DOI:10.4274/tnd.2020.87405
Turk J Neurol 2020;26:133-137

The Relationship Between Mean Platelet Volume, Platelet Count, Platelet Lymphocyte Ratio, and Recanalization Success in First-pass Thrombectomy of Middle Cerebral Artery Occlusions

Trombektomi ile Tedavi Edilen Orta Serebral Arter Oklüzyonlarında İlk Geçiş Sonunda Rekanalizasyonun Ortalama Trombosit Hacmi, Trombosit Sayısı ve Trombosit Lenfosit Oranı ile İlişkisi

Nihat Şengeze[1], Semih Giray[2]

[1]Suleyman Demirel University Faculty of Medicine, Department of Neurology, Isparta, Turkey
[2]Gaziantep University Faculty of Medicine, Department of Neurology, Gaziantep, Turkey

Abstract

Objective: Platelet activation plays an important role in the development of cerebral arterial occlusion. Mean platelet volume (MPV) and platelet count are reported to be good indicators of platelet activity. The aim of this study was to investigate the relationship between MPV, platelet count, and the platelet-lymphocyte ratio with endovascular recanalisation success in acute middle cerebral artery (MCA) M1 occlusions.

Materials and Methods: Ninety-one patients with acute stroke with MCA M1 occlusions who were treated with endovascular mechanical thrombectomy between January 2015 and January 2019 were included in the study. Complete blood count, routine biochemical tests, erythrocyte sedimentation rate, clotting time, aPTT, and INR values of all patients were evaluated. The patients were separated into two groups, those who were recanalized successfully with at least thrombolysis in cerebral infarction score (TICI) 2b at the first pass, and those whose recanalisation procedure was unsuccessful with ≤TICI 2a.

Results: Among the 91 patients included in the study, 61.5% (n=56) were women. The mean age was 62.3±13.4 years. The median National Institute of Health stroke scale score was 16 (14-19), platelet count was 261.360±78.100/µL, and MPV was 10.2±0.96 fL. There were 48 (52.7%) patients in the poor recanalization (≤ TICI 2a) group and 43 (47.3%) in the successful recanalization (≥ TICI 2b) group after the first pass. There were no statistically significant differences between recanalization success and MPV values, platelet counts, and platelet-lymphocyte ratio (PLR) after the first pass (p values respectively; 0.37, 0.12, and 0.26).

Conclusion: Our study revealed that there was no statistical relationship between first-pass thrombectomy success of MCA M1 occlusions and MPV, platelet count, and PLR values. It is essential to investigate other factors beyond MPV, platelet count, and PLR value in the recanalization success of MCA M1 occlusions.

Keywords: Mechanical thrombectomy, middle cerebral artery occlusion, mean platelet volume, platelet count, platelet-lymphocyte ratio, ischemic stroke

Öz

Amaç: Trombosit aktivasyonu serebral arteriyel oklüzyon gelişmesinde önemli bir role sahiptir. Ortalama trombosit hacminin (MPV) ve trombosit sayısının trombosit aktivitesinin iyi bir göstergesi olduğu bildirilmektedir. Bu çalışmada MPV'nin, trombosit sayısının ve trombosit lenfosit oranının endovasküler yolla tedavi edilen orta serebral arter M1 oklüzyonlarında, ilk geçişte rekanalizasyon ile ilişkisinin araştırılması amaçlandı.

Gereç ve Yöntem: Çalışmaya Ocak 2015-Ocak 2019 yılları arasında akut iskemik inme kliniği ile hastaneye başvuran ve orta serebral arter M1 oklüzyonu saptanan, endovasküler mekanik trombektomi ile tedavi edilen 91 hasta dahil edildi. Çalışmaya alınan bütün olguların hemogram, rutin biyokimyasal inceleme, eritrosit sedimentasyon hızı, pıhtılaşma zamanı, aPTT, INR değerleri incelendi. Çalışma sonucunda hastalar ilk geçiş ile en az TICI 2b rekanalize olan ile ilk geçiş sonrası TICI 2a ve altı yeterli rekanalize olmayan olgular olarak iki gruba ayrıldı.

Bulgular: Çalışmaya dahil edilen 91 hastanın %61,5 (n=56) kadındı. Tüm hastaların yaş ortalaması 62,3±13,4 idi. Hastaların başvuru anında National Institute of Health stroke skala skoru ortalaması 16 (14-19), trombosit sayısı ortalaması 261,360±78,100/µL, MPV ortalaması 10,2±0,96 fL olarak saptandı. İlk pas ile TICI 2a ve altında rekanalize olmayan grupta 48 (%52,7) ve ilk pas ile TICI 2b ve üzeri rekanalize olan grupta ise 43 (%47,3) hasta saptandı. İlk pas sonrası TICI 2b ve üzeri başarılı rekanalizasyon MPV değeri, trombosit sayısı ve trombosit lenfosit oranı (TLO) ile karşılaştırıldığında istatistiksel olarak anlamlı bir farklılık saptanmadı (sırasıyla p değeri 0,37, 0,12 ve 0,26).

