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Original research paper

Complete blood count parameters and inflammation-related biomarkers in patients with colorectal carcinoma

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ABSTRACT

The aim of this study was to determine whether there are differences in complete blood count parameters (CBC) and inflammation-related biomarkers, MPV/PC, PLR, NLR, LWR, LMR, NMR, and LCR, among patients with colorectal carcinoma (CRC) and patients with colorectal adenomas. The study included 155 patients who were divided into two groups according to histopathological analysis – 74 adenomas patients and 81 CRC patients. A routine examination of CBC was conducted on Sysmex XN1000 whereas CRP was measured on Alinity ci-series. Statistical analysis was performed by ROC curve analysis using MedCalc Statistical Software. In CRC patients, hemoglobin concentration, hematocrit, MCV, MCH, and MCHC were lower, while RDW was higher ($p < 0.001$), compared to patients with adenomas. Total leukocyte count ($p = 0$ .006), absolute neutrophils ($p = 0.005$), and absolute monocytes ($p = 0.007$) were lower while relative eosinophils ($p = 0.001$) and relative basophils ($p = 0.001$) were higher in CRC patients. Platelet count ($p < 0.001$) was significantly higher and MPV ($p = 0.003$) was significantly lower in CRC patients. Furthermore, MPV/PC ($p < 0.001$) was significantly lower and PLR ($p < 0.001$) was significantly higher in CRC. Moreover, Receiver Operating Characteristic (ROC) analysis revealed poor diagnostic accuracy, for all tested parameters (AUC was 0.7 or less). PC, MPV, MPV/PC, and PLR were significantly different between study groups, but ROC analysis revealed poor diagnostic accuracy. Lower hemoglobin levels in CRC patients are possibly due to more frequent and excessive bleeding. Higher levels of basophils and eosinophils in CRC patients are indicators of inflammatory reaction, which is linked to CRC.

Keywords: colorectal cancer, complete blood count, inflammation-related biomarkers

INTRODUCTION

Colorectal carcinoma (CRC) is the third most common cancer in the world. It is the second leading cause of cancer-related deaths worldwide, with almost 900,000 deaths in 2020 (1). Older age and family history are some of the major risk factors for the development

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of CRC, with most cases diagnosed in individuals over 50 years old (2, 3). Additionally, obesity, diet, cigarette smoking, and conditions like polyps in the colon and inflammatory bowel disease (IBD) increase the risk of developing CRC (2, 4). Current screening tests include colonoscopy, fecal occult blood test (FOBT), and fecal immunochemical test (FIT). Colonoscopy is the most commonly used screening method since it can detect CRC with the highest efficiency, despite an unpleasant patient experience and high costs (5). Since symptoms of CRC usually occur in the late stage of the disease, such as blood in stool, dark and black stool, cramps, bloating, and constipation, it is of great importance to have a good screening test to recognize the development of the disease promptly (6).

Chronic inflammation in general, has been linked to the development and progression of many malignant diseases, including CRC (7). It is associated with immunosuppression and tissue damage, heightening the risk of tumorigenesis (4). Consequently, chronic gut diseases such as Crohn's disease and ulcerative colitis, represent a risk for the development of CRC. Commonly observed conditions in patients with chronic inflammatory diseases or different malignancies include thrombocytosis, anemia, leukocytosis, and hemoglobinemia, which can be determined using a complete blood count (CBC) (6). The complete blood count is one of the most widely used laboratory tests and plays an important role in the diagnosis of various diseases. Numerous studies report various hematology-associated inflammatory markers that could play a role in the prognosis and monitoring of CRC (2, 7, 8). These are known as platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), lymphocyte-to-leukocyte-ratio (LWR), neutrophil-to-monocyte ratio (NMR), and lymphocyte to CRP ratio (LCR) (6, 7). Of all listed, NLR and PLR are the most investigated inflammation-related biomarkers. NLR and PLR are linked to various malignancies, including CRC (9). Studies suggest that PLR and NLR are good prediction markers of survival since CRC patients with high NLR and PLR have worse overall survival (OS) and disease-free survival (DFS) (9, 10). Other highly researched ratios are LCR and LMR, where low values of these ratios are linked to lower OS and DFS among CRC patients (9). Fewer studies examined LWR and NMR in CRC patients. Some of these studies suggest that lower LWR is related to substantially low OS and DFS, which also depends on specific tumor location (11).

Nevertheless, as far as we know, there are not many studies focusing on the differences between CRC and adenomas. Therefore, the aim of this study was to determine whether there are differences in CBC parameters and inflammation-related hematological biomarkers, mean platelet volume to platelet count ratio (MPV/PC), PLR, NLR, LWR, LMR, NMR, and LCR among patients with CRC and patients affected by adenomas.

