RESEARCH COMMUNICATION

Prevalence of Colorectal Cancer in Relatives of Iranian Patients Diagnosed with Colorectal Cancer

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Abstract

Background: A high rate of colorectal cancer occurrence is established in individuals with a positive family history of this type of cancer. Objectives: The aim of this study was to investigate the prevalence of colorectal cancer in first degree and second degree relatives of colorectal cancer patients. Methods: Family medical histories of 489 first degree relatives of colorectal cancer patients were obtained by a questionnaire. 249 average risk patients with no family history of colorectal cancer were included as control patients. Results: In our study from a total of 489 case patients, 153 (31.3%) had at least one close relative affected by colon cancer. Case-control analysis showed an odd ratio of 3.1 (95% CI, 2.07 to 6.27) for one and 5.7 (CI, 2.39 to 13.56) for two affected relatives. Cases with a positive family history had a 3.006 times greater risk in developing colorectal cancer if a first degree relative was affected comparing with a 4.898 time greater risk if a second degree family member was diagnosed with colorectal cancer .Our study indicated a higher risk for developing colorectal cancer in male family relatives 50 years and older. Rectal area was found the most tumor side affected in case and control patients. Conclusion: First-degree relatives of patients with colorectal cancer had an increased risk of developing this type of cancer. The risk was greater when diagnosis was in male, elderly patients and other first-degree relatives were affected.

Key Words: Colorectal cancer - familial factors - colonoscopy screening - high risk patients

Asian Pacific J Cancer Prev, **10**, 91-93

Introduction

Colorectal cancer results from both genetic and environmental factors, and their interactions. Studies have shown that between one in every six and one in every five people (16%-20%) with colorectal cancer has a first degree relative diagnosed with colorectal cancer. Epidemiological studies on high risk populations (China, Iran) evidenced a strong familiarity for esophageal cancer with up to 60% of the affected patients reporting a positive familial history. About 10-15% gastric cancer patients show a positive family history for this neoplasm.The aim of this study was to evaluate the risk of colorectal cancer in relatives of patients with a positive family history for this type of cancer.

A high rate of cancer occurrence is established in individuals with a positive family history of Cancer. Patients with a family history of CRC have an estimated relative risk, two to six times greater than patients without it. This depends on the age at diagnosis, the number and proximity of affected relatives and the frequency of tumors in the genealogy (Martellucci et al., 2008). A history of colorectal cancer in a first-degree relative nearly doubles the risk of developing this type of cancer. Approximately 3 to 4 percent of patients with colorectal cancer have a cancer susceptibility syndrome caused by one of two autosomal dominant, highly effective genes.

Important risk factors for developing adenomatous polyps were revealed in relatives of CRC patients after total colonoscopy. However, male gender and closer degree of relation to a CRC case were independently and significantly associated with a greater incidence of simple and advanced adenomatous polyps, even after correcting the age of relatives (Neklason et al., 2008).

Two inherited disorders, which are transmitted in an autosomal dominant fashion, are associated with the greatest risk of developing colon cancer: Familial Adenomatous polyposis (FAP) and Hereditary Nonpolyposis Colorectal Cancer (HNPCC) (Lynch et al., 1993; Ponz de Leon et al., 1993; Burt et al., 1995). HNPCC is more common than FAP, accounting for about 2 to 3 percent of all colorectal adenocarcinomas (Mecklin. 1987; Lynch et al., 1993; Rodriguez-Bigas et al., 1997; Aaltonen et al., 1998; Samowitz et al., 2001). An autosomal recessive polyposis syndrome, termed MUTYH in association with polyposis, has also been

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described, although the full clinical picture is not yet completely understood (Sieber et al., 2003; Jo et al., 2005).

Among the multiple cancer family syndromes, several are known to be associated with the development of colon cancer. These disorders may be diagnosed during evaluation of the index patient or during screening of family members who are at risk (Mandel et al., 1993). Early detection of colorectal cancer in family members of patients diagnosed with this type of cancer by effective colonoscopy screening may reduce death rate due to earlier diagnosis.

Materials and Methods

The study used a case control design to analyze the data collected from a total of 738 patients. Of these patients, 489 cases were diagnosed with colorectal cancer and 249 controls were randomly chosen among average risk patients with a normal total colonoscopy result. Family medical histories were obtained by a questionnaire completed by all case and control patients. The questionnaires covered personal information (age, sex, habits and medical backgrounds), occurrence of colorectal or any other type of cancer in first degree (parents, siblings and offspring) and second degree family members of the patients. For patients diagnosed with colorectal cancer, extra information such as age at diagnosis, tumor sites and pathologic reports were included in the cancer registry. Chi-square test was used for the analysis of nominal data in detecting statistically significant differences between case and control groups. Odd ratios (ORs) and 95% confidence intervals (CIs) were using appropriate unconditional logistic regression. All statistical analysis was performed using SPSS version 13.0 (SPSS, IL, USA).

