Short Communication

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Evaluation of Colonoscopy Screening Results in the First-Degree Relatives of Patients with Familial Colorectal Cancer X-Type

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ABSTRACT

BACKGROUND AND OBJECTIVE: Colorectal cancer is one of the growing cancers in Iran and one of the few preventable cancers in the World Health Organization. One of the most important ways to early diagnose this malignancy and its underlying lesions (polyps) and subsequently to prevent it is screening. Colorectal cancer is one of the growing cancers in Iran and one of the few preventable cancers in the World Health Organization. One of the most important ways of early detection of this malignancy and its underlying lesions (polyps) and consequently its prevention is screening. Different protocols have been developed for the diagnosis of first degree relatives of known hereditary cases such as HNPCC and FAP, but the diagnosis plan for first degree relatives has not been defined as a group of familial colorectal cancers without known mutations (type X colorectal cancer). The purpose of this study was to evaluate the results of colonoscopy screening in first-degree relatives of these patients.

METHODS: This cross-sectional study was performed on the families of patients with suspected Lynch syndrome who had no deficiency in the expression of repair proteins. Data were collected from the medical records system of colorectal cancer patients who had been enrolled in the system for prevention and early detection of colorectal cancer at Shahid Beheshti University of Medical Sciences Research Center from 1387 to 1397.

FINDINGS: The results of colonoscopy revealed that 18 out of 77 subjects had 23% polyps or tumors in their colon, out of which 55% were polyps and the rest were adenomas. About 60% of polyps were in the rectum and sigmoid and the rest in the colon and cecum. Also, 4 patients in this screening showed tumors in their colon, all of which were newly diagnosed, and 2 patients in this screening were diagnosed with inflammatory bowel disease.

CONCLUSION: According to the results of this study, in the case of colon polyps, the families of these patients appear to be at high risk like those of Lynch syndrome families and need regular colonoscopy care.

KEY WORDS: *Colorectal Cancer, Colorectal Cancer Familial, Lynch Syndrome, Colorectal Cancer X-type.*

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Introduction

Colorectal cancer is the third most commonly diagnosed malignancy in the world. In Iran, the standardized incidence rates for men and women were 11.31 and 10.89% respectively, and in Mazandaran were 12.47% and 12.61%, respectively (1). Age, inflammatory bowel disease, having a personal or family history of colorectal cancer or colon polyps, inherited syndromes and lifestyle are the most important risk factors for this malignancy (2 and 3). The molecular basis of X-type familial colorectal cancer is still poorly understood (4).

The median age of onset of cancer in the X-type familial colorectal cancer is about 55 years, which is about 5-10 years later than Lynch syndrome (median age of 45 years). The incidence of extra-colon cancers in X-type familial colorectal cancer (10%) is lower than Lynch syndrome (5-7). Colorectal cancer is a silent malignancy, and involves people who may have no significant markers, such as bleeding or abdominal pain, and worse they are diagnosed when the tumor growth is too large to be cured (8).

Most colorectal cancers start from uneven, non-cancerous growth of a polyp, if the polyp or polyps are removed from the colon it may prevent cancer, so screening for this malignancy can reduce both the incidence and death rate (9). Those who were diagnosed with early-stage cancer had a five-year survival rate of 93.2%, while those with high-grade cancer had a five-year survival rate of 47.7%. (10). Most cases of colorectal cancer are single-stage, accounting for about 70 to 80 percent of colon cancers. In this type of cancer, age and environmental factors play a greater role than genetic-hereditary factors (2).

Approximately 5 to 10 percent of these cancers fall into the hereditary branch, most notably hereditary nonpolyposis colorectal cancer or Lynch syndrome and other familial adenomatous polyposis cancers. Numerous other Hamartomatous polyposis syndromes are also associated with an increased risk including of Peutz–Jeghers syndrome, Juvenile polyposis syndrome. Hereditary gastrointestinal syndromes are divided into general categories of polyposis and non-polyposis. In the first category, FAP and in the second category, HNPCC is the most common and most important syndromes (11). Today, the third group has been classified as colorectal cancer (about 20%), although clinical criteria and family history are present in these patients, initial genetic screening tests do not indicate defects in the function of the repair system genes. Extensive studies have shown that screening is very effective in reducing mortality from colorectal cancer. But in general, these tests fall into two groups. The first group of tests that exclusively screen for colorectal cancer and have a moderate impact on prevention, including: Fecal Occult Blood Test, Guyak Test, Immunochemical Test, Fecal DNA Search Test, and Measurement of Serum Tumor Markers. Second group of tests mainly examine the colon structure. This includes endoscopy, flexible sigmoidoscopy, barium enema, and CT colonography. In these methods, colonoscopy is both a screening method and sometimes a treatment because the polyp is visible in the intestine and can be removed simultaneously (2).

