

# Clinical application of susceptibility-weighted imaging in the evaluation of leptomeningeal collateralization

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## Abstract

The feasibility of using susceptibility-weighted imaging (SWI) in a clinical setting was assessed for quantifying leptomeningeal collateralization.

Eighteen patients with stroke and acute infarction underwent diffusion-weighted imaging, SWI, perfusion-weighted imaging, and magnetic resonance angiography within 3 days after symptom onset. Lesions were evaluated by the Alberta Stroke Program Early CT score (ASPECTS), based on mean transit time, SWI, and cerebral blood volume (CBV).

For evaluating ischemic penumbra and leptomeningeal collateralization, the SWI-ASPECTS significantly correlated, respectively, with mean transit time and CBV-ASPECTS (Spearman test,  $r=0.793$  and  $0.682$ ;  $P<.001$ , both).

The SWI may be useful to quantify leptomeningeal collateralization in patients with acute cerebral infarction.

**Abbreviations:** ASPECTS = the Alberta Stroke Program Early CT score, CBV = cerebral blood volume, CT = computed tomography, DWI = diffusion-weighted imaging, MRA = magnetic resonance angiography, MRI = magnetic resonance imaging, mRS = modified Rankin scale, MTT = mean transit time, NIHSS = National Institutes of Health Stroke scale, PWI = perfusion-weighted imaging, rtPA = recombinant tissue plasminogen activator, SWI = susceptibility-weighted imaging.

**Keywords:** leptomeningeal collateralization, penumbra, perfusion-weighted imaging, stroke, susceptibility-weighted imaging

## 1. Introduction

Thrombolytic therapy with recombinant tissue plasminogen activator (rtPA) for patients with acute cerebral infarction can effectively promote revascularization and improve prognosis.<sup>[1,2]</sup> Currently, thrombolytic therapy is guided by assessments of collateral circulation and the ischemic penumbra, as reflected, respectively, by cerebral blood volume (CBV) and mean transit time (MTT).<sup>[3,4]</sup>

Nearly one-third of patients who receive endovascular thrombolysis or stents did not achieve a satisfactory clinical prognosis,<sup>[5]</sup> perhaps due to invalid recanalization.<sup>[6,7]</sup> This may be associated with the presence of collateral circulation, especially the opening of leptomeningeal collaterals. Leptomeningeal collaterals provide a vascular network that may maintain enough cerebral blood to prolong or indefinitely sustain the viability of brain tissue beyond an occlusion. Good flow through collaterals has been associated with a large penumbra and small infarct core. By prolonging the survival time of the penumbra, the time window for viable reperfusion may also increase.<sup>[6,7]</sup> Good

collaterals therefore limit infarct core expansion and determine the final infarct volume.<sup>[6,7]</sup>

Early identification of leptomeningeal collaterals is crucial for the clinical treatment of patients with ischemic stroke. Some imaging techniques have limited clinical application because of the need for radionuclides or contrast agents. Such methods include digital subtraction angiography, computed tomography (CT) angiography, and perfusion-weighted imaging (PWI).<sup>[7]</sup>

A relatively new high-resolution magnetic resonance imaging (MRI) technique that has been used to detect the leptomeningeal collaterals in stroke patients is susceptibility-weighted imaging (SWI).<sup>[8]</sup> SWI does not require radionuclides or contrast agents, because endovascular deoxygenated hemoglobin acts as an endogenous contrast agent. Compared with conventional imaging techniques, SWI provides good contrast-to-noise ratio for small blood vessels.<sup>[9–11]</sup> In addition, numerous studies have shown that the status of the ischemic penumbra and collaterals can be obtained using SWI.<sup>[3,9–12]</sup> However, there has been only one study of the feasibility of using SWI to evaluate leptomeningeal collateralization, to the best of our knowledge,<sup>[8]</sup> and results were demonstrated qualitatively; leptomeningeal collateralization was not quantified.

We hypothesize that SWI can quantify leptomeningeal collaterals in stroke patients. The present study assessed the feasibility of using SWI to quantify leptomeningeal collaterals relative to more conventional imaging methods, particularly PWI. Eighteen stroke patients with acute infarction were evaluated using SWI, with comparisons to PWI, diffusion-weighted imaging (DWI), and magnetic resonance angiography (MRA).

## 2. Methods

### 2.1. Patients

The Medical Ethics Committee of Bengbu Medical College approved this study, and all patients gave informed consent prior

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to inclusion. The study population comprised 18 patients (15 men and 3 women; aged  $53.8 \pm 8.8$  years, 22–65 years) with acute cerebral infarction who were admitted to the Department of Neurology at First Affiliated Hospital of Bengbu Medical College between June 2015 and June 2016.

