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Total Colonoscopy Detects Early Colorectal Cancer More Frequently than Advanced Colorectal Cancer in Patients with Fecal Occult Blood

Takuji Ozaki[1,2], Akira Tokunaga[1,2], Naoto Chihara[1,2],
Masanori Yoshino[1,2], Hideki Bou[1,2], Masao Ogata[1,2],
Masanori Watanabe[1,2], Hideyuki Suzuki[1,2] and Eiji Uchida[1]

[1]Surgery for Organ Function and Biological Regulation, Graduate School of Medicine, Nippon Medical School
[2]Institute of Gastroenterology, Nippon Medical School Musashi Kosugi Hospital

Abstract

The efficacy of total colonoscopy following a positive result of the fecal occult blood test (FOBT) for the early detection of colorectal cancer and polyps was evaluated. A total of 1,491 patients with positive FOBT results underwent total colonoscopy at the Institute of Gastroenterology, Nippon Medical School, Musashi Kosugi Hospital, from April 2002 through July 2009. Abnormalities were found in 1,312 of the 1,491 patients (88.0%). Ninety-six of the 1,491 patients (6.4%) were found to have early cancer, but 59 patients (4.0%) were found to have advanced cancer. The early cancers were treated with endoscopic mucosal resection or endoscopic submucosal dissection in 81 patients, with laparoscopy-assisted colectomy in 10 patients, and with open surgery in 5 patients. Fifty-one of the 59 patients with advanced colorectal cancer underwent conventional open surgery, and 8 patients underwent laparoscopic surgery. The cancers detected were more likely to be early cancers than advanced cancers. In addition to malignancies, other abnormalities found included inner or external hemorrhoids, diverticula of the colon, ulcerative colitis, ischemic colitis, infectious colitis, and colorectal polyps. Our results show that a high percentage of lesions detected with total colonoscopy following a positive FOBT result are early colorectal cancers and polyps.
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Key words: fecal occult blood test, total colonoscopy, colorectal cancer surveillance

Introduction

The incidence of colorectal cancer has increased with the westernization of diets in Japan. Screening examinations for colorectal cancer have been established in Japan, and many people have undergone secondary prevention measures as a result of early detection using a variety of means. Most screening programs involve an endoscopic examination or contrast enema radiography as a secondary screening method after immunologic fecal

Correspondence to Takuji Ozaki, MD, Institute of Gastroenterology, Nippon Medical School Musashi Kosugi Hospital, 1−396 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211−8533, Japan
E-mail: Otakuji0128@aol.com
Journal Website (http://www.nms.ac.jp/jnms/)

occult blood tests (FOBTs) have been performed. Randomized studies performed outside Japan have confirmed reductions in colorectal cancer mortality as a result of screening with FOBTs[3-19]. A variety of reports have also been published in Japan[20-24] since the implementation of colorectal cancer screening using FOBTs in 1992 as a result of the Health and Medical Services for the Aged Law[25]. Because the immunologic FOBT specifically reacts with human hemoglobin alone, dietary or oral medication restrictions are not necessary, and this test is an excellent screening method for asymptomatic individuals. The manual recommended by the Ministry of Health, Labour and Welfare and the Japanese Society of Gastroenterological Mass Survey stipulates that a detailed examination be performed in individuals with positive test results, even when the result of only 1 of the 2 tests is positive. Thus, it is desirable to conduct a detailed examination using such methods as contrast enema radiography and endoscopy in any person with at least 1 positive test result. The secondary screening examination used in persons with a positive FOBT during a screening examination for colorectal cancer varies with the facilities and staffing at individual institutions[23]. At some institutions, contrast radiography, a combination of sigmoidoscopy and contrast enema radiography, is most often performed[26]; however, the Ministry of Health, Labour and Welfare recommends that total colonoscopy be performed if possible, because of the advantages of superior sensitivity and diagnostic power and the ability to perform tissue examinations and endoscopic therapy simultaneously during examinations[27,28]. Colorectal examinations, including the necessary preparations, causes patients discomfort, and because avoiding a second colonoscopic examinations is desirable, total colonoscopy is performed, in principle, as a secondary examination at our hospital the first time a positive FOBT result is obtained. The number of reports describing a tendency for cancer of the right colon has increased in recent years[29], and 1 report has even suggested that fecal occult blood reactions are more sensitive for the right colon, where mingling with the feces occurs more easily[30], once again suggesting the usefulness of a total colonoscopy as a secondary screening examination. The FOBT is convenient and inexpensive, but detection of cancer lesion is impossible unless it bleeds, and the test has the additional drawback of detecting hemorrhoid bleeding. Moreover, both false-positive and false-negative results are impossible to avoid. The FOBT has some limitations, and reliable screening for early colorectal cancers, which rarely bleed, is impossible. A variety of other potential screening methods, such as genes studies and the use of markers other than hemoglobin, have been assessed, but a dependable alternative to the FOBT has not yet been found. The detection of early-stage colorectal cancer is highly desirable because of its curability. The present study was designed to determine whether early-stage colorectal cancer could be detected more frequently with total colonoscopy following a positive FOBT result.

