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Opportunistic Screening for Colorectal Cancer

Xu An-gao
Huizhou Medicine Institute, Huizhou First Hospital, Guangdong
China

1. Introduction

Two major screening models are currently available in the world for colorectal cancer: systematic screening and opportunistic screening. Systematic screening covers all segments of the population in a certain area and requires the participation of specialized institutions and professionals as well as huge financial support. It is a population-based active screening. Opportunistic screening targets those who seek medical treatment and screens for disease of interest during patients' treatment or examination. Compared with systematic screening, opportunistic screening has the advantages of good compliance and no need for additional examination with slightly increased cost. The key to opportunistic screening for colorectal cancer is to identify the population at high risk for colorectal cancer and determine who need such screening. The criteria for identification of high-risk population for colorectal cancer include mainly family history, personal history, laboratory testing, and age: ① hereditary non-polyposis colorectal cancer (HNPCC) family members aged ≥ 10 years; ② individuals with first-degree relatives with familial polyposis aged ≥10 years; ③ individuals with first-degree relatives with colorectal cancer and aged ≥ (the age of the diagnosis of colorectal cancer in the affected relatives minus 10 years) (i.e. first-degree relatives who are 10 years younger than a colorectal cancer patient are at high risk for the cancer. For example, the first-degree relatives aged 50 years or older of a 60-year-old colorectal cancer patient are high-risk population for colorectal cancer.); ④ previous history of colorectal cancer or colorectal adenoma; ⑤ ulcerative colitis or Crohn's disease unhealed for more than 10 years; ⑥ history of biliary tract disease or cholecystectomy for more than 10 years; ⑦ history of lower abdominal radiotherapy for more than 10 years; ⑧ history of chronic schistosomiasis in the colon; ⑨ history of chronic appendicitis; ⑩ unexplained positive fecal occult blood test; ⑪ unexplained elevated serum CEA level; and ⑫ age of 50 years and older.

Development of screening models for colorectal cancer depends on disease risk stratification of individuals in the population. The risk of colorectal cancer development in individuals in a natural population with no symptoms of colorectal cancer is stratified into four levels: ① Level III high risk. Individuals in this subgroup have the highest risk and about 5% of colorectal cancer cases occur in this population, who should undergo screening every 3 months to 1 year. ② Level II high risk. About 15-20% of colorectal cancer cases occur in this population, who should undergo screening every 1 to 5 years. ③ Level I high risk. About 70% to 80% of colorectal cancer cases occur in this population, who should undergo screening at a frequency of 5 to 10 years. Stratifying the population at high risk for colorectal

cancer into levels I, II, III high-risk subgroups will help choose screening methods and the timing of screening. ④ Low-risk subgroup. This population is at low risk for colorectal cancer and no screening is thus needed.

Major screening methods for colorectal cancer include digital rectal examination, fecal occult blood test, sigmoidoscopy, full colonoscopy and genetic testing. Full colonoscopy can serve as the preferred modality for opportunistic screening for colorectal cancer. If full colonoscopy is performed only after the discovery of distal colorectal tumor via sigmoidoscopy, there will be a missed diagnosis rate of 72.0%.

Our study shows that by performing opportunistic screening among high-risk populations, the average direct cost for each detected case of colorectal cancer is about 50,000 RMB yuan, four times less than the cost of systematic screening. For each detected case of colorectal tumor (cancer and adenoma combined), the direct cost of opportunistic screening on average is 2,000 RMB yuan. These data show favorable cost-effectiveness of opportunistic screening for colorectal cancer. In addition, of the colorectal cancers detected among high-risk populations, the proportion of colorectal cancers staged at Duke's A and B is 45% and 33% respectively. In contrast, of the colorectal cancers detected among symptomatic hospital-visiting patients, the proportion of colorectal cancers staged at Duke's A and B is 4% and 29%, respectively. Previous research has established that the 5-year survival rate following surgery of Dukes' A colorectal cancer can reach as high as 90%, which demonstrates the good social benefit of opportunistic screening.

Worldwide, the incidence rate of colorectal cancer ranks only after lung cancer and breast cancer. Overall, colorectal cancer accounts for 9% and 10% of malignant tumors in men and women respectively. Colorectal cancer thus poses a serous public health problem and increases greatly the burden of disease. In recent two decades, the incidence and mortality rates of colorectal cancer in the world increase significantly, with the incidence rate increasing from an annual average of about 2% to 6.4% and the average mortality rate increasing by 3.3% annually.

