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Original Article

Types of intraparenchymal hematoma as a predictor after revascularization in patients with anterior circulation acute ischemic stroke

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ABSTRACT

Background: Intracranial hemorrhage after revascularization for acute ischemic stroke is associated with poor outcomes. Few reports have examined the relationship between parenchymal hematoma after revascularization and clinical outcomes. This retrospective study aimed to investigate the risk factors and clinical outcomes of parenchymal hematoma after revascularization for acute ischemic stroke.

Methods: Ninety-three patients underwent revascularization for anterior circulation acute ischemic stroke. Patient characteristics and clinical outcomes were compared between patients with and without post procedural parenchymal hematoma using the following parameters: age, sex, occlusion location, presence of atrial fibrillation, diffusion-weighted imaging-Alberta stroke program early computed tomography score (DWI-ASPECTS), National Institute of Health Stroke Scale (NIHSS) score, recombinant tissue plasminogen activator, thrombolysis in cerebral infarction > 2b, door-to-puncture time, onset-to-recanalization time, number of passes, and modified Rankin Scale scores.

Results: Parenchymal hematomas were not significantly correlated with age, sex, occlusion location, atrial fibrillation, DWI-ASPECTS, NIHSS score, recombinant tissue plasminogen activator, thrombolysis in cerebral infarction > 2b, door-to-puncture time, onset-to-recanalization time, and number of passes, but were significantly correlated with poor clinical outcomes ($P = 0.001$) and absence of the anterior communicating artery evaluated using pre procedural time-of-flight magnetic resonance angiography ($P = 0.03$).

Conclusion: Parenchymal hematoma was a predictor of poor outcomes. In particular, the absence of the anterior communicating artery on pre procedural time-of-flight magnetic resonance angiography is a potential risk factor for parenchymal hematoma after revascularization for anterior circulation acute ischemic stroke.

Keywords: Cerebral hemorrhage, Cerebral revascularization, Cerebrovascular accident, Stroke, Thrombectomy

INTRODUCTION

Rapid, safe, and effective endovascular thrombectomy (EVT) to restore blood flow and ameliorate functional outcomes remain the primary goal of acute ischemic stroke (AIS) management,[7] and treatment outcomes depend on the age, reperfusion grade, and site of vessel occlusion.[1,3] Intracranial hemorrhage (ICH) after revascularization for AIS is one of the factors associated with poor outcomes.[15] However, the relationship between hematoma subtypes after revascularization and clinical outcomes remains controversial.

Collateral circulation is considered an important factor in determining the prognosis and response in recanalization therapy for AIS. Collateral circulation has been evaluated using computed tomography (CT) angiography, CT perfusion,[18] arterial spin labeling, and perfusion magnetic resonance imaging (MRI).[16] It also appears that the presence of the anterior communicating artery (A-com) evaluated by time-of-flight/magnetic resonance angiography (TOF/MRA) leads to good revascularization outcomes for anterior circulation AIS.[14] Based on the results of this literature review,[14] we speculated that the absence (including anatomical "hypoplasia") of A-com on TOF/MRA could be a factor in poor collateral circulation.

The aim of this retrospective study was to investigate the risk factors, including A-com evaluated by TOF/MRA, and clinical outcomes of the hemorrhagic complication patterns after revascularization for anterior circulation AIS at our hospital.

MATERIALS AND METHODS

This single-center retrospective cohort study included 93 patients who underwent revascularization for anterior circulation AIS at our hospital between April 2014 and September 2019. We investigated on the anterior circulation lesions, including intracranial internal carotid artery (ICA), middle cerebral artery (MCA), and T occlusions.

All patients underwent EVT with a stent retriever and direct thromboaspiration. Recombinant tissue plasminogen activator (rt-PA) was administered before EVT in applicable cases, and an 8/9-French guiding balloon catheter was navigated into the ICA using the femoral approach. Thereafter, a microcatheter was passed through the occlusion site using a microguidewire through the aspiration catheter. The stent retriever, with a diameter of 4.0–6.0 mm, was retrieved during thromboaspiration with the aspiration catheter after temporary blockade of ICA flow. The postprocedural revascularization grade was evaluated by assigning the thrombolysis in cerebral infarction (TICI) grade.[21] The door-to-puncture (D2P) time and onset-to-recanalization (O2R) time were also recorded.

