

Risk Factors, Susceptibility Vessel Sign and Thrombosis Pathology for Prognosis in Patients With Different Subtypes of Acute Ischemic Stroke Treated With Mechanical Thrombectomy

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Purpose: This study highlights the relationship between stroke subtypes, thrombosis pathology, and susceptibility vessel sign (SVS) and identifies probable risk factors affecting recanalization and outcomes in endovascular treatment.

Methods: A prospective study was conducted in which 53 acute ischemic stroke patients received intravenous thrombolysis and mechanical thrombectomy (MT) from January 2017 to December 2019 in a native hospital. The recanalization was evaluated using modified cerebral infarction thrombolysis grade and prognosis at 3 months using modified Rankin Scale (mRS). The risk factors were identified using univariate and multivariate logistic regression analyses. The thrombus samples were stained to determine their composition. Magnetic sensitivity-weighted imaging was used to determine SVS.

Results: Age, locations of occlusion, and treatments were significantly different of TOAST (Trial of Org 10172 in Acute Stroke Treatment) subtypes ($P < 0.05$). The time from door to puncture (TDP) and time of operation (TO) were significantly lower in the successful recanalization group ($P < 0.05$). National Institutes of Health Stroke Scale (NIHSS), MT, TDP, time from onset to recanalization (TOR), and TO have significant differences between the two groups of $mRS \leq 2$ and > 3 . The occurrence of symptomatic intracranial hemorrhage (sICH) significantly affected the mRS score. The red and mixed thrombi were common in patients with positive SVS whereas the white thrombi were associated with the negative SVS.

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Conclusion: Improved recanalization and prognosis was observed in early MT and when endovascular operations time was reduced.

Key words: Susceptibility vessel sign – Thrombosis pathology – Acute ischemic stroke – Stroke subtypes – Mechanical thrombectomy

Acute ischemic stroke (AIS) is the most common type of stroke and accounts for 60% to 80% of all the stroke population.^{1–3} Endovascular operation is the most ideal treatment for AIS to date. Therefore, endovascular therapy (EVT) is the preferred treatment strategy for AIS caused by large vessel occlusion (AIS-LVO), which can significantly improve the vascular recanalization and clinical outcomes of AIS patients.⁴ Many factors such as locations of occlusion, thrombi composition, and TOAST (Trial of Org 10172 in Acute Stroke Treatment) subtypes are associated with successful reperfusion.⁵

Revealing the composition of thrombi provides insight into the diagnosis of stroke subtypes and predicts the success rate of recanalization after intravenous thrombolysis and/or EVT as per previous studies.⁶ Histological analysis of thrombi, obtained from intracranial blood vessels, has been made possible by the development of endovascular technology. Etiology of ischemic stroke and the thrombus composition could help in improving the prognosis of this disease.^{6,7}

Thrombus is a collection of fibrin and platelets; comes in different sizes, shapes, and colors; and consists of red and white blood cells. Thrombus forms within a blood vessel or cardiac chamber, adjacent to the endothelium or endocardium. Depending on the relative number of platelets and red blood cells, the thrombus is classified into 3 major groups such as white thrombus (characterized by a predominance of platelets), red thrombus (characterized by a predominance of red blood cells), and mixed thrombus (features of white and red thrombus). The hemoglobin in thrombus and its degraded products are magnetically sensitive with different magnetic sensitivity due to the different iron-containing states.

In recent years, the magnetic sensitivity-weighted imaging (SWI) technique has been gradually developed and applied in clinical diagnosis.⁸ The SWI technique is based on magnetic susceptibility differences between different tissues. Susceptibility vessel sign (SVS) on the SWI gradient-echo image, caused by a loss in MR signal due to arterial thrombosis in the presence of hypointensity in the artery, is highly sensitive in detecting the intra-arterial thrombus in

stroke. The SVS is highly specific in occlusive thrombus, and is associated with larger infarct volume in AIS. SVS not only helps in the clinical diagnosis of cerebral ischemic infarction, but also helps in identifying stroke subtypes, assessing the severity and clinical prognosis, and helping in the selection of treatment options for AIS.⁹ Studies demonstrated that preoperative SVS evaluation helps in predicting reperfusion and clinical outcomes after EVT.^{8,10,11}

In this study, we identified the risk factors affecting the rate of recanalization and use of SVS to analyze thrombosis pathology and further identify probable risk factors affecting the prognosis of different subtypes of AIS.

Methods

Study population

This is a prospective study that enrolled 53 stroke patients with acute anterior circulation and large-artery atherosclerosis (LAA). They underwent intravenous thrombolysis and intravascular treatments in the neurology department from January 2017 to December 2019. The ethics committee of the native hospital approved this study. Written informed consent was given by the subjects.

