BRIEF ARTICLE

Colorectal cancer screening: Comparison of transferrin and immuno fecal occult blood test

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Abstract

AIM: To evaluate the sensitivity and specificity of transfesrrin dipstick test (Tf) in colorectal cancer (CRC) screening and precancerous lesions screening.

METHODS: Eight hundreds and sixty-one individuals at high-risk for CRC were recruited. Six hundreds and eleven subsequently received the three fecal occult blood tests and colonoscopy with biopsy performed as needed. Fecal samples were obtained on the day before colonoscopy. Tf, immuno fecal occult blood test (IFOBT) and guaiac fecal occult blood test (g-FOBT) were performed simultaneously on the same stool. To minimize false-negative cases, all subjects with negative samples were asked to provide an additional stool specimen for a second test even a third test. If the results were all negative after testing three repeated samples, the subject was considered a true negative. The performance characteristics of Tf for detecting CRC and precancerous lesions were examined and compared to those of IFOBT and the combination of Tf, IFOBT and g-FOBT.

RESULTS: A total of six hundreds and eleven subjects met the study criteria including 25 with CRC and 60 with precancerous lesions. Sensitivity for detecting CRC was 92% for Tf and 96% for IFOBT, specificities of Tf and IFOBT were both 72.0% (95% CI: 68.2%-75.5%; χ^2 = 0.4, P > 0.05); positive likelihood ratios of those were 3.3 (95% CI: 2.8-3.9) and 3.4 (95% CI: 2.9-4.0), respectively. In precancerous lesions, sensitivities for Tf and IFOBT were 50% and 58%, respectively (χ^2 = 0.8, P > 0.05); specificities of Tf and IFOBT were 71.5% (95% CI: 67.6%-75.1%) and 72.2% (95% CI: 68.4%-75.8%); positive likelihood ratios of those were 1.8 (95% CI: 1.3-2.3) and 2.1 (95% CI: 1.6-2.7), respectively; compared to IFOBT, g-FOBT+ Tf+ IFOBT had a significantly higher positive rate for precancerous lesions (83% *vs* 58%, respectively; χ^2 = 9.1, P < 0.05). In patients with CRC and precancerous lesions, the sensitivities of Tf and IFOBT were 62% and 69% (χ^2 = 0.9, P > 0.05); specificities of those were 74.5% (95% CI: 70.6%-78.1%) and 75.5% (95% CI: 71.6%-79.0%); positive likelihood ratios of those were 2.5 (95% CI: 2.0-3.1) and 2.8 (95% CI: 2.3-3.5). Compared to IFOBT alone, combining g-FOBT, IFOBT and Tf led to significantly increased sensitivity for detecting CRC and cancerous lesions (69% *vs* 88%, respectively; χ^2 = 9.0, P < 0.05).

CONCLUSION: Tf dipstick test might be used as an additional tool for CRC and precancerous lesions screening in a high-risk cohort.

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Key words: Transferrin; Immuno fecal occult blood test; Colorectal cancer; Precancerous lesions; Transferrin dipstick test

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INTRODUCTION

Colorectal cancer (CRC) is one of the major diseases threatening human health. In the United States, CRC is the third most frequently diagnosed cancer among men and women, and the third leading cause of cancer death[1]. In China, the prevalence of CRC has risen in recent years, possibly attributable to changes in the population's lifestyle and dietary habits[2,3]. In most cases, CRC is believed to arise within precancerous lesions that develop slowly over many years[4,5].

Currently, many tools are be used for CRC screening. CRC screening tests recommended by the American Cancer Society (ACS) can be grouped into 2 categories: (1) tests that primarily detect CRC, which include tests that look for blood, such as guaiac fecal occult blood test and fecal immunochemical test, or exfoliated DNA [single-strand DNA (sDNA)] in stools; and (2) tests that can detect cancer and advanced lesions, which include endoscopic and radiological exams, i.e., colonoscopy, double-contrast barium enema (DCBE), and computed tomography colonography (CTC) (or virtual colonoscopy)[6]. However, these tests all have certain limitations.

