

**ORIGINAL ARTICLE**

**ARAŞTIRMA YAZISI**

**OUR EXPERIENCE WITH INTRAVENOUS TROMBOLYTIC TREATMENT IN ACUTE  
MCA M2-M3 OCCLUSIONS**

**Seda BOSTAN, Özlem AYKAÇ, Atilla Özcan ÖZDEMİR**

**Eskişehir Osmangazi University Faculty of Medicine, Department of Neurology, Eskişehir, TURKEY**

**ABSTRACT**

**INTRODUCTION:** Trombectomy is commonly used in acute middle cerebral artery, especially in M1 and M2 segment, occlusions. The decision of iv tPA or thrombectomy in M2-M3 segment occlusions is still controversial. In our study, we aimed to assess good clinical outcomes, mortality and hemorrhage rates in acute ischemic stroke patients with MCA M2-M3 occlusion who were treated with iv tPA.

**METHODS:** In our study, we analyzed data from 38 patients admitted to the emergency department between April 2015-March 2019, whose CT-angiographies showed M2-M3 occlusion. Age, gender, NIHSS and ASPECT scores at admission and iv tpa time period data were collected. Intracerebral hemorrhage and mortality rates, Mrs score at third month after iv rtpa treatment were also assessed

**RESULTS:** There was no statistically significant relationship between NIHSS score at admission, ASPECT score or t-PA time period; but multivariate analysis showed that NIHSS score at admission was the most relevant variable with good clinical outcome. Among all variables, age is found to be the most relevant and statistically significant variable with good clinical outcome. Symptomatic intracranial hemorrhage was not observed in any of the 38 patients. At third month assessment, 18 patients' mRS score was 0-1 (excellent outcome), 2 patients' mRS score was 2 (good outcome) and 18 patients' mRS score was 3-6 (poor outcome); %47,3, %5,2 and %47,3 respectively.

**DISCUSSION and CONCLUSION:** Results from our study is found to be better than other studies with iv. trombolysis and similar to those with endovascular treatment in MCA M2-M3 occlusions in literature. Therefore we conclude that trombolytic treatment must be considered in a patient with acute MCA M2-M3 occlusion before thrombectomy plan.

**Keywords:** IV trombolytic, endovascular treatment, middle cerebral artery, tPA, MCA M2-M3 occlusion, acute stroke.

**AKUT MCA M2-M3 OKLÜZYONLARINDA İNTRAVENÖZ TROMBOLİTİK TEDAVİ DENEYİMİMİZ**

**ÖZET**

**GİRİŞ ve AMAÇ:** Orta serebral arter (MCA) oklüzyonlarında özellikle M1 M2 segment oklüzyonlarında trombektomi yaygın olarak uygulanırken, M2-M3 segmenti oklüzyonlarında tedavi tercihi hala tartışmalıdır. Çalışmamızda M2-M3 oklüzyonu olan ve intravenöz trombolitik tedavi verilen akut iskemik inme hastalarının iyi klinik sonuçları, mortalite ve kanama oranlarını değerlendirmeyi amaçladık.

**YÖNTEM ve GEREÇLER:** Nisan 2015- Mart 2019 tarihleri arasında acil servise başvuran ve nörogörüntülemesinde M2-M3 oklüzyonu saptanarak trombolitik tedavi uyguladığımız 38 hastayı değerlendirdik. Hastaların yaşı, cinsiyeti, acile başvurusundaki NIHSS değeri, ASPECT skoru ve iv rt PA zaman dilimi verileri ve iv rt PA sonrası hemoraji, mortalite ve 3. Aydaki mRS skorları analiz edildi.

**BULGULAR:** Başvurudaki NIHSS değeri, ASPECT skoru ve iv rt PA zaman dilimi ile iyi klinik sonuçları arasında anlamlı ilişki bulunmasa da, çoklu değişken analiziyle bakıldığında iyileşmeyle en çok ilgili olan başvurudaki NIHSS değeri olarak bulundu (p=0,27). Tüm değişkenlere bakıldığında ise iyileşmeyi en çok etkileyen faktör yaş olarak saptandı (p=0,01). Hiçbir hastada semptomatik hemoraji gözlenmedi. 3 ay sonrasında 38 hastadan mRS skoru 0-1 olan (çok iyi outcome) 18 hasta (%47,3), mRS 2 olan (iyi outcome) 2 hasta (%5,2) ve mRS skoru 3-6 olan (kötü outcome) 18 hasta (%47,3) bulunmaktaydı.

