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RESEARCH ARTICLE

The Importance of Platelet Count and Mean Platelet Volume, Platelet Distribution Width, and Monocytes Count in the Differentiation of Colorectal Cancer and Colon Polyps

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ABSTRACT

Aim: Mean platelet volume (MPV) is a marker of platelet activity that has been found to be lower in people with colon cancer than in healthy people. In order to forecast the probability of colon cancer development in colon polyps, we looked at the predictive values of MPV, platelet distribution width (PDW), platelet count/MPV (Plt/MPV) and monocyte (Mo) count.

Method: This was a retrospective study. The study comprised colonoscopy procedures performed at a single hospital between 02.01.2019 and 05.05.2021. Colon polyps detected during colonoscopy in 425 patients were included. Colon polyps that underwent polypectomy were separated into two groups based on histopathological analysis into benign and malignant. Standard complete blood count parameters were assessed in both groups and Plt/MPV, Plt/PDW, neutrophil/lymphocyte ratio (NLR), and Mo/lymphocyte ratio (MLR) values were calculated.

Results: The total number of polyps removed was 754. Haemoglobin and red cell distribution width values were statistically lower in the adenocarcinoma group ($p<0.001$ for both). When the values of NLR, MLR, Plt/PDW, and Plt/MPV were compared, the Plt/PDW and MLR were significantly higher in the adenocarcinoma group ($p=0.036$ and $p=0.004$, respectively).

Conclusion: The Mo count and MLR and Plt/PDW ratios were useful for detecting malignancies that may arise from colon polyps in this retrospective cohort. Polyps detected in patients with a high Mo count or MLR or Plt/PDW ratio measured before the procedure may be associated with a higher risk of cancer but these results should be confirmed in larger prospective studies.

Keywords: Colorectal polyps, monocytes count, platelet count/platelet distribution width

Introduction

Colorectal cancers (CRC) are the most prevalent cancers of the gastrointestinal tract and the fourth most common cancer in developed countries.[1] CRC are usually at an advanced stage by the time they manifests symptoms. The mortality rate from CRC has fallen by more than 20% as a result of the rapid development of early detection techniques and efficient treatment.[2] Despite this, only 40% of people with CRC are detected at an early stage.[3]

Most CRC develop from normal-looking mucosa to adenoma, dysplasia, and carcinoma. Most CRC develop against a background of a pre-existing polyp (adenoma).[4] The majority of colon polyps, however, do not progress to cancer. High-grade, dysplastic, villous adenomas are more prone to develop into cancer. Early detection is critical in CRC, as it is in other malignancies. After the age of 50, a routine colonoscopy is suggested to detect colorectal malignancies early. Recent evidence suggests that patients with no abnormalities at previous colonoscopy have a significantly lower risk of CRC.[5] Screening colonoscopy was linked to a 67% reduction in CRC incidence and a 65% reduction in death in a cohort trial of average-risk patients.[6]

The tumor structure and the patient's inflammatory response have a complicated relationship.[7] Platelet count and mean

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platelet volume (Plt and MPV) are inversely connected, resulting in a relatively constant total platelet mass.[8] Studies have revealed that thrombotic activity develops in more than 76% of cancer patients. Platelets are non-nucleated cells produced from megakaryocytes in the bone marrow, play a key role in blood clotting but are also linked to inflammation and thrombosis.[9] Tumor cells are associated with various cytokines that stimulate platelet production, such as platelet-derived growth factor, vascular endothelial growth factor and other growth factors.[10] The enhanced destruction of large platelets in an inflammatory milieu can cause a decrease in MPV, possibly because larger platelets are more sensitive to stimulation, and thus larger platelets are more likely to be selectively cleaved in this situation. MPV is a marker of platelet activity that has been found to be lower in people with colon cancer than in healthy people.[11] Platelet distribution width (PDW), like MPV, is a simple platelet index that measures platelet activity and is measured during a routine complete blood count (CBC).[12] MPV and PDW show similar increases in platelet activation.[13]

Blood monocytes (Mo) from patients with CRC at different stages have been shown to be activated by various immunomodulators, inducing specific cytolytic activity against tumor cells, and the Mo could also recognize and lyse tumorigenic cells, but did not affect non-tumorigenic cells. Even after repeated doses of radiotherapy and chemotherapy, the tumoricidal activity of Mo has been reported in blood Mo from patients.[14] Moreover, a six-fold increase in Mo count has been reported in metastasizing colorectal tumours compared to the normal intestine.[15] Therefore, the Mo count may be expected to increase in colorectal tumours.

