

An Evaluation of Mass Screening Using Fecal Occult Blood Test for Colorectal Cancer in Japan: A Case-Control Study

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There is as yet no firm evidence showing that mass screening for colorectal cancer using fecal occult blood tests (FOBTs) reduces the mortality from this cancer. Therefore we evaluated the effectiveness of the screening by a case-control study in Miyagi Prefecture, Japan. The study included as case subjects 28 individuals who had died from colorectal cancer and had had an opportunity to participate in the mass screening before the date of diagnosis as colorectal cancer, and 3 controls for each case subject randomly selected from residents who were alive on the date of death of case subjects and matched by sex, age (within 3 years) and living area using residential files. For each set, i.e., a case subject and 3 controls, screening histories before the date of the diagnosis of the case as colorectal cancer were examined. Both the case subjects and the controls who had participated in the screening at least once within 3 years before the date of diagnosis of the case were classified as "screened." The 28 case subjects consisted of 12 males and 16 females (average age: 60.8 years). The odds ratio of death from colorectal cancer for the screened versus the non-screened persons was 0.24 (95% confidence interval = 0.08-0.76) by the Mantel-Haenszel method. The present study suggests that mass screening using FOBTs for colorectal cancer significantly reduces the mortality from this cancer epidemiologically.

Key words: Mass screening — Colorectal cancer — Fecal occult blood test — Case-control study

There has been a gradual increase in the mortality from colorectal cancer in Japan, and it is anticipated that the annual incidence of colorectal cancer in the year 2000 (88,000 cases) will be more than twice as great as that in 1985 (40,000 cases).¹⁾ For early detection and treatment of colorectal cancer to reduce the mortality, several attempts at mass screening using fecal occult blood tests (FOBTs) have been made. It is generally accepted that FOBTs are able to detect earlier cancer among asymptomatic persons. The best method to accomplish an evaluation of the effectiveness of mass screening using FOBTs is randomized controlled trial (RCT). At present, four RCTs are being conducted to estimate the effectiveness of mass screening using FOBTs in the US and Europe.²⁻⁵⁾ RCT not only requires enormous cost and time, but also is unsuitable for the Japanese national character.⁶⁾ Furthermore, since the number of mass screening programs for various purposes has been increasing in Japan year by year, the application of RCT was considered inappropriate. Therefore to evaluate the effectiveness of this screening, we adopted the case-control method, which has been widely used to evaluate mass screening for cervical cancer⁷⁻¹⁰⁾ and other cancers. The data of 13 municipalities in Miyagi Prefecture, where mass screening for colorectal cancer had been performed for more than 3 years during 1983-90, were examined in this

study. These municipalities are located in the northern part of Miyagi Prefecture, and their main industries are farming and/or fishing. In these areas, screening for colorectal cancer including FOBTs had not been carried out by general physicians or public health services. The participants, men and women residents between the ages of 45 and 69 years at the first screening, were screened by FOBTs and recommended to take part in the screening every year. The rate of screened persons among all target residents was 28.8% (67,609/236,468). FOBTs used were predominantly a guaiac test (Hemoccult II, Smith-Kline Diagnostics, CA, USA) over 3 consecutive days and also immunochemical tests, reversed passive hemagglutination (RPHA) (Immudia Hem-Sp, Fujirebio, Tokyo)¹¹⁾ or latex agglutination (Immunocult, Chuugai, Tokyo) for 2 consecutive days in some cases. Positives for FOBTs received a diagnostic work-up examination, including digital examination, fiberoptic sigmoidoscopy (observation up to about 50 cm from anal verge) and double contrast barium enema on the same day at the Cancer Detection Center of the Miyagi Cancer Society.

