CT-based Higher Thrombus Density is associated with Secondary Embolism during Mechanical Thrombectomy: A Preliminary Observation

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Background: Secondary embolism (SE) during mechanical thrombectomy (MT) for acute ischemic stroke (AIS) is the main reason for incomplete recanalization, while its risk factors are largely unknown. This study addresses a potential relationship between thrombus density on preinterventional computed tomography (CT) and the occurrence of SE. *Methods:* We reviewed anterior circulation AIS patients who underwent MT from July 2015 to January 2019 in our center. Thrombus density was measured in Hounsfield Units (HU) on 1-mm and 5-mm preinterventional nonenhanced CT (NECT). Thrombus density, baseline characteristics, procedural, and clinical outcomes were compared between patients with SE and those without SE. Logistic regression was conducted to identified potential risk factors of SE. *Results:* Sixty-four consecutively patients were included, of whom SE was identified in 16 (25.0%) patients. Compared with those without SE, patients with SE showed a higher thrombus density on both 1-mm (72.85 versus 64.28, $P = .005$) and 5-mm NECT (60.31 versus 49.71, $P < .001$), a higher proportion of atrial fibrillation (75.0% versus 45.8%, $P = .043$), a lower clot burden score (.5 versus 6.0, $P = .029$), and a higher proportion of front-line contact aspiration strategy (50.0% versus 16.7%, $P = .020$). Multivariate regression analysis showed that only thrombus density was the independent predictor of SE (for the model including HU values on 1-mm NECT, OR 1.11, 95%CI 1.01-1.23, $P = .029$; for the model including HU values on 5-mm NECT, OR 1.09, 95%CI 1.02-1.17, $P = .018$). *Conclusions:* Higher thrombus density was the independent predictor for SE. Further studies are needed to investigate its role in the optimization of thrombectomy strategy.

Key Words: Acute ischemic stroke—mechanical thrombectomy—secondary embolism—CT—thrombus density

Introduction

Mechanical thrombectomy (MT) has become the standard treatment for acute ischemic stroke (AIS) with large vessel occlusion.[1] Most patients could achieve so-called "successful recanalization" (modified Thrombolysis in Cerebral Infarction [mTICI] 2b-3), while only about half of them could get favorable outcomes (modified Rankin Scale [mRS] score 0-2),[2-7] partially because the poorer outcome of incomplete recanalization (mTICI 2b) compared with complete recanalization (mTICI 2c-3).[8,9]

Secondary embolism (SE) is probably the most common reason for incomplete recanalization during MT,[9] which could increase the number of maneuvers and the risk of hemorrhagic transformation, therefore lead to a more unsatisfactory outcome. Specific devices and combination techniques,

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Received March 20, 2019; revision received June 14, 2019; accepted July 21, 2019.

Financial Disclosure: This work was supported by the Beijing Hospital Clinical Research 121 Project grant number (121-2016006).

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1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104311

such as balloon guiding catheter (BGC), EmboTrap thrombectomy system and stent retriever assisted vacuum-locked extraction (SAVE) technique, might reduce the incidence of SE.[10-16] However, stent retriever (SR) and contact aspiration (CA) are still front-line strategies in most cases; routine use of these specific devices or techniques for prevention of SE might be not cost-efficient. Therefore, predicting this adverse event preoperatively and choosing optimal strategies accordingly seem to be quite essential.[12,17,18]

As reported, the histologic characteristics of thrombi could determine its fragility, therefore impact the incidence of SE during MT.[17,18] Although we could not obtain specific histopathologic features of thrombus before MT, several studies have demonstrated the significant association between histologic components and thrombus density on nonenhanced computed tomography (NECT).[18-20] Hence, our aim was to detect the potential correlation between thrombus density on preinterventional NECT and incidence of SE for patients with anterior circulation AIS.