EXPERIMENTAL

Study design

This study was conducted in collaboration with the Department of Gastroenterology and Hepatology and the Department of Clinical Chemistry, Clinical Hospital Centre Sestre milosrdnice in Zagreb, and the Department of Medical Biochemistry and Hematology, Faculty of Pharmacy and Biochemistry, University of Zagreb. Patients were

recruited from December 2019 to February 2024 in the Department of Gastroenterology and Hepatology, Clinical Hospital Centre Sestre milosrdnice in Zagreb. Sample analyses were performed at the Department of Clinical Chemistry, Clinical Hospital Centre Sestre milosrdnice in Zagreb.

Clinical subjects

The study included 155 patients who were suspected of having CRC based on clinical signs and symptoms. All patients underwent colonoscopy. Based on colonoscopy findings and histopathological analysis patients were divided into two groups, 74 patients with colorectal adenomas and 81 patients with confirmed CRC. The histopathological analysis was performed according to current national guidelines and the latest studies (12). Group of patients with adenomas [71 (35–90) years] and patients with confirmed CRC [72 (41–93) years] did not differ in age ($p = 0.074$).

The study was approved by the Ethics Committee of Clinical Hospital Centre Sestre milosrdnice, Zagreb, Croatia (EP-19243/17-6) and the University of Zagreb Faculty of Pharmacy and Biochemistry, Croatia (251-62-03-19-29). All participants signed the informed consent.

Samples

After 12 hours of overnight fasting, blood samples were collected in K_3EDTA-tubes (Greiner Bio-One, Austria) for routine examination of complete blood count or in tubes with clot activator for sera CRP concentration (Greiner Bio-One, Austria). Sera samples were obtained after 30 minutes of spontaneous clotting and centrifuged at 2000 g for 10 minutes at room temperature. Sera and K_3EDTA-blood samples were immediately analyzed.

Methods

A routine examination of complete blood count was conducted on Sysmex XN1000 (Sysmex Inc, Kobe, Japan) whereas C-reactive protein (CRP) was measured using Alinity ci-series (Abbott Diagnostics, USA).

MPV/PC values were calculated from the mean platelet volume (MPV) and platelet count (PC), PLR from the platelet count and the absolute lymphocyte count, NLR from absolute neutrophil count and absolute lymphocyte count, LWR from the absolute lymphocyte count and leukocyte count, LMR from absolute lymphocyte count and absolute monocyte count, NMR from absolute neutrophil count and absolute monocyte count and finally, LCR from absolute lymphocyte count and CRP.

Statistical analysis

Data are presented as median and interquartile range (Q1-Q3) or as mean and standard deviation. The distribution was tested using the Kolmogorov-Smirnov goodness of fit test. Data were analyzed using the *t*-test or Mann-Whitney rank sum test. Diagnostic accuracy was tested by Receiver Operating Characteristic (ROC) analysis. p values less than 0.05 were considered statistically significant. Statistical analysis was performed using MedCalc® Statistical Software version 22.014 (MedCalc Software Ltd, Belgium).

RESULTS AND DISCUSSION

The obtained results of our studies are presented in the form of tables and discussed accordingly.

Differences in complete blood count parameters

Complete blood count parameters in both CRC and adenoma patients are shown in Table I. In CRC patients, hemoglobin concentration ($p = 0.001$), hematocrit ($p = 0.004$), as well as erythrocyte indices, mean corpuscular volume (MCV; $p = 0.002$), mean corpuscular hemoglobin (MCH; $p < 0.001$), and mean corpuscular hemoglobin concentration (MCHC; $p = 0.002$) were lower while red blood cell distribution width (RDW; $p < 0.001$) was higher compared to patients with adenomas.

