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Effects of thrombus characteristics on clinical outcome and success of recanalization in acute ischemic stroke

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Abstract

Background: Despite current developments in mechanical thrombectomy (MT), successful recanalization cannot be achieved in all patients. One of the factors related to this is the characteristics of the thrombus. In this study, we aimed to evaluate the effects of thrombus length and permeability on procedural success and clinical outcome. *Methods:* Patients with intracranial ICA, middle cerebral artery M1, or M2 occlusions, who underwent MT between November 2019 and January 2022 were included in the study. Thrombus length, density and permeability were calculated and the relationship between recanalization success and modified Rankin Scores (mRS) at the 3rd month was evaluated. Good clinical outcome was defined as an mRS score of 2 or less. *Results:* Forty-six of the 79 patients included in the study had a good clinical outcome. Although thrombus length was shorter and permeability was higher in patients with good clinical outcome, statistical significance was not achieved. There was a positive correlation between thrombus density, thrombus length and the number of passes, and a negative correlation between permeability. There was no significant difference in thrombus length, density and permeability between patients with and without successful recanalisation. Thrombus length was found to be a predictor of clinical outcome at 3 months in univariate analysis, whereas only age was found to be an independent predictor in multivariate analysis.
Conclusions: In conclusion, despite certain findings not achieving statistical significance, the observed trends offer valuable insights for future research. A comprehensive understanding of thrombus nature could guide personalized stroke treatment strategies in the future.

Keywords: Stroke, Thrombus length, Thrombus permeability, Endovascular treatment, Thrombectomy

INTRODUCTION

Stroke continues to be a critical public health concern worldwide, posing a major burden on healthcare systems due to its high morbidity and mortality rates.[1] Ischemic strokes, largely attributable to thromboembolic occlusions in cerebral arteries, represent the most prevalent stroke subtype.[2] Over the past decade, mechanical thrombectomy (MT) has emerged as a standard of care for patients with acute ischemic stroke caused by large vessel occlusion (LVO), demonstrating a substantial improvement in functional outcomes compared to intravenous thrombolysis alone.[3,4]

However, despite the considerable advances in MT techniques and devices, not all patients achieve successful recanalization and desirable long-term clinical outcomes. One variable that may influence this heterogeneity is the characteristics of the occlusive thrombus. In recent studies on thrombus length, density and permeability, there are studies reporting an effect on procedural success and good clinical outcome, as well as studies reporting that no relationship has been demonstrated.[5–9]

Nonetheless, data on the precise relationship between thrombus radiological features and procedural and clinical outcomes after MT are somewhat conflicting and are still under investigation. The aim of this study was to evaluate the relationship between radiological features of thrombus and clinical outcome and procedural success in mechanical thrombectomy.

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METHODS

Patient selection

After obtaining ethical approval from Bolu Abant Izzet Baysal Traning and Research Hospital Clinical Research Ethics Committee (21.02.2023-2023/35), the files of acute ischemic stroke patients who underwent mechanical thrombectomy at Bolu Abant Izzet Baysal Training and Research Hospital Stroke Center between November 2019 and January 2022 were retrospectively scanned. Inclusion criteria were patients who underwent endovascular treatment (EVT) for intracranial internal carotid artery (ICA), middle cerebral artery M1, M2, or tandem occlusions, and who had undergone both computed tomography (CT) and CT angiography (CTA) examinations. Patients from whom we could not obtain three-month clinical outcome data or informed consent were excluded from the study.

The files of 142 patients who underwent mechanical thrombectomy due to anterior circulation stroke within the study date range were evaluated, 29 patients were excluded from the study because CTA examination was not performed, 12 patients were excluded from the study because CTA images taken at an external center could not be accessed, and 22 patients were excluded because 3rd month clinical outcome information was not available (Figure 1).

Data acquisition

We recorded the age, sex, admission and discharge National Institutes of Health Stroke Scale (NIHSS)[11] scores, identified stroke etiologies, three-month modified Rankin Scale (mRS)[12] scores, times from symptom onset to femoral puncture, and recanalization, number of passes during the thrombectomy procedure, and recanalization success rates of patients who met the inclusion criteria. Stroke etiology was determined according to the TOAST[13] classification. Successful recanalization was defined as a Thrombolysis in Cerebral Infarction (TICI)[14] score of 2b or higher, and a good clinical outcome was defined as an mRS score of 2 or less.

