Original Article

Immunologic Fecal Occult Blood Test for Colorectal Cancer Screening

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Abstract

Background To clarify the limitations of immunologic fecal occult blood tests (IFOBT) as a screening method for colorectal cancer (CRC), we analyzed data from a total colonoscopy (TCS) and an IFOBT independently performed in asymptomatic average-risk adults, undergoing a complete medical check-up on a single day.

Methods Colonoscopic screening examinations were performed by IFOBT on 7,797 asymptomatic adults enrolled for a complete medical check-up at our hospital between July 1998 and July 2002.

Results A total of 19 cancers and 53 large adenomas (10 mm or more in diameter) were detected using TCS: 18 in early stages of cancer and 1 in advanced stages of cancer. The sensitivity of IFOBTs for cancer was 52.6% and for large adenoma was 24.5%. Seven cancers (36.8%) were found in the proximal colon, and 34 large adenomas (64.2%). Of the 12 cancers found in the distal colon, 7 (58.3%) had a positive IFOBT. On the other hand, 3 of the 7 proximal cancers (42.9%) had a positive IFOBT. The positive rates of IFOBT for large adenoma found in the distal and proximal colon were 7 out of 19 (36.8%) and 6 out of 34 (17.6%) respectively. There was a tendency for lesions in the proximal colon to have a lower IFOBT positive rate than those in the distal colon. From the results above, approximately one half of both cancers and large adenomas would have been missed using just IFOBT as a screening test.

Conclusion The sensitivity of IFOBT for screening for cancers and large adenomas was lower in the proximal colon than in the distal colon.

Key words Asymptomatic subjects, Total colonoscopy, Colorectal cancer screening, Fecal occult blood test, Complete medical check-up

Introduction

The mortality and morbidity from colorectal cancer (CRC) continues to increase in Japan as well as in the Western world.[1] At the present time, methods to primarily prevent CRC have not yet been established, so secondary prevention is very important. Several large prospective randomized controlled studies have shown that fecal occult blood test (FOBT) plays an important role as a secondary preventive measure.[2–4] However, the FOBT method is not sufficient to obtain survival benefit or to detect cancers at an early stage. To counteract these disadvantages, a more sensitive modality is necessary, such as total colonoscopy (TCS). The aim of the present study is to clarify the problems of an immunologic fecal occult blood test (IFOBT) based on a comparison of data obtained from TCS and IFOBT independently performed on a patient in a single day.

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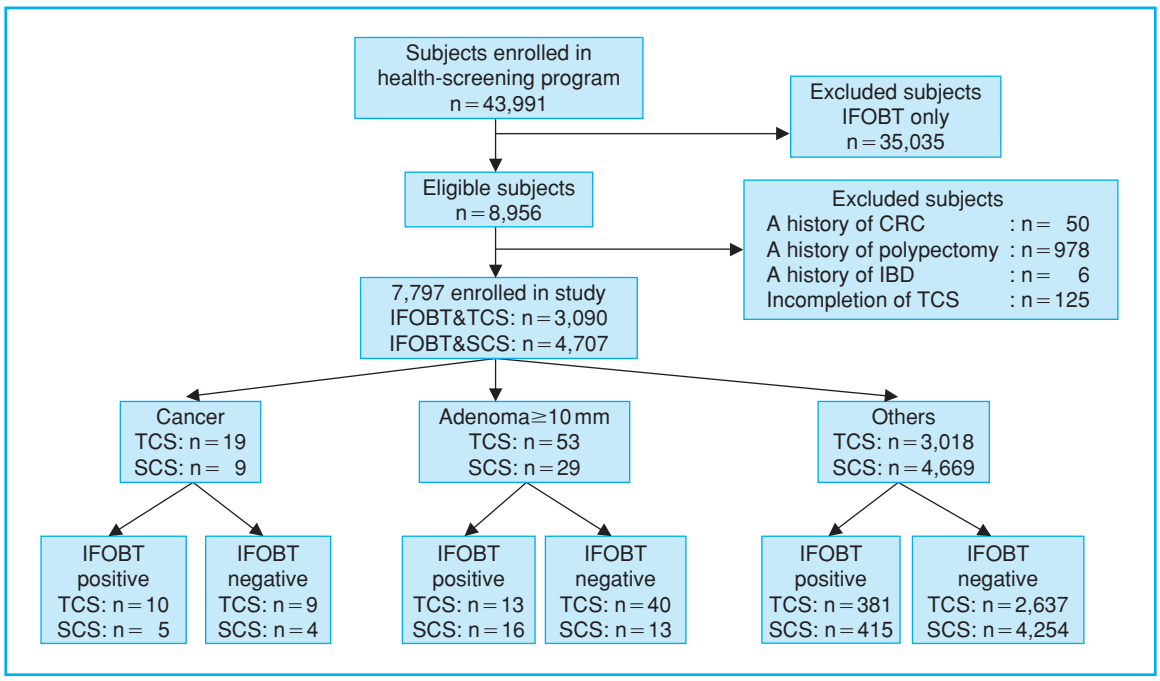