Patients and Methods

Patient Characteristics

A total of 1,491 patients (773 male and 718 female) underwent total colonoscopy after receiving a positive FOBT result from April 2002 through July 2009. The patients who had a positive FOBT result and definite bleeding based on a rectal examination or other examination underwent total colonoscopy on the same day or on the following day; as a rule, asymptomatic patients with a positive FOBT result were thoroughly examined within 2 weeks to 1 month. In accordance with the 3rd edition of the Gastrointestinal Endoscopy Guidelines[1] we confirmed the patient's history, present medical conditions (such as pacemaker, asthma, glaucoma, prostatic hyperplasia, liver cirrhosis, allergies, hemorrhagic diathesis, and pregnancy), and oral medications, including anticoagulants, and antiplatelet drugs. After the patient consulted a specialist, a decision was made as to whether any present medications could be temporarily discontinued; if discontinuation was possible, the patient was instructed as to how long the medication should not be taken. A medical database containing the retrospectively documented characteristics of the enrolled patients was analyzed.

Endoscopic Techniques

The endoscopic procedures were performed by 6 faculty gastrointestinal (GI) endoscopists, who were certified as specialists in colonoscopy by the Japan Gastroenterological Endoscopy Society. Endoscopic diagnosis was performed on the basis of the observation of the endoscopic films by 2 specialists in GI endoscopy.

Informed Consent

We obtained written informed consent after an oral explanation of the need for the test, the adverse effects of the preparations and premedication, the types and frequency of possible complications, and the methods for managing such complications. If the patient was a minor or elderly person, we provided an explanation to the family and obtained their consent.

Preparation before Colonoscopy

The preparations for the examination consisted of, first, confirming the absence of symptoms of stenosis before the patient received any medication. The patient was then asked to consume a test meal on the day before the examination and to take a laxative (Laxoberon®, 1 tablet; and Pursennid®, 4 tablets) before going to bed on the night before the examination. On the day of the examination, the patient was asked to drink an isotonic solution of magnesium citrate (Magcorol P®, 100 g dissolved in 1,800 mL of water) over a 2-hour period. We used an intestinal lavage solution (Niflec®, 2 L) in patients with nephropathy. If nausea or vomiting developed while the patient took the medication, administration was discontinued, and the adverse effect was managed by asking the patient to rest or by giving the patient an enema. For patients with severe constipation, we prescribed a mild laxative for several days before the examination and controlled defecation. If an elderly patients was unable to drink the lavage solution, we used the modified Brown method. In patients with massive bleeding followed by hemorrhagic shock, we performed the examination without any preparation or by administering an enema for emergency examinations, e.g., in cases of sigmoid volvulus, or in the active phase of ulcerative colitis.

Premedication

1）Spasmolytics

Before administering premedication, we checked for the presence of diseases, such as glaucoma, prostatic hyperplasia, and arrhythmias. To suppress colorectal motility we usually injected scopolamine butylbromide intramuscularly or intravenously. When scopolamine butylbromide was contraindicated, we either did not administer a spasmolytic or we used glucagon.

2）Sedatives and analgesics

In accordance with the patient's wishes or in cases in which adhesions after abdominal surgery or dolichocolon was present, we explained the complications, such as respiratory depression, respiratory arrest, associated with the use of sedatives and analgesics. After obtaining consent, we used sedatives or analgesics on the condition that a family member was present during the examination. Emergency equipment and intubation material were kept on hand, and access to a blood vessel was secured. The patient's blood pressure, pulse, and the partial pressure of oxygen were monitored throughout sedation or analgesia. We used pethidine hydrochloride as an analgesic and midazolam as a sedative. After the examination was completed, we confirmed definite awakening and allowed patients to leave the hospital after prohibiting them from operating a motor vehicle.