Diagnosis of stroke and stroke subtype classification

The inclusion criteria included: (1) age ≥ 18 years; (2) endovascular treatment of AIS performed according to the indications Guidelines for Early Endovascular Interventional Diagnosis and Treatment of Acute Ischemic Stroke in China 2018; (3) AIS caused by large vessel occlusion (LVO) in the anterior circulation confirmed by magnetic resonance angiography (MRA) and/or digital subtraction angiography (DSA) and those vessels including internal carotid artery, the M1 segment of a middle cerebral artery, and tandem internal carotid and middle cerebral artery M1 occlusion; (4) use of intravenous thrombolysis with a recombinant tissue-type plasminogen activator (rt-PA) within 4.5 hours and urokinase within 6 hours in AIS patients with EVT; (5) for AIS patients with EVT, time from onset to operation within 6 hours or the cerebral ischemic penumbra confirmed for patients with unknown

causes; (6) DWI and SWI performed before EVT; and (7) modified Rankin scale (mRS) < 2.

The exclusion criteria included: (1) intracerebral hemorrhage or active bleeding; (2) severe heart, liver, or kidney dysfunctions; (3) preoperative blood glucose <2.7 mmol/L or >22.2 mmol/L; and (4) DWI-ASPECT score < 6.

Stroke etiology and TOAST classification

TOAST classification was used to identify the etiology of AIS and explore its probable role in affecting prognosis, outcome, and management of AIS.^{12,13} This study included only 3 subtypes of the TOAST classification: (1) LAA; (2) cardioembolism; and (3) stroke of unknown etiology including no specific cause determined or lack of necessary examinations.

Data collection

Clinical and imaging data including age, sex, history of smoking, hypertension, diabetes, atrial fibrillation, coronary heart disease and cerebral infarction, TOAST subtypes, National Institutes of Health Stroke Scale (NIHSS) score at the onset, DWI-ASPECTS score, vascular occlusion site, time of operation, number of thrombectomies, whether the occluding blood vessel is complicated with atherosclerotic primary stenosis, salvage therapy, postoperative modified cerebral infarction thrombolytic therapy (mTICI), blood flow classification, symptomatic cerebral hemorrhage, mRS scores, pathological analysis of emboli, and signs of SVS at 3 months were collected. Improvement of patients' neurological function was evaluated using the NIHSS score, and the neurological status at 3 months was evaluated using the mRS score. mRS ≤ 2 is concluded as a good prognosis and mRS ≥ 3 is concluded as a poor prognosis. The modified treatment in cerebral infarction (mTICI) score was used to assess postoperative vascular reperfusion, which reflects increased use of endovascular therapies. At the end of the procedure, mTICI 2B or 3 is considered as successful reperfusion. Any type of intracranial hemorrhage with a decline in the NIHSS score ≥ 4 is known as symptomatic cerebral hemorrhage (sICH).

MRA and SVS

SVS was classified as present (SVS+) or absent (SVS-) according to magnetic SWI differences in different tissues. SVS is a dark-filling defect with a blooming artifact within the artery.^{11,14} The vessel signal is wider than the diameter of other arteries. However, in the absence of such changes, SVS is

negative. The SWI images were reviewed by 2 radiologists independently with no MRA and clinical data, and the presence or absence of SVS was concluded. In case of inconsistency, further discussions were done to finalize the decision. Baseline MRA determined the arteries of acute occlusion and these were divided into M1 occlusion and M2 occlusion. In the case of positive SVS, the volume and length of clots were measured and location was noted.

EVT of AIS

The AIS patients underwent 1-stop MRI, including MR DWI, MRA, and SWI, and the location of occlusion on the internal carotid artery or middle cerebral artery was identified. Intravenous thrombolytic treatment with alteplase was initiated within 4.5 hours after the onset of symptoms, and intravenous thrombolysis with urokinase was performed within 6 hours from the onset of symptoms. Thrombolysis followed by mechanical thrombectomy (MT) was carried out.⁴ All procedures were completed by the same person. Using the Seldinger technique, the right common femoral artery was punctured and a 5-French sheath was placed into the common femoral artery. Through the sheath, an 8 F Cobra Guide Catheter was inserted and selective cerebral angiography was performed. In case angiography was unsuccessful after the thrombectomy, the balloon dilatation and stent implantation were initiated. Intravenous microcatheter injection of tirofiban in combination with hydrochloride sodium chloride injection was given to reduce the formation of acute and subacute thrombosis.¹⁵ All patients underwent computed tomography (CT) examination after the operation to confirm extravasation and bleeding of the contrast medium, and the dose of tirofiban hydrochloride was adjusted with antibiotic treatment.