Methods and Materials

Patients Selection and Treatment Protocol

This was a retrospective observational study, with most clinical data collected prospectively. We reviewed consecutive AIS patients with large vessel occlusion in anterior circulation (including intracranial internal carotid artery [ICA], middle cerebral artery, and anterior cerebral artery) who underwent MT in our center (Beijing Hospital, National Center of Gerontology) from July 2015 to January 2019. Patients who were suspected suffering from AIS underwent at least NECT or mostly one-stop CT (including NECT, CT angiography, CT perfusion). There was no specific restriction on the National Institutes of Health Stroke Scale (NIHSS), Alberta Stroke Programme Early CT Score (ASPECTS), and duration from onset to treatment. The endovascular treatments (EVTs) indication was evaluated by the attending neurointerventionalist (J.L. or P.Q.).

In our center, patients eligible for intravenous thrombolysis (IVT) treatment were treated with .9 mg/kg of tPA (tissue-type plasminogen activator). All the EVTs were mostly performed under conscious sedation, and the BGCs were not used. Three kinds of front-line strategies were usually adopted, including SR (Solitaire [Medtronic, Minneapolis, MN]), CA (ACE [Penumbra, Alameda, CA]), and a combination of SR and aspiration (Solumbra). If the front-line strategy did not work for a maximum of 3 passes, the rescue therapy including Solumbra, percutaneous transluminal angioplasty and/or stenting might be adopted according to the judgment of the operator.

Baseline Characteristics

We recorded the following baseline characteristics for each patient: demographic features (age and gender), atrial fibrillation (AF), hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, stroke or transient ischemic attacks history, smoking history, current use of anticoagulant, and antiplatelet drugs; imaging information including baseline ASPECTS, clot burden score (CBS), thrombus density on 1-mm and 5-mm reconstructed NECT; stroke features including NIHSS on admission, duration from onset (defined as last seen well time) to puncture, preoperative IVT, lesion location, and stroke etiology.

CBS was scored according to Tan et al based on maximum intensity projection.[21] The lesion location was classified as intracranial ICA, the first segment of the middle cerebral artery (M1), tandem lesion, and distal part. The distal artery was defined as the second or third segment of the middle cerebral artery (M2/M3) or anterior cerebral artery. Stroke etiology was categorized according to Trial of Org 10172 in Acute Stroke Treatment classification.[22]

Imaging Protocol and Thrombus Density Measurement

All patients included underwent NECT on admission, and most of them additionally underwent one-stop CT using a 320 × .5 mm detector rows CT scanner (Aquilion ONE, Canon Medical Systems). The parameters for NECT were as follows: 80 kV, 200 mAs, and 5-mm reconstructed slice thickness; while the one-stop scanning parameters were as follows: 80 kV, 100 mAs, and 1-mm reconstructed slice thickness. Contrast allergy was the exclusion criteria for one-stop CT. As for patients with a clinical history of renal hypofunction, we would evaluate the risk of contrast related acute kidney injury and the benefit of acute stroke treatment carefully.

Measurement of thrombus density was conducted by 2 trained raters (GFY and RYC) independently. First, the thrombus location was determined by contrast-enhanced CT and cerebral angiography during MT. Then, we would draw round region of interest (ROI) accounting for about half to two-thirds of the vascular area, and placed the round region of interests in the center of the artery approximately 2 mm behind the occlusion site, as well as the corresponding position of the contralateral artery. The mean Hounsfield Unit (HU) value of thrombus and the contralateral artery on 1-mm and 5-mm NECT were recorded, respectively. The inter-rater reliability of measurements was evaluated by the interclass correlation coefficient (ICC). The ICC for HU value of thrombus and contralateral artery on 1-mm NECT was .902 and .852, respectively; while the ICC for HU value of thrombus and contralateral artery on 5-mm NECT was .935 and .912, respectively; these results showed high inter-rater agreement (all>.75). Besides, we calculated the relative HU (rHU) (thrombus density/contralateral artery density) and ΔHU (thrombus density-contralateral artery density).

Procedural and Clinical Outcomes

SE was identified when an intracranial artery was patency on the preinterventional angiogram or preoperative CTA, while occluded during or after intervention procedure, including both visible embolisms in a new-territory and a distal part of the primary occluded vessel.

