

RESEARCH ARTICLE

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The Recurrence Rate of Colorectal Polyps among Patients with Average Risk of Colorectal Cancer

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Abstract

Background: CRC is going to be an important issue in Middle East countries. Also, the main parts of this cancer develop from benign adenomas. **Aim:** To understand the recurrence rate of colorectal polyps among average-risk subjects. **Method:** In a prospective study, the average-risk patients with colorectal adenoma were enrolled in this study based on inclusion criteria. The patients were consulted annually by an expert gastroenterologist. A control colonoscopy was programmed after three years of follow-up. It was not an obligation to follow our program, and each patient could exit the study at any time. The patient who developed one of the exclusion criteria was also withdrawn from the study by the gastroenterologist of this study. **Results:** 237 patients were enrolled in this study. Of them, 102 patients completed their 3-year follow-up. Among these participants, 62 (60.8%) were male and 40 (39.2%) were female, with a mean age of 57.05 ± 12.87 years. Additionally, 20 (19.6%) subjects had adenomatous polyps at the end of the study. Patients with recurrent colorectal polyps tend to be raised in large ones with a tubulovillous morphology. The polyps were more commonly located in the sigmoid colon, rectum. Furthermore, high-grade dysplasia was recorded in 5 patients. Tubulovillous polyp had higher chance of recurrence than patients with tubular polyp. **Conclusion:** We believe the colonoscopy screening needs to be set up in regions previously considered low-risk for CRC. Also, it may be valuable to control colonoscopy for less than three years in patients with dysplasia.

Keywords: Colorectal cancer- polyp- colonoscopy

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Introduction

Colorectal cancers (CRC) stand as the second most common cause of cancer-related deaths and the fourth most commonly diagnosed cancer [1]. Based on different studies, CRC has diverse geographical incidence among different ethnicities [2]. CRC has traditionally been more common in Western countries, likely due to lifestyle and dietary factors. However, recent studies have shown that while the incidence of CRC is decreasing in older adults due to screening programs, it is unfortunately increasing in younger people under the age of 50. [3]. Additionally, an increasing incidence of CRC has been observed in developing countries, including those in the Middle East, which were previously considered to be low-risk regions for this cancer [4]. In a retrospective study on patients who underwent total colonoscopy in a tertiary center in Iran, it was demonstrated that the prevalence of advanced adenoma as a precursor of CRC is not related to age and gender [5]. Another survey conducted among average-risk Iranians who underwent screening colonoscopies revealed

a significant prevalence of adenomas and advanced adenomas [6]. In this context, the data from Lebanon illustrate that CRCs are responsible for about 17% of all diagnosed cancers[7].

Furthermore, A study from the United Arab Emirates (UAE) found that (CRC) may affect younger populations in the region more frequently than in Western countries [8]. Studies in Saudi Arabia and the United Arab Emirates demonstrated that CRC incidence is soaring similarly, making it one of the primary lethal cancers in both genders in this region [9]. CRC is going to pose an elusive challenge in prevention, diagnosis, and treatment in the countries of the Middle East [10, 7-9, 11].

Mortality and curability of CRCs are highly dependent on the stage in which the disease is diagnosed; studies illustrate that the 5-year survival of CRCs diagnosed in early stages can be as high as 92%, while for advanced diseases, this rate plunges dramatically to about 8% [12]. Thus, it is believed that screening people at average risk has been introduced to play an essential role an essential role in detecting polyps and CRCs in the early stages as

they are typically asymptomatic, which causes a decline in CRC rate in countries with CRC screening programs [3]. colonoscopy is assumed to be THE method of choice, serving both as a screening tool for colorectal cancer and a therapeutic method for removing precancerous growths or polyps [13, 14].