Several published randomized trials have showed that the most widely accepted test method, fecal occult blood test (FOBT), can reduce CRC incidence[7] and mortality rate[8]. However, guaiac fecal occult blood test (g-FOBT) has been criticized for its high false positive because it detects non-human haem in food[9,10]. Compared with that of g-FOBT, the sensitivity of immuno fecal occult blood test (IFOBT) is significantly higher[11-13]. IFOBT specifically detects human hemoglobin (Hb) in stool by antibody-antigen reaction, which has no restrictions on diet or drug intake. However, Hb is unstable in feces because it can be degraded by bacteria. Furthermore, Hb can not be used to detect lesions that are not accompanied by bleeding[14-17]. Fecal DNA test was developed based on the molecular genetics of CRC. It is suggested that the occurrence of most CRCs has close relationship with chromosomal instability, with mutations progressively accumulating in the *adenomatous polyposis coli* gene, the p53 tumor-suppressor gene, and the K-ras oncogene[18]. Despite relatively high specificity[19], fecal DNA test has many problems[20], including the lack of adequate fecal DNA makers, complex extraction steps, and so on. Furthermore, population-based studies showing the capability of the method to decrease mortality of CRC have been lacking[21]. Other non-invasive methods include testing for faecal calprotectin, which has high sensitivity but low specificity[22].

DCBE is a preferred method for screening in children, old people and those who can not undergo colonoscopy. However, its false positive and false negative ratios are both higher than those of colonoscopy[15,23]. Colonoscopy can detect CRC in the entire colonic lumen and is the most sensitive and specific test. A report showed that the incidence and mortality of CRC rate were reduced to 67% and 65%, respectively, after colonoscopy screening in an average-risk cohort[24]. However, colonoscopy is invasive and has risks to certain extent[25]. High costs and painful procedure has prevented colonoscopy from being used as a method for large-scale screening of CRC. Practically it is only used for final diagnostic test of positive patients. In 2008, two additional tests have been added to CRC screening guidelines of the ACS[26]: sDNA and CTC. CTC is a minimally invasive method for examination of the whole colon. It is safe and the entire colon can be examined thoroughly. A recently study shows that for ≥ 10 mm colorectal lesions, the sensitivity of CTC is similar to that of colonoscopy. However, for < 10 mm and flat neoplasms, the sensitivity of CTC is lower than colonoscopy[27]. Additionally, CTC can not perform biopsy and is an expensive procedure. For these reasons, our study sought to develop a method to improve the sensitivities and specificities of CRC and precancerous lesions screening.

Transferrin (Tf), which is present in plasma by the release of neutrophil-specific granules, is undetectable in normal human gastrointestinal tract. Detection of Tf in feces or contents in the stomach indicates bleeding in gastrointestinal tract. Unlike hemoglobin, Tf is resistant to degradation by digestive enzymes and bacteria. Thus, compared to hemoglobin, Tf is more stable in feces[28]. It has been reported that fecal Tf is elevated in patients with colorectal tumor, compared to healthy individuals[29]. Recently, a number of proteomic studies showed that Tf could be used as a marker expressing in a number of cancers[30,31]. Saitoh *et al*[32] and Hirata *et al*[33] compared fecal Tf with IFOBT in clinical studies and found that Tf was as useful as IFOBT in diagnosing colorectal diseases. However, these two studies did not analyze patients with precancerous lesions. Sheng *et al*[34] compared fecal Tf with IFOBT for their sensitivities in detecting CRC and precancerous lesions in CRC patients. However, the subjects of this study were CRC patients, and specificity was not analyzed.

So far, Tf has not been recommended as a method for CRC screening by the ACS. Based on the above studies, we assumed that the sensitivity and specificity of Tf in detecting CRC and precancerous lesions were equal or superior to IFOBT. Using a combination of the three measurements (g-FOBT, Tf and IFOBT) appears to increase the sensitivity of diagnosis in high-risk population. In order to investigate whether Tf can be applied in the screening of CRC and precancerous lesions, we conducted this study to compare the effectiveness of Tf and IFOBT in the detection of colorectal cancer and precancerous lesions.

MATERIALS AND METHODS

Study materials

The stool specimen collection, colonoscopy and patho-logic examination were performed in the Eighth Hospital of Wuhan City which is a hospital specializing in anorec-tal diseases. G-FOBT, IFOBT and Tf kits were purchased from Baso Diagnostics Inc and WHPM Inc.

