Colorectal Cancer Screening in Asymptomatic Adults: Comparison of Colonoscopy, Sigmoidoscopy and Fecal Occult Blood Tests

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Background and Purpose: Fecal occult blood tests (FOBT) and flexible sigmoidoscopy have previously been recommended for colon cancer screening. More recently, studies have recommended colonoscopy due to the high rates of advanced neoplasm not detected by FOBT and sigmoidoscopy. Previous studies of the effectiveness of colonoscopic screening in Taiwan were limited to families of patients with colorectal cancer. This study compared colonoscopy, sigmoidoscopy and FOBT for colorectal cancer screening in asymptomatic adults.

Methods: Screening colonoscopies and FOBT were performed in asymptomatic adults enrolled in our health-screening program between January 1997 and December 2000. Advanced neoplasm was defined as the presence of a polyp larger than 1 cm, polyps with villous or severe dysplastic features, or cancer. The junction of the splenic flexure and descending colon was defined as the boundary of the proximal and distal colon, and it was presumed that the distal colon would be examined using sigmoidoscopy in all patients. Data on the prevalence of polyps, advanced neoplasm, and cancer among different age groups were obtained. The results of chemical and immunologic FOBT were compared. The anatomic distributions of advanced neoplasm and cancer were analyzed.

Results: A total of 7,411 colonoscopic examinations were included in the analysis. Advanced neoplasms were present in 93 examinations (1.3%), including 16 cancers (0.2%). Chemical FOBT detected 20.2% of advanced neoplasms and 37.5% of cancers. Immunologic FOBT detected 48.3% of advanced neoplasms and 87.5% of cancers. If sigmoidoscopy had been performed in place of colonoscopy, 26.9% of advanced neoplasms and 12.5% of cancers would not have been detected.

Conclusions: Colonoscopy can detect neoplastic lesions undetectable by FOBT and sigmoidoscopy in asymptomatic subjects. These results suggest that colonoscopy should be the method of choice in colon cancer screening.

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Key words:
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occult blood

Colorectal cancer is the third most common cancer in Taiwan. The mortality rate has increased rapidly from 8.18 per 100,000 population in 1991 to 15.22 in 2000 [1, 2]. It is generally accepted that colon carcinoma arises from colonic polyps [3–5]. Accumulating evidence supports the validity of colon cancer screening. Fecal occult blood tests (FOBT) and sigmoidoscopy have been widely adopted for colon cancer screening. Three prospective controlled trials observed a 15 to 33% reduction in colon cancer resulting from the use of FOBT [6–8]. Three case-controlled studies also found that sigmoidoscopy can reduce the mortality of colon cancer [9, 10], or the risk of developing colon cancer [11]. Thus, the combined use of FOBT and sigmoidoscopy to screen for colorectal cancer has been recommended [12, 13]. Because of the cost, discomfort,

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and potential risks associated with colonoscopic examination, colonoscopy has been indicated only for individuals at increased risk of colorectal cancer, and has not been recommended as a screening procedure for the general population. Recently, three studies reported that high rates (52% and 46%) of advanced proximal neoplasms were found in the proximal colon without the presence of distal adenomas [14, 15], and 29.7% of the examinations that identified advanced proximal colonic neoplasms found no neoplasms in the distal colon [16]. These reports led to the proposal that colonoscopy should replace sigmoidoscopy and FOBT for colon cancer screening.

Previous studies of the value of colonoscopic screening in Taiwan were limited to families of patients with colorectal cancer [17, 18], and showed that 42% of adenomatous polyps and 75% of cancers were beyond the reach of conventional flexible sigmoidoscopy [18]. A previous study from Taiwan found that sigmoidoscopy in high-risk patients with neoplasm of the large bowel has a sensitivity of 68% [18]. No studies of colonoscopic screening in the asymptomatic population in Taiwan have been published in a peer-reviewed journal.

Since its inception in 1990, the screening program at the Koo Foundation at Sun Yat-Sen Cancer Center (KFSYSCC) has adopted the combined use of colonoscopic examination and FOBT tests. The data generated by this screening program for colorectal neoplasms in the past decade formed the basis for this study.