The recurrence rate of colonic polyps has a wide range that can reach up to 40% [15]. Although knowledge about whether polypectomy is effective at reducing CRC risk in routine clinical practice is limited, Studies in this regard are not sufficient, and previous studies revealed a higher incidence of developing neoplasia and cancer among patients with adenoma or advanced adenoma [16]. The recurrence of polyps and its consequent outcome recently become an essential issue in CRC prevention. Many patients may be missed due to the first negative screening. According to the literature, some factors triggering the recurrence of polyps include polyp characteristics and number, male sex, elderly, obesity, dyslipidemia, and metabolic syndromes [17-20]. Considering the facts discussed above, the variations noticed in recurrence rate between different countries, and the lack of sufficient and consistent data in our region to our knowledge, we decided to conduct this study to investigate the recurrence rate of adenomatous polyps among average-risk subjects who have undergone colonoscopy at a tertiary hospital in Tehran.

Materials and Methods

In a prospective study for screening of CRC in Endoscopy Department of Firoozgar Hospital, which affiliates to Iran University of Medical Sciences (IUMS), Tehran, Iran, the adult subjects classified as average risk for CRC underwent total colonoscopy in a tertiary center. Individuals considered to be at average risk for colorectal cancer, as defined by the American Gastroenterology Association [21], are those without a personal or family history of the disease, no history of inflammatory bowel disease (IBD), no history of hereditary colorectal polyposis syndromes, and no other known risk factors for colorectal cancer [22]. Of them, the subjects with colonic adenoma were invited for follow-up colonoscopies Three years. The primary outcome of this study is to evaluate the recurrence rate in an average-risk population.

Patient selection

Between 2017 and 2019, we offered screening colonoscopies to subjects without lower gastrointestinal complaints. Two expert gastroenterologists at our center interrogated and examined them.

The exclusion criteria were history of previous total colonoscopy, history of colorectal polyp or cancers, polyposis syndromes like FAP and HNPCC, rectal bleeding, iron deficiency anemia, colorectal cancer in first-degree relatives, recent change of bowel habits, spontaneous weight loss during last six months, chronic abdominal pain, positive fecal occult blood test (FOBT), inflammatory bowel disease (IBD) and any contraindication for colonoscopy e.g, severe co-morbidity diseases. Moreover, patients with previous surgeries on

the gastrointestinal tract were excluded.

Colonoscopy data

For bowel preparation, participants were instructed to self-administer Polyethylene glycol (PEG) 24 hours before the procedure, along with dietary restrictions. The adequacy of bowel preparation was assessed by the physicians as good, fair, or poor. Participants with poor bowel preparation were advised to undergo a second colonoscopy.

Sedation during colonoscopy was achieved using a combination of intravenous midazolam and meperidine under the supervision of an anesthesiologist. The average withdrawal time was 20 minutes. All colonoscopies were performed using a Fujinon Colonoscopy 2200 (Fujifilm Endoscopy; Fuji Photo Film Co, Midtown West, Tokyo, Japan). The total insertion length was recorded based on the segment, and cecal intubation was confirmed by visualizing the ileocecal region or inserting the colonoscope into the terminal ileum.

For participants who did not have a complete colonoscopy, a second-look colonoscopy was performed. The characteristics and location of any polyps detected were noted. If multiple lesions were found in the same participant, the finding was classified as more advanced.

Histopathology

All polypoid lesions were removed, or biopsies were obtained and sent to the hospital's central lab for histopathologic evaluation. The size of the lesion was measured objectively by endoscopists. Advanced adenomas carry at least one of these three features: villous architecture of over 25%, more than 10mm in size, and high-graded dysplasia seen in histopathology [23].

One experienced gastrointestinal pathologist performed a histopathological assessment. High-grade dysplasia and carcinoma in situ [9] are considered one category. WHO guidelines, as well as revised Vienna Criteria, were used to categorize polyp histology (22-25).

Ethics

Ethical approval was obtained from the Gastrointestinal Research Center -Iran University of Medical Sciences research board. This study was performed concordant with the Helsinki Declaration of Ethical Principles. All patients were informed about colonoscopy and CRC screening programs, and written informed consent was taken.