Study group

From January 2010 to September 2010, 861 subjects at high-risk (a personal history of curative-intent resection of CRC or intestinal polyps; family history of colorectal cancer; having the following two or more: chronic diar-rhea, chronic constipation, abdominal pain, dark stool, blood or mucus on stool) were recruited. The inclusion criteria were as following: age over 14 years, male or fe-male. Subjects with age < 14 years were excluded. All participants provided written informed consent and were instructed on diet and drug restrictions three days before and during the period of stool collection.

Fecal samples collection and IFOBT and Tf analysis

All fecal samples were collected the day before colonos-copy and processed in accordance with manufacturer's instructions. We applied the fecal sample on the strip and the result was read out within 5 min (the result was invalid after 5 min). A red bar in control area (C) only was considered as negative. A red bar in both the testing area (T) and the control area (C), was considered as positive. If there was no red bar in the control area(C), the test was considered invalid. Tf, IFOBT and g-FOBT were per-formed simultaneously on the same stool. To minimize false-negative cases, all subjects with negative samples were asked to provide an additional stool specimen for a second test; if the second test still gave negative result, a third test would be conducted. As long as one of the three tests showed positive results, the subject was consid-ered to have a positive sample. If the results were all neg-ative after testing three repeated samples, the subject was considered a true negative. Approximately 10% of the samples were repeated and the concordance was 100%.

Statistical analysis

The positive rate of Tf alone, IFOBT alone, Tf com-bined with IFOBT (Tf + IFOBT), Tf and IFOBT com-bined with g-FOBT (Tf + IFOBT + g-FOBT), as well as their respective specificity, likelihood ratio, odd ratio and 95% confidence interval were calculated to compared the sensitivity of Tf, IFOBT, Tf+ IFOBT and Tf + IFOBT + g-FOBT in detecting CRC and precancerous lesions. χ^2 and McNemar's test were conducted to determine the significance of difference. $P < 0.05$ in a two-tailed test was considered statistically significant. Analyses were per-formed using SPSS version 17.0.

RESULTS

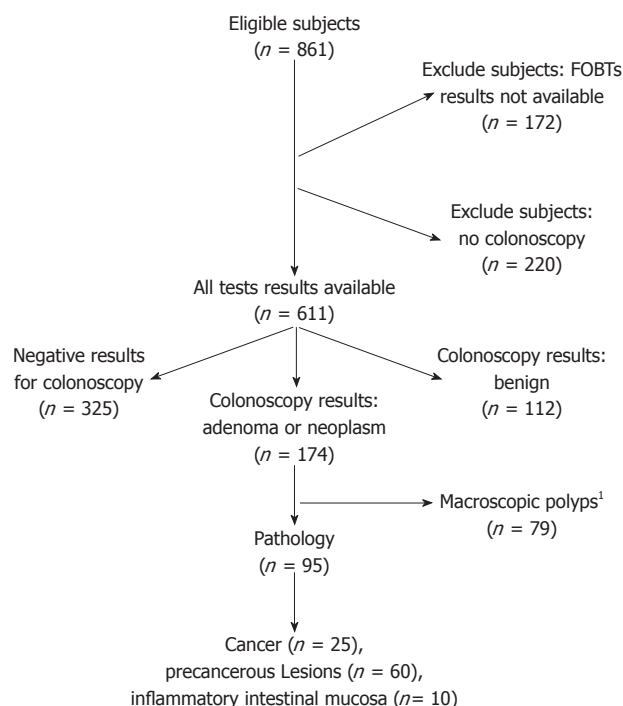Subject enrollment flow is described in Figure 1. Of the

Figure 1 Flow diagram of the study. [1]Includes polyps that were less than 3 mm in diameter, broadbased, sessile and fat.