Table I. Complete blood count parameters in study groups

	Colorectal adenoma *N* = 74	CRC *N* = 81	*p*
Erythrocyte ($\times 10^{12}$ L^{-1})	4.57 ± 0.55	4.46 ± 0.57	0.238
Hemoglobin (g L^{-1})	137 (129–145)	130 (107–137)	**0.001**
Hematocrit (L L^{-1})	0.411 (0.391–0.436)	0.396 (0.333–0.414)	**0.004**
MCV (fL)	89.3 (87.0–92.4)	86.0 (81.2–91.0)	**0.002**
MCH (pg)	30.0 (29.0–31.1)	28.6 (25.5–30.5)	**< 0.001**
MCHC (g L^{-1})	333 (327–340)	329 (317–335)	**0.002**
RDW (%)	13.2 (12.8–14.0)	14.3 (13.3–16.2)	**< 0.001**
Leukocyte ($\times 10^{9}$ L^{-1})	8.26 (6.90–11.10)	7.20 (6.20–9.23)	**0.006**
Neutrophils ($\times 10^{9}$ L^{-1})	5.70 (4.49–8.02)	4.82 (3.88–6.05)	**0.005**
Neutrophils (%)	67.4 ± 8.6	66.1 ± 8.7	0.330
Lymphocytes ($\times 10^{9}$ L^{-1})	1.81 (1.50–2.30)	1.58 (1.29–2.10)	0.059
Lymphocytes (%)	21.7 ± 7.2	22.5 ± 7.5	0.471
Eosinophils ($\times 10^{9}$ L^{-1})	0.10 (0.05–0.17)	0.14 (0.10–0.23)	**0.019**
Eosinophils %	1.3 (0.5–2.1)	2.0 (1.1–3.1)	**0.001**
Monocytes ($\times 10^{9}$ L^{-1})	0.70 (0.60–0.89)	0.63 (0.50–0.78)	**0.007**
Monocytes (%)	8.7 ± 2.2	8.3 ± 2.1	0.282
Basophils ($\times 10^{9}$ L^{-1})	0.04 (0.02–0.07)	0.05 (0.02–0.10)	0.253
Basophils (%)	0.5 (0.3–0.7)	0.6 (0.5–1.0)	**0.001**
Platelet ($\times 10^{9}$ L^{-1})	218 (184–258)	277 (223–319)	**< 0.001**
MPV (fL)	9.8 ± 1.3	9.2 ± 1.2	**0.003**
S-CRP (g L^{-1})	6 (3–18)	4 (2–11)	0.070

MCV – mean corpuscular volume, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, RDW – red blood cell distribution width, MPV – mean platelet volume. Data are shown as median (interquartile range: Q1-Q3) or as mean ± standard deviation. Tested by Mann-Whitney test or *t*-test.

Leukocyte count ($p = 0.006$), absolute neutrophils ($p = 0.005$), and absolute monocytes ($p = 0.007$) were lower, while absolute eosinophils ($p = 0.019$), relative eosinophils ($p = 0.001$) and relative basophils ($p = 0.001$) were higher in CRC patients.

The platelet count was significantly higher ($p < 0.001$), and MPV was significantly lower ($p = 0.003$) in CRC patients compared to patients with adenomas.

Among all inflammation-related biomarkers calculated from complete blood count parameters, only MPV/PC and PLR showed significant differences between the two study groups, as shown in Table II. MPV/PC was lower ($p < 0.001$), while PLR was higher ($p < 0.001$) in CRC patients.

Table II. Hematology-associated inflammatory markers from complete blood count in study groups

	Colorectal adenoma *N* = 74	CRC *N* = 81	*p*
MPV/PC	0.05 (0.03–0.06)	0.03 (0.03–0.04)	**< 0.001**
PLR	119.71 (102.16–147.03)	167.46 (124.58–222.45)	**< 0.001**
NLR	3.33 (2.54–4.18)	2.99 (2.38–4.08)	0.321
NMR	8.04 (6.33–10.05)	8.00 (6.35–9.85)	0.983
LMR	2.50 (1.94–3.29)	2.60 (2.10–3.27)	0.492
LWR	0.21 (0.18–0.25)	0.22 (0.18–0.26)	0.432
LCR	0.27 (0.09–0.56)	0.36 (0.16–0.68)	0.153

MPV/PC – MPV/platelet count, PLR – platelet count/absolute lymphocyte ratio, NLR – neutrophils/lymphocyte ratio, NMR – neutrophils/monocyte ratio, LMR – absolute lymphocyte/absolute monocyte ratio, LWR – absolute lymphocyte/leukocyte ratio, LCR – absolute lymphocyte/CRP ratio. Data are shown as median (interquartile range) or as mean ± standard deviation. Tested by Mann-Whitney test or *t*-test.

Diagnostic accuracy

We tested diagnostic accuracy for all parameters that were different between patients with adenomas and CRC, the area under the curve with 95 % confidence interval [AUC (95 % CI)], sensitivity, specificity, and cut-off values, which are all part of Table III.

Although all P values were statistically significant, ROC analysis revealed poor diagnostic accuracy. For all the tested parameters, AUC values were 0.7 or less.

