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Thrombus magnetic susceptibility is associated with recanalization and clinical outcome in patients with ischemic stroke

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ABSTRACT

In acute ischemic stroke patients with large vessel occlusion, the characteristics of the occluding thrombus on neuroimaging may be associated with recanalization after endovascular thrombectomy (EVT); however, the relationship between magnetic susceptibility of thrombus and clinical outcome remains unclear. We utilized quantitative susceptibility mapping (QSM) MRI to assess the magnetic susceptibility of thrombus in acute ischemic stroke patients undergoing EVT, and to evaluate its relationship with recanalization and functional outcomes. Patients with documented intracranial artery occlusion were consecutively recruited from one research center of the RESCUE-RE study (a registration study for Critical Care of Acute Ischemic Stroke After Recanalization). All the recruited patients underwent a 3D multi-echo MRI scan on a 3.0 T scanner for both susceptibility-weighted imaging (SWI) and QSM quantification of the thrombus. Among 61 patients included in the analyses, 51 (75.0 %) patients achieved thrombolysis in cerebral infarction (TICI) 2b/3 and 22 (36.1 %) patients had favorable functional outcomes. Successful recanalization was significantly associated with a higher thrombus magnetic susceptibility mean value (0.27 ± 0.09 vs 0.20 ± 0.09 ppm, p = 0.020) and lower coefficient of variation (0.42 ± 0.12 vs 0.52 ± 0.19, p = 0.024). ROC curve analysis showed the optimal cutoff value for thrombus susceptibility for predicting good clinical outcomes was 0.25 ppm (sensitivity 86.4 %, specificity 69.2 %). In multivariable logistic regression analyses, increased thrombus magnetic susceptibility was independently and significantly associated with good functional outcomes (adjusted odds ratio 15.11 [95 % confidence interval 2.64–86.46], p = 0.002). This study demonstrated that the increased thrombus magnetic susceptibility is associated with successful recanalization and favorable functional outcomes for intracranial artery occluded stroke patients.

1. Introduction

In acute ischemic stroke patients with large vessel occlusion, endovascular thrombectomy (EVT) has been proved to be one of the most effective treatments. However, about 20 % of the patients receiving EVT failed to reopen (Phipps and Cronin, 2020). The occlusion site, thrombus composition and clot size may all be associated with recanalization (Dutra et al., 2019; Staessens et al., 2020; Xu and Ariëns, 2020). Determining the characteristics of the occluding thrombus on neuroimaging has the potential for improving the vessel reopening and clinical outcome.

The MRI susceptibility vessel sign (SVS), defined as the hypointense blooming signals on T2*-weighted or susceptibility-weighted imaging (SWI), demonstrates the existence of local paramagnetic contents such

Abbreviations: CV, coefficient of variation; EVT, endovascular thrombectomy; IVT, intravenous alteplase treatment; mRS, modified Rankin Scale score; ppm, parts per million; NPV, negative predictive value; PH, parenchymal hematoma; PPV, positive predictive value; ROI, region of interest; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; SVS, susceptibility vessel sign; TICI, thrombolysis in cerebral infarction.

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as deoxyhemoglobin and methemoglobin (Cho et al., 2005). Many studies reported that patients with SVS receiving EVT were more likely to recanalize and improve clinical outcomes (Belachew et al., 2021; Bourcier et al., 2015; Bourcier et al., 2018; Darcourt et al., 2019; Liu et al., 2019). However, on the same issue, several studies showed negative results (Soize et al., 2015; Kang et al., 2017). One potential contributing factor to this discrepancy is that SVS is qualitative, and SWI contrast is bloomed, not localized and varies with vessel orientations. Quantitative susceptibility mapping (QSM) is a potential quantitative MRI (qMRI) technique that can resolve the issue by quantifying the magnetic susceptibility of the thrombi in the occluded vessels (de Rochefort et al., 2008; Haacke et al., 2015; Liu et al., 2015; Shmueli et al., 2009; Wang and Liu, 2015; Wei et al., 2019). Compared with the simple qualitative evaluation using SVS or other image signs, the voxel-wise quantitative measurement of the magnetic susceptibility value in thrombus might accurately reflect and evaluate its characteristics and components (Chen et al., 2022a,b).

This study aims to assess the magnetic susceptibility value of thrombus in patients treated with EVT, and to explore its association with successful recanalization and favorable functional outcomes.