Complications

In cases with severe adhesions in which there was a high risk of perforation or in cases in which insertion was difficult, we performed a contrast enema examination. In cases of perforation, we performed, if possible, plication with clips, monitored the patient closely, and, when necessary, selected surgical treatment. In addition, if a colorectal polyp was identified during the colonoscopic screening examinations, we performed a biopsy of the polyp but did not perform a polypectomy on the day of the examination. At a later date, the patient was admitted overnight, and polypectomy was performed.
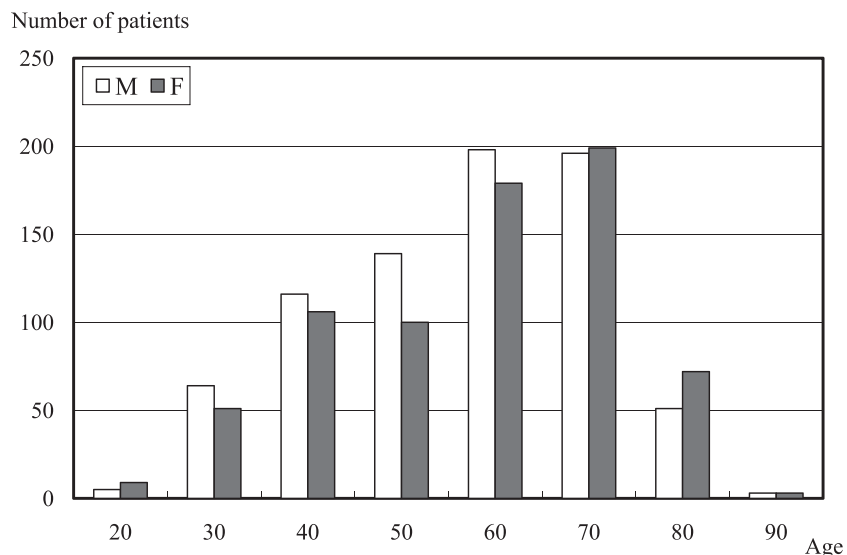
Number of patients

Fig. 1　Age distribution of patients who underwent total colonoscopy following a positive FOBT result. The open bars indicate the number of male patients, and the closed bars indicate the number of female patients.
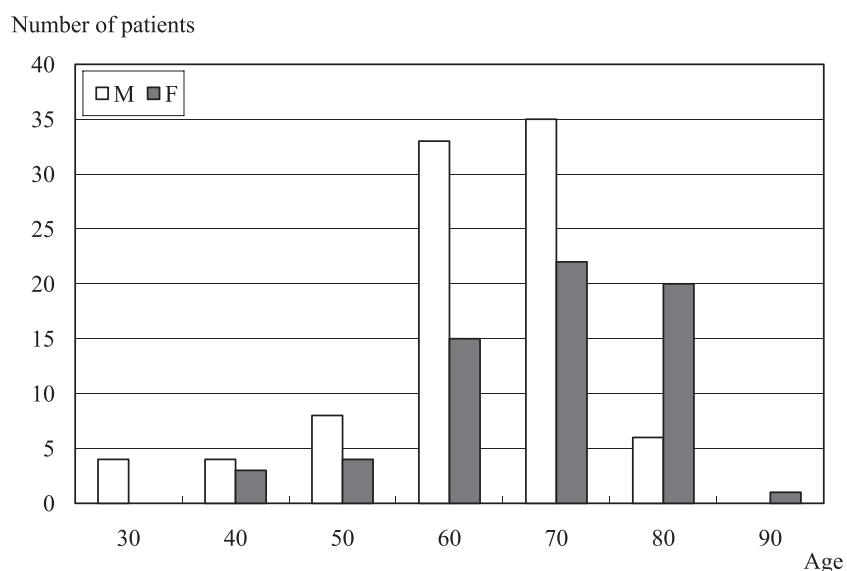
Number of patients

Fig. 2　Age distribution of cancer patients who had lesions detected with total colonoscopy following a positive FOBT result. The open bars indicate the number of male patients, and the closed bars indicate the number of female patients.