For inclusion, all the patients were characterized by the following: new infarction locus detected by DWI; hospital admission within 3 days of symptom onset; 1st-ever ischemic stroke, or a previous stroke with hemiplegia sequelae that did not affect the neurologic score; aged 18–75 years, either gender; and a National Institutes of Health Stroke Scale (NIHSS) score of 4–20. DWI was applied as selection criteria, because higher signal intensities in DWIs can be observed in regions with acute infarction. Nevertheless, we also considered medical history, clinical symptoms, and NIHSS score. Patients with any of the following were excluded from this analysis: cerebral hemorrhage, tumor, or trauma detected by head CT; severe cardiovascular, renal, or hemorrhagic disease; history of allergy; current pregnancy; or psychologic or neurologic diseases such as autism.

For early-stage evaluation, the NIHSS score was determined on the day the patients arrived for initial neurologic evaluation. All patients underwent cranial SWI, PWI, MRI, DWI, and MRA within 3 days of symptom onset. The severity of neurologic damage was evaluated using NIHSS scores. Some patients underwent MRA 1 week after symptom onset to measure if revascularizations had occurred. None of the patients underwent any reperfusion treatments, such as thrombolytic therapy with rtPA, or endovascular interventions. Routine treatments were

administered after admission, including antiplatelet aggregation drugs, aspirin, clopidogrel, or combined statin therapy.

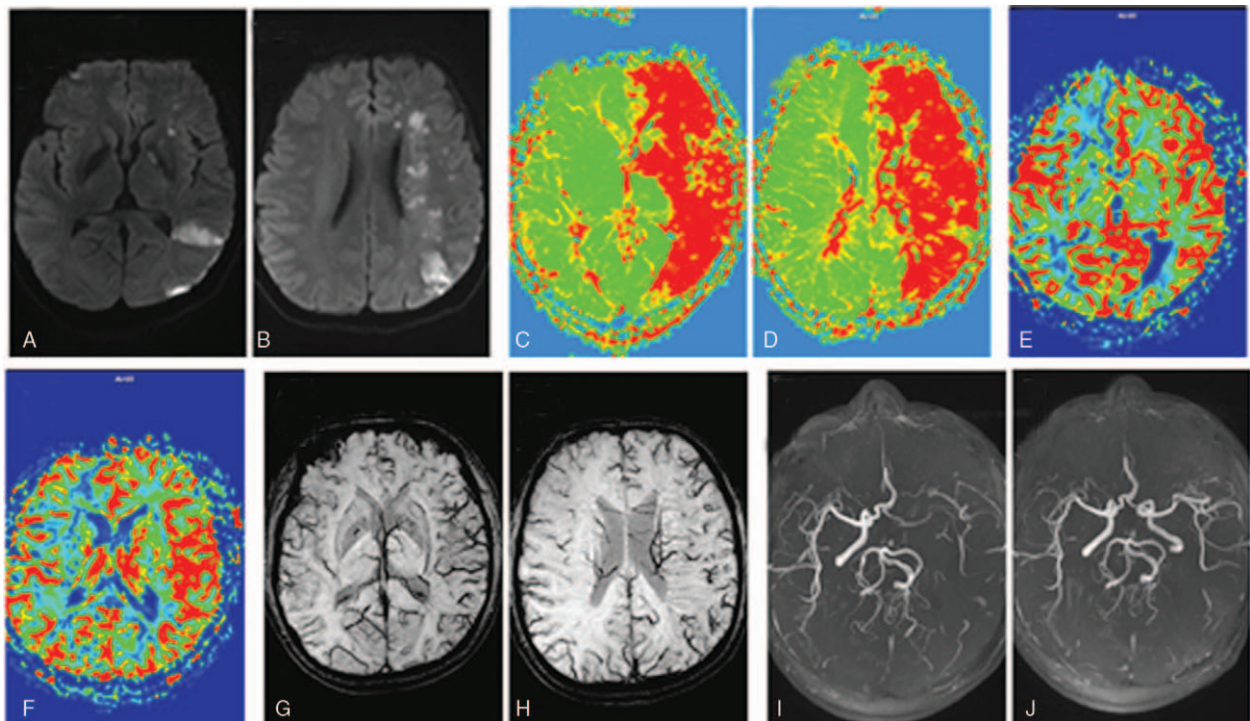
## 2.2. Image analysis

All images were collected as Digital Imaging and Communications in Medicine (DICOM)-format data and imported to an OsiriX image viewer for analysis. For SWI and PWI studies, the size of abnormal signal intensities or densities were evaluated in an observer-blinded fashion by 2 neuroradiologists using the 10-point quantitative topographic Alberta Stroke Program Early CT score (ASPECTS).<sup>[13]</sup> For calculating ASPECTSs, 1 point was subtracted from a maximum of 10 for each area of ischemic change, including prolonged MTT, increased CBV, and prominent vessels in SWI (Fig. 1). Disagreements between the neuroradiology raters were resolved by consensus. The prominent vein on SWI was defined as a local prominence of hypointense vessels with either increased vessel number or diameter in the target area, when compared with the nontarget area<sup>[12]</sup> (Fig. 1).