Sonuç: Çalışmamızda orta serebral arter M1 tıkanıklıklarının endovasküler tedavi sonucu rekanalizasyonu ile MPV, trombosit sayısı ve trombosit lenfosit oranı değeri arasında istatistiksel olarak anlamlı bir ilişki elde edilememiştir. Sonuç olarak orta serebral arter M1 tıkanıklığının endovasküler tedavi sonucu rekanalizasyonunda MPV, platelet sayısı ve TLO değeri dışı başka faktörlerin araştırılacağı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Mekanik trombektomi, orta serebral arter oklüzyonu, ortalama trombosit hacmi, platelet sayısı, platelet lenfosit oranı, iskemik inme

Address for Correspondence/Yazışma Adresi: Nihat Şengeze MD, Suleyman Demirel University Faculty of Medicine, Department of Neurology, Isparta, Turkey
Phone: +90 555 258 18 97 E-mail: nihatsengeze@yahoo.com ORCID: orcid.org/0000-0002-2821-3708
Received/Geliş Tarihi: 16.10.2019 **Accepted/Kabul Tarihi:** 23.01.2020

Introduction

Platelet activation plays an important role in the development of ischemic cerebrovascular disease. Platelet size, measured as mean platelet volume (MPV), is a good indicator of platelet-specific activities such as platelet aggregation, thromboxane A2, platelet factor 4, and thromboglobulin release. The increase of MPV has been shown in conditions such as diabetes mellitus, myocardial infarction, smoking, and renal artery stenosis. Its relationship with stroke risk, severity, and prognosis has also been investigated in studies on ischemic stroke (1). Studies have shown that large-volume platelets are more reactive and have increased hemostatic capacity than small ones (2).

In addition, many recent studies have shown that the platelet-lymphocyte ratio (PLR) value obtained by dividing the platelet count by lymphocyte count is an inflammatory marker. Some studies have shown an increase in PLR in coronary artery disease and ST-elevated myocardial infarction and stroke, and this was associated with unfavorable prognosis and mortality (3,4).

In recent meta-analyses, 80% recanalization was achieved with stent-retrievers. However, only 54% of patients had successful recanalization, the others resulted in futile recanalization. The possibility of futile recanalization is associated with an increase in the number of passes. There are few studies comparing the characteristics of the thrombus with recanalization rates (5). The aim of this study was to investigate the relationship between MPV, platelet count, and PLR in endovascular treatment of middle cerebral artery (MCA) M1 occlusions with first-pass recanalization.

Materials and Methods

Of the 322 patients admitted to the hospital with stroke for endovascular therapy between January 2015 and January 2019, 91 patients with MCA M1 occlusion who were treated with endovascular therapy were included in the study. Four patients treated with intra-arterial thrombolytic therapy were excluded. Hemogram, routine biochemical examinations (blood glucose, urea, creatinine, blood, urea, nitrogen), erythrocyte sedimentation rate, clotting time (PT), aPTT, and INR values of all subjects included in the study were examined. Blood parameters were examined as values at the time of first admission. Digital subtraction angiography (DSA) of the patients recorded how much recanalization was achieved for each of pass of three. In our laboratory, the MPV normal range is 8-12 fL and the platelet normal range is 130.000-400.000/µL.

For endovascular treatment strategy, intravenous (IV) recombinant tissue plasminogen activator (tPA) was given to all eligible patients in the IV tPA window, but intra arterial (IA) tPA was given as much as possible to other patients. Patients underwent IA tPA primarily in the endovascular procedure and mechanical thrombectomy was performed in patients with no or insufficient response. At the end of the study, the rate of recanalization with the first pass was evaluated using the thrombolysis in cerebral infarction score (TICI) in patients with stroke (6). We selected all successfully recanalized patients (TICI 2b or TICI 3), with TICI 2b defined as reperfusion in more than two-thirds of the initially involved territory (mTICI scale). TICI grades were determined from the last follow-up run of interventional DSA images. At the end of the study, the patients were divided into two groups, those recanalized successfully at the first pass with at least TICI 2b, and those non-recanalized successfully with ≤ TICI 2a.