Fig. 1 Study profile

IFOBT: immunologic fecal occult blood test; TCS: total colonoscopy; SCS: sigmoidoscopy; CRC: colorectal cancer; IBD: inflammatory bowel diseases

Materials and Methods

Study subjects (Fig. 1)

We performed a cross-sectional analysis of asymptomatic adults who underwent both a colonoscopic examination and an IFOBT, independently performed in a single day in complete medical check-up conducted at our hospital in the period from July 1998 through July 2002. The study was approved by the institutional review board of Akita Red Cross Hospital. Of 43,991 subjects enrolled for a complete medical check-up at our hospital, 8,956 were screened by both IFOBT and colonoscopy at their request. A total of 7,797 (87.1 percent) of examinations were included in this analysis. Of the total of 7,797 colonoscopic examinations, 3,090 consisted of TCS and 4,707 consisted of sigmoidoscopy (SCS). The average age of the subjects was 52.7 ± 7.9 years (mean age ± SD) (TCS; 53.4 ± 8.2 years, SCS; 52.5 ± 7.6 years) and the male-female ratio was 3.4:1 (TCS; 5.6:1, SCS; 2.8:1). The subjects were excluded from the study if they met the following criteria: 1) a personal history of CRC and colonoscopic treatment of colorectal neoplasm, 2) a history of altered bowel habits or rectal bleeding, or 3) a known history of inflammatory bowel diseases (IBD), familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC). The analysis was based on data obtained from colonoscopic examinations (TCS and SCS), pathologic findings and IFOBT of 7,797 examinees.

Study procedures

Eligible subjects received a polyethylene glycol-based electrolyte solution for bowel preparation. Two stool samples from each of the two consecutive days before bowel preparation were sent for IFOBT. As a rule, colonoscopies were performed with no use of conscious sedation. All lesions found were photographed and their sites, size, morphological findings and classification of pit pattern were recorded by the study doctors. In our study, all the endoscopists had substantial experience with colonoscopy.

Histological evaluation

All retrieved lesions were sent to pathological

Table 1 Results of IFOBT in relation to total colonoscopic findings

	Cancer (early/advanced)	Large adenoma (adenoma≥10 mm)	Small adenoma (adenoma<9 mm)	Others
IFOBT positive (n=404)	10 (9/1)	13	37	344
IFOBT negative (n=2,686)	9 (9/0)	40	216	2,421
Overall (n=3,090)	19 (18/1)	53	253	2,765

IFOBT: immunologic fecal occult blood test

Table 2 Sensitivity, specificity, positive predictive value and negative predictive value of IFOBT for cancer and large adenoma