The aim of this study was to investigate the use of parameters measured by or derivable from CBC in order to forecast the probability of colon cancer development in colon polyps. The predictive values of MPV, PDW, Plt/MPV ratio and Mo count was retrospectively investigated in patients undergoing polypectomy.

Materials and Methods

The study comprised data from patients undergoing colonoscopy procedures performed at Hitit University Çorum Erol Olçok Training and Research Hospital performed by the General Surgery Department, Gastroenterology Surgery Sub-Division Member and in the Gastroenterology Clinic between 02.01.2019 and 05.05.2021 were included. The patients included in the study were those older than 18 years of age and those who had polyps on colonoscopy. Patients who underwent polypectomy during colonoscopy were included in the study. The data were scanned retrospectively using the Hospital Information Management System, with the approval of the hospital's chief physician and the approval of the ethics committee. Patients under the age of 18, those with diseases that may affect blood values, such as cirrhosis or chronic kidney failure, and patients with ulcerovegetative mass lesions during colonoscopy were not included in the study. Ethics committee approval was received from Hitit University Faculty of Medicine, Non-Interventional Research Ethics Committee in 2021 (approval number: 2021-78).

Colonoscopy procedures were performed by specialist doctors. One of two different procedures was performed in patients who underwent polypectomy. In all cases, an Olympus Medical Systems variable stiffness colonoscope (Olympus, Tokyo, Japan) was used. The distal tip of this instrument was 12.2 mm in diameter, while the insertion tube was 12.0 mm in diameter (working length, 133 cm; diameter of the accessory canal, 3.2 mm). The appendix orifice and ileocecal valve were identified during a complete colonoscopy. Polyps were removed if they were discovered during any colonoscopy. The location of each polyp was documented. A snare was put on the polyp for hot snare polypectomy, and the current was administered while the snare was closed. For an endoscopic mucosal resection procedure, 1 to 3 mL of epinephrine diluted 1:10,000 in saline was injected submucosally into each polyp. A detailed visual assessment of the region was performed by the same endoscopist after each polypectomy to establish whether polyp eradication was complete. The adequacy of resection was assessed visually in a standard manner. The presence of residual tumor was determined according to the experience and discretion of the endoscopist.

Patient demographic information, such as age and gender, was recorded. All the colon polyps detected during colonoscopy procedures were grouped according to size, location, polyp type, and histopathological features. Parameters from the CBC performed in all patients prior to the colonoscopy procedure were collected, including white blood cell count (WBC), Mo count, lymphocyte count (Ly), Plt, neutrophil count (Ne), MPV, PDW, red cell distribution width (RDW) and haemoglobin (Hb) values. Additionally, Plt/MPV, Plt/platelet distribution volume ratio (Plt/PDW), Ne to lymphocyte count ratio (NLR), Mo count to lymphocyte count ratio (MLR) values were calculated from the blood samples taken.

Polypectomy was undertaken on colon polyps that were discovered during the colonoscopy process. Excised colon polyps were separated into two groups based on histopathological report: benign and malignant. The CBC parameters derived from pre-colonoscopy blood samples were compared between the benign and malignant polyp groups.

Statistical Analysis

SPSS for Windows, version 22.0, was used for statistical comparison of data (SPSS Inc., Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to assess if the parameters followed a normal distribution. Mean ± standard deviation was used to represent normally-distributed continuous variables. A receiver operating characteristic (ROC) curve analysis was used to measure diagnostic capabilities, and ROC curves and Youden index were created to examine the trade-off between sensitivity and specificity. A p-value of <0.05 was assumed to define statistical significance. The statistical power and power analysis were calculated with the open-source software G*Power version 3.1.9.2. A priori sample size was calculated as 35 patients in each group for a power of 0.80, the alpha error probability of 0.05, and the effect size of 0.80 according to the primary outcome measure.

