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Predictors of intracranial hemorrhage in patients with large vessel occlusion stroke who underwent successful recanalization of the anterior system

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ABSTRACT

Aim: To determine the causes of intracranial hemorrhage (ICH) following endovascular thrombectomy (EVT) in patients with large vessel system (LVO). ICH is a cause of fatal birth defects and morbidity. This study was designed to evaluate the causes of ICH after successful mechanical thrombectomy (MT) in patients with acute ischemic stroke.

Methods: This retrospective study included isolation of anterior circulation LVO with ASPECTS scores > 6, where symptoms were successfully treated with recanalization from 6 hours onwards. The study aimed to investigate the causes of intracranial hemorrhage occurring within 24 hours.

Results: The study included 123 patients with a history of LVO ischemic stroke. ICH developed in 37 (30%) patients. Low ASPECT score (p<0.01), high 24-hour NIHS score (p<0.01), high passage rates (p<0.01), low lymphocyte count (p<0.01), high 3-month MRS score (p<0.01), presence of hyperlipidemia (p<0.05), low first-pass recanalization rate (p<0.01), presence of distal embolism (p<0.01), and growth rate of cardioembolic stroke etiology (p<0.01) were associated with the progression of ICH development. In a multivariate logistic regression model, cardioembolic etiology was found to be an independent predictor of ICH.

Conclusion: A low ASPECT score, high 24-hour NIHS score, high pass counts, low lymphocyte counts, high 3-month MRS score, presence of hyperlipidemia, low first-pass recanalization rate, and presence of distal embolism indicated the progression of ICH. The etiology of cardioembolic stroke was an independent vision of ICH.

Keywords: Acute ischemic stroke, endovascular thrombectomy, intracranial hemorrhage, embolism.

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1. Introduction

Strokes are a global health problem and are among the leading causes of death and disability worldwide [1]. The advent of reperfusion therapy has revolutionized the management of acute ischemic stroke (AIS), providing significant benefits to those affected. Endovascular thrombectomy (EVT) has been shown to improve outcomes in selected patients with LVO ischemic stroke within a 24-hour time window and to provide significant benefits, including a reduction in long-term functional disability and mortality [2]. ICH is a common complication after EVT and has been reported to occur in up to 46.1% of patients in clinical trials [3]. The occurrence of ICH after reperfusion therapy increases the likelihood of poor functional outcomes and death

[4]. Hemorrhagic complications, particularly ICH, can reduce the benefit ratio of endovascular treatment or even render it ineffective. Therefore, identifying predictors of ICH after EVT in real-world practice is crucial for continuously improving the effectiveness of this new treatment strategy. Reliably identifying patients at high risk for ICH may be useful for clinicians when making treatment decisions, informing patients and their families about prognosis, and personalizing follow-up protocols [5]. The aim of this study was to evaluate the relationship between clinical, radiological, and treatment-related characteristics and the occurrence of ICH in a cohort of patients with anterior circulation ischemic stroke treated with EVT.

2. Materials and methods

2.1. Patients: This was a retrospective analysis of data collected from consecutive anterior system ischemic stroke patients who underwent endovascular treatment at a stroke center from January 2023 to December 2023.

Inclusion criteria were age ≥ 18≤80, patients presenting within 6 hours of the last known well, pre-EVT Alberta Stroke Program Early CT score (ASPECTS) ≥6, pre-disease modified Rankin scale (mRS) <2, and thrombolysis in cerebral infarction (TICI) final reperfusion of 2b-3. The choice of technique in EVT was made at the operator's discretion using left-lobe, aspiration, or combined methods. Balloon guiding was used depending on the operator's preference. No IVTPA was administered to any patient after the procedure, and no rescue stents were applied.

Exclusion criteria were missing follow-up data, post-TICI <2b, pre-EVT NIHSS < 6, pre-EVT ASPECTS < 6, premorbid mRS ≥ 3, active liver disease with Last known well more than 6 hours ago, and bleeding diathesis.

ICH was defined as one of the following subtypes according to the European Cooperative Acute Stroke Study-II (ECASS-II) [6]: hemorrhagic infarction (HI)-1: small petechiae along the margins of the infarct; HI-2: more confluent petechiae within the infarcted area, but without space-occupying effect; parenchymal hematoma (PH)-1: blood clot not exceeding 30% of the infarcted area with some mild space-occupying effect; and PH-2: dense blood clot(s) exceeding 30% of the infarct volume with significant space-occupying effect. All subtypes were included in the ICH group.

