

# Clinical Impact of Intracerebral Hemorrhage after Hyperacute Extracranial Stenting in Patients with Ischemic Stroke

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**Purpose:** Emergent intracranial occlusions causing acute ischemic stroke are often related to extracranial atherosclerotic stenosis. This study aimed to investigate the association between post-procedure intracerebral hemorrhage (ICH) and emergent extracranial artery stenting and assess their effects on clinical outcomes in patients with acute ischemic stroke.

**Materials and Methods:** We retrospectively analyzed patients undergoing hyperacute endovascular treatment for cervicocephalic vascular occlusion in three Korean hospitals between January 2011 and February 2016. Patients who had extracranial artery involvement and were treated from 24 hours of symptom onset to puncture were included in this study, and they were divided into the extracranial stenting (ES) and non-ES groups. Any type of petechial hemorrhages and parenchymal hematoma was defined as ICH for the current study.

**Results:** In total, 76 patients were included in this study. Among them, 56 patients underwent ES, and 20 patients did not. Baseline characteristics, risk factors, laboratory data, treatment methods, successful reperfusion rates, and baseline stenotic degrees of extracranial internal carotid artery did not differ between these two groups. However, atrial fibrillation was more frequent in patients without than with ES ( $P=0.002$ ), and post-procedure ICH was more frequent in patients with than without ES ( $P=0.035$ ). Logistic regression models revealed that ES was independently associated with post-procedure ICH (odds ratio [OR], 7.807; 95% confidence interval [CI], 1.213–50.248;  $P=0.031$ ), and ICH was independently associated with poor clinical outcomes (OR, 0.202; 95% CI, 0.054–0.759;  $P=0.018$ ); however, ES itself was not associated with clinical outcomes (OR, 0.530; 95% CI, 0.117–2.395;  $P=0.409$ ). Notably, ICH and ES had interaction for predicting good outcomes ( $P=0.041$ ).

**Conclusion:** Post-procedure ICH was associated with ES and poor clinical outcomes. Therefore, ES should be cautiously considered in patients with hyperacute stroke.

**Key Words:** Carotid stenosis; Stents; Cerebral infarction; Endovascular procedures; Cerebral hemorrhage

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## INTRODUCTION

Extracranial atherosclerosis (ECAS) is observed in about 10–20% of stroke patients and is not a rare cause of acute ischemic stroke.<sup>1,2</sup> Retrospective single-arm studies have shown that acute ischemic stroke patients undergoing emergent endovascular treatment (EVT) for acute extracranial internal carotid artery (ICA) occlusion show high recanalization rates and early neurologic improvement.<sup>3–5</sup> In addition, several studies have demonstrated that patients with extracranial occlusion combined with intracranial artery tandem occlusion have better outcomes after EVT.<sup>6–8</sup> Mechanical thrombectomy-based EVT is now considered a reasonable treatment especially for intracranial large artery occlusions.<sup>9</sup> However, symptomatic intracranial hemorrhage (ICH) is observed in about 30–40% patients with acute large-artery occlusion after EVT,<sup>10,11</sup> and it is thus considered a significant contributing factor for poor functional outcomes.

Carotid artery stenting is an EVT option for patients with extracranial carotid stenosis. Cases of extracranial stenting (ES) for ECAS-related occlusion in hyperacute stroke are increasing presently; however, the relationship between ES and the prevalence of post-procedural hemorrhagic transformation (HT) remains unclear. Therefore, we investigated the association between ES and the prevalence of post-procedural HT and assessed the effect of ES on clinical outcomes in patients with hyperacute stroke.

## MATERIALS AND METHODS

### Study population and inclusion criteria

We retrospectively analyzed patients in the Acute Stroke due to Intracranial Atherosclerotic occlusion and Neurointervention-Korean Retrospective (ASIAN-KR) registry. This registry collected data on patients (aged  $\geq 18$  years) who underwent EVT for cervicocerebral artery occlusion causing ischemic stroke at three comprehensive stroke centers in Korea between January 2011 and February 2016.<sup>12</sup> Inclusion criteria were as follows: 1) onset-to-puncture time within 24 hours; 2) underlying etiology was proven as ECAS; or 3) patients underwent EVT for extracranial artery steno-occlusive disease.

All clinical data were de-identified and allocated study identification numbers. The protocol of data collection was approved by the Institutional Review Board of each hospital and was implemented in accordance with the ethical stan-

dards of the 1964 Declaration of Helsinki and its later amendments.