2. Materials and methods

2.1. Study design and Subjects

Subjects were recruited from one research center of the RESCUE-RE study (a registration study for Critical Care of Acute Ischemic Stroke After Recanalization), which is an ongoing, prospective, observational cohort study (Liu et al., 2021; Wei et al., 2020). The study protocol was evaluated and approved by the medical ethics committee of all participating centers, and written informed consent was obtained from all participants or their legal representatives. The study had been registered in the Chinese Clinical Trial Registry.

Patients who met the following criteria were consecutively recruited: (1) age $\geq$ 18 years old; (2) acute ischemic stroke confirmed by MRI with documented intracranial artery occlusion (including middle cerebral artery, basilar artery, and vertebral artery V4 segment) and treated with EVT; (3) pre-stroke modified Rankin Scale score (mRS score) $\leq$ 2; (4) patients were followed up for 3 months.

2.2. MRI protocol

Subjects were scanned on a 3.0 T MRI scanner (Ingenia; Philips, Best, the Netherlands) with a 32-channel phased-array head coil. The multi-contrast MRI protocol includes diffusion-weighted imaging (DWI), T1- and T2-weighted imaging, fluid-attenuated inversion recovery imaging (FLAIR), 3D time-of-flight MR angiography (TOF MRA), and 3D multi-echo SWI. The fast 3D SWI protocol used a flow-compensated 4-echo gradient-echo pulse sequence with first TE = 6 ms, delta TE = 6.7 ms, TR = 30 ms, flip angle = 15°, FOV = 230 × 187 × 149 mm^3, acquisition voxel size = 0.6 × 0.9 × 2.5 mm^3 and reconstruction voxel size = 0.53 × 0.53 × 1.25 mm^3. The scan time was 00:59 with the scan acceleration factor = 7 (3.5 in left–right direction and 2 in superior-inferior direction) using the sensitivity encoding parallel imaging method (Pruessmann et al., 1999). The SWI was generated from the multi-echo data using the vendor-provided SWIp sequence. The raw magnitude and phase images of each echo were saved for QSM calculation.

2.3. Image analysis

The multi-echo magnitude and phase images were reformatted to the nifti format (https://nifti.nimh.nih.gov/nifti-1) for quantitative susceptibility calculation and region of interest (ROI) analysis. The QSM (with the unit of parts per million [ppm]) was calculated from the multi-echo images using Laplacian-based phase unwrapping, V-SHARP background phase removal, and iterative LSQR QSM algorithm in the STI Suite toolbox (V2.2) (Li et al., 2015; Wang and Liu, 2015; Wu et al., 2012) in MATLAB (Mathworks, Natick, MA). The normal-appearing white matter in centrum semioval was used as QSM reference (Chen et al., 2022a,b). The QSM map was then loaded in 3D Slicer (https://www.slicer.org/) for ROI drawing (Fedorov et al., 2012). For each subject, the 3D thrombus ROI was manually drawn on the hyperintense region of the corresponding thrombus on the QSM image, as illustrated in Fig. 1. The thrombus was identified by reviewing multi-modality MRIs as hyperintensity on QSM, bloomed hypointensity on SWI, thrombus-related occlusion on MRA /DSA and infarction in occlusion-related territories on DWI. Two investigators performed the ROI drawing (J.C. and Z.Z.) blinded to the clinical data.

For each subject, the volume of the 3D thrombus ROI, and the mean, median, standard deviation, maximum and minimum of the quantitative susceptibility within the ROI (e.g., in Fig. 1) were calculated. In addition, image histogram features, including skewness, kurtosis, and coefficient of variation (CV), were also calculated in MATLAB (Mathworks, Natick, MA) to reflect the susceptibility distribution in the thrombus ROI.

For each subject, the SVS was defined as a hypointense signal on SWI in the corresponding symptomatic occlusive vessels, with the diameter of the vessels exceeding the contralateral ones (Cho et al., 2005). The SVS diameter was obtained by measuring the maximum diameter perpendicular to the SVS long axis.

2.4. Outcome measurements

The primary favorable outcome was functional independence (mRS score of 0 – 2) at 90 days post EVT. The secondary favorable outcome was successful recanalization, defined as thrombolysis in cerebral infarction (TICI) grading system 2b – 3 after mechanical thrombectomy. The 90-day outcomes were obtained through clinic interview or telephone follow-up by trained researchers blinded to the baseline clinical information.

