

Left Sided Colorectal Adenomatous Polyps Have More Risk for High Grade Dysplasia

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Abstract- Colorectal cancer is the second leading cause of cancer death worldwide. Through risk assessment of malignancy in polyps, screening programs can achieve the best results. This study aimed to determine the association between the grade of dysplasia and the location of colorectal polyps. 240 colorectal adenomatous polyps which were referred to department of pathology at Rasoul-e-Akram Hospital between 2005 and 2009 met the inclusion criteria. Demographic data and information about size of polyps, grade of dysplasia and location of polyps were collected and analyzed by Chi-square and t-test. 124 (58.8%) patients were male and 87 (41.2%) were female. The mean age of the patients was 61.6 years. 47 (19.6%) polyps were right-sided and 193 (80.4%) were left sided. 39 (16.2%) polyps had high grade dysplasia. 27 (12.8%) patients had 56 synchronous polyps (23.3%). 176 (73.3%), 39 (16.2%) and 25 (10.5%) polyps were of tubular, tubulovillous and villous types respectively. The greatest dimension of 110 (45.8%) polyps was <0.5 cm, 97 (40.4%) 0.5-1 cm, 22 (9.2%) between 1 and 2 cm and finally 11 (4.6%) >2 cm. High grade dysplasia was detected in 3 (6.3 %) of right-sided and 36 (18.6%) of left-sided polyps. The obtained results revealed that size of polyp and amount of villous component were strongly associated with high grade dysplasia. Left side location of polyps was independently associated with high grade dysplasia. Left-sided colorectal polyps must be treated more seriously, especially the larger ones with villous component. There was no association between age and gender and the grade of dysplasia.

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Introduction

Colon cancer is the second leading cause of cancer death worldwide (1). Colorectal cancers are the third or fourth common cancers reported in Iranian men and the fourth or second in Iranian women, excluding skin cancer (2,3). 17% of colorectal cancers in Iranian population occur in patients younger than 40 years of age at the time of diagnosis. This proportion is similar to proportions seen in many other Middle Eastern countries probably due to the young age-structure of these countries and relatively low rates of colorectal carcinoma in older individuals (4).

Adenocarcinoma constitutes 85% of colorectal malignancies and originates from adenomatous polyps. The progression of adenoma to adenocarcinoma is a well-accepted concept and the base for screening

program of colorectal carcinomas by colonoscopy (5-7). The progression of adenoma with low grade dysplasia to adenocarcinoma takes time. Hence, not all the adenomatous polyps progress into invasive adenocarcinoma, so risk determination of adenomatous polyp for changing into adenocarcinoma is very important for how to treat the polyp.

In the past years, the risk assessment of adenomatous polyp for progression into adenocarcinoma was not important as all the polyps were resected by segmental colectomy. Now there are many techniques such as endoscopic mucosal resection, photodynamic treatment and laparoscopic colectomies for adenomatous polyps that require an accurate risk assessment of malignancy by an endoscopist (8-10).

There are many studies in literature which have demonstrated the strong association between the size of

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polyp and the presence of villous architecture in polyps with high risk of progression into malignancy (11). We found few scientific papers in which the grade of dysplasia was studied in association to the location of colorectal adenomatous polyps (12-19) especially in Iranian population (18,19). This study aimed to evaluate the association between the location of colorectal adenomatous polyps and the grade of dysplasia.

Materials and Methods

In this retrospective study, medical files of 211 patients with colorectal adenomatous polyps were studied. These polyps were resected by endoscopy, segmental or total colectomy in Rasoul-e-Akram Hospital between 2005 and 2009. We included all the polyps which were of adenomatous type and their precise location in colon and size were mentioned in pathology reports. Patients with synchronous polyps including those who had both left-sided and right-sided polyps were included in our study, but each polyp was separately evaluated. We excluded the polyps whose histological slides or paraffin embedded blocks were not available. However, rare cases of familial adenomatous polyposis and patients with a previous history of colorectal cancers were excluded from this study.