Table 1. Family History of Cases and Controls

		Cases	Controls
Family History of CRC	+	153 (31.3%)	24 (9.6%)
	-	336 (68.7%)	225 (90.4%)
Total		489 (100%)	249 (100%)

Table 2. Patients with a Positive Family History of Colorectal Cancer under and over 50 Years old

	Female	Male	Total
Patients <50	35 (22.9%)	41 (26.8%)	76 (49.7%)
Patients ≥50	31 (20.2%)	46 (30.1%)	77 (50.3%)
Total	66 (43.1%)	87 (56.9%)	153 (100%)

Table 3. Tumor Sites of Patients Diagnosed with Colorectal Cancer

Anal Canal	4	(0.8%)
Ascending Colon	45	(9.2%)
Cecum	40	(8.2%)
Descending Colon	19	(3.9%)
Hepatic Flexure	6	(1.2%)
Rectosigmoid	49	(10.0%)
Rectum	99	(20.2%)
Sigmoid	64	(13.1%)
Splenic Flexure	11	(2.2%)
Transverse Colon	18	(3.7%)

A two-sided P-value <0.05 was considered to be statistically significant.

Results

From a total of 489 case patients, 153 patients (31.3%) had at least one close relative affected by colon cancer and 336(68.7%) had no family member with this condition. Of 153 case patients 58.4% had a first degree family member (sibling or parent) and 41.6% had a second degree family member diagnosed with colorectal cancer. (see Table 1). Cases with a positive family history in first degree relatives had a 3.006 (CI, 1.73 to 5.22) times greater risk in developing colorectal cancer. This risk was 4.898(CI 2.29 to 10.49) times greater for cases with a second degree family member diagnosed with colorectal cancer.

Our study indicated 1.37 times greater risk (CI0.99 to 1.89) for case patients diagnosed at 50 years or older. Male patients have a 1.68 (CI, 1.22 to 2.31) times greater chance of developing colorectal cancer comparing to female patients.From a total of 153 case patients with a positive family history of colorectal cancer 87 (56.9%) were male and 66 (43.1%) were female patients. From 87 male patients 41(26.8%) were under 50 years of age and 46 (30.1%) were 50 years and over. In 66 female patients 35(22.9%) were under 50 and 31(20.3%) were 50 years old and over (see Table 2).

Studying the tumor sites of patients diagnosed with colorectal cancer indicated that the rectal area was the most affected site with a total of 22.1% reported cases in contrast with the anal canal which was considered the least (0.89%) (see Table 3).

Discussion

This study found consistent increase in the risk of colorectal cancer among men and women with a family history of the disease. The result of our study is similar to results reported in several other studies (Conio et al., 1987; St John et al., 1993; Johns and Houlston., 2001; Butterworth et al., 2006).

In one study 302 patients affected by large bowel carcinoma with a positive history of colorectal cancer in first degree family members and some pathological and clinical features were investigated. Patients with inherited forms of polyposis of the large bowel were excluded. Thirty-six (11.9%) had at least one close relative affected by intestinal cancer. No relationship between family history and pathological features (anatomic distribution, stage and grading) was found. Moreover no difference in prognosis between patients with a family history and those without was shown. These results suggest no relationship between a first degree family history and the natural history of the disease (Conio et al., 1987).

An increased risk due to a positive family history depended on the number of family members affected, whether they were first-degree relatives, and the age onset of the disease. In general, the raise in lifetime risk, ranged from about two- to six folds according to measured factors. The results of a systematic review provided precise

estimatation of these risks. The highest risk belonged to people with multiple first-degree relatives or relatives who had developed colorectal cancer at a relatively young age (e.g. younger than 50 years) (Butterworth et al., 2006). Risk for colorectal cancer was greater for relatives of patients with colon cancer comparing to rectal cancer.

The purpose of another study was to quantify any possible risk for colorectal cancer in first-degree relatives of patients with common colorectal cancer and to define possible markers for risk increase. In this case-control family study relatives of colorectal cancer patients and matched control patients from a one-surgeon practice were investigated (Johns and Houlston., 2001). Family medical histories were obtained for 7493 first-degree relatives and 1015 spouses of 523 case-control pairs. Reported diagnoses of colorectal cancer in relatives were verified in 79% of cases. The odds ratio was 1.8 (95% CI, 1.2 to 2.7) for one and 5.7 (CI, 1.7 to 19.3) for two affected relatives. By matched analysis of risk in relatives, the increased risk for parents and siblings were 2.1 times greater for case patients than for control patients (CI, 1.4 to 3.1); 3.7 times greater (CI, 1.5 to 9.1) when case patients were diagnosed before 45; and 1.8 times greater (CI, 1.2 to 2.9) when case patients were diagnosed at 45 years or older; and was independent of gender, type of relative, site of cancer, and type of cancer (single or multiple). The cumulative incidence among first-degree relatives was greater for case patients than for control patients ($P < 0.001$) (St John et al., 1993).

