

The predictive value of platelet/mean platelet volume ratio in predicting colon diverticulitis relapse

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Abstract. – **OBJECTIVE:** Diverticulitis is a health problem that has increased in frequency recently. It has a wide spectrum from simple inflammation to fecal peritonitis, sepsis and even mortality. Thus, it is important to predict diverticulitis, especially recurrent diverticulitis, and take measures to prevent it. In this study, we investigated the predictive value of the PLT/MPV ratio, which is an inflammation marker in predicting the recurrence of diverticulitis disease.

PATIENTS AND METHODS: In this study, 132 patients diagnosed with diverticulitis were analyzed retrospectively. Patients' gender, age, localization of diverticulitis, number of diverticula in computed tomography (CT), hospitalization status, length of hospitalization, control colonoscopies, polyps' number and localizations in colonoscopies, presence of malignancy, need for surgery, and recurrences were not reported. White blood cell (WBC), Neutrophil (NE), Lymphocyte (LY), Hemoglobin (Hb), PLT, MPV, Albumin, Creatine Kinase (CK) and C-reactive protein (CRP) levels were examined. The patients were divided into two groups as those who did not relapse concerning diverticulitis and those who did, and statistical analysis was performed between the two groups about related parameters.

RESULTS: Among all patients, recurrence was seen in 11 (10.1%) patients. The patients were divided into two groups according to their recurrence status and statistical significance was sought between the data. The calculated PLT/MPV ratio of patients who did not relapse was 25.61 ± 8.05 and 34.98 ± 11.37 for those who had a relapse ($p=0.006$). The sensitivity for MPV was 81.8%, a specificity of 57.1% and a cut-off of 9.85. The cut-off value for PLT was 207.5 with 100% sensitivity and 33.7% specificity. A cut-off value of 25.11 was found for PLT/MPV with 100% sensitivity and 49% specificity.

CONCLUSIONS: PLT/MPV ratio was significantly higher in relapsed cases. Since it is easily accessible and inexpensive, it will guide phy-

sicians for diagnosis concerning early detection of relapse cases and initiation of appropriate treatment.

Key Words:

Colon diverticulitis, Relapse, Platelet, Mean platelet volume.

Introduction

Colon diverticulosis, i.e., pouch-like protrusions in the wall of the large intestine, is the most common anatomical change in the human colon. It is detected incidentally, either endoscopically or radiologically. While left colon diverticulosis is common in western societies, right colon diverticulosis is more common in Asian societies¹. The global prevalence of diverticulosis is increasing in both developed and developing countries, possibly due to changes in diet and lifestyle. The reason for this is the increase in the number of patients diagnosed endoscopically and radiologically and interpreted as a western lifestyle². While the disease is mostly asymptomatic, it becomes symptomatic with inflammation of the diverticulum and is defined as diverticulitis. Complications, such as abscess, fistula, obstruction, bleeding and perforation, may develop after this inflammation process³.

The pathogenesis of diverticulosis is not fully understood. However, various changes may occur in the structure of the colon wall, including loss of the elastic function of the colon wall and accumulation of immature collagen fibers in the extracellular matrix⁴. There are various challenges in the process of diagnosing diverticulitis. Diverticulum pathologies generally present with diverticulitis in the left colon and bleeding in the

right colon. Typically, abdominal pain, changes in bowel habits, bloating, fever, nausea, and vomiting develop and are seen in approximately 25% of individuals with diverticulosis⁵. The severity of acute diverticulitis may range from simple inflammation limited to the colon wall to diffuse peritonitis due to diverticulum perforation. Therefore, early diagnosis and treatment of diverticular disease are critical. The pathogenesis of diverticular disease is less well understood than diverticulosis, but it is thought to be related to conditions, such as genetic predisposition and intestinal microbiota imbalance⁶.

