

Clinical applications of susceptibility weighted imaging in patients with major stroke

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Abstract Susceptibility weighted imaging (SWI) is a newly developed magnetic resonance (MR) protocol. Recent studies have found that SWI may be useful in the field of cerebrovascular diseases, especially for detecting the presence of prominent veins, microbleeds and the susceptibility vessel sign (SVS). Some authors have even suggested that SWI can be used to predict outcome. We conducted a prospective study of patients hospitalized with middle cerebral artery territory infarction receiving MRI within 2 days of stroke onset. The presence of prominent veins, microbleeds and SVS in SWI was analyzed along with hospital characteristics of the patients. A total of 44 patients were enrolled. Among the 44 patients, 15 (34.1%) patients showed prominent veins, 19 (43.2%) showed SVS, and 14 (31.8%) showed microbleeds. The presence of SVS and prominent veins was not associated with prognosis. Though not statistically significant ($p = 0.06$), patients with SVS were more likely to develop later brain edema. SVS was significantly associated with arterial occlusion ($p = 0.008$) based on the MR angiogram, and microbleeds were significantly associated with later hemorrhagic transformation ($p = 0.018$). In our study, SWI could not be used to predict outcome as previously suggested. However,

the presence of microbleeds may predict further hemorrhagic transformation, and the presence of SVS could be used to detect intra-arterial thrombus. Patients with SVS were also more likely to develop later brain edema. Including SWI in routine MR protocols for major acute ischemic stroke would be worthwhile.

Keywords Susceptibility weighted imaging · Stroke

Introduction

Susceptibility weighted imaging (SWI) has gradually developed into a useful clinical tool in the field of cerebrovascular diseases [1–5]. It has been applied widely, including for detection of intracerebral hemorrhage, hemorrhagic transformation, cerebral venous thrombosis and assessment of brain tissue at risk for infarction [6]. Within the field of acute ischemic stroke, the presence of prominent veins, microbleeds and the susceptibility vessel sign in SWI has been considered to be useful in evaluating stroke severity, treatment and prognosis [4, 7–9].

The presence of prominent veins was hypothesized to be caused by the increased oxygen extraction fraction (OEF), which reflects the ratio of deoxyhemoglobin to oxyhemoglobin in the capillaries and veins. Since the OEF is increased in the penumbra following acute ischemic stroke [4], these hypointense signals shown by SWI could possibly represent the penumbra. The prominent veins were also considered to be the presentation of collateralization [4]. The susceptibility vessel sign could be used to detect intra-arterial thrombus and was thought to be useful in assessing the extent of infarct and prognosis [10]. SWI, which is exquisitely sensitive to magnetic field inhomogeneity, can detect microbleeds within the infarct. The sensitivity of

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SWI may enable earlier diagnosis along with assessment of severity and disease progression. However, whether this improved detection can predict further symptomatic hemorrhagic transformation is not certain at the moment [11].

Although SWI is thought to be useful in evaluating acute ischemic stroke, it is yet not included in routine neuroimaging protocols. Thus, the aim of this study was to identify whether the presence of prominent veins, microbleeds and the susceptibility vessel sign in SWI is useful in clinical application for major acute ischemic stroke.

Materials and methods

Patients

We conducted a prospective study of patients hospitalized with middle cerebral artery (MCA) territory infarction receiving SWI within 2 days of stroke onset. The data were collected in a university hospital with a catchment area of 1.5 million inhabitants in the metropolitan area. The following criteria were established for inclusion in the study: initial brain computed tomography (CT) showed no evidence of intracranial hemorrhage and presence of an infarct within the MCA territory detected at initial or follow-up imaging. Data of these patients were prospectively registered into a computerized database and, a total of 44 patients were recruited. The local institutional ethics committee approved this study, and informed consent was obtained from each patient or the patient's relatives.

Among these MCA territory infarction patients, the diagnosis was confirmed both by trained neurologists and positive findings of magnetic resonance imaging (MRI). The severity of stroke was assessed by the National Institutes of Health Stroke Scale (NIHSS) on admission and discharge. Stroke subtypes were classified by the Trial of ORG 10172 in Acute Stroke Treatment (TOAST). Global outcomes were assessed with the modified Rankin Scale (mRS) at the 6th month after stroke onset. Stroke risk factors such as hypertension (H/T) and diabetes mellitus (DM) were identified. Time from stroke onset to MRI (days), the presence of infection (pneumonia and urinary tract infection) and the antithrombotics used were also recorded. Antiplatelets were administered in 41 (93.2%) patients; heparin was administered in one patient; and two patients did not receive antithrombotics because of complications such as upper gastrointestinal bleeding. None of the patients received thrombolytic therapy.

