

Evaluation of risk factors for the recurrence of colorectal polyps and colorectal cancer

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Background/aim: Colorectal adenomatous polyps are precursors of colorectal cancer (CRC), which can be prevented with surveillance colonoscopy. This study aimed to assess risk factors for the recurrence of colorectal polyps and CRC following polypectomy.

Materials and methods: In this single-center trial, a total of 510 patients who applied to the endoscopy unit of Hacettepe University Hospital for various reasons and who were diagnosed with at least one colorectal adenomatous polyp between 2000 and 2010 were retrospectively analyzed. Patients with colorectal adenomatous polyps or CRC recurrences were examined in terms of clinical and histological risk factors.

Results: A total of 190 (37.1%) patients had surveillance colonoscopy. Among them, 127 (66.3%) were found to have polyp recurrence. Of the parameters defined for polyp recurrence, no association was found between the number of polyps (1–2, ≥3) (1–3, ≥4) in the first colonoscopy and diabetes mellitus, hypertension, hyperlipidemia, sex, family history of colon malignancy, smoking, alcohol usage, size of polyp (<10 mm, ≥10 mm), or advanced histologic type of polyp. The only significant difference was observed in patients who had left-sided colon polyps. In the basal colonoscopy, 130 patients had been diagnosed with CRC, and a significant correlation was found between the number of polyps (1, ≥2) and polyp size (≥10 mm), anemia, high sedimentation rate (>25), and CRC. In the first surveillance colonoscopy, CRC was detected in 12 patients. There was a significant correlation between the development of CRC and advanced histological type, anemia with high erythrocyte sedimentation rate, polyp size (<10 mm, ≥10 mm), and the number of polyps (<3, ≥3).

Conclusion: Patients with left-sided colon polyps had a high risk of developing colorectal polyp recurrence. Moreover, the risk of developing CRC increased in patients who had advanced histology, a polyp larger than 10 mm, or more than three polyps.

Key words: Colorectal adenomatous polyps, recurrence, colorectal cancer

1. Introduction

Neoplastic colorectal polyps include adenomatous polyps and carcinomas. Nonneoplastic colorectal polyps include hyperplastic, hamartomatous, and inflammatory polyps. Although colorectal polyps are usually asymptomatic due their hidden growth pattern, they may also be present with ulceration and bleeding. They are most frequently found during endoscopic or radiologic imaging studies. Colorectal polyps are precursors of colorectal cancer (CRC), and removing these polyps has been shown to reduce the risk of developing CRC (1,2). To further minimize the risk of CRC, patients with adenomatous polyps are usually placed in a surveillance program of periodic colonoscopy to remove missed synchronous or new metachronous adenomas and cancers (3). The risk of a polyp developing into a cancer is variably determined by a number of criteria, such as the size and number of detected polyps, the histological type (villous

or tubular), morphology (sessile or polypoid), and degree of dysplasia. Characteristics of the baseline colonoscopy are also an important predictor for developing subsequent neoplasia and determining appropriate intervals for postpolypectomy surveillance. Several recent studies have suggested that basal colonoscopy findings stratify adenomas into low- or high-risk (i.e. adenoma ≥10 mm, villous adenoma, adenoma with high-grade dysplasia, or invasive cancer) groups for recurrent adenomas during surveillance colonoscopy (3,4). CRC arises from both genetic and environmental factors and their interaction. Genetic predisposition is the dominant risk factor for some individuals; however, environmental factors (including diet, exercise, smoking, and obesity) are stronger risk factors for most people (5). Most cases of CRC occur in patients with average risk who have no family or medical history of cancer predisposition. Since increasing age and male sex are associated with an increased incidence

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of CRC, current guidelines recommend that screening should start after 50 years of age even if risk factors are absent (6). This study aimed to assess the risk factors for the recurrence of colorectal polyps and CRC following polypectomy.