The risk of acute diverticulum recurrence is generally approximately 20-35% in five years⁷⁻¹⁰. Relapse usually occurs <12 months after the first attack and the risk of complications is very low¹⁰. This situation imposes a considerable economic burden on health services. Various strategies have been implemented to prevent the recurrence of diverticulitis. These are dietary practices, pharmacological treatments and surgery. In addition to preventing recurrence, it is clinically important to predict recurrence. There is not enough information in the literature to determine risk factors for diverticulitis recurrence¹¹.

Platelets (PLT) are the smallest and yet highly reactive blood morphotic components. The mean platelet volume (MPV) value is the best indicator of platelet function and activation and can be easily measured with routine complete blood count tests. Literature data show that MPV can provide crucial information about the course and prognosis in many pathological conditions, such as acute pancreatitis, ulcerative colitis, rheumatoid arthritis, and celiac disease¹²⁻¹⁵.

Based on this information, we predict that changes in the PLT/MPV ratio showing increased inflammation can be used as a biomarker to predict and detect diverticulitis recurrence in patients.

Patients and Methods

This study was planned as a retrospective cohort study to include patients diagnosed with diverticulitis between 01.01.2013–01.05.2021 in the Department of General Surgery of Hitit University Faculty of Medicine Erol Olçok Training and Research Hospital after ethics committee approval was obtained from Hitit University Faculty of Medicine Non-Invasive Research Ethics Committee on 28.06.2021 (Ethics Com-

mittee Decision No: 2021-73, Application No: 2021-131). Patients diagnosed with diverticulitis between the specified dates were included in the present study. Patients with cancer, thrombocytopenia, hyperthyroidism, heart disease, diabetes, atrial fibrillation, vitamin D deficiency and obesity that would affect MPV and platelet values were excluded from this study. In addition, after eliminating the patients whose information could not be reached, who did not follow up and who did not want to be included, 132 patients who met the criteria in this study were retrospectively analyzed from computer records, patient files and doctor's records. Twenty-three patients who did not meet the criteria were excluded from this study.

Patients' gender, age, comorbidities, localization of diverticulitis, number of diverticula in computed tomography (CT), Modified Hinchey classifications, hospitalization status, length of hospitalization, control colonoscopies, polyps' number and localizations in colonoscopies, presence of malignancy, need for surgery and recurrences were not reported. White blood cell (WBC), Neutrophil (NE), Lymphocyte (LY), Hemoglobin (Hb), PLT, MPV, Albumin, Creatine Kinase (CK) and C-reactive protein (CRP) levels were examined.

The patients were divided into two groups as those who did not relapse concerning diverticulitis and those who did, and statistical analysis was performed between the two groups concerning related parameters.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows software (version 26; IBM Corp., Armonk, NY, USA). Categorical variables, such as gender, number of additional diseases, localization of diverticulitis, number of diverticula on CT, Modified Hinchey classifications, hospitalization needs, control colonoscopy status and results, need for operation and recurrence, were reported as numbers and percentages. Numerical variables, such as age, length of hospitalization, WBC, NE, LY, Hb, Plt, MPV, Albumin, CK and CRP values, were reported as mean value \pm standard deviation and median value in parentheses. Relationships between variables were investigated using Pearson and Spearman correlation coefficients. The statistical difference of categorical variables between the groups was evaluated using the Chi-Square

test. Data normality distribution in numerical data was evaluated with the Shapiro Wilks test. The *t*-test (Student's *t*-test) was used to compare the mean age, Hb, MPV between the two groups. Mann-Whitney U test was used in line with data distribution for comparisons of WBC, NE, LY, Plt, Alb, CK, CRP, and length of hospitalization between the two groups. The cut-off values with optimal sensitivity and specificity, which distinguish the groups according to recurrence, were found by drawing the ROC curve and calculating the area under it and the Youden index. Subsequently, risk analyses were performed according to cut-offs. For the statistical significance level, $p < 0.05$ was accepted as meaningful.