Clinicopathological Studies

The clinicopathological findings were described according to the Japanese Classification of Colorectal Carcinoma[2], and pathologic diagnosis was performed on the basis of the light microscopic observation of the specimen by 2 specialists in GI pathology.

Results

Total colonoscopy was performed in all 1,491 patients with a positive FOBT result, and malignant lesions were identified in 10.4% of the patients. The lesions consisted of early cancer in 96 patients and advanced cancer in 59 patients. According to the sites occupied by the lesions, 36.8% were in the right colon.

Age Distribution

The mean age of the patients with a positive FOBT result was 62.0 ± 14.2 years, with most of the patients in their 60s or 70s (**Fig. 1**). The mean age of the patients with cancer was 70.5 ± 10.2 years (**Fig. 2**).
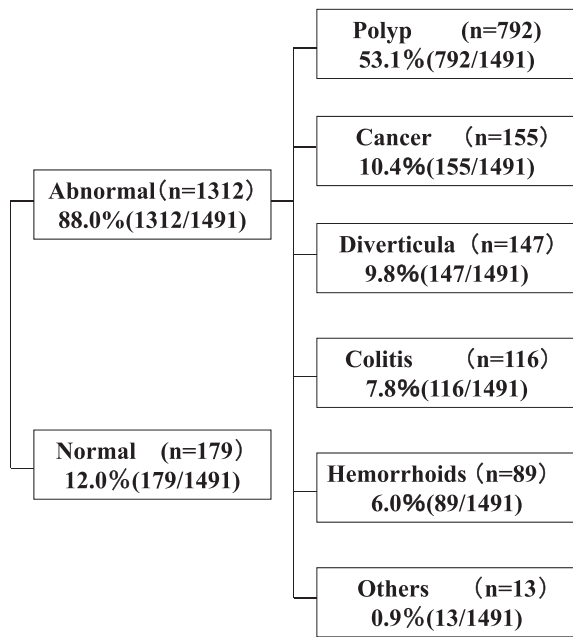
Disease Characteristics

The incidence of morbidity among patients undergoing total colonoscopy after receiving a positive FOBT result was 88.0%. The most common abnormality was colorectal polyps (53.1%), followed by colorectal cancer (10.4%), diverticula (9.8%), colitis (7.8%), and hemorrhoids (6.0%). Other abnormal findings, in decreasing order of frequency, were inflammatory bowel disease, internal hemorrhoids, and others (e.g., ulcers, fissures, and telangiectasia.) (**Fig. 3**). According to the Japanese classification for colorectal carcinoma, the disease was stage 0 in 73 cases (47.1%), stage I in 35 cases (22.6%), stage II in 19 cases (12.3%), stage IIIa in 17 cases (10.9%), stage IIIb in 4 cases (2.6%), and stage IV in 7 cases (4.5%); thus, a higher percentage of detected cancers were early-stage cancers than advanced cancers (**Fig. 4**). Endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) was performed for 81 patients with early-stage cancer. Laparoscopic surgery was performed for 10 patients with early cancer and 8 patients with advanced cancer. Open surgery was performed for 5 patients with early cancer and 51 patients with advanced cancer (**Fig. 4**).

