

Retrospective Analysis of Demographic, Clinical, Biochemical, and Histopathological Findings of Gastrointestinal Polyps

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Abstract

Introduction: In this study, we aimed to demonstrate the histopathological, clinical, demographic, and biochemical features of upper and lower gastrointestinal (GI) tract polyps. Additionally, we aimed to investigate the effect of polyp localization on endoscopic intervention indications, polyp size, and biochemical, histopathological, and demographic characteristics.

Materials and Methods: Endoscopic procedures performed in the endoscopy unit at the Van Yüzüncü Yıl University Dursun Odabaş Medicine Center between 2016-2021 were scanned. In total, 900 patients with polyps in the upper or lower GI tract were included in this study. Endoscopic procedure reports, biochemical data (C-reactive protein (CRP), sedimentation, hemoglobin, platelet, leukocyte, red cell distribution width, and ferritin values), histopathological data, endoscopic procedure indications, and demographic data of the patients were evaluated by statistical analysis.

Results: Polyps were divided into three groups according to polyp size: diminutive polyps 61.3% (n=552); small polyps 30.3% (n=273); and large polyps 8.3% (n=75). The polyps were also divided into three groups according to their histological features: neoplastic polyps (including; adenomatous polyps (38.3%), and serrated polyps (0.3%), malignant polyps (3.7%), and non-neoplastic polyps (57.2%). The incidence of adenomatous and malignant polyps was significantly higher in the left colon, whereas that of non-neoplastic polyps were significantly higher in the upper GI tract (p=0.001). The incidence of adenomatous polyps was significantly higher in large polyps (p=0.001). We determined the CRP and leukocyte values to be significantly higher in large polyps than in other polyp sizes (p=0.01, p=0.008, respectively). The platelet count was significantly higher in malignant polyps (p=0.026).

Conclusion: This study revealed significantly higher leukocyte counts in polyps with lower GI tract and left colon localization. Additionally, higher platelet counts in polyps with malignant pathology and higher CRP levels and leukocyte counts in large polyps were detected.

Key words: Polyps; endoscopy; colonoscopy; inflammation.

Introduction

Polyps are defined as luminal lesions that protrude into the mucosal surface of the GI tract. They are most commonly observed in the colonic mucosa of the gastrointestinal system (GIS) (1). Gastric polyps are mostly asymptomatic and are incidentally detected during endoscopy performed for another reason (2). Currently, the prevalence of gastric polyps has also increased with the increase in the rate of endoscopy and has been found to be between 2%-6% (3). Although gastric polyps are usually asymptomatic, large polyps may present with abdominal pain, anemia, GI bleeding, or gastric outlet obstruction (4). Colon polyps are frequently multiple and are most commonly found in the rectosigmoid region, and the incidence decreases as one moves towards the cecum (5).

Although polyps are usually asymptomatic, they rarely present with overt or occult rectal bleeding or, more rarely, with obstruction by large sizes. Polyps are classified according to their shape (stalked, sessile, flat, or depressed), number, size, location, general appearance, and histologic features. Histological features determine the carcinogenic potential of polyps (6). Endoscopy is the gold standard for diagnosing GI polyps. In addition to its diagnostic features, it also has therapeutic features. In this respect, it is superior to the other imaging methods. Most colorectal cancers (CRC) develop from polyps especially from adenomatous polyps (7). Adenomatous polyps, which are considered precursor lesions in the development of CRC, transform into cancer within an average of 7-10 years (8). Early detection and eradication of polyps by

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colonoscopy results in a 76-90% reduction in the incidence of CRC (9). Systemic inflammation correlates with the development of polyps, although they do not significantly correlate with the size or number of polyps (10). The correlation between leukocyte count, platelet count, and sedimentation rate in patients with gastrointestinal polyps is a complex interplay of inflammatory markers that can provide insights into the pathological state of the gastrointestinal tract. These markers are often used to assess the inflammatory status and potential malignancy of polyps, particularly in the context of CRC, so they could potentially indicate more severe or malignant polyp pathology (11-13). However, these markers collectively reflect the inflammatory status and potential malignancy of polyps, providing valuable insights into disease progression and prognosis. In summary, while leukocyte count, platelet count, and sedimentation rate are individually significant markers in the context of colorectal cancer, their direct correlation with gastrointestinal polyps specifically is less frequently studied. In this study, we aimed to analyze the demographic, clinical, histopathological, and biochemical characteristics of polyps found in both the upper and lower GI tracts and to determine the relationship between the localization of the polyps and the histopathological features of the polyps, their effects on the biochemical status, and demographic characteristics such as age and sex. In addition, we aimed to determine the relationship between the histopathological features of polyps and polyp localization, biochemical values, clinical presentation, and demographic characteristics of patients (age and sex).