861 participants in this study, 250 subjects who have tak-en neither FOBTs nor colonoscopy, or have taken only one of the tests were excluded in this survey. Six hundred and eleven subsequently received both FOBTs and colo-noscopy with biopsy performed as needed. Among them, 286 were found to have abnormalities by colonoscopy, while 447 were classified as low risk population includ-ing no abnormalities (325 cases) and benign lesions (122 cases). Benign lesions included chronic enteritis, chronic schistosomiasis bowel disease, intestinal diverticula, co-lorectal erosive inflammation (a total of 112 cases) and inflammatory intestinal mucosa by biopsy (10 cases). One hundred and seventy-four subjects were found to have polyps or neoplasm. Pathological examination showed CRC (25 cases), precancerous lesions (60 cases), inflam-matory intestinal mucosa (10 cases); Polyps (79 cases) that were less than 3 mm in diameter, broad-based, sessile and flat were not subjected to biopsy. Precancerous le-sions included tubular adenoma, villous adenoma, tubular villous adenoma and hyperplastic polyp with moderate-severe dysplasia (with histological confirmation).

The overall demographic information of 611 subjects (Table 1). There were 310 men and 301 women among the participants, with a median age of 50 years (range 14-85 years). Among them, 10 men and 15 women had CRC, with a median age of 62 years; 35 men and 25 women had precancerous lesions, with a median age of 56 years.

The positive rate of g-FOBT, Tf, Tf+ IFOBT, and g-FOBT+ Tf+ IFOBT in fecal samples from five groups of participants is shown in Table 2. In CRC, the positive rates of Tf and IFOBT were 92% and 96%, respectively ($\chi^2 = 0.4$, $P > 0.05$). In precancerous lesions, the positive

Table 1 Patient demographics

Charac-teristic	No. of participants	Colorectal cancer	Precancerous lesions	Polyp	Abnor-mality	Low risk
Total	611	25	60	79	286	447
Sex						
Male	310	10	35	49	152	216
Female	301	15	25	30	134	231
Age, yr						
Median	50	62	56	53	53	48
Range	14-85	39-85	24-84	25-84	17-85	14-81

rates for Tf and IFOBT were 50% and 58%, respectively ($\chi^2 = 0.8$, $P > 0.05$); compared to IFOBT, g-FOBT+ Tf+ IFOBT had a significantly higher positive rate for precancerous lesions (83% *vs* 58%, respectively; $\chi^2 = 9.1$, $P < 0.05$). In CRC and precancerous lesions, the positive rates for Tf and IFOBT were 62% and 69% ($\chi^2 = 0.9$, $P > 0.05$), whereas g-FOBT+ Tf+ IFOBT also provided significantly higher positive rate compared to IFOBT alone (88% *vs* 69%, respectively; $\chi^2 = 9.0$, $P < 0.05$). For Tf alone, a difference in positive rate was observed for detecting CRC and precancerous lesions (92% *vs* 50%, respectively; $\chi^2 = 13.3$, $P < 0.05$).

The performance characteristics of various tests examined by our study (Table 3). For detecting CRC, The specificities of Tf and IFOBT were both 72.0% (95% CI: 68.2%-75.5%); positive likelihood ratios of those were 3.3 (95% CI: 2.8 - 3.9) and 3.4 (95% CI: 2.9-4.0), respectively. For detecting precancerous lesions, specificities of Tf and IFOBT were 71.5% (95% CI: 67.6%-75.1%) and 72.2% (95% CI: 68.4%- 75.8%); positive likelihood ratios of those were 1.8 (95% CI: 1.3-2.3) and 2.1 (95% CI: 1.6-2.7), respectively. For detecting both CRC and precancerous lesions, specificities of Tf and IFOBT were 74.5% (95% CI: 70.6%-78.1%) and 75.5% (95% CI: 71.6%-79.0%); positive likelihood ratios of those were 2.5 (95% CI: 2.0-3.1) and 2.8 (95% CI: 2.3-3.5), respectively. In these tests, the specificity of Tf and IFOBT for detecting CRC was the same. Likelihood ratio can accurately reflect how likely it is that patients with CRC will test positive. The likelihood ratio showed that Tf and IFOBT detected CRC (3.3 and 3.4, respectively) more effectively than they detected precancerous lesions (1.8 and 2.1, respectively).

DISCUSSION

The data from our study demonstrated that the sensitivities and specificities of Tf and IFOBT were similar in the detection of colorectal cancer and precancerous lesions in high-risk cohort. These results suggest that when using Tf alone, the sensitivity and specificity have no visible difference compared to using IFOBT alone; when combining these three methods, the sensitivity can be enhanced.

