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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

EFFECT OF INTRAVENOUS THROMBOLYTIC THERAPY ON MECHANICAL THROMBECTOMY OUTCOMES IN ACUTE ISCHEMIC STROKE PATIENTS WITH BASILAR ARTERY OCCLUSION

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ABSTRACT

INTRODUCTION: The aim of the study is to determine the effect of intravenous thrombolytic therapy on mechanical thrombectomy outcomes in stroke patients with basilar occlusion who have a high risk of mortality.
METHODS: The data of acute stroke patients who applied to our hospital between January 2018 and June 2022, who had basilar artery occlusion and underwent mechanical thrombectomy, were retrospectively analysed and included in the study. Patients' demographic characteristics, comorbidities, medications, blood pressure at admission to the emergency room, NIHSS, radiological imaging results, symptom onset time, intravenous recombinant tissue plasminogen activator (IV tPA) treatment and contraindications were examined. The posterior circulation Alberta stroke program early computed tomography score (pc-ASPECT) and the basilar artery on computed tomography angiography (BATMAN) scores were evaluated by examining brain computed tomography (CT) and CT angiography results. The results of the patients who received combined IV tPA and endovascular thrombectomy (EVT) were compared with the patients who underwent EVT alone. Post-procedure recanalization results, EVT complications, functional outcomes at discharge and 3-month outcomes were compared between the two groups. Clinical outcome was determined using the modified Rankin scale (mRS). Those with mRS 0-2 were included in the good clinical outcome group, whereas those with mRS 3-6 were included in the poor clinical outcome group.
RESULTS: The results of the patient group treated with combined IVtPA and EVT were compared with the group treated with EVT alone.The rate of patients who achieved complete recanalization after the procedure was 53.3% in the direct EVT group, compared to 42.9% in the combined group. Intracranial bleeding after EVT was13.3% in the direct EVT group,while it was7.1% in the combined group. After EVT, reocclusion was observed in 3(56.7%)patients in the direct EVT group and in2(14.3%) patients in the combined group. MRS was 31.1%in the0-2 direct EVT group and 35.7%in the combined group.While mRS3-6 was 68.9%in the directEVT group,it was 64.3%in the combined group.There was no statistically significant difference between the groups. Binary logistic analysis showed that advanced age increased the risk of poor outcome.Those with type3 aortic arch increased the risk of poor outcomes 10.5 times compared to those with type1.
DISCUSSION AND CONCLUSION: There was no statistically significant effect of the treatment type on mRS in the patient groups who received direct EVTand IVtPA plusEVT combination.Advanced age was found to be directly associated with poor clinical outcome.
Keywords: Basilar artery occlusion, direct EVT, bridging therapy.

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BAZİLER ARTER OKLÜZYONU OLAN AKUT İSKEMİK İNME HASTALARINDA İNTRAVENÖZ TROMBOLİTİK TEDAVİNİN MEKANİK TROMBEKTOMİ SONUÇLARI ÜZERİNE ETKİSİ