For late-stage neurologic evaluation, the modified Rankin scale (mRS) was used 90 days after stroke onset, with mRS  $\leq 2$  indicating a good clinical prognosis.

## 2.3. Imaging techniques

The MRI data were obtained with a 3.0T Siemens Tim Trio whole-body MRI system (Siemens, Munich, Germany) with a standard head coil. Each patient was given a conventional MRI,



**Figure 1.** Patient experienced a cerebral infarction caused by acute occlusion of the left internal carotid artery. The admission magnetic resonance angiography (MRA) (I) and diffusion-weighted imaging (DWI) were confirmed (A and B). The patient had an National Institutes of Health Stroke scale score of 20 on admission and mean transit time (MTT) on perfusion-weighted imaging (PWI) (C and D) MTT prolonged in the area of the responsible vessel, MTT - Alberta Stroke Program Early CT score (MT-ASPECTS) was 2 points; cerebral blood volume (CBV) in the PWI showed (E and F) CBV in the lesion area increased compared with the healthy area CBV, CBV-ASPECTS was 1 point; in the susceptibility-weighted imaging (SWI) (G and H). The presence of a large number of small and prominent blood vessels (PV) in the same region, SWI-ASPECTS is 2 points; review of the head after treatment MRA (J) prompted the left internal carotid artery to achieve recanalization, mRS for 90 days after 2 points, the prognosis Better, reflected on SWI, PV grade=2, suggesting that the cortex pia mater is better in the patient and the patient has an effective revascularization.

3-dimensional time-of-flight MRA, spin echo-echo planar imaging (SE-EPI), magnetic resonance perfusion, and SWI. The entire cranial anatomy was scanned in the sagittal, coronal, and axial planes. The images were obtained in the following sequence: DWI; T1-weighted spin echo (T1-SE); T2-weighted fast spin echo; and T2-weighted fast fluid-attenuated inversion-recovery.

The following parameters were used for DWI: repetition time (TR), 93 milliseconds; and echo time (TE), 3800 milliseconds. For T1-SE, the parameters were: TR, 440 milliseconds; and TE, 2.5 milliseconds. For T2-weighted fast spin echo, TR, TE, and inversion time (TI) were 3000, 93, and 2371.5 milliseconds, respectively. The parameters for T2-weighted fast fluid-attenuated inversion-recovery were: slice thickness, 6 mm; interslice gap, 1.2 mm; field of view (FOV), 199 mm × 220 mm; and matrix, 464 × 512. For SWI, the magnitude and phase images were obtained with the following parameters: TR/TE, 49/40; flip angle, 15°; bandwidth, 80 kHz; slice thickness, 2 mm; 64 slices in a single slab; iPAT factor, 2; and matrix, 177 × 256 pixels.

Postprocessing was performed and 2-mm maximum intensity projection images were generated. For magnetic resonance perfusion, patients received an intravenous bolus injection of gadolinium-DTPA (diethylenetriamine penta-acetic acid; 0.2 mmol/kg) at a rate of 4.5–5.0 mL/s during the 6th SE-EPI scan, using a Medrad high-pressure syringe. Magnetic resonance perfusion was performed using the following parameters in 1 excitation: TR, 1400 milliseconds; TE, 32 milliseconds; inversion angle, 70°; FOV, 23 cm × 23 cm; slice thickness, 5 mm; interslice gap, 1.5 mm; and matrix, 128 × 128.

#### 2.4. Statistical analysis

Analyses were performed using SPSS 17.0. Because the data were not normally distributed, nonparametric tests were used for comparison. The values are presented as mean and standard deviation, median and range, or number and percentage. Spearman correlation test was used to analyze the correlation between the clinical data and the SWI-, MTT-, and CBV-ASPECTS. A *P*-value <.05 was considered statistically significant.

### 3. Results

Eighteen patients with cerebral infarction (Table 1) were classified as to SWI cortical pial branch. SWI, MTT, and CBV were scored according to the ASPECTS criteria. There was no statistical association between the general clinical information of the patients and ASPECTS of SWI, MTT, or CBV (Table 1). There was a positive association between the ASPECTS of SWI and MTT ( $r=0.682$ ,  $P<.001$ , Fig. 2), and between the ASPECTS of SWI and CBV ( $r=0.793$ ,  $P<.001$ , Fig. 3, Table 2). These results showed that SWI can reflect collateral circulation quantitatively.

