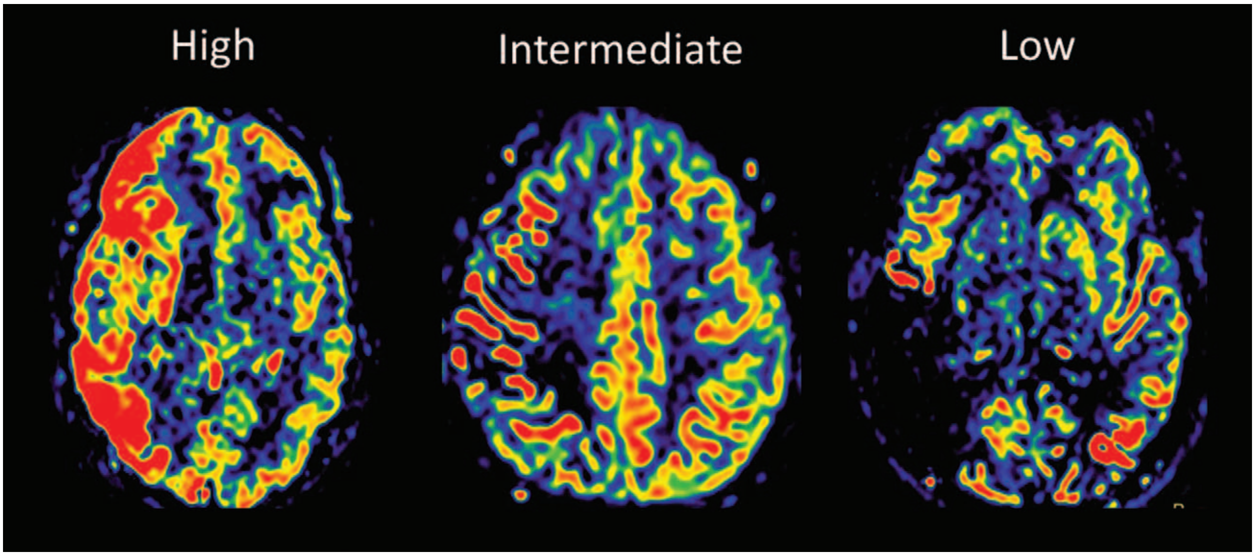

Figure 1. Grading of the color ASL images. High (full gyriform high signal intensity), intermediate (area of low signal intensity with partial gyriform high signal intensity), and low grade (area of low signal with or without peripheral spotty high signal intensity). ASL=arterial spin labeling.

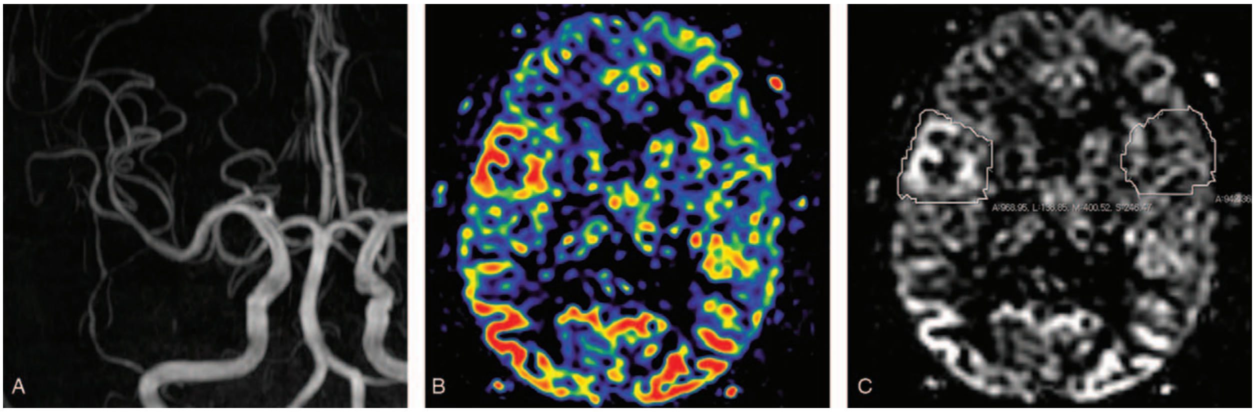

Figure 2. Representative case of recanalized MCA (M1) infarction in a 74-year-old woman. MRI was performed on hospital day 1. On 3D TOF-MRA, occluded segment on CT angiography was recanalized (A). Color ASL images of both groups could be graded as intermediate grade (B). The ASL signal ratio was calculated by manually drawing ROI (C), and the result was 1.73. ASL=arterial spin labeling, CT = computed tomography, MCA=middle cerebral artery, MRA=magnetic resonance angiography, MRI=magnetic resonance imaging, ROI=region of interest, TOF=time of flight.