ÖZ

GİRİŞ ve AMAÇ: Çalışmanın amacı, mortalite riski yüksek olan akut baziler arter oklüzyonu olan inme hastalarında intravenöz trombolitik tedavinin mekanik trombektomi sonuçları üzerinde etkisini belirlemektir.
YÖNTEM ve GEREÇLER: 2018- 2022 tarihler arasında hastanemize başvuran, baziler arter oklüzyonu olan ve mekanik trombektomi işlemi uygulanan akut inme hastalarının verileri retrospektif olarak incelenerek çalışmaya dahil edildi. Hastaların demografik özellikleri, komorbiditeleri, başvuru sırasındaki NIH inme ölçeği, radyolojik görüntüleme sonuçları, semptom başlangıç zamanı, intravenöz doku plazminojen aktivatörü (IV-tPA) tedavisi ve kontrendikasyonları incelendi. Beyin bilgisayarlı tomografi (BT) ve BT anjiyografi sonuçları incelenerek pc-ASPECT (Posterior Circulation Alberta Stroke Program Early Computed Tomography Score) ve BATMAN (the Basilar Artery on Computed Tomography Angiography) skorları değerlendirildi. IV tPA ve endovasküler tedavi (EVT) uygulanan hasta grubu ile direkt EVT uygulanan hastaların sonuçları karşılaştırıldı. İki grubun işlem sonrası rekanalizasyon sonuçları, EVT komplikasyonları, taburculuk ve 3 ay sonrasındaki fonksiyonel sonuçları karşılaştırıldı. Klinik sonlanım, modifiye rankin skalası(mRS) kullanılarak belirlendi. mRS 0-2 olanlar iyi, mRS 3-6 olanlar ise kötü klinik sonlanım grubuna alındı.
BULGULAR: IV tPA artı EVT kombinasyonu uygulanan hasta grupu ile direct EVT uygulanan grubun sonuçları karşılaştırıldı. İşlem sonrası tam rekanalizasyon sağlanan hastaların oranı direct EVT grubunda %53.3 iken, kombine grupta %42.9 idi. EVT sonrası intrakranial kanama direkt EVT grubunda %13.3 iken, kombine grupunda %7.1 idi. EVT sonrası distal emboli toplam %27.1 oranında gözlemlendi. Bunlardan %22.2'si direct EVT grubunda, %42.9'u ise kombine grubunda idi. İki grup arasında istatiksel olarak anlamlı fark saptanmadı. EVT sonrası reoklüzyon direct EVT grubunda 3 (%56.7) hastada izlenirken, kombine grupta 2 (%14.3) hastada görüldü. MRS 0-2 direkt EVT grubunda % 31.1, kombine grupta ise %35.7 idi. MRS 3-6 direkt EVT grubunda %68.9 iken, kombine grupta %64.3 idi. Gruplar arasında istatiksel olarak anlamlı fark saptanmadı. Binary lojistik analizinde ileri yaş kötü sonlanım riskini 1.054 kat artırırdı. Tip 3 akus aortu olanların kötü sonlanım riski tip 1 olanlara göre 10.5 kat artırdı.
TARTIŞMA ve SONUÇ: Direk EVT ve IVtPA artı EVT kombinasyonu uygulanan hasta gruplarında tedavi şeklinin mRS üzerinde istatistiksel olarak anlamlı bir etkisi bulunmadı. İleri yaşın kötü klinik sonlanım üzerinde direkten etkisi görüldü.
Anahtar Sözcükler: Baziler arter oklüzyonu, direct EVT, köprüleme tedavi.

INTRODUCTION

Basilar artery occlusion accounts for only 1% of all ischemic strokes (1). It leads to severe neurological deficits, coma, locked-in syndrome, and death in 80% of patients (2). Today, successful outcomes are achieved with mechanical thrombectomy, especially in patients with anterior circulation large vessel occlusion. However, it may be difficult to achieve similar results in patients with posterior circulation large vessel occlusion. Even if successful recanalization is achieved, it does not always result in a good clinical outcome ('futile recanalization') (3). In the literature review, studies comparing the results of mechanical thrombectomy with or without intravenous thrombolytic therapy in patients with acute ischemic stroke showed greater efficacy of combined therapy on functional outcomes. High good clinical outcome and low mortality rates were reported at 3 months (3).

Randomized controlled trials (RCTs) conducted in recent years have shown that direct endovascular treatment (EVT) is not less effective than combined treatment in anterior circulation acute ischemic stroke patients with large vessel occlusion (4). This situation remains unclear for posterior circulation. Although the safety of EVT has been proven in patients with basilar artery occlusion (BAO), the effectiveness of EVT in patients with BAO is not superior to that of medical treatment, according to current data (4). In the BASICS study, no significant results were achieved between endovascular therapy and medical therapy in terms of functional outcome (5).

In this study, we aimed to determine the effect of intravenous thrombolytic therapy on mechanical thrombectomy outcomes in acute ischemic stroke patients with basilar artery occlusion.

METHODS

The study was carried out in Eskişehir Osmangazi University Faculty of Medicine, Department of Neurology. The data of acute ischemic stroke patients who applied to our hospital between 01.01.2018 and 01.06.2022, who had basilar artery occlusion and underwent

mechanical thrombectomy, were reviewed retrospectively. We examined patients' demographic characteristics, comorbidities, medications, blood pressure at admission to the ER, National Institutes of Health Stroke Scale (NIHSS) results, radiological imaging results, time parameters relative to stroke symptom onset, use of intravenous recombinant tissue plasminogen activator (IV tPA) and contraindications for IV tPA. The results of brain computed tomography (CT) and brain-neck CT angiography were analysed to determine posterior circulation Alberta stroke program early computed tomography score (pc-ASPECT) and the Basilar Artery on Computed Tomography Angiography (BATMAN) Score (Figure 1 and 2) (6,7). The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification was utilized for stroke aetiology. In addition, the results of patients who underwent IV tPA and EVT were compared with those who underwent direct EVT. Post-procedure recanalization results, EVT complications, functional outcomes at discharge and 3-month outcomes were compared between the two groups. Recanalization results were evaluated with modified thrombolysis in cerebral infarction score (mTICI). Clinical outcome was determined using the modified Rankin scale (mRS) score. Those with MRS 0-2 were included in the good clinical outcome group, while those with mRS 3-6 were included in the poor clinical outcome group.