Currently, the incidence rate of colorectal cancer in China is 16.3/100,000 for men, 12.2/100,000 for women, and 14.2/100,000 for the whole population. The mortality rate of colorectal cancer in China is 8.0/100,000 for men, 5.9/100,000 for women, and 6.9/100,000 for the whole population. In recent years, with changes in lifestyle, dietary structure, and environment in China, the incidence and mortality rates of colorectal cancer are on the rise and its incidence rate ranks the fourth in malignant tumors. Its incidence rates in the 1990s increased by 31.9% in urban areas and 8.5% in rural areas as compared with the incidence rates in the 1990s. It is expected that colorectal cancer cases will be nearly doubled by 2030, with 400,086 new cases and 211,714 deaths.

Because colorectal cancer often presents no symptoms in the early stage, patients do not seek timely medical treatment. By the time clinical symptoms of colorectal cancer appear, their condition will usually have progressed to intermediate or advanced stages which are associated with increased disease burden and poor prognosis. Previous studies suggest that at least 80% of colorectal cancers derive from colorectal adenoma and that the transition from colorectal adenoma to colorectal cancer lasts over 5 years, with an average of 10 to 15 years, which makes early detection of lesions through screening possible. Considerable evidence based on research has confirmed that colorectal cancer screening in the population can identify precancerous disease and precancerous lesions of colorectal cancer as well as early colorectal cancer. Treatment can be prescribed, thereby reducing the incidence and mortality rates of colorectal cancer, and economic burden of colorectal cancer.

Population at risk of colorectal cancer has a likelihood of colorectal cancer development 2 to 4 times higher than the general population. High-risk population screening is an important part of secondary prevention of colorectal cancer. The focus of current medical model is shifting towards "early prevention". Strengthening the screening of colorectal cancer will contribute to "early prevention" and early diagnosis and early treatment, and will ultimately improve 5-year survival rate of colorectal cancer patients.

1.1 Overview

Two major screening models are currently available for colorectal cancer: systematic screening and opportunistic screening. Systematic screening covers all segments of the population in a certain area and requires the participation of specialized institutions and professionals as well as huge financial support. It is a population-based active screening. Opportunistic screening targets those who seek medical treatment and screens for disease of interest during patients' treatment or examination. Compared with systematic screening, opportunistic screening has the advantages of good compliance and no need for additional examination with slightly increased cost. Therefore, opportunistic screening among the population at high risk of colorectal cancer is feasible and also of great significance for early diagnosis of colorectal cancer. Opportunistic screening can be performed at outpatient departments or health examination centers, with no need of special financial support or additional personnel. Hence, it is individual-based passive screening. Our study shows that for each detected case of colorectal cancer, the average direct cost of systematic screening is about four times as much as that of opportunistic screening.

The main targets of opportunistic screening can be divided into three categories: ① individuals seeking health examination in the hospitals (community or health examination centers); ② individuals seeking medical treatment for disease other than colorectal cancer but having high risk factors for colorectal cancer (individuals present no clinical manifestations of colorectal tumors but have definite positive family history or personal history); ③ outpatients with no symptoms of colorectal cancer.

2. Definition of high-risk population for colorectal cancer

High-risk population refers to a group of individuals at high risk of a certain disease. Currently there is no unified definition of high-risk population for colorectal cancer in the international community. In general, identification of high-risk population for colorectal cancer is conducted by integrating family history, personal history, laboratory tests and age.

Family history

1. hereditary non-adenomatous colorectal cancer (HNPCC) family members aged ≥ 10 years;
2. first-degree relatives with familial polyposis aged ≥ 10 years;
3. individuals with first-degree relatives with colorectal cancer and aged ≥ (the age of the diagnosis of colorectal cancer in the affected relatives minus 10 years) (i.e. first-degree relatives 10 years younger than the colorectal cancer patient are high-risk population. For example, the first-degree relatives aged 50 years or older of a 60-year-old colorectal cancer patient are high-risk population for colorectal cancer.);

Personal History

4.   previous history of colorectal cancer or colorectal adenoma;
5.   ulcerative colitis or Crohn's disease unhealed for more than 10 years;
6.   history of biliary tract disease or cholecystectomy for more than 10 years;
7.   history of lower abdominal radiotherapy for more than 10 years;
8.   history of chronic colonic schistosomiasis;
9.   history of chronic appendicitis;

Laboratory tests

10. unexplained positive fecal occult blood test;
11. unexplained elevated serum CEA level;

Advanced age

12. age of 50 years and older.