In addition, 7 of the 18 patients enrolled in the review MRA had SWI cortical pial branch grade=2. This result suggested that the cortex was soft. There were 5 improved meningeal openings and 4 revascularizations (up to 80%) were achieved.

At the 90-day follow-up, 5 patients were better (mRS at 0–2, Fig. 1) and 2 patients had mRS=2. Among these 7 patients, the SWIs showed cortical pial branches grade=0, suggesting that the cortical pial circulation did not open effectively. Although the recanalization occurred later, the 90-day prognosis was poor in 2 patients (mRS was 3–4, Fig. 4).

**Table 1**

**Correlations of clinical data with imaging parameters\*.**

		<i>P</i> -value		
		SWI	MTT	CBV
Age, y		0.295	0.463	0.730
Mean ± SD	53.8 ± 8.8	—	—	—
Median (range)	55 (22–65)	—	—	—
Female	3 (17%)	0.522	0.845	0.787
Hypertension	9 (50%)	0.459	0.103	0.698
Diabetes mellitus	4 (22%)	0.257	0.724	0.310
Hyperlipidemia	12 (67%)	0.148	0.620	0.293
Hyperhomocysteinemia	4 (22%)	0.060	0.605	0.076
Smoking	9 (50%)	0.232	0.568	0.350
Drinking	7 (39%)	0.200	0.478	0.464

CBV=cerebral blood volume, MTT=mean transit time, SWI=susceptibility-weighted imaging. Spearman's correlation test was used to analyze the correlation of clinical data with SWI, MTT and CBV.

\* Reported as *n* (%), unless indicated otherwise.

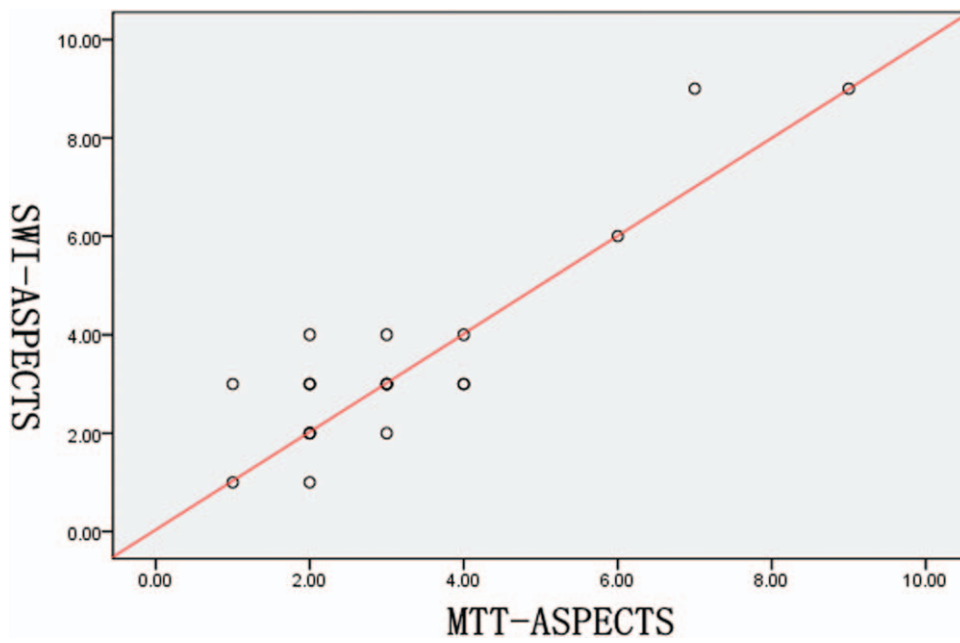
### 4. Discussion

In this study, we hypothesized that collateral circulation had occurred, especially the cortical bronchi, which protects the ischemic penumbra. Since SWI can characterize tiny blood vessels, the feasibility of SWI was evaluated for quantifying leptomeningeal collateralization in a clinical setting. The SWI results showed that these patients had a large number of prominent vessels after routine treatment. Together with the clinical follow-up results, this indicated that revascularization occurred in some patients. These results suggest that, although patients may have missed the optimal time window for thrombolytic therapy, there was still a possibility of recanalization.