2. Materials and methods

A total of 600 patients over the age of 18 who were admitted to the endoscopy unit of the gastroenterology department of Hacettepe University Hospital for various reasons and who were diagnosed with at least one colorectal adenomatous polyp between 2000 and 2010 were retrospectively analyzed. We excluded 90 patients who had inflammatory bowel disease, familial adenomatous polyposis, or missing information. The demographic characteristics of the patients, their habits, the drugs that they used, their comorbid diseases, and their symptoms during the diagnostic course were analyzed. Colonoscopy findings and the histological characteristics of the polyps were also recorded. The total number of polyps, their size, and the location of each polyp were also recorded. Adenomas were classified as follows: tubular, tubulovillous, villous, and serrated adenomas. Polyps larger than 10 mm, three or more adenomatous polyps, and significant villous component were defined as advanced polyps. Polyps larger than 5 mm were removed by standard snare excision and those smaller than 5 mm were removed by biopsy forceps.

Ethics committee approval was obtained prior to study initiation. Patients who had polyp recurrences were examined for risk factors such as comorbid disease, pathologic features, size, and number of polyps.

2.1. Statistical analysis

Data were analyzed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). The histological findings of the polyps and clinical characteristics of the patients were analyzed by descriptive statistics (mean, median, percentage, standard deviation, and minimum and maximum values). In the comparison between continuous variables of the two groups, either Student's t-test or the Mann-Whitney U test was used. Fisher's exact test or the chi-square test was used for analysis of categorical variables. Risk factors were analyzed with chi-square analysis. Odds rates were calculated with logistic regression. All tests of significance were two-tailed, and $P < 0.05$ was considered as statistically significant.

3. Results

A total of 510 patients were enrolled in the study. Of the 510 patients, 354 (69.4%) were men. The median age was 64 years old (range: 30–96), with 63.5% of the patients being older than 60 years old (Table 1). A total of 869 polyps (median: 1; range: 1–9) were established in the first basal colonoscopy. The number of polyps detected in the basal colonoscopy was one and two in 62.2% and 21.2%

of the patients, respectively. Most polyps were smaller than 10 mm (54.5%), with a mean size of 11.4 ± 13 mm (range: 1–80 mm). Of the polyps detected in the basal colonoscopy, 68.1% were left-sided (rectum, sigmoid and descending colon) and 31.9% were right-sided (cecum, ascending and transverse colons). Comorbid diseases and the medication history of all patients are shown in Table 1. Gastrointestinal (GIS) hemorrhage was the most common indication for performing colonoscopy (32%). Adenomatous and tubular changes were observed in 293 (33.7%) and 154 (17.7%) of all polyps, respectively. Anemia was found in 220 (43.1%) patients, with a mean hemoglobin value of 12.9 ± 2.2 g/dL (range: 5.4–18.9 g/dL). The erythrocyte sedimentation rate (ESR) could be monitored in 235 patients, with a mean value of 25.1 ± 26 mm/h (range: 1–140).

Of the patients, 190 (37.1%) had surveillance colonoscopy. Among them, 127 (66.3%) were found to have polyp recurrence (total of 196 polyps and a median of 1 (range: 1–8) polyp). Median time to first surveillance colonoscopy was 11 (range: 1–152) months. According to polyp features, 126 of 190 patients were in the high-risk group. The recurrence rate of polyps for the first, second, and third year was 76 (40%), 104 (55%), and 114 (58.7%), respectively. Of the parameters defined for recurrence, no association was found between the number of polyps in the basal colonoscopy (1–2, ≥ 3) (1–3, ≥ 4), diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), sex, family history of colon malignancy, smoking, alcohol use, size (< 10 mm, ≥ 10 mm), and advanced histologic type (Tables 2 and 3). There was a significant difference between adenomatous polyp recurrence and left-sided polyps ($P = 0.02$) (Table 2).

In the basal evaluation colonoscopy, 130 patients had been diagnosed with CRC and significant correlations were found between the number of polyps (1, ≥ 2) and the size of the polyp (≥ 10 mm), anemia, high sedimentation rate (> 25 mm/h), carcinoembryonic antigen (CEA) (> 4 ng/mL), and CRC (Table 4). In the first surveillance colonoscopy, CRC was found in 12 patients, five of whom had an advanced histological type of CRC. There was a significant correlation between the development of CRC and advanced histological type (OR = 5 (1.3–18.0); $P = 0.02$), anemia with high ESR, polyp size (< 10 mm, ≥ 10 mm), and the number of polyps (< 3 , ≥ 3).