2.5. Statistics analysis

Continuous variables are expressed as mean with standard deviation or median with interquartile range, and categorical variables are presented as percentages. We used normality testing to assess the variable distribution. We used Student's *t*-test, ANOVA test and Mann-Whitney *U* test to compare the continuous variables, and Pearson's c^2 test and Fisher's exact test to analyze categorical variables between groups. Correlations of QSM susceptibility and thrombus volume were analyzed by Pearsons's correlation coefficient analysis. The optimal cutoff value of thrombus susceptibility in predicting outcomes was defined using the receiver operating characteristic (ROC) methodology. The diagnostic values (sensitivity, specificity, positive predictive value, negative predictive value) and 95 % confidence interval (CI) for predicting favorable clinical outcomes based on the thrombus characteristics were calculated. Multivariate logistic regression was utilized to obtain the odds ratios (OR) and 95 % CI for the independent associations between thrombus susceptibility and the outcomes, adjusting for confounders including National Institutes of Health Stroke Scale (NIHSS) score, the time between onset to groin puncture, site of occlusion, intravenous alteplase treatment (IVT) and stroke etiology. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS (Version 24; IBM, SPSS; Chicago, IL) and MedCalc (V.19.1; MedCalc Software, Belgium).

3. Result

From January to December 2019, 73 patients with documented intracranial artery occlusion (including MCA, BA, and 4th segment of VA) underwent QSM examination before EVT. After excluding 10 patients with severe image artifacts, 1 with pre-stroke mRS > 2 and 1 lost