Materials and Methods

In our study, 900 patients with polyps diagnosed using endoscopic procedures performed in the Van Yüzüncü Yıl University Dursun Odabaş Medicine Center endoscopy unit between 01.01.2016 and 31.12.2021 were included. With the help of the data processing department of our hospital, the file numbers of the patients were accessed and retrospectively scanned with polyp expression in the pathology reports. Biochemical data (CRP, sedimentation, hemoglobin, hemoglobin, platelet, leukocyte, red cell distribution width, and ferritin values), histopathologic data (polyp pathology results and polyp sizes), endoscopic procedure indications (overt GI bleeding, positive fecal blood occult test, anemia, and CRC screening), and

demographic data of the patients were recorded. Upper GI endoscopy and colonoscopy were performed using a Fujinon EG-530 Video Endoscopy System. Patients aged 18-90 years who underwent upper GI endoscopy or colonoscopy were included in our study. Patients aged >18 or >90 years and those whose endoscopic procedure reports were not available were excluded from the study.

Ethical approval: Van Yüzüncü Yıl University Medical Faculty Clinical Research Ethics Committee with the decision number 2022/10-22 on 14.10.2022. The requirement for informed consent was waived owing to the retrospective nature of the study.

Statistical analysis: To calculate the sample size of our study, the power (Power of the Test) for each variable was determined by taking at least 80% and Type-1 error 5%. Kolmogorov-Smirnov ($n > 50$) and Skewness-Kurtosis tests were used to determine whether the continuous measurements in the study were normally distributed and parametric tests were applied since the measurements were normally distributed. Descriptive statistics for the study variables were expressed as mean, standard deviation, minimum, maximum, number (n), and percentage (%). The Independent 'T-test' or One-Way Analysis of Variance (ANOVA) was used to compare continuous measurements according to 'categorical groups.' Following the analysis of variance, "Duncan test" was used to determine different groups. The chi-square test was used to determine the relationship between categorical variables and groups. Pearson's correlation coefficients were calculated to determine the relationship between continuous measurements. The statistical significance level (α) was set at 5% and SPSS (IBM SPSS for Windows, ver.26) statistical package program was used for the analysis.

Results

Of the 900 patients included in the study, 464 (51.6%) were male and 436 (48.4%) were female. The mean patient age was 59.7 years. The polyps were divided into two groups according to their localization: the upper GI tract (30.6%, $n=275$) and lower GI tract (69.4 %, $n = 625$). In addition, polyps detected in the lower GI tract were divided into two groups, the right and left colon, for further analysis. 3 groups were formed and analyzed as upper GI tract, right colon and left colon; the rate of polyps in the upper GI tract was 30.6% ($n=275$), the rate of polyps in the right colon was 19.4% ($n=175$), and that in the left

colon was 50% (n=450). The rate of polyps in the lower GI tract was significantly higher than that in the upper GI tract (p =0.001). In the lower GI tract, the rate of polyps in the left colon was significantly higher than that in the other locations (p=0.001). The distribution of all polyps in the GI tract according to their localization is shown in Figure-1