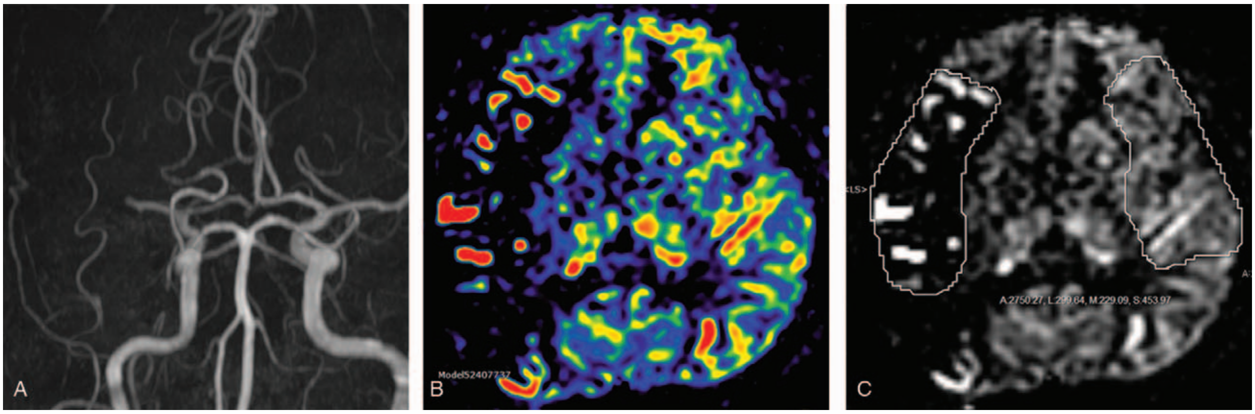

Figure 3. Representative case of non-recanalized MCA (M1) infarction in a 57-year-old man. MRI was performed on hospital day 1. On 3D TOF-MRA, there was still noted occluded right MCA (A). Color ASL image could be graded as intermediate grade (B). The ASL signal ratio was calculated by manually drawing ROI (C), and the result was 4.71. ASL=arterial spin labeling, MCA=middle cerebral artery, MRA=magnetic resonance angiography, MRI=magnetic resonance imaging, ROI=region of interest, TOF=time of flight.

Table 2

Comparison of the ASL signal ratio between non-recanalized and recanalized MCA infarct.

	ASL signal ratio		
ASL signal grade	**Non-recanalization (n = 17)**	**Recanalization (n = 18)**	***P* value***
High (n = 8)	N/A	2.07 ± 0.44	N/A
Intermediate (n = 21)	3.02 ± 1.00	1.98 ± 0.69	.011
Low (n = 6)	2.25 ± 0.79	N/A	N/A
All (n = 35)	2.75 ± 0.96	2.00 ± 0.60	.010

ASL = arterial spin labeling, MCA = middle cerebral artery, N/A = not applicable.
* *P*-values were derived from the independent *t* test.

Table 3

Comparison of the ASL signal ratio between patients with and without hyperintense vessel sign on FLAIR among non-recanalized MCA infarct.

	ASL signal ratio	***P* value***
Hyperintense vessel sign on FLAIR		.049
Yes (n = 11)	3.09 ± 0.85	
No (n = 6)	2.11 ± 0.88	

Data are the mean of the ASL signal ratio and standard deviation.
ASL = arterial spin labeling, FLAIR = fluid attenuated inversion recovery, MCA = middle cerebral artery.
* *P*-values were derived from the independent *t* test.

on FLAIR. Finally, correlation analysis was performed between patients' ASL signal ratios and NIHSS scores.

2.5. Statistical analysis

All variables were expressed as group means and standard deviations. Independent *t* tests were used to compare the mean ASL signal ratios between the groups. Simple correlation analysis and Pearson correlation coefficient were used to assess the statistical relationship between the ASL signal ratio and NIHSS score. Statistical analyses were performed using a commercially available software (SPSS, version 18 for Windows, SPSS, Chicago, IL).