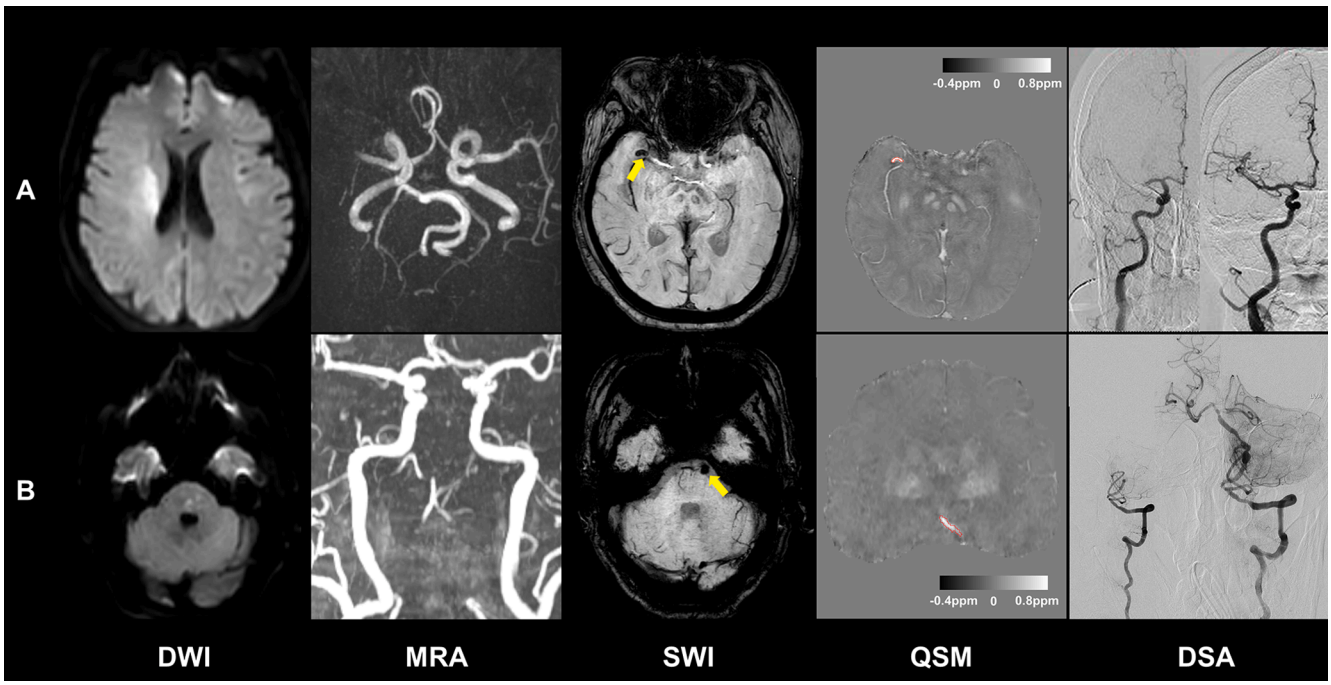

Fig. 1. Case illustration of QSM measurement. The SVS can be observed as depicted by the yellow arrow. The QSM is calculated from the multi-echo MRI phase images, and the ROI was drawn on the QSM image as depicted by the red contour. The thrombus was identified by reviewing multi-modality MRIs as hyperintensity on QSM, bloomed hypointensity on SWI, thrombus-related occlusion on MRA/DSA and infarction in occlusion-related territories on DWI. (A) A 63-year-old female patient imaged 330 min after the onset of right hemiparesis and aphasia. MRI demonstrated acute left paraventricular infarctions on DWI, middle cerebral artery occlusion on MRA, and the susceptibility vessel sign on SWI (yellow arrow). QSM showed hyperintense signals in the thrombus with the mean susceptibility value of 0.44 ppm measured in the ROI (in red contour, drawn in axial view at the central slice of the thrombus). DSA revealed that the occluded middle cerebral artery achieved successful recanalization with TICI 3 after endovascular thrombectomy. (B) A 56-year-old male patient imaged 22 h following the onset of coma. MRI demonstrated acute brainstem infarctions on DWI, bilateral vertebral artery occlusion on MRA and the susceptibility vessel sign on SWI (yellow arrow). QSM showed hyperintense signals in the thrombus with the mean susceptibility value of 0.39 ppm measured in the ROI (in red contour, drawn in coronal view at the central slice of the thrombus). DSA revealed the right vertebral artery occlusion, and after endovascular thrombectomy the occluded vertebral artery recanalized, with TICI 2b grade. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

follow-up, a total of 61 patients (mean age 61.74 ± 10.48 years, 63.9 % males) were included in the final analysis. The median baseline NIHSS score was 14 (interquartile range, 12–18). The ischemic stroke etiology included 36 (59.0 %) large-artery atherosclerosis, 21 (34.4 %) cardioembolism, 2 (3.3 %) artery dissection and 2 (3.3 %) undetermined etiology. Forty-one thrombi were located in the MCA (including 35 in M1 segment and 6 in M2 segment), 13 at BA and 7 at the 4th segment of the VA. IVT was administered to 20 (32.8 %) patients before the MRI scan and EVT. The median time from stroke onset to MR scan and groin puncture was 326 and 535 min, respectively. The median number of retriever passes was 1, with the interquartile range of 1–2. Of 49 patients with successful recanalization, recanalization was achieved with the first pass in 28 patients (57.1 %, Table 1).

A total of 22 (36.1 %) patients had favorable functional outcomes (mRS score 0–2) at 90 days, and TICI 2b/3 were achieved in 51 (75.0 %) patients. The demographic and clinical baseline data of patients with different functional outcomes and recanalization status are shown in Table 1. The SVS was present in 50 (82.0 %) patients, which was more frequent among the recanalization group than the non-recanalization group, but without statistical significance (Table 1).

The mean susceptibility of thrombus on QSM using the normal-appearing white matter as reference was 0.26 ± 0.10 ppm. The mean susceptibility of reference tissue for all subjects was −0.019 ± 0.014 ppm. The interobserver agreement of the mean thrombus susceptibility measured by the intraclass correlation coefficient was 0.95. The values for QSM per clinical outcome group separately passed normality tests (Kolmogorov-Smirnov and Shapiro-Wilk tests, Supplementary Table S1). Univariate analysis showed that the means, minimum value, maximum value, and median of susceptibility were significantly different between favorable and unfavorable outcomes groups (Table 2). Similarly, the mean susceptibility values and CV were significantly associated with recanalization (Table 2). Pearson's correlation indicated no statistically significant relationship between thrombus susceptibility and volume ($p = 0.228$). ANOVA test showed thrombus susceptibility had no statistically significant correlation with occlusion site ($p = 0.057$).