Statistical Analysis

The SPSS Windows 23 software was used for statistical analysis of the data obtained from the study. One-way ANOVA was used to compare the groups with respect to normally distributed continuous variables, and the Kruskal-Wallis test was used for other continuous variables. The chi-square test or Fisher's exact test was used to analyze categorical variables. Grouped data were compared using the chi-square test. In univariate analyses, non-normally distributed continuous variables were compared using the Mann-Whitney U test. Data are expressed as mean ± standard deviation (normal distributed data, mean-range normal non-distributed data) and percentage (%). The relationship between continuous variables was tested using Pearson's correlation analysis and Spearman analysis for non-parametric variables. The results were evaluated at 95% confidence intervals and $p<0.05$ as the level of significance.

Results

Of the 91 patients included in the study, 61.5% (n=56) were women. The mean age of all patients was 62.3±13.4 years. Forty-six patients (50.5%) had a right-sided stroke. The median (per 25-75) of National Institute of Health stroke scale score (NIHSS) was 16 (14-19), the median platelet count was 261.360±78.100/µL, and the median MPV was 10.2±0.96 fL.

Twenty (22%) of the patients received IV tPA and 65 (71.4%) received IA tPA. Mortality occurred in 35 (38.5%) patients at the end of the third month. At the end of the third month, there were 28 (30.8%) patients with modified Rankin scale (mRS) 0-2.

The comparison of demographic data in terms of recanalization success and stroke risk factors in the patients using the chi-square test is presented in Table 1. There was no significant difference between the two groups in terms of stroke risk factors. This showed that the patients were homogeneously distributed in groups separated according to the success of recanalization. The comparison of the success of recanalization with clinical evaluation scores, and laboratory and imaging data performed using the chi-square and Mann-Whitney U test is given in Table 2. When the blood values of the patients were examined, there was a significant difference between the two groups in terms of leukocyte values for successful and unsuccessful recanalization ($p=0.007$). There was no statistically significant difference between the successful and unsuccessful recanalization groups in terms of NIHSS scores, ASPECT scores, and stroke etiology (Table 1 and 2).

There were 48 (52.7%) patients in the poor recanalization (≤ TICI 2a) group and 43 (47.3%) patients in the successful recanalization (≥ TICI 2b) group at the first pass. There were no patients recanalized by thromboaspiration. There were no statistically significant differences between the recanalization success and MPV values, platelet counts, and PLR after the first pass (Table 3) (p values respectively; 0.37, 0.12, and 0.26).

Discussion

Increased platelet activation contributes to atherosclerosis and is a crucial step in the initiation of the pathologic process

in ischemic stroke. MPV is considered as an indicator of platelet function and activation, because large platelets contain more dense granules and produce more prothrombotic factors than small platelets. High MPV levels have been shown to be an independent marker for stroke recurrence and cardiovascular events. Moreover, MPV elevation and increased PLR have been reported to have prognostic value in terms of poor clinical outcome and mortality in stroke and myocardial infarction (3,4,7).

The pathophysiologic causes of large vessel occlusions may preclude achieving rapid and complete revascularization; these include proximal carotid or vertebral occlusions, either because of dissection or atherosclerosis, intracranial atherosclerosis with superimposed acute thrombus, and multiple vessel embolic events. Treatment standards in patients with stroke with large vessel obstruction have been redefined with the use of stent retrievers. Nevertheless, the lack of rapid and complete recanalization in some patients is troublesome for interventional neurologists. The

Table 1. Comparison of demographic data in terms of recanalization success and stroke risk factors in patients

Stroke risk factors	First-pass recanalization success		
	Unsuccessful	Successful	
	n (%)	n (%)	*p
Hypertension	31 (48.4%)	33 (51.6%)	0.205
Atrial fibrillation	14 (45.1%)	17 (54.9%)	0.297
Smoking	11 (55%)	9 (45%)	0.819
Diabetes	18 (66.7%)	9 (33.3%)	0.084
History of CABG	2 (50%)	2 (50%)	0.910
Coronary artery disease	8 (40%)	12 (60%)	0.196
Stroke history	4 (66.7%)	2 (33.3%)	0.480
Hyperlipidemia	16 (47.1%)	18 (52.9%)	0.401

*Chi-square test, CABG: Coronary artery bypass grafting

Table 2. Comparison of the success of recanalization with clinical evaluation scores, laboratory and imaging data in patients