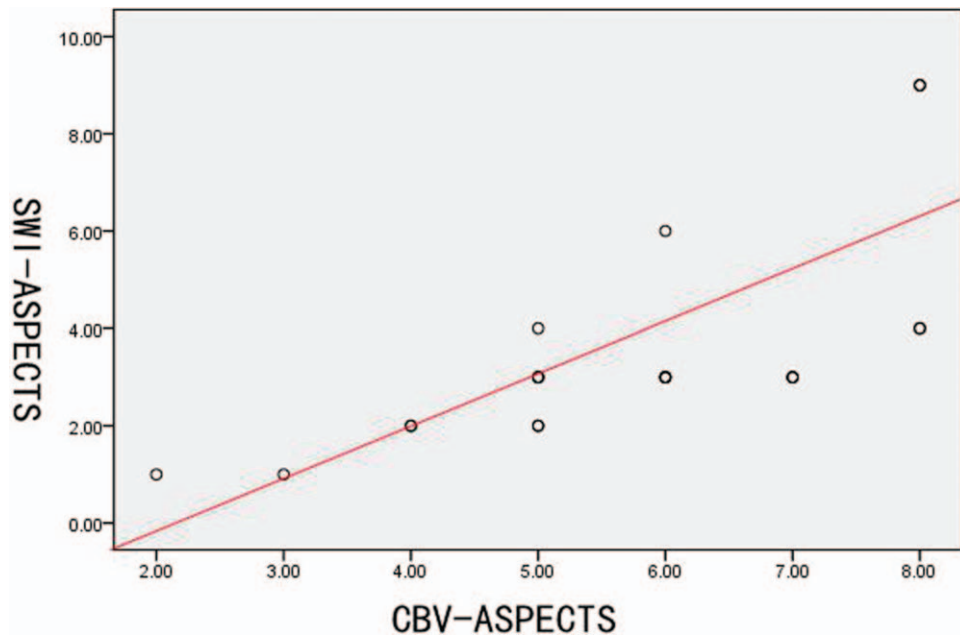
Leptomeningeal collaterals are direct arteriolo-arteriolar connections between major cerebral arteries that provide a route for retrograde filling of pial arteries distal to an occluded artery. They provide a vascular network with the potential to maintain cerebral blood flow at levels that prolong or indefinitely sustain brain tissue viability beyond an occlusion.<sup>[14]</sup> Good flow through collateral pathways is associated with a large penumbra and small infarct core at baseline.<sup>[15,16]</sup> By extending the survival time of penumbra, it has been shown that we can extend the time window for viable reperfusion.<sup>[15,16]</sup> Healthy collaterals therefore limit infarct core expansion and determine final infarct volumes.

Collateral circulation is established during acute cerebral infarction, and has an important role in protecting the ischemic penumbra and avoiding further expansion of the core infarct size.<sup>[16,17]</sup> The medial cranial circulation can be roughly divided as 1st-degree (Willis ring) or 2nd-degree (mainly referring to the ophthalmic and cortical pial branches).<sup>[18,19]</sup> Liebeskind<sup>[20]</sup> believed that cortical pial branches can be used as a factor to evaluate the clinical prognosis of acute cerebral infarction. In a study with mice, cortical pial branches were fully expanded within seconds of an acute occlusion of the internal carotid artery.<sup>[21]</sup>

Zhang et al<sup>[22]</sup> analyzed the number and diameter of cortical pial blocs in the occluded middle cerebral artery blood supply area in an animal model of acute cerebral infarction to assess infarct size. Digital subtraction angiography was also performed in patients with acute cerebral infarction with acute occlusion of



**Figure 2.** The scatter plot showing the correlation between the susceptibility-weighted imaging (SWI)- and mean transit time (MTT) - Alberta Stroke Program Early CT score (ASPECTS). The SWI-ASPECTS positively correlated with the MTT-ASPECTS (Spearman test,  $r=0.682$ ,  $P < .001$ ).



**Figure 3.** The scatter plot showing the correlation between the susceptibility-weighted imaging (SWI)- and cerebral blood volume (CBV) - Alberta Stroke Program Early CT score (ASPECTS). The SWI-ASPECTS positively correlated with the CBV-ASPECTS (Spearman test,  $r=0.793$ ,  $P < .001$ ).

the middle cerebral artery, showing that retrograde perfusion of the cortical pial branch into the responsible vascular hypoperfusion region has an important role in maintaining the ischemic penumbra.<sup>[13,18,23]</sup>

At present, studies have suggested that CBV observed on PWI can determine the status of collateral circulation in patients with acute cerebral infarction, and can be used as a predictor of vascular recanalization after thrombolysis.<sup>[24]</sup> Therefore, acute cerebral infarction can determine the establishment of collateral