The following procedural information was collected: the front-line treatment strategies, whether switched to other treatment strategies, the number of maneuvers, recanalization outcomes, duration from puncture to reperfusion, duration from onset to reperfusion, and procedure time. The successful and complete recanalization was defined as mTICI 2b-3 and mTICI 3, respectively. The clinical outcomes were evaluated by the mRS score after 90 days from onset, and functional independence or favorable outcome was defined as mRS score 0-2. The hemorrhagic events were classified according to the Heidelberg Bleeding Classification.[23]

Statistical Analysis

AIS patients included were assigned to SE group or no SE group; and the differences in HU value of thrombus, baseline characteristics, procedural, and clinical outcomes were examined between the 2 groups. Normality test was conducted for continuous variables. The continuous variables conforming to normal distribution would be expressed as mean ± standard deviation (SD), and student *t* test would be used to detect the differences. The median (interquartile range, IQR) and Mann-Whitney *U* test were used for continuous variables inconsistent with normal distribution. For categorical data, it was expressed as count (percent), and chi-square test was used to detect the difference. Univariate and multivariate logistic regression was also performed to detect the risk factors of SE. All tests used α-level of .05 for significance. All statistical analysis was performed with SPSS software (version 23.0; SPSS, Chicago, IL).

Results

Baseline Characteristics

A total of 64 patients (median age, 75 years; 34 male) were included in the present study. The baseline characteristics were shown in Table 1. The mean NHISS on admission was 15.07 (SD, 6.47); the median baseline ASPECTS was 8 (IQR, 5-8); and median CBS was 6 (IQR, 0-8). The proportion for each etiology subtype was as follows: cardiogenic embolism in 36 patients (56.3%), large artery atherosclerosis in 15 patients (23.4%), other determined causes in 4 patients (6.3%), and cryptogenic stroke in 9 patients (14.1%). The proportion for each lesion location was as follows: ICA in 23 patients (35.9%), M1 in 24 patients (37.5%), tandem lesion in 5 patients (7.8%), and distal part in 12 patients (18.8%). As for thrombus density, the mean HU, rHU, and ΔHU on 1-mm NECT (n = 52) was 66.75 (±10.17), 1.14 (±17) and 8.04 (±9.34), respectively; while the mean HU, rHU, and ΔHU on 5-mm NECT (n = 64) was 52.36 (±10.66), 1.10 (±.17), and 4.47 (±7.68), respectively.

SE was identified in 16 (25.0%) of the 64 patients. Compared with no SE group, patients of SE group showed a higher proportion of AF (75.0% versus 45.8%, $P = .043$), a lower CBS (.5 versus 6.0, $P = .029$), a higher thrombus density in HU (72.85 versus 64.28, $P = .005$), rHU (1.22 versus 1.11, $P = .033$), and ΔHU (12.31 versus 6.31, $P = .035$) on 1-mm reconstructed NECT, as well as higher HU (60.31 versus 49.71, $P < .001$), rHU (1.20 versus 1.07, $P = .007$), and ΔHU (9.63 versus 2.75, $P = 001$) on 5-mm reconstructed NECT. For the other baseline characteristics, no significant difference was observed between these 2 groups.

Procedural and Clinical Outcomes

The procedural and clinical outcomes were shown in Table 2. Among 64 patients, 23 patients (35.9%) received front-line SR; 16 patients (25.0%) received front-line CA; 20 patients (31.3%) underwent front-line Solumbra and the other 5 patients (7.8%) underwent front-line percutaneous transluminal angioplasty and/or stenting. Nineteen patients (29.2%) were switched to other strategies due to failure of front-line strategy; the median maneuvers of thrombectomy was 2 (IQR, 1-3); the median procedure duration was 130 minutes (IQR, 85.5-190.50). Finally, 54 patients (84.4%) got successful recanalization and 46 patients (71.9%) achieved complete recanalization; any hemorrhage events were observed in 27 patients (42.2%), in which 17 (26.6%) was parenchymal hemorrhage. After 90 days from onset, 32 (50.0%) patients achieved favorable outcomes, and 14 patients (21.9%) were dead.