Results

Of the patients included in the present study, 48.6% were male, and 51.4% were female. The mean age and standard deviation of ages were calculated as 57.08 ± 15.62 years. Of the patients, 62 had no chronic disease, 23 of them had one, 20 of them had two, four of them had three or more chronic diseases. Inflamed diverticula were mostly seen in the sigmoid colon with 66.1% on CT. Sigmoid colon diverticulum was followed by descending colon with 15.6%, rectosigmoid with 8.3%, ascending colon with 6.4% and cecum with 3.7%. Multiple diverticula were seen on CT in 70.6% of the patients, while 29.4% were solitary.

According to the Modified Hinchey classification, 90.8% of the patients were Stage 1, 8.3% ($n=9$) were M-Hinchey 2, and 0.9% were M-Hinchey 4 ($n=1$). WBC, NE, LY, PLT mean and standard deviations at admission were 10.59 ± 3.53 ; 7.44 ± 3.14 ; 2.16 ± 0.85 ; it was found as 255.44 ± 73.80 $10^9/L$, respectively. Hb mean and standard deviation were calculated as 13.22 ± 1.94 mg/dL. The mean of MPV, Alb, CK, and CRP were calculated as 9.79 ± 1.06 ; 39.30 ± 4.86 ; 106.69 ± 103.69 ; 76.80 ± 81.08 , respectively.

While 65.1% of the patients were hospitalized and followed up, 34.9% were eligible for outpatient treatment. The mean length of hospitalization of the hospitalized patients was 4.76 ± 3.31 days. Only four of the patients required interventional or surgical procedures. After discharge, only 34.9% ($n=38$) of the patients came to the control colonoscopy appointment. Malignancy was observed in three of 38 patients. Among all patients, recurrence was seen in 11 (10.1%) pa-

tients. The patients were divided into two groups according to their recurrence status and statistical significance was sought between the data.

There was no statistically significant difference between the gender distribution of the patients, their average age and the distribution of additional disease numbers ($p=0.529$, $p=0.443$, $p=0.609$, respectively) (Table I).

The most common localization of diverticulitis in both groups was the sigmoid colon (67.3% vs. 66.1%), and there was no significant difference between localization distributions ($p=0.495$). Multiple diverticular appearances were more common in both groups, but no significant difference was observed ($p=0.728$). Modified Hinchey classification distributions of the patients in the groups did not differ statistically significantly ($p=0.431$). There was no significant difference between the two groups concerning the need for hospitalization and the number of patients who needed surgery ($p=0.510$ and $p=0.351$). The patients without recurrence were hospitalized for 4.76 ± 3.31 days, while the patients with recurrence were hospitalized for 8.33 ± 3.98 days, which was statistically significant ($p=0.001$). In this study, 72.7% of the patients with recurrence had a control colonoscopy. The rate of those who did not relapse was 34.9%, which was statistically significant ($p=0.015$). However, no correlation was found between the rate of malignancy and recurrence ($p=0.519$).

There was no significant difference between the mean WBC, NE, LY, Albumin, CK, and CRP between the two groups ($p=0.448$; $p=0.357$; $p=0.960$; $p=0.246$; $p=0.863$; $p=0.389$, respectively). The mean Hb was 13.36 ± 1.93 in non-relapsed patients and 12.00 ± 1.64 in relapsed patients, which were statistically significant ($p=0.027$).

The mean Plt of the patients who did not relapse was 249.43 ± 70.28 , the mean of those with relapse was 309.00 ± 86.00 . There was a statistically significant difference between the two groups ($p=0.029$). Likewise, the mean MPV of the patients who did not relapse was 9.89 ± 1.03 and 8.94 ± 1.01 for the patients who did relapse, which is statistically significant ($p=0.005$).

The calculated PLT/MPV ratio of the patients who did not relapse was 25.61 ± 8.05 and 34.98 ± 11.37 for the patients who had relapsed, and this was statistically significant ($p=0.006$). Cut-off values were calculated for MPV, Plt and PLT/MPV ratio by performing ROC curve analysis (Figure 1). A sensitivity of 81.8%, a specificity of 57.1% and a cut-off value of 9.85 were found for MPV; it was observed to increase the risk

Table I. Comparison of variables in diverticulitis cases.