Subjects presenting any one or more of the following symptoms are symptomatic of colorectal cancer and diagnostic testing is indicated. ①altered bowel habits (diarrhea, constipation, etc.); ② stool changes (thinning stool, blood stool, mucus stool, etc.); ③ tenesmus (feeling of unsatisfied defecation); ④abdominal mass; ⑤intestinal obstruction; ⑥ unexplained lower abdominal discomfort or abdominal pain; ⑦unexplained anemia; ⑧ unexplained weight loss or systemic cancer symptoms (such as fatigue, fever, etc.).

Subjects less than 50 years of age who do not meet the criteria of colorectal cancer high-risk populations and present no symptoms of colorectal cancer have low risk of colorectal cancer development and no screening is needed. If screening is required by an individual, fecal occult blood test in conjunction with colonoscopy can be employed.

3. Risk stratification of high-risk colorectal cancer populations

To achieve good cost-effectiveness and feasibility, screening can be performed in the population with high prevalence. Usually there are three ways of looking for population with high prevalence: ① questionnaire-based search for high-risk groups. High-risk populations are more likely to develop a certain disease than asymptomatic populations; ② conducting screening among a group of subjects with a particular clinical symptom or who are positive for a certain test; ③ conducting opportunistic screening at outpatient departments of hospitals or community medical centers. No matter which method is chosen, risk stratification of individuals is the first step of screening. On the basis of previous studies at home and abroad, we stratify the risk of asymptomatic individuals developing colorectal cancer into four levels. 1. Level III high risk. Individuals in this subgroup have the highest risk, who include ①HNPCC family members aged ≥ 10 years; ② individuals with first-degree relatives with familial polyposis aged ≥10 years; ③ ulcerative colitis or Crohns disease unhealed for more than 10 years. About 5% of colorectal cancer cases occur in the level III high-risk population. 2. Level II high risk. Subjects at level II high risk of colorectal cancer include: ① individuals with history of colorectal cancer; ② individuals with history of colorectal adenoma; ③ individuals with first-degree relatives with colorectal cancer and aged ≥ (the age of the affected relatives minus 10 years); ④ individuals with first-degree relatives with colorectal adenoma and aged ≥ (the age of the affected relatives minus 10 years);⑤ individuals with cholecystectomy performed more than 10 years ago; ⑥individuals with history of lower abdominal radiotherapy for more than 10 years；⑦

individuals with chronic colonic schistosomiasis; ⑧ individuals with chronic appendicitis。 About 15-20% of colorectal cancer cases occur in the level II high-risk population. 3. Level I high risk. Individuals at this risk level refer to a group of subjects who have an age of 50 years and older, present no colorectal cancer symptoms, and do not meet the criteria of levels II and III high-risk populations. About 70% to 80% of colorectal cancer cases occur in the level I high-risk population. Stratifying the population at high risk for colorectal cancer into levels I, II, III high-risk subgroups will help choose screening methods and the timing of screening. 4. Low-risk subgroup. Individuals at this risk level refer to a group of subjects under 50 years who have no symptoms of colorectal cancer and do not meet the criteria of levels II and III high-risk populations. This population is at low risk of colorectal cancer and no screening is thus needed.

4. Strategies of opportunistic screening for colorectal cancer

A complete colorectal cancer screening program should include determination of the population to be screened, the choice of screening methods, screening monitoring of different populations. There are various methods available for colorectal cancer screening and there is no generally accepted consensus worldwide as to which method is to be chosen and what program is most effective. American Cancer Society (ACS), United States Preventive Service Task Force (USPSTF), US Multisociety Task Force On Colorectal Cancer, American Society for Gastrointesinal Endoscopy (ASGE) and National Comprehensive Cancer Network (NCCN) have issued their own colorectal cancer screening guidelines [2-5]. The United Kingdom, Canada, and China also have developed their own screening guidelines. On the basis of these aforementioned guidelines, we developed an opportunistic screening program for colorectal cancer.