The incidence of SE showed a significant difference among front-line strategies ($P = .045$). Because of the limited sample size, dichotomy was made for treatment strategy according to whether adopted front-line CA technique or not. In the SE group, more patients underwent front-line CA technique (50.0% versus 16.7%, $P = .020$) compared with no SE group. There was no significant difference in other procedural information, including whether switched to other strategies, the number of maneuvers, reperfusion time, and recanalization outcomes. Moreover, no significant difference was shown in all the clinical outcomes such as favorable outcome, any hemorrhage event, parenchymal hemorrhage, and death.

SE Predictors

The results of logistic regression for prediction of SE were shown in Table 3. The univariable analysis suggested that AF (OR 3.55, 95%CI 1.00-12.58, $P = .050$), CBS (OR 0.83, 95%CI .70-.98, $P = .031$), front-line CA strategy (OR 5.00, 95%CI 1.45-17.27, $P = .011$), HU on 1-mm (OR 1.13, 95%CI 1.03-1.24, $P = .008$), rHU on 1-mm (OR 86.02, 95%CI 1.10-6759.70, $P = .045$), ΔHU on 1-mm (OR 1.09, 95%CI 1.00-1.18, $P = .045$), HU on 5-mm (OR 1.12, 95%CI 1.04-1.20, $P = .002$), rHU on

Table 1. *Baseline characteristics*

	All patients (n = 64)	SE (n = 16)	No SE (n = 48)	*P* value
Age, y	75 (62-81)	72 (66.5-79.5)	76 (61-81.75)	.721
Sex, male	32 (50.0%)	7 (43.8%)	25 (52.1%)	.564
Atrial fibrillation	34 (53.1%)	12 (75.0%)	22 (45.8%)	.043
Hypertension	50 (78.1%)	12 (75.0%)	38 (79.2%)	1
Diabetes mellitus	27 (42.2%)	4 (25.0%)	23 (47.9%)	.108
Dyslipidemia	31 (48.4%)	9 (56.3%)	22 (45.8%)	.470
Stroke or TIA history	19 (39.7%)	5 (31.3%)	14 (29.2%)	1
Smoking history	22 (34.4%)	4 (25.0%)	18 (37.5%)	.362
Coronary artery disease	28 (43.8%)	8 (50.0%)	20 (41.7%)	.561
Current anticoagulant use	4 (6.3%)	0 (0%)	4 (8.3%)	.551
Current antiplatelet use	29 (45.3%)	10 (62.5%)	21 (39.6%)	.111
Stroke etiology				.726
CE	36 (56.3%)	11 (68.8%)	25 (52.1%)	
LAA	15 (23.4%)	3 (18.8%)	12 (25.0%)	
Other determined	4 (6.3%)	0 (0%)	4 (8.3%)	
Cryptogenic	9 (14.1%)	2 (12.5%)	7 (14.6%)	
Thrombus location				.371
ICA	23 (35.9%)	8 (50.0%)	15 (31.3%)	
M1	24 (37.5%)	4 (25.0%)	20 (41.7%)	
Tandem	5 (7.8%)	2 (12.5%)	3 (6.3%)	
Distal	12 (18.8%)	2 (12.5%)	10 (20.8%)	
Preoperative IVT	21 (32.8%)	4 (25.0%)	17 (35.4%)	.442
NIHSS	15.07 ± 6.47 (n = 58)	15.75 ± 5.62 (n = 16)	14.81 ± 6.81 (n = 42)	.625
Duration from onset to puncture, min	268 (177.5-418.75)	214 (169.75-288)	278.5 (184.5-455.0)	.182
ASPECTS	8 (5-8)	6 (4.25-8)	8 (5-8)	.134
Clot burden score	6 (0-8)	.5 (0-6)	6 (1-8)	.029
Thrombus density on 1-mm NECT	n = 52	n = 15	n = 37	
HU	66.75 ± 10.17	72.85 ± 8.88	64.28 ± 9.70	.005
rHU	1.14 ± .17	1.22 ± .19	1.11 ± .16	.033
ΔHU	8.04 ± 9.34	12.31 ± 9.86	6.31 ± 8.67	.035
Thrombus density on 5-mm NECT				
HU	52.36 ± 10.66	60.31 ± 11.33	49.71 ± 9.10	<001
rHU	1.10 ± .17	1.20 ± .18	1.07 ± .16	.007
ΔHU	4.47 ± 7.68	9.63 ± 8.41	2.75 ± 6.66	.001