Fig. 3 Diseases and their incidences of detection with total colonoscopy following a positive FOBT result.
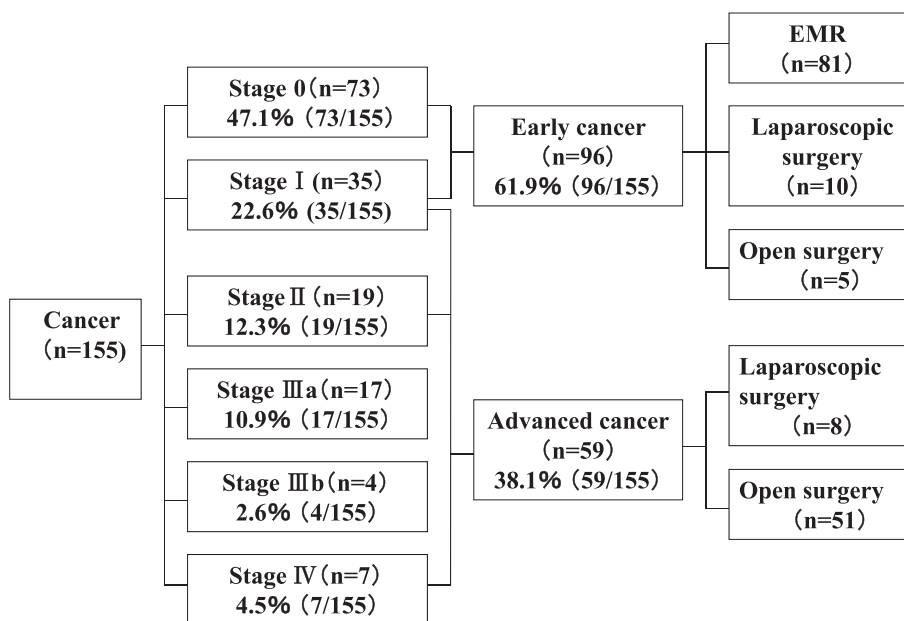
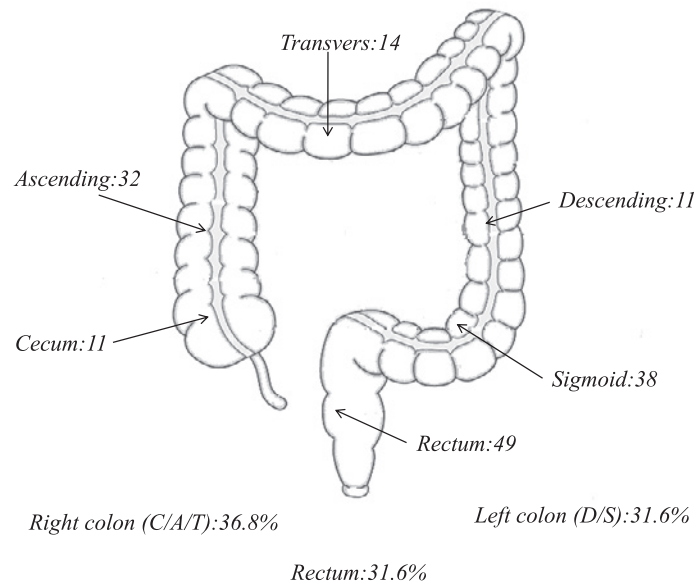Fig. 4 Treatment of cancer according to stage (Japanese Criteria).

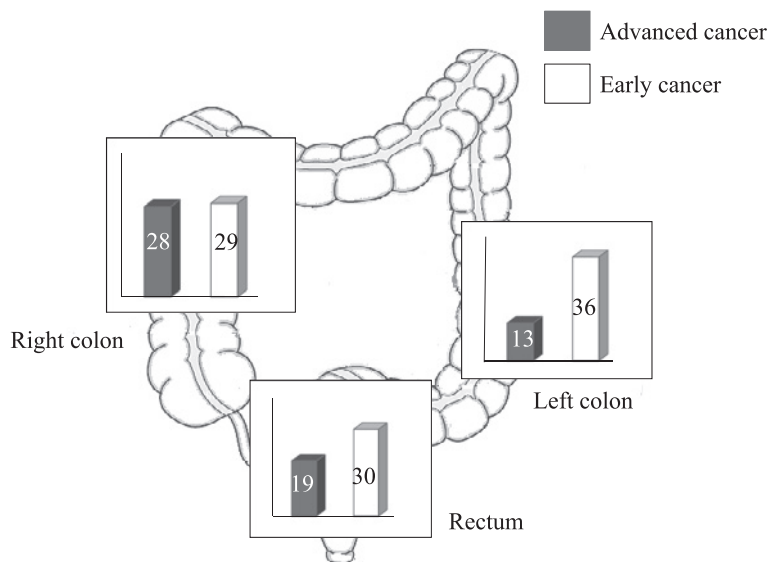Fig. 5 Location of colorectal cancers detected with total colonoscopy following a positive FOBT result.

Fig. 6 Depth of invasion of colorectal cancers detected with total colonoscopy following a positive FOBT result.

Location and Depth of Colorectal Cancer

Fifty-seven cases (36.8%) of colorectal cancer were located in the right colon (11 in the cecum, 32 in the ascending colon, and 14 in the transverse colon), 49 cases (31.6%) were in the left colon (11 in the descending colon, 38 in the sigmoid colon), and 49 cases (31.6%) were found in the rectum **(Fig. 5)**. Twenty-nine early cancers and 28 advanced cancers were detected in the right colon, 36 early and 13 advanced cancers were located in the left colon, and 30 early and 19 advanced cancers were found in the rectum **(Fig. 6)**.