All patients underwent DW MRI before and after EVT as part of the evaluation for new ischemic lesions, and the presence or absence of the A-com was simultaneously recorded using TOF/MRA by two neurosurgeons (Y. M. and K. N.). In this study, the presence or absence of A-com is visually assessed by TOF/MRA signal intensity, which is a functional assessment of blood flow. The "presence" of A-com is defined when signal intensity is visually present on TOF/MRA, and the "absence" of A-com is defined when is absent. In other words, the absence of A-com includes the cases where the A-com is anatomically hypoplastic. Moreover, the DW Alberta Stroke Program Early CT Score (DW-ASPECTS) was used to assess the degree of the ischemia, and periprocedural neurologic findings were evaluated using the National Institutes of Health Stroke Scale (NIHSS).

ICH was noted using CT within a day after EVT. The Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) criteria were used to classify ICH [Table 1].[20] Symptomatic ICH (SICH) was recorded when the NIHSS score increased by >4 points, and clinical outcomes were evaluated using the modified Rankin Scale (mRS) on discharge. An mRS score of 0–2 was defined as a good outcome, whereas scores of 3–6 were regarded as poor outcomes.

First, univariate analysis was performed to determine any association between SITS-MOST and clinical outcomes. Subsequently, patient characteristics and clinical outcomes were compared between the parenchymal hematoma (PH) (n = 21) and non-PH groups (hemorrhagic infarction [HI] and no hemorrhage, n = 72), and the risk and prognostic factors were investigated. Predictors for PH were analyzed using multiple logistic regression analysis; the covariates were age, sex, NIHSS score, TICI grade, O2P, and absence of the A-com. Continuous variables are expressed as mean ± standard deviation, whereas categorical variables are expressed as percentages. Fisher's exact test was used to analyze categorical variables, whereas the Mann–Whitney U-test was used for continuous variables. $P < 0.05$ was

Table 1: Intracranial hemorrhage definitions of the SITS-MOST.

HI1	Small petechiae along the margins of the infarct
HI2	Confluent petechiae within the infarcted area without space-occupying effect
PH 1	Local or intra-ischemic confluent hematoma in ≤30% of the infarcted area with some space-occupying effect
PH 2	Local or intra-ischemic confluent hematoma >30% of the infarcted area with a substantial space-occupying effect
PHr1	Small to medium hematoma located remote from the infarct (s), with mild space-occupying effect
PHr2	Large confluent hematoma located remote from the actual infarct (s), with substantial space-occupying effect

SITS-MOST: Safe implementation of thrombolysis in stroke-monitoring study, HI1: Hemorrhagic infarction Type 1, HI2: Hemorrhagic infarction Type 2, PH 1: Parenchymal hemorrhage Type 1, PH 2: Parenchymal hemorrhage Type 2, PHr1: Remote parenchymal hemorrhage Type 1, PHr2: Remote parenchymal hemorrhage Type 2 considered statistically significant. This study was conducted in accordance with the Declaration of Helsinki, and the study design was approved by the Fukuoka University Medical Ethics Committee (human subject assurance number: R19-002). Informed consent was obtained from the patients.

RESULTS

[Table 2] summarizes the association between SITS-MOST and clinical outcomes. HI was noted in 26 patients (28%), PH in 21 patients (23%), and no hemorrhage in 46 patients (49%). The PH and non-PH groups were not significantly correlated in terms of HI1, HI2, PH 2, remote parenchymal hematoma 1 (PHr1), or PHr2; however, PH1 ($P = 0.04$), total PH ($P = 0.002$), and no hemorrhage ($P = 0.006$) were significantly correlated with poor outcomes on discharge (mRS scores, 3–6).