Brain imaging

In the emergency room, a baseline brain CT scan was done. MRI according to our protocol was then performed within

2 days after stroke onset. MR imaging was performed on a 3-T imager (Siemens) equipped with a 12-channel receiver head coil. The MRI protocol included: diffusion-weighted imaging (DWI), 3D time-of-flight (TOF) MR angiogram (MRA) of the intracranial arteries, SWI, T2-fluid attenuated inversion recovery (FLAIR), T2-weighted imaging and T1-weighted imaging. A second follow-up brain CT was performed 7 days after the MRI study in all patients. All images were read by two neuro-radiologists who were blinded to the pattern of stroke symptoms and clinical data of the recruited patients. The susceptibility vessel sign on SWI was defined as presence of hypointensity within the MCA, in which the diameter of the hypointense signal within the vessel exceeded the contralateral vessel diameter. Prominent veins were defined by comparing the images to normal control subjects whose images were obtained before the study. Microbleed was defined as multiple punctate hypointensities with no continuity within the infarct area (Fig. 1). MRA was used as the reference standard for establishing the diagnosis of occlusion of the MCA.

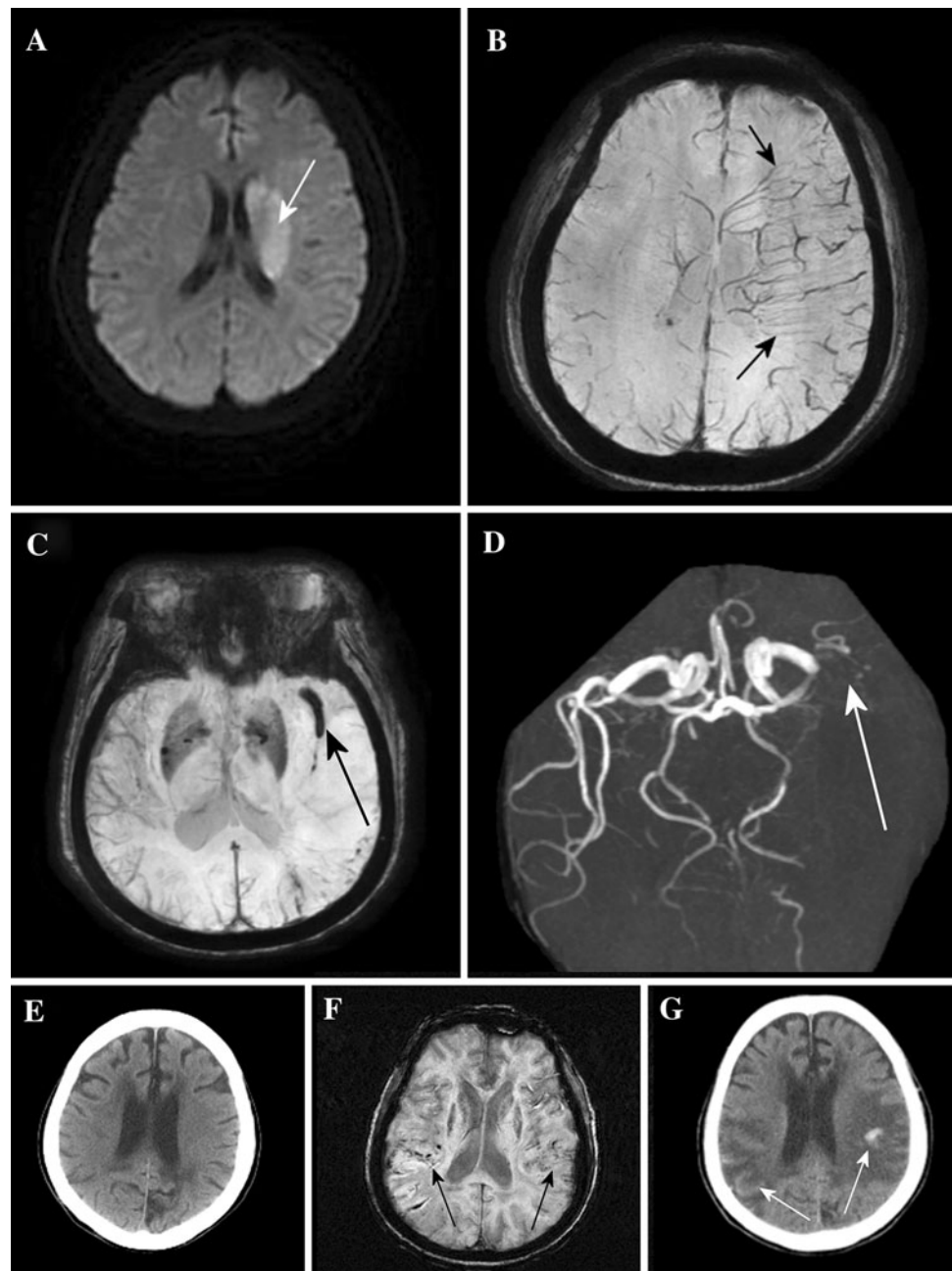
Statistics

Statistical analysis was performed with SPSS 12.0 package, and $p < 0.05$ was set to be statistically significant. To evaluate the differences between two groups, we used the two-tailed *t*-test for analyzing continuous variables and the chi-square test for categorical variables. Results of continuous normally distributed variables are expressed as mean value \pm standard deviation. Wilcoxon rank sum test was used when continuous variables failed tests for normality. Fisher's exact test was used when numbers tested were too small for chi-square analysis. For NIHSS, median, range and the Wilcoxon 2-sample test were used to determine significance. To evaluate the differences between multiple groups, we used the Kruskal-Wallis test for analyzing continuous variables and chi-square test for categorical variables. The diagnostic value of the susceptibility vessel sign with regard to the presence of arterial occlusion was expressed as sensitivity and specificity. The diagnostic value of microbleeds with regard to the presence of later hemorrhagic transformation was also expressed as sensitivity and specificity. Binary logistic regression using outcome as dependent variable was also performed for further analysis.