Exclusion Criteria: Posterior circulation acute ischemic stroke patients who did not undergo thrombectomy and anterior circulation stroke patients were excluded from the study.

Statistical Analysis: Data were analysed with IBM SPSS V23. Conformity to normal distribution was analysed using the Shapiro-Wilk test. The Chi-square test, Yates correction, and Fisher's Exact tests were used to compare categorical data according to groups. Independent two-sample t-test was used to compare data with normal distribution according to pairwise groups, and the Mann-Whitney U test was used to compare data without normal distribution. Analysis results were expressed as mean ± standard deviation and median (minimum–maximum) for quantitative data, and frequency (percent) for categorical data. The value of significance was accepted as $p<0.050$. Binary logistic regression analysis was used to examine risk factors associated with poor outcomes.

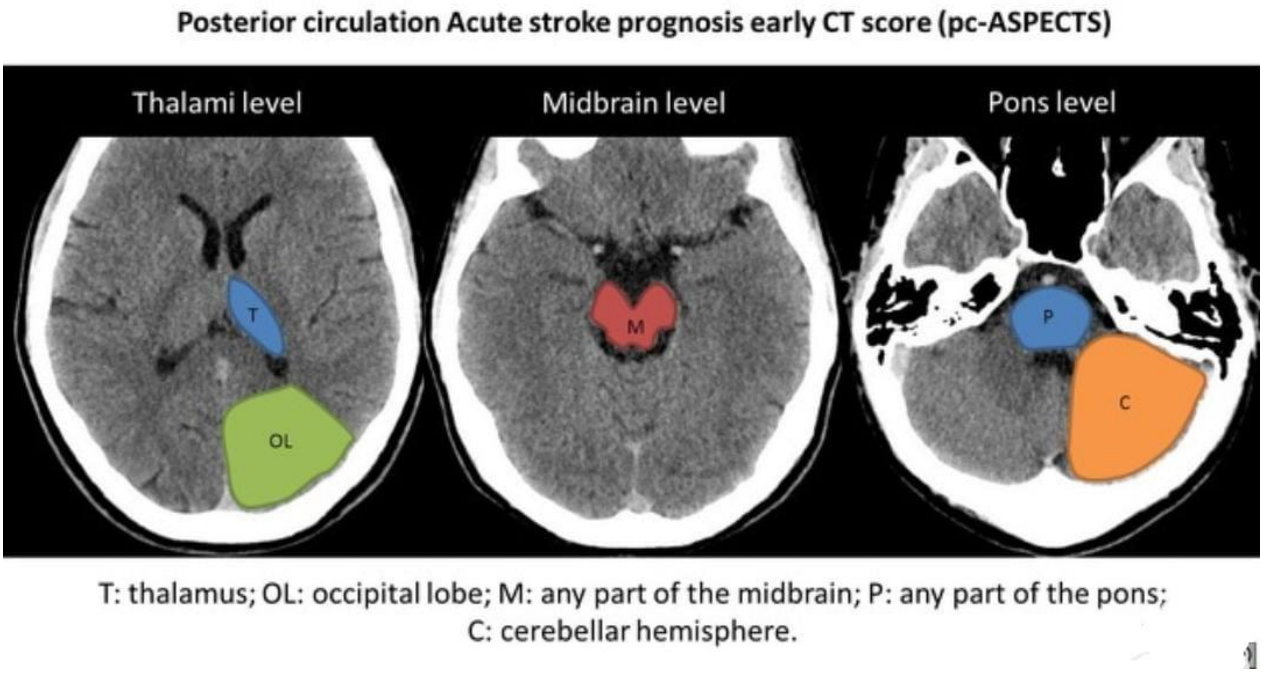

Figure 1. Posterior circulation - Acute stroke prognosis early CT score (pc-ASPECTS) illustration (Alwalid O. Radiopaedia). The pc-ASPECT assigns the posterior circulation 10 points: two points each are subtracted for early ischemic changes in midbrain or pons and 1 point each for early ischemic changes in left or right thalamus, cerebellum or PCA-territory, respectively.