**Corresponding author:** Seda Bostan MD, Eskişehir Osmangazi University Faculty of Medicine, Department of Neurology, Eskişehir, Turkey

**Phone:** 02222392979

**E-mail:** sedabostan@yahoo.com

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**TARTIŞMA ve SONUÇ:** Çalışmamızda literatürdeki MCA M2-M3 oklüzyonlarındaki trombolitik tedavi sonuçlarından daha iyi, endovasküler tedavi serilerinin sonuçlarına benzer bulgular saptandı. Akut MCA M2-M3 oklüzyonlarında trombektomi planı öncesinde trombolitik tedavi verilebilir.

**Anahtar Sözcükler:** IV trombolitik, endovasküler tedavi, orta serebral arter, tPA, MCA M2-M3 oklüzyonu, akut inme.

## INTRODUCTION

Ischemic stroke is one of the most important causes of morbidity and mortality in the world. The efficacy and reliability of intravenous recombinant tissue plasminogen activator (iv rtPA) therapy in ischemic stroke has long been known and is safely used in acute stroke patients (1). With the development of endovascular treatments, this treatment has been started to be widely used due to hemorrhage rates similar to IV rtPA in proximal large vessel occlusions and good clinical outcomes (2,3).

The vertical branch of the middle cerebral artery (MCA), starting from the sylvian fissure and extending to the operculum, is called the M2 segment (4). The M3 segment starts from the circular sulcus of the insula and terminates at the surface of the sylvian fissure (Figure 1) (4, 5). Isolated MCA M2 occlusion occurs in 9-38% among all stroke causes [6]. Although the vascular regions affected by acute ischemia of M2 occlusion are smaller than M1 occlusion, 50% of M2 occlusion patients may end up with mortality or severe disability.

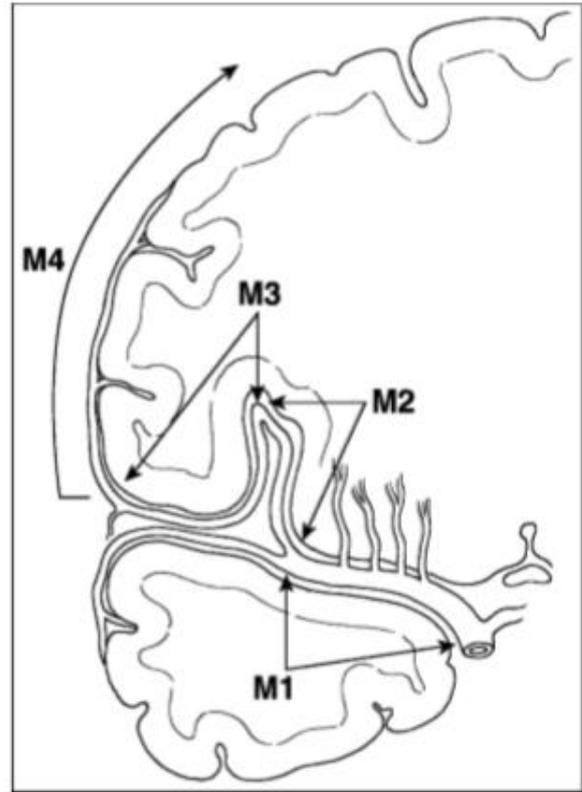
Although thrombectomy in M2 segment is common in large vessel occlusions, the preference for IV rtPA or thrombectomy in M2-M3 occlusions is still controversial.

Studies evaluating the effectiveness of IV rtPA relative to the location of occlusion are insufficient. This study aims to present recovery and mortality rates, clinical outcomes and hemorrhage rates of acute stroke patients with M2-M3 occlusion and treated with IV rtPA.

## MATERIAL AND METHODS

Approval of the Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine was obtained for our research.

The study was conducted with 38 patients admitted to Eskişehir Stroke Center, between April 2015 and March 2019, with presenting acute ischemic stroke clinic manifestation and received IV rtPA treatment due to M2-M3 occlusion of



**Figure 1.** Branches of the middle cerebral artery (5).

middle cerebral artery (MCA) as diagnosed in CT-angiographies taken in the emergency department. Prospective clinical and neuroimaging data were evaluated retrospectively.

Demographic data and clinical characteristics of the patients were recorded. The severity of stroke on hospital admission was assessed by the National Institutes of Health Stroke Scale (NIHSS).

Occlusion localization was recorded in neuroimaging. The vertical segment of the MCA was named M2 and the opercular segment was named as M3 [5].