ROC curve analysis showed that the optimal cutoff value for thrombus mean susceptibility for predicting good clinical outcomes was 0.25 ppm (Fig. 2), with the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 86.4 %, 69.2 %, 61.3 %, and 90.0 %, respectively. Moreover, that was superior to the SVS for predicting favorable functional independence, with sensitivity, specificity, PPV, and NPV of 86.4 %, 20.5 %, 38.0 %, and 72.7 %, respectively. The ROC curve analysis showed that the optimal cutoff value for SVS diameter for predicting favorable outcomes was 4.0 mm.

Univariate and multivariate logistical regression analyses were performed to assess the relationship between the thrombus characteristics (SVS and mean susceptibility) and clinical outcome (Table 3). Univariate analysis showed an odds ratio value of 1.63 (95 % CI 0.39–6.93; $p = 0.731$) for the SVS, whereas the odds ratio value for mean susceptibility was 14.25 (3.53–57.78; $p < 0.001$). According to a literature review and univariate analysis, the NIHSS score, the time between onset to groin puncture, site of occlusion, IVT, stroke etiology, infarct volume and PH-2 (parenchymal hematoma) hemorrhage were utilized as adjusted variables in the multivariate logistical model. Multivariate analysis showed that the thrombus susceptibility (≥0.25 ppm) on QSM was significantly associated with favorable outcomes, with an adjusted odds ratio of 15.11 (2.64–86.46, $p = 0.002$, Table 3).

Table 1
Characteristics of enrolled Participants by Recanalization and Clinical Outcome.

Baseline Characteristics	Total	Recanalization			90-d functional Outcome		
		TICI 2b/3 (n = 49)	**TICI 0–2a (n = 12)**	**p**	**mRS ≤ 2 (n = 22)**	**mRS > 2 (n = 39)**	**p**
Age, y, mean + SD	61.74 ± 10.48	62.12 ± 10.80	60.17 ± 9.30	0.57	62.73 ± 8.36	61.18 ± 11.57	0.58
Male, n (%)	39 (63.9)	31 (63.3)	8 (66.7)	1.00	15 (68.2)	24 (61.5)	0.60
B-NIHSS, Median (IQR)	14 (12–18)	14 (12–18)	14 (11–22)	0.97	15 (12–22)	14 (12–18)	0.30
Medical history, n (%)							
Atrial fibrillation	14 (23.0)	21 (41.2)	6 (35.3)	0.67	3 (13.6)	11 (28.2)	0.19
Hypertension	49 (80.3)	38 (77.6)	11 (91.7)	0.75	20 (90.9)	29 (74.4)	0.18
Diabetes	25 (41.0)	21 (42.9)	4 (33.3)	0.43	10 (45.5)	15 (38.5)	0.54
Current smoke	27 (44.3)	22 (44.9)	5 (41.7)	0.84	12 (54.5)	15 (38.5)	0.23
Occlusion location, n (%)				0.29			0.40
MCA	41 (67.2)	35 (71.4)	6 (50.0)		15 (68.2)	26 (66.7)	
BA	13 (21.3)	9 (18.4)	4 (33.3)		6 (27.3)	7 (17.9)	
VA	7 (11.5)	5 (10.2)	2 (16.7)		1 (4.5)	6 (15.4)	
Stroke etiology, n (%)				0.68			0.06
Atherosclerotic	36 (59.0)	28(57.1)	8 (66.7)		17 (77.3)	19 (48.7)	
Cardioembolic	21 (34.4)	18 (36.7)	3 (25.0)		5 (22.7)	16 (41.0)	
Other	4 (6.6)	3 (6.1)	1 (8.3)		0	4 (10.3)	
Intravenous rt-PA, n (%)	20 (32.8)	17 (34.7)	3 (25.0)	0.73	11 (50.0)	9 (23.1)	0.03
Procedure time, min, median (IQR)							
Onset to MR scan	326 (248–484)	334 (235–493)	293 (260–444)	0.54	326 (253–508)	315 (233–480)	0.94
Onset to groin puncture	535 (453–712)	537 (455–698)	530 (450–720)	0.88	510 (428–736)	560 (469 ~ 702)	0.39
Number of retriever passes, median (IQR)	1 (1–2)	1 (1–2)	1 (1–2.75)	0.24	1.5 (1–2)	1 (1–2)	0.47
SVS characteristics							
SVS, n (%)	50 (82.0)	41 (83.7)	9 (75.0)	0.68	19 (86.4)	31 (79.5)	0.73
SVS diameter, mm	4.08 ± 1.09	4.23 ± 1.10	3.46 ± 0.83	0.03	4.18 ± 1.00	4.03 ± 1.14	0.59
ASITN/SIR collateral grading				0.52			0.55
0–1	10 (16.4)	7 (14.3)	3 (25.0)		3 (13.6)	7 (17.9)	
2–3	50 (82.0)	41 (83.7)	9 (75.0)		18 (81.8)	32 (82.1)	
4	1 (1.6)	1 (2.0)	0 (0)		1 (4.5)	0 (0)	
Infarct volume on MRI-DWI, cm^3	22.55 ± 33.06	22.93 ± 33.99	20.98 ± 30.25	0.86	22.52 ± 31.60	22.57 ± 34.26	0.99
PH-2 Hemorrhage	7 (11.5)	5 (10.2)	2 (16.7)	0.62	4 (18.2)	3 (7.7)	0.41