Risk stratification	Starting time of screening	Frequency of colonoscopy
I. Level I high risk		
1. More than 50 years old	50 years old	Every 10 years
II. Level II high risk		
2. Family history of colorectal cancer		
①First-degree relatives developing colorectal cancer at an age <60 years	40 years old or 10 years earlier than the age of onset of the youngest affected relative	Every 3-5 years if the first colonoscopy is normal
②First-degree relatives developing colorectal cancer at an age ≥60 years	40 years old	Every 3-5 years if the first colonoscopy is normal
3. Family history colorectal adenoma		
①First-degree relatives developing colorectal adenoma at an age <60 years	40 years old or 10 years earlier than the age of onset of the youngest affected relative	Every 5 years if the first colonoscopy is normal

Risk stratification	Starting time of screening	Frequency of colonoscopy
②First-degree relatives developing colorectal adenoma at an age ≥60 years	Individually determined	Every 10 years if the first colonoscopy is normal
4. Personal history of colorectal cancer ①Personal history of colon cancer	One year after surgical resection of the cancer	Re-examination at the 3rd year if the first one is normal and later every 5 years
②Personal history of rectal cancer	One year after surgical resection of the cancer	Re-examination at the 4th year if the first one is normal and later every 5 years Every 3-6 months in the first 2-3 years following low resection when no pelvic radiotherapy or mesorectal excision is performed
5. Personal history of colorectal adenoma ①Colonic adenomas ≤2, diameter <1cm and mild atypical hyperplasia	Not earlier than 5 years after surgery	Every 5 years
②Advanced tumors or adenomas >3	One year after surgery	Every 3 years
③Villous adenoma accompanied by possible incomplete excision	Within 2-6 months after surgery	Every 3 years
6. Cholecystectomy performed more than 10 years ago	At the time of knowledge	Every 5 years
7. History of lower abdominal radiotherapy performed more than 10 years ago	At the time of knowledge	Every 5 years
8. Chronic colonic schistosomiasis	At the time of knowledge	Every 5 years
9. Chronic appendicitis	At the time of knowledge	Every 5 years
III. Level III high risk		
HNPCC family history	20-25 years old or 10 years earlier than the age of onset of the youngest family member	Every 1-2 years and every 1 year after 40 years old
FAP family history ①Genetic test of FAP proband (+)		
Genetic test of FAP relatives (+)	10-12 years old	Every 1 year and, if no polyp is present, every 1 year until the age of 40 years. Then every 3-5 years.

Risk stratification	Starting time of screening	Frequency of colonoscopy
Genetic test of FAP relatives (-)	10-12 years old	Every 7-10 years until the age of 40 years. Then every 5 years.
②Genetic test of FAP proband (-)	10-12 years old	Every 1 year and, if no polyp is present, every 1 year until the age of 40 years.Thereafter, every 3-5 years.
Inflammatory bowel disease (ulcerative colitis or extensive Crohn's colitis)	10 years after onset	Every 1-2 years

Note: HNPCC: hereditary non-polyposis colorectal cancer; FAP: familial adenomatous polyposis

Table 1. Opportunistic screening programs for colorectal cancer

5. Screening methods and benefits

Screening methods for colorectal cancer mainly include digital rectal examination, fecal occult blood test, sigmoidoscopy, full colonoscopy and genetic testing. We recommend full colonoscopy as the preferred examination for opportunistic screening of the population at high risk of colorectal cancer. This recommendation is based on the following reasons. First, colonoscopy is needed to reach a definite diagnosis when other screening methods are positive. Second, colonoscopy is the only screening modality capable of both diagnosis and treatment. Third, if colonoscopy is performed only after distal colon cancer is found with sigmoidoscopy, there will be a missed diagnosis rate of 72.0%. If full colonoscopy cannot be used as the examination of choice for screening subjects, immunoassay fecal occult blood test can be performed daily for three consecutive days and, if positive, full colonoscopy can be then conducted.

A total of 3704 high-risk subjects were screened using full colonoscopy and 807 patients with colorectal tumors were identified, including 11 with colorectal cancer and 796 with colorectal adenomatous polyps, with a detection rate of colorectal tumor 22.8% and a detection rate of colorectal cancer 0.3%. Compared with the diagnosis of the 2675 subjects with colorectal cancer symptoms who sought medical help at the gastrointestinal departments, Dukes' A and B stage colorectal cancers accounted for 45% and 33% (78% combined) of the colorectal cancers detected in the high-risk population respectively whereas Dukes' A and B stage colorectal cancers accounted for 4% and 29% (33% combined) of the colorectal cancers detected in the symptomatic subjects seeking medical help at hospitals. This indicates that screening among high-risk population is an effective way for early detection of colorectal cancer. Previous research has established that the 5-year survival rate of Dukes' A colorectal cancer following surgery can reach as high as 90%, showing colorectal cancer screening will greatly enhance the survival rate of patients and yield good social benefits.