Statistics

Statistical analysis was done using IBM SPSS software version 26, with a significance level of $p < 0.05$. Continuous variables were expressed as mean±standard deviation (SD), and categorical variables were presented as frequencies and percentages (%). The chi-square test and Fisher's exact test were utilized to compare proportions in various categories. A logistic regression model was employed to evaluate. In which polyp recurrence as dependent variable and sex, age, Type of polyp, Polyp location and Grade of dysplasia as independent variables considered. The findings were reported as odds ratios (OR) with corresponding 95% confidence intervals [24].

Results

The present study comprised 237 patients diagnosed with adenomatous polyps; 102 patients completed the three-year follow-up and re-colonoscopy. The main reason for not continuing this study is nonadherence to continue the study, migration, and digestive diseases that interfered with the endoscopy results. Among 102 participants, 62 (60.8%) were male and 40 (39.2%) were female, with a mean age of 57.05 ± 12.87 years. Additionally, 20 (19.6%) subjects had recurrent adenomatous polyps. The basic characteristics of the patients are summarized in Table 1. According to these findings, there are significant associations between the type of polyps and dysplasia with polyp recurrence. Regarding the age of the participants, by advancing the age, the recurrence of polyps increased as most patients aged more than 60 years old. Furthermore, we could not find a significant association between age and gender with polyp recurrence. Moreover, among recurrence polyps, the tubulovillous was the prominent type, followed by tubular and villous adenoma.

As illustrated in Tables 2 and 3, twenty patients had experienced recurrence. They are usually raised from large polyps with villous components and are located on the left side of the colon. Furthermore, high-grade dysplasia was recorded in 5) 25%) patients with the male gender prominent. Regarding the type of polyps, tubulovillous and tubular types were more prominent in 9 (45%) and

8(40%) patients, respectively the main part of adenoma is located in the rectosigmoid colon.

The results of the simple logistic regression model for each variable are presented in Table 4. The odds ratio for tubulovillous polyp type was 4.75, indicating that the likelihood of polyp recurrence in patients with tubulovillous polyp type was 4.75 times higher compared to patients with tubular polyp type (OR=4.75, 95% CI: 1.43–15.74, P-value=0.011). Additionally, the probability of polyp recurrence in patients with high-grade dysplasia in the first round of evaluation is 8.11 times higher than in those with low-grade dysplasia at that time (OR=8.11, 95% CI: 2.65–24.3, P-value<0.001). Nevertheless, our study showed no correlation between gender, age, and polyp location with polyp recurrence.

Discussion

The study focused on the average risk of colorectal cancer and identified factors like advanced age, presence of Villous features, and left-side polyps as contributors to the recurrence of adenomatous polyps, which could potentially lead to colorectal cancer according to previous reports [25-27]. Understanding patient and polyp characteristics can aid in identifying individuals at higher risk for recurrence, with periodic surveillance colonoscopy recommended for those with adenomatous polyps [28, 29].

Our study revealed that follow-up colonoscopy can be considered a valuable method in following patients with