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Cancer	52.6%	87.2%	2.5%	99.7%
(95% CI)	(30.1–75.1)	(86.0–88.4)	(1.0–4.0)	(97.5–99.9)
Large adenoma (adenoma≥10 mm)	24.5%	87.1%	3.2%	98.5%
(95% CI)	(12.9–36.1)	(85.9–88.3)	(1.5–4.9)	(98.0–99.0)

IFOBT: immunologic fecal occult blood test; CI: confidence interval

laboratories in our center for processing. Interpretation of the histopathological features was performed by a single pathologist who had considerable experience in gastroenterologic pathology. In cases having some kind of tumor, the classification of the tumor was based on the most advanced lesions. The distal part included the sigmoid colon and the rectum. The proximal part included the descending colon and all proximal portions of the colon. Early colorectal cancer has been defined as intramucosal carcinoma and carcinoma invading the submucosal layer in Japan. Advanced colorectal cancer was defined as a lesion in which malignant cells had infiltrated beyond the submucosal layer.[5]

Statistical analysis

Management of the study database and all statistical analyses were performed by StatView for Windows software (Version5.0, SAS Institute, Cary, NC, USA).

The results were shown as rates or proportions. χ^2 test was used to compare proportions. Statistical significance was taken as $P<0.05$. Descriptive statistical analyses included the calculation of rates and proportions for categorical data and means and standard deviation for continuous data.

Results

We assessed the sensitivity of IFOBT as a screening test. Of the 3,090 subjects who underwent TCS, 404 (13.1%) had positive IFOBT results. Cancer was detected in 19 subjects. 10 had positive IFOBT results. Among all the 53 subjects with large adenoma (10 mm or more in diameter), 13 had positive IFOBT results. The sensitivity of IFOBT for cancer was 52.6%, the specificity was 87.2%, and the positive predictive value was 2.5%. As for large adenomas, the sensitivity was 24.5%, the specificity was 87.1%, and the positive predictive value was 3.2% (Table 1, 2).

Nineteen cancer subjects would have been diagnosed using TCS as a screening test: 18 in the early stages of cancer and 1 in advanced stage cancer. Twelve (63.2%) subjects had cancers in the distal colon, and 7 (36.8%) in the proximal colon. Among 53 subjects with large adenoma, 34 (64.2%) were found in the proximal colon

Table 3 Relation between location and IFOBT positive rate of cancer and large adenoma found among the subjects who underwent TCS

	Distal colon	Proximal colon	Overall	*P* value
Cancer	12	7	19	
IFOBT positive (%)	7 (58.3)	3 (42.9)	10	$P=0.7125$
Large adenoma (adenoma≥10 mm)	19	34	53	
IFOBT positive (%)	7 (36.8)	6 (17.6)	13	$P=0.2340$

IFOBT: immunologic fecal occult blood test; TCS: total colonoscopy

Table 4 The Rate of detection of cancer and large adenoma of TCS and SCS

Variable	Overall (n=7,797)	TCS (n=3,090)	SCS (n=4,707)	*P* value
The rate of detection of cancer (%)	28 (0.36)	19 (0.615)	9 (0.191)	$P=0.0043$
early cancer (%)	27 (0.35)	18 (0.583)	9 (0.191)	$P=0.0375$
advanced cancer (%)	1 (0.01)	1 (0.032)	0	—
The rate of detection of Large adenoma (adenoma≥10 mm) (%)	82 (1.05)	53 (1.72)	29 (0.62)	$P<0.0001$

TCS: total colonoscopy; SCS: sigmoidoscopy

and 19 (35.8%) were in the distal colon.

Of the 12 cancers found in the distal colon, 7 (58.3%) had positive IFOBT results. On the other hand, 3 out of 7 cancers (42.9%) in the proximal colon had positive IFOBT results. The rate of positive IFOBT results for large adenomas which were found in the distal and proximal colon were 7 out of 19 (36.8%) and 6 out of 34 (17.6%) respectively. Cancers and large adenomas in the proximal colon tended to have a much lower rate of positive IFOBT results than those in the distal colon (Table 3).