2.2. Evaluation and Analysis of Patient Data: We collected patient data, including demographic characteristics, clinical data, and laboratory parameters. Patient characteristics included age, gender, smoking status, alcohol consumption, hypertension, diabetes, atrial fibrillation (AF), asthma, hyperlipidemia (HL), and coronary heart disease (CHD). Clinical data included initial systolic blood pressure (BP), initial diastolic BP, initial NIHS score, symptom-to-puncture time (time from onset to inguinal puncture), puncture-to-recanalization time (time from inguinal puncture to reperfusion), and Alberta Stroke Program Early Computer Tomography score (ASPECTS).Laboratory parameters included blood glucose (BG), lymphocyte count, neutrophil count, red blood cell distribution width (RDW), and platelet (PLT) count.

2.3. Statistics: Statistical analyses were performed using IBM SPSS Statistics regarding the study design and variable characteristics. Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) depending on the distribution normality, while categorical variables were expressed as frequencies and percentages (n, %). The normality of the data distribution was assessed using visual inspection (histograms and Q-Q plots) and statistical tests.

For univariate analysis, differences between groups (Bleeding vs. No Bleeding) were evaluated using the Mann-Whitney U test for non-normally distributed continuous variables (e.g., ASPECTS, NIHSS, time intervals) and the Student's t-test for normally distributed variables. Categorical variables were compared using the Pearson Chi-square test or Fisher's exact test, as appropriate.

To identify independent predictors of intracranial hemorrhage (bleeding) at 24 hours, a binary logistic regression analysis was conducted using the 'Enter' method. All variables that were clinically relevant or showed statistical significance in the univariate analysis were included in the multivariate model. The model's goodness-of-fit was assessed using the Hosmer-Lemeshow test, and the explained variance was estimated using Nagelkerke' R^2. The model's discriminative ability was evaluated via classification accuracy tables. The results of the regression analysis were reported as Odds Ratios (OR) with 95% Confidence Intervals (CI). A two-tailed *p*-value of <0.05 was considered statistically significant for all analyses.

3. Results

Tables 1 and 2 present the association of demographic, clinical, laboratory, and some predictive data with intracranial hemorrhage.

A total of 123 patients (70 women (56.9%) and 53 men (43.1%) who met the inclusion criteria between 2023-2024 were included in the study. The mean age was 67.2±12.8 years, the mean ASPECT score at presentation was 9.1±0.9, and 19 patients (15.4%) had a history of previous stroke. IV TPA was administered in 63 (51.2%) patients. The mean symptom-to-puncture time was 191.61±85.25 minutes, and the mean puncture-to-canalization time was

Table 1. Association of demographic, clinical, and laboratory data with ICH.

Variables	All Group (n=123)	No Bleeding (n=86)	ICH (n=37)	Statistical analyses	
	$\bar{X}$ (sd)	$\bar{X}$ (sd)	$\bar{X}$ (sd)	U/t	*p*
Age	67.25(12.81)	66.9(13.54)	68.08(11.04)	1588.5	*0.99*
Admission ASPECT	9.11(0.97)	9.29(0.87)	8.68 (1.06)	2151.0	*0.00***
Symptom onset time	191.61(85.25)	185.66(88.52)	205.43(76.45)	1350.5	*0.18*
Puncture recanalization time	48.18(18.36)	48.31(18.42)	47.86(18.47)	1635.5	*0.81*
Admission NIHS score	10.54(3.72)	10.15(3.74)	11.46(3.55)	-1.86	*0.07*
24-hour NIHS score	5.93 (4.32)	4.88 (3.66)	8.35 (4.79)	916.0	*0.00***
Number of Passes	2.15 (0.98)	1.99 (0.98)	2.54(0.9)	1070.0	*0.00***
Leukocyte	9.01(3.27)	9.01(3.43)	9(2.9)	1524.5	*0.72*
Neutrophil (10^9/L)	6.4 (3.24)	6.57 (3.42)	6 (2.77)	1688.5	*0.59*
Lymphocyte (10^9/L)	2.14 (1.29)	2.3 (1.34)	1.79 (1.11)	2012.5	*0.02**
PLT (10^9/L)	247.97(108.14)	248.55 (119.88)	246.62 (75.46)	1476.5	*0.53*
RDW (%)	14.63(1.95)	14.69(2.1)	14.49(1.56)	1465.0	*0.49*

ICH: intracranial hemorrhage. RDW: Red cell distribution width.