Symptom-to-door, door-to-imaging, door-to-needle and symptom-to-needle times, predicted etiology of stroke, and presence of complications were recorded.

NIHSS scores, modified Rankin scores (mRS) and symptomatic and asymptomatic hemorrhage rates at 24 hours and 3 months after treatment were recorded.

Three months after treatment, patients with mRS 0-2 were deemed to have clinically good outcomes.

It was defined as the NIHSS score as least 8 points higher than the baseline score per hour. Groups of patients who recovered dramatically and who did not were compared.

**Statistical Analysis:** The data of the study were evaluated in IBM SPSS Statistics 21.0 program (IBM Corp, Released 2012, IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp). Categorical data were given as frequency distribution and percentage. Chi-square test was used for the analysis of the table created based on the categorical variables.  $p < 0.05$  was considered statistically significant.

## RESULTS

Of 38 patients, 6 out of 21 patients in the good clinical outcome group were female (28.6%), 15 were male (71.4%), and 9 out of 17 patients in the poor clinical outcome group were female (52.9%), and 8 (47.1%) were male. There was no significant difference between the two groups in terms of gender ( $p = 0.13$ ).

Although there was no significant correlation, when evaluated individually, between the NIHSS value, ASPECT score and IV rtPA time frame and

good clinical outcome, the NIHSS value at the admission was found to be the most correlated with the good clinic outcome according to the multivariate analysis ( $p = 0.27$ ) (Table I).

When we looked at all variables, age was the factor most affecting the recovery ( $p = 0.01$ ).

The mean age of the group with poor clinical outcome was 73.7 ( $\pm 6.7$ ), and the mean age of the group with good clinical outcome was 60.9 ( $\pm 13.5$ ).

Of patients under the age of 65, 93.8% improved dramatically, while the dramatic improvement rate was 27.3% in patients over the age of 65.

No symptomatic hemorrhage was observed in any of the 38 patients, who received intravenous thrombolytic therapy.

No asymptomatic hemorrhagic transformation was observed in any of the 21 patients in the good clinical outcome group. In the poor clinical outcome group, type 3 petechial hemorrhage was observed in 3 (17.6%) of 17 patients, and type 2 petechial hemorrhage was observed in 1 (17.6%) patients.

The mortality rate of 38 patients given intravenous thrombolytic therapy was 5.2% (2 patients). One of these two patients died due to a non-cerebral condition, caused by heart failure. Three months later, of the 38 patients, 0 patients had (47.3%) a mRS score of 0-1 (very good outcome), 2 patients (5.2%) had a mRS score of 18-3 (good outcome), and 2 patients (47.3%) had a mRS score of 6-18 (poor outcome) (Figure II).

**Table I.** Distribution of patient data in good and poor clinical outcome groups.

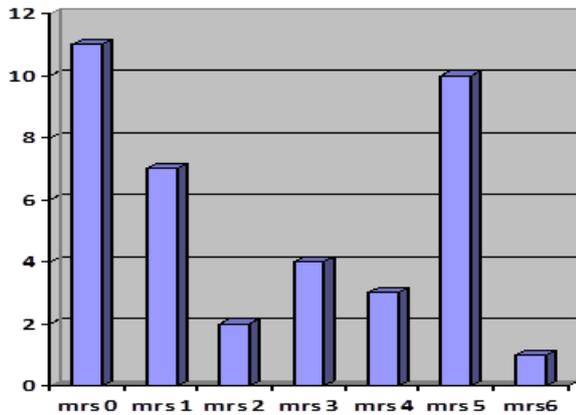
Criteria		Good Clinic Outcome	Poor Clinic Outcome	Total
Gender	M	16 (76,2%)	7 (41,2%)	23 (60,5%)
	F	5 (23,8%)	10 (58,8%)	15 (39,5%)
Aspect Score	ASPECT $\leq 7$	2 (9,6%)	3 (17,7%)	5 (13,2%)
	ASPECT $> 7$	19 (90,4%)	14 (82,3%)	33 (86,8%)
Age	Mean ( $\pm$ SD)	73,7 ( $\pm 6,7$ )	60,9 ( $\pm 13,5$ )	66,6 (12,6 $\pm$ )
NIHSS Scor	NIHSS $< 8$	18 (85,7%)	5 (31,3%)	23 (60,5%)
	NIHSS $> 8$	3 (14,3%)	12 (68,7%)	15 (39,4%)
Fischer Hemoraji Classification	Patechial type 1	0	3 (17,6%)	3 (7,8%)
	Patechial type 2	0	3 (17,6%)	3 (7,8%)

## DISCUSSION

In our study, the rate of patients who were functionally independent (mRS 0-2) in the third month was 52.6%, the mortality rate was 5.26%, and the symptomatic hemorrhage rate was 0%. The asymptomatic hemorrhagic transformation rate was 7.8% in petechial type 1, and 7.8% in petechial type 2, which was 15.7% in total. Our

study also supports that intravenous thrombolytic therapy is an effective and reliable treatment method in patients suffering from acute ischemic stroke due to acute MCA M2-M3 occlusion.