The rate of detection of cancer in the TCS group was 19/3,090 (0.615%) consisting of 18/3,090 (0.583%) of early colorectal cancers and 1/3,090 (0.032%) of advanced colorectal cancers, and that in SCS group was 9/4,707 (0.191%) consisting of 9/4,707 (0.191%) of early stage cancers and 0/4,707 (0%) of advanced stage cancers. The difference in the detection rate between TCS and SCS reached statistical significance. The corresponding figures for large adenoma were 53/3,090 (1.72%) of the subjects who received TCS and 29/4,707 (0.62%) of the subjects who received SCS. A statistically significant difference was also found for the detection rate of large adenoma between two groups (Table 4).

There were no complications among the 3,090 subjects who underwent TCS examinations and the 263 subjects who underwent colonoscopic treatment. Colonoscopies are usually performed at our center without intravenous sedation. None of the subjects in this study required the use of medication for conscious sedation. The completion rate for total colonoscopy was 96.1% under these conditions.

Discussion

The purpose of this study was to clarify the limitations of IFOBT as a screening test for CRC by examining the data of the rate of detection and location of cancers and large adenomas, and the relation between the location and the sensitivity of IFOBT for average-risk asymptomatic adults. In large randomized controlled studies in the West[2,3,4] there is evidence that as a screening test chemical FOBT can reduce the mortality of

CRC in the screened group. However, it is not clear whether screening with the FOBT method would have given individuals the benefit of a complete medical check-up. That is to say, to obtain longer survival after detection of colorectal cancer or the higher rate of detection of cancers in the early stage, we need more sensitive modalities than IFOBT can provide. Based on the results of this study, the sensitivity of IFOBT for cancer (large adenoma) was 52.6% (24.5%). In addition more than half of colorectal neoplasms were underdiagnosed with use of IFOBT alone as a screening test. The sensitivity of IFOBT for cancer in this study was much lower than that previously reported.[6] This may be due to the result that most of the cancers detected in complete medical check-up at our hospital were not advanced cancers, but early stage cancers.

Many people have pointed out that a significant number of colorectal neoplasms have been underdiagnosed with use of chemical FOBT alone due to its low sensitivity in detecting colonic neoplasms.[7,8,9] Therefore, the use of SCS has been recommended as a more sensitive screening strategy. Analyses from case-control studies[10,11] also suggested that SCS examination reduced the mortality of cancer. However, two recent studies[12,13] confirm that sigmoidoscopic screening would fail to detect a substantial proportion of asymptomatic colorectal cancers or polyps associated with a high risk of cancer. As 64.2% of large adenoma (36.8% of cancer) was found in the proximal colon from the result obtained in this study, about half of the sum of cancer and large adenoma would be missed using SCS alone as a primary screening procedure. Even combining SCS with IFOBT, 52.8% of large adenoma (21.1% of cancer) would have been missed because the IFOBT-positive rates were lower for proximal large adenoma (17.6%) and cancer (42.9%). In short, it is impossible to detect the lesions in the proximal colon using SCS, and yet IFOBT has difficulty in finding lesions in the proximal colon because of its lower sensitivity. Thus, TCS has been recommended as a screening modality since it can not only detect colonic neoplasms with a high degree of accuracy, but also accurately examine the entire colon.[14] However, before TCS can be widely used as a primary screening modality, there are several problems to solve: manpower, cost-effectiveness, technical factors and so on.

In summary, this study demonstrates the lower positivity of IFOBT for colonic lesions in the proximal colon as compared with in the distal colon. A complete medical check-up is needed to be of benefit to individuals, rather than mass screening. Therefore, we believe that a screening modality that enables us to accurately examine the entire colon, such as TSC, is desirable for complete medical check-up.

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