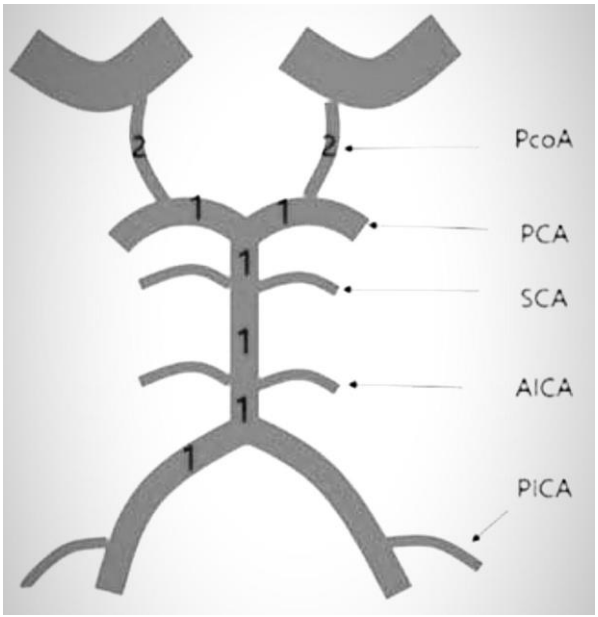

Figure 2. Schematic illustration of collateral scores (BATMAN) (Kwak and Park, Stroke. 2020). Basilar artery on computed tomography angiography score allocated 2 points for each posterior communicating artery (PCoA), 1 point for hypoplastic PCoA, and 1 point for each of the other segments giving a maximum score of 10.

RESULTS

Interventional neurology acute stroke registry records of Eskisehir Osmangazi University Faculty of Medicine, Department of Neurology were retrospectively analysed. A total of 59 patients who underwent interventional procedures between 2018 and 2022 were included in the study after the exclusion of patients with anterior circulation acute stroke..

General Characteristics: 57.6% of the patients were male. In terms of comorbidities, the rate of hypertension was 47.5%, diabetes mellitus 18.6%, previous stroke 23.7%, atrial fibrillation 19.3%, coronary artery disease 15.3%, and active smokers 33.9%. Of the patients with basilar artery occlusion, 16.9% were antiaggregant users, 3.4% were direct oral anticoagulant (DOAC) users, and 13.6% were warfarin users (Table 1). Almost all of these patients had missed doses and irregular drug use. EVT treatment was applied to 5 (%35.7) patients after full dose IV tPA treatment, while EVT treatment was applied to 9 (64.3%) patients before the full dose was administered. Direct EVT treatment was immediately applied to 45 patients due to various reasons such as symptom-to-door time, collateral status, and age of the patient.

The results of the patient group treated with combined IV tPA and EVT were compared with the patient group treated with EVT alone. While the median symptom-to-door time (min) was 131.0 in the direct EVT treatment, it was 59.0 in the combined IV tPA and EVT treatment. The median values obtained show statistically significant differences by the treatment modality (p=0.046). While the median door-to-imaging time (min) was 20.0 in direct EVT treatment, it was 11.5 in combined IV tPA and EVT. The median door-to-imaging times (min) show a statistically significant difference in direct EVT and combined IV tPA and EVT treatments (p=0.047) (Table 1).

The rate of patients with mTICI 3 post-procedure recanalization level, that is, complete recanalization, was 53.3% in the direct EVT group, while it was 42.9% in the IVtPA and EVT combination group. First-pass recanalization was observed in 20 (44.4%) patients in the direct EVT group, while it was observed in 8 (57.1%) patients in the combined group. 24-hour intracranial bleeding, which is one of the complications after EVT, was seen in 6 (13.3%) patients in the direct EVT group and in only 1 (7.1%) patient in the combined group. Distal embolism was observed in a total of 16 (27.1%) patients after EVT. Of these, 10 (22.2%) patients were in the direct EVT group, while 6 (42.9%) patients were in the combined IV tPA and EVT group. After EVT, reocclusion was observed in 3 (56.7%) patients in the direct EVT group, while it was observed in 2 (14.3%) patients in the combined group. Good clinical outcome (mRS 0-2) was 31.1% in the direct EVT group and 35.7% in the other group. Poor clinical outcome (mRS 3-6) was 68.9% in the direct EVT group, compared to 64.3% in the other group. There was no statistically significant difference between the two groups (p= 0.753) (Table 2).

At 3 months, mRS was 0 in 10 (22.2%) patients in the direct EVT group and in 3 (21.4%) patients in the combined IV tPA and EVT group. At 3 months, 3 (6.7%) patients with mRS 1 were in the direct EVT group, while 2 (14.3%) patients were in the other group. There was only 1 (1.7%) patient with MRS 2 and this patient was in the direct EVT group. At 3 months, 3 (6.7%) patients with mRS 5 who were included in the poor clinical outcome group were in the direct EVT group, while 2 (14.3%) patients were in the other group. While 26 (57.8%) of the MRS 6 patients, who died within 3 months, were in the direct EVT group, 7

Table 1. Baseline characteristics of all patients.