48.18±18.36 minutes.

ICH developed in 37 (30%) patients. Low ASPECT score (*p*<0.01), high 24-hour NIHS score (p<0.01), high number of passes (*p*<0.01), low lymphocyte count (*p*<0.01), presence of hyperlipidemia (*p*<0.05), low first-pass recanalization rate (*p*<0.01), presence of distal embolism (*p*<0.01), and increased rate of cardioembolic stroke etiology (*p*<0.01) were found to be associated with the development of ICH.

Table 3 presents the results of multivariate logistic regression analysis of some predictors. In the multivariate logistic regression model, cardioembolic etiology of stroke was found to be an independent predictor of ICH (*p*<0.02).

Table 2. Results of some predictors in patients with intracranial hemorrhage.

Variables	**Categories**	**No Bleeding (n=86)**	**ICH (n=37)**	χ^2	*p*
		n (%)	**n (%)**		
Sex	Female	51 (59.3)	19 (51.4)	0.67	*0.434*
	Male	35 (40.7)	18 (48.6)		
Hypertension	No	23 (26.7)	14 (37.8)	1.51	*0.281*
	Yes	63 (73.3)	23 (62.2)		
Diabetes	No	56 (65.1)	28 (75.7)	1.33	*0.299*
	Yes	30 (34.9)	9 (24.3)		
Coronary artery disease	No	42 (48.8)	21 (56.8)	0.65	*0.437*
	Yes	44 (51.2)	16 (43.2)		
Congestive Heart Failure	No	52 (60.5)	21 (56.8)	0.15	*0.837*
	Yes	34 (39.5)	16 (43.2)		
Asthma and/or COPD	No	79 (91.9)	33 (89.2)	0.23	*0.731*
	Yes	7 (8.1)	4 (10.8)		
Atrial fibrillation	No	43 (50)	19 (51.4)	0.02	*1*
	Yes	43 (50)	18 (48.6)		
Alcohol Consumption	No	83 (96.5)	37 (100)	1.32	*0.553*
	Yes	3 (3.5)	0 (0)		
Smoker	No	62 (72.1)	26 (70.3)	0.04	*1*
	Yes	24 (27.9)	11 (29.7)		
Previous Stroke History	No	77 (89.5)	27 (73)	5.43	*0.026*
	Yes	9 (10.5)	10 (27)		
Hyperlipidemia	No	36 (41.9)	24 (64.9)	5.48	*0.028*
	Yes	50 (58.1)	13 (35.1)		
IV TPA	No	45 (52.3)	27 (73)	4.54	*0.045*
	Yes	41 (47.7)	10 (27)		
First-pass recanalization	No	52 (60.5)	33 (89.2)	10	*0.003***
	Yes	34 (39.5)	4 (10.8)		
Distal embolism	No	63 (73.3)	18 (48.6)	6.97	*0.012***
	Yes	23 (26.7)	19 (51.4)		
Embolism in a different vessel	None	83 (96.5)	36 (97.3)	0.05	*1*
	Yes	3 (3.5)	1 (2.7)		
Subtype of stroke	Cardioembolic	16 (18.6)	13 (35.1)	7.04	*0.031**
	other	70 (81.4)	24 (64.9)		

ICH: intracranial hemorrhage. COPD: Chronic obstructive pulmonary disease. TPA: Tissue plasminogen activator.

Table 3. The results of multivariate logistic regression analysis of some predictors.