Histopathological analysis of thrombus

The harvested thrombus samples were placed in 10% paraformaldehyde, fixed for 24 to 48 hours, and embedded in paraffin. Five micrometer paraffin-embedded sections were prepared (4 slices for each sample). Hematoxylin and eosin (H&E) staining was performed and a quantitative analysis of fibrin, platelets, and the number of red/white blood cells was done using ImageJ software. According to the quantitative results, when the proportion of fibrin >60%, it is defined as white thrombi, and when the proportion of red blood cells >50%, it is defined as red thrombi. The rest is considered as mixed thrombi.¹⁶

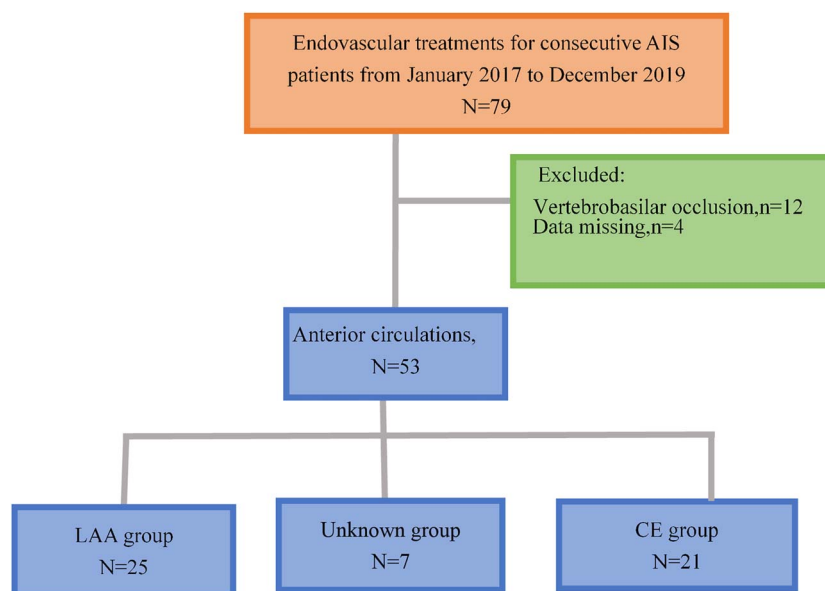


Fig. 1 Selection of patients in this study.

Statistical analysis

All statistical analyses were done using Statistical Package for the Social Sciences (SPSS) 17.0 software. The data were presented as mean $\pm$ SD. Normality tests of data were performed as a prerequisite for statistical tests. One-way analysis of variance (ANOVA) was used to compare normal data and the Kruskal-Wallis test was used for non-normal data. A chi-square test was used for count data. Related risk factors were analyzed using univariate and multivariate logistic regression. The value of $P < 0.05$ was considered statistically significant.

Result

Clinical characteristics in different subtypes of AIS

A total of 53 AIS patients receiving intravenous thrombolysis and MT from January 2017 to December 2019 were enrolled (Fig. 1). The preoperative evaluations, surgical procedures, and postoperative examinations were provided in Figs. S1–S6. First, on the general clinical characteristics of included patients, the age was different with different TOAST subtypes ($P < 0.05$, Table 1). Specifically, the average age of the LAA group was significantly lower, whereas the age of the unknown group was significantly higher. Moreover, the difference in the location of occlusion was significant ($P < 0.05$). The proportion of M1 occlusion in the unknown group was significantly higher and the proportion of Tandem occlusion in the LAA group

was significantly higher. Furthermore, use of rescue treatments was significantly different ($P < 0.05$). Balloon plus tirofiban accounts for a relatively higher proportion in the LAA group, and NO represents a relatively smaller amount in the LAA group.

Clinical features affecting thrombolysis in cerebral infarction (mTICI)

We performed a multivariate logistic regression analysis to explore the risk factors and clinical features associated with mTICI, and independent factors affecting mTICI were identified. With the single-factor analysis, there were significant differences in TDP and TO in different groups (Table 2). Among these, the TDP and TO were significantly lower in successful reperfusion ($P < 0.05$). Furthermore, TDP and TO were included in the multivariate logistic regression, and the odds ratio (OR) of TDP and TO were 1.042 (0.993–1.094) and 1.01 (0.985–1.035), respectively, indicating that a higher TDP and TO suggest a higher probability of mTICI failure.