Baseline characteristics		Total	Direct EVT		IV tPA+EVT		p value
			Mean ± s.d n(%)	Median (Min-Max) n(%)	Mean ± s.d n(%)	Median (Min-Max) n(%)	
Age (years)			57.8 ± 11.9	60 (28- 81)	58.6 ± 16.1	52 (37 -91)	0.862
Gender	Female	25 (42.4)	19 (42.2)		6 (42.9)		1.000[Y]
	Male	34 (57.6)	26 (57.8)		8 (57.1)		
Medical history							
Atrial fibrillation		11 (19.3)	7 (15.6)		4 (33.3)		0.219[f]
Hypertension		28 (47.5)	23 (51.1)		5 (35.7)		0.483[Y]
Diabetes mellitus		11 (18.6)	9 (20)		2 (14.3)		1.000[f]
Coronary artery disease		9 (15.3)	6 (13.3)		3 (21.4)		0.431[f]
Prior stroke		14 (23.7)	13 (28.9)		1 (7.1)		0.152[f]
Obesity		9 (15.3)	8 (17.8)		1 (7.1)		0.671[f]
Smoking (active user)		20 (33.9)	15 (33.3)		5 (35.7)		1.000[f]
Smoking (former user)		6 (10.2)	6 (13.3)		0 (0)		0.319[f]
Chronic alcoholism		2 (3.4)	2 (4.4)		0 (0)		1.000[f]
Prior drugs							
Anticoagulant use		10 (16.9)	9 (20)		1 (7.1)		0.425[f]
- DOACs		2 (3.4)	2 (4.4)		0 (0)		1.000[f]
- Warfarin		8 (13.6)	8 (17.8)		0 (0)		0.179[f]
Baseline systolic blood pressure			163.4 ± 31.9	151 (110-256)	165.1 ± 24.9	170.5 (114-200)	0.457
Baseline diastolic blood pressure			92.5 ± 14.5	90 (70-140)	95.7 ± 12.3	100 (71-115)	0.322
Baseline NIHSS			22.3 ± 7.6	23 (8- 37)	21 ± 5.3	19.5(14-29)	0.557
Pc-ASPECT score			8.5 ± 1.5	9 (4- 10)	9 ± 1.4	9.5 (6- 10)	0.185
with contrast pc-ASPECT score			7.8 ± 1.8	7 (4 -10)	8.2 ± 2	8.5 (3- 10)	0.324
BATMAN score			5.5 ± 2.4	6 (0- 9)	5.6 ± 1.5	5 (3- 9)	0.714
Symptom-to-door time (min.)			177.6 ± 179.3	131 (12- 960)	82.9 ± 68.1	59 (10-236)	**0.046**
Door-to-imaging time (min.)			42 ± 102.4	20 (2-660)	15.4 ± 12.2	11.5 (2-50)	**0.047**
Symptom-to-recanalization time (min.)			319.2 ± 244.2	275 (30- 1255)	230.8 ±95.2	220 (100-416)	0.267
Door-to-femoral puncture time (min)			171.7 ± 270.1	100 (19- 1500)	140.5 ± 62.6	117 (75-300)	0.053
Femoral puncture-to-microcatheter time (min.)			18.4 ± 14.4	15 (3-79)	38.6 ± 54.7	20 (5- 210)	0.330
Femoral puncture-to-recanalization time (min.)			45.1 ± 32.6	35 (8- 160)	43 ± 27.4	40 (0- 90)	0.871
Discharge mRS			4.1 ± 2.4	5 (0- 6)	4.2 ± 2.4	5.5 (0- 6)	0.857
90-Day mRS			4.1 ± 2.6	6 (0- 6)	3.9 ± 2.7	5.5 (0- 6)	0.730

(50%) patients were in the other group (Table 2), (Figure 3).

Examination of risk factors associated with poor outcomes by binary logistic regression analysis as univariate and multivariate models showed that advanced age increased the risk of poor outcomes 1.054 times according to the univariate model (p=0.037). A high pc-ASPECT score reduces the risk of poor clinical outcomes and has a protective effect (OR=0.551; p=0.034). Those with type 3 aortic arch have a 10.5 times higher risk of poor outcomes than those with type 1 (p=0.043). There was no statistically significant effect associated with other factors (p>0.050). There was no statistically significant effect of the independent variables in the multivariate model (p>0.050) (Table 3).

DISCUSSION AND CONCLUSION

Basilar artery occlusion is a disease with a very poor natural course, resulting in disability and death (4). Previous studies yielded inconclusive and conflicting results on the comparison between EVT and standard medical treatment in patients with acute ischemic stroke associated with BAO (5,8,9).

In BASICS and BEST studies, which are randomized controlled studies, EVT and standard medical treatment groups were compared, and no significant difference was observed in terms of good functional outcome (5,8). Although successful recanalization rates have increased as a result of EVT performed with improved mechanical thrombectomy tools, poor clinical

Table 2. Stroke etiology of patients, EVT techniques, results of procedures, postprocedure complications and clinical outcome rates.

