RESEARCH COMMUNICATION

Colonoscopy Screening Results in at Risk Iranian Population

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Abstract

Objectives: To investigate the prevalence of colorectal adenomas and other advanced lesions in first degree relatives of Iranian patients diagnosed with colorectal cancer by colonoscopy and pathologic evaluation. Methods: Iranian colorectal cancer patients (probands) were identified through pathologic reports of the regional cancer registry. First degree relatives (siblings, parents and offspring) of probands were evaluated for the existence of polyps and precancerous lesions via colonoscopy screening. Control patients were chosen among average risk population with no family history of colorectal cancer who agreed to colonoscopy screening. Results: A total of 184 subjects underwent colonoscopy screening from April 2007 to March 2009. From 90 cases among families of probands, 70 (77.8%) had a normal colonoscopy result, 18 (20%) demonstrated polyps and 2 (2.2%) were diagnosed with colorectal cancer. Colonoscopy screening in 94 average risk control patients discovered polyps in 4 (4.3%) cases and the other 90 (95.7%) patients had normal total colonoscopy results. Mean age of cases with advanced lesions was 48.4±10.2 and 41.5±18.4 in control patients with polyps. The incidence of polyps was significantly higher in males, and in family case patients compared to controls. Conclusions: Based on colonoscopy screening, the prevalence of colorectal adenoma and precancerous lesions in first degree relatives of patients diagnosed with colorectal cancer is significantly higher than in the average risk population.

Keywords: Colorectal cancer - colonoscopy screening - high risk patient - average risk patient

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Introduction

Colorectal cancer (CRC) is the third most common cancer diagnosed among men and women and the second leading cause of death from cancer in the United States. CRC can largely be prevented by the detection and removal of adenomatous polyps, and survival is significantly better when CRC is diagnosed while still localized (Levin et al., 2008).

Between one in every six and one in every five people (16%-20%) with colorectal cancer has a first-degree relative - a parent or sibling-with colorectal cancer. Studies have shown that a history of colorectal cancer in a first-degree relative nearly doubles the risk of developing the disease (Chan et al., 2008).

Colonoscopy is considered to be the gold standard for early detection of colon adenomas and colorectal cancer.

The incidence of colorectal cancer is uncommon before the age of 40, but rises progressively to 3.7/1000 per year by the age of 80. The lifetime occurrence for patients at average risk is 5 percent, with 90 percent of cases occurring after age 50. Patients with one first-degree relative experience a 2-fold higher risk of CRC and patients with two or more relatives, a 4-fold increased risk, independent of age at diagnosis (Butterworth et al., 2006).

A number of studies suggest that screening for colorectal cancer by colonoscopy, with removal of precancerous lesions, reduces the risk of death from colon cancer. Due to the known familial risk for colorectal cancer, first degree relatives (parent, sibling or child) of patients with colon cancer or adenomatous polyps are advised to have screening colonoscopy. According to current guidelines, screening procedures should start at age 40 years or 10 years younger than the earliest diagnosis in their family (Ruthotto et al., 2007).

Recommendations for CRC screening, as with other screening, must take into account the effectiveness, sensitivity, false-positive rate, safety, and convenience of the test. In addition, cost and cost-effectiveness of the screening program need to be considered in the context of what is best for the individual patient, as well as for clinical policy in general.

According to previous studies first degree relatives (parent, sibling, offspring) of patients with colorectal cancer have a higher risk of developing this type of cancer comparing to the normal population. Therefore colonoscopy is a recommended procedure for advanced screening of precancerous lesions. However, a well defined screening and consensus guideline has not yet been developed for these families in Iran. In April 2007 we started a screening program for early detection of adenomatous polyps and CRC in asymptomatic high

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risk Iranians.

This study has been conducted to evaluate the prevalence of precancerous lesions in first degree family members of patients with colorectal cancer and to develop a consensus guideline for future screening of high risk population in Iranian patients.

Materials and Methods

We started a screening program for early detection of precancerous lesions in high risk Iranian population from April 2007 to March 2009. Colorectal cancer (CRC) patients (probands) were identified from regional cancer registry, via pathology lab results. First-degree relatives (siblings, parents, and offspring) of probands were invited to a counseling session. The patients were fully informed about the advantages of advanced colonoscopy for early detection of precancerous lesions. All relatives who agreed to colonoscopy screening were included in our study. Blood samples were taken for genetic study.