Results

The study comprised 425 participants who had colorectal polyps removed during colonoscopy. Of the patients included in the study, 277 (65.2%) were male and 148 (34.8%) were female. Forty-two (9.9%) of these patients had adenocarcinoma as their final pathology result. According to the diagnosis of adenocarcinoma or other polyps, the patients were separated into two groups. There were 383 (90.1%) patients in the benign group and 42 (9.9%) patients in the adenocarcinoma group. The total number of polyps removed was 754 (Table 1). Of the polyps, 30 (4%) were removed from the cecum, 103 (13.7%) from the ascending colon, 135 (17.9%) from the transverse colon, 131 (17.4%) from the descending colon, 177 (23.5%) were from the sigmoid colon and 178 (23.6%) from the rectum. There was no difference between the two groups in terms of polyp excision location (p=0.146). Percentages according to polyp subtypes are given in Table 1.

There was no statistical difference between the groups in terms of age and gender (p=0.898 and p=0.089, respectively). Patients with multiple polyps were more likely to develop adenocarcinoma than those with single polyps. The mean largest diameter of polyps in the adenocarcinoma group were significantly larger than those in the other polyp group (Table 1). When CBC data were examined, it was found that lymphocyte counts were significantly lower in adenocarcinoma (p=0.013). Moreover, Hb and RDW values were also significantly lower in the adenocarcinoma group (p<0.001 for both). When the values for NLR, MLR, Plt/PDW, and Plt/MPV were compared, it was found that the Plt/PDW and MLR were significantly elevated in the adenocarcinoma group compared to the other polyp group (p=0.036 and p=0.004, respectively) (Table 2).

ROC curve analysis was used to calculate the diagnostic utility of the found values (Table 3). According to the ROC curve and the Youden index [1-(1-sensitivity) + (1-specifity)], Mo was shown to be the most valuable laboratory value in predicting the diagnosis of adenocarcinoma with a sensitivity of 86% and a specificity of 83% (Table 3). In this retrospective cohort the probability of polyps being malignant was 2.42 times higher in patients with a pre-colonoscopy Mo count >0.85.

Discussion

The results of this single-center retrospective analysis suggest that a number of commonly available absolute and derived CBC values may aid in the early detection of CRC. These parameters include the absolute Mo count, which had the best combination of sensitivity and specificity for predicting adenocarcinoma in polyps in this cohort, but consideration should also be given to the MLR, Hb value and Plt/PDW ratio parameters.

Colon polyps are the most common cause of CRC. Colon polyps may cause symptoms, depending on the size or amount of bleeding. The intensity of systemic inflammation should be considered while classifying circulating small and large platelets.[16] Cancer is a systemic inflammatory condition in which many pro-inflammatory cytokines are secreted. High-grade inflammation is negatively correlated with MPV. When an adenoma develops into a carcinoma, the malignant cells invade the mucosal layer, causing a systemic inflammatory response. MPV is also linked to disease activity/severity and is an indication of inflammatory disorders.[17] In patients with CRC, low MPV readings are expected.

It has been reported that the MPV is significantly lower in CRC patients.[11] The MPV values of patients in whom colon polyps were benign or contained adenocarcinoma did not differ significantly in our research. We suspect that the reason for this difference from the study of Wu et al.[11] that CRC patients were selected in the earlier study, while in our study, patients were selected for having polyps excised, only some of which were later found to be adenocarcinoma. Therefore, we believe that our findings can be explained because the activity of the inflammatory process is reduced in malignancies that are followed by polyps.

The mechanism that results in the association between Plt/MPV ratio and the formation or advancement of malignant tumors is unknown. Nonetheless, there are more studies about MPV and Plt independently than there are about the Plt/MPV ratio. Cho et al.[18] reported that the Plt/MPV ratio was more useful than MPV alone in discriminating

Table 1. Demographic and clinical characteristics of all patients and those with adenocarcinoma or other type of polyp