Variables		Whole group (n = 109)	No recurrence (n = 98)	Recurrence (n = 11)	Statistical significance
Demographic data					
Gender	Man	53 (48.6%)	49 (50%)	4 (36.4%)	0.529
	Woman	56 (51.4%)	49 (50%)	7 (63.6%)	
Age		57.47±15.60 (58)	53.64±16.07 (55)	0.443	0.609
Number of additional diseases	0	62 (56.9%)	54 (55.1%)	8 (72.7%)	
	1	23 (21.1%)	22 (22.4%)	1 (9.1%)	
	2	20 (18.3%)	18 (18.4%)	2 (18.2%)	
	3+	4 (3.7%)	4 (4.1%)	0 (0%)	
Radiological imaging					
Diverticulitis	Cecum	4 (3.7%)	4 (4.1%)	0 (0%)	0.495
	Ascending column	7 (6.4%)	5 (5.1%)	7 (6.4%)	
	Descending colon	17 (15.6%)	15 (15.3%)	17 (15.6%)	
	Sigmoid	72 (66.1%)	66 (67.3%)	72 (66.1%)	
	Rectosigmoid	9 (8.3%)	8 (8.2%)	9 (8.3%)	
Number of diverticulum	Solitary	32 (29.4%)	28 (28.6%)	4 (36.4%)	0.728
	Multiple	77 (70.6%)	70 (71.4%)	7 (63.6%)	
Modified Hinchey Score	1	99 (90.8%)	90 (91.8%)	9 (81.8%)	0.431
	2	9 (8.3%)	7 (7.1%)	2 (18.2%)	
	4	1 (0.9%)	1 (1%)	0 (0%)	
Laboratory values					
WBC		10.59±3.53 (10.25)	10.54±3.60 (10.22)	11.06±2.89 (10.81)	0.448
NE		7.44±3.14 (6.71)	7.39±3.14 (6.59)	7.94±3.19 (7.5)	0.357
LY		2.16±0.85 (2.11)	2.17±0.86 (2.13)	2.13±0.72 (1.96)	0.96
Hb		13.22±1.94 (13.2)	13.36±1.93 (13.35)	12.00±1.64 (11.60)	0.027
Plt		255.44±73.80 (246)	249.43±70.28 (245)	309.00±86.00 (278)	0.029
MPV		9.79±1.06 (9.90)	9.89±1.03 (9.9)	8.94±1.01 (9)	0.005
Alb (n=91)		39.30±4.86 (40)	39.54±4.67 (40)	36.75±6.36 (36.5)	0.246
CK (n=93)		106.69±103.69 (78)	96.58±72.77 (79)	182.11±221.20 (66)	0.863
CRP (n=73)		76.80±81.08 (50.4)	74.05±77.86 (47.80)	102.73±111.14 (57.30)	0.389
Plt/MPV		26.55±8.85 (26,17)	25.61±8.05 (25,45)	34.98±11.37 (28,65)	0.006
Hospitalization data					
Need for hospitalization		71 (65.1%)	65 (66.3%)	6 (54.5%)	0.51
Length of Hospitalization (n=71)		4.76±3.31 (4)	4.43±3.07 (4)	8.33±3.98 (7)	0.001
Need for pperation		4 (3.7%)	3 (3.1%)	1 (9.1%)	0.351
Control colonoscopy					
Control colonoscopy		38 (34.9%)	30 (30.6%)	8 (72.7%)	0.015
Malignancy in control colonoscopy (n=38)		3 (7.9%)	2 (6.7%)	1 (12.5%)	0.519
Relapse		11 (10.1%)	-	-	-

of recurrence five times (OR 6, 95% CI 1.231-29.233). 100% sensitivity and 33.7% specificity and a cut-off value of 207.5 for PLT were found. A cut-off value of 25.11 was found for PLT/MPV with 100% sensitivity and 49% specificity (Tables II and III).

Discussion

We retrospectively analyzed the cases diagnosed with diverticulitis and followed up in our

clinic, we found the recurrence rate to be 10.1%. In our study, we showed that the ratio of PLT/MPV in relapsed cases was statistically low in non-relapsed cases. To our knowledge, there is no other study on the ratio of PLT/MPV in diverticulitis in the literature.