Demographic data and information about size of

polyps, grade of dysplasia, histological type and location of polyps were collected from medical files. Age was stratified into 10-year groups, dysplasia as low and high, location of polyp as right or left according to midpoint of transverse colon, histologic types as tubular, tubulovillous and villous and size as <0.5, 0.5-1, >1 & ≤2 and finally >2 cm. We also reviewed the histological type of polyps and their degree of dysplasia by H&E slides. The data was collected in a checklist and analyzed by software program SPSS 17 using Chi-square and t-test. The P -value<0.05 was considered as statistically significant.

Results

A total of 240 adenomatous polyps of 211 patients were included in the study.

124 (58.8%) patients were male and 87 (41.2%) were female. In women, we noted 94 (39.1%) polyps, of which 78 (82.9%) had low grade dysplasia and 16 (17.1%) had high grade dysplasia. In men, we noted 146 (60.9%) polyps, of which 123 (84.2%) had low grade dysplasia and 23 (15.8%) high grade dysplasia. The frequency of the location of polyps according to gender is shown in Table 1. There was no association between gender and the grade of dysplasia or the location of colorectal polyps ($P>0.05$).

Table 1. Frequency of gender of colonic adenomatous polyps according to location of polyps.

Gender	Location of polyps						Total
	Cecum	Ascending colon	Transverse colon	Descending colon	Sigmoid	Rectum	
Female	2	7	6	18	33	28	94
Male	7	18	17	26	45	33	146
Total	9	25	23	44	81	61	240

There was no association between gender and location of polyps.

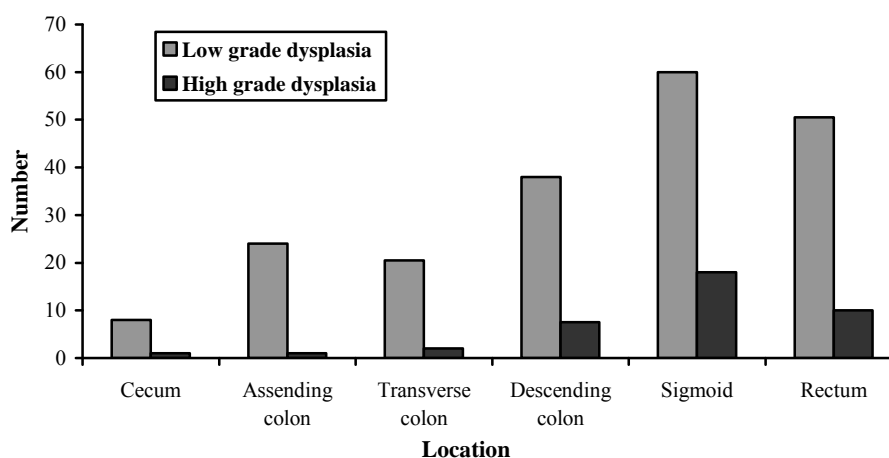


Figure 1. Location of colorectal adenomatous polyps and their degree of dysplasia.

High grade dysplasia is more prevalent in left-sided colorectal polyps.

High grade dysplasia in colorectal polyps

The mean age of the patients was 61.6 years, ranging between 13 and 97 years. The age stratification of the patients according to the grade of dysplasia and the location of polyps is shown in Tables 2 and 3. 35 (74.4%) of right-sided polyps were resected from men and 12 (25.6%) from women. 112 (76.1%) of left-sided polyps were resected from men and 35 (23.9%) from women. Also, there was no association between age and high grade dysplasia or the location of colorectal polyps ($P>0.05$).

47 (19.6%) polyps were right-sided and 193 (80.4%) were left-sided. 39 (16.2%) polyps had high grade dysplasia and 201 (83.8%) had low grade dysplasia (Figure 1).

27 of 211 patients had synchronous resected polyps (12.8%). 56 of 240 polyps were synchronous (23.3%). 184 patients had 1 polyp, 25 patients had 2, and 2 others had 3 resected synchronous polyps. 7 (3.3%) patients had synchronous left and right colonic polyps. 15 of 240 polyps were synchronous left and right sided colonic polyps (6.2%).