### Evaluation methods

Premorbid and 3-month modified Rankin Scale (mRS) scores, National Institutes of Health Stroke Scale (NIHSS) scores, conventional vascular risk factors, and laboratory findings on admission were collected. A 3-month mRS score of 0 to 2 or no change compared with the premorbid mRS score was defined as a good outcome, and a 3-month mRS score of 3 to 6 or an increase compared with the premorbid mRS score was classified as a poor outcome.

The location of the initial occlusion site was determined using baseline computed tomography (CT) angiography, magnetic resonance angiography, or digital subtraction angiography. Stenotic degree of extracranial artery associated with hyperacute stroke was assessed based on the North American Symptomatic Carotid Endarterectomy Trial criteria.<sup>13</sup> Alberta Stroke Program Early CT Scores (ASPECTS) were determined using non-contrast CT in the anterior-circulation territory in patients with hyperacute stroke. Final reperfusion was evaluated using the modified thrombolysis in cerebral infarction (mTICI) scale,<sup>14</sup> and mTICI grades 2b or 3 were defined as successful reperfusion. Post-procedural ICH was graded based on the criteria defined by the European Cooperative Acute Stroke Study, and was defined as presence of any grade of ICH for the current study.<sup>15</sup> Subarachnoid hemorrhage was classified according to the modified Fisher scale.<sup>16</sup>

### Endovascular procedures

Endovascular devices were selected at the discretion of neurointerventionists based on consensus within each stroke team. Contact aspiration and stent retrieval were routinely used as a frontline method. Contact aspiration is a method of a forced arterial suction thrombectomy, which uses the Penumbra system (Penumbra Inc., Alameda, CA, USA). Stent retrieval is a method of clot removal by capturing and removing the thrombus with a stent retriever, such as the Solitaire AB/FR (Medtronic, Irvine, CA, USA) or Trevo (Stryker, Kalamazoo, MI, USA). Balloon guide catheters, adjuvant local lytic infusion, intracranial or extracranial angioplasty, and/or stenting were implemented as needed.

### Statistical analysis

Data are expressed as mean  $\pm$  standard deviations, median

(interquartile ranges), or numbers (percentages). Comparative analyses of clinical characteristics and treatment outcomes were performed between the ES and non-ES (NES) groups. Differences between the groups were analyzed using  $\chi^2$  tests for categorical variables, the Mann-Whitney U-test for ordinal variables, or t-tests for continuous variables. To evaluate the relation between ES and the prevalence of post-procedural ICH or further clinical outcomes, we performed multivariate logistic regression analyses with major confounders. A P of <0.05 was considered significant. Statistical analyses were performed using the SPSS statistical package (version 25.0, IBM SPSS, Armonk, NY, USA).