	Total n(%)	Direct EVT n(%)	IV tPA+EVT n(%)	p value
Post-procedure recanalization scale				
mTICI 0	1 (1.7)	1 (2.2)	0 (0)	
mTICI 2a	7 (11.9)	6 (13.3)	1 (7.1)	
mTICI 2b	17 (28.8)	12 (26.7)	5 (35.7)	0.607[x2]
mTICI 2c	4 (6.8)	2 (4.4)	2 (14.3)	
mTICI 3	30 (50.8)	24 (53.3)	6 (42.9)	
First pass recanalization	28 (47.5)	20 (44.4)	8 (57.1)	0.600[y]
Secondary pass recanalization	10 (16.9)	6 (13.3)	4 (28.6)	0.227[y]
ADAPT	26 (48.1)	19 (46.3)	7 (53.8)	
Isolated stent	12 (22.2)	10 (24.4)	2 (15.4)	---
Solumbra	1 (1.9)	0 (0)	1 (7.7)	
ARTS	1 (1.9)	1 (2.4)	0 (0)	
Intra-arterial tPA therapy	10 (17.2)	6 (13.3)	4 (30.8)	0.208[f]
Salvage technique balloon angioplasty	11 (18.6)	9 (20)	2 (14.3)	1.000[f]
Rescue technique permanent stent	10 (16.9)	10 (22.2)	0 (0)	0.098[f]
Complications after EVT				
Intracranial bleeding in the first 24 hours after EVT	7 (11.9)	6 (13.3)	1 (7.1)	1,000[f]
Post-EVT intracranial hemorrhage type				
Type 1 hematoma	3 (42.9)	3 (50)	0 (0)	
Type 2 hematoma	2 (28.6)	1 (16.7)	1 (100)	---
Subarachnoid hemorrhage	2 (28.6)	2 (33.3)	0 (0)	
Distal embolism after EVT	16 (27.1)	10 (22.2)	6 (42.9)	0,172[f]
Vessel rupture during EVT	1 (1.7)	1 (2.2)	0 (0)	1.000[f]
Dissection during EVT	6 (10.2)	5 (11.1)	1 (7.1)	1.000[f]
Reocclusion after EVT	5 (8.5)	3 (6.7)	2 (14.3)	0.583[f]
Vasospasm after EVT	7 (11.9)	6 (13.3)	1 (7.1)	1.000[f]
Decompression after EVT	2 (3.4)	1 (2.2)	1 (7.1)	0.421[f]
Cardioembolic stroke	16 (29.1)	13 (28.9)	3 (30)	
Extracranial atherosclerotic disease	11 (20)	9 (20)	2 (20)	
Intracranial atherosclerotic disease	18 (32.7)	16 (35.6)	2 (20)	0.548[x2]
Extracranial dissection	2 (3.6)	2 (4.4)	0 (0)	
Intracranial dissection	1 (1.8)	1 (2.2)	0 (0)	
Stroke of undetermined cause	7 (12.7)	4 (8.9)	3 (30)	
Good clinical outcome (mRS 0-2)	19 (32.2)	14 (31.1)	5 (35.7)	0.753[f]
Poor clinical outcome (mRS 3-6)	40 (67.8)	31 (68.9)	9 (64.3)	0.753[f]

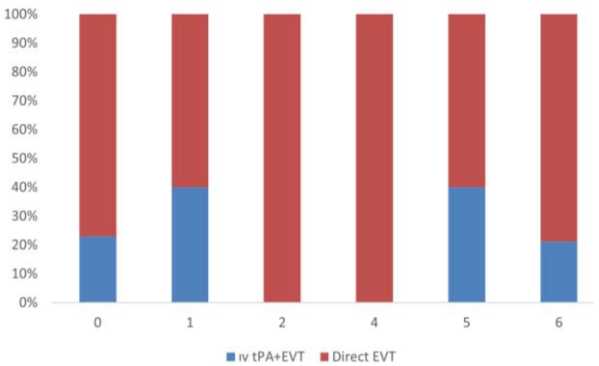

Figure 3. 100% stacked column graph of 3rd month mRS scores by groups.

outcome rates are still high (7). However, the ATTENTION and BAOCHE studies, which were published in 2022, indicated that good functional outcome rates (mRS 0-3) were higher in the EVT group than in the best medical treatment group (10,11).