Platelets and platelet count

Platelets play a significant role in the tumorigenesis of various types of cancer. They contribute to cell proliferation, inflammation, and metastasis (8, 9). PC is a parameter of CBC that has been widely studied in CRC patients, along with hemoglobin. Thrombocytosis is observed in many types of cancers and is associated with tumor growth and metastasis (11). Platelets contribute to tumor growth *via* different mechanisms. For example, by secreting different angiogenesis-regulating proteins and growth factors, such as vascular endothelial growth factor (9). In our study, we observed significantly higher PC and significantly

Table III. Diagnostic accuracy of complete blood count parameters and inflammation-related biomarkers from complete blood count in study groups

	AUC (95% CI)	*p*	Sensitivity	Specificity	Cut-off
Hemoglobin	0.66 (0.58–0.73)	< 0.001	40.74	85.14	≤ 122 g L^{-1}
Hematocrit	0.63 (0.55–0.71)	0.003	35.80	87.84	≤ 0.366 L L^{-1}
MCV	0.65 (0.57–0.72)	0.001	51.90	79.70	≤ 86.1 fL
MCH	0.67 (0.59–0.74)	< 0.001	58.02	78.38	≤ 28.9 pg
MCHC	0.64 (0.56–0.72)	0.001	46.91	75.68	≤ 326 g L^{-1}
RDW	0.70 (0.62–0.77)	< 0.001	55.56	78.38	> 14.1 (%)
Leukocyte	0.63 (0.55–0.70)	0.005	81.48	41.89	≤ 9.4×10^9 L^{-1}
Neutrophils	0.63 (0.55–0.71)	0.004	80.25	44.59	≤ 6.31×10^9 L^{-1}
Eosinophils	0.61 (0.53–0.69)	0.017	46.91	75.68	> 0.17×10^9 L^{-1}
Eosinophils	0.66 (0.58–0.73)	< 0.001	51.85	72.97	> 1.9 (%)
Monocytes	0.63 (0.54–0.70)	0.005	58.02	62.16	≤ 0.66×10^9 L^{-1}
Basophils	0.66 (0.58–0.73)	< 0.001	48.15	74.32	> 0.6 (%)
Platelet	0.72 (0.65–0.79)	< 0.001	69.14	70.27	> 238×10^9 L^{-1}
MPV	0.63 (0.55–0.71)	0.004	58.02	66.22	≤ 9.3 fL
PLR	0.71 (0.64–0.78)	< 0.001	62.96	77.03	> 150.88
MPV/PC	0.72 (0.64–0.79)	< 0.001	81.48	55.41	≤ 0.04

MCV – mean corpuscular volume, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, RDW – red blood cell distribution width, MPV – mean platelet volume, MPV/PC – MPV/platelet count, PLR – platelet count/absolute lymphocyte. Tested by ROC curve analysis; results are shown as area under the curve (AUC) with 95% confidence interval (95% CI), sensitivity, specificity, and optimal cut-off value.

lower MPV in CRC patients. Furthermore, MPV/PC was lower, while PLR was higher in CRC patients. A meta-analysis conducted on nine retrospective cohort studies examined the role of platelet count in CRC patients. The analysis included 3413 CRC patients. The studies showed that elevated platelet count is associated with shorter OS and DFS rates in CRC patients (13). Additionally, the study conducted in 2018 on 783 patients with CRC and 463 patients with colorectal adenomas examined platelet indices as diagnostic biomarkers. The study showed that PC is significantly higher in patients with more advanced TNM stages and in CRC patients compared to those with colorectal adenomas (14). Numerous recently conducted studies have focused not only on PC but also on MPV, MPV/PC ratio, and PLR as new clinical markers. A considerable number of studies have shown a connection between MPV and different types of cancer, including CRC (2, 15). A study conducted in 2019 showed that the MPV/PC ratio was significantly lower in the CRC group than in both the adenomatous polyp and control groups. Furthermore, they suggested that MPV/PC is a useful diagnostic marker for distinguishing between benign and malignant CRC and early and advanced CRC (14). Many studies have observed a decrease in MPV values across TNM stages of CRC, but no significant correlation has been found (2, 8).

Platelet to lymphocyte ratio

For a while, PLR has been the focus of studies researching different malignancies, including CRC and adenomas. Although studies suggest different cut-off values, many indicate that PLR is a good prediction marker for OS and DFS (7, 9, 10). Research conducted in 2021 on 71 CRC patients who underwent neoadjuvant chemoradiotherapy studied different inflammatory markers and their connection to OS and DFS. The study showed that PLR, as well as NLR, significantly correlated with OS. They used two different tests to determine the significant correlation between PLR and DFS, where PLR showed a substantial correlation in one test and nearly reached significance in the other (7). Additionally, Feng *et al.* examined the significance of NLR, PLR, and MPV for predicting colorectal adenomatous polyp and CRC. Studies showed that NLR and PLR are significantly increased in the CRC group compared to the adenomatous polyp group, while MPV is significantly lower in the CRC group (16). In contrast to the study, which found a relationship between CRC and NLR, we did not observe significant differences in NLR values between study groups.