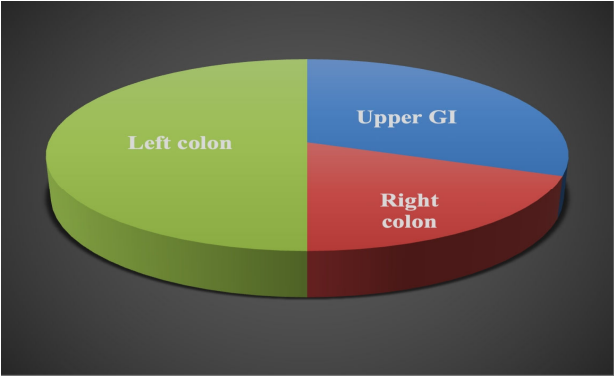


Figure 1. Localization of polyps detected in the gastrointestinal tract

Polyps were divided into three groups according to polyp size: <5 mm polyps are classified as dimunitive, 61.3% (n=552); 5–10 mm polyps are classified as small, 30.3% (n=273); and >10 mm polyps are classified as large, 8.3% (n=75). The mean polyp sizes in the upper GI tract, right colon, and left colon were 4.75 ± 5.35 mm, 4.5±4.1 mm and in the left colon 5.92±7.17 mm. The size of the polyps in the left colon was found to be significantly larger than that in the right colon and upper GI tract (p = 0.008) (Table-1). The distribution of all polyps in the GI tract according to their size is shown in Figure-2. When polyp localization was evaluated according to sex, the rate of polyps in the upper GI tract was significantly higher in women (62.9%, n=173) than in men (37.1%, n=102) (p = 0.001). The rate of polyps in the left colon (n = 257 and 57.1%, n = 193 and 42.9%, respectively) and the rate of polyps in the right colon (n = 105 and 60%, n = 70 and 40%, respectively) was also significantly higher in men than in women (p = 0.001)

Table 1: The polyp sizes detected in the gastrointestinal tract

		Polyp Size					<i>*p</i>
		N	Mean	Std. Dev.	Min.	Max.	
Polyp localization-1	Upper GI	275	4.75 mm	5.35	.00	40.00	.008
	Right colon	175	4.50 mm	4.10	1.00	30.00	
	Left colon	450	5.92 mm	7.17	1.00	60.00	
Polyp localization-2	Upper GI	275	4.75 mm	5.35	.00	40.00	.085
	Lower GI	625	5.52 mm	6.48	1.00	60.00	

GI: gastrointestinal tract

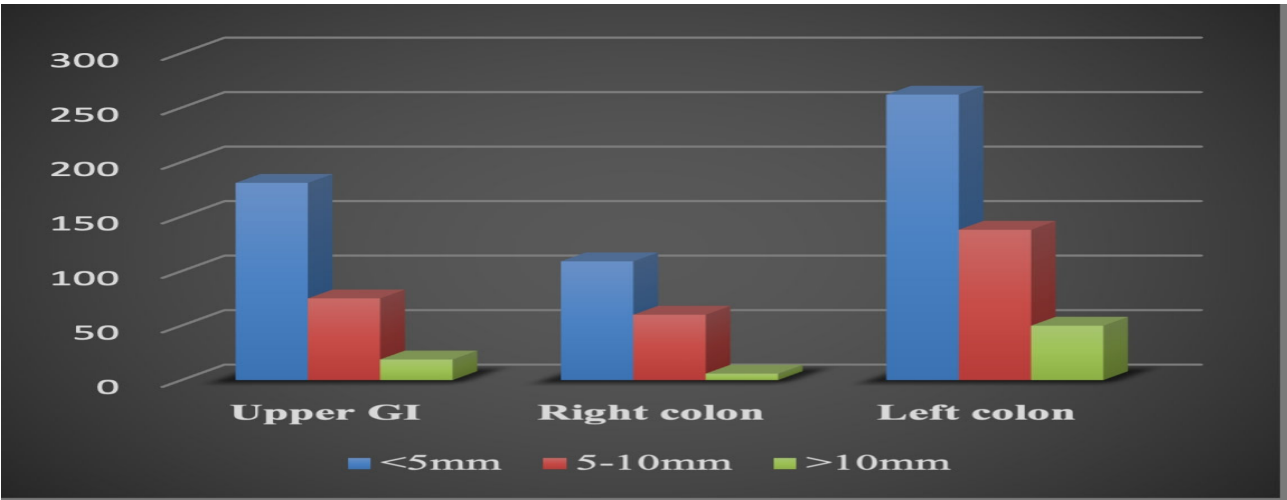


Figure 2. Distribution of polyps in the gastrointestinal tract according to polyp size