Table 1. Baseline Characteristic of the Study Participants

Variable	patients with polyp (N=237)	Follow up (N=102)	No recurrence* (N=82)	Recurrence* (N=20)	P_value*
Sex N(%)					
Male	154 (65)	62 (60.8)	47 (57.3)	15 (75)	0.1461
Female	83 (35)	40 (39.2)	35 (42.7)	5 (25)	
Age(year) N(%)					
20-39	24 (10.1)	12 (11.8)	11 (13.4)	1 (5)	0.4942
40-60	102 (43)	40 (39.2)	33 (40.2)	7 (35)	
>60	111 (46.8)	50 (49)	38 (46.3)	12 (60)	
Type of polyp N(%)					
Hyperplastic	52 (21.9)	30 (29.4)	30 (36.6)	0 (0)	
Tubular	140 (59.1)	46 (45.1)	38 (46.3)	8 (40)	<0.0012
Villous	10 (4.2)	8 (7.8)	5 (6.1)	3 (15)	
Tubulovillous	35 (14.8)	18 (17.6)	9 (11)	9 (45)	
polyp locationN (%)					
Cecum	8 (3.4)	3 (2.9)	3 (3.7)	0 (0)	0.6462
Ascending colon	35 (14.8)	12 (11.8)	10 (12.2)	2 (10)	
Transverse colon	16 (6.8)	11 (10.8)	7 (8.5)	4 (20)	
Descending colon	32 (13.5)	17 (16.7)	13 (15.9)	4 (20)	
Sigmoid	89 (37.6)	41 (40.2)	33 (40.2)	8 (40)	
Rectum	57 (24.1)	18 (17.6)	16 (19.5)	2 (10)	
Dysplasia N(%)					
High	35 (14.8)	19 (18.6)	9 (11)	10 (50)	<0.0011
Low	202 (85.2)	83 (81.4)	73 (89)	10 (50)	

*, recurrence percent is from the follow-up patients. 1. chi-square test, 2. Fisher's exact test; significant and showed in Bold Font.

Table 2. Changes in Patients with Polyp Recurrence

Variable	Before polyp recurrence (N=20)	After polyp recurrence (N=20)	P-value
Type of polyp N(%)			0.012¹
Tubular	8 (40)	12 (60)	
Villous	3 (15)	4 (20)	
Tubulovillous	9 (45)	4 (20)	
Site of polyp N(%)			<0.001¹
Ascending colon	2 (10)	1 (5)	
Transverse colon	4 (20)	4 (20)	
Descending colon	4 (20)	5 (25)	
Sigmoid	8 (40)	7 (35)	
Rectum	2 (10)	3 (15)	
PolypSize			0.293 ¹
1cm	2 (10)	10 (50)	
1-2cm	1 (5)	6 (30)	
>2cm	17 (85)	4 (20)	
Grade of dysplasia N(%)			0.302 ²
High	10 (50)	5 (25)	
Low	10 (50)	15 (75)	

¹, Kappa test; ², McNemar's test; significant and showed in Bold Font.

colorectal polyps, as we calculated a recurrence rate of 19.6%. Compared to other studies, our results are lower than those of previous studies from developed countries in an average-risk population [17]. Studies from Western countries state that polyps' recurrence rate varies between 20 to 40 percent for an average surveillance time of 3 years [30, 31]. Rotermund et al. stated in their meta-analysis that total recurrence rates for large colorectal polyps in developed countries were 11.0% after 12 months of

follow-up and 14.6% for 24-month follow-up [32]. Also, the researchers from the eastern developed countries show no difference in recurrence rates for colorectal polyps compared to Western countries [33, 34]. This discrepancy between our results and their findings may related to the fact that our patients were at average risk for CRC [35, 30, 31]. In this regard, environmental factors like lifestyle, diet, and genetic differences may also be effective. Lower compliance with follow-up colonoscopy, which causes

Table 3. The Relationship between the Degree of Dysplasia and Other Variables before and after Polyp Recurrence

