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ORIGINAL RESEARCH

Diagnostic value of occult fecal blood testing for colorectal cancer screening

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Abstract

AIM: To evaluate the diagnostic value of occult fecal blood testing in mass colorectal cancer screening.

METHODS: A reverse passive hemagglutination reaction fecal occult blood test (RPHA-FOBT) and colorectal cancer risk factor quantitative method were used as preliminary screening for colorectal cancer. A 60-cm fiber optic colonoscopy was used to validate the preliminary screen and was used to detect colorectal cancer in a community of 75813 subjects.

RESULTS: Compared to the 60-cm fiber optic colonoscopy as a standard reference, FOBT has a sensitivity of 41.9%, specificity of 95.8%, Youden's index of 0.38, and positive predictive value of 0.68%. These results increased with subject age from the first detection. A 3-year follow up in the target mass showed that all new cases had initially been FOBT-negative.

CONCLUSION: The value of FOBT as an indicator of colorectal cancer in mass screening is limited.

Key words: Colorectal neoplasms/diagnosis; Occult blood; Mass screening; Risk factors; Colonoscopy

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INTRODUCTION

Fecal occult blood testing (FOBT) was first reported by Greegor in 1967 as a useful index in mass colorectal cancer screening[1]. Immunochemical FOBT is currently used worldwide[2-5] to detect early colorectal cancer, but the sensitivity, specificity, and positive predictive value of this method varies greatly with the differences in the selected masses. Reverse passive hemagglutination reaction fecal occult blood testing (RPHA-FOBT) was established by Zhou *et al*[4] in 1987. Since then, this method has been used among patients and colorectal cancer high risk populations with histories of rectal polyps or ulcers. The sensitivity for the two groups was 89% and 64%, respectively, and the positive predictive values were 100% and 1.5%, respectively. These results were statistically significantly different[6]. The value of RPHA-FOBT as a mass screening indicator and its relationship with a 3-year cumulative incidence rate (CIR) of colorectal cancer in a population aged ≥30 years is reported in this study.

MATERIALS AND METHODS

RPHA-FOBT and colorectal cancer risk factor quantitative methods[7] were implemented as a preliminary screening procedure, and a 60-cm fiber optic colonoscopy was performed as an accurate screening from May 1989 to May 1990 in Jianshan County, an area of the highest colorectal cancer incidence rate in China[8]. In this study, 75813 subjects were randomly selected from ten towns in Jianshan County. Of the 62611 subjects tested (82.6%), 43 colorectal cancer cases were identified, with a total detection rate of 68.7/10.5. A total of 70% of the 43 cases were classified as either Dukes A or B, the early stages of colorectal cancer.

The entire population studied was surveyed for colorectal cancer incidence. Fifty-three new cases were identified from May 1990 to May 1992, totaling 96 cases within 3 years from May 1989 to May 1992, making the CIR 153.3 per 10^5 people.

RPHA-FOBT kits were purchased from the Basic Medical Sciences Institute of Zhejiang Medical University[3,4]. Fecal samples were sent to the local hospital by the examiners, smeared on slides, and transferred to the Lab of Cancer Research Institute of Zhejiang

Table 1 Diagnostic value of PRHA-FOBT (passive hemagglutination reaction fecal occult blood testing) by age group

Sex	*n*	Sensitivity (%)	Specificity (%)	J	PV (+)
Men	30177	43.5	95.9	0.39	0.81
Women	32434	40	95.7	0.36	0.56
Total	62611	41.9	95.8	0.38	0.68

Table 2 Diagnostic value of PRHA-FOBT (reversed passive hemagglutination reaction fecal occult blood testing) by age group

Age (yrs)	Sex	Case/mass	Sensitivity (%)	Specificity (%)	PV(+) (%)
30-39	Men	23/30177	43.5	95.9	0.81
	Women	20/32434	40	95.7	0.56
	Total	43/62611	41.9	95.8	0.68
40-49	Men	22/19026	40.9	95.9	1.15
	Women	18/20517	38.9	95.6	0.77
	Total	40/39543	40	95.8	0.94
50-59	Men	19/10891	47.4	95.9	1.96
	Women	15/12497	46.7	95.3	1.18
	Total	34/23388	47.1	95.6	1.52
≥ 60	Men	8/4856	50	95.2	1.68
	Women	9/6219	55.6	94.8	1.53
	Total	17/11075	52.9	95	1.6

Table 3 CIR1 and CIR3 (One-year cumulative incidence rate and three-year cumulative incidence rate) by sex and RPHA-FOBT (reversed passive hemagglutination reaction fecal occult blood testing) Results

Sex	FOBT (+)				FOBT (-)			
	n	CIR1	CIR3	u^1	*n*	CIR1	CIR3	u^1
Men	1236	809.1	809.1	0	28941	44.9	148.6	4.01[b]
Women	1417	564.6	564.6	0	31017	38.7	112.3	3.35[b]
Total	2653	678.5	678.5	0	59958	41.7	130.1	5.55[b]

[b]$P < 0.01$; [1]$u = (|x1 - x2|)/\sqrt{x1 + x2}$.