		All polyps (n=754)	Other polyps (n=709)	Adenocarcinoma (n=45)	p
Gender	Male	516 (68.4%)	486 (68.5%)	30 (66.7%)	0.792
	Female	238 (31.6%)	223 (31.5%)	15 (33.3%)	
Age	Min-max (median) Mean ± SD (median)	20-89 (65)	64.33±11.63 (65)	67.62±12.31 (68)	0.069
Location	Cecum	30 (4%)	29 (4.1%)	1 (2.2%)	0.146
	Ascending	103 (13.7%)	98 (13.8%)	5 (11.1%)	
	Transverse colon	135 (17.9%)	133 (18.8%)	2 (4.4%)	
	Descending	131 (17.4%)	120 (16.9%)	11 (24.4%)	
	Sigmoid	177 (23.5%)	163 (23.0%)	14 (31.1%)	
	Rectum	178 (23.6%)	166 (23.4%)	12 (26.7%)	
Polyp size	Mean ± SD	4.47±3.40	4.31±3.11	7.05±5.96	**<0.001***
	Min-max (median)	1-27 (3)	1-27 (3)	3-25 (5) high red	
Polyp types	Inflammatory	65 (8.6%)			
	Hyperplastic	158 (21%)			
	Adenoma	486 (64.5%)			
	Adenocarcinoma	45 (6%)			
	Serrated	7 (1.3%)			
Adenoma polyp subtypes (474)	Tubular	394 (83.2%)			
	Tubulovillous	54 (11.4%)			
	Villous	19 (4.1%)			
Dysplasia (14.7% | 111)	Low grade	73 (65.8%)			
	Moderate	2 (1.8%)			
	High grade	36 (4.8%)			
Differentiation for adenocarcinomas (12)	Well differentiated	7 (58.3%)			
	Moderately differentiated	4 (33.3%)			
	Poorly differentiated	1 (8.3%)			

Statistically significant values are bold*. SD: Standard deviation

between cancer and healthy individuals in a study carried out in patients with hepatocellular carcinoma. Wu et al.[11] stated that the Plt/MPV ratio showed superior diagnostic performance compared to MPV, NLR, or PLR alone to distinguish CRC from benign colorectal polyps. The Plt/MPV ratio was slightly higher in colon adenocarcinoma polyps in our study, but this was not significant. We believe that this may be due to the low number of adenocarcinomatous polyps.

PDW, another platelet index, is a measure of variation in platelet size. The relationship between PDW and cancer is unclear.[19] The variation of MPV and PDW in different cancer types is inconsistent. PDW was found to be higher in gastric and lung cancers, but lower in thyroid and breast cancers.[19] Although PDW values were lower in patients with polyps with colon cancer in our study, again the difference was not significant. Nonetheless, the Plt/PDW ratio was found to be higher in adenocarcinomas. Thus, we believe that evaluating PDW in conjunction with Plt, rather than separately, will yield more diagnostic utility.

A high MLR may be a sign of high tumor burden, as both a high Mo count and low lymphocyte count reflect suppressed immune activity.[20] MLR levels were shown to be elevated in cancers of the right colon and rectum in the MIMIC trial.[21] MLR values were higher from patients with polyps with adenocarcinoma in our analysis, which is in agreement with the findings of the MIMIC trial.

Table 2. Examination of all patients and comparison between patients with and without adenocarcinoma

		All patients (n=425)	Benign (n=383)	Adenocarcinoma (n=42)	Statistical significance
Gender	Male	277 (65.2%)	250 (65.3%)	27 (64.3%)	0.898
	Female	148 (34.8%)	133 (34.7%)	15 (35.7%)	
Age	(Years)	65 (20-89)	64 (20-89)	69.5 (43-86)	0.089
Polyp count		1 (1-12)	1 (1-12)	2 (1-10)	**<0.001**
Solitary/multiple	Solitary	259 (60.9%)	253 (66.1%)	6 (14.3%)	**<0.001**
	Multiple	166 (39.1%)	130 (33.9%)	36 (85.7%)	
WBC	Unit	7.62±2.64 (7.21)	7.63±2.66 (7.18)	7.55±2.48 (7.25)	0.911
Ne	Unit	4.72±2.30 (4.23)	4.71±2.31 (4.19)	4.86±2.31 (4.45)	0.651
Ly	Unit	2.07±0.78 (2.02)	2.10±0.79 (2.04)	1.79±0.53 (1.70)	**0.013**
Hb	Unit	13.10±2.21 (13.4)	13.24±2.16 (13.4)	11.85±2.34 (11.25)	**<0.001**
Plt	Unit	250.14±87.88 (238)	248.86±88.09 (237)	261.81±86.12 (251.5)	0.294
MPV	Unit	10.40±1.06 (10.4)	10.41±1.07 (10.4)	10.21±1.00 (10.2)	0.127
Mo	Unit	0.78±0.30 (0.58)	0.72±0.30 (0.57)	0.87±0.27 (0.64)	**<0.001**
PDW	Unit	12.39±2.23 (12.1)	12.47±2.20 (12.1)	11.64±2.38 (11.7)	**0.019**
PMR		25.24±17.99 (23.3)	25.14±18.68 (23.07)	26.13±9.89 (23.91)	0.173
PLT/PDW		21.23±9.60 (19.78)	20.95±9.44 (19.57)	23.78±10.73 (22.04)	**0.036**
NLR		2.68±2.15 (2.08)	2.64±2.13 (2.07)	3.12±2.35 (2.34)	0.124
MLR		0.33±0.21 (0.28)	0.33±0.21 (0.27)	0.41±0.23 (0.33)	**0.004**
Polyp type	Benign	383 (90.1%)			
	Adenocarcinoma	42 (9.9%)			