4. Discussion

CRC is the third most common type of cancer worldwide (7). In Turkey, CRC is the fourth most common cancer type in men and the third most common type in women. As many as 95% of all CRCs develop from adenomatous polyps (8). CRC can be prevented with surveillance colonoscopy (9). According to colonoscopy series, the

Table 1. Demographic features of patients.

	n	%
Sex		
Female	156	30.6%
Male	354	69.4%
Age, years		
<40	22	4.3%
40–49	44	8.6%
50–59	117	22.9%
60–69	142	27.8%
≥70	182	35.7%
Number of polyps		
1	317	62.2%
2	108	21.2%
3	39	7.6%
≥4	45	8.8%
Size of polyps		
<10 mm	330	64.7%
≥10 mm	180	35.3%
Pathology		
Adenomatous change	293	33.7%
Tubular	154	17.7%
Tubulovillous	76	8.7%
Villous	12	1.3%
Adeno cancer	130	14.9%
Hyperplasic	74	8.5 %
Polyp location		
Cecum	31	3.6%
Ascending colon	81	9.4%
Hepatic flexure	37	4.3%
Transverse colon	126	14.6%
Splenic flexure	17	2%
Descending colon	115	13.3%
Sigmoid colon	115	13.3%
Rectum	274	31.6%

	n	%
Symptoms		
Hematochezia	146	28.6%
Stomachache	135	19.2%
Constipation	72	14.1%
Weight loss	59	11.6%
Diarrhea	46	9%
Melena	17	3%
Drugs used by patients		
ACE	74	14.5%
ARB	46	9%
ASA	50	9,8%
Statin	31	6%
Oral antidiabetics	32	6.2%
Size of polyps		
<10 mm	330	64.7%
≥10 mm	180	35.3%
Comorbid diseases		
DM	93	18.2%
HT	153	30%
HL	103	20.2%
Acromegaly	6	1.2%
Smoking	134	26.3%
Alcohol	52	10.2%

prevalence of colorectal adenomas is 15%–30% (10,11). With the introduction of high-quality basal colonoscopies, which allow for a complete and meticulous inspection of all colonic mucosa and a complete removal of all neoplastic lesions, this rate has increased to 50% (12). The incidence rate of metachronous polyps in follow-up colonoscopies varies in accordance with the frequency of follow-up and patient characteristics (12%–60%) (13). The number, size, and pathologic features of polyps in the basal colonoscopy are defined as the risk factors for polyp recurrence (14).

Erlangen et al. reported that the parameters for the risk of polyp recurrence are advanced histological type (tubulovillous and villous), family history of colon cancer, the presence of more than two polyps, and polyps larger than 10 mm. In our study, surveillance colonoscopies were performed in 190 (37%) patients, with 127 (66.8%) patients showing recurrences. However, we were not able to confirm the results of Erlanger et al. since 83.4% of our cases had only one or two polyps. In addition, the number of surveillance colonoscopies was lower than that

Table 2. Features of patients with surveillance colonoscopy and recurrence of colorectal adenomatous polyps.