[Table 3] summarizes the relationship between patient characteristics and clinical outcomes in the PH and non-PH groups. The mean age was 77 ± 11 years, and 51 patients (55%) were female. The occlusion location was in the ICA in 28 cases (30%) and the MCA in 60 cases (65%), and there was T occlusion in 5 cases (5%). Moreover, atrial fibrillation was observed in 54 cases (58%). The pre-EVT DW-ASPECTS was 7 ± 2.1, and the pre-EVT NIHSS score was 18 ± 7.3. rt-PA was administered in 51 cases (55%). Reperfusion (TICI > 2b) was noted in 72 cases (77%) and absence of the A-com in 29 cases (31%). Furthermore, the D2P was 101 ± 48 min and O2R was 259 ± 91 min. The number of passes was 1 in 49 cases (53%), and a poor outcome (mRS score, 3–6) was recorded in 63 cases (68%). Age, sex, occlusion location, presence of atrial fibrillation, pre-EVT DW-ASPECTS, pre-EVT NIHSS score, administration of rt-PA, TICI > 2b, D2P, O2R, and the number of passes were not significantly correlated between the two groups. However, the number of poor outcomes (mRS score, 3–6) and absence of the A-com were significantly higher in the PH group ($P = 0.001$, $P = 0.03$).

[Table 4] summarizes the investigation of predictors of PH in the multiple logistic regression analysis, which revealed that the absence of the A-com significantly predicted PH (odds ratio, 4.05; 95% confidence interval, 1.30–12.60; $P = 0.01$).

DISCUSSION

Revascularization using a stent retriever has increased the recanalization rates and resulted in good clinical outcomes in AIS with large vessel occlusion. However, the influence of overall ICH elicited by EVT requires further investigation. Kaesmacher *et al*.[10] reported that the risk of HI following MCA occlusion and subsequent EVT is primarily determined by factors that influence infarct severity and that successful

Table 2: Association between SITS-MOST and clinical outcomes.

SITS-MOST	Good clinical outcome group (mRS 0–2), *n*=30	Poor clinical outcome group (mRS 3–6), *n*=63	*P*-value	
HI, *n* (%)				
HI1	3 (10)	7 (11)	>0.5	>0.5
HI2	5 (17)	11 (17)	>0.5	
PH, *n* (%)				
PH 1	1 (3)	12 (19)	0.04*	0.002*
PH 2	0 (0)	7 (11)	>0.1	
PHr1	0 (0)	1 (2)	>0.1	
PHr2	0 (0)	0 (0)	>0.5	
No hemorrhage, *n* (%)	21 (70)	25 (40)	0.006*	

SITS-MOST: Safe implementation of thrombolysis in stroke-monitoring study, HI: Hemorrhagic infarction, mRS: Modified Rankin Scale, PH: Parenchymal hematoma, PHr: Remote parenchymal hematoma, **P*<0.05, ***P*<0.01

Table 3: Relationship between the patient characteristics and clinical outcomes in the PH and non-PH groups.

Patient characteristics and clinical outcomes	PH group, *n* =21	Non-PH group, *n* = 72	*P*-value
Age (mean ± SD, years)	79.6 ± 11	77.9 ± 9.0	>0.1
Sex			
Male, *n* (%)	13 (62)	29 (40)	>0.05
Female, *n* (%)	8 (38)	43 (60)	
Occlusion location			
ICA, *n* (%)	9 (43)	19 (26)	>0.1
MCA, *n* (%)	11 (52)	49 (68)	>0.1
T, *n* (%)	1 (5)	4 (6)	>0.5
Af (+)	10 (48)	44 (61)	>0.1
Pre DW-ASPECTS	5.8 ± 2.5	6.8 ± 1.9	>0.1
Pre NIHSS	20.9 ± 6.7	18.5 ± 7.4	>0.5
rt-PA, *n* (%)	10 (48)	41 (57)	>0.1
Reperfusion (TICI > 2b), *n* (%)	17 (81)	55 (76)	>0.5
A-com (-)	11 (52)	18 (25)	0.03*
D2P (min)	98 ± 42	115 ± 49	>0.1
O2R (min)	269 ± 93	266 ± 91	>0.5
1 pass (number of passes)	10 (48)	39 (54)	>0.5
mRS: 3–6 on discharge, *n* (%)	20 (95)	43 (60)	0.001**

A-com (-): The absence of an anterior communicating artery, Af (+): The presence of atrial fibrillation, D2P: Door-to-puncture time, DW-ASPECTS: Diffusion-weighted magnetic resonance imaging-Alberta stroke program early CT Score, ICA: Internal carotid artery, n: number of patients, MCA: Middle cerebral artery, mRS: Modified Rankin Scale, NIHSS: National institutes of health stroke scale, O2R: Onset-to-recanalization time, PH: Parenchymal hematoma, SD: Standard deviation, T: Tandem-occlusion, TICI: Thrombolysis in cerebral infarction, **P* < 0.05, ***P* < 0.01

Table 4: The investigation of predictors of PH in the multiple logistic regression analysis.