Analysis of risk factors affecting the prognosis of AIS

With single-factor analysis, there were significant differences in NIHSS, MT, TDP, TOR, and TO in different groups, which affected the mRS score (Table 3). Specifically, a lower mRS score was associated with a lower NIHSS, MT, TDP, TOR, and TO ($P < 0.05$). However, the ASPECTS (Alberta Stroke

Table 1 Clinical characteristics in different subtypes of acute ischemic stroke^a

	LAA	CE	Unknown	c ² /F	P
Age	59 (51–63.5)	68 (61–71)	73 (40–76)	8.507	0.014
NIHSS	16 (14–19.5)	20 (15.5–22)	15 (14–18)	3.52	0.172
DWI-ASPECTS	7 (6–8)	7 (6–8)	7 (6–7)	0.027	0.987
TOD	230 (185–259)	190 (120–240)	180 (130–260)	4.011	0.135
TDI	40 (20–60)	55 (47.5–60)	40 (20–50)	5.999	0.051
MT	2 (1–2.5)	2 (1–2)	2 (1–4)	0.077	0.962
TDP	100 (90–125)	110 (90–120)	100 (80–120)	0.671	0.715
TO	97.6 ± 36.66	95.71 ± 42.05	110.71 ± 71.09	0.313	0.733
TOR	424.56 ± 52.32	389.38 ± 92.14	407.14 ± 68.55	1.34	0.271
IVT					
rt-PA	13 (52%)	13 (61.9%)	3 (42.9%)	0.969△	0.649△
Urokinase	12 (48%)	8 (38.1%)	4 (57.1%)		
Sex					
M	23 (92%)	15 (71.4%)	6 (85.7%)	3.325△	0.198△
F	2 (8%)	6 (28.6%)	1 (14.3%)		
Locations of occlusion					
M1	12 (48%)	12 (57.1%)	6 (85.7%)	11.63△	0.012△
ICA-T	5 (20%)	9 (42.9%)	1 (14.3%)		
Tandem	8 (32%)	0 (0%)	0 (0%)		
Rescue Treatments					
Balloon + tirofiban + stent	8 (32%)	0 (0%)	1 (14.3%)	34.038△	<0.001△
Tirofiban	3 (12%)	8 (38.1%)	2 (28.6%)		
NO	0 (0%)	11 (52.4%)	3 (42.9%)		
Balloon + tirofiban	14 (56%)	2 (9.5%)	1 (14.3%)		
sICH					
No	20 (80%)	16 (76.2%)	6 (85.7%)	0.315△	1△
Yes	5 (20%)	5 (23.8%)	1 (14.3%)		
SVS					
–	12 (48%)	5 (23.8%)	1 (14.3%)	4.012△	0.169△
+	13 (52%)	16 (76.2%)	6 (85.7%)		
Pathology					
White	13 (52%)	7 (33.3%)	2 (28.6%)	5.076	0.269
Red	5 (20%)	10 (47.6%)	2 (28.6%)		
Mixed	7 (28%)	4 (19%)	3 (42.9%)		

^aCE, DWI-ASPECTS, DWI-Alberta Stroke Program Early Computed Tomography Score; ICA-T, IVT, LAA, large-artery atherosclerosis; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; NO, rt-PA, recombinant tissue-type plasminogen activator; sICH, symptomatic intracranial hemorrhage; SVS, susceptibility vessel sign; TDI, TDP, time from door to puncture; TO, time of operation; TOD, TOR, time from onset to recanalization.

Program Early Computed Tomography Score) was significantly higher in the mRS score ≤ 2 group. The female AIS patients had a lower mRS score and improved prognosis compared to male patients. In the multivariate logistic regression analysis, the occurrence of sICH influenced the mRS score with the OR of 60.359 (1.877–1941.402) significantly. This showed that the occurrence of sICH in patients resulted in a higher risk of poor prognosis.

SVS could help identify thrombosis pathology

On a histopathological analysis, we found that the white thrombi were negatively associated with SVS, but red and mixed thrombi were common in the SVS-positive population of AIS (Table 4). They

could even go further and show the correlation of SVS negative white thrombi patients with success (mRS < 2) and sICH. It was concluded that the SVS could help in identifying the thrombosis pathology and the etiology of ischemic stroke.

Discussion

The first-line treatment for AIS with anterior circulation occlusion is MT.⁴ Thrombosis, LAA, and cardioembolism are the main causes of AIS-LVO; however, the specific pathogenesis in 40% of patients remains unclear.¹⁷ The results of this study suggest that there is no significant difference in the NIHSS score, DWI-ASPECTS score, time from onset to puncture, time from puncture to recanalization,