Abbreviations: SE, secondary embolism; TIA, transient ischemic attacks; CE, cardiogenic embolism; LAA, large artery atherosclerosis; NHISS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Programme Early CT Score; IVT intravenous thrombolysis; NECT, non-enhanced computed tomography; HU, Hounsfield Unit.

Results are shown as mean ± SD, median (IQR) or number (%).

5-mm (OR 93.27, 95%CI 2.57-3386.99, P = .013), and ΔHU on 5-mm NECT (OR 1.14, 95%CI 1.04-1.25, P = 005) could be predictive factors of SE during MT for AIS patients.

Because of the limited positive cases, only CBS, front-line CA technique and thrombus density were included in multivariate analysis. As significant collinearity was observed among mean HU, rHU, and ΔHU both on 1-mm and 5-mm NECT, mean HU value of thrombus on 1-mm and 5-mm was included in multivariate regression, respectively. In multivariate model 1, only the thrombus density on 1-mm NECT was an independent predictor for SE (OR 1.11, 95%CI 1.01-1.23, P = 029). Similarly, only the thrombus density on 5-mm NECT showed an independent predictive value for SE in multivariate model 2 (OR 1.09, 95%CI 1.02-1.17, P = 018).

Discussion

For patients with anterior circulation AIS, our results suggested that the incidence of SE was 25.0% during MT. Compared with no SE group, patients with SE showed a higher thrombus density on NECT, a lower CBS, a higher proportion of AF, and a higher proportion of front-line CA strategy. In multivariate analysis, only higher thrombus density was the independent risk factor for SE. The clinical outcomes showed no significant difference between these 2 groups, which might be limited by our sample size.

The fragility of thrombus might be a potential mechanism for SE, which was determined by the histologic features of the thrombus. After histopathologic analysis

Table 2. *Procedural and clinical outcomes*

	All patients (n = 64)	SE (n = 16)	No SE (n = 48)	*P* value
Front-line strategy				.045
PTA/S	5 (7.8%)	0 (0%)	5 (10.4%)	
SR	23 (35.9%)	3 (18.8%)	20 (41.7%)	
CA	16 (25.0%)	8 (50.0%)	8 (16.7%)	.020
Solumbra	20 (31.3%)	5 (31.3%)	15 (31.3%)	
Switched to other strategy	19 (29.2%)	4 (25.0%)	15 (30.6%)	.911
Number of maneuvers	2 (1-3) (n = 58)	2 (1-3) (n = 15)	1 (1-3) (n = 43)	.255
Duration from puncture to reperfusion, min	75 (57-125.25) (n = 58)	67.50 (57.75-104.75) (n = 16)	87 (56.5-147) (n = 42)	.334
Procedure duration, min	130 (85.5-190.50)	127.5 (95.25-165.75)	135 (82.50-207.25)	.846
Duration from onset to reperfusion, min	348 (250-536.75) (n = 58)	293 (240.25-381.50) (n = 16)	360.5 (252.5-583.5) (n = 42)	.172
Successful recanalization	54 (84.4%)	15 (93.8%)	39 (81.3%)	.427
Complete recanalization	46 (71.9%)	11 (68.8%)	35 (72.9%)	1
Favorable outcomes	32 (50.0%)	8 (50.0%)	24 (50.0%)	1
Any hemorrhage events	27 (42.2%)	8 (50.0%)	19 (39.6%)	.465
Parenchymal hemorrhage	17 (26.6%)	5 (31.3%)	12 (25.0%)	.870
Death	14 (21.9%)	3 (18.8%)	11 (22.9%)	1

Abbreviations: SE, secondary embolism; PTA/S, percutaneous transluminal angioplasty and/or stenting; SR, stent retriever; CA, contact aspiration; Solumbra, a combination of stent retriever and aspiration.