Materials and Methods

Study design

A cross-sectional analysis of asymptomatic adults who underwent colonoscopic examinations in our health-screening program from January 1997 through December 2000 was performed. The analysis was based on data generated from colonoscopic examinations, pathologic findings and FOBT of 7,617 examinees. Among them, 206 examinations were excluded for reasons including incomplete colon examination, presence of related symptoms (anemia, bloody stool, diarrhea, weight loss), history of colorectal cancer, colitis, or inflammatory bowel disease (IBD) or previous positive FOBT, location or size of lesion not defined, or no pathologic examination (Table 1). Ineligible patients accounted for 3.0% of the entire health-screening population. A total of 7,411 examinations met the criteria for inclusion in this analysis.

Screening program

Enrollment in the screening program was voluntary. After enrollment, eligible examinees were asked to complete a questionnaire that included reasons for health screen, presence of abdominal symptoms, past medical and surgical history, personal and family history, medication, and history of allergies. We defined an asymptomatic subject as one who had no known history of colorectal cancer, IBD, rectal bleeding, recent changes in bowel habits, weight loss, anemia, or positive FOBT on prior examinations. Individuals with a personal history of colonic polyps or a family history of colon cancer were not excluded from joining the program. Well-trained and board-certified gastroenterologists performed all screening colonoscopies.

Table 1. Reasons for exclusion from the study

Reason for exclusion	No. of patients
Incomplete examination	84
No pathology	52
Previous history of colon cancer	14
Lesion site not defined	14
Lesion size not defined	13
History of colitis or inflammatory bowel disease	12
History of rectal cancer	6
Diarrhea	4
History of positive fecal occult blood test	3
Blood per rectum	2
Anemia	1
Weight loss	1
Total	206

Study procedures

After examinees enrolled in the screening program, they were asked to follow diet instructions for 3 days prior to stool collection. Stool specimens were sent for FOBT on the day of colonoscopic examination. Colonoscopy was performed under conscious sedation, and the report was recorded on a standardized computer form that included the size and location of the polyps or tumor, if present. We defined the junction of the splenic flexure and descending colon as the boundary of the proximal and distal colon, and presumed that only the distal colon could be reached if sigmoidoscopy were performed.

The examinees also underwent a complete health screening examination, which included a medical history, physical examination, laboratory tests, electrocardiography (ECG) and chest roentgenography. Examinations were classified on the basis of the most advanced lesion identified. The lesion was categorized as either hyperplasia, tubular villous adenoma (including villotubular adenoma) with or without dysplasia, adenocarcinoma or other pathologies.

Advanced neoplasm was defined as a polyp larger than 1 cm, polyps with villous or severe dysplastic features, and cancer.

Stool specimens were analyzed both chemically (color reaction of toluidine with peroxidase, CFOBB test; Shih-Yung Instruments Co., Taipei, Taiwan) and immunologically (OC-Hemodia for human hemoglobin, OC-light; Eiken Chemical Co., Tokyo, Japan).

Statistical analysis

Statistical analysis was performed with SAS software (SAS Institute, Cary, NC, USA). Rates and proportions were calculated for categoric data, and means and standard errors for continuous data. Patients without polyps served as the reference group. Standard logistic-regression methods were used to calculate relative risks for FOBT positivity according to pathology. The relative risk was adjusted for age and sex. The Mantel-Haenszel test was used to determine whether FOBT positivity increased with pathologic severity.

Results

The age distribution of the study population is shown in Table 2. Mean age was 46.8 ± 9.9 years and the male to female ratio was 1.23. The completion rate for colonoscopy was 98.9%. Major complications included perforation in two individuals, which were managed surgically, and bleeding in five, managed by epinephrine injection, heat coagulation or hemoclip at the time of occurrence. No blood transfusion or hospital admission was needed. There was no mortality from colonoscopy.