There had been several comparative studies of Tf and IFOBT previously. Saitoh *et al*[32] found that the sensitivities of Tf and IFOBT for detecting CRC were similar (53.8% and 61.5%, respectively). The study used enzyme-linked immunosorbent assay (ELISA) kit for fecal Tf and Latex agglutination for IFOBT. Hirata *et al*[33] found that the sensitivities of Tf and IFOBT were both 50%, whereas combining both methods gave a slightly higher sensitivity of 61.1%. The study measured the Tf and Hb quantitatively by sandwich ELISA. Both studies analyzed the sensitivity for detecting colorectal diseases (colon cancer, colorectal polyps, ulcerative colitis, Crohn's disease, *etc.*) but not precancerous lesions. In addition, in both previous studies, each patient was tested only once with one stool specimen. In contrast, our study strove to minimize false negative results by testing up to three stool specimens from a single patient, hence achieving a more accurate estimation of sensitivity. Sheng *et al*[34] found that the positive ratio of Tf and IFOBT for detecting colorectal cancer were 80% and 75%, respectively. For detecting precancerous lesions, the positive ratios were 72% (Tf) and 44% (IFOBT). The difference is statistically significant. Combining the two methods gave a positive ratio of 78% in detecting precancerous lesions. Three possible reasons might explain the differences between Sheng *et al*[34] and our study. First, the tested subjects were different. The previous study tested CRC patients. Our study tested those who are at high-risk. Second, the sample size was different. Our study had 611 samples, compared to 110 in the previous study. Third, the design of the studies was different. The previous study took only one stool specimen from an individual patient and retested the sample if the result was negative. We took at least one specimen from every participant and up to three specimens from those showing negative results. None of the three previous studies analyzed the specificities of colorectal cancer and precancerous lesions detection. The difference in specificity may be caused by variation in other factors, such as degradation of hemoglobin, samples, experiment and the quality of reagents, *etc.*

The study shows that Tf and IFOBT both have false positive and false negative results in colorectal cancer and precancerous lesions screening. IFOBT specifically detects the Hb in stool by antibody-antigen reaction. Anti-Hb antibody do not react with animal blood, fruits and vegetables in the testing material, and do not confer peroxidase activity, which obviously reduce the false positive rate. However, the test has several problems, including (1) some participants' hemoglobin may not be recognized by the anti-Hb antibody used in the test; (2) hemoglobin can be degraded by bacteria, resulting in the loss of antigen; (3) the symptom of bleeding in early colorectal lesions is intermittent; and (4) the massive bleeding causes an excessive amount of antigen to be present in the reaction system and hence the "pre-band phenomenon". These are all possible causes of false negative results in the detection using IFOTB. Tf, a type of β1 globulin with a molecular weight of 77 KD, transports extracellular iron into cells through membrane receptor-mediated endocytosis[35]. Tf can resist degradation caused by digestive enzymes and bacteria, and is more stable than hemoglobin in stool. But Tf can only be detected at a concentration

Table 2 Positive rate of three fecal occult blood tests in fecal samples from colorectal cancer patients, precancerous lesions subjects, polyp subjects, abnormality subjects and low risk subjects *n* (%)

Disease (N)	g-FOBT		Tf		IFOBT		Tf+ IFOBT		g-FOBT+ Tf+ IFOBT	
	+[1]	-[1]	+[1]	-[1]	+[1]	-[1]	+[1]	-[1]	+[1]	-[1]
CRC (25)	25 (100)	0 (0)	23 (92)	2 (8)	24 (96)	1 (4)	25 (100)	0 (0)	25 (100)	0 (0)
Precancerous lesions (60)	36 (60)	24 (40)	30 (50)	30 (50)	35 (58)	25 (42)	40 (67)	20 (33)	50 (83)	10 (17)
Polyp (79)	35 (44)	44 (56)	29 (37)	50 (63)	20 (25)	59 (75)	34 (43)	45 (57)	49 (62)	30 (38)
Abnormality (286)	153 (53)	133 (47)	126 (44)	160 (56)	128 (45)	158 (55)	162 (57)	124 (43)	203 (71)	83 (29)
Low risk (447)	148 (33)	299 (67)	105 (23)	342 (77)	109 (24)	338 (76)	154 (34)	293 (66)	221 (49)	226 (51)

[1]*n* (*n*/N × 100%). Tf: Transferrin; IFOBT: Immuno fecal occult blood test; g-FOBT: Guaiac-fecal occult blood test; CRC: Colorectal cancer.