Occlusion of the MCA M2 segment generally responds positively to intravenous thrombolytic therapy. However, in cases where thrombolytic



**Figure II.** 3rd-month MRS scores of the patients receiving t-PA therapy in our study..

therapy is contraindicated and patients admitted more than 4.5 hours later, endovascular treatment should be considered (4). Distal localization of the M2 segment is technically difficult to reach due to its small diameter and thin wall, and the risk of periprocedural complications is high (4).

In a study of 1080 diseases conducted by Saber et al., the functional independence rate of patients suffering from acute ischemic stroke due to M2 occlusion was 59%, and the mortality and symptomatic hemorrhage rates were 16% and 10%, respectively (7). The clinical outcome, symptomatic hemorrhage and mortality rates of our study were similar to those of acute ischemic stroke patients with M2 occlusion, who underwent thrombectomy in the literature (Table II).

Thanks to newly developed technological devices for endovascular treatment, mechanical thrombectomy is increasingly preferred for distal occlusions (8). In a study conducted by Kim et al., it was reported that thromboaspiration had 72% successful recanalization rate and thrombectomy with stent retriever devices had an 87.5% successful recanalization rate. In the same study, good functional termination rate was 84% in thromboaspiration group and 75% in stent retriever group (9).

In another study, 288 out of 522 patients with acute M2 segment occlusion underwent endovascular treatment, and 234 underwent medical treatment. Good clinical outcomes were 62.8% and 35.4% for the endovascular treatment

and medical treatment group, respectively. This difference was statistically significant ( $p=0.001$ ). Intracerebral hemorrhage rates were 5.6% and 2.1%, and no significant difference was found between the two groups (10). It is, therefore, suggested that endovascular thrombectomy is superior to medical treatment in the treatment of acute MCA M2 occlusion. While difficulties exist in the endovascular approach in the M2 segment, the risk of periprocedural complications for endovascular treatment of M1 and M2 occlusions was found to be similar thanks to the development of new thrombectomy techniques (11).

In another study by Qurashi et al., 34 out of 51 patients with MCA M2 occlusion underwent endovascular treatment and 17 underwent thrombolytic therapy. Intracranial hemorrhage rates of the groups were 5.9% and 11.8%, respectively. The proportion of patients with very good outcomes (mRS 0-1) in the third month was 38.2% and 17.6%, respectively. In the third month, the proportion of patients with good outcomes (mRS score 0-2) was found to be 52.9% in the endovascular treatment group, and 41.2% in the tPA group. Although MCA M2 occlusions have a higher rate of good clinical outcome with thrombectomy and a lower risk of hemorrhage, there is no clear data for M2-M3 occlusions in the literature.

Small number of patients and the retrospective nature of the research were among the limitations of our study. Prospective analysis of data from more patients is needed.

As a result, thrombolytic therapy in MCA M2-M3 occlusions is an effective and reliable method. Evaluation of vascular structures with non-invasive imaging techniques prior to the decision of treatment is important for prognosis. Thrombolytic therapy should be started prior to thrombectomy plan in acute MCA M2-M3 occlusions. Intravenous thrombolytic therapy should be started in cases with M2-M3 occlusion in the centers where endovascular treatment is not performed. In addition, in elderly patients with M2-M3 occlusion and elongated arch with severe internal carotid proximal and distal tortuosity, intravenous thrombolytic therapy alone may be considered instead of endovascular therapy.

**Table II.** Comparison of the data of our study with the data of the studies in the literature.

Treatment Method	Saber H et al.	Sarraj A. et al.		Qureshi A et al.		Our study
	Thrombectomy	Thrombectomy	IV tPA	Thrombectomy	IV tPA	IV tPA
Number of patients	1080	288	234	34	17	38
Symptomatic Hemorrhage rate	10%	5.6%	2.1%	5.9%	11.8%	0%
3. month MRS 0-2	59%	62.8%	35.4%	52.9%	41.2%	52.6%
Mortality	16%			5.9%	35.3%	5.2%

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