Measurement of thrombus radiological characteristics

Measurements of thrombus length and radiological characteristics were made by investigator AO, an interventional neurologist with 6 years of experience, who was blinded to the clinical outcomes of the patients.

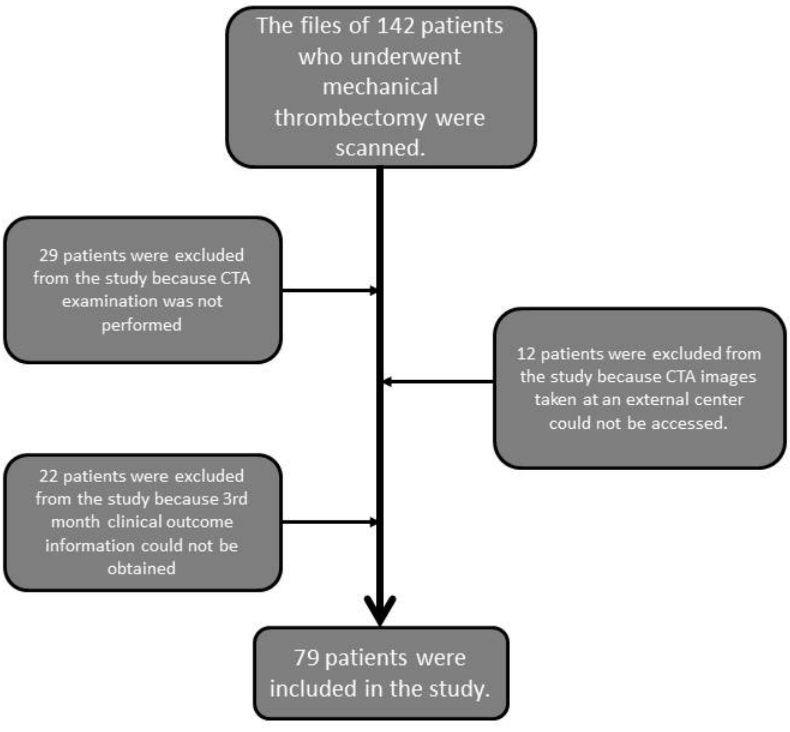

Figure 1. Flow chart of the study

Thrombus Density and Permeability: The average density measurements obtained from three areas (proximal, middle, and distal) on thin-slice (<2.5mm) non-contrast CT (NCCT) were calculated as the thrombus density. The adjusted thrombus density was obtained by subtracting the same vessel's contralateral Hounsfield Unit (HU) value from the thrombus density. Thrombus permeability was calculated by subtracting the NCCT density from the average density in the late venous phase of the CTA study of the occluded segment.

Thrombus Length: The thrombus length was calculated by averaging measurements made in at least two planes on Maximum Intensity Projection (MIP) images.

Statistical methods

Data analysis was performed using SPSS 20.0 (IBM Inc., Chicago, IL, USA) statistical software. Numeric data were reported as mean and standard deviation, while categorical data were reported as numbers and percentages. The independent sample T-test was used to compare two independent groups meeting the criteria for normal distribution; otherwise, the Mann-Whitney U test was used. The relationship between continuous variables was assessed using Pearson and Spearman correlation analysis, depending on whether the data were normally distributed. Binary logistic regression analysis was used to evaluate the relationship between binary dependent variables and independent variables.