Our series of studies have shown that for every detected case of colorectal cancer, the average direct cost of systematic screening is 200,000 RMB yuan whereas the average direct cost of opportunistic screening is only about 50,000 RMB yuan, 4 times less than the cost of systematic screening. For each detected case of colorectal tumor (cancer and adenoma), opportunistic screening costs 2,000 RMB yuan on average. This shows the great economic benefit of opportunistic screening for colorectal cancer.

6. Issues and suggestions

Screening should cover more of the target population. The biggest drawback of opportunistic screening is that only those who seek medical help at hospitals or undergo health examination are screened while those potential patients who do not seek medical treatment are excluded from the screening. Therefore, some high-risk populations may be missed during the screening and the effectiveness of the screening is thus impaired. We can step up the publicity of screening programs, use information systems to manage residents' health records, keep track of personal information of those who do not undergo screening, and then invite them for screening. By doing so, more of the target population may be covered.

The awareness of the significance of screening on the part of patients and physicians needs to be improved. Adequate education and training are necessary for the success of opportunistic screening, which can raise the awareness of screening among patients and physicians, particularly the latter. Mandel et al. reported that with physicians' consultation and advice, 81% of FOBT-positive patients were willing to accept subsequent colonoscopy. Therefore, to improve screening efficiency, it is of considerable importance to educate general practitioners and gastroenterologists about the importance of screening. At present, most of the colorectal cancer screening work is done by community physicians and other first-line medical staff, who often lack knowledge and training in epidemiology. Studies have shown that community health providers in the U.S. often base their choice of colorectal cancer screening programs on patients' wishes, rather than following relevant national screening guidelines. Therefore, education among medical practitioners about the importance of screening and the establishment of specialized agencies responsible for guidance and monitoring of colorectal cancer screening may help clinicians to implement and enforce screening guidelines.

Government support is not enough. Many countries now have no comprehensive national statistics for colorectal cancer screening and thus can not develop a national screening strategy. The high cost of screening is also an important factor that reduces patients' compliance. Accordingly, we call upon the attention of our society and government for colorectal cancer screening, strive for the support of the national basic medical insurance, and advocate the coverage of colorectal cancer screening by medical insurance. These efforts will help us to carry out large-scale screening programs for colorectal cancer to achieve early diagnosis and early treatment.

7. Summary

Natural population screening and opportunistic screening are two screening models currently prevalent in many countries. Although both screening programs are intended to reduce cancer incidence and mortality rates, they are different in many aspects, especially in their anti-cancer strategy. Population-based screening programs have been mainly conducted as a preventive policy in local regions with government support. It needs responsibility for the program's implementation, such as population registration and quality assurance follow-up and evaluation. In this regard, natural population screening in many countries has not yet evolved into mature systematic screening. In contrast, opportunistic screening depends on individual members of a certain population requesting screening or their health advisors recommending screening. Although there is no conclusive evidence about its effectiveness, it has been implemented in clinical settings in different modes and holds great promise for clinical application.

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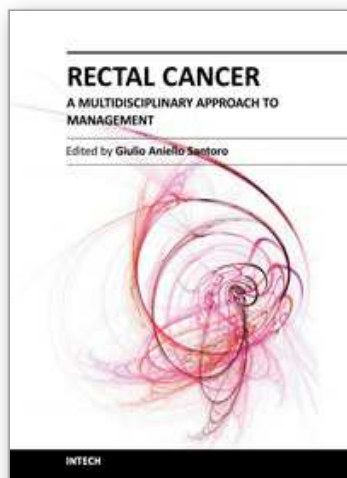
Rectal Cancer - A Multidisciplinary Approach to Management
Edited by Dr. Giulio A. Santoro

Dramatic improvements in medicine over the last few years have resulted in more reliable and accessible diagnostics and treatment of rectal cancer. Given the complex physiopathology of this tumor, the approach should not be limited to a single specialty but should involve a number of specialties (surgery, gastroenterology, radiology, biology, oncology, radiotherapy, nuclear medicine, physiotherapy) in an integrated fashion. The subtitle of this book "A Multidisciplinary Approach to Management" encompasses this concept. We have endeavored, with the help of an international group of contributors, to provide an up-to-date and authoritative account of the management of rectal tumor.

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