Results

The basic characteristics of the patients are shown in Table 1. Among the 44 patients, 15 (34.1%) showed prominent veins (Fig. 1), 19 (43.2%) showed the

Fig. 1 Prominent veins. Brain MRI obtained 5 h after stroke onset. **a** DWI showed the hyperintense acute infarct in the left M1 territory (*white arrow*). **b** SWI showed prominent vessels and hypointense signals (*black arrows*) over the left MCA territory, indicating increased oxygen extraction. Susceptibility vessel sign: **c** SWI showed the susceptibility vessel sign (*black arrows*). **d** MRA showed occlusion of the left MCA (*white arrow*). Microbleeds: **e** Initial brain CT showed no hemorrhage. **f** SWI showed multiple punctate hypointensities over bilateral parietal lobes (*black arrows*). **g** Brain CT followed 1 week later, showing hemorrhagic transformation (*white arrows*). Figures above were obtained from three different patients



susceptibility vessel sign, and 14 (31.8%) showed microbleeds in SWI. In brain CT 1 week after MRI, 20 (45.5%) patients showed hemorrhagic transformation, and 8 (18.2%) showed prominent brain edema. As to the 6-month outcome, 34 (77.3%) patients had poor (mRS 4–6) outcomes.

In univariate analysis regarding the presence of prominent veins (Table 2), only age ($p = 0.055$) had a low level correlation with prominent veins. The prognosis, presence of later hemorrhagic transformation and edema, stroke worsening or improving (NIHSS change) were not associated with the presence of prominent veins. In univariate

analysis regarding the presence of the susceptibility vessel sign (Table 3), variables including prognosis, presence of later hemorrhagic transformation, stroke worsening or improving (NIHSS change) were not associated with the presence of the susceptibility vessel sign. However, there was a low level correlation between the susceptibility vessel sign and later brain edema ($p = 0.06$). Binary logistic regression using outcome as dependent variable did not show any significant finding.