The polyps were divided into three groups according to their pathology: Neoplastic polyps 39.1% (n=352); malignant polyps, 3.7% (n=33); and non-neoplastic polyps, 57.2% (n=515). Neoplastic polyps were also divided into two groups as adenomatous polyps 38.7% (n=349), and serrated polyps 0.3% (n=3). Adenomatous polyps were more common in men than in women ($p = 0.001$). Adenomatous and malignant polyps were significantly more common in the left colon (n = 227, 65%; n = 16, and 48.5%, respectively), whereas non-neoplastic polyps were significantly more common in the upper GI tract (n = 258, 50.1%) ($p = 0.001$). The distribution of polyp pathologies according to localization is shown in Figure-3. Analysis of the relationship between polyp size and polyp pathology revealed that the rate of non-neoplastic pathology in diminutive and small polyps was significantly higher (n = 341, 66.2% and n = 141, 27.4%, respectively) than that in other pathologies ($p = 0.001$). In large polyps, the rate of adenomatous polyps (n = 34) was significantly higher than that of other pathologies ($p = 0.001$). When the relationship between polyp size and polyp localization was examined, the number of polyps of all three sizes was

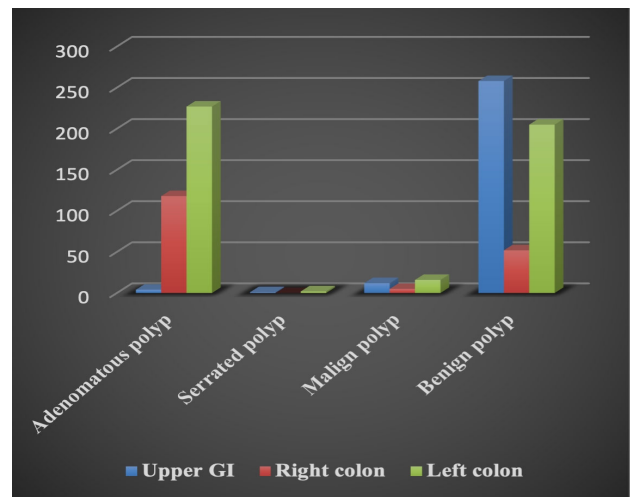


Figure 3: Distribution of pathological findings of polyps in the gastrointestinal tract according to polyp localization

significantly higher in the left colon than in other locations ($p=0.01$). In addition, the incidence of diminutive polyps at all three locations was significantly higher than that of polyps of other sizes ($p = 0.01$) (Table-2). The detection rate of polyps in the left colon was significantly higher than that in other locations for all endoscopic indications ($p = 0.007$).

Table 2: Characteristics of polyps in the upper gastrointestinal tract, right colon and left colon

		Polyp localization						P
		Upper Gastrointestinal Tract		Right colon		Left colon		
		n	%	n	%	n	%	
Polyp size	Diminutive polyps	181	32.8	109	19.7	262	47.5	.010
	Small polyps	75	27.5	60	22	138	50.5	
	Large polyps	19	25.3	6	8	50	66.7	
Polyp pathology	Neoplastic polyps (Adenomatous polyp)	4	1.1	118	33.8	227	65	.001
	Neoplastic polyps (Serrated polyp)	1	33.3	0	0	2	66.7	
	Malign	12	36.4	5	15.2	16	48.5	
	Non-neoplastic polyps	258	50.1	52	10.1	205	39.8	
Endoscopic procedure indication	Anemia	20	28.2	15	21.1	36	50.7	.007
	Overt Gastrointestinal bleeding	7	10.9	15	23.4	42	65.6	
	Positive fecal occult blood test	8	18.2	11	25	25	56.8	
	Screening endoscopic procedure	240	33.3	134	18.6	347	48.1	
Sex	Male	102	37.1	105	60	257	57.1	0.001
	Female	173	62.9	70	40	193	42.9	

The detection rate of diminutive polyps was significantly higher in CRC screening than that in other sizes ($p = 0.001$). There was no significant difference between polyp pathology and indications for endoscopic procedures

($p=0.119$) (Table-3). Biochemical values were compared according to sex, polyp location, polyp size, polyp pathology, and endoscopic procedure indications.