RESULTS

A total of 79 patients, including 34 males and 45 females, were included in the study. At the three-month follow-up, 46 patients exhibited a good clinical outcome. Demographic data and technical information about the procedure for patients with and without good clinical outcomes at three months are presented in Table 1. Upon comparison of the clinical, radiological, and EVT-related technical and duration data of patients with and without good clinical outcomes, it was noted that those with good clinical outcomes had significantly lower admission NIHSS scores and fewer passes during the procedure. The permeability of the thrombus in patients with a

Table 1: Comparison of data of patients with good and poor clinical outcome

	Good clinical outcome (n=46)	Poor clinical outcome (n=33)	*p*
Age (years)	69.17±13.97	74.24±11.41	0.091
Gender M/F (n)	21/25	13/20	0.580
Witnessed/unwitnessed stroke (n)	38/8	27/6	0.928
Right/Left (n)	25/21	17/16	0.803
IVT (n)	13	10	0.844
sICH (n)	0	4	0.027*
≥TICI2b recanalization (n)	43	22	0.002**
First pass recanalization (n)	20	7	0.04*
NIHSS	12.69±4.41	16.12±5.91	0.004**
ASPECT	9 (7-10)	9 (5-10)	0.022*
Thrombus density (HU)	38.63±9,56	40.69±10.17	0.359
Thrombus adjusted density (HU)	6.30±9.50	7.57±9.95	0.567
Thrombus permeability (HU)	21.52±16.12	16.93±9.44	0.148
Thrombus length (cm)	1.51±0.97	1.94±0.92	0.065
Onset- door (min)	199.58±249.52	201.60±243.03	0.971
Onset- femoral puncture (min)	287.52±252.44	299.33±248.48	0.837
Femoral puncture-recanalization (min)	55.68±34.78	69.55±40.11	0.12
Onset-recanalization time (min)	345.93±250.85	391.37±261.32	0.457
Number of passes (n)	2.34±1,41	3.21±1,83	0.021*

*p<0.05 ** p<0.01, M:Male, F:Female, IVT: intravenous thrombolytic treatment, sICH: symptomatic intracranial hemorrhage, NIHSS: National Institutes of Health Stroke Scale good clinical outcome was higher (21.52±16.12 HU) compared to those with poor clinical outcomes (16.93±9.44 HU), but this difference did not reach statistical significance. Similarly, although the thrombus length was smaller in patients with good clinical outcomes, the difference was not statistically significant (Table 1). (1.51±0.97 vs 1.94±0.92 cm).

Successful recanalisation was achieved in sixty-five patients. Comparing patients in whom successful recanalization was achieved with those in whom it was not, it was found that patients with successful recanalization had shorter symptom-to-recanalization times (p=0.008), shorter femoral puncture-to-recanalization times (p=0.017), and fewer passes during the procedure (p=0.03). No differences were observed between groups in terms of thrombus length, density, and permeability (Table 2).

Correlation analysis revealed that thrombus density and corrected density positively correlated with femoral puncture-to-recanalization time, number of passes during the procedure, and thrombus length, but negatively correlated with thrombus permeability. Thrombus permeability negatively correlated with the number of passes during the procedure. Thrombus length positively correlated with thrombus density and NIHSS score but negatively correlated with the ASPECT score. No significant correlation was found between the three-month mRS score and thrombus density, corrected density, or permeability (Table 3).

According to the TOAST classification in etiology, cardioembolism was found in 47 patients, large vessel atherosclerosis in 11 patients, and coagulopathy in 1 patient. Twenty patients had a cryptogenic stroke. There was no significant difference between thrombus densities, corrected densities, thrombus permeability and thrombus lengths of patients with cardioembolic etiology and those with large vessel atherosclerosis (Table 4).

In the univariate logistic regression analysis, age, admission NIHSS score, thrombus length, ASPECT score, presence of first pass recanalization, and number of passes were found to be predictors of the 3rd month clinical outcome, while in the multivariate analysis, only age was found to be an independent predictor of the 3rd month clinical outcome (Table 5, 6).

DISCUSSION

In our study, we examined the effects of the radiological characteristics of the thrombus on clinical outcomes and procedural success. Although statistical significance was not achieved, we found that the thrombus length was shorter and its permeability was higher in those with a good clinical outcome. Additionally, we found that thrombus density and length were positively correlated, and that density and permeability were negatively correlated. Our findings echo those of Gavriliuc *et al*., showing that clot length does not significantly impact clinical outcome after thrombectomy.[9] This is somewhat contrary to other studies, like those by Gralla *et al*. and Seker *et al*., which suggested that occlusion length is a

Table 2: Comparison of the data of patients with and without successful recanalization