Variable	Before Polyp Recurrence (N=20)			After Polyp Recurrence (N=20)			
	High Dysplasia (N=10)	Low Dysplasia (N=10)	P-value ¹	High Dysplasia (N=5)	Low Dysplasia (N=15)	P-value ¹	
Sex N (%)	Men	8 (80)	7 (70)	1	4 (80)	11 (73.3)	1
	Women	2 (20)	3 (30)		1 (20)	4 (26.7)	
Age N (%)	<40 years	0 (0)	1 (10)	0.17	0 (0)	1 (6.7)	0.702
	40 – 59 years	2 (20)	5 (50)		1 (20)	6 (40)	
	60 – 80 years	8 (80)	4 (40)		4 (80)	8 (53.3)	
Type of polyp N (%)	Tubular	1 (10)	7 (70)	0.022	1 (20)	11 (73.3)	0.03
	Villous	2 (20)	1 (10)		1 (20)	1 (6.7)	
	Tubulovillous	7 (70)	2 (20)		3 (60)	3 (20)	
Site of polyp N (%)	Ascending colon	2 (20)	0 (0)	0.385	0 (0)	1 (6.7)	0.643
	Transverse colon	2 (20)	2 (20)		0 (0)	4 (26.7)	
	Descending colon	1 (10)	3 (30)		1 (20)	4 (26.7)	
	Sigmoid	5 (50)	3 (30)		3 (60)	4 (26.7)	
	Rectum	0 (0)	2 (20)		1 (20)	2 (13.3)	
Polyp Size N (%)	1cm	1 (10)	1 (10)	1	2 (40)	7 (47)	0.222
	1-2cm	1 (10)	0 (0)		2 (40)	6 (40)	
	>2cm	8 (80)	9 (90)		1 (20)	2 (13)	

¹Fisher's exact test. Significant and showed in Bold Font.

Table 4. Simple Logistic Regression Results

Variable	OR	95%CI(OR)		P-value
Female ^a	0.45	0.15	1.35	0.153
Age (year)	1.02	0.98	1.07	0.228
Type of polyp ^b				
Villous	2.85	0.56	14.43	0.206
Tubulovillous	4.75	1.43	15.74	0.011
High dysplasia ^c	8.11	2.65	24.79	<0.001
Polyp location ^d				
Cecum	0	0	—	0.999
Ascending colon	0.65	0.09	4.29	0.655
Transverse colon	1.86	0.35	9.79	0.466
Sigmoid	0.79	0.2	3.07	0.731
Rectum	0.41	0.06	2.58	0.34

^a, The reference group is male; ^b, The reference group is tubular; ^c, The reference group is low dysplasia; ^d, The reference group is descending colon;; significant and showed in Bold Font.

limited patient compliance, could also be effective, as mentioned in previous reports [36, 37].

Nevertheless, more data about screening and follow-up for colorectal premalignant lesions in the Middle East region need to be collected. This is an area which previously considered low-risk for CRC [38, 39]. During the last decade, there was a rising trend in colorectal premalignant and malignant lesions due to industrialization in this region [40, 23]. This development in the facilities' accessibility to healthcare providers could change the incidence and recurrence of colorectal premalignant lesions and require a consensus on this issue.

There is a lack of studies aiming for the estimation of the recurrence of colorectal premalignant lesions in Iran; a multi-center clinical trial study and a large polyps surveillance study that also enrolled subjects of the Middle East reported 17% and a 5% recurrence rate during the median average time of surveillance colonoscopy 6-month period respectively [41, 42]. Those previous studies enrolled symptomatic and high-risk subjects, and in contrast, our study was implemented on a group of average-risk subjects; in addition, some of these studies conducted follow-up colonoscopies on patients with a history of CRC, which results in a higher recurrence rate.

In recent studies, advanced age has been mentioned as a risk factor for colorectal premalignant lesions [43, 44]. Although we found that the incidence and recurrence of adenomatous polyps increased with age. However, there is no statistical significance between recurrent polyps and advancing age. In other words our study found no statistical association between age and recurrence rate. This discrepancy between our findings and the reports from Western countries might be indictable with previous research from Iran that proposed that young people are higher risk of CRC compared to the same studies worldwide [45, 46]. This fact mentions the importance of follow-up colonoscopies in patients with colorectal premalignant lesions aged 40-59, as transforming premalignant lesions to CRC requires about one decade [45, 47, 21].