Statistically significant values are bold*. Ly: Lymphocyte count, Hb: Heamoglobin value, Plt: Platelet count, MPV: Mean platelet volume, Mo: Monocyte count, PDW: Platelet distribution width, Plt/MPW: Plateletcount to mean platelet volume ratio, Plt/PDW: Platelet count to platelet distribution width ratio, NLR: Neutrophil count to lymphocyte count ratio, MLR: Monocyte count to lymphocyte count ratio

Table 3. Complete blood count parameter diagnostic utility for adenocarcinoma including values for cut-off, sensitivity, specificity, area under the curve, odds ratios and Youden index (J)

	Diagnostic values				
	Cut-off	Sensitivity	Specifity	AUC (SE)	J
Ly	1.62	50.0%	73.4%	0.487 (0.047)	0.234
Hb	12.60	64.2%	64.3%	0.512 (0.052)	0.285
Plt	240.50	47.8%	47.6%	0.524 (0.045)	-0.046
MPW	10.35	51.4%	52.4%	0.491 (0.050)	0.038
Mo	0.85	86.0%	83.0%	0.556 (0.047)	0.69
PDW	11.95	54.9%	52.9%	0.520 (0.049)	0.078
Plt/MPW	23.70	46.2%	45.2%	0.517 (0.046)	-0.086
Plt/PDW	20.62	44.4%	42.9%	0.599 (0.044)	-0.127
NLR	2.23	42.8%	42.9%	0.580 (0.052)	-0.143
MLR	0.29	43.1%	42.9%	0.559 (0.052)	-0.14
Solitary/multiple	-	85.7%	66.1%		

Ly: Lymphocyte count, Hb: Heamoglobin value, Plt: Platelet count, MPV: Mean platelet volume, Mo: Monocyte count, PDW: Platelet distribution width, Plt/MPW: Plateletcount to mean platelet volume ratio, Plt/PDW platelet count to platelet distribution width ratio, NLR, neutrophil count to lymphocyte count ratio, MLR: Monocyte count to lymphocyte count ratio

Study Limitations

The fact that our study was single-centred can be considered as a limitation. It also had a retrospective design that could not completely resolve the confounding factors and will produce a certain degree of bias. The results may have been influenced by the large number of polyps analyzed and the low frequency of adenocarcinoma polyps. We therefore suggest that our results should be validated by larger, prospective, multicenter studies.

Conclusion

We believe that the absolute Mo count and the MLR and Plt/PDW ratios have diagnostic utility in detecting malignancies that may arise from colon polyps. We further suggest that polyps detected in patients with a high Mo count or elevated MLR or Plt/PDW ratios have a higher risk of cancer. Our results should be validated by larger prospective studies but in the meantime we propose a more thorough colonoscopic examination and screening in these patients.

Ethics

Ethics Committee Approval: Ethics committee approval was received from Hitit University Faculty of Medicine, Non-Interventional Research Ethics Committee in 2021 (approval number: 2021-78).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.D., H.K., Concept: D.D., Design: D.D., Data Collection or Processing: D.D., E.G.A., H.K., Analysis or Interpretation: V.B.T., Literature Search: D.D., V.B.T., Writing: D.D., E.G.A., H.K., V.B.T.

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