Patient factors	Odds ratio	95% Confidence interval	*P*-value
Age	1.05	0.99–1.12	>0.1
Female	0.21	0.05–0.79	0.02*
Pre NIHSS	1.05	0.97–1.14	>0.1
Reperfusion (TICI>2b)	1.26	0.32–5.02	>0.5
A-com (-)	4.05	1.30–12.60	0.02*
O2R	1	0.99–1.01	>0.5

A-com (-): The absence of an anterior communicating artery, NIHSS: National institutes of health stroke scale, O2R: Onset-to-recanalization time, TICI: Thrombolysis in cerebral infarction, *$P<0.05$, **$P<0.01$

recanalization acted protectively against subsequent HI. The results of their study supported the notion that HI as an ICH subtype was not a "benign" imaging sign because overall ICH including HI and PH was associated with more severe neurologic disability. Another study revealed that both PH and HI after EVT are functional prognostic exacerbating factors in AIS patients[6] Conversely, other studies have shown that overall ICH after rt-PA therapy was not necessarily a poor outcome factor.[12,13] Indeed, our present study also showed that PH was significantly correlated with poor outcomes after EVT.

The PH subtype could also be a significant factor in the clinical outcomes of AIS treatment. It has been reported that the occurrence of both SICH and PH 2 after EVT leads to poor outcomes.[8] Our study showed that all seven cases of PH 2 resulted in SICH. However, we could not demonstrate whether this was significantly correlated with poor outcomes because the number of cases was too small.

Interestingly, our study showed that the absence of the A-com on pre procedural TOF-MRA was an independent risk factor of PH after EVT. Multiple logistic regression analyses revealed that the absence of the A-com significantly predicted PH [Table 4]. Delayed initiation of treatment,[14] low value of ASPECTS,[17] insufficient collateral circulation,[2] ICA occlusion,[9] and tandem lesions[19] is considered to contribute to the "enlargement of the ischemic core" and has been shown to be risk factors of post-EVT ICH. Kaesmacher *et al*.[10] reported that the incidence of PH after EVT was time-dependent and that the risk increases with more extensive early ischemic damage. Moreover, Boisseau *et al*.[4] demonstrated that angiographic poor collaterals were identified as independent predictors of PH after EVT. Considering the abovementioned factors, the absence of the A-com could reduce cerebral blood flow through collateral circulation to the ischemic core and lead to extensive early ischemic damage in patients with anterior circulation AIS. Consequently, ischemia-reperfusion injury was more likely to cause post-EVT PH under the absence of the A-com.

Other previously reported risk factors of SICH or PH include the use of MERCI Retriever,[14,19] emergency stent placement,[5] cardiogenic embolism,[11] intravenous rt-PA therapy, and urokinase selective intra-arterial infusion.[19] Atrial fibrillation and intravenous rt-PA therapy did not significantly differ in our patients with and without PH. Our study also showed that the number of passes was not a recognized risk factor of PH after EVT.

The limitations of our study included the following: the choice of EVT devices depended on the site of the arterial occlusion and the preference of the surgeon. Our results require validation by future prospective studies that will not be limited by such selection bias. In addition, the 90-day outcome data were not available for analysis; this limited our ability to evaluate patient long-term outcomes. As rehabilitation often improves neurological assessments, we expect our rate of good clinical outcomes to have further increased after 90 days. This study enrolled a relatively small sample size; therefore, future studies with a larger number of cases should be conducted to confirm the present findings.

CONCLUSION

Our study showed that PH, not overall ICH, was a poor prognostic factor of clinical outcomes after revascularization in patients with anterior circulation AIS. In particular, the absence of the A-com on pre procedural TOF-MRA tended to be an independent risk factor for post-EVT PH. We consider that strict post procedural blood pressure control and careful imaging observations and administration of antithrombotics are important after EVT, especially when the A-com is absent, to prevent poor clinical outcomes caused by PH.

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Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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