Hemoglobin

In CRC, hemoglobin (Hb) is most commonly investigated in the context of occult bleeding and less commonly in the blood. Blood in the stool is a common symptom of CRC and of adenomas. Nevertheless, there are some differences between the amount of blood and the frequency of bleeding between the two. Usually, colorectal bleeding is more frequent and excessive in CRC patients than in adenoma patients, which could explain lower levels of blood hemoglobin in CRC patients (16–18). A retrospective study conducted in 2023 examined the significance of inflammation-related markers in distinguishing early colon cancer and adenomatous polyps. The study included 216 patients with CRC and 126 with colorectal adenomatous polyps. They showed that Hb levels are significantly lower in CRC patients than in colorectal adenomatous polyp patients. Furthermore, they also showed that age, carcinoembryonic antigen (CEA), less monocyte count, and Hb were independent risk factors for the diagnosis of stage I colorectal cancer (16). In accordance with the published paper, we also showed that CRC patients have significantly lower Hb concentration as well as hematocrit, MCV, MCH, MCHC, and higher RDW values.

Neutrophil count

Neutrophil count in cancer patients has been usually studied in the context of NLR. Neutrophilia is commonly seen in CRC patients since colorectal carcinoma cells secrete granulocyte-macrophage colony-stimulating factor, which recruits neutrophils (19, 20). Recent studies report that CRC patients with high neutrophil count have worse OS and progression-free survival (7, 21). Neutropenia is typically observed in colorectal cancer patients undergoing chemotherapy (22–24). Furthermore, several studies have demonstrated a connection between neutropenia and DFS in these patients (22, 23). However, limited research has been done on neutrophil count differences between CRC and colorectal adenomas. A retrospective study conducted on CRC patients in addition to colorectal adenomatous polyp patients showed no significant difference between neutrophil counts in those groups (16).

Eosinophils

Eosinophils are types of white blood cells that are mainly studied concerning allergies. However, many studies have shown their connection to the tumor microenvironment and their role in tumorigenesis (25, 26). Eosinophils release multiple cytokines and chemokines that play a role in the inflammatory response and can cause various changes in cancer. Eosinophilia is commonly seen in different malignancies, such as Hodgkin lymphoma and eosinophilic leukemia, but it can also be present in some solid tumor cancers. Many studies examined the role of eosinophils and tumor-associated tissue eosinophilia (TATE) in the context of different solid tumors such as cervical cancer, esophageal carcinoma, prostate cancer, and CRC (26, 27). In accordance, we also observed eosinophilia in CRC patients compared to the patients with adenomas. A retrospective cohort study conducted on 8334 pairs of CRC patients and matched controls studied whether trends in peripheral blood eosinophil numbers are associated with CRC diagnosis. The study showed that the risk of CRC diagnosis was higher when the absolute number of eosinophils in peripheral blood increased linearly. They suggested that positive linear change in an absolute number of eosinophils is an independent predictor of CRC (28). Another study conducted a meta-analysis of 26 investigations to examine the role of TATE in different solid tumors. The study showed that the presence of TATE was associated with better OS in patients with solid tumors such as CRC and esophageal carcinoma (26).

Inflammation-related biomarkers

In addition to the previously discussed MPV/PC, PLR, and NLR, other inflammation--related biomarkers such as LWR, LMR, NMR, and LCR are studied in different types of cancer, including CRC. Chan *et al.* found that elevated LMR was independently associated with better OS, and the rate of histologically high-grade tumors was higher in the patients with low LMR (29). Furthermore, tumors with low LMR were more likely to be found in the left-sided colon in CRC patients who underwent curative surgery. Li *et al.* reported that lower LMR was independently associated with worse OS and DFS in CRC patients with curative resection (Stage I-III) (30). LCR was also shown to significantly and independently correlate with worse OS and DFS in CRC patients (31, 32). Retrospective research done in 2021 reported that LWR is correlated with sex and tumor location in CRC patients who received neoadjuvant therapy. Additionally, the study showed that a high LWR was associated with longer OS and DFS but suggested that it was not an independent predictor of the two (10). Only a few studies investigated the role of NMR in CRC or colorectal adenomas. Kostakis *et al.* studied different preoperative parameters in colorectal cancer. The study showed that NMR was connected with the stage of the disease, the size of the tumor, and the presence of distant metastasis. Patients with stage IV disease and distant metastasis had higher NMR (33).