Designating the location of polyps in our study was an

essential goal in our research because of the recurrence risk associated with establishing a polyp. The most common site was the rectosigmoid colon, followed by the ascending colon. In previous studies, the rectum was the most common site of colorectal adenoma [2, 48, 23]. Also, some studies implicated the highest number of colorectal polyps in the sigmoid colon [49]. there is almost a consensus that the distal part of the colon is the most common site of colorectal premalignant lesions. Despite the higher rates of polyps detected in the rectosigmoid region that may become sooner symptomatic [50], Our results are proportionate with the studies of European and Western countries, which reported higher recurrence rates in the proximally located polyps. [51]. Martinez et al., in a large colonoscopy surveillance study, stated that proximally located polyps are associated with higher recurrence rates, 45.2% to 27.7% [52]. This was disproportionate with some Eastern countries' scientists and some Western countries [43, 53, 24]. Facciorusso et al., in a study from Italy, found an OR of 1.31 for right-sided polyps' recurrences, which were statistically insignificant [24]. As we mentioned before, these findings might be signs of Western lifestyle and changes in the diet of the Iranian population. In addition, our results suggest that sigmoidoscopy alone is not recommended for a surveillance plan because of the limited accessibility of sigmoidoscopy to the proximal part of the colon. It also warns the colonoscopist to be aware of proximal polyps, which have higher recurrence rates and malignant potentials.

As we want to assess the role of gender on the recurrence of polyps, the male gender was not significantly accompanied by a higher recurrence rate. The results contradict previous studies in the eastern countries [34, 54, 55]. We have found a slightly higher polyp recurrence rate in men than women, which was not statistically significant. Yamaji et al. mention that the recurrence rate per year was 12.4% and 6.5% for asymptomatic Japanese men and women, respectively [34]. This study includes surveillance colonoscopy for malignant colorectal lesions; hence, more prevalence of CRC in men has been previously accepted [6, 39]. This finding may be due to our

study population and genetic and environmental factors. As mentioned by other studies, in the Iranian population, we cannot determine diverse colonoscopy screening and colonoscopy surveillance based on sex [2].

It has been previously mentioned that the most common colorectal premalignant lesion is the tubular polyp [56]; however, it carries the lowest risk of recurrence and transition to carcinoma (p-value:0.03%) [57]. Based on the villous structure at the base of the polyps, tubulovillous and villous adenoma are distinguishable with the latter carries, the most risk of dysplasia and malignant transformation [56]. We found a majority of recurrence rates in tubulovillous and tubular polyps. They also carried the highest proportion of high-grade dysplastic lesions in our study. Polyps with high-grade dysplasia, the intermediate stages of the adenoma-carcinoma transition sequence, had a greater recurrence rate than lesions with low-grade dysplasia, as shown in previous studies [34, 58, 59]. In our study, there was a significant difference between recurrence rates based on dysplasia. Yamaji et al. measured the hazard ratio of adenoma with higher dysplastic features and carcinoma in situ of 6.6, which was highly suggestive of a higher risk of recurrence [34]. These findings elucidate the role of precise histological evaluation of colorectal lesions to determine further follow-up colonoscopies in patients with colorectal premalignant lesions.

Our studies had some limitations; first of all, the number of participants may be due to patients' adherence to reassessment, and second, many of them with normal first colonoscopy results did not follow the physician's recommendation. For this reason, patients' follow-up needs to be more prolonged.

In conclusion, our study found that patients with colorectal polyps exhibiting tubular and villous features are at an increased risk of polyp recurrence and subsequent development of malignant characteristics. Given the potential for malignancy in advanced adenomas, more frequent surveillance colonoscopies may be warranted in this population. Finally, our findings clarify the importance of follow-up colonoscopies due to increasing recurrence rates of adenomas.

Author Contribution Statement

MS, HA, and FZ conceptualized and designed the study. HA administrated and supervised the project. MS, HA, FZ, and MRA provided methodological consults. MO, MRA, AS, and AHB investigated and collected the data. RP, MS, and PH validated the data. PH and MS analyzed the data. MS, HA, drafted the manuscript. All authors critically revised and approved the final manuscript. HA are the guarantors and take responsibility for the paper as a whole.

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Conflict of interest

The authors declare no conflict of interest.

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