## RESULTS

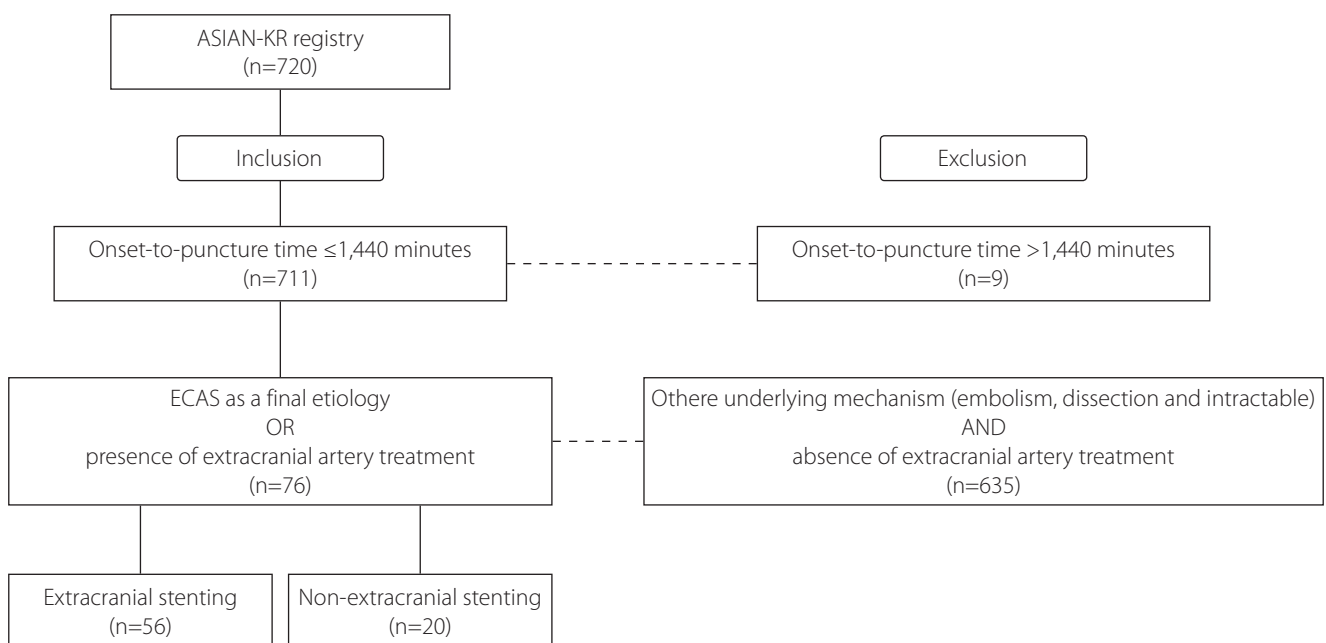
### Baseline characteristics

Among the 720 registered patients, 76 patients were eligible based on the inclusion criteria (Fig. 1). Baseline characteristics of patients are summarized in Table 1. Among the 76 eligible patients, 56 patients underwent ES, and 20 patients did not undergo any extracranial treatment or underwent other extracranial treatments without stenting (such as balloon-angioplasty and contract aspiration). Atrial fibrillation was more prevalent in the NES group than in the ES group (35.0% vs.

7.1%,  $P=0.002$ ); however, other variables including laboratory data; percentages of hypertension, diabetes mellitus, dyslipidemia, or smoker; NIHSS or ASPECTS score on admission; or systolic or diastolic blood pressure did not differ between the two groups.

### Treatment methods and outcomes associated with ES

Comparative analyses of treatment methods and outcomes between these two groups are summarized in Table 2. Overall procedure time or treatment methods, except for the ES, were not different between the two groups. The rates of successful reperfusion were similar in these two groups, regardless of ES (80.0% vs. 85.7%,  $P=0.547$ ). Functional outcomes, based on the mRS score, did not differ between the ES and NES groups. However, the prevalence of post-procedural cerebral hemorrhage after emergent extracranial EVT was associated with ES (odds ratio [OR], 7.807; 95% confidence interval [CI], 1.213 to 50.248;  $P=0.031$ ) (Table 3). Notably, multivariate analyses with potential major confounders in a logistic regression model revealed that the presence of ES was the only independent predictor for the prevalence of hemorrhage after emergent extracranial EVT (OR, 7.807; 95% CI, 1.213 to 50.248;  $P=0.031$ ). Good outcomes at 3 months were more commonly observed in patients without than



**Fig. 1.** Flowchart of this study. ASIAN-KR, Acute Stroke due to Intracranial Atherosclerotic occlusion and Neurointervention-Korean Retrospective; ECAS, Extracranial Atherosclerosis.