Complications

The success rate for total colonoscopy was nearly 100%. No serious complications such as perforation, occurred in this series.

Table 1　Overview of screening results using fecal occult blood tests[13]

Variable	Mandel et al.[3,4]	Hardcastle et al.[8,9] Hardcastle and Justin[10]	Kewenter et al.[11,12]	Kronborg et al.[5-7]	Ozaki et al.
Study site	Minnesota	United Kingdom	Sweden	Denmark	Japan
Years of study	1975−1992	1981−1995	1982−present	1985−1995	2002−2009
Number of FOBT-positivity patients	4562	3210	3006	1400	1491
Probability of any colorectal cancer	2.2	9.9	5	17.2	10.4
Probability of early colorectal cancer	No available	7	3	14	6.4

Discussion

Because of its simplicity, low cost, and noninvasiveness, FOBT is widely recognized as a cost-effective and comprehensive screening test, and its use has been assessed in randomized trials. Nevertheless, its specificity and sensitivity are limited. A reduction in colorectal cancer mortality as a result of FOBT screening has been confirmed by reports of randomized studies performed all over the world[3-24]. Regarding the significance of FOBT for the detection of colorectal cancer, **Table 1** shows a comparison of previous results. According to the report of Ransohoff and Lang[13], the rate of finding any colorectal cancer ranges from 2.2% to 17.2%, while the rate of detecting an early colorectal cancer ranges from 3.0% to 14.0%. A positive screening result was associated with a rate of early colorectal cancer detection of about 7% in a trial performed in the United Kingdom and of 14% in a trial performed in Denmark. Moreover, the probability of finding early-stage colorectal cancer was about 3% in a trial performed in Sweden and was not reported in a Minnesota study. While the inspection methods differed in each country, in our hospital, FOBT is performed twice in each case, and a single positive result is regarded as an indication for a colonoscopy. The incidence of early cancer was 6.4% in the present study. Endoscopy, on the other hand, has been shown to be the best method for detecting colorectal cancer and its precursor lesions, polyps. Primary endoscopic screening is increasingly favored over the FOBT protocol.

The present study was designed to evaluate whether total colonoscopy performed after a positive FOBT result is useful for detecting early colorectal cancer. In this series, 792 patients were found to have colorectal polyps, and 155 patients (10.4%) were found to have colorectal cancer, consisting of 96 (6.4%) cases of early cancer and 59 (4%) cases of advanced cancer. More than 50% of the patients who underwent total colonoscopy had colorectal polyps, and 546 of the 792 patients (69%) underwent EMR or ESD. Total colonoscopy following a positive FOBT result has been shown to detect colorectal polyps, which have the potential to transform into cancer.

A major advantage of endoscopy is the potential for tissue sampling and interventional procedures[27,28]. Colonoscopic polypectomy has been shown to prevent colorectal cancer. Thirty-six percent of the colorectal cancers were located in the right colon: the cecum, ascending colon, or transverse colon. These results indicate that a sigmoidoscopy would be of limited use for detecting cancer in the right colon, especially advanced cancer; thus, total colonoscopy is strongly recommended. An increased incidence of cancers of the right colon and a decrease in rectal lesions have been reported[29]. One report has even concluded that the FOBT is more sensitive for detecting cancers of the right colon, where mingling with the feces is more likely to occur[30]. Endoscopic resection, including polypectomy, or mucosal and submucosal resection, was performed in 70% of the patients with colorectal polyps without any major complications. Furthermore, laparoscopic surgery, rather than open surgery, was selected for cases of early-stage cancer, and open surgery, rather than laparoscopic surgery,

was performed for most patients with advanced cancer. Among the patients with advanced cancer, 7 had stage IV metastatic colorectal cancer, indicating that some colorectal cancers grew rapidly with minimal symptoms. Whether total colonoscopy following a positive FOBT result is the optimal method for detecting early cancer remains questionable, and further detection protocols might be needed. To establish a novel screening or detection system for colorectal cancer, computed tomography colonography has been recognized as an alternative method for detecting colorectal cancer in an FOBT-positive screening population. A high diagnostic accuracy for the detection of adenoma and carcinoma and a sensitivity similar to that of colonoscopy has been shown for this method. Computed tomography colonography might also increase the acceptability of and the adherence to screening, since it is less invasive and better tolerated[31,32].

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