176 (73.3%), 39 (16.2%) and 25 (10.5%) polyps were of tubular, tubulovillous and villous types respectively. 110, 97, 22 and 11 polyps were <0.5 cm, 0.5-1 cm, >1&≤2 cm and >2 cm in greatest dimension respectively (Figure 2).

Table 2. The age stratification of grade of dysplasia in colonic polyps.

Age	Grade of dysplasia		Total
	Low	High	
<20	3	0	3
20-29	2	0	2
30-39	9	4	13
40-49	18	3	21
50-59	51	7	58
60-69	52	16	68
70-79	50	6	56
80<	16	3	19
Total	201	39	240

There was no association between age and grade of dysplasia.

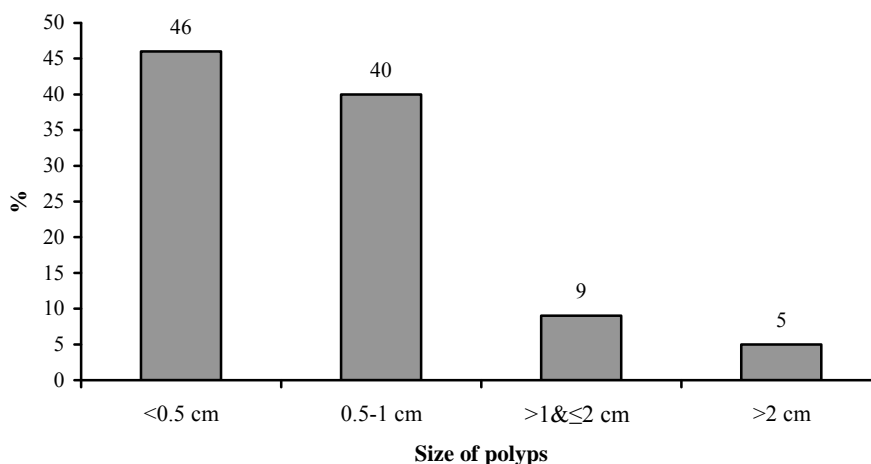


Figure 2. Size of colorectal adenomatous polyps.

Most polyps are 0.5-2 cm in greatest diameter.

Table 3. The age stratification of colonic adenomatous polyps according to their location.

Age	Location						Total
	Cecum	Ascending colon	Transverse colon	Descending colon	Sigmoid	Rectum	
<20	0	0	0	1	0	2	3
20-29	0	0	0	0	0	2	2
30-39	0	1	1	1	5	5	13
40-49	0	4	4	6	4	3	21
50-59	2	10	7	13	12	14	58
60-69	5	6	5	8	25	19	68
70-79	1	2	5	10	25	13	56
80<	1	2	1	5	7	3	19
Total	9	25	23	44	78	61	240

There was no association between age and location of polyps.

3 (6.3 %) and 36(18.6%) of right and left sided polyps had high grade dysplasia respectively (Figure 1). The difference was statistically significant ($P<0.001$). Histological type of polyps was also strongly associated with the grade of dysplasia, as 5.7%, 38.5% and 56% of tubular, tubulovillous and villous adenomas had high grade dysplasia ($P<0.001$).

Discussion

Our study revealed that left-sided colorectal polyps were more prevalent than right-sided ones, which is in agreement with previous studies. In the study by Gschwantler *et al.* performed on a large sample including 7590 adenomatous polyps, a total of 5810 (76.5%) adenomas were localized in the left side of the colon, and 1780 (23.5%) adenomas were localized in the right side (16). In the study by Patel *et al.*, the majority of the polyps were left-sided (20). Also 92% of polyps in the study by Tony *et al.* were left-sided (21). In the previous study on Iranian population performed by Khodadoostan *et al.* (19) and Bafandeh *et al.* (22), left-sided colorectal polyps were more prevalent.

In the present study, although the frequency of left-sided polyps was greater than right-sided ones, high grade dysplasia was significantly different ($P<0.001$).

A study by Rerknimitr *et al.* in Taiwan in 2003 showed that right-sided colorectal polyps were more prevalent than rectosigmoid polyps. Also, right-sided colonic cancers were detected more often than rectosigmoid cancers (12). Their results are in disagreement with ours regarding higher prevalence of right-sided colonic polyps, yet they did not study the association between the location of polyps and the grade of dysplasia. Moreover, the sample size of their study was smaller than our study.