A case subject was defined as an individual who had died from colorectal cancer before March 1991, and had had an opportunity to participate in the mass screening before the date of diagnosis as colorectal cancer. Case subjects were collected through inquiries by public health

nurses and reports from local hospitals and identified from the death certificates and the records of the Miyagi Cancer Registry. Three controls for each case subject were selected at random from among the residents who were confirmed to be alive on the date of death of the case subjects, matched by sex, age (within 3 years) and living area, using the file of all residents. For each set, i.e., a case subject and 3 controls, screening histories within 3 years before the date of the diagnosis of the case subject as colorectal cancer were investigated from the records of screenees kept at the Miyagi Cancer Society. Individuals who had participated in the screening at least once within 3 years before the date were regarded as "screened." Relative risk of the "screened" was estimated from the odds ratio along with the 95% confidence interval, using the Mantel-Haenszel method.¹²⁾

Case subjects consisted of 28 patients, including 12 males and 16 females with an average age of 60.8 years (Table I). Seven patients (25%) belonged to the "screened" category, and the percentage was lower than that of screened controls (48%, 40/84). In Table II, case subjects are classified according to the respective matched number of screened controls. The odds ratio of death from colorectal cancer for screened versus non-screened persons was 0.24 (95% confidence interval = 0.08–0.76). This study suggests that mass screening using FOBTs leads to a significant reduction in mortality from colorectal cancer.

As regards the effectiveness of mass screening for colorectal cancer using FOBTs, Mandel *et al.* from the Minnesota group reported that a 33% decline in mortality was observed in the annually screened group as com-

pared with the control group.¹³⁾ This report was the first to establish the effectiveness of the screening by RCT; the other 3 RCT study groups have not yet reported their conclusions. According to Mandel's report,¹³⁾ rehydration was adopted to improve the low sensitivity of the Hemoccult test. Therefore, specificity was decreased and the increase in cost was substantial. The estimated benefit was smaller than that anticipated at first, and they concluded that it is necessary to evaluate the cost-effectiveness. On the other hand, Selby *et al.* reported that an odds ratio of 0.69 (95% confidence interval = 0.52–0.91) was observed for exposure to at least one screening FOBT (Hemoccult II) during a 5-year interval by a case-control study.¹⁴⁾ The present study is the first one suggesting the epidemiological effectiveness of the screening using FOBTs in Japan. Differences in the sensitivity of FOBTs used and in the prevalence of this cancer might influence the evaluation of the effectiveness, so this Japanese report is considered to be significant.

The case-control study used has some potential biases, especially self-selection bias. It is generally considered that when there are many individuals with lower risks for colorectal cancer in a "screened" group, the effectiveness of the screening might be overestimated. In the present study, we did not take into consideration the risk factors of colorectal cancer, i.e., dietary habit, family history of colorectal cancer or polyps, etc. Nevertheless, when several study groups dealing with different populations in different areas achieve common conclusions by case-control study, the result can be regarded as established. Another problem is that the FOBTs used were not a single test, but a guaiac test over 3 days and immunochemical tests for 2 days. It is generally accepted that the sensitivity and specificity of immunochemical tests are higher than those of a guaiac test,¹⁵⁾ and most screening groups have switched from the guaiac test to immunochemical tests in Japan. If immunochemical tests with excellent sensitivity and specificity were used, it is anticipated that the odds ratio would be lower and the above conclusion would remain valid.

In the future, it will be necessary to reevaluate the effectiveness by strict criteria, i.e., the effect of length from the last negative screening (screening interval), differences between guaiac test and immunochemical tests, the effect of number of feces collected, and so on. Furthermore, analysis of the effectiveness by age group and sex, and cost-effectiveness analysis should be performed.

This study was supported in part by a Grant-in-Aid for Cancer Research (No. 1-12, Chairman: Prof. S. Hisamichi 1990 and No. 3-2, Chairman: Prof. Y. Yoshida 1991) from the Ministry of Health and Welfare, Japan

(Received July 27, 1993/Accepted August 13, 1993)

Table I. Age and Sex Distribution of Case Subjects

Age	Male	Female	Total
45–50	1	1	2
50–54	0	2	2
55–59	6	1	7
60–64	4	4	8
65–69	1	6	7
70–74	0	2	2
Total	12	16	28

Table II. Odds Ratio and Distribution of Case Subjects and Controls According to the Number of Matched Controls Screened

Case subjects	Number of matched controls screened				Odds ratio (95%CI)
	0	1	2	3	
Screened	0	2	2	3	0.24
Non-screened	7	7	3	4	(0.08–0.76)

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