Results are shown as median (IQR) or number (%).

Table 3. *Logistic regression for prediction of secondary embolism*

Variables	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI) Model 1	*P* value	Multivariate OR (95% CI) Model 2	*P* value
Age, per 1-y increase	1.02 (.97-1.07)	.444				
Atrial fibrillation	3.55 (1.00-12.58)	.050				
CBS, per 1-score increase	.83 (.70-.98)	.031	.89 (.72-1.11)	.305	.92 (.76-1.12)	.425
Frontline CA	5.00 (1.45-17.27)	.011	3.60 (.73-17.81)	.116	2.93 (.71-12.06)	.136
HU on 1-mm	1.13 (1.03-1.24)	.008	1.11 (1.01-1.23)	.029		
rHU on 1-mm	86.02 (1.10-6759.70)	.045				
ΔHU on 1-mm	1.09 (1.00-1.18)	.045				
HU on 5-mm	1.12 (1.04-1.20)	.002			1.09 (1.02-1.17)	.018
rHU on 5-mm	93.27 (2.57-3386.99)	.013				
ΔHU on 5-mm	1.14 (1.04-1.25)	.005				

Abbreviations: OR, odds ratio; CI, confidence interval; CBS, clot burden score; HU, Hounsfield Unit.

of thrombi in 85 AIS patients, Kaesmacher et al found an association between erythrocyte composition and periprocedural thrombus fragmentation, though it was not a significant factor in multivariable regression.[17] Several studies have demonstrated the significant positive correlation between thrombus density on NECT and the RBC composition,[18-20] which could provide a foundation for prediction of histologic characteristics before MT. By analyzing histopathology and imaging information for 180 cases of AIS patients, Sporns et al confirmed the positive association between erythrocyte composition and rHU value of thrombus.[18] However, they drew an opposite conclusion showing clot with less RBC composition (lower rHU) were prone to occur SE. Given the relationship between histopathology and imaging, our results were closer to Kaesmacher et al, suggesting the correlation between higher thrombus density and the increased risk of SE. Through an in vitro experiment regarding the role of erythrocytes for fibrin structure and clot mechanical properties, Gersh et al found that a higher RBC proportion could increase the ratio of viscous modulus to elastic modulus of the clot, and alter the fibers arrangement around the cells,[24] which might be an underlying mechanism for the fragility of RBC-rich thrombus.

Treatment strategy might be another important factor impacting SE. Our results showed that patients who underwent front-line CA technique were prone to occur

SE (50% versus 16.7%, $P = .020$) compared with other front-line strategies. In the contact aspiration vs stent retriever for successful revascularization (ASTER) trial, front-line CA showed a comparable incidence of new territory embolism (3.7% versus 2.7%) with front-line SR.[7] After reviewing 97 cases of AIS patients, Maegerlein et al also found no significant difference of new territory embolism between CA and SR (2.8% versus 8.2%).[25] It seemed that the risks of SE between front-line SR and CA were comparable, but these 2 studies only reported the embolism in new territory, while we include embolisms both in a new-territory and a distal part of the primary occluded vessel. Although there is no standard definition for SE, our definition might be more comprehensive. Recently, Yeo et al reviewed relevant articles and displayed both new territory embolism and distal embolism respectively. As suggested, the proportion of SE events was approximately 10%-48% during aspiration technique, while the incidence was about 5.6%-23% during SR.[12] It seemed that a higher incidence of SE was in aspiration group compared with SR, but still less research was based on the aspiration technique, and more studies should be made.