Table 3: Polyp size and pathological findings according to endoscopic procedure indications

		Endoscopic Procedure Indications								P
		Overt Gastrointestinal bleeding		Positive fecal occult blood test		Screening endoscopic procedure		Anemia		
		n	%	n	%	n	%	n	%	
Polyp size	Dimunitive polyps	33	51.6	25	56.8	464	64.4	30	42.3	.005
	Small polyps	22	34.4	16	36.4	202	28	33	46.5	
	Large polyps	9	14.1	3	6.8	55	7.6	8	11.3	
	Neoplastic polyps (Adenomatous polyps)	32	50	22	50	265	36.8	30	42.3	
	Neoplastic polyps (Serrated polyps)	0	0	0	0	3	0.4	0	0	
Polyp pathology	Malign	1	1.6	1	2.3	30	4.2	1	1.4	.389
								40	56.3	
	Non-neoplastic polyps	31	48.4	21	47.7	423	58.7			

Table 4a: Biochemical values of polyps according to their localization, size, pathological findings, and indications for endoscopic procedures

	Sedimentation rate (mm/h)				C-Reactive Protein (mg/L)				Hemoglobin (g/dL)			
	N	Mean	Std. Dev	P	N	Mean	Std. Dev.	p	N	Mean	Std. Dev.	p
Upper GI	275	22.18	23.24	.198	275	12.392	23.45	.671	275	68.87	912.14	.326
Right colon	175	20.77	22.23		175	13.061	26.02		175	14.406	2.21	
Left colon	450	19.27	19.59		450	14.301	32.42		450	14.12	2.38	
Upper GI	275	22.18	23.24	.106	275	12.39	23.45	.453	275	68.87	912.14	.134
Lower GI	625	19.69	20.36		625	13.95	30.74		625	14.207	2.33	
Dimunitive polyps	552	19.203	20.105	.056	552	12.22	25.91	.001	552	41.709	643.79	.721
Small polyps	273	21.87	22.01		273	12.53	24.92		273	13.8	2.46	
Large polyps	75	24.45	26.207		75	26.11	50.54		75	13.72	2.66	
Adenomatous polyps	349	21.49	22.42	.124	349	12.707	27.54	.077	349	14.19	2.47	.863
Serrated Polyps	3	12.33	12.85		3	13.01	16.96		3	14.52	1.64	
Malign Polyps	33	27.03	27.44		33	26.24	43.63		33	13.502	2.37	
Non-neoplastic Polyps	515	19.37	20.01		515	13.18	28.24		515	43.45	666.53	
Anemia	71	29.54	26.78	.001	71	16.22	30.63	.333	71	10.680	1.62	.001
Overt GI bleeding	64	15.82	12.97		64	9.25	16.12		64	13.880	2.804	
Positive fecal occult blood test	44	18.18	16.08		44	8.66	10.47		44	13.883	2.22	
Screening endoscopic procedure	721	20.106	21.35		721	13.87	30.08		721	14.477	1.98	

GI: gastrointestinal tract

When the relationship between biochemical values and polyp localization was examined, leukocyte

counts were found to be significantly higher in lower GI polyps than in upper GI polyps (P =

0.008). Among the lower GI polyps, leukocyte counts were significantly higher in the left colon polyps than in the right colon polyps ($p = 0.022$). When the relationship between polyp size and biochemical values was analyzed, CRP and leukocyte values were significantly higher in large polyps compared to polyps of other sizes ($p=0.001$; and $p=0.008$, respectively). When the relationship between platelet count and polyp

pathology was analyzed, platelet counts were significantly higher in malignant polyps than in other pathologies ($p=0.026$). The mean sedimentation rate and platelet count were significantly higher in patients who underwent endoscopic procedures for anemia than in those who underwent endoscopic procedures for other indications ($p=0.001$ and $p=0.006$, respectively) (Table-4a, Table-4b).

Table 4b: Biochemical values of polyps according to their localization, size, pathological findings, and indications for endoscopic procedures