With high-resolution video colonoscopy, total colonoscopy was performed and all detected lesions were removed and histo pathologically assessed by expert pathologist. For all participants a questionnaire was completed. Clinical manifestations, past medical history, positive family history for cancer, demographic and epidemiological information were obtained in the questionnaires. The pattern of malignancy occurrence through two generations of a proband was drawn in shape of a pedigree.

Colonoscopy results of 90 first degree relatives of probands was compared to colonoscopy results of 94 age and sex matched, average risk control patients with no family history of colorectal cancer.

SPSS 13.0 software (SPSS, IL, USA) was used for statistical analysis. Chi-square test was used for the analysis of nominal data in detecting statistically significant differences between different groups. The t-test and Mann-Whitney U test were employed to compare the means of continuous data. P values below 0.05 were considered significant.

Results

Total colonoscopy was performed on 184 case and control patients who agreed to colonoscopy screening. 90 case patients were selected among first degree relatives (sibling, parents and offspring) of patients diagnosed with colorectal cancer. 94 control patients were among average risk population with no family history of colorectal cancer. From 90 colonoscopies performed on case patients, 70 (77.8%) patients had normal colonoscopy results and 20 (22.2%) were reported positive for a lesion. From the 20 colonoscopies with abnormal results, 18 (20%) were polyps and 2 (2.2%) were colorectal cancer. In 94 average risk control patients who underwent colonoscopy screening 90 (95.7%) had a normal report, and only 4(4.3%) were detected with a lesion (Table 1).

Studying the colonoscopy results of first degree relatives (siblings, parents and offspring) of probands indicated 20 (22.2%) cases with a lesion and 70 (77.8%) cases with a normal total colonoscopy report. From the 20 lesions detected the most common lesion detected was tubular adenoma with mild dysplasia in 7 of 20 (35%) cases (Table 2). Rectum was the most affected site with an abnormal lesion.

Incidence of polyp was significantly higher in case patients comparing to controls (P value=0.001).

Mean age of patients diagnosed with polyp was (48.89±10.53) in case patients and (41.50±18.41) for controls.

Mean age of polyp incidence in case and control patients was not significantly different (P value=0.774).

Incidence of polyp was higher in males in both case (72.2%) and control (75.0%) patients.

Table 1. Colonoscopy Results in Case and Control Patients

		FH		Total
		No	Yes	
CRC	n	0	2	2
	%	0	2.22	1.10
Normal	n	90	70	160
	%	95.7	77.78	86.95
Polyp	n	4	18	22
	%	4.3	20.00	11.95
Total	n	94	90	184
	%	100	100	100

Table 2. Advanced Lesions Detected in Colonoscopy Screening of First Degree Relatives of Patients Diagnosed with CRC

Pathology	Frequency	Percent
adenocarcinoma	2	10
high grade dysplasia villus	1	5
hyper plastic polyp	1	5
mild inflamed	1	5
moderate dysplasia	1	5
tubovillus dysplasia	2	10
tubular	1	5
tubular adenoma mild dysplasia	7	35
villus adenoma	3	15
villus moderate dysplasia	1	5
Total	20	100

Table 3. Colonoscopy Sites of Detected Lesions

Location	frequency	percent
Anal verge	1	5
Ascending	1	5
Descending	3	15
Rectum	7	35
Sigmoid	4	20
Splenic Flexure	2	10
Transverse	2	10
Total	20	100

Discussion

Colorectal cancer results 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 in most people (Little et al., 1999; Potter et al.,

1999).

Colorectal cancer (CRC) is the third most common cancer diagnosed among men and women and the second leading cause of death from cancer in the United States. CRC can largely be prevented by detection and removal of adenomatous polyps, and survival is significantly better when CRC is diagnosed while still localized. Most colorectal cancers arise from adenomatous polyps, some of which progress from small (<5 mm) to large polyps (>1.0 cm), and then to dysplasia and cancer. This progression probably takes at least 10 years in most people (Eddy et al,. 1990). The risk of developing colon cancer is 2.5- to 3 fold increased among relatives of those affected. However, in most families, no hereditary syndrome can be identified (Thorpe et al., 2005).