	Surveillance colonoscopy, n = 190 (%)	Recurrence of polyps, n = 127 (%)	No recurrences of polyps, n = 63 (%)	P
Sex				
Female	65 (34.2)	43 (33.9)	22 (34.9)	
Male	125 (65.8)	84 (66.1)	41 (65.1)	0.82
Age, years				
<40	11 (5.8)	7 (5.5)	4 (6)	0.52
40–49	19 (10)	12 (9.4)	7 (11)	0.71
50–59	36 (18.9)	26 (20.5)	10 (15.8)	0.44
60–69	53 (27.9)	36 (28.3)	17 (26.9)	0.84
≥70	71 (37.4)	46 (36.2)	25 (39.6)	0.64
Number of polyps				
1	119 (62.1)	78 (61.3)	41 (65)	0.78
2	41 (21.3)	27 (21.3)	14 (22.2)	0.78
3	13 (6.8)	8 (6.3)	5 (7.9)	0.44
≥4	17 (8.9)	13 (10.2)	4 (6.3)	0.30
Size of polyp				
<10 mm	97 (51.1)	62 (48.8)	35 (55.5)	
≥10 mm	93 (48.9)	65 (51.2)	28 (44.4)	0.83
Polyps location				
Cecum	8 (4.2)	1 (0.7)	7 (11.1)	
Ascending colon	16 (8.2)	12 (9.4)	4 (6.3)	
Hepatic flexure	6 (3.2)	4 (3.1)	2 (3.1)	
Transvers colon	28 (14.7)	18 (14.1)	10 (15.8)	
Splenic flexure	7 (3.7)	4 (3.1)	3 (4.7)	
Descending colon	27 (14.2)	22 (17.3)	5 (7.9)	
Sigmoid colon	49 (25.8)	48 (37.7)	1 (1)	
Rectum	49 (25.8)	44 (34.6)	5 (7.9)	
Left-sided polyp	132 (69.4)	95 (74.8)	37 (57.8)	0.024
Pathology				
Tubular	51 (26.8)	35 (27.5)	16 (25.3)	
Tubulovillous	30 (22.6)	21 (16.5)	9 (14.3)	
Villous	7 (3)	4 (3.1)	3 (4.7)	
Hyperplasic	12 (6.3)	6 (4.7)	6 (9.5)	
High-risk patients	126 (66.3)	84 (66.1)	42 (66.6)	0.94
Comorbid disease				
DM	38 (20)	24 (18.9)	14 (22.2)	0.59
HT	49 (25.7)	33 (25.9)	16 (25.3)	0.55
HL	39 (20.5)	23 (18.1)	16 (25.3)	0.24
Smoking	54 (28.4)	38 (29.9)	16 (25.3)	0.51
Alcohol	14 (7.4)	10 (7.8)	4 (6.3)	0.47

DM: Diabetes mellitus; HT: hypertension; HL: hyperlipidemia; ACE: angiotensin converting enzyme; ARB: angiotensin 2 receptor blocker; ASA: acetylsalicylic acid.

Table 3. Risk factors for recurrence of colon polyps.

	Odds ratio	P
Sex (male/female)	1.01 (0.55–1.85)	
Family history of malignity	0.46 (0.14–1.50)	0.16
Family history of colon malignity	1.09 (0.42–2.80)	0.52
Smoking	0.79 (0.40–1.57)	0.51
Alcohol	0.79 (0.23–2.63)	0.47
DM	1.22 (0.58–2.57)	0.59
HL	1.53 (0.74–3.17)	0.24
Polyp number: 1–2/≥3	0.79 (0.34–1.84)	0.59
Polyp number: 1–3/≥4	1.1 (0.95–1.20)	0.12
Polyp size: <10 mm/≥10 mm	0.76 (0.41–1.40)	0.38
Histological type: Tubulovillous/villous	1.06 (0.47–2.39)	0.53
Left-sided colon polyps	2.08 (1.09–3.96)	0.02

Table 4. Risk factors for CRC.

Parameters	Odds ratio	P
1, 2–5, 6 or a higher polyp number		0.203
Polyp size (<10 mm, ≥10 mm)	13 (7.4–22.8)	0.0001
1, ≥2 polyps	1.6 (1.02–2.4)	0.01
Anemia	2.13 (1.4–3.1)	0.0001
ESR >25	2.6 (1.3–5.1)	0.03
CEA >4 ng/mL	1.9 (1.2–3.1)	0.006
CA19-9 >35 U/mL	1.0 (0.6–1.7)	0.91
Smoking	1.32 (0.8–2)	0.19
Alcohol consumption	0.62 (0.3–1.2)	0.18
DM	0.86 (0.5–1.46)	0.58
HL	0.87 (0.52–1.4)	0.59
Family history	0.75 (0.3–1.8)	0.54
Anemia and high rate of sedimentation	1.8 (1.1–2.4)	0.0001

found in the literature, which may be attributed to the fact that patients may have not have attended their follow-up examinations.

The baseline colonoscopy needs to be of high quality for the baseline adenoma characteristics to be used for planning surveillance intervals. The US Multi-Society Task Force on Colorectal Cancer and the American Society

for Gastrointestinal Endoscopy further extended the recommended surveillance interval to 5–10 years for those with 1 to 2 small (tubular) adenomas. In patients with 3 or more colorectal adenomas, regardless of size, a 3-year surveillance interval is recommended (15). Several studies have shown that compliance with guidelines remains poor. The rate of first-year surveillance colonoscopy and polyp

recurrence (40%) was higher in our study. This might be explained by the fact that high-quality basal colonoscopy could not be performed because the records of the patients in the study were relatively old.