Table 2 Monofactor and multivariate logistic regression analysis on mTICI^a

	Monofactor		Multivariate			
	Success (N = 46)	Failure (N = 7)	P	P	OR	95% CI
Age	61.22 ± 12.76	61 ± 10.26	0.966			
NIHSS	16 (14–20)	19 (18–22)	0.112			
ASPECTS	7 (6–8)	6 (6–8)	0.49			
TOD	205.33 ± 61.38	176.57 ± 67.99	0.26			
TDI	46.5 (30–60)	90 (40–90)	0.064			
MT	2 (1–2)	3 (2–3)	0.061			
TDP	104.46 ± 21.04	138.57 ± 33.88	0.001	0.095	1.042	0.993–1.094
TO	80 (60–120)	160 (120–180)	0.011	0.439	1.010	0.985–1.035
TOR	395 (357.5–454.75)	420 (400–580)	0.299			
IVT						
rt-PA	25 (86.2%)	4 (13.8%)	1△			
Urokinase	21 (87.5%)	3 (12.5%)				
Sex						
M	38 (86.4%)	6 (13.6%)	1△			
F	8 (88.9%)	1 (11.1%)				
Stroke etiology						
LAA	22 (88%)	3 (12%)	1△			
CE	18 (85.7%)	3 (14.3%)				
Unknown	6 (85.7%)	1 (14.3%)				
Occlusion						
M1	27 (90%)	3 (10%)	0.643△			
ICA	12 (80%)	3 (20%)				
Tandem	7 (87.5%)	1 (12.5%)				
Rescue treatments						
Balloon + tirofiban + stent	8 (88.9%)	1 (11.1%)	0.743△			
Tirofiban	10 (76.9%)	3 (23.1%)				
NO	13 (92.9%)	1 (7.1%)				
Balloon + tirofiban	15 (88.2%)	2 (11.8%)				
sICH						
No	35 (83.3%)	7 (16.7%)	0.322△			
Yes	11 (100%)	0 (0%)				
SVS						
–	17 (94.4%)	1 (5.6%)	0.401△			
+	29 (82.9%)	6 (17.1%)				
Pathology						
White	19 (86.4%)	3 (13.6%)	1△			
Red	15 (88.2%)	2 (11.8%)				
Mixed	12 (85.7%)	2 (14.3%)				
DM						
0	44 (88%)	6 (12%)	0.352△			
1	2 (66.7%)	1 (33.3%)				
AF						
0	34 (89.5%)	4 (10.5%)	0.389△			
1	12 (80%)	3 (20%)				
HT						
0	31 (86.1%)	5 (13.9%)	1△			
1	15 (88.2%)	2 (11.8%)				
Smoke						
0	22 (81.5%)	5 (18.5%)	0.42△			
1	24 (92.3%)	2 (7.7%)				
Dyslipidemia						
0	41 (91.1%)	4 (8.9%)	0.061△			
1	5 (62.5%)	3 (37.5%)				
Stroke						
0	41 (87.2%)	6 (12.8%)	1△			
1	5 (83.3%)	1 (16.7%)				

Table 2 Continued.

	Monofactor		Multivariate			
	Success (N = 46)	Failure (N = 7)	P	P	OR	95% CI
CVD						
0	42 (85.7%)	7 (14.3%)	1△			
1	4 (100%)	0 (0%)				

^aAF, atrial fibrillation; ASPECTS, CE, CI, confidence interval; CVD, cardiovascular disease; DM, diabetes mellitus; F, female; HT, hypertension; ICA, IVT, LAA, large-artery atherosclerosis; M, male; MT, mechanical thrombectomy; mTICI, modified treatment in cerebral infarction; NIHSS, NIHSS, National Institutes of Health Stroke Scale; NO, OR, odds ratio; rt-PA, recombinant tissue type plasminogen activator; sICH, symptomatic intracranial hemorrhage; SVS, susceptibility vessel sign; TDI, TDP, time from door to puncture; TO, time of operation; TOD, TOR, time from onset to recanalization.

operation time, number of thrombectomy, and intravenous thrombolysis before thrombectomy. These results suggest that different TOAST subtypes are independent of the choices of therapies. Moreover, we found that age differed significantly among the 3 TOAST groups. The average age of onset of acute atherosclerotic ischemic stroke is 59 years, which is younger than AIS patients with cardioembolism and unknown reasons. Also, the

location of occlusion is significantly different. This study shows that the middle cerebral artery M1 segment occlusion is the most common, especially in the unknown etiology of AIS, and the rate is as high as 85.7%.¹⁸ Internal carotid artery T-type occlusion represents the highest proportion of AIS patients with cardioembolism. In a previous study including 640 patients with MT in the anterior circulation, the proportion of internal carotid artery