Complete colonoscopy has advantages, most importantly full access to the intestine with the possibility of simultaneous biopsy or polyp resection when viewed in the colon. Although Sigmoidoscopy and fecal occult blood tests, are cost-effective and non-invasive, but they are ineffective in identifying malignancies, especially in the early stages (2). Other screening methods such as virtual colonoscopy, fecal DNA testing and serum proteomics are under study, but none have been routinely approved for use in the patient's bedside (9).

The most important and cheapest way to prevent colon cancer and rectal cancer is lifestyle change. Studies have now shown that not smoking, proper physical activity, and weight control can significantly reduce the risk. Clinical trials with dietary interventions such as increased fiber, fruits and vegetables, reduced fat and red meat have shown the effect of diet on cancer (12). Due to the silence of this cancer and the absence of symptoms until its advanced stages and the necessity of screening to prevent the progression of the disease, this study aimed to investigate the results of colonoscopy screening in first degree relatives of patients with X-type familial colorectal cancer.

Methods

This cross-sectional study was done after obtaining permission from the Ethics Committee of Shahid Beheshti University of Medical Sciences with code IR.SBMU.MSP.REC.1393.787 and obtaining written consent from the family of patients suspected with Lynch Syndrome that had no defects in the expression of repair proteins and the data were extracted from medical records. Patients with colorectal cancer who were operated on were randomly selected from the patients registered in the system of prevention and early detection of colorectal cancer of Shahid Beheshti

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University of Medical Sciences Gastroenterology Research Center from 1387 to 1397. Patients whose clinical and pathological information was valid and whose surgical pathology block was available and patients who were able to track their life status were included in the study. Patients who were diagnosed at a stage that did not undergo surgery by the decision of the medical team, also, patients whose clinical and pathological information was not valid or their surgical pathology block was unavailable, as well as patients with FAP syndrome or other hereditary polyposis syndromes were excluded. In the first stage, suspected cases of Lynch syndrome were identified by examining the medical records and genealogy of patients and they were referred to the Cancer Lab for evaluation of MSI and IHC-MMR.genealogy was drawn for those who were suspected of inherited syndromes, after obtaining a verbal consent.Among the patients, those who had the Amsterdam criteria but, their both molecular tests were negative, were selected as the target population. The first-degree relatives were then contacted and an appointment was made between them and genetic specialist. At this meeting, screening in these patients was described as having a positive family history and even considering the negative result of screening test by a geneticist and the benefits and benefits of complete colonoscopy was described for relatives by specialist.Complete colonoscopy with anesthesia was performed by an specialist doctor and experienced team. Data were analyzed using SPSS software and statistical tests such as Mann Whitney U, T test and X2-test and $P<0.05$ was considered significant.

Results

The relatives of 27 major patients with colorectal cancer who had the Amsterdam criteria in clinical history but did not show any defect in the expression of repair proteins in their screening tests, including MMR and MSI, were randomly selected and their first- and second-degree relatives were invited to evaluate the colon. The mean age of these patients was 52±7.2 years, 55% of whom were male and 45% were female. Eleven tumors (41%) were located in different parts of the colon and the rest (59%) were located in rectosigmoid. More than 60% of the tumors were in the first and second stages and 33% of the patients died. Medical records and biopsy data showed that 13 people (18%) of these patients had a history of gastric malignancies, uterine polyp or colon polyp and the rest had no malignancy in their records. The mean age of diagnosis in the relatives group was 44±5.3 years, and most of them had received chemotherapy in addition to surgery, indicating a high tumor stage at the time of diagnosis. 16 relatives (21%) had colonoscopy, 13 relatives (17%) had endoscopy and 6 relatives (7.8%) had pelvic and abdominal ultrasound. In 64 cases (82%) of relatives no previous malignancies were reported and in 7 cases (9%) of relatives had polyps or tumors already. 78% of participants in the study had colon cancer in their family history and 22% of participants in the family had ovarian cancer in addition to colon cancer. 47% of participants had two patients in the family, 30% had 3 cases and 23% had more than 3 cases in the family. In 31% of the participants, the patient was their first family members and in 45% of the participants, the patient was their first and second family members. In this study, 63% of cases were in the first and second stage of tumor and 36% in stage 3 and 4. Colonoscopy revealed that 18 of 77 patients (23%) had polyps or tumors in their colon, 55% of polyps were hyperplastic and the rest were adenomas (Table 1).