Recurrence rates after acute diverticulitis disease may vary as much as 4-32%, as reported in the previous studies^{8,16-19}. Patients may present with recurrent diverticulitis, stricture, fistula, chronic gastrointestinal or non-gastrointestinal symptoms. Although recurrence rates are higher

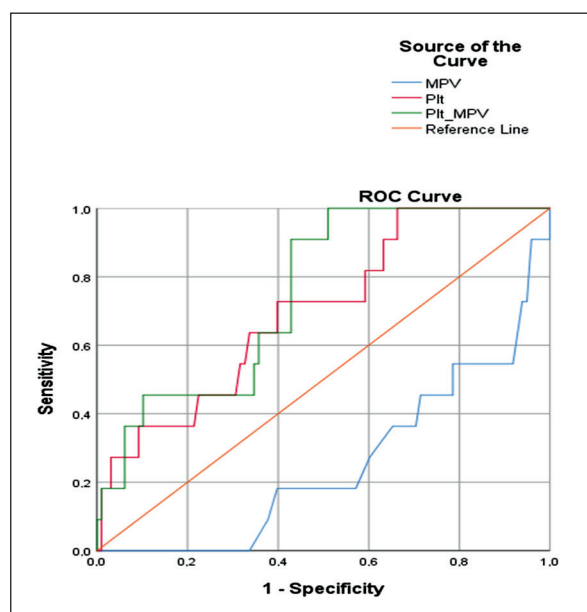


Figure 1. ROC curve for PLT, MPV and PLT/MPV.

in studies with small numbers of cases, these rates are lower in large-scale cohort studies⁶.

Conditions, such as young age, female gender, abscess on tomography and obesity, are seen as risk factors for diverticulitis recurrence. Many retrospective studies have shown that the recurrence of diverticulitis increases significantly under the age of 50^{7,20,21}.

The presence of an abscess in the first attack is a risk factor for diverticulitis recurrence²². In a retrospective study by Devaraj et al²³, it was seen that 61% of diverticulitis cases with an abscess on tomography and treated non-surgically presented with recurrence within an average of 3.5 months, and the majority of them were complicated diverticulitis again. These results suggest that recurrent diverticulitis attacks may be more severe. In our study, the recurrence rate was 10.1%, and the length of hospitalization was significantly higher in relapsed cases than in others. Thus, it is significant for patient management to diagnose recurrent diverticulitis cases easily and quickly.

PLT is the smallest and surprisingly active blood component. They are activated at the site of inflammation by agonists, such as adenosine diphosphate, thromboxane A2, and platelet-activating factor. Activated platelets secrete IL-1, IL-6 and TNF alpha from their cytoplasmic granules and these are the first molecules to accumulate in the injury site. It is an important blood component in the initiation of inflammatory processes²⁴.

The MPV value represents the mean platelet volume. Increased degradation of large platelets during inflammation may lead to a reduction in MPV, possibly because larger platelets are more sensitive to stimulation and significantly larger platelets are more likely to be selectively lysed, resulting in an increased PLT/MPV ratio²⁵. It has been observed that there is an inverse correlation between the MPV value and the number of PLT. Thus, it has been understood that the PLT/MPV ratio is a more useful parameter than PLT or MPV alone²⁶.

Recurrence of diverticular disease may present with simple diverticulum attack and perforation, resulting in severe sepsis. Apart from this, given that Mortensen et al²⁷ found a serious relationship between diverticulitis and colon cancer in a study conducted with an 18-year follow-up, it is crucial to prevent the recurrence of diverticulitis. Thus, unnecessary and costly procedures can be avoided if the probability of recurrence is calculated before deciding on diet, antibiotic therapy and surgery.