Two-third of polyps is adenomas. The prevalence of adenomas is about 25 percent by the age of 50 and 50 percent by the age of 70. Large adenomatous polyps (>1 cm) are most likely to progress to cancer but are less common, accounting for 11 percent of all adenomas in one necropsy study (Williams et al., 1982). Hyperplastic polyps account for most of the remaining polyps and are typically small and distal. They usually do not progress to cancer, although there are reports of sporadic cancers arising from hyperplastic polyps (Hawkins et al., 2001) and a rare syndrome, hyperplastic polyposis, which may be associated with an increased risk of colorectal cancer (Burt et al., 2000).

The risk of CRC increases with adenoma size, number, and histology. The finding of one adenomatous polyp suggests that this type of colon tissue has the propensity to form polyps and should be evaluated for other lesions in the colon and rectum.

The role of polyps as a precursor for cancer, high lights the important benefits of colonoscopy screening and polypectomy.

Persons with a familial risk of colorectal cancer (CRC) account for about 25% of all CRC cases. The adenoma prevalence in relatives of CRC patients 50-60 years of age is 17-34%; data on younger individuals are scarce. In one study the aim was to prospectively define the adenoma prevalence in 40- to 50-year-old first-degree relatives of CRC patients compared to controls. Using high-resolution video colonoscopy, each detected polyp was removed and histopathologically assessed. Each participant completed demographic and epidemiological questionnaire: Of 228 subjects in the risk group 36.4% had polypoid lesions compared to 20.9% of 220 controls (p<0.001). Forty-three (18.9%) subjects in the risk group had adenomas compared to 18 (8.2%) in the control group (p=0.001). High-risk adenomas (>10 mm and/or of villous type) were found in 12 persons in the risk group compared to 5 controls (not significant). In the risk group most lesions (52%) were located proximal to the sigmoid colon compared to 29% in controls Menges et al., 2006).

In another study the rate of cancer and adenomas increased with age and it was higher among males, 55% of screen-detected cancers were at TNM stage I. The positive predictive value (PPV) was 7.4% for cancer and 32.9% for AA at first screening, and 4.5% for cancer and 20.5% for AA at repeat screening. Overall 89.0% of FS were classified as complete. Among subjects referred to colonoscopy the prevalence of proximal Adenoma and cancer ranged from 5.4 to 11.1%. The overall DR (subjects with at least one advanced lesion) ranged from 3.5 to 7.0%. In conclusion, during 2005 the organized programs for colorectal cancer screening in Italy increased considerably, covering about one third of the eligible population at a national level (Zorzi et al., 2005).

The National Polyp Study Work Group, as an example, followed 1418 patients in who complete colonoscopic examination led to the removal of one or more polyps in the colon or rectum. During a mean follow-up of six years, the incidence of colon cancer was 88 to 90 percent lower than in patients who had similar risk but in whom polyps were not removed and 76 percent lower than in the general population. The study cohort consisted of 1418 patients who had a complete colonoscopy during which one or more adenomas of the colon or rectum were removed. The patients subsequently underwent periodic colonoscopy during an average follow-up of 5.9 years, and the incidence of colorectal cancer was ascertained. The incidence rate of colorectal cancer was compared with that in three reference groups, including two cohorts in which colonic polyps were not removed and one general-population registry, after adjustment for sex, age, and polyp size. Ninety-seven percent of the patients were followed clinically for a total of 8401 person-years, and 80 percent returned for one or more of their scheduled colonoscopies. Five asymptomatic early-stage colorectal cancers (malignant polyps) were detected by colonoscopy (three at three years, one at six years, and one at seven years). No symptomatic cancers were detected. The numbers of colorectal cancers expected on the basis of the rates in the three reference groups were 48.3, 43.4, and 20.7, for reductions in the incidence of colorectal cancer of 90, 88, and 76 percent, respectively ($P < 0.001$) (Winawer et al., 1993).

Colorectal cancer (CRC) is the third most common cancer diagnosed among men and women. Studies have shown that a history of colorectal cancer in a first-degree relative nearly doubles the risk of developing this disease. Colonoscopy screening is considered to be the gold standard for early detection of colon adenomas and colorectal cancer.

In this study the prevalence of colorectal adenoma and precancerous lesions in the Iranian population was significantly higher in first degree relatives of probands .The presentation of lesions was prominent in male patients and in the rectum area. We identified a significant number of advanced cancers at an early stage suggesting that colonoscopy screening could be a useful tool in early identification of CRC. We recommend colonoscopy screening for early detection of precancerous lesions for first degree relatives of colorectal cancer patients.

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