A recent meta-analysis of DIRECT-MT, DEVT, SKIP, and MR CLEAN-NO IV studies reported an increase in the success of revascularization after EVT in patients who underwent IV-tPA. However, combined IV tPA and EVT treatment has been shown to cause higher revascularization, less functional dependence, and less complication compared to patients treated with EVT alone (12). In our study, we compared the results of the patient group who received IV tPA and EVT combined and the patients who received EVT alone. The rate of patients with mTICI 3 recanalization was 42.9% in the combined IV tPA and EVT group, and 53.3% in the direct EVT group. Consistent with the results of many studies (4,12), no statistically significant difference was noted between the two groups in our study. Complications such as symptomatic intracranial haemorrhage were observed in 13.3% of the direct EVT group and in 7.1% of the patients who

Table 3. Evaluation of risk factors affecting poor clinical outcome.

	Univariate		Multivariate	
	OR (%95 CI)	p	OR (%95 CI)	p
Age (years)	1.054 (1.004 – 1.106)	**0.034**	1.057 (0.954 – 1.172)	0.292
Baseline systolic blood pressure	1.014 (0.994 – 1.035)	0.178	1.041 (0.978 – 1.107)	0.204
Baseline diastolic blood pressure	1.034 (0.99 – 1.081)	0.130	0.975 (0.876 – 1.086)	0.649
Baseline NIHSS	1.04 (0.961 – 1.125)	0.331	1.027 (0.896 – 1.177)	0.706
Pc-ASPECT score	0.551 (0.318 – 0.955)	**0.034**	0.286 (0.014 – 5.827)	0.416
with contrast pc- ASPECT score	0.645 (0.446 – 0.933)	**0.020**	1.441 (0.162 – 12.839)	0.743
BATMAN score	0.849 (0.643 – 1.122)	0.250	0.741 (0.463 – 1.186)	0.212
Symptom-to-recanalisation time (min.)	1.004 (0.999 – 1.009)	0.154	1.003 (0.997 – 1.009)	0.291
Femoral puncture-to-recanalisation time (min.)	1.017 (0.995 – 1.04)	0.128	1.003 (0.964 – 1.043)	0.887
Type of treatment (Referance: Direct EVT)	0.813 (0.23 – 2.872)	0.748	1.018 (0.107 – 9.722)	0.987
Sex (Referance: Female)	1.35 (0.449 – 4.058)	0.593	4.839 (0.546 – 42.887)	0.157
Aortic arch type (Reference: Type 1)				
Type 2	1.575 (0.44 – 5.638)	0.485	0.169 (0.008 – 3.538)	0.252
Type 3	10.5 (1.076 – 102.478)	**0.043**	6.859 (0.1 – 468.711)	0.372
Distal embolism after EVT (Reference: No)	1.607 (0.441 – 5.86)	0.472	1.693 (0.268 – 10.695)	0.576
Dissection during EVT (Reference: No)	2.571 (0.279 – 23.7)	0.405	1.446 (0.006 – 373.443)	0.897

underwent combined IV tPA and EVT.

A recent randomized controlled trial showed that direct EVT therapy within 4.5 hours of symptom onset was equally effective compared to bridging therapy (combined IV tPA and EVT). Due to limited patient data on posterior circulation, direct EVT therapy was not recommended for patients with BAO. Although an increase was observed in haemorrhagic transformation in the group undergoing bridging treatment, similar results were reported between the two groups in terms of symptomatic intracranial bleeding (4). Several studies reported that IVtPA was associated with an increased risk of haemorrhagic transformation, delayed initiation of the EVT procedure, adverse thrombus migration, and fragmentation, resulting in thrombi that were out of reach for mechanical thrombectomy (13,14,15,16). IVtPA before EVT appeared to be ineffective in patients with long clots, low clot burden scores, proximal occlusions, long symptom-to-treatment time or with calcific emboli (13,17).

In the study of Nappini et al., distal embolism was shown to be more common in patients who underwent direct EVT (4). Although no statistically significant difference was observed between the two groups in our study, the rate of distal embolism was 42.9% in the combined IV tPA and EVT group, while it was 22.2% in the direct EVT group.

In their multicentre cohort study conducted in 2022, Nie et al. showed that patients receiving combined IVtPA and EVT displayed a better clinical outcome (13).

In another study conducted by Siow et al. in 2022, they compared the results between bridging IVtPA and direct EVT, reporting that the rate of favourable functional outcome was similar on day 90. Subgroup analysis showed that patients with intracranial atherosclerotic stenosis had a higher rate of positive functional outcome in bridging therapy in 90 days compared to patients who underwent direct EVT. Symptomatic intracranial bleeding rates were similar between the two treatment groups (5.0% in bridging with IVtPA versus 4.4% in direct EVT) (18).