Abbreviations: ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology / Society of Interventional Radiology; BA, basilar artery; B-NIHSS, Baseline National Institutes of Health Stroke Scale; IQR, interquartile range; IVT, intravenous thrombolysis; MCA, middle cerebral artery; mRS, modified Rankin Scale; PH, parenchymal hematoma, SVS, susceptibility vessel sign; TICI, Thrombolysis in Cerebral Infarction score; and VA, vertebral artery.

Table 2
QSM Image Features of Thrombus Susceptibility.

Variables	Total	Recanalization			90-d functional Outcome		
	(n = 61)	TICI 2b/3 (n = 49)	TICI 0–2a (n = 12)	p	mRS ≤ 2 (n = 22)	mRS > 2 (n = 39)	p
Volume, mm^3	91.51 ± 73.53	94.94 ± 75.49	77.48 ± 66.02	0.466	70.52 ± 65.37	103.35 ± 76.01	0.094
Means, ppm	0.26 ± 0.10	0.27 ± 0.09	0.20 ± 0.09	0.020*	0.33 ± 0.07	0.22 ± 0.09	<0.001*
SD, ppm,	0.11 ± 0.03	0.11 ± 0.03	0.10 ± 0.04	0.306	0.11 ± 0.03	0.10 ± 0.03	0.548
Minimum value, ppm	0.06 ± 0.07	0.06 ± 0.06	0.02 ± 0.07	0.053	0.11 ± 0.03	0.02 ± 0.06	<0.001*
Maximum value, ppm	0.57 ± 0.18	0.59 ± 0.18	0.48 ± 0.19	0.063	0.64 ± 0.17	0.53 ± 0.18	0.036*
Medians, ppm	0.25 ± 0.10	0.26 ± 0.10	0.19 ± 0.08	0.019*	0.32 ± 0.07	0.21 ± 0.08	<0.001*
Skewness	0.46 ± 0.30	0.47 ± 0.30	0.44 ± 0.34	0.751	0.39 ± 0.27	0.51 ± 0.32	0.136
Kurtosis	2.76 ± 0.46	2.79 ± 0.46	2.64 ± 0.47	0.308	2.69 ± 0.36	2.80 ± 0.51	0.366
CV	0.44 ± 0.14	0.42 ± 0.12	0.52 ± 0.19	0.024*	0.34 ± 0.05	0.50 ± 0.14	<0.001*

Abbreviations: CV, coefficient of variation; mRS, modified Rankin Scale score; SD, standard deviation; and TICI, thrombolysis in Cerebral Infarction score.
*Significant p values.

4. Discussion

Using MRI data from the prospective registry study of acute ischemic stroke treated with EVT, we demonstrated that the value and distribution of magnetic susceptibility in thrombus are associated with recanalization and clinical outcomes. Specifically, the increased susceptibility of thrombus was a strong predictor of favorable clinical outcomes at 90 days, independent of demographics, clinical and radiographic characteristics.