In our study, we did not find differences in LWR, LMR, NMR, and LCR between patients with CRC and adenomas patients. The reasons for this discrepancy in obtained results could be the differences in study design. Namely, herein, we determined the diagnostic accuracy for parameters, which showed different results between study groups, but ROC analysis revealed poor diagnostic accuracy for all tested parameters. Many previously conducted studies determined the diagnostic accuracy of CBC parameters and inflammation-related biomarkers, with some of them showing good diagnostic accuracy

(8, 14, 15). Lalošević *et al.* used ROC analysis to determine the best cut-off values of NLR, PLR, and MPV for CRC detection (8). They used AUC to determine the diagnostic accuracy of the three. AUC showed good diagnostic performance of NLR and PLR. Furthermore, AUC showed even greater diagnostic accuracy when MPV was combined with NLR and PLR. In addition, Wu *et al.* used ROC analysis to determine the sensitivity, specificity, and diagnostic values of MPV and MPV/PC in colorectal cancer (15). They calculated AUC to evaluate MPV and MPV/PC diagnostic accuracy. The analysis showed that MPV/PC has superior diagnostic performance compared to using MPV, NLR, or PLR alone in differentiating colorectal cancer from benign colorectal polyps. Again, the different study designs and selected groups could be a reason for the discrepancy in results.

CONCLUSIONS

In conclusion, we demonstrated statistically significant differences between the two groups in MPV/PC and PLR, with MPV/PC being lower and PLR higher in CRC patients, although ROC analysis revealed poor diagnostic accuracy. Lower hemoglobin levels were observed in CRC patients, possibly due to more frequent and excessive bleeding than in colorectal adenoma patients (16–18). We observed higher levels of basophils and eosinophils in CRC patients. Both basophils and eosinophils are indicators of inflammatory reactions linked to CRC and could be a possible explanation for observed data (28). While neutrophilia is commonly observed in CRC patients, our study found lower neutrophil levels in CRC patients compared to adenocarcinoma patients (6). Furthermore, Feng *et al.* did not find a significant difference in neutrophil count between CRC and adenomatous polyps patients (16). We also demonstrated higher PC and lower MPV in CRC patients compared to adenoma patients, which is in accordance with recent studies (14, 16). Although all *p* values were statistically significant for the listed parameters, ROC analysis revealed poor diagnostic accuracy, and more research is required. Also, we did not find statistically significant differences in NLR, NMR, LMR, LWR, and LCR between CRC and adenoma patients.

REFERENCES

1. WHO, WHO global survey on the inclusion of cancer care in health-benefit packages 2020–2021; https://iris.who.int/bitstream/handle/10665/375828/9789240088504-eng.pdf?sequence=1
2. A. Alsalman, M. A. Al-Mterin, A. Abu-Dayeh, F. Alloush, K. Murshed and E. Elkord, Associations of complete blood count parameters with disease-free survival in right-and left-sided colorectal cancer patients, *J. Pers. Med.* **12**(5) (2022) Article ID 816 (13 pages); https://doi.org/10.3390/jpm12050816
3. B. Baran, N. Mert Ozupek, N. Yerli Tetik, E. Acar, O. Bekcioglu and Y. Baskin, Difference between left-sided and right-sided colorectal cancer: A focused review of literature, *Gastroenterol. Res.* **11**(4) (2018) 264–273; https://doi.org/10.14740/gr1062w
4. H. Zhao, L. Wu, G. Yan, Y. Chen, M. Zhou, Y. Wu and Y. Li, Inflammation and tumor progression: Signaling pathways and targeted intervention, *Signal Transduct. Target. Ther.* **6** (2021) Article ID 263 (46 pages); https://doi.org/10.1038/s41392-021-00658-5
5. I. A. Issa and M. Noureddine, Colorectal cancer screening: An updated review of the available options, *World J. Gastroenterol.* **23**(28) 5086–5096; https://doi.org/10.3748/wjg.v23.i28.5086