3. Results

Demographic information, clinical data, and ASL signal grades of the non-recanalized and recanalized MCA groups are shown in Table 1. High or intermediate grades on color ASL images were found more in patients with recanalized MCA ($P < .01$) (Table 1, Fig. 2). High or intermediate ASL signal grade may represent either luxury perfusion in recanalized MCA or ATA in non-recanalized MCA.

Patients with non-recanalized MCA had a higher ASL signal ratio than those with recanalized MCA (2.75 ± 0.96 vs 2.00 ± 0.60, $P = .010$) (Table 2) (Fig. 3). Among patients with intermediate grade of their color ASL image, those with non-recanalized MCA had a higher ASL signal ratio than those with recanalized MCA (3.02 ± 1.00 vs 1.98 ± 0.69, $P = .011$) (Table 2). Therefore, ATA can be discriminated from luxury perfusion by calculating ASL ratio. ATA of non-recanalized MCA had a higher ASL ratio than luxury perfusion (recanalized MCA).

Among 17 patients with non-recanalized MCA, those with hyperintense vessel sign on FLAIR had a higher ASL signal ratio (3.09 ± 0.85 vs 2.11 ± 0.88, $P = .049$) (Table 3). Initial and final NIHSS scores were significantly and negatively correlated with the ASL signal ratio. The Pearson correlation coefficient for the initial and final NIHSS score was –0.549 and –0.699, respectively ($P = .023$ and .003) (Fig. 4). The mean hospital day was 19.4 ± 15.3 in non-recanalized group.

4. Discussion

Our data demonstrated that the ASL signal ratios had correlation with the recanalization status, pial collateral flow, and NIHSS score. Among patients with intermediate color ASL signal grade, ASL signal ratios were higher in patients with non-recanalized

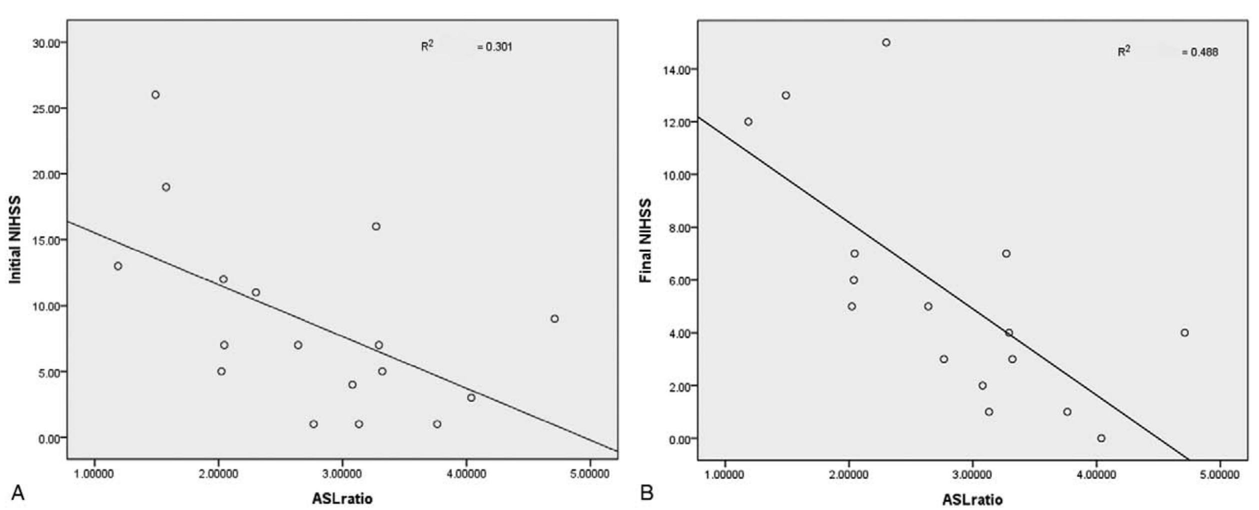

Figure 4. Simple correlation analysis of the ASL signal ratio and NIHSS score. Initial (A) and final (B) NIHSS scores showed a significant negative relationship with the ASL ratio (Pearson correlation coefficient: $r = -0.549$, $P = .023$, $R^2 = 0.301$ and $r = -0.699$, $P = .003$, $R^2 = 0.488$, respectively). ASL = arterial spin labeling, NIHSS = National Institutes of Health Stroke Scale.