Data regarding combined analysis of prominent veins and the susceptibility vessel sign are shown in Table 4. Although none of the variables were statistically

Table 1 Descriptive statistics of the patients

Variables	Patients (<i>n</i> = 44)
Age	71.91 ± 13.68
Sex (M/F)	18/26
Hypertension	27 (61.4)
Prominent veins	15 (34.1)
Susceptibility vessel sign	19 (43.2)
SWI microbleeds	14 (31.8)
One week CT hemorrhagic transformation	20 (45.5)
One week CT brain edema	8 (18.2)
TOAST	
Large artery	11 (25.0)
Small vessel	2 (4.5)
Cardioembolism	11 (25.0)
Undetermined	20 (45.5)
DM	10 (22.7)
NIHSS admission	18.5 (1–33)
NIHSS discharge	15 (0–38)
Pneumonia	15 (34.1)
Urinary tract infection	15 (34.1)
6-month mRS	
Good (0–3)	10 (22.7)
Poor (4–6)	34 (77.3)
Antithrombotics	
None	2 (4.5)
Aspirin	21 (47.7)
Clopidogrel	19 (43.2)
Heparin	1 (2.3)
Dipyridamole	1 (2.3)
MRI (days)	1.25 ± 0.78

Data are presented as mean ± standard deviation or *n* (%). Median and range for NIHSS

significant, none of the patients with positive prominent veins and negative susceptibility vessel sign had later brain edema. All the patients with negative prominent veins and a positive susceptibility vessel sign had poor outcomes.

MRA demonstrated MCA occlusion related to the clinically affected hemisphere in 33 (75.0%) patients. The susceptibility vessel sign was significantly associated with arterial occlusion ($p = 0.008$) based on the MR angiogram, and microbleeds were significantly associated with later hemorrhagic transformation ($p = 0.018$). When using the susceptibility vessel sign as a diagnostic tool for the presence of arterial occlusion based on MRA, the sensitivity was 54.5% and the specificity was 90.9%. When using microbleeds in SWI as a diagnostic tool for the presence of later hemorrhagic transformation, the sensitivity was 50.0% and the specificity was 83.3%.

Discussion

SWI is a modern MR technique that is a high-resolution three-dimensional sequence, wherein the phase images are used to enhance the conspicuity of small veins and other paramagnetic substances. It is exquisitely sensitive to paramagnetic substances, such as deoxygenated blood, blood products, iron and calcium [12–14]. The clinical utility of this technique covered a wide range of neurological disorders such as trauma, tumors, vascular malformations, multiple sclerosis, venous thrombosis and stroke [15–18]. Especially the presence of prominent veins, microbleeds and the susceptibility vessel sign in SWI were suggested to be helpful in evaluating patients with acute ischemic stroke [7–9]. This study focused on assessing the usefulness of these findings in patients with acute MCA territory infarction.

The presence of prominent veins was hypothesized to represent the penumbra and also considered to be the presentation of collateralization. Whether the presence of prominent veins was actually useful in assessing acute ischemic stroke patients remained unclear [8]. Previous studies have already found that it is impossible to state that SWI has the ability to show the OEF penumbra (misery perfusion) [7]. In our study, prominent veins were present in 15 (34.1%) patients. Theoretically, patients with collateralization should have better outcomes. However, the presence of prominent veins was not associated with prognosis, presence of later hemorrhagic transformation and edema, stroke worsening or improving. The usefulness of the presence of prominent veins seems to be limited.

Previous study has shown that the presence of the susceptibility vessel sign at echo-planar gradient-echo MRI can provide fast and accurate detection of acute proximal MCA thrombotic occlusion [9]. Thus, the susceptibility vessel sign in SWI was thought to be useful in detecting intra-arterial thrombus. Some authors even suggested that the susceptibility vessel sign could be used to assess the extent of infarct and prognosis [4, 10, 19]. In our study, the susceptibility vessel sign was present in 19 (43.2%) patients. It was not associated with prognosis, presence of later hemorrhagic transformation, stroke worsening or improving. However, there was low level correlation between the susceptibility vessel sign and later brain edema ($p = 0.06$). With study limited so far by the small case numbers, determining whether the susceptibility vessel sign can be used to predict later brain edema may need further studies. Concerning the detection of intra-arterial thrombus, the susceptibility vessel sign was significantly associated with arterial occlusion ($p = 0.008$) based on the MR angiogram. When MRA was used as the reference standard for establishing the diagnosis of occlusion of the MCA, the susceptibility vessel sign had a sensitivity of