	Successful recanalization (n=65)	Unsuccessful recanalization (n=14)	*p*
Age (years)	71.108±13,48	72.141±11.79	0.791
NIHSS	13.89±4.91	15.21±7.11	0.404
Thrombus density (HU)	39.38±9.97	40±9.33	0.833
Thrombus adjusted density (HU)	6.98±9.71	6.14±9.71	0.769
Thrombus permeability (HU)	19.80±14.53	18.71±10.45	0.792
Thrombus length (cm)	1.65±1.00	1.78±0.80	0.682
Onset- door (min)	185.26±226.41	270.85±319.47	0.239
Onset- femoral puncture (min)	276.60±231.99	366.07±317.37	0.225
Femoral puncture-recanalization (min)	57.29±32.92	88.77±55.30	0.017*
Onset-recanalization time (min)	334.96±227.67	571.55±345.92	0.008**
Number of passes (n)	2.46±1.53	3.85±1.74	0.003**

*p<0.05 ** p<0.01 NIHSS: National Institutes of Health Stroke Scale

Table 3: Correlation of thrombus characteristics with clinical outcome and radiological data

		Thrombus density (HU)	Thrombus adjusted density (HU)	Thrombus permeability (HU)	Thrombus length (cm)
mRS (3rd month)	*r*	0.043	-0.022	-0.133	0.169
	p	0.706	0.846	0.242	0.150
NIHSS	*r*	0.118	0.040	-0.046	0.357
	p	0.301	0.728	0.689	0.002**
ASPECT	*r*	-0.117	-0.076	-0.078	-0.310
	p	0.306	0.505	0.495	0.007**
Femoral puncture-recanalization time (min)	*r*	0.276	0.261	-0.187	-0.040
	p	0.017*	0.025*	0.111	0.621
Onset- door time (min)	*r*	-0.121	-0.094	0.026	-0.018
	p	0.286	0.410	0.822	0.879
Onset-recanalization time (min)	*r*	-0.073	-0.064	-0.001	-0.037
	p	0.539	0.585	0.993	0.761
Number of passes (n)	*r*	0.311	0.234	-0.283	0.164
	p	0.005**	0.038*	0.012*	0.162
Thrombus length (cm)	*r*	0.322	0.262	-0.183	
	p	0.005**	0.024*	0.118	
Thrombus permeability (HU)	*r*	-0.466	-0.372		-0.183
	p	0.000**	0.001**		0.118

*p<0.05 ** p<0.01, NIHSS: National Institutes of Health Stroke Scale, mRS: modified rankin scale.

crucial determinant of efficiency and complication rate in thrombectomy.[7,15] Similar to the study of Gavriliuc *et al*., a positive correlation was found between thrombus length and admission NIHSS scores in our study.[9]

We observed that successful recanalization was associated with shorter symptom-to-recanalization and femoral puncture-to-recanalization times and fewer passes during the procedure. These findings are in alignment with studies by Baek *et al*. , Rossi *et al*., and Spiotta *et al*. , which have previously highlighted the significance of thrombus volume, clot area, and time to thrombectomy.[6,16,17]

However, our study did not find a significant association between thrombus density and recanalization outcomes, which contrasts with studies by Ye *et al*., Mokin *et al*., and Qazi *et al*. that suggested that thrombus density plays a key role in determining reperfusion outcomes.[8,18,19] On the other hand, the results of our study are similar to the studies by Baek *et al*. and Spiotta *et al*.[6,17] One possible explanation for this discrepancy could be differences in the population studied, as well as the variability in stroke severity and thrombectomy techniques used. In the study of Mokin *et al*., it was reported that thrombus

Table 4: Comparison of thrombus features according to etiology

	Non-cardioembolic (n=11)	Cardioembolic (n=47)	*p*
Thrombus density (HU)	45.091±9.47	39.04±10.04	0.075
Thrombus adjusted density (HU)	12.72±10.18	6.29±9.68	0.055
Thrombus permeability (HU)	19.54±11.74	18.19±11.17	0.721
Thrombus length (cm)	2.28±1.32	1.70±0.90	0.087

Table 5: Evaluation of factors associated with prognosis by univariate logistic regression analysis