In another study the increased risk in patients with a family relative diagnosed with colorectal cancer in a family relative was evaluated as following: with CRC 2.25 (95% CI = 2.00-2.53), colon 2.42 (95% CI = 2.20-2.65), and rectal 1.89 (95% CI = 1.62-2.21) cancer; parent with CRC 2.26 (95% CI = 1.87-2.72); sibling with CRC 2.57 (95% CI = 2.19-3.02); more than one relative with CRC 4.25 (95% CI = 3.01-6.08); relative diagnosed with CRC before age 45, 3.87 (95% CI = 2.40-6.22); and a relative with CRA 1.99 (95% CI = 1.55-2.50. Individuals with a family history of CRC had a significantly elevated risk of developing CRC compared with those without such a history. Risks were greatest for relatives of patients' diagnosed young, those with two or more affected relatives, and relatives of patients with colonic cancers (Johns and Houlston., 2001).

First-degree relatives of patients with colorectal cancer had an increased risk for this type of cancer. This risk was decreased if diagnosis was at a younger age and was greater when other first-degree relatives were affected. Understanding of familial and hereditary risks for colonic cancer is leading to a better understanding of this disease and is suggesting more preventive strategies.

References

Aaltonen, LA, Salovaara, R, Kristo, P, et al (1998). Incidence of hereditary nonpolyposis colorectal cancer and the feasibility of molecular screening for the disease. *N Engl J Med*, **338**, 1481.

Burt RW, DiSario JA, Cannon-Albright L (1995). Genetics of colon cancer: Impact of inheritance on colon cancer risk. *Annu Rev Med*, **46**, 371.

Butterworth, AS, Higgins, JP, Pharoah, P (2006). Relative and absolute risk of colorectal cancer for individuals with a family history: a meta-analysis. *Eur J Cancer*, **42**, 216.

Conio M, Bonelli L, Martines H, et al (1987). Colorectal cancer in patients with family history. *Int J Colorectal Dis*, **2**, 190-2.

Jo, WS, Bandipalliam, P, Shannon, KM, et al (2005). Correlation of polyp number and family history of colon cancer with germline MYH mutations. *Clin Gastroenterol Hepatol*, **3**, 1022.

Johns, LE, Houlston, RS (2001). A systematic review and meta-analysis of familial colorectal cancer risk. *Am J Gastroenterol*, **96**, 2992.

Lynch HT, Smyrk TC, Watson P, et al (1993). Genetics, natural history, tumor spectrum, and pathology of hereditary nonpolyposis colorectal cancer: An updated review. *Gastroenterology*, **104**, 1535.

Mandel, JS, Bond, JH, Church, TR, et al (1993). Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med*, **328**, 1365.

Martellucci J , Civitelli S , Dhamo A , Tanzini G (2008). Familial colorectal cancer: a concept revisited 2008. *Colorectal Dis*, **11**, 133-7.

Mecklin JP (1987). Frequency of hereditary colorectal carcinoma. *Gastroenterology*, **93**, 1021.

Neklason DW, Thorpe B L., Ferrandez A, et al (2008). Colonic adenoma risk in familial colorectal cancer - a study of six extended kindreds. *Am J Gastroenterol*, **103**, 2577-84.

Ponz de Leon, M, Sassatelli, R, Benatti, P, et al (1993). Identification of hereditary nonpolyposis colorectal cancer in the general population: The 6-year experience of a population-based registry. *Cancer*, **71**, 3493.

Rodriguez-Bigas MA, Boland CR, et al (1997). A National Cancer Institute workshop on hereditary nonpolyposis colorectal cancer syndrome: Meeting highlights and Bethesda guidelines. *J Natl Cancer Inst*, **89**, 1758.

Samowitz, WS, Curtin, K, Lin, HH, et al (2001). The colon cancer burden of genetically defined hereditary nonpolyposis colon cancer. *Gastroenterology*, **121**, 830.

Sieber, OM, Lipton, L, Crabtree, M, et al (2003). Multiple colorectal adenomas, classic adenomatous polyposis, and germ-line mutations in MYH. *N Engl J Med*, **348**, 791.

St John, DJ, McDermott, FT, Hopper, JL, et al (1993). Cancer risk in relatives of patients with common colorectal cancer. *Ann Intern Med*, **118**, 785.