**Table 1. Baseline characteristics of patients with emergent extracranial steno-occlusive disease**

	No extracranial stenting (n=20)	Extracranial stenting (n=56)	P-value
Age	67.9±7.7	69.1±8.8	0.588
Sex, men	16 (80.0)	49 (87.5)	0.413
Hypertension	13 (65.0)	38 (67.9)	0.815
Diabetes mellitus	5 (25.0)	21 (37.5)	0.312
Dyslipidemia	7 (35.0)	17 (30.4)	0.701
Atrial fibrillation	7 (35.0)	4 (7.1)	0.002
Smoker	6 (30.0)	21 (37.5)	0.547
Intracranial occlusion sites			0.620
ICA, T-type	11 (55.0)	29 (51.8)	
MCA, M1	7 (35.0)	21 (37.5)	
MCA, M2	0 (0.0)	1 (1.8)	
Vertebrobasilar artery	2 (10.0)	2 (3.6)	
None, extracranial ICA only	0 (0.0)	3 (5.4)	
Initial NIHSS score, median	16 (10.5–21)	14 (10–19)	0.469
ASPECTS score, median	7 (6–8) (n=15)	7 (5.8–9) (n=50)	0.534
Hemoglobin (g/dL)	13.3±1.2	13.7±1.6	0.275
White blood cell ( $\times 10^9/L$ )	9.8±3.2	9.8±3.3	0.958
Platelet ( $\times 10^9/L$ )	253.2±111.4	254.7±65.2	0.942
Glucose (mg/dL)	124.3±34.8	144.0±65.5	0.097
Total cholesterol (mg/dL)	169.0±45.0	173.8±46.9	0.692
Low-density lipoprotein (mg/dL)	111.5±40.4	108.6±43.7	0.792
High-density lipoprotein (mg/dL)	41.4±7.8	41.4±10.2	0.994
Triglyceride (mg/dL)	112.7±80.3	147.9±217.8	0.484
Erythrocyte sedimentation rate (mm/hr)	19.6±20.9	18.6±14.3	0.815
C-reactive protein (mg/dL)	2.0±4.3	1.0±2.4	0.316
Initial systolic blood pressure (mmHg)	162.2±29.0	157.8±27.7	0.551
Initial diastolic blood pressure (mmHg)	85.5±18.4	85.9±14.1	0.905

Values are presented as mean±standard deviation or number (%).

ICA, internal carotid artery; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score.

with any post-procedural cerebral hemorrhage (68.0% vs. 42.3%,  $P=0.031$ ).

As observed in Table 4, the association between ES and better clinical outcomes was not demonstrated in multivariate logistic regression analyses (OR, 0.530; 95% CI, 0.117 to 2.395;  $P=0.409$ ). However, good outcomes after EVT were the absence of any post-procedural intracerebral hemorrhage (OR, 0.202; 95% CI, 0.054 to 0.759;  $P=0.018$ ). Because ES had an interaction with post-procedural intracerebral hemorrhage ( $P=0.041$ ), we speculate that ES has an indirect impact on worse clinical outcomes.

## DISCUSSION

In the present study, we found that the prevalence of post-procedural ICH was relatively higher in patients who underwent emergent ES than in those who did not. Good outcomes after hyperacute extracranial artery treatment were attributable to multiple factors such as younger age, lower initial NIHSS score, successful reperfusion, and the absence of any ICH after EVT. Post-procedural ICH was related emergent extracranial artery stenting and associated with poor functional outcomes.

**Table 2. Comparisons of treatment methods and outcomes**

	No extracranial stenting (n=20)	Extracranial stenting (n=56)	P-value
IV thrombolysis	9 (45.0)	25 (44.6)	0.978
Onset to puncture time (minutes)	448.5±351.0	384.1±245.8	0.375
Procedure time (minutes)	78.1±58.7	78.8±41.0	0.948
Use of balloon guide catheter	6 (30.0)	17 (30.4)	0.976
Remote aspiration with balloon guide catheter	14 (70.0)	36 (64.3)	0.644
Stent retrieval	6 (30.0)	17 (30.4)	0.976
Contact aspiration	16 (80.0)	37 (66.1)	0.244
Local tirofiban infusion	4 (20.0)	7 (12.5)	0.413
Final reperfusion success	16 (80.0)	48 (85.7)	0.547
Post-procedure intracerebral hemorrhage			0.160
None	17 (85.0)	33 (58.9)	
Hemorrhagic infarct type 1	0 (0.0)	6 (10.7)	
Hemorrhagic infarct type 2	1 (5.0)	10 (17.9)	
Parenchymal hematoma type 1	0 (0.0)	3 (5.4)	
Parenchymal hematoma type 2	2 (10.0)	4 (7.1)	
Post-procedure subarachnoid hemorrhage			0.646
None	19 (95.0)	52 (92.9)	
Fisher grade 1	0 (0.0)	1 (1.8)	
Fisher grade 2	0 (0.0)	2 (3.6)	
Fisher grade 3	0 (0.0)	0 (0.0)	
Fisher grade 4	1 (5.0)	1 (1.8)	
Modified Rankin Scale, median	2 (1–3)	2 (1–4)	0.516

Values are presented as mean±standard deviation or number (%). IV, intravenous.