In the study of Khodadoostan *et al.*, most of the carcinomas arose from right-sided colonic polyps (19). This study is also in disagreement with ours.

O'Brien *et al.* studied 3371 adenomatous polyps and showed that left-sided polyps of colon, located distal to the splenic flexure, have more chance for high grade dysplasia than right-sided ones (13). The results are in agreement with ours, but in this study, increased frequency of high-grade dysplasia in left-sided colonic adenomatous polyps was mainly related to villous component and larger size of polyps rather than to location itself. The adjusted odds ratio was 1.4 for left-sided location ($P<0.11$).

Terry *et al.* in 2002 studied the risk factors which can cause colorectal polyps to progress to

adenocarcinoma through a pooled analysis of 4 case-control studies. They divided colorectal polyps into proximal, distal and rectal polyps and applied multivariate logistic model to adjust pathologic predictors such as age, gender and many other variables including family history, smoking status, diet and alcohol consumption. At last, they conclude that rectal location of polyps is associated with advanced polyps defined as polyps having high grade dysplasia, carcinoma in situ and intramural carcinoma (OR, 2.4; 95% CI, 1.1-5.2). Larger size and tubulovillous histology were also associated with advanced polyps (14).

Kristjansdottir *et al.* studied 3315 colonic adenomas removed from 2,385 patients by colonoscopy. The use of multiple logistic regression analysis showed that size, multiplicity, tubulovillous/villous histology, location in rectum, and age were, in order of importance, independent risk factors for high grade dysplasia (15). The large sample size of study makes the study results more reliable.

The results of the two above-mentioned studies are like our results, regarding high prevalence of high grade dysplasia in rectal polyps.

Gschwantler *et al.* evaluated the patients who had undergone total colonoscopy in Australia between 1978 and 1996 (16). 7590 adenomatous polyps were resected from 4216 patients. 86.6% of these polyps had low grade dysplasia and 13.4% had high grade dysplasia. Left-sided polyps had more chance for high grade dysplasia (OR, 2.1; 95% CI, $P<0.001$) in this study. They concluded although left-sided polyps are more common in age >60 years, often have size >0.5 cm, and show more tubulovillous and villous architecture, left side location of colorectal adenomatous polyps is associated with high grade dysplasia independently of age, size and histological type. Their results are in concordance to our data.

The study of Blumberg, performed in Pittsburgh University in 2009 revealed that colonic polyps with high-grade dysplasia on endoscopic biopsy and polyps located distal to the splenic flexure are associated with the highest risk of cancer (17). Their results are similar to ours, but we divided the polyps into right and left sided according to midpoint of transverse colon.

The study of Khatibzadeh *et al.*, which was performed in Milad Hospital in Iran in the year 2005, applied multivariate logistic regression test to show that the location of polyp after splenic flexure can be a risk factor for high grade dysplasia (18). This study and the previously mentioned study were alike.

High grade dysplasia in colorectal polyps

Finally, our study revealed that in addition to well-known risk factors such as size and amount of villous architecture, there is a statistically significant association between left side location of adenomatous polyps and high grade dysplasia. According to our study, it is essential that left-sided colorectal adenomatous polyps be treated and followed more seriously, especially those that have a larger size or villous histology.

More studies especially prospective multivariate studies with larger sample sizes including different races accompanied by patient follow-ups and review articles are required to solve the probable bias towards confounding factors such as race, family history, multiplicity, body mass index, dietary fiber and fat, smoking status, alcohol consumption, physical activity, hormone replacement therapy, parity and education (14).

Most adenomas of colon do not progress to cancer. There are molecular alterations in the progression of early adenomas to intermediate and late adenomas and finally carcinoma as K-ras and p53 mutations and deletion of DCC (deleted in colorectal cancer) (23). The location of adenomatous polyp may be related to intermediate steps between adenoma-carcinoma sequence and the molecular hits. By applying immunohistochemical staining or molecular tests, further studies are required to evaluate the association between the location of colorectal adenomatous polyps and molecular changes.

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