	WBC (u/L)				Platelet				RDW (f/L)			
	N	Mean	Std. Dev.	p	N	Mean	Std. Dev.	p	N	Mean	Std. Dev.	p
Upper GI	275	7131.6	275	.022	275	276723.6 3	85235.03	.565	275	20.51	91.302	.296
Right colon	175	7763.2	175		175	285651.4 2	95876.22		175	13.93	1.86	
Left colon	450	8064.7	450		450	278340	90795.33		450	15.01	17.303	
Upper GI	275	7131.6	2417.2	.008	275	276723.6 3	85235.03	.575	275	20.51	91.302	.123
Lower GI	625	7980.2	5031.7		625	280387.2	92227.16		625	14.71	14.71	
Diminutive polyps	552	7519.05	2573.5	.008	552	276713.7 6	83668.09	.413	552	17.35	65.61	.821
Small polyps	273	7724.19	2879.1		273	281315.0 1	97305.40 3		273	15.11	13.78	
Large polyps	75	9195.6	12437.7		75	290613.3 3	107417.2		75	15.11	3.35	
Adenomatous polyp	349	8086.87	6124.68	.185	349	282126.0 7	90291.61	.026	349	14.09	1.79	.710
Serrated Polyp	3	8666.66	1939.93		3	282333.3 3	87956.42		3	15.06	0.602	
Malign Polyp	33	8107.87	2797.34		33	322181.8 1	129014.1 5		33	14.4	2.402	
Non-neoplastic Polyps	515	7442.75	2834.99		515	274563.1	86440.37					
Anemia	71	7149.85	2489.11	.472	71	312802.8 1	123612.7 1	.006	71	16.202	3.95	.967
Overt GI bleeding	64	7616.56	2871.22		64	266859.3 7	83390.05		64	14.37	2.61	
Positive fecal occult blood test	44	7089.77	2033.27		44	264363.6 3	64715.86		44	13.82	1.54	
Screening endoscopic procedure	721	7825.02	4766.39		721	277976.4 2	87498.86		721	16.86	58.01	

GI: gastrointestinal tract, WBC: leukocyte, RDW: red blood cell distribution width

Discussion

Polyps are defined as luminal lesions that protrude into the mucosal surface of the GI tract (1). It was

not possible to specify a specific localization for small polyps, whereas large polyps are frequently located in the distal colon (14). In our study, we found that large polyps were more frequently

located in the left colon, which is in accordance with the literature. When the sizes of gastric polyps were examined, diminutive and small polyps were reported to be 64%–87% in the literature and 60.2%–88% in studies conducted in our country (15). In our study, similar to the literature, diminutive and small polyps were found in higher numbers in the upper GI tract. In a study by Kefeli et al. (16), the incidence of colorectal polyps <5 mm in size was 68.2%. Oymacı et al. (17) reported the incidence of colon polyps <5 mm in size as 58.4%. In our study, we found a higher rate of diminutive and small polyps in the lower GI tract, which is consistent with the literature. In addition, we found that polyps in all three sizes were more common in the left colon than in other locations. It can be suggested that the most important characteristics of polyps in terms of the risk of malignancy development are their histological features. The prevalence of adenomatous polyps varies, but a significant proportion of colorectal polyps are adenomatous polyps that belong to the neoplastic polyp group and constitute approximately 2/3 of all colon polyps (18). In a study by Şahintürk et al. (19), adenomatous polyps were found in 74.3% and hyperplastic polyps in 11.9%. In our study, adenomatous polyps in the colon were observed at the highest rate, which is in accordance with the literature. In addition, non-neoplastic polyps in the upper GI tract were found at a significantly higher rate. Male sex has been reported as a risk factor for adenomatous polyps (17). In our study, we found that adenomatous polyps were significantly more common in the male gender in accordance with the literature. CRCs are frequently localized to the left colon, in accordance with the most common localization of colon polyps (20). In the present study, malignant polyps were most commonly found in the left colon. Some indications for upper GI endoscopy include occult or overt GI bleeding, positive fecal occult blood test results, upper abdominal symptoms, dysphagia and odynophagia (21). Indications for colonoscopy include lower GI symptoms such as abdominal pain, unexplained iron deficiency anemia, diarrhea, and CRC screening in the age range recommended by guidelines (22). In our study, the indications for endoscopic procedures in the patients included overt GI bleeding, positive fecal occult blood test results, anemia, and screening. In a study conducted at the Mayo Clinic in the United States of America in 2013, which examined the results of colonoscopy in 1921 patients, the indications for colonoscopy were polyp screening, polyp follow-