It is well known that EVT's such as mechanical thrombectomy are preferred to intravenous thrombolysis for intracranial large artery occlusions.<sup>9,17</sup> Whereas EVT's for intracranial large artery occlusions have had sufficient evidences of efficacy and safety, evidences for emergent ES have barely been achieved. Nevertheless, accumulating evidence has indicated the safety and efficacy of emergent endovascular stenting in hyperacute stroke. It was reported that endovascular therapy of tandem occlusions with extracranial internal carotid artery revascularization as the first step had a high recanalization rate and led to an acceptable rate of good clinical outcomes. However, little is known about the hemorrhagic risk after ES. A retrospective study about the hemorrhagic risk after emergent EVT with intracranial or ES showed that patients undergoing emergent stenting had higher grades of hemorrhagic subtypes, and acute phase stenting was an independent predictor of sICH after adjustment for potential confound-

ers and the procedure duration. However, this study had a single-center retrospective design, and the sample size was small (24 patients) in the emergent stenting group.<sup>18</sup> Notably, TITAN study did not find a definite association between extracranial ICA stenting and post-procedural hemorrhage, although procedure-related complications after 90 days of EVT, including any ICH, were lower in the intracranial thrombectomy with ICA stenting group than in the intracranial thrombectomy only group.<sup>19</sup> However, while final successful reperfusion rate was similar between ES and NES groups in the current study, reperfusion success rate was significantly higher in the ICA stenting group than thrombectomy only group in the TITAN study. Reperfusion failure may increase the final infarct volume, which, in turn, can cause larger area of breakdown of blood-brain barrier and the risk of hemorrhagic transformation. Therefore, it is difficult to ascertain that ES-based EVT is safer than NES-based.

**Table 3. Risk factors of intracerebral hemorrhage after EVT**

	Univariate analysis			Multivariate analysis	
	No hemorrhage (n=50)	Any hemorrhage (n=26)	P-value	OR (95% CI)	P-value
Age	68.7±8.2	68.9±9.2	0.944	1.018 (0.947–1.094)	0.623
Sex, men	42 (84.0)	23 (88.5)	0.600	1.139 (0.165–7.878)	0.895
Hypertension	33 (70.2)	17 (68.0)	0.846		
Diabetes mellitus	19 (40.4)	7 (28.0)	0.296	0.657 (0.149–2.896)	0.579
Atrial fibrillation	7 (14.9)	2 (8.0)	0.400		
Smoker	15 (31.9)	10 (40.0)	0.493		
Dyslipidemia	16 (34.0)	8 (32.0)	0.861		
Prior history of TIA or stroke	7 (14.9)	4 (16.0)	0.901	3.083 (0.402–23.658)	0.279
Prior usage of antiplatelets	12 (25.5)	7 (28.0)	0.821	1.199 (0.263–5.466)	0.815
Prior usage of anticoagulants	1 (2.1)	1 (4.0)	0.645	15.776 (0.084–2975.334)	0.302
Initial NIHSS score, median	14 (10–19.3)	15.5 (10.8–20.3)	0.781	0.999 (0.904–1.104)	0.984
Intracranial occlusion location			0.405		
ICA, T-type	27 (54.0)	13 (50.0)			
MCA, M1	17 (34.0)	11 (42.3)			
MCA, M2	0 (0.0)	1 (3.8)			
Vertebrobasilar artery	3 (6.0)	0 (0.0)			
None, only extracranial ICA	3 (6.0)	0 (0.0)			
ASPECTS score, median	8 (5.5–9) (n=41)	6 (6–8) (n=24)	0.071		
Hemoglobin (g/dL)	13.3±1.6	14.1±1.2	0.036		
White blood cell (×10 <sup>9</sup> /L)	9.6±3.2	10.3±3.3	0.372		
Platelet (×10 <sup>9</sup> /L)	253.7±88.5	255.6±58.4	0.921		
Glucose (mg/dL)	135.2±44.4	145.7±81.5	0.545		
Total cholesterol (mg/dL)	163.4±45.0	190.0±44.0	0.016		
Low-density lipoprotein (mg/dL)	101.6±40.0	124.0±44.8	0.029		
High-density lipoprotein (mg/dL)	39.1±9.1	45.8±9.1	0.003		
Triglyceride (mg/dL)	149.0±231.3	118.7±68.8	0.517		
Initial systolic blood pressure (mmHg)	160.2±28.4	156.6±27.3	0.593		
Initial diastolic blood pressure (mmHg)	86.9±14.2	83.6±17.1	0.370		
IV thrombolysis	23 (46.0)	11 (42.3)	0.759	1.735 (0.327–9.199)	0.518
Onset to puncture time (minutes)	388.0±270.5	426.1±290.8	0.571	1.001 (0.998–1.004)	0.414
Procedure time (minutes)	81.1±45.6	73.8±46.9	0.512	0.995 (0.980–1.010)	0.516
Use of balloon guide catheter	33 (66.0)	17 (65.4)	0.957		
Remote aspiration with balloon guide catheter	17 (34.0)	6 (23.1)	0.325		
Stent retrieval	12 (24.0)	11 (42.3)	0.099		
Contact aspiration	35 (70.0)	18 (69.2)	0.945		
Local tirofiban infusion	5 (10.0)	6 (23.1)	0.124		
Extracranial stenting	33 (66.0)	23 (88.5)	0.035	7.807 (1.213–50.248)	0.031
Successful reperfusion	42 (84.0)	22 (84.6)	0.944		
Good outcomes at 3 months	34 (68.0)	11 (42.3)	0.031		