Table 3 Monofactor and multivariate logistic regression analysis on mRS^a

	Monofactor		Multivariate			
	Good (mRS ≤ 2) (N = 29)	Poor (mRS > 3) (N = 24)	P	P	OR	95% CI
Age	61 (51–67.5)	67 (52.5–75.25)	0.109			
NIHSS	15.48 ± 4.73	18.29 ± 2.87	0.011	0.103	1.562	0.913–2.672
ASPECTS	8 (6.5–9)	6 (6–7)	0.001	0.105	0.271	0.056–1.316
MT	1 (1–2)	2 (2–3.75)	0.001	4.888	4.888	0.475–50.267
TDP	100 (90–120)	120 (100–140)	0.033	0.972	0.972	0.897–1.054
TO	74.83 ± 25.69	127.29 ± 44.01	<0.001	1.022	1.022	0.965–1.082
TOR	379.55 ± 67.97	443.08 ± 64.43	0.001	1.024	1.024	0.998–1.051
Sex						
M	21 (47.7%)	23 (52.3%)	0.031	0.857	0.746	0.031–18.002
F	8 (88.9%)	1 (11.1%)			1	
Stroke etiology						
LAA	14 (56%)	11 (44%)	0.861			
CE	12 (57.1%)	9 (42.9%)				
Unknown	3 (42.9%)	4 (57.1%)				
sICH						
No	28 (66.7%)	14 (33.3%)	0.001	0.021	1	1.877–1941.402
Yes	1 (9.1%)	10 (90.9%)			60.359	
SVS						
–	10 (55.6%)	8 (44.4%)	0.93			
+	19 (54.3%)	16 (45.7%)				
Pathology						
White	12 (54.5%)	10 (45.5%)	0.477			
Red	11 (64.7%)	6 (35.3%)				
Mixed	6 (42.9%)	8 (57.1%)				

^aCE, ASPECTS, Alberta Stroke Program Early Computed Tomography Score; F, female; LAA, large-artery atherosclerosis; M, male; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage; SVS, susceptibility vessel sign; TDP, time from door to puncture; TO, time of operation; TOR, time from onset to recanalization.

Table 4 Correlation of SVS and thrombosis pathology^a

	SVS		χ^2	<i>p</i>
	–	+		
White	16 (88.9%)	6 (17.1%)	24.395△	<0.001△
Red	1 (5.6%)	16 (45.7%)		
Mixed	1 (5.6%)	13 (37.1%)		

^aSVS, susceptibility vessel sign.

T-type occlusion was 24.3% whereas that of cardioembolism was 32.9%, which is much higher than the proportion of LAA.¹⁹

Moreover, the study also finds that tandem lesions (internal carotid artery and middle cerebral artery) are more common in aortic atherosclerotic stroke with a proportion of 32%. This is probably caused by acute occlusion and embolism based on severe stenosis in the initial carotid artery and the middle cerebral artery, which suggests that we should pay attention to and actively treat the extracranial stenosis of the internal carotid artery. Furthermore, one of the severe complications of MT is symptomatic cerebral hemorrhage.²⁰ No significant differences were observed among the 3 groups of this study. However, a real-world ACTUAL study from China including 632 patients with AIS from 21 cerebrovascular disease centers reports that 16% of patients developed symptomatic cerebral hemorrhage within 72 hours of MT, and the mortality rate of patients with symptomatic cerebral hemorrhage is as high as 65.3%, which is significantly higher than that of patients without cerebral hemorrhage.²⁰

Continuous successful recanalization is an important prognostic factor related to clinical outcomes that can significantly improve the clinical prognosis of AIS patients.^{4,21} With advanced technology and continuous optimization of procedures, the recanalization rate of thrombectomy can be as high as 90%, but the proportion of patients with good prognosis after EVT treatment is only 40% to 50%. This study shows that TDP (admission–puncture time) and TO (puncture–recanalization time) are significantly associated with successful reperfusion with mTICI 2B or 3. A recent retrospective study comprising 6756 patients with anterior circulation vascular occlusion and intravascular reperfusion therapy shows that reducing the time from admission to treatment could improve the patient's prognosis and decrease the mortality rate. Consistently, our findings further confirm that reducing the time from onset to admission

and promoting intravascular reperfusion as soon as possible are critically important for AIS patients.²²

A multivariate logistic regression analysis was done to further identify the specific factors that influence the mRS score and AIS prognosis, and identify many prognostic factors that are related to clinical outcomes of AIS. Results indicated that the NIHSS score and longer recanalization time including MT, TDP, TOR, and TO are significantly lower in patients of the good prognosis group (mRS < 2), compared to that in the poor prognosis group (mRS ≥ 3). It is worth noting that male patients could develop more severe outcomes compared to female AIS patients, and this finding is consistent with previous reports.^{23,24} This study finds that decreasing the time of vascular recanalization is related to better prognosis of patients.²⁵ Moreover, sICH being the most serious complication after intravascular recanalization influences the clinical outcomes of AIS patients. Occurrence of sICH is more common in AIS patients in the poor prognosis group probably due to intravascular operations, hyperperfusion after EVT, and use of anti-thrombotic and antiplatelet drugs.