Medical University.

RESULTS

Diagnostic value of RPHA-FOBT in mass colorectal cancer screening

FOBT sensitivities in this natural community were 43.5% in males and 40.0% and females, but the specificity was over 95%. There was no statistical significance in Youden's index (J) between males and females (0.39 *vs* 0.36, $u = 0.199$, $P > 0.05$, Table 1).

The total positive predictive value (PV) of RPHA-FOBT was 0.68% (Table 1). This indicated that endoscopic screening is too large of a scale for epidemiologists, as only approximately seven subjects among 1000 that screened positive with RPHA-FOBT. There was no statistical significance in the positive predictive value (0.81% *vs* 0.56%, $\chi^2 = 0.583$, $P > 0.05$) between men and women.

Relationship between age and RPHA-FOBT

Colorectal cancer prevalence rates vary with age, and the mass screening results correlated well with the prevalence rate. As the American Association of Cancer has suggested, people over the age of 40 should take the FOBT annually[9]. As shown in Table 2, the diagnostic index increased with the initial age of screening; *i.e.*, the sensitivity rose from 43.5% to 50.0% in men, and from 40.0% to 55.6% in women, and the positive predictive value (PV+) increased by 1%.

Follow-up of the target population

We surveyed 62611 subjects for three years to observe the long-term values of the RPHA-FOBT results for colorectal cancer. We compared the one-year CIR (CIR1) and three-year CIR (CIR3) in FOBT-positive and -negative subjects in females and males. Because FOBT-positive subjects underwent endoscopic screening, there was no change between CIR1 and CIR3 of the FOBT-positive subjects ($u = 0$), while there were statistically significant differences between CIR1 and CIR3 of FOBT-negative females and males. In FOBT-negative males and females, the CIR3 was 2.3 and 1.9 times higher than CIR1, respectively. These results demonstrate that many colorectal cancer patients were misdiagnosed because of their negative FOBT results (Table 3), and the false negative rate was very high.

DISCUSSION

We used RPHA-FOBT and the colorectal cancer risk factor quantitative method as preliminary screening procedures, and a 60-cm fiber optic colonoscopy, which could reach the splenocolic curve, as the accuracy screening procedure in FOBT-positive subjects and the high risk population indicated by the quantitative method. We determined the FOBT diagnostic values by comparing the results from FOBT to the results of the 60-cm fiberoptic colonoscopy. It was previously reported[10] that 82% of 3147 Chinese colorectal cancer patients had their cancer initiate in the colon below the splenocolic curve, suggesting that approximately 20% of cases cannot be identified by this method. However, because of its ease of use and simple preparation, it is still considered a relatively reliable and practical method for reference standard. We examined more than 3000 subjects by 60-cm fiberoptic colonoscopy in our study, and no new cases were identified during a 3-year follow up.

There have not been any similar reports in China about the application of RPHA-FOBT and its value in mass screening. In some studies abroad[2,5,6,11], the sensitivity of immunochemical FOBT ranged from 33% to 50%, which was similar to our results (Table 1). However, our results differed from the previous studies among a special population using the same materials and methods[3,4], suggesting that more than 50% of cases in a normal population cannot be detected using FOBT. The specificity of RPHA-FOBT is over 95%, but when estimated together with other diagnostic indexes, such as the Youden's index (0.39 in males, 0.36 in females in this study), its practical value for screening colorectal cancer was limited.

PV(+), the percentage of patients among FOBT-positive subjects, is another useful index to estimate the diagnostic value of FOBT. Hardcastle *et al*[12] identified 618 FOBT-positive subjects in 27651 individuals, among which 65 subjects were colorectal cancer patients, giving a PV(+) of 10.5%, which is higher than results (PV(+) 4.8%) reported by Kewenter *et al*[13]. The PV(+) reported by Gregorio *et al*[6] was 7.5%, while the PV(+) in our study (0.68%), which was significantly lower than previous reports.

As Gregorio *et al*[6] reported, the PV(+)s of FOBT were 3% and 9%, respectively, in population less than or more than 60 years old. The difference was significant, but the difference in PV(+) between sexes was not significant (male 7%, female 10%), similar to our results (Table 2). Results in our study suggested that the older the initial age of screening, the higher the rate of PV(+). The PV(+) in our study was lower than in previous other reports. The PV(+) would increase if we defined older initial ages of the screened population to reduce the workload in the screening.

The long-term value of FOBT as a colorectal cancer diagnostic index is not perfect. The CIR1 and CIR3 values were similar in FOBT-positive male and female subjects, but compared to CIR1, the CIR3 in FOBT-negative males and females was approximately 3.3 and 2.9 times higher ($P < 0.01$). The results in Table 3 show that these FOBT-negative subjects should also be monitored to quickly identify and treat new cases.

In summary, when used alone, FOBT is not a satisfactory indicator in mass colorectal cancer screening. Therefore, it is necessary to search for and develop new testing methods, or "concentrate" the target mass. We recommend that the initial age of screening should serve as an important factor in mass colorectal cancer screening.

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