Values are presented as mean±standard deviation or number (%) unless otherwise indicated.

EVT, endovascular treatment; OR, odds ratio; CI, confidence interval; TIA, transient ischemic attack; NIHSS, National Institutes of Health Stroke Scale; ICA, internal carotid artery; MCA, middle cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; IV, intravenous.

**Table 4. Predicting factors associated with good clinical outcomes**

	Univariate analysis			Multivariate analysis	
	Poor outcomes (n=31)	Good outcomes (n=45)	P-value	OR (95% CI)	P-value
Age	71.9±9.5	66.6±7.0	0.007	0.918 (0.848–0.993)	0.033
Sex, men	27 (87.1)	38 (84.4)	0.747	0.841 (0.162–4.353)	0.837
Hypertension	22 (71.0)	29 (64.4)	0.552		
Diabetes mellitus	10 (32.3)	16 (35.6)	0.766	0.687 (0.177–2.665)	0.587
Atrial fibrillation	7 (22.6)	4 (8.9)	0.095	0.216 (0.027–1.718)	0.147
Smoker	7 (22.6)	20 (44.4)	0.050		
Dyslipidemia	8 (25.8)	16 (35.6)	0.369		
Premorbid mRS score, median	0 (0–1)	0 (0–0)	0.635		
Initial NIHSS score, median	19 (11–22)	14 (10–17)	0.126	0.895 (0.801–0.999)	0.049
Initial occlusion site			0.453		
ICA, T-type	15 (48.4)	25 (55.6)			
MCA, M1	11 (35.5)	17 (37.8)			
MCA, M2	1 (3.2)	0 (0.0)			
Vertebrobasilar artery	3 (9.7)	1 (2.2)			
None, only extracranial ICA	1 (3.2)	2 (4.4)			
ASPECTS score, median	6.5 (4.3–8.8) (n=24)	6 (7–9) (n=41)	0.610		
Onset to puncture time (minutes)	461.3±332.8	359.5±224.2	0.144	0.998 (0.996–1.000)	0.117
Puncture to final time (minutes)	89.7±55.2	71.0±36.9	0.104		
Prior history of TIA or stroke	5 (16.1)	8 (17.8)	0.851		
Prior usage of antiplatelets	6 (19.4)	14 (31.1)	0.253		
Prior usage of anticoagulants	1 (3.2)	2 (4.4)	0.789		
Initial systolic blood pressure (mmHg)	156.0±26.1	161.0±29.2	0.450		
Initial diastolic blood pressure (mmHg)	85.6±12.6	85.9±16.9	0.929		
Hemoglobin (g/dL)	13.4±1.6	13.7±1.4	0.354		
White blood cell (×10 <sup>9</sup> /L)	10.6±3.6	9.3±2.9	0.090		
Platelet (×10 <sup>9</sup> /L)	234.8±69.4	267.7±83.3	0.075		
Glucose (mg/dL)	143.3±73.9	135.7±47.7	0.586		
Total cholesterol (mg/dL)	174.5±46.9	171.1±46.1	0.753		
Low-density lipoprotein (mg/dL)	111.0±46.6	108.3±40.3	0.787		
High-density lipoprotein (mg/dL)	43.0±10.2	40.4±9.1	0.255		
Triglyceride (mg/dL)	152.7±286.9	129.1±83.3	0.604		
IV thrombolysis	11 (35.5)	23 (51.1)	0.178	1.059 (0.236–4.752)	0.940
Use of balloon guide catheter	17 (54.8)	33 (73.3)	0.095		
Remote aspiration with balloon guide catheter	7 (22.6)	16 (35.6)	0.226		
Stent retrieval	14 (45.2)	9 (20.0)	0.019		
Contact aspiration	19 (61.3)	34 (75.6)	0.183		
Local tirofiban infusion	4 (12.9)	7 (15.6)	0.747		
Extracranial stenting*	23 (74.2)	33 (73.3)	0.933	0.530 (0.117–2.395)	0.409
Successful reperfusion	23 (74.2)	41 (91.1)	0.047	13.892 (2.132–90.538)	0.006
Post-procedure intracerebral hemorrhage, any type*	15 (48.4)	11 (24.4)	0.037	0.202 (0.054–0.759)	0.018
Post-procedure subarachnoid hemorrhage, any type	3 (9.7)	2 (4.4)	0.294		