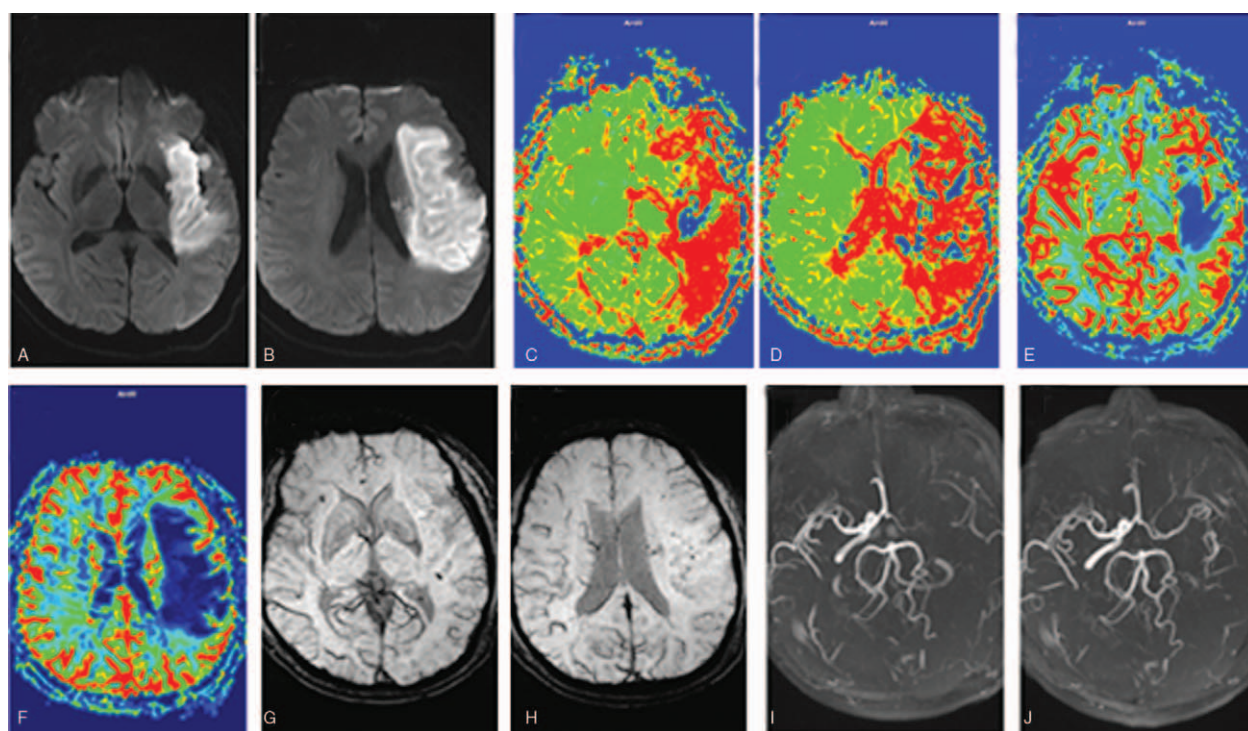
**Table 2**

**SWI-ASPECTS, CBV-ASPECTS, and MTT-ASPECTS.**

		SWI	MTT	CBV
ASPECTS	Mean ± SD	3.45 ± 2.087	3.18 ± 1.943	5.73 ± 1.638
	Median (range)	5.7 (1–9)	3 (1–9)	2.64 (2–8)

$P < .001$  between SWI-ASPECTS and MTT-ASPECTS.  $P < .001$  between SWI-ASPECTS and CBV-ASPECTS.

CBV = cerebral blood volume, MTT = mean transit time, SWI = susceptibility-weighted imaging.



**Figure 4.** Patient showed cerebral infarction caused by an acute occlusion of the left internal carotid artery. Magnetic resonance angiography (MRA) (I) and diffusion-weighted imaging (DWI) admissions were confirmed (A and B). The National Institutes of Health Stroke scale score at admission was 16 points, and the mean transit time (MTT) at perfusion-weighted imaging (PWI) (C and D) MTT prolonged in the lesion area, MTT - Alberta Stroke Program Early CT score (ASPECTS) was 3 points; in the CWI of PWI (C and E), the cerebral blood volume (CBV) showed a smaller range of increase in CBV than in the healthy side, CBV-ASPECTS was 6 points; in the susceptibility-weighted imaging (SWI) (CWI). (G and H) In the same region, the prominent vein was absent, SWI-ASPECTS was 7 points; after the treatment, the head MRA (J) showed that the left middle cerebral artery was recanalized, and the mRS after 90 days was 4 points. The poor prognosis was reflected in the SWI. On the contrary, the prominent vein grade = 0 suggested that the cortical pia mater was not opened effectively, and although there was revascularization in the later period, the prognosis of the patient was not improved and it was an ineffective revascularization.

circulation and openness by CBV measurement.<sup>[3,25]</sup> When acute cerebral infarction occurs along with low perfusion in brain tissue, the deoxygenated-to-oxygenated hemoglobin ratio varies according to the oxygen extraction fraction.<sup>[26]</sup>

In such a condition, there is a prominent vein in the area of the vascular blood supply on SWI, indicating the identification of cortical pia mater by SWI. When perfusion is low, the oxygen extraction fraction of the tissue increases compensatorily, and the ratio of deoxygenated-to-oxygenated hemoglobin in the blood increases, leading to an increase in the magnetic sensitivity between the tissues, which highlights many tiny blood vessels (shown as prominent veins in SWI) that are difficult to find under normal conditions. Santhosh et al<sup>[27]</sup> pointed out that the prominent vein near the meninges on SWI may be collateral circulation including cortical pia mater.