Table 2 Characteristics of patients with and without prominent veins

	Positive (<i>n</i> = 15)	Negative (<i>n</i> = 29)	<i>p</i> value
Age	67.20 ± 12.99	74.34 ± 13.60	0.055*
Sex (M/F)	8/7	10/19	0.228
Hypertension	7 (46.7)	20 (69.0)	0.150
DM	1 (6.7)	9 (31.0)	0.127*
SWI microbleeds	3 (20.0)	11 (37.9)	0.314*
One week hemorrhage	5 (33.3)	15 (51.7)	0.246
One week brain edema	3 (20.0)	5 (17.2)	1.000*
TOAST			0.091
Large artery	7 (46.7)	4 (13.8)	
Small vessel	1 (6.7)	1 (3.4)	
Cardioembolism	2 (13.3)	9 (31.0)	
Undetermined	5 (33.3)	15 (51.7)	
6 month mRS			0.227
Good (0–3)	5 (33.3)	5 (17.2)	
Poor (4–6)	10 (66.7)	24 (82.8)	
Antithrombotics			0.684
None	0 (0.0)	2 (6.9)	
Aspirin	8 (53.3)	13 (44.8)	
Clopidogrel	7 (46.7)	12 (41.4)	
Heparin	0 (0.0)	1 (3.4)	
Dipyridamole	0 (0.0)	1 (3.4)	
Pneumonia	5 (33.3)	10 (34.5)	0.939
Urinary tract infection	3 (20.0)	12 (41.4)	0.195*
NIHSS admission	19 (2–21)	18 (1–33)	0.472*
NIHSS discharge	15 (0–28)	15 (0–38)	0.543*
NIHSS change	3 (–9 to 17)	2 (–20 to 22)	0.709*
MRI (days)	1.07 ± 0.80	1.34 ± 0.77	0.250*

Data are presented as mean ± standard deviation or *n* (%); *p* value by χ^2 or two-tailed *t* test

* Fisher's exact test or Wilcoxon rank sum test

54.5% and a specificity of 90.9%. The low sensitivity and high specificity indicate that when the susceptibility vessel sign is present, there is probably MCA occlusion. However, when the susceptibility vessel sign is not present, whether the MCA is occluded or not cannot be determined with certainty. Thrombolytic therapy may have greater benefits in patients who have thrombi in major arteries. MRA was used to detect major cerebral artery stenosis or occlusion caused by intra-arterial thrombus in acute ischemic stroke. Since the susceptibility vessel sign represented detection of intra-arterial thrombus and was associated with arterial occlusion or stenosis based on MRA, it could be useful when considering thrombolytic therapy.

We have also analyzed simultaneously the presence of prominent veins and the susceptibility vessel sign. The results showed that none of the patients with positive prominent veins and negative susceptibility vessel sign had later brain edema. All the patients with negative prominent veins and positive susceptibility vessel signs had poor outcomes. However, none of the variables were statistically significant. Limited by the small case numbers, we cannot

draw a solid conclusion from this combined analysis of prominent veins and the susceptibility vessel sign.

Previous studies have demonstrated the presence of microbleeds in more than one-fourth of the patients with acute ischemic stroke and less than 10% of the healthy population [20]. Microbleeds appear as punctate hypointense signals in SWI, and these represent small hemosiderin deposits adjacent to the small vessels [11]. The presence of multiple microbleeds may represent increased microvascular vulnerability. Hemorrhagic transformation of acute ischemic stroke is observed in approximately 20–40% of all patients within the first week of stroke onset and could be a devastating complication [21]. Whether the presence of microbleeds could predict further hemorrhagic transformation remained unclear [11, 22]. Our results showed that microbleeds were detected in 14 (31.8%) patients and were significantly associated with later hemorrhagic transformation (*p* = 0.018). When follow-up brain CT was used as the reference standard for establishing the diagnosis of hemorrhagic transformation, the presence of microbleeds has a sensitivity of 50.0% and a specificity of 83.3%. These results indicate that when