The hemoglobin in thrombus and its degraded products are common magnetic sensitive substances.²⁶ Magnetic sensitivity and SVS signs on the SWI sequence provide a more specific and sensitive method for the AIS diagnosis and subtype classification.^{27,28} This study confirms that SVS sign is more common in stroke patients with cardioembolism subtype and undetermined etiology. Furthermore, SVS-positive thrombus was found to be mainly composed of red blood cells (red thrombi). Red thrombi are usually considered as sensitive to thrombolytic agents and venous thrombolysis would bring more benefits for AIS patients with positive SVS and a higher chance of vascular recanalization.²⁹ In contrast, SVS-negative thrombus is mainly composed of blood platelets (white thrombi), which are insensitive to venous thrombolysis. Furthermore, this study finds that white thrombi are more common in the LAA group, red thrombi are more common in the CE group (47.6%), and mixed thrombi are more common in the group of unknown etiology. Similarly, recent studies have found that patients with cardioembolism have a higher proportion of red blood cells.³⁰ Compared to noncardiogenic thrombi, AIS patients with positive SVS and cardiogenic thrombi are more suitable for venous thrombolysis. This result confirms the selection of recanalization techniques for different TOAST subtypes in treating AIS, and it is also important to consider different etiology and TOAST subtypes for stroke secondary prevention.^{14,31}

However, histopathology types of thrombi did not clearly correlate with MT outcome; the procedure can benefit both the SVS positive and negative patients.

There are still some limitations to the study. First, this study is single-centered with small sample size. The selection bias should be considered when interpreting the results of this study. Second, the SVS is only determined by radiologists and further quantitative analysis of SVS is absent. Other susceptibility artifacts, such as calcium in the vessel wall or clot, could affect the SVS results. Third, other than H&E staining, more specific histopathological investigations could have been performed. More multicentered prospective studies with a larger number of patients are needed to further provide insights for AIS diagnosis and treatment.

Acknowledgments

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References

- Dargazanli C, Deverdun J, Lionnet C, Michau S, Ozluk E, Corlobé A *et al.* Quantitative susceptibility mapping in superficial hemosiderosis of the central nervous system. *J Neuroradiol* 2015;**42**(6):370–372
- Molina CA. Monitoring and imaging the clot during systemic thrombolysis in stroke patients. *Expert Rev Cardiovasc Ther* 2007;**5**(1):91–98
- Williams GR, Jiang JG, Matchar DB, Samsa GP. Incidence and occurrence of total (first-ever and recurrent) stroke. *Stroke* 1999;**30**(12):2523–2528
- Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM *et al.* Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;**387**(10029):1723–1731
- Grau AJ, Weimar C, Buggle F, Heinrich A, Goertler M, Neumaier S *et al.* Risk factors, outcome, and treatment in subtypes of ischemic stroke: the German stroke data bank. *Stroke* 2001;**32**(11):2559–2566
- Chueh JY, Wakhloo AK, Hendricks GH, Silva CF, Weaver JP, Gounis MJ. Mechanical characterization of thromboemboli in acute ischemic stroke and laboratory embolus analogs. *AJNR Am J Neuroradiol* 2011;**32**(7):1237–1244
- Mehta BP, Nogueira RG. Should clot composition affect choice of endovascular therapy? *Neurology* 2012;**79**(13 Suppl 1):S63–67
- Soize S, Batista AL, Rodriguez Regent C, Trystram D, Tisserand M, Turc G *et al.* Susceptibility vessel sign on T2* magnetic resonance imaging and recanalization results of mechanical thrombectomy with stent retrievers: a multicentre cohort study. *Eur J Neurol* 2015;**22**(6):967–972
- Kim SK, Yoon W, Heo TW, Park MS, Kang HK. Negative susceptibility vessel sign and underlying intracranial atherosclerotic stenosis in acute middle cerebral artery occlusion. *AJNR Am J Neuroradiol* 2015;**36**(7):1266–1271
- Kimura K, Sakamoto Y, Iguchi Y, Shibasaki K. Clinical and MRI scale to predict very poor outcome in tissue plasminogen activator patients. *Eur Neurol* 2011;**65**(5):291–295
- Bourcier R, Volpi S, Guyomarch B, Daumas-Duport B, Lintia-Gaultier A, Papagiannaki C *et al.* Susceptibility vessel sign on MRI predicts favorable clinical outcome in patients with anterior circulation acute stroke treated with mechanical thrombectomy. *AJNR Am J Neuroradiol* 2015;**36**(12):2346–2353
- Amort M, Fluri F, Weisskopf F, Gensicke H, Bonati LH, Lyrer PA *et al.* Etiological classifications of transient ischemic attacks: subtype classification by TOAST, CCS and ASCO—a pilot study. *Cerebrovasc Dis* 2012;**33**(6):508–516
- Paradowski B, Maciejak A. TOAST classification of subtypes of ischaemic stroke: diagnostic and therapeutic procedures in stroke. A four-year observation. *Cerebrovasc Dis* 2005;**20**(5):319–324
- Cho KH, Kim JS, Kwon SU, Cho AH, Kang DW. Significance of susceptibility vessel sign on T2*-weighted gradient echo imaging for identification of stroke subtypes. *Stroke* 2005;**36**(11):2379–2383
- Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL *et al.* Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. *Stroke* 2013;**44**(9):2650–2663
- Marder VJ, Chute DJ, Starkman S, Abolian AM, Kidwell C, Liebeskind D *et al.* Analysis of thrombi retrieved from cerebral arteries of patients with acute ischemic stroke. *Stroke* 2006;**37**(8):2086–2093
- Ekizoğlu E. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *Turk J Neurol* 2016;**22**:35–36.
- Giray S, Ozdemir O, Baş DF, İnanç Y, Arlier Z, Kocatürk O. Does stroke etiology play a role in predicting outcome of acute stroke patients who underwent endovascular treatment with stent retrievers? *J Neurol Sci* 2017;**372**:104–109