Pathology

Among the 7,411 examinations, 719 (9.7%) had abnormal findings including hyperplastic polyps (135, 1.8%), tubular adenomas (533, 7.2%), villous adenomas (35, 0.5%), and cancers (16, 0.2%). Advanced neoplasm was present in 93 examinations (1.3%), including 40 tubular adenomas larger than 1 cm, two tubular adenomas with severe dysplastic change, 35 villous adenomas, and 16 cancers (Table 3). Of 16 examinees diagnosed with cancer (11 men and five women), eight had carcinoma *in situ*, four had Dukes stage A lesions, two had Dukes stage B lesions, and one had a Dukes stage C lesion; the remaining examinee underwent surgery in another hospital and the final Dukes staging was unknown.

The prevalence of polyps, advanced neoplasm, and cancer stratified by age are shown in Table 2. Other pathologic findings were made in 63 subjects, including carcinoid tumors, colitis, hamartomatous polyps, inflammatory polyps, juvenile polyps, leiomyoma, lipoma, lymphoid polyps, retension polyps, and xanthoma. These individuals were excluded from the analysis.

Fecal occult blood tests

FOBT results and relative risks for various pathologies were compared with normal findings on colonoscopy (Table 3). Using immunologic FOBT, positive results were found in 8.4% of patients with normal colonoscopic findings, 16.8% of patients with polyps on colonoscopy, 48.3% of patients with advanced neoplasm on colonoscopy, and 87.5% of patients with cancer on colonoscopy. Using chemical FOBT, positive results were found in 11.2% of patients with a normal examination, 12.8% of patients with polyps, 20.2% of patients with advanced neoplasm, and 37.5% of patients with cancer.

Location of advanced neoplasms

Advanced proximal colonic neoplasms were found in 32 examinations (34.4%). Among these, 25 patients had no coexisting lesions identified in the distal colon (Figure, A). Had these examinees undergone only sigmoidoscopy, their proximal lesions would not have been detected (26.9%).

Table 2. Characteristics of colonoscopic examinees and prevalence of polyps and advanced neoplasms by age

Age range (yr)	No. examined (%)	No. of polyps (%)	No. of advanced neoplasms (%)	Cancer (%)
≤ 20	6 (0.08)	0 (0.0)	0 (0.0)	0 (0.0)
21–30	233 (3.14)	7 (3.0)	1 (0.4)	0 (0.0)
31–40	1,780 (24.02)	108 (6.3)	6 (0.3)	0 (0.0)
41–50	3,076 (41.51)	263 (8.6)	27 (0.9)	5 (0.1)
51–60	1,513 (20.42)	201 (13.3)	32 (2.1)	3 (0.2)
61–70	717 (9.67)	119 (16.6)	23 (3.2)	8 (1.1)
71–80	83 (1.12)	20 (24.1)	4 (4.8)	0 (0.0)
≥ 81	3 (0.04)	1 (33.3)	0 (0.0)	0 (0.0)
Total	7,411	719	93	16

Table 3. Colonoscopic findings according to the most advanced lesion present and its correlation with fecal occult blood tests (FOBT)

Finding	No. of patients (%)	Immunologic FOBT			Chemical FOBT (%)		
		Positivity (%)	Adjusted relative risk	95% CI	Positivity (%)	Adjusted relative risk	95% CI
No polyps	6,692 (90.3)	8.4	1		11.2	1	
Polyps	719 (9.7)	16.8	2.0	(1.6–2.5)	12.8	1.1	(0.9–1.4)
Advanced neoplasm	93 (1.3)	48.3	8.9	(5.8–13.7)	20.2	1.8	(1.1–3.0)
Cancer	16 (0.2)	87.5	63.3	(14.2–282)	37.5	4.1	(1.5–11.5)
Mantel-Haenszel test for trend		$X^2 = 237$, $p < 0.0001$			$X^2 = 20.1$, $p < 0.001$		

CI = confidence interval.

Furthermore, among the 16 cancerous lesions, five (31.3%) were proximal, of which two (12.5%) were without any distal lesions (Figure, B). Had these examinees undergone only sigmoidoscopy, their proximal lesions would not have been detected.