Laboratory, imaging and clinical evaluation	First-pass recanalization success		
	Unsuccessful	Successful	
	Median (25-75)	Median (25-75)	**p
Leukocyte	11076 (9022-14112)	8500 (7100-11000)	0.007*
Hemoglobin	12.4 (11.2-14.2)	13 (10.8-14.3)	0.474
Creatinine	0.81 (0.61-1.0)	0.7 (0.6-0.9)	0.111
NIHSS score	16 (14-19)	16 (14-19)	0.949
ASPECT score	9.5 (8-10)	10 (8-10)	0.445
	n (%)	n (%)	*p
mRS (0-2)	12 (42.9)	16 (57.1)	0.208
Mortality at third month	18 (51.4)	17 (48.6)	0.842
Symptomatic hemorrhage	11 (57.9)	8 (42.1)	0.391

*Chi-square test, **Mann-Whitney U test, NIHSS: National Institute of Health stroke scale score, mRS: Modified Rankin scale

Table 3. Comparison of the success of recanalization MPV, platelet and PLR values in patients

MPV, platelet and PLR values	First pass recanalization success		
	Unsuccessful	Successful	
	Median (25-75)	Median (25-75)	**p
MPV	10.4 (9.5-11)	10.1 (9.4-10.7)	0.369
Platelet	255 (213-335)	237 (196-305)	0.124
PLR	146.6 (104.9-249.6)	139 (95.3-200)	0.259

**Mann-Whitney U test, MPV: Mean platelet volume, PLR: Platelet lymphocyte ratio

location, pathophysiologic causes (e.g. atherosclerosis, embolism, dissection) of large vessel occlusion affects the outcome of recanalization.

Zaidat et al. (8) reported that first-pass successful recanalization (TICI 3 recanalization was considered successful) rates were measured as 25.1%. Furthermore, Zaidat et al. (8) showed that recanalization with the first pass reduced symptomatic intracranial hemorrhage to 5.6% and mortality to 16%. In addition, the rate of endothelial trauma due to mechanical thrombectomy will be lower in these patients. In other words, first-pass recanalization is very important for both post-stroke complications, good clinical outcomes, and low mortality rates. It has been shown that clinical outcomes are better in patients with MCA M1 occlusion who are treated with mechanical thrombectomy and recanalized successfully at the first pass.

Recent studies demonstrated the superiority of mechanical thrombectomy over IV thrombolytic therapy in patients with stroke with large vessel occlusion. However, despite mechanical thrombectomy treatment, 29-67.4% of patients have poor clinical outcomes (mRS >2). Although long-term adverse outcomes in endothelial injury due to mechanical thrombectomy have not been observed in studies so far, it is important to achieve recanalization with a minimal mechanical effect (9,10,11). Platelets participate in the process of thrombosis and atherosclerosis, which are activated in the early thromboembolic phase of ischemic stroke. Activated platelets will release thromboxane A2 and high expression of glycoprotein Ib and glycoprotein IIb/IIIa receptors, which contribute to thrombosis and stroke (12). On the other hand, high MPV values were accepted as an indicator of platelet size and activity. Larger platelets are known to produce greater amounts of substances such as thromboxane B2 and fibrinogen with larger granules and thus have more thrombogenic activity (7).

In our study, there was no statistically significant difference between recanalization success and MPV values, platelet counts, and PLR after the first pass (p values respectively; 0.37, 0.12, and 0.26). Thus, although these data can be obtained with a simple hemogram analysis, it shows that these parameters alone cannot be prognostic indicators for first-pass recanalization success according to our study data. However, increased lymphocyte count is an another parameter that may affect the success of recanalization. It is a parameter that may affect recanalization that is possibly worth investigating in patients with stroke.

In our study, 11 (26.8%) out of 41 patients with MPV values 10.4 and above and 17 (34%) out of 50 patients with MPV value less than 10.4 had an mRS scale score of ≤2. Although patients whose MPV values were less than 10.4 had favorable clinical outcomes, there was no statistically significant difference between the two groups (p=0.461). Peng et al. (7) showed that successful recanalization was achieved in 53% of patients in their stroke study due to acute anterior circulation obstructions, including 153 patients treated with mechanical thrombectomy. When the results of the third month clinical outcome (mRS) of the Peng et al. (7) study were examined, it was shown that MPV values over 10.4 fl were associated with poor clinical outcomes. In that study, the rate of successful recanalization was lower in patients with higher MPV values, although not statistically significant. This also shows that different results can be obtained regarding MPV with studies involving more patients.

In a study in which thrombus volume was calculated using cerebral computed tomography angiography, it was stated that the success of recanalization decreased with increasing thrombus volume and earlier and successful recanalization was achieved with decreasing thrombus volume (5). The relationship between increased MPV and PLR values and thrombus volume may also be a parameter affecting the success of recanalization.