6. P. S. Virdee, I. R. Marian, A. Mansouri, L. Elhussein, S. Kirtley, T. Holt and J. Birks, The full blood count blood test for colorectal cancer detection: A systematic review, meta-analysis, and critical appraisal, *Cancers* **12** (2020) Article ID 2348 (37 pages); https://doi.org/10.3390/cancers12092348
7. M. S. Mekić, I. Pedišić, H. Šobat, V. V. Boras, I. Kirac, L. Štefančić, M. Šekerija, B. Vrdoljak and D. Vrdoljak, The role of complete blood count parameters in patients with colorectal cancer, *Acta Clin. Croat.* **57**(4) (2018) 624–629; https://doi.org/10.20471/acc.2018.57.04.03
8. M. Stojkovic Lalosevic, A. Pavlovic Markovic, S. Stankovic, M. Stojkovic, I. Dimitrijevic, I. Radoman Vujacic, D. Lalic, T. Milovanovic, I. Dumic and Z. Krivokapic, Combined diagnostic efficacy of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) as biomarkers of systemic inflammation in the diagnosis of colorectal cancer, *Dis. Markers* (2019) Article ID 6036979 (7 pages); https://doi.org/10.1155/2019/6036979
9. T. Yamamoto, K. Kawada and K. Obama, Inflammation-related biomarkers for the prediction of prognosis in colorectal cancer patients, *Int. J. Mol. Sci.* **22**(15) (2021) Article ID 8002 (14 pages); https://doi.org/10.3390/ijms22158002
10. W. Jia, L. Yuan, H. Ni, B. Xu and P. Zhao, Prognostic value of platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and lymphocyte-to-white blood cell ratio in colorectal cancer patients who received neoadjuvant chemotherapy, *Technol. Cancer Res. Treat.* **20** (2021) 1–10; https://doi.org/10.1177/15330338211034291
11. A. Braun, H. J. Anders, T. Gudermann and E. Mammadova-Bach, Platelet-cancer interplay: Molecular mechanisms and new therapeutic avenues, *Front. Oncol.* **11** (2021) Article ID 665534 (27 pages); https://doi.org/10.3389/fonc.2021.665534
12. A. Demirović and B. Krušlin, Recommendations for histopathology report of colorectal carcinoma specimens, *HAZU* **530** (2017) 67–72; https://doi.org/10.21857/ygjwrc642y
13. X. D. Rao, H. Zhang, Z. S. Xu, H. Cheng, W. Shen and X. P. Wang, Poor prognostic role of the pretreatment platelet counts in colorectal cancer: A meta-analysis. Vol. 97, *Medicine* (Baltimore) **97**(23) (2018) Article ID e10831 (7 pages); https://doi.org/10.1097/MD.0000000000010831
14. X. Zhu, Y. Cao, P. Lu, Y. Kang, Z. Lin, T. Hao and Y. Song, Evaluation of platelet indices as diagnostic biomarkers for colorectal cancer, *Sci. Rep.* **8**(1) (2018) Article ID 11814 (7 pages); https://doi.org/10.1038/s41598-018-29293-x
15. Y. Y. Wu, X. Zhang, Y. Y. Qin, J. Q. Qin and F. Q. Lin, Mean platelet volume/platelet count ratio in colorectal cancer: A retrospective clinical study, *BMC Cancer* **19**(1) (2019) Article ID 314 (7 pages); https://doi.org/10.1186/s12885-019-5504-9
16. Z. Feng, H. Lin, X. Yang, S. Cao, X. Gu, Z. Zhang and W. Deng, Diagnostic value of inflammation-related indicators in distinguishing early colon cancer and adenomatous oolyps, *Cancer Control.* **30** (2023) 1–10; https://doi.org/10.1177/10732748231180745
17. B. G. Ellis and M. R. Thompson, Factors identifying higher risk rectal bleeding in general practice, *Br. J. Gen. Pract.* **55**(521) (2005) 949–955.
18. J. Tibble, G. Sigthorsson, R. Foster, R. Sherwood, M. Fagerhol and I. Bjarnason, Faecal calprotectin and faecal occult blood tests in the diagnosis of colorectal carcinoma and adenoma, *Gut* **49**(3) (2001) 402–408; doi.org/10.1136/gut.49.3.402
19. W. Zheng, J. Wu, Y. Peng, J. Sun, P. Cheng and Q. Huang, Tumor-associated neutrophils in colorectal cancer development, progression and immunotherapy, *Cancers* **14**(19) (2022) Article ID 4755 (20 pages); https://doi.org/10.3390/cancers14194755
20. Z. Fan, Y. Li, Q. Zhao, L. Fan, B. Tan, J. Zuo, K. Hua and Q. Ji, Highly expressed granulocyte colony-stimulating factor (G-CSF) and granulocyte colony-stimulating factor receptor (G-CSFR) in human gastric cancer leads to poor survival, *Med. Sci. Monit.* **24** (2018) 1701–1711; https://doi.org/10.12659/MSM.909128