up, stool irregularity, GI bleeding, and anemia (23). The number of endoscopic procedures performed for CRC screening was higher than for other indications. Considering that endoscopy can reduce morbidity and mortality related to malignancy by detecting polyps at an early stage, CRC screening is important. Moreover, the fact that the number of those who underwent screening endoscopy was the highest in our study indicates that the CRC screening strategy has taken place in our population. C-reactive protein (CRP) is an acute-phase reactant and sensitive indicator of systemic inflammation. In addition, leukocyte counts also increase during inflammation, although the subgroup cells (neutrophilic or lymphocytic) differ depending on the type of inflammation (24). As the relationship between local inflammation and CRC is well known, we investigated the relationship between CRP, sedimentation rate, leukocyte values, and polyps, which may be neoplasm precursors. The results of studies investigating the relationship between colon polyps and CRP are controversial. In a study by Tsilidis et al. (25), no relationship was found between the presence of colorectal adenoma and CRP. However, Gunter et al. found that each 1 unit increase in CRP level was associated with a 15% decrease in the development of colorectal adenomas (24). However, in a study by Kigawa et al. (26), a positive correlation was found between CRP levels and the presence of colorectal adenoma, and CRP levels were also positively correlated with the number of polyps and polyp size. In our study, we could not examine the presence of colonic polyps with inflammatory markers because there was no control group without polyps; however, we found significantly higher CRP levels and leukocyte counts in large polyps compared to diminutive and small polyps. Oset et al. (27) found that CRP levels were higher in adenomas localized to the proximal colon. In our study, we found no difference between CRP values and polyp localization; however, leukocyte values were significantly higher in polyps with lower GI tract localization than in those with upper GI tract localization. The correlation between leukocyte count, platelet count, and sedimentation rate in patients with gastrointestinal polyps is a complex interplay of inflammatory markers that can provide insights into the pathological state of the gastrointestinal tract. In one study conducted by Bilinski et al. (28), the presence of increased inflammation was identified by histopathology in adenomatous and hyperplastic polyps. In a study by Uçmak et al. (29) of 379 patients who

underwent colonoscopic polypectomy, no significant difference was found between polyp pathology and leukocyte levels. However, cancer patients had significantly lower lymphocyte counts than those with hyperplastic and adenomatous polyps. These findings suggest that immune dysregulation, as reflected in leukocyte profiles, may play a significant role in the pathogenesis of gastrointestinal polyps. Our findings indicate that the leukocyte count was significantly higher in left colon polyps than in right colon polyps. Additionally, the leukocyte count was significantly higher in large polyps than diminutive or small polyps. Platelet count is a significant marker in the context of gastrointestinal polyps and CRC. Thrombocytosis, or elevated platelet count, has been associated with poor prognosis and increased risk of metastasis in CRC patients. In a study by Elbassiouny et al. (13), which included 169 patients with colorectal adenocarcinoma, showed abnormal platelet count (≥ 310) was prognostic and predictor of significant decrease in progression-free survival and overall survival. Additionally, Lin et al. (30) investigated the relationship between the platelet and the biological features in 150 patients with CRC in China. They found that elevated platelet counts were significantly correlated with advanced TNM clinical stages of CRC as well as poorer survival. In our study, we found higher platelet counts in polyps with malignant pathology than in polyps with other pathologies, which is in accordance with the literature.

Study limitations: First, although both upper and lower GI polyps were evaluated, the number of cases was limited. In addition, because there was no control group in the study, the presence of polyps and other parameters could not be compared. Finally, this study is limited to single-centre data and does not include data from different geographical regions. This may have an impact on the generalizability of the results. To clarify the contradictory results in the literature, we are of the opinion that planning a study with a larger number of patients in which upper and lower GI polyps are evaluated separately and a control group will also allow a clearer presentation of the clinicopathologic features of GI polyps.

Conclusion

This study revealed significantly higher leukocyte counts in polyps with lower GI tract and left colon localization. Additionally, higher platelet counts were detected in polyps with malignant pathology. Lastly, significantly higher CRP levels and leukocyte counts were detected in large

polyps. We conclude that simple biochemical tests (CRP) and complete blood counts (leukocyte and platelet values) performed before colonoscopy may predict polyp localization, polyp size, and polyp histology in patients.

Ethical approval: Ethics Committee permission was obtained from Van Yüzüncü Yıl University Medical Faculty Clinical Research Ethics Committee with the decision number 2022/10-22 on 14.10.2022.

Conflict of interest: The authors have no conflict of interest regarding this study.

Financial disclosure: No financial support has been received for this study.

Author contributions: Concept (YYÜ, NGS), Design (YYÜ), Data Collection and/or Processing (NGS), Analysis and/or Interpretation (YYÜ, NGS, SE)

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