Table 3 Characteristics of patients with and without susceptibility vessel sign

	Positive (<i>n</i> = 19)	Negative (<i>n</i> = 25)	<i>p</i> value
Age	72.32 ± 10.76	71.60 ± 15.75	0.868*
Sex (M/F)	6/13	12/13	0.272
Hypertension	9 (47.4)	18 (72.0)	0.096
DM	4 (21.1)	6 (24.0)	1.000*
SWI microbleeds	4 (21.1)	10 (40.0)	0.211*
One week hemorrhage	8 (42.1)	12 (48.0)	0.697
One week brain edema	6 (31.6)	2 (8.0)	0.060*
TOAST			0.202
Large artery	3 (15.8)	8 (32.0)	
Small vessel	1 (5.3)	1 (4.0)	
Cardioembolism	3 (15.8)	8 (32.0)	
Undetermined	12 (63.2)	8 (32.0)	
6 month mRS			0.474*
Good (0–3)	3 (15.8)	7 (28.0)	
Poor (4–6)	16 (84.2)	18 (72.0)	
Antithrombotics			0.327
None	0 (0.0)	2 (8.0)	
Aspirin	10 (52.6)	11 (44.0)	
Clopidogrel	7 (36.8)	12 (48.0)	
Heparin	1 (5.3)	0 (0.0)	
Dipyridamole	1 (5.3)	0 (0.0)	
Pneumonia	8 (42.1)	7 (28.0)	0.328
Urinary tract infection	5 (26.3)	10 (40.0)	0.343
NIHSS admission	19 (5–33)	18 (1–27)	0.610*
NIHSS discharge	12 (2–38)	15 (0–38)	0.859*
NIHSS change	3 (–20 to 18)	3 (–18 to 22)	1.000*
MRI (days)	1.05 ± 0.78	1.40 ± 0.76	0.128*

Data are presented as mean ± standard deviation or *n* (%); *p* value by χ^2 or two-tailed *t* test

* Fisher’s exact test or Wilcoxon rank sum test

Table 4 Combined analysis of prominent veins and susceptibility vessel sign

	PV (+) SVS (+) <i>n</i> = 7	PV (+) SVS (–) <i>n</i> = 8	PV (–) SVS (+) <i>n</i> = 12	PV (–) SVS (–) <i>n</i> = 17	<i>p</i> value
Age	64.14 ± 11.98	69.88 ± 14.03	77.08 ± 6.61	72.41 ± 16.85	0.189
Sex (M/F)	3/4	5/3	3/9	7/10	0.422
Hypertension	2 (28.6)	5 (62.5)	7 (58.3)	13 (76.5)	0.182
DM	0 (0.0)	1 (12.5)	4 (33.3)	5 (29.4)	0.291
SWI microbleeds	1 (14.3)	2 (25.0)	3 (25.0)	8 (47.1)	0.356
One week hemorrhage	4 (57.1)	1 (12.5)	4 (33.3)	11 (64.7)	0.068
One week edema	3 (42.9)	0 (0.0)	3 (25.0)	2 (11.8)	0.139
6 month mRS					0.133
Good (0–3)	3 (42.9)	2 (25.0)	0 (0.0)	5 (29.4)	
Poor (4–6)	4 (57.1)	6 (75.0)	12 (100.0)	12 (70.6)	
NIHSS admission	19 (10–21)	19 (2–21)	20 (5–33)	17 (1–27)	0.760
NIHSS discharge	9 (4–28)	15.5 (0–20)	15.5 (2–38)	15 (0–38)	0.434
NIHSS change	3 (–9 to 17)	3 (0–4)	2.5 (–20 to 18)	2 (–18 to 22)	0.773

Data are presented as mean ± standard deviation or *n* (%); *p* value by χ^2 or Kruskal-Wallis test

PV prominent veins, SVS susceptibility vessel sign

microbleeds were present, there was possibly later hemorrhagic transformation. However, when microbleeds were not present, whether later hemorrhagic transformation would occur was not predictable.

Looking over our data, SWI did not provide useful information for predicting outcome as previously suggested. However, it did provide helpful information other than conventional MR protocols. The presence of the susceptibility vessel sign could be used to detect intra-arterial thrombus, which may be very helpful when considering thrombolytic therapy. The presence of microbleeds may predict further hemorrhagic transformation. The usefulness of the presence of prominent veins seems limited in this study. However, whether it could represent the penumbra was not addressed in this study and needs further study to confirm. Altogether, we felt that SWI would be worthwhile to include in routine MR protocols for major acute ischemic stroke.

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Conflicts of interest The authors report no conflicts of interest.

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