About 60% of polyps were in the rectum and sigmoid and the rest in the colon and cecum. In 67% of cases the polyp size was less than 5CM and in 33% the polyp size was more than 5 CM . Also, 4 patients in this screening showed tumors in their colon that were all newly diagnosed and in 2 patients IBD was diagnosed in this screening. 57 people (74%) had normal colon and 18 people had (23%) polyps. In 12 patients with polyps (66%), the number of polyps was 1 to 2 and in 6 cases (33%) more than 2 polyps were observed (Table 1). In this study, 15 patients (55%) underwent surgery only and 12 patients (45%) underwent surgical and sidelong treatment.

Table 1. Colon evaluation results of 18 abnormal relatives

Variable	Subgroup	Number (Percent)
Polyp type	Adenoma	8(44)
	Hyperplastic	10(55)
Polyp place	Colon and Cecum	7(39)
	Rectosigmoid	11(61)
Polyp size	Less than 5	12(67)
	More than 5	5(33)
Number of polyps	1 to 2	12(66)
	More than 2	6(33)

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Discussion

In this study, 21.5% of patients had a history of inflammatory bowel disease, indicating the importance and prevalence of inflammatory bowel cancer (CAC). Iravani et al. in a study conducted in middle-risk individuals, approximately 26% of people with intestinal polyps accounted for nearly half of the hyperplastic polyps and 15% of adenocarcinoma polyps (13). In the above study, nearly 30% of patients were younger than 50 years old and more importantly 70% were diagnosed over 50 years old. In this study, most tumors were in distal with a small percentage in the proximal and 90% of them had non-mucinous phenotype. In this study, 30% of cancers were by screening, and the most common complication was rectal bleeding (13).

In the Fakheri et al. study, a total of 70 patients had a family history of colorectal cancer. Also, 38% of patients less than 45 years old had right colon involvement and 38% had left colon involvement (14). Hunt et al.,in a study of 110 patients with a history of colorectal cancer in 3 of the relatives, observed dysplastic and metastatic polyps in two cases. In this study, there were 3 lesions in the right colon, 5 lesions in the left and 5 lesions in the rectum (15).

In our study, 11 tumors (41%) were located in different parts of the colon and the rest (59%) were in rectosigmoid.In 2006, Pahlavan et al., Retrospectively studied all cases of colorectal cancer registered in Tehran's reference hospitals. In this study, 200 patients (57%) were males and 43% were females with a mean age of 55.15±14.5 years and 16.5% of patients were younger than 40 years (16). In a study in Shiraz, clinical features of 491 patients with malignancy were evaluated; the majority (57.2%) of the patients were males and 23% of the population were under 45 years old and 32% were over 65 years old. Also, 27% of patients in their first-degree family had a history of colorectal cancer. However, the most common complication in this study was abdominal pain (60.7%). The study also found that nearly half of the tumors had a good pathological phenotype (17), which was 40% in our study. In the study of Mahmodlou et al., clinical and demographic data of 546 colorectal cancer patients collected from private and educational hospitals in Urmia, mean age was 55.2±11.5 years, 23% of patients were less than 40 years old. Rectal involvement with a prevalence of nearly 45% was the most important finding in this study. The incidence of tumors at different stages of involvement was 6%, 37%, 33% and 24% for the first to fourth stages, respectively (18). In a study of 218 patients, Golfam et al reported that 60% of CRC cases were in the rectum and sigmoid was in the second stage with 17%, and the incidence of tumor in the transverse colon is one of the few (19).

Ghanadi et al. evaluated the file of 112 diagnosed patients and found that the most common sites of involvement were sigmoid in men (40%) and rectal and sigmoid in women (34.6% each). It has also been shown in the study that most tumors are in the left intestine and the incidence of colorectal cancer in first-degree relatives of patients is high, therefore, controlling the disease by obtaining a pedigree is very useful and practical (20).

In our study, 59% of patients had rectosigmoid involvement. In 61% of cases, the site of polyp involvement in close relatives was rectosigmoid. Contrary to our study, in 2005 Mahdavinia et al compared tumor location in colorectal cancer with starting at an early age and beginning at an old age, which did not find a significant difference between tumor location in these two groups. Also, nearly 30% of colorectal cancer patients who were young, in their first degree family, they had a history of colorectal cancer (21). Nikbakht et al reported in their study that in 27 patients (22.5%) colorectal cancer were seen in a relative (22).

In this study, 21.5% of patients had a history of inflammatory bowel disease, indicating the importance and prevalence of colorectal cancer due to inflammation. Type X colorectal cancer may be genetically different from Lynch Syndrome and these patients are less likely to have extra-intestinal involvement than patients with Lynch syndrome, but in terms of colon polyps, the families of these patients appear to be at high risk like those of Lynch syndrome families and need regular colonoscopic care.

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