Most previous susceptibility-related MRI studies focused on the image signs like SVS (Belachew et al., 2021; Bourcier et al., 2015; Bourcier et al., 2018; Cho et al., 2005; Darcourt et al., 2019; Kang et al., 2017; Liu et al., 2019; Soize et al., 2015) due to the easy clinical availability. The present study is one of the first studies to explore the thrombus properties and outcome associations by the quantification MRI method. Using QSM to quantify the magnetic susceptibility of thrombus, our study revealed that increased susceptibility could be a more accurate predictor than the SVS for recanalization and independent functional outcome. Previous thrombus susceptibility characteristics, such as SVS and its length and width, are usually determined on T2*-weighted or SWI MRI (Belachew et al., 2021; Bourcier et al., 2015; Bourcier et al., 2018; Cho et al., 2005; Darcourt et al., 2019; Kang et al., 2017; Liu et al., 2019; Soize et al., 2015). Bourcier et al (2015) found the SVS was associated with good functional outcome for patients with anterior circulation stroke after EVT. Darcourt et al. (2019) reported SVS to predict recanalization and early clinical improvement. In recent research including patients presenting both anterior and posterior circulation stroke in larger populations, SVS was also demonstrated to

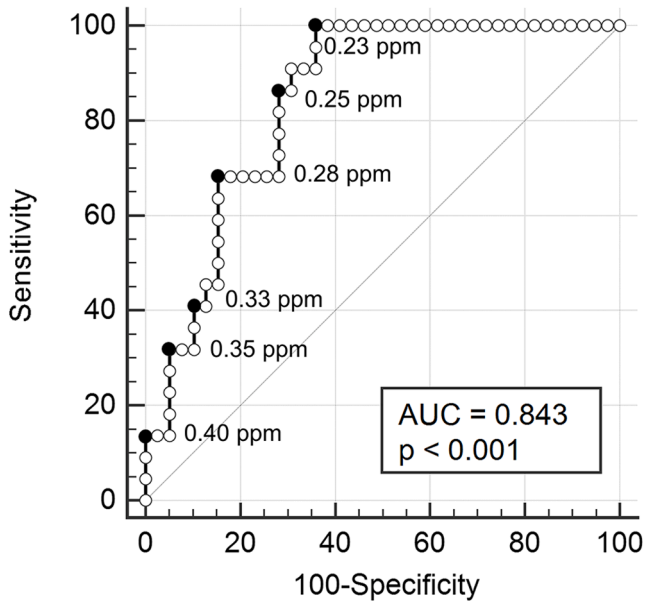

Fig. 2. Receiver-operating characteristics (ROC) analysis of thrombus susceptibility for predicting favorable outcomes after endovascular treatment. AUC, area under the curve.

Table 3
Univariate and multiple logistic regression analysis of thrombus characteristics and favorable outcomes.

Variables	Favorable outcome, n (%)	Univariate		Multivariate *	
		OR (95 %CI)	p value	aOR (95 % CI)	p value
Susceptibility (≥0.25 ppm)	19 (86.4)	14.25 (3.53–57.78)	<0.001	15.11 (2.64–86.46)	0.002
SVS (+)	19 (86.4)	1.63 (0.39–6.93)	0.731	1.73 (0.25–11.81)	0.575
SVS diameter (≥4.0 mm)	12 (54.5)	1.40 (0.49–4.00)	0.529	1.98 (0.50–7.91)	0.332

Abbreviations: SVS, susceptibility vessel sign; OR, odds ratio; CI, confidence interval.
*Adjusted for the NIHSS score, time between onset to groin puncture, site of occlusion, IVT, stroke etiology, infarct volume and parenchymal hematoma −2 hemorrhage.

be a predictor of successful reperfusion and better clinical functional outcome after EVT (Belachew et al., 2021). SWI/ T2*-weighted MRI enhances the visualization of the thrombus as blooming hypointense signals, known as SVS, which can be easily accessible in clinical practice. However, due to the inherent defect of all-or-nothing qualitative evaluation, SVS cannot make a detailed evaluation of the components of the thrombus. QSM, on the other hand, can map the underlying susceptibility of each voxel in the thrombus using the MRI phase information (Liu et al., 2015). QSM has been demonstrated to show greater accuracy in assessing microbleeds and hematoma in intracranial hemorrhagic disease (Liu et al. 2012; Zhang et al., 2018), and our previous study has reported the utility of QSM in distinguishing stroke subtypes in acute ischemic stroke (Chen et al., 2022a,b).