In the Mosimann et al. (13) study, 711 patients treated with mechanical thrombectomy were examined for early reocclusion within the first 48 hours. Early reocclusion was very rare (n=16, 2.3%). Patients deemed high risk for reocclusion had high platelet elevation at admission to hospital, atherosclerotic stenosis at the occlusion site, and residual embolic fragment residue after thrombectomy.

In conclusion, although platelet values and other similar parameters have been the subject of many studies related to endovascular treatment of ischemic stroke, it is thought that the effects of unsuccessful recanalization are multifactorial and that no single parameter can guide the prognostic point of view. As a result of the study, the identification of the more difficult and poor recanalization cases in endovascular therapy will shed light on the different treatment strategies for these patients.

This study has some limitations. Our study is based on retrospective data. The other limitations include the fact that different types of stent retrievers were used in each case for recanalization, IV and IA thrombolytic therapy use was not standardized, the source of thrombus etiologies in patients could not be standardized, and the time from the onset of stroke symptoms to endovascular treatment of patients was different. The symptom-to-groin puncture time and recanalization time data were also limitations of this study, but they did not directly affect the study goal and outcome.

Conclusion

Although it is stated that high MPV levels and platelet counts during the acute period may play a role in the development of ischemic stroke in all patients with stroke, in our study, no statistical relationship was found between first-pass thrombectomy success of MCA M1 occlusions and MPV, platelet count, and PLR values. There is a need to further investigate other factors beyond MPV, platelet count, and PLR in the recanalization success of MCA M1 occlusions.

Ethics

Ethics Committee Approval: Gaziantep University Ethics Committee decision no. 2019/171.

Informed Consent: It was taken before the endovascular procedure and put in the patient file.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Ş., S.G., Concept: S.G., Design: S.G., Data Collection or Processing: N.Ş., Analysis or Interpretation: N.Ş., S.G., Literature Search: N.Ş., Writing: N.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Güldiken B, Ozkan H, Kabayel L. Mean Platelet Volume and Peripheral Blood Count Response in Acute Ischemic Stroke. Balkan Medical Journal 2008;25:130-135.
2. Ozdemir O, Soylu M, Alyan O, et al. Association between mean platelet volume and autonomic nervous system functions: Increased mean platelet volume reflects sympathetic overactivity. Exp Clin Cardiol 2004;9:243-247.
3. Osadnik T, Wasilewski J, Lekston A, et al. The platelet-to-lymphocyte ratio as a predictor of all-cause mortality in patients with coronary artery disease undergoing elective percutaneous coronary intervention and stent implantation. J Saudi Heart Assoc 2015;27:144-151.
4. Jin P, Li X, Chen J, et al. Platelet-to-neutrophil ratio is a prognostic marker for 90-days outcome in acute ischemic stroke. J Clin Neurosci 2019;63:110-115.
5. Baek JH, Yoo J, Song D, et al. Predictive value of thrombus volume for recanalization in stent retriever thrombectomy. Sci Rep 2017;7:15938.
6. Fugate JE, Klunder AM, Kallmes DF. What is meant by "TICI"? AJNR Am J Neuroradiol 2013;34:1792-1797.
7. Peng F, Zheng W, Li F, et al. Elevated mean platelet volume is associated with poor outcome after mechanical thrombectomy. J Neurointerv Surg 2018;10:25-28.
8. Zaidat OO, Castonguay AC, Linfante I, et al. First Pass Effect: A New Measure for Stroke Thrombectomy Devices. Stroke 2018;49:660-666.
9. Kurre W, Pérez MA, Horvath D, Schmid E, Bäzner H, Henkes H. Does mechanical thrombectomy in acute embolic stroke have long-term side effects on intracranial vessels? An angiographic follow-up study. Cardiovasc Intervent Radiol 2013;36:629-636.
10. Park S, Hwang SM, Song JS, Suh DC, Lee DH. Evaluation of the Solitaire system in a canine arterial thromboembolic occlusion model: is it safe for the endothelium? Interv Neuroradiol 2013;19:417-424.
11. Singh P, Doostkam S, Reinhard M, Ivanovas V, Taschner CA. Immunohistochemical analysis of thrombi retrieved during treatment of acute ischemic stroke: does stent-retriever cause intimal damage? Stroke 2013;44:1720-1722.
12. Gao F, Chen C, Lyu J, et al. Association between platelet distribution width and poor outcome of acute ischemic stroke after intravenous thrombolysis. Neuropsychiatr Dis Treat 2018;14:2233-2239.
13. Mosimann PJ, Kaesmacher J, Gautschi D, et al. Predictors of Unexpected Early Reocclusion After Successful Mechanical Thrombectomy in Acute Ischemic Stroke Patients. Stroke 2018;49:2643-2651.