Thus in this study, we speculated that the prominent veins that extended from the pia mater to the deep layers of the cortex on SWI should be the cortical pia mater. There was a significant positive correlation between the SWI- and MTT-ASPECTS, and between the SWI- and CBV-ASPECTS. In the prominent vein region near the pia mater, the CBV on PWI is increased and the MTT is prolonged compared to SWI. The underlying mechanism may be that, because of acute cerebral infarction, hypoperfusion of blood flow around the brain results in changes in the magnetic sensitivity in the lesion. Pia mater collateral circulation, which is an important part of cerebral infarction peripheral tissue collateral circulation and is formed by the slow flow of small blood vessels, showed low intravascular blood oxygen satura-

tion. Therefore, we believe that SWI-ASPECTS can evaluate the collateral circulation in patients with acute cerebral infarction, especially the opening of cortical pial branches. The large prominent vein near the meninges on SWI can be considered the cortex pia mater.

This study also revealed the phenomena of effective and ineffective revascularization (Fig. 1), where ineffective recanalization refers to revascularization in the acute phase of cerebral infarction. Although revascularization occurs, the patient may not achieve clinical improvement.<sup>[6,7]</sup> This may be due to re-occlusion of the responsible blood vessel after thrombolysis, or the collateral circulation. In particular, the degree of opening of the cortical pial branches is not perfect, and the ischemic penumbra cannot be protected before and after thrombolysis.<sup>[6,7]</sup> Therefore, the clinical symptoms of patients after thrombolysis do not effectively improve. This is consistent with the results of Huang et al's<sup>[28]</sup> retrospective analysis of 44 cerebral infarction patients within 2 days of onset.

The present study is limited by the small number of cases. The phenomena observed in the present study require further study for confirmation.

In this study, we believe that collateral circulation, especially in the cortical pia mater, may be an important factor in effective revascularization. The known factors affecting recanalization after thrombolysis include early thrombolysis time, blood glucose level, history of atrial fibrillation, and collateral circulation, and especially the opening of cortical pial branches.<sup>[29-32]</sup> When the clinical thrombolytic treatment window in patients with acute cerebral

infarction is missed, the collateral circulation may still effect revascularization, and improve the clinical prognosis. The results of the present study suggest that SWI has significant potential and applicability for assessing clinical prognosis quantitatively.