Values are presented as mean±standard deviation or number (%) unless otherwise indicated.

OR, odds ratio; CI, confidence interval; mRS: modified Rankin Scale; NIHSS; National Institutes of Health Stroke Scale; ICA, internal carotid artery; MCA, middle cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; TIA, transient ischemic attack; IV, intravenous.

\*Both variables had interaction (P=0.041).

Several reasons may explain the relative high risk of ICH following ES in the current study. Many studies have suggested that hyperacute ICH after extracranial carotid artery stenting is mainly associated with abrupt cerebral hyperperfusion in the chronically hypoperfused areas.<sup>20-23</sup> The high rate of cerebral hyperperfusion after stenting is associated with the underlying diseases causing microangiopathy, high degrees of stenosis with the poor collateral flow, high degrees of stenosis on the contralateral carotid artery, and recent stroke history.<sup>20,21</sup> In addition, these post-procedural hemorrhages just after extracranial carotid artery stenting could result from rupture of small perforating arteries after rapidly normalized perfusion pressure in the chronically hypoperfused areas.<sup>24</sup> Prior usage of antiplatelets or anticoagulants might also increase the risk of post-procedural hemorrhage. In our current study, no significant correlation was observed between prior antiplatelet/anticoagulant medication and post-procedural hemorrhage. However, peri- or post-procedural antiplatelet treatment might potentially affect the incidence of ICH in the current study. As large infarct volume or microbleeds are seen on CT or magnetic resonance imaging, physicians may skip antiplatelet medication to escape hemorrhagic transformation. In contrast, physicians cannot skip the medication if ES is permanently deployed to escape in-stent thrombosis. Therefore, the occurrence of ICH after stenting might be caused by sudden hyperemia/hyperperfusion combined with post-stent prevention, such as antiplatelets.

Many studies have improved the process of EVT for intracranial large artery occlusion (LAO) in patients with acute ischemic stroke and tandem occlusion from ECAS disease. It is suggested that sufficient dilation of stenosis cervical artery is important for the successful use in stent-retrieval thrombectomy or spontaneous recanalization in cases of refractory LAO.<sup>25</sup> Therefore, it is necessary to perform balloon angioplasty or stenting for maintaining a good extracranial artery perfusion status. Our study showed that ES had an increased risk on post-procedure ICH; therefore, balloon angioplasty could be used as an alternative method, and cautious local administration of glycoprotein IIb/IIIa inhibitor, such as tirofiban, could be used to prevent re-occlusion of the extracranial artery after mechanical thrombectomy.

This study has several limitations. First, this study was a retrospective study; thus, the findings in the current study cannot be generalized. For escaping potential biases, we recruited multicenter data. Second, ICH after ES in patients with posterior circulation stroke was not well evaluated. Therefore,

further studies must be implemented with a large amount of data related to extracranial vertebral artery stenting. Third, no exact data on pre- or post-stenting prevention were available; therefore, we could not exactly examine whether post-procedural ICH was related to stenting or/and antiplatelet medication during the stenting period. Therefore, further studies with a standardized dosage of antiplatelet medications before and after stenting are needed.

## CONCLUSION

Emergent extracranial artery stenting has been used as a treatment option for hyperacute stroke patients with extracranial artery stenosis. This study found that ICH more frequently occurred in patients who underwent ES and was related to poor clinical outcomes in which ICH and ES had interaction. The findings indicate that ES must be cautiously considered in patients with ECAS-related acute ischemic stroke.

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