MCA than those with recanalized MCA. Among patients with non-recanalized MCA, ASL signal ratio had significant correlation with hyperintense vessel sign on FLAIR and final NIHSS score.

Collateral perfusion in ischemic stroke has a strong correlation with the clinical outcomes.[7,8] DSA is a standard method for visualization of collateral perfusion but has little role in diagnostic work-up for patients with acute ischemic stroke.[9] In clinical practice, dynamic CTA is increasingly investigated for the visualization of collateral flow, and various efforts have been made to visualize collateral flow using conventional MRI and dynamic susceptibility contrast MR perfusion.[10–12] ATA on ASL is also a promising technique for the assessment of collateral flow.[5,13] ATAs are related to the delayed arrival of the blood by pial collateral flow in patients with acute ischemic stroke.

Visual assessment of color ASL images showed that high signal grades were found only in the recanalization group, whereas intermediate grades could be found in both the non-recanalization and recanalization groups. Partial gyriform high ASL signal intensities, that is, intermediate grade of patients with non-recanalized MCA may represent ATA of the pial collateral vessels. In contrast, the same partial gyriform high intensities in patients with recanalized MCA may be associated with post-recanalization luxury perfusion. Therefore, in the case of intermediate ASL signal grades, it can be difficult to distinguish an ATA from luxury perfusion, particularly when the occluded vessel is a small distal branch, because it is not always easy to check the recanalization status on CTA or MRA. Among patients with intermediate ASL signal grades, those with non-recanalized MCA had a higher ASL signal ratio than those with recanalized MCA. Therefore, the ASL signal ratio could be used to differentiate the pial collateral vessels from post-recanalization luxury perfusion.

The hyperintense vessel sign on FLAIR has been reported to have relationship with the pial collaterals and less ischemic injury to tissue.[5] One possible explanation is that the stationary blood is due to slow antegrade or retrograde collateral circulation.[5] In our study, there was a correlation between a high ASL signal ratio and hyperintense vessel sign on FLAIR ($P=.049$). This result may support the suggestion that intermediate ASL signal grade with high signal ratio is related to a hyperintense vessel sign on FLAIR and better outcome in acute infarct. Furthermore, our study showed a significant negative correlation between the ASL signal ratios and NIHSS scores. Therefore, we propose that signal grade on color ASL and the ASL signal ratio have potential to be prognostic factors in acute infarct.

The ASL signal intensity can be affected by many factors including age, steno-occlusive conditions, and underlying disease.[1,14] Therefore, the quantitative use of ASL signal intensity may be inappropriate. However, when we use the ratio of ASL signal intensity between lesion and contralateral side, individual characteristics which may affect ASL signal can be corrected.[15,16] In addition, when measuring the ASL signal, we used the maximum intensity of ASL signal within the ROI, instead of the mean value. This allowed us to minimize the effect of unwanted signals, such as hemorrhage or cerebrospinal fluid, because we could not exclude them during manual drawing of the ROI on PACS.

Our study has some limitations. First, our study was retrospective and had small sample volume. A prospective study with large sample size should be performed in the future. Second, ASL MRI results could not be correlated with DSA or CT perfusion at the time of MRI. In our institution, CTA or MRA are the main diagnostic tool for acute ischemic stroke, and DSA or CT perfusion were performed for only few selected patients. Third, PLD time of 1600 ms could be small for elderly patients. Further evaluation with optimized PLD time would be required in the future. Fourth, we used visual scaling for ASL signal. So, the reproducibility tests will be necessary. Fifth, there were uncontrolled factors including hospital time, treatment options, location, and size of the infarct. A well-controlled further study would be needed.

In conclusion, the ASL signal ratio could help to differentiate between the pial collaterals and post-recanalization luxury perfusion. A higher ASL ratio was significantly related with the hyperintense vessel sign on FLAIR and lower NIHSS score.

Author contributions

Conceptualization: Dong Woo Park, Young-Jun Lee.
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Formal analysis: Junyoung Lee.
Methodology: Young-Jun Lee.
Resources: Young-Jun Lee.
Validation: Junyoung Lee, Dong Woo Park, Young Seo Kim, Hyun Young Kim, Young-Jun Lee.
Writing – original draft: Dong Woo Park, Young Seo Kim, Hyun Young Kim.
Writing – review & editing: Dong Woo Park, Young Seo Kim, Hyun Young Kim.

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