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## Author contributions

**Conceptualization:** Song Luo.

**Investigation:** Lijuan Yang.

**Methodology:** Song Luo, Lijuan Yang.

## References

- [1] Anonymous Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Group. *N Engl J Med* 1995;333:1581–7.
- [2] Lansberg MG, Bluhmki E, Thijs VN. Efficacy and safety of tissue plasminogen activator 3 to 4.5 hours after acute ischemic stroke: a metaanalysis. *Stroke* 2009;40:2438–41.
- [3] Park HS, Cha JK, Kim DH, et al. The rCBV ratio on perfusion-weighted imaging reveals the extent of blood flow on conventional angiography after acute ischemic stroke. *Clin Neurol Neurosurg* 2014;122:54–8.
- [4] McVerry F, Liebeskind DS, Muir KW. Systematic review of methods for assessing leptomeningeal collateral flow. *AJNR Am J Neuroradiol* 2012;33:576–82.
- [5] Lum C, Ahmed ME, Patro S, et al. Computed tomographic angiography and cerebral blood volume can predict final infarct volume and outcome after recanalization. *Stroke* 2014;45:2683–8.
- [6] Hussein HM, Georgiadis AL, Vazquez G, et al. Occurrence and predictors of futile recanalization following endovascular treatment among patients with acute ischemic stroke: a multicenter study. *AJNR Am J Neuroradiol* 2010;31:454–8.
- [7] Liebeskind DS. Of mice and men: essential considerations in the translation of collateral therapeutics. *Stroke* 2008;39:e187–8.
- [8] Verma RK, Hsieh K, Gratz PP, et al. Leptomeningeal collateralization in acute ischemic stroke: impact on prominent cortical veins in susceptibility-weighted imaging. *Eur J Radiol* 2014;83:1448–54.
- [9] Cho ZH, Ro YM, Lim TH. NMR venography using the susceptibility effect produced by deoxyhemoglobin. *Magn Reson Med* 1992;28:25–38.
- [10] Lee BC, Vo KD, Kido DK, et al. MR high-resolution blood oxygenation level-dependent venography of occult (low-flow) vascular lesions. *AJNR Am J Neuroradiol* 1999;20:1239–42.
- [11] Tsui YK, Tsai FY, Hasso AN, et al. Susceptibility-weighted imaging for differential diagnosis of cerebral vascular pathology: a pictorial review. *Neurol Sci* 2009;28:7–16.
- [12] Luo S, Yang L, Wang L. Comparison of susceptibility-weighted and perfusion-weighted magnetic resonance imaging in the detection of penumbra in acute ischemic stroke. *J Neuroradiol* 2015;42:255–60.
- [13] Barber PA, Demchuk AM, Zhang J, et al. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. *Lancet* 2000;355:1670–4.
- [14] Bang OY, Saver JL, Buck BH, et al. Impact of collateral flow on tissue fate in acute ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2008;79:625–9.
- [15] Miteff F, Levi CR, Bateman GA, et al. The independent predictive utility of computed tomography angiographic collateral status in acute ischaemic stroke. *Brain* 2009;132:2231–8.
- [16] Liu J, Wang Y, Akamatsu Y, et al. Vascular remodeling after ischemic stroke: mechanisms and therapeutic potentials. *Prog Neurobiol* 2014;115:138–56.
- [17] Shuaib A, Butcher K, Mohammad AA, et al. Collateral blood vessels in acute ischaemic stroke: a potential therapeutic target. *Lancet Neurol* 2011;10:909–21.
- [18] Hendrikse J, van Raamt AF, van der Graaf Y, et al. Distribution of cerebral blood flow in the circle of Willis. *Radiology* 2005;235:184–9.
- [19] Brozici M, van der Zwan A, Hillen B. Anatomy and functionality of leptomeningeal anastomoses: a review. *Stroke* 2003;34:2750–62.
- [20] Liebeskind DS. Collateral circulation. *Stroke* 2003;34:2279–84.
- [21] Morita Y, Fukuuchi Y, Koto A, et al. Rapid changes in pial arterial diameter and cerebral blood flow caused by ipsilateral carotid artery occlusion in rats. *Keio J Med* 1997;46:120–7.
- [22] Zhang H, Prabhakar P, Sealock R, et al. Wide genetic variation in the native pial collateral circulation is a major determinant of variation in severity of stroke. *J Cereb Blood Flow Metab* 2010;30:923–34.
- [23] Bang OY, Saver JL, Buck BH, et al. UCLA, Collateral Investigators Impact of collateral flow on tissue fate in acute ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2008;79:625–9.
- [24] Sohn SW, Park HS, Cha JK, et al. Relative CBV ratio on perfusion-weighted MRI indicates the probability of early recanalization after IV t-PA administration for acute ischemic stroke. *J Neurointerv Surg* 2016;8:235–9.
- [25] Cortijo E, Calleja AI, Garcia-Bermejo P, et al. Relative cerebral blood volume as a marker of durable tissue-at-risk viability in hyperacute ischemic stroke. *Stroke* 2014;45:113–8.
- [26] Tamura H, Hatazawa J, Toyoshima H. Detection of deoxygenation-related signal change in acute ischemic stroke patients by T2-weighted magnetic resonance imaging. *Stroke* 2002;33:967–71.
- [27] Santhosh K, Kesavadas C, Thomas B, et al. Susceptibility weighted imaging: a new tool in magnetic resonance imaging of stroke. *Clin Radiol* 2009;64:74–83.
- [28] Huang P, Chen CH, Lin WC, et al. Clinical applications of susceptibility weighted imaging in patients with major stroke. *J Neurol* 2012;259:1426–32.
- [29] Ribo M, Molina C, Montaner J, et al. Acute hyperglycemia state is associated with lower t-PA induced recanalization rates in stroke patients. *Stroke* 2005;36:1705–9.
- [30] Saqqur M, Uchino K, Demchuk AM, et al. Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. *Stroke* 2007;38:948–54.
- [31] Liebeskind DS, Tomsick TA, Foster LD, et al. Collaterals at angiography and outcomes in the Interventional Management Stroke (IMS) III trial. *Stroke* 2014;45:759–64.
- [32] Nambiar V, Sohn SI, Almekhlafi MA, et al. CTA collateral status and response to recanalization in patients with acute ischemic stroke. *AJNR Am J Neuroradiol* 2014;35:884–90.