In BAO, intracranial atherosclerosis is reported as the etiological cause in 80.97% of stroke cases in Asian studies, which is higher compared to anterior circulation large artery occlusion. Therefore, IV tPA and EVT combined may theoretically yield more benefits primarily in acute stroke patients with BAO (13). In our study, although the patients belonged to the Turkish society, intracranial atherosclerotic stenosis was detected more than cardioembolic strokes with a slight difference. While direct EVT was applied to 35.6% of these patients, bridging therapy was applied to 20%.

It is assumed that thrombolytic agents flow through the collateral vessels and reach even the distal end of the thrombus effectively. It is argued that mechanical thrombectomy procedures from the narrowed lumen due to intracranial stenosis are not effective in embolic strokes and strokes associated with other aetiologies where collateral development is more limited, and IV tPA treatment prior to EVT may be beneficial in cases with a high risk of occlusion (18,19).

IV tPA therapy potentially softens or dissolves the thrombus, resulting in more effective EVT and better functional outcomes. Therefore, ischemic stroke patients with BAO may potentially be candidates for IV tPA bridging therapy (18).

In a multicentre, open-label, international, randomized, controlled study conducted by Langezaal et al in 2021, they showed that EVT and medical treatment could not exclude the benefit of EVT in patients with BAO, although no effective difference was found on good functional outcomes (5). In another multicentre, prospective, non-randomized cohort study conducted in 2020, the results of 829 patients (patients receiving standard medical treatment and EVT combined with standard medical treatment) showed better results in the combined group. What was accepted as standard medical treatment was IV tPA or IV tPA using urokinase, antiplatelet drugs, systematic anticoagulation or combinations of these medical treatments (9).

Recently, several studies have reported prognostic factors associated with clinical outcomes in patients with acute BAO after EVT. Although there were some differences in the cut-off value, the baseline low NIHSS score (NIHSS<15) prior to EVT was shown as an independent indicator of good outcomes in all studies. In addition, posterior circulation acute stroke prognosis early CT score (high pc-ASPECT score), use of MRI prior to EVT, good collateral status (high BATMAN or posterior circulation collateral score), time to recanalization within 6 hours, and successful recanalization were defined as independent predictors of good outcome (7,20,21,22,23). In our study, examination of the risk factors affecting clinical outcomes by binary logistic regression analysis showed that patients' age, pc-ASPECT scores, as well as the types of the aortic arch, were among the factors. NIHSS was not shown to exert a positive effect on functional outcomes in our study. Advanced age was found to increase the risk of poor outcomes. Higher pc-ASPECT scores reduced the risk of poor outcomes and exerted a protective effect. Those with type 3 aortic arch were 10.5 times more likely to have a poor outcome than those with type 1 aorta, which is associated with the prolongation of treatment time due to higher arc types with tortuousness and wider vascular origins. This directly affects the clinical outcome (24,25).

In our study, symptom-to-door time and door-to-imaging time showed a statistically significant difference between the two groups. While the median symptom-to-door time was 131 minutes in the direct EVT group, it was 59 minutes in the combined IV tPA and EVT group. This was because many patients missed the IV tPA time window (4.5 hours from the onset of stroke symptoms). These patients were gathered in the direct EVT group. Logistic analysis of the time from the onset of stroke symptoms to the time of recanalization showed no significant effect in terms of poor clinical outcome in both groups.

Contrary to many, there are studies in the literature that argue that the time from symptom onset to recanalization is not associated with positive results (7). It is thought that the concept of time (from the onset of stroke symptoms to the initiation of treatment) should not be an absolute criterion for EVT in patients with acute BAO (7).

In most available studies, successful recanalization (Thrombolysis in Cerebral Infarction 2b, 3) is an indicator of a positive result (7). Although the direct EVT group was mostly mTICI 3 in our study, successful recanalization exerted no significant effect on functional results in both groups.

Thrombectomy with direct aspiration has been reported to cause shorter procedure time, better reperfusion, and better clinical outcome compared to thrombectomy with stent-retriever in patients with large vessel occlusion stroke of the anterior circulation (26). However, it has been emphasized that fewer rescue devices are needed in EVT treatment with stent retriever. It has also been shown that the time from femoral puncture to reperfusion is longer. It has been shown that there is no significant difference between direct aspiration and stent-retriever use in terms of complication rates and mortality (27,28). The results are similar to our study.

The retrospective and single-centre design of the study and the small number of the patients constituted the limitations of our study.

In conclusion, it was observed that the treatment method exerted no statistically significant effect on 3-month mRS in the patient groups who received direct EVT and IVtPA and EVT combined. No significant difference was observed between the two groups in terms of bleeding rates and distal embolism.

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Ethics

Ethics Committee Approval: The study was approved by Ethics Committee of Eskişehir Osmangazi University (Date: 22.11.2022, No: 40).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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