Apart from histologic characteristics and treatment strategy, several other factors were also reported to be associated with SE. In the present study, lower CBS could increase the risk of SE, which is reasonable because large clots might be difficult to retrieve through 1 pass. Besides, it was reported that preoperative IVT could increase the risk of distal embolization,[12,17,26] as thrombolysis might reduce thrombotic stability and increase fragility. However, this association was not observed in this study. Similarly, the current use of anticoagulant and antiplatelet drugs also showed no significant difference between the 2 groups in our study. In addition, posterior circulation occlusion was reported as an independent risk factor for SE, which might be due to the difficulty in proximal flow arrest.[12] More effort should be made for the prediction of SE, which could help optimize thrombectomy strategy.

As reported, specific devices and techniques could effectively prevent SE to some extent. The BGC has been valid reduce the distal emboli by proximal flow control in vitro simulation experiment,[27,28] and recent meta-analysis also demonstrated that using BGC during MT could significantly improve the proportion of first-pass recanalization and complete recanalization compared with no BGC group.[29] Besides, the EmboTrap thrombectomy system, specifically designed for prevention of distal embolism during MT, could also reduce fragmentation during MT compared with the solitaire system in vitro. As reported, the whole SE events of EmboTrap were 12% in the anterior circulation and 7.8% in the posterior circulation, while its efficiency was still lack of comparison with other thrombectomy devices.[12] Furthermore, several new techniques have been reported to be able to reduce SE events, such as SAVE,[14] CAPTIVE[15], and retrograde semiretrieval technique.[16] More studies should be performed to confirm the effectiveness and safety of these devices or techniques. Currently, SR and CA were still the front-line strategies in most stroke centers; the risk factors for SE might be an implication of adopting these specific treatment modalities.

This study has several limitations. First, the retrospective nature and the limited sample size reduced the credibility of our conclusion. Second, we did not distinguish SE in new-territory or a distal part of the primary occluded vessel, because the similar underlying mechanism could be attributed to the fragility of thrombus. Third, some patients did not undergo one-stop CT, so the thrombus density on 1-mm reconstructed NECT was not available. Fourth, there was no specific restriction to baseline ASPECTS and NIHSS for EVTs, which would reduce our comparability with other studies, yet might be closer to real-world research. Fifth, there was no standard protocol for thrombectomy in our center, and different front-line strategies were adopted in the same period. Sixth, we did not calculate a cut-off for HU value for prediction of SE events, because the CT scanners and the parameters might be different from center to center and lack of comparability. Seventh, the variation of the circle of Willis could impact the blood flow and pressure at the occluded artery, which might influence the occurrence of SE to some extent and could also be a confounding factor. We did not analyze it in the present study, yet we would further study this issue in the future. Finally, our imaging information was lack of verification of histologic outcomes, which might reduce the persuasiveness of our conclusion, but we are collecting thrombus specimens for analysis in the future.

Conclusion

For patients with anterior circulation AIS, higher thrombus density on NECT, lower CBS, AF, and front-line CA technique might be risk factors for SE. The multivariate analysis suggested that only higher thrombus density was the independent predictor for SE, which could be an implication of adopting specific treatment strategies for prevention of this adverse event. More studies with high quality are needed for prediction and prevention of SE events during MT, therefore further improving the clinical outcomes of AIS patients.

Author Contribution

G.F.Y. designed the study, measured the thrombus density, collected clinical data, made telephone follow-up, analyzed and interpreted data, wrote and revised the manuscript. R.Y.C. measured the thrombus density, collected clinical data, made telephone follow-up, and analyzed data. J.L. designed the study, confirmed the procedural information, made outpatient follow-up, revised the manuscript. P.Q. confirmed the procedural data, made outpatient follow-up, participated in data analysis and interpretation. J.C. monitored the acquisition of imaging information, revised the manuscript.

D.M.W. designed the study, monitored the study, and revised the manuscript. He is the guarantor.

Acknowledgments

We thank the Department of Neurology, Radiology, and Anesthesiology of Beijing Hospital for the diagnosis and treatment of patients with acute ischemic stroke.

Conflict of Interest

None declared.

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