Tursi et al²⁸ developed the Diverticular Inflammation and Complication Assessment (DICA) classification to predict diverticulum recurrence. In this method, it was found that the persistence of mucosal changes after an acute diverticulitis attack may have a prognostic role in determining the risk of diverticulitis recurrence, and it has been shown for the first time that endoscopic examination may be useful in predicting the outcome of the disease, so it has become quite popular. The PLT/MPV used in our study is a more accessible, non-invasive and cost-effective method that can be used easily in developing countries.

Since diverticular disease and colon cancer have similar etiology, PLT/MPV ratios were higher in cases with colon cancer in the study of Wu et al²⁶, and colon cancer rates were higher in patients with diverticulitis in the study of Mortensen et al²⁷. Thus, we think that colonoscopy should be performed in patients with a high PLT/MPV ratio. In cases, such as colonoscopy, which cannot be performed due to risks in the acute period, it would be beneficial to examine the patients, especially about colon cancer, with other imaging and laboratory methods during hospitalization.

When we compared the cases with and without relapse in our single-center study in which diverticulitis cases of eight years were screened retrospectively, a statistically significant difference was found between the two groups in terms

Table II. MPV, Plt and Plt/MPV ratio cut-off values.

	Cut-off	Diagnostic values				ROC curve			Odds ratio		
		Sensitivite	Spesifite	PPV	NPV	Area (SE)	95 CI%	<i>p</i>	Odds ratio	95 CI%	<i>p</i>
MPV	9.85	81.80%	57.10%	17.60%	96.60%	0.747 (0.072)	0.606-0.889	0.007	6	1.231-29.233	0.023
Plt	207.5	100.00%	33.70%	14.50%	100.00%	0.701 (0.078)	0.549-0.853	0.029	*	*	0.032
Plt/MPV	25.11	100.00%	49.00%	18.00%	100.00%	0.751 (0.065)	0.625-0.878	0.006	*	*	0.002

*Odds Ratio was not calculated since there was no recurrence in test negativity.

Table III. Recurrence distribution according to cut-off values.

	Cut-off	No recurrence (n = 98)	Recurrence (n = 11)	Statistical significance
MPV	> 9.85	56 (57.1%)	2 (18.2%)	0.023
	< 9.85	42 (42.9%)	9 (81.8%)	
Plt	< 207.5	33 (33.7%)	0 (0%)	0.032
	> 207.5	65 (66.3%)	11 (100%)	
Plt/MPV	< 25.11	48 (49%)	0 (0%)	0.002
	> 25.11	50 (51%)	11 (100%)	

of MPV, PLT, and PLT/MPV rates. To our knowledge, our study is the first study to investigate the PLT/MPV value with diverticulitis. The rate of PLT/MPV was higher in relapsed cases than in non-relapsed cases. Control colonoscopy rates were also significantly higher in relapsed cases. Although the probability of malignancy was not statistically significant in control colonoscopies, it was high in recurrent diverticulitis. However, our work will provide valuable insights into further studies.

Conclusions

Since it is easily accessible and inexpensive, PLT/MPV ratio can guide physicians in diagnosis concerning early detection of relapse cases and initiation of appropriate treatment. We also think that PLT/MPV ratio can reduce the burden of diverticular disease on the health system.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Institutional Review Board Statement

This study was planned as a retrospective cohort study to include patients diagnosed with diverticulitis between 01.01.2013-01.05.2021 in the Department of General Surgery of Hitit University Faculty of Medicine Erol Olçok Training and Research Hospital after ethics committee approval was obtained from Hitit University Faculty of Medicine Non-Invasive Research Ethics Committee on 28.06.2021 (Ethics Committee Decision No: 2021-73, Application No: 2021-131).

Authors' Contribution

Conceptualization, Visualization: R.T. and V.B.T., Data curation, Formal Analysis: M.B.T. and M.B.Y., Investigation, Methodology: O.A. and R.T., Resources, Validation: F.Ş. and R.T., Software: M.B.Ö and F.Ş., Supervision: M.B.Y. and M.B.T., Approval of final manuscript: all authors Writing Original Draft: O.A. and R.T. Writing – Review and Editing: R.T., V.B.T. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

The data presented in this study are available on request from the corresponding author.

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