	B value	*p*
Age (years)	1.032	0.095
NIHSS	1.141	0.007*
ASPECT	0.614	0.028*
Thrombus density (HU)	1.022	0.355
Thrombus permeability (HU)	0.973	0.157
Thrombus length (cm)	1.592	0.074
Thrombus adjusted density (HU)	1.014	0.562
Onset- femoral puncture (min)	1	0.834
Femoral puncture-recanalization (min)	1.01	0.125
Onset-recanalization time (min)	1.001	0.453
First pass recanalization	2.857	0.043
Number of passes (n)	1.395	0.026

ASPECT: The Alberta stroke program early CT score, NIHSS: National Institutes of Health Stroke Scale, collateral, * $p < 0.05$

density was higher in patients who were successfully recanalized with the SR technique.[8] In the study of Ye *et al*., when all patients were evaluated, they reported that although there was no correlation between thrombus density and successful recanalization, the SR technique tended to be more successful in high-density thrombus and contact aspiration in low-density thrombi.[19] Contrary to the results of these studies, in our study, no significant difference was found between the thrombus densities of the patients with and without successful recanalization in the MT procedure performed with the combined technique.

While not statistically significant, our study did observe a trend toward higher thrombus permeability in patients with good clinical outcomes. This observation is consistent with the literature suggesting that thrombus permeability may have a role in stroke outcome. For instance, Padmos *et al*. highlighted the importance of collateral flow and thrombus permeability in stroke[20], and Gensicke *et al*. found an impact of thrombus permeability on recanalization.[20] Further studies such as Huang *et al*. and Santos *et al*. have also suggested a value of thrombus imaging in predicting outcomes after endovascular therapy and associated permeable thrombi with higher treatment success.[21,22]

In a study by Berndt *et al*. in which the relationship between thrombus permeability and histopathological features of thrombus was evaluated, it was reported that permeability was higher in cardioembolic fibrin-rich thrombi. It is thought that fibrin-rich clots are more organized, allowing for easier penetration of the contrast agent. The reason for the lower permeability in the erythrocyte-rich clot was attributed to the tightly bound conglomerate with high hemoglobin content. In addition, it was stated in this study that thrombus permeability and cardioembolic origin could be recognized and it could be helpful in detecting the etiology in cryptogenic strokes.[23] Similarly, a negative correlation was found between thrombus density and permeability in our study. This situation can be interpreted

Table 6: Multivariate logistic regression analysis

	B value	*p*
Age (years)	1.056	0.033*
NIHSS	1.108	0.088
ASPECT	0.681	0.170
Thrombus length (cm)	0.993	0.981
First pass recanalization	1.549	0.583
Number of passes (n)	1.235	0.393

ASPECT: The Alberta stroke program early CT score, NIHSS: National Institutes of Health Stroke Scale, collateral, * $p < 0.05$

as the permeability of fibrin-rich thrombi is higher. In our study, as expected, thrombus corrected density in patients with large vessel atherosclerosis was higher than in patients with cardioembolic etiology, but statistical significance was not achieved. We did not find any significant difference between the two groups in terms of thrombus permeability. This may be due to the small number (n=11) in the large vessel atherosclerosis group. The positive correlation between thrombus length and thrombus density in our study can be explained by the presence of stasis around the original thrombus in long thrombi and associated erythrocyte accumulation.

This study found a correlation between thrombus characteristics, such as density, corrected density, length, and permeability, and procedure-related parameters like time to recanalization and the number of passes during the procedure. Such findings support the idea that these thrombus characteristics could potentially predict procedural success and clinical outcomes, a concept suggested by Berndt *et al*., Pilato *et al*., and Benson *et al*.[24–27]

The most important limitations of our study are that it was single-centre, retrospective, there was no control group, only combined technique was applied and the number of patients was small.

In conclusion, this study contributes to the growing body of literature investigating the relationships between thrombus characteristics, procedural parameters, and clinical outcomes in acute ischemic stroke. Despite some findings not reaching statistical significance, the trends observed provide valuable insights for future research. Larger studies are required to confirm our observations and further elucidate the complex relationships between these variables. Moreover, understanding the nature of thrombus, including its density, permeability, and length, could help to tailor the stroke treatment strategies in the future.

DISCLOSURE

Conflict of interest: None

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