21. J. Yang, X. Guo, M. Wang, X. Ma, X. Ye and P. Lin, Pre-treatment inflammatory indexes as predictors of survival and cetuximab efficacy in metastatic colorectal cancer patients with wild-type RAS, *Sci. Rep.* **7**(1) (2017) Article ID 17166 (9 pages) ; https://doi.org/10.1038/s41598-017-17130-6
22. T. Sunaga, S. Suzuki, M. Kogo, T. Kurihara, S. Kaji, N. Koike, N. Harada, M. Suzuki and Y. Kiuchi, The association between neutropenia and prognosis in stage III colorectal cancer patients receiving adjuvant chemotherapy, *Eur. J. Cancer Care* **23**(3) (2014) 394–400; https://doi.org/10.1111/ecc.12120
23. P. H. Cashin, L. Ghanipour, M. Enblad and D. L. Morris, Neutropenia in colorectal cancer treated with oxaliplatin-based hyperthermic intraperitoneal chemotherapy: An observational cohort study, *World J. Gastrointest. Oncol.* **12**(5) (2020) 549–558; https://doi.org/10.4251/wjgo.v12.i5.549
24. S. Hamauchi, K. Yamazaki, T. Masuishi, Y. Kito, A. Komori, T. Tsushima, Y. Narita, A. Todaka, M. Ishihara, T. Yokota, T. Tanaka, N. Machida, S. Kadowaki, A. Fukutomi, T. Ura, Y. Onozawa, M. Ando, M. Tajika, K. Muro, H. Yasui, K. Mori and H. Taniguchi, Neutropenia as a predictive factor in metastatic colorectal cancer treated with TAS-102, *Clin. Colorectal Cancer* **16**(1) (2017) 51–57; https://doi.org/10.1016/j.clcc.2016.07.005
25. H. Reichman, D. Karo-Atar and A. Munitz, Emerging roles for eosinophils in the tumor microenvironment, *Trends Cancer* **2**(11) (2016) 664–675; https://doi.org/doi: 10.1016/j.trecan.2016.10.002
26. G. Hu, S. Wang, K. Zhong, F. Xu, L. Huang, W. Chen and P. Cheng, Tumor-associated tissue eosinophilia predicts favorable clinical outcome in solid tumors: A meta-analysis, *BMC Cancer* **20**(1) (2020) Article ID 454 (9 pages); https://doi.org/10.1186/s12885-020-06966-3
27. G. Varricchi, M. R. Galdiero, S. Loffredo, V. Lucarini, G. Marone, F. Mattei, G. Marone and G. Schiavoni, Eosinophils: The unsung heroes in cancer? *Oncoimmunology* **7**(2) (2018) Article ID e1393134 (12 pages); https://doi.org/10.1080/2162402X.2017.1393134
28. Y. Rosman, T. Hornik-Lurie, K. Meir-Shafrir, I. Lachover-Roth, A. Cohen-Engler, A. Munitz and R. Confino-Cohen, Changes in peripheral blood eosinophils may predict colorectal cancer – A retrospective study, *World Allergy Organization J.* **15**(10) (2022) Article ID 100696 (8 pages); https://doi.org/doi: 10.1016/j.waojou.2022.100696
29. J. C. Chan, D. L. Chan, C. I. Diakos, A. Engel, N. Pavlakis, A. Gill and S. J. Clarke, The lymphocyte-to-monocyte ratio is a superior predictor of overall survival in comparison to established biomarkers of resectable colorectal cancer, *Ann. Surg.* **265**(3) (2017) 539–546; https://doi.org/10.1097/SLA.0000000000001743.
30. Y. Li, H. Jia, W. Yu, Y. Xu, X. Li, Q. Li and S. Cai, Nomograms for predicting prognostic value of inflammatory biomarkers in colorectal cancer patients after radical resection, *Int. J. Cancer* **139**(1) (2016) 220–231; https://doi.org/10.1002/ijc.30071
31. Y. Okugawa, Y. Toiyama, A. Yamamoto, T. Shigemori, S. Ide, T. Kitajima, H. Fujikawa, H. Yasuda, J. Hiro, S. Yoshiyama, T. Yokoe, S. Saigusa, K. Tanaka, Y. Shirai, M. Kobayashi, M. Ohi, T. Araki, D. C. McMillan, C. Miki, A. Goel and M. Kusunokit, Lymphocyte-C-reactive protein ratio as promising new marker for predicting surgical and oncological outcomes in colorectal cancer, *Ann. Surg.* **272**(2) (2020) 342–351; https://doi.org/10.1097/SLA.0000000000003239
32. S. Suzuki, T. Akiyoshi, K. Oba, F. Otsuka, T. Tominaga, T. Nagasaki, Y. Fukunaga and M. Ueno, Comprehensive comparative analysis of prognostic value of systemic inflammatory biomarkers for patients with stage ii/iii colon cancer, *Ann. Surg. Oncol.* **27**(3) (2020) 844–852; https://doi.org/10.1245/s10434-019-07904-9
33. I. D. Kostakis, A. G. Vaiopoulos, Z. Garoufalia, A. G. Papavassiliou, S. Kykalos, G. Kouraklis and G. Tsourouflis, What can preoperative blood tests tell us about colorectal cancer? *JBUON* **23**(1) (2018) 84–95.