19. Sun B, Shi Z, Pu J, Yang S, Wang H, Yang D *et al.* Effects of mechanical thrombectomy for acute stroke patients with etiology of large artery atherosclerosis. *J Neurol Sci* 2019;**396**: 178–183
20. Hao Y, Yang D, Wang H, Zi W, Zhang M, Geng Y *et al.* Predictors for symptomatic intracranial hemorrhage after endovascular treatment of acute ischemic stroke. *Stroke* 2017;**48**(5): 1203–1209
21. Jahan R, Saver JL, Schwamm LH, Fonarow GC, Liang L, Matsouaka RA *et al.* Association between time to treatment with endovascular reperfusion therapy and outcomes in patients with acute ischemic stroke treated in clinical practice. *JAMA* 2019;**322**(3):252–263
22. Hassan AE, Shariff U, Saver JL, Goyal M, Liebeskind D, Jahan R *et al.* Impact of procedural time on clinical and angiographic outcomes in patients with acute ischemic stroke receiving endovascular treatment. *J Neurointerv Surg* 2019; **11**(10):984–988
23. Madsen TE, DeCrose-Movson E, Hemendinger M, McTaggart RA, Yaghi S, Cutting S *et al.* Sex differences in 90-day outcomes after mechanical thrombectomy for acute ischemic stroke. *J Neurointerv Surg* 2019;**11**(3):221–225
24. Sheth SA, Lee S, Warach SJ, Gralla J, Jahan R, Goyal M *et al.* Sex differences in outcome after endovascular stroke therapy for acute ischemic stroke. *Stroke* 2019;**50**(9):2420–2427
25. Chalos V, de Ridder IR, Lingsma HF, Brown S, van Oostenbrugge RJ, Goyal M *et al.* Does sex modify the effect of endovascular treatment for ischemic stroke? *Stroke* 2019;**50**(9): 2413–2419
26. Chalela JA, Haymore JB, Ezzeddine MA, Davis LA, Warach S. The hypointense MCA sign. *Neurology* 2002;**58**(10):1470
27. Kim SK, Yoon W, Kim TS, Kim HS, Heo TW, Park MS. Histologic analysis of retrieved clots in acute ischemic stroke: correlation with stroke etiology and gradient-echo MRI. *AJNR Am J Neuroradiol* 2015;**36**(9):1756–1762
28. Niesten JM, van der Schaaf IC, van Dam L, Vink A, Vos JA, Schonewille WJ *et al.* Histopathologic composition of cerebral thrombi of acute stroke patients is correlated with stroke subtype and thrombus attenuation. *PLoS One* 2014;**9**(2):e88882
29. Yamamoto N, Satomi J, Harada M, Izumi Y, Nagahiro S, Kaji R. Is the susceptibility vessel sign on 3-Tesla magnetic resonance T2*-weighted imaging a useful tool to predict recanalization in intravenous tissue plasminogen activator? *Clin Neuroradiol* 2016;**26**(3):317–323
30. Almekhlafi MA, Hu WY, Hill MD, Auer RN. Calcification and endothelialization of thrombi in acute stroke. *Ann Neurol* 2008;**64**(3):344–348
31. Fitzgerald S, Mereuta OM, Doyle KM, Dai D, Kadirvel R, Kallmes DF *et al.* Correlation of imaging and histopathology of thrombi in acute ischemic stroke with etiology and outcome. *J Neurosurg Sci* 2019;**63**(3):292–300