Sporadic colon cancers are mainly localized in the right and left colon (29% in the rectum) in approximately 40% and 60% of all cases, respectively. According to the literature published after 1980, there is increased evidence of a shift towards the proximal colon. The localization of the polyps in our study was similar to the literature; however, left colon polyps (68.9%) and rectum polyps (31.6%) were observed to be more common. The rate of right colon polyps in our study (31.9%) was also lower than that in the literature. This may be related to missing polyps in the right colon due to inadequate cecal intubation rates and noncompliance with the withdrawal time (16).

There was a significant correlation between patients with left-sided colon polyps and polyp recurrence. This can be explained in several ways: colonoscopists may pay more attention to the sites where the excision of polyps is performed and polyps may be incompletely removed, suggesting that there may be missing colon polyps left behind. The rate of missed colorectal polyps is 20% (17), which can be linked to an inability to implement high-quality colonoscopies.

In asymptomatic people, the prevalence of colorectal adenomas increases with age, especially in patients over the age of 50 (10,11). It has been discovered in autopsies that the prevalence of colorectal adenomas is 50% at the age of 70 (12). CRC and adenomas are observed two to three times more frequently in males. Nusko et al. (18) reported that 63.7% of patients with polyps were male. Similar to these results, 67.8% of patients with polyps in our study were male. In our study, the median age was 63 years old, and 82.5% of the cases were observed after the fifth decade.

It has been found that the etiology of CRC and adenomas involves environmental factors, especially dietary factors (e.g., a fatty diet). It was proven by necropsy that there is a relationship between CRC and HL. The production of bile increases with a fatty diet and the increase of bile oxidation leads to an increase in tumor activation (19). There was HL in 20.2% of the patients in our study. However, the correlation between the recurrence of polyps and HL was not found to be significant. These findings may be related to the fact that Turkey is a Mediterranean country and our diets are different from those in western countries. Moreover, in Turkey, the rate of bread consumption as a source of fiber is more frequent than that reported in western societies.

The relation between smoking and CRC risk has long been known (20). The relationship between smoking and CRC is more obvious in the long term. It has also been found in previous studies that CRC is more commonly observed in patients with DM (21). It was observed that there was an increase in the recurrence rate of malignancy in patients with insulin resistance. However, the conditions mentioned above were not investigated in our study since our study was retrospective, so we were not able to exactly calculate how long patients had been exposed to smoking. We also could not exactly determine whether or not these patients had DM and if surveillance colonoscopy was inadequate.

As polyps are generally asymptomatic, they can only be diagnosed with screening. When polyps are symptomatic, their diameter is generally greater than 10 mm and rectal bleeding is the most common finding. In addition, abdominal discomfort, change in bowel habits, and rectal prolapses are other symptoms. GIS bleeding was similarly found to be higher; however, interestingly, constipation was found to be lower according to the literature data in our study.

CRC was detected in 130 patients during the basal colonoscopy in this study. We found a significant correlation between CRC and the number of polyps (1, ≥ 2), size of the polyp (>10 mm), anemia, and high ESR and CEA levels (25 and 4, respectively). For CRC screening, older patients who have extreme anemia with a high ESR should be taken into consideration. In the first surveillance colonoscopy, 12 patients were diagnosed with CRC, and these patients had advanced histological types in the basal colonoscopy. Parameters such as a large number of polyps (≥ 3) and advanced histologic type and size (≥ 10 mm) also indicate a high risk for the development of CRC.

Aside from its retrospective nature, the major limitations of our study were the relatively low number of patients who had surveillance colonoscopy and an intrinsic selection bias. Since the dysplasia grade of most patients was missing, we could not evaluate this parameter as a risk factor.

In conclusion, patients with left-sided colon polyps are at risk for polyp recurrences. Furthermore, a significant correlation was observed between the development of CRC and advanced histological type, anemia with high ESR, polyp size (<10 mm, ≥ 10 mm), and the number of polyps (<3 , ≥ 3). In our study, the rate of left-sided polyps was found to be higher than that reported in the literature. Flexible sigmoidoscopy is still important in Turkey during the course of treatment. However, taken together with the small number of cases included in this study, more studies that include a larger number of patients are needed to support our findings.

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