The present study showed that not only the diameter of SVS on SWI (which was consistent with previous studies, Bourcier et al., 2018; Darcourt et al., 2019; Kang et al., 2017), but also the quantification and distribution of susceptibility of thrombus on QSM were associated with successful recanalization after EVT treatment. Histogram analysis further revealed that in successfully recanalized vessels, the thrombus susceptibility is higher (in mean/median value) and relatively more homogeneous (smaller CV for recanalization). Thrombi can be distinct in content and structure: Platelet-rich thrombi consist of platelets, dense fibrin structure and leukocytes; while erythrocyte-rich thrombi are less complex, predominated by red blood cells (Xu and Ariëns, 2020; Staessens et al., 2020). In red blood cells, paramagnetic materials like deoxyhemoglobin and methemoglobin, can lead to an increase in magnetic susceptibility. Meantime, thrombectomy is more effective for red blood cell-rich thrombus than fibrin-rich thrombus (Gunning et al., 2018 Hashimoto et al., 2016; Yuki et al., 2012;). This might help explain the association with the quantification of thrombus susceptibility and recanalization in patients receiving EVT treatment. Future histologic studies are needed to confirm the correlation between QSM imaging characteristics and detailed thrombus contents.

Recent studies demonstrated that magnetic susceptibility-related imaging signs were associated with better functional outcome in patients receiving EVT (Dutra et al., 2019). Our study designed a fast qMRI method for such patients, using the SWI acquisition without additional scan time. We implemented the fast SWI/QSM protocol using parallel imaging technique (Pruessmann et al., 1999), which takes only about 1 min to acquire. The fast-imaging speed favors many clinical applications, especially for stroke patients. With the next-generation image reconstruction techniques for MRI, like compressed sensing (Lustig et al., 2008) or deep learning (Knoll et al., 2020), the acquisition can be further accelerated or the resolution can be further improved in the same acquisition time. The QSM processing also takes about 10 min for each case to finish offline. With the emerging deep learning-based processing approaches, like QSMnet (Yoon et al., 2018), the instant on-console multi-modality (e.g., QSM with DWI/MRA/perfusion) evaluation is expected in the near future. QSM MRI, as a part of qMRI, gives a quantitative and detailed evaluation of the occluding thrombus, associating with the vessel reopening and clinical outcome.

In patients with acute proximal large artery occlusion, EVT has been recommended as the standard treatment. In daily practice, the key criteria for EVT include the occlusion site, NIHSS score, Alberta Stroke Program Early CT Score and symptom onset time. The present study demonstrated that the increased magnetic susceptibility of thrombus is significantly associated with recanalization and favorable functional outcomes for acute intracranial artery occluded patients. The novel QSM MRI technique may be helpful in EVT treatment selection for patients with acute ischemic stroke. Further multi-center external validation is required to be generalized in clinical practice.

This study has several limitations. Firstly, all participants were recruited from one single center. Thus, a large multi-center cohort was required to validate the conclusion. Secondly, about one-third of patients received intravenous thrombolysis before MRI scan and EVT treatment. The tissue plasminogen activator may dissolve the fibrin scaffold, but not the deoxyhemoglobin and hemosiderin content in the clot. As the increased susceptibility value is mainly contributed by the content of the deoxyhemoglobin and hemosiderin, the susceptibility value of thrombus may not change dramatically after the EVT procedure, as long as the thrombus structure holds. Logistic regression analysis including intravenous alteplase treatment information was used in the present study to control this possible confounding factor. Thirdly, another limitation of the present study is the lack of external validation. Thus, our results should be interpreted with caution, and further studies are required to validate the superiority of QSM susceptibility of thrombus in prognostic models for the outcome of EVT in ischemic stroke.

In conclusion, using QSM MRI, the quantification and distribution of magnetic susceptibility can be accessed in thrombi. The increased susceptibility is associated with superior functional outcome and successful recanalization after EVT.

CRediT authorship contribution statement

Jie Chen: Conceptualization, Formal analysis, Investigation,

Methodology, Writing – original draft, Writing – review & editing, Funding acquisition. **Zhe Zhang:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Ximing Nie:** Formal analysis, Investigation. **Yuyuan Xu:** Formal analysis, Investigation. **Chunlei Liu:** Conceptualization, Investigation, Methodology, Writing – review & editing. **Xingquan Zhao:** Conceptualization, Methodology. **Zhongrong Miao:** Conceptualization, Methodology. **Yongjun Wang:** Conceptualization, Methodology, Funding acquisition. **Liping Liu:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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