Variables	B	p	aOR(95% CI)
Admission ASPECT	-0.23	0.68	0.8 (0.27-2.33)
IV TPA	2.15	0.07	8.61 (0.82–90.15)
Symptom onset time	-0.01	0.32	0.99 (0.98–1.01)
Puncture recanalization time	-0.02	0.43	0.98 (0.94–1.03)
First-pass recanalization	-2.87	0.06	0.06 (0–1.12)
Distal embolism	-1.45	0.10	0.24 (0.04-1.33)
Embolism in a different vessel	3.89	0.47	48.95(0-1881217.93)
Cardioembolic subtype	**3.23**	**0.02**	**25.22 (1.54–413.43)**
24-hour NIHS score	0.11	0.43	1.12 (0.84–1.48)
Sex	0.02	0.61	1.02 (0.95–1.09)
Hypertension	1.35	0.24	3.86 (0.41–36.33)
Diabetes	1.41	0.18	4.08 (0.51–32.36)
Coronary artery disease	-1.09	0.36	0.34 (0.03–3.48)
Congestive heart failure	0.49	0.63	1.64 (0.22–12.11)
Asthma and/or COPD	0.53	0.78	1.7 (0.04–76.78)
Atrial fibrillation	1.39	0.38	4.01 (0.18–89.45)
Alcohol Consumption	19.35	1.00	253,417,443.91 (0-0)
Smoking	0.08	0.94	1.09 (0.11–10.3)
Previous Stroke History	-1.48	0.27	0.23 (0.02–3.22)

4. Discussion

Recent advances in reperfusion therapies for acute ischemic stroke have led stroke specialists to focus on cerebral hemorrhagic complications. ICH following acute ischemic stroke has a significant impact on patient outcomes, and controlling the risk of bleeding plays an important role in recanalization decisions. ICH following reperfusion therapy for AIS was not a rare complication after the procedure. We found it occurred in 30% of our series. This was seen to be a lower rate than previously published studies, which found approximately 40%. [7,8]. This retrospective study identified one potential predictor of ICH following EVT in patients with AIS due to anterior circulation LVO. cardioembolic etiology of stroke was an independent predictor of ICH. Additionally, low ASPECTS at admission, high 24-hour NIHS score, patients with multiple passages, low lymphocyte count, presence of hyperlipidemia, low first-pass recanalization rate, and presence of distal emboli were associated with an increased risk of ICH. Previous studies have associated a high admission NIHS score with ICH [9]. In our study, ICH was associated with the 24-hour NIHS score, not the admission NIHS score. Our findings do not clarify whether ICH leads to higher 24-hour NIHSS scores or whether a higher 24-hour NIHSS reflects more severe strokes that are intrinsically prone to ICH. Previous studies have associated lower ASPECTS scores with ICH risk, consistent with our findings [10,11]. These findings suggest that patients with large infarct cores are vulnerable to ICH.

Contrary to the results of our study, a retrospective study found that a high number of passes was not significant in terms of ICH. However, in this study, almost all patients had 3 or fewer passes [12]. Other studies in the literature have found that an increase in the number of passes is associated with ICH [9,11]. Similarly, a multicenter study has shown that a pass count greater than 3 is an independent predictor of ICH [8]. A high pass count has been associated with hemorrhagic transformation due to endothelial damage caused by mechanical stress and radial force [13-15].

Due to rapid arterial occlusion, cardioembolic stroke typically has a smaller penumbra and a larger infarct core, which may increase the risk of ICH [16,17]. Furthermore, the high rate of anticoagulant use in these patients is thought to contribute to the elevated risk of ICH. cardioembolic stroke is a risk factor for ICH in AIS patients due to disruption of the blood-brain barrier (BBB) [18]. Cardiogenic embolism has been reported as an independent predictor of ICH in many studies [19,20], which was also confirmed in our study. However, a recent systematic review of endovascular treatment in patients with AF did not show an increase in ICH risk compared to patients without AF [21].

Our results cannot be generalized; this study has several limitations: First, we included a relatively small retrospective patient series. This may have affected the results of multivariate analyses and reduced the effect of other variables. Second, blood pressure records could not be obtained after EVT. Considering the importance of blood pressure values in the development of ICH, recording them could have contributed to the study. Another limitation is that INR values were not available in all patients and were excluded from the evaluation. This could have affected the results in patients with cardioembolic stroke.

4.1. Conclusions: In this study, low ASPECT score, high 24-hour NIHS score, high number of passes, low lymphocyte count, high 3-month MRS score, presence of hyperlipidemia, low first-pass recanalization rate, and presence of distal embolism were associated with ICH. Cardioembolic etiology of stroke was an independent predictor of ICH. Reliably identifying patients at high risk for ICH after EVT, especially those with cardioembolic etiology, may be useful for clinicians when making treatment decisions.

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