Discussion

This study has provided valuable information regarding the benefit and risk of colonoscopic examination and FOBT in asymptomatic adults in Taiwan. Among 7,411 examinations, 719 neoplasms (9.7%) were found. This number is much lower than that reported by Imperiale et al [15], Lieberman and Weiss [16] and Shieh et al [18]. The prevalence of polyps and advanced neoplasms increased significantly with age ($p < 0.05$). Several studies have shown a correlation between the prevalence of colonic adenomas in a given country and the frequency of colon cancer [19–21]; the prevalence of adenoma and cancer increase with age [19, 21, 22]. Our study population was in a geographic area with a lower prevalence of colon cancer than in these previous studies. Most of our examinees (68.7%) were between 31 and 50 years of age, and only a small proportion had a family history of colorectal cancer. These factors probably influenced the prevalence of neoplasm in our study.

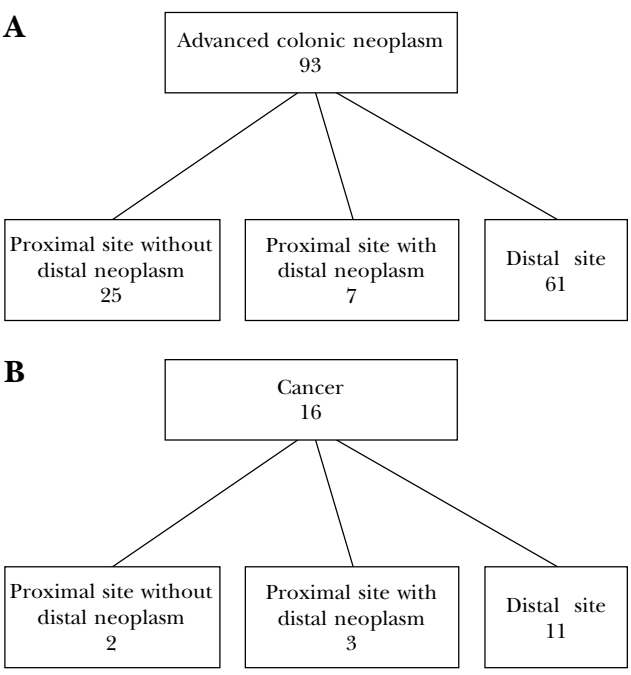

Figure. *Numbers of advanced colonic neoplasms (A) and cancers (B) stratified by location.*

This study assessed both chemical and immunologic FOBT. Using both methods, the FOBT-positive rate increased with pathologic severity and this trend was statistically significant. Previous studies indicate that the sensitivity of chemical FOBT is 1 to 16% [6, 23–28], with a false-positive rate of 2 to 4% with nonrehydrated slides, and 8 to 16% with hydrated slides. We found a false-positive rate of 8.4% with immunologic FOBT and 11.2% with chemical FOBT. This high false-positive rate would result in unacceptably high rates of indication for work-up if FOBT was used for screening. Previous studies have revealed the superiority of immunologic (e.g., HemeSelect) to chemical methods (e.g., Hemoccult) [29–32]. The results of this study are compatible with the published data.

This study found that 26.9% of examinations yielded advanced proximal colonic neoplasm without distal colonic neoplasm. In previous studies, 52% and 46% of patients with advanced proximal neoplasms had no distal adenomas or polyps [14, 15]. Lieberman and Weiss showed that 29.7% of examinations that identified advanced proximal colonic neoplasm found no

neoplasm in the distal colon [16]. The anatomic distribution of advanced neoplasms was similar in all studies.

In summary, this study found a similar anatomic distribution of advanced neoplasm and cancer in this Taiwanese population compared to previous studies in Western populations. It confirmed that immunologic FOBT rather than chemical FOBT should be used for colon cancer screening. The purpose of colon cancer screening includes detection and removal of colon polyps, followed by detection of colorectal cancer in its early stage. This study found that immunologic FOBT effectively detected cancers in the early stage (87.5%), but its positive rates were lower for advanced neoplasms (48.3%) and polyps (16.8%). Chemical FOBT had poor results in detecting cancers (37.5%), advanced neoplasms (20.2%), and polyps (12.8%). Use of screening sigmoidoscopy alone would have missed 26.9% of advanced neoplasms and 12.5% of cancers. The results of this study indicate that colonoscopy should be employed in colon cancer screening, as it can not only detect early-stage colon cancer, but also prevent the development of colon cancer by the identification and removal of colon polyps.

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