Table 3 Sensitivity, specificity, positive likelihood ratio and odd ratio of three fecal occult blood tests for detection of colorectal cancer, precancerous lesions and colorectal cancer + precancerous lesions

Test	No. of neoplasms detected	Sensitivity%		Specificity%		Likely ratio(+) (95% CI)	Odd ratio (95% CI)
		n/total	% (95% CI)	*n*/total	% (95% CI)		
CRC							
g-FOBT	25	25/25	100 (86.7-100)	367/586	62.6 (58.6-66.5)	2.7 (2.4-3.0)	-
Tf	25	23/25	92 (75.0-97.8)	422/586	72 (68.2-75.5)	3.3 (2.8-3.9)	29.6 (6.8-126.9)
IFOBT	25	24/25	96 (80.5-99.3)	422/586	72 (68.2-75.5)	3.4 (2.9-4.0)	61.8 (8.3-460.2)
Tf+ IFOBT	25	25/25	100 (86.7-100)	358/586	61.1 (57.1-65.0)	2.6 (2.3-2.8)	-
g-FOBT+ Tf+ IFOBT	25	25/25	100 (86.7-100)	266/586	45.4 (41.4-49.4)	1.8 (1.7-2.0)	-
Precancerous lesions							
g-FOBT	60	36/60	60 (47.4-71.4)	343/551	62.3 (58.1-66.2)	1.6 (1.3-2.0)	2.5 (1.4-4.3)
Tf	60	30/60	50 (37.7-62.3)	394/551	71.5 (67.6-75.1)	1.8 (1.3-2.3)	2.5 (1.5-4.3)
IFOBT	60	35/60	58.3 (45.7-70.0)	398/551	72.2 (68.4-75.8)	2.1 (1.6-2.7)	3.6 (2.1-6.3)
Tf+ IFOBT	60	40/60	66.7 (54.1-65.3)	338/551	61.3 (57.2-65.3)	1.7 (1.4-2.1)	3.2 (1.8-5.6)
g-FOBT+ Tf+ IFOBT	60	50/60	83.3 (72.0-90.7)	256/551	46.5 (42.3-50.6)	1.6 (1.4-1.8)	4.3 (2.2-8.7)
CRC+ precancerous lesions							
g-FOBT	85	61/85	71.8 (61.4-80.2)	343/526	65.2 (61.0-69.2)	2.1 (1.7-2.5)	4.8 (2.9-7.9)
Tf	85	53/85	62.4 (51.7-72.0)	392/526	74.5 (70.6-78.1)	2.5 (2.0 -3.1)	4.8 (3.0-7.8)
IFOBT	85	59/85	69.4 (59.0-78.2)	397/526	75.5 (71.6-79.0)	2.8 (2.3-3.5)	7.0 (4.2-11.5)
Tf+ IFOBT	85	65/85	76.5 (66.4-84.2)	338/526	64.3 (60.1-68.2)	2.1 (1.8-2.5)	5.8 (3.4-9.9)
g-FOBT+ Tf+ IFOBT	85	75/85	88.2 (79.7-93.5)	256/526	48.7 (44.4-53.0)	1.7 (1.5-1.9)	7.1 (3.6-14.1)

Tf: Transferrin; IFOBT: Immuno fecal occult blood test; g-FOBT: Guaiac-fecal occult blood test; CRC: Colorectal cancer; CI: Confidence interval.

greater than 10 ng/mL. The ratio of hemoglobin and Tf is 5.4:1 in specimens containing blood. Thus, if the subject has low level of Tf, or the bleeding is very trivial, the testing threshold can not be reached and false negative results will be the outcome. Our study tested the stool specimen repeatedly, therefore reduced the error rate. All subjects underwent standard colonoscopic examination with biopsy performed as needed. In this way, an accurate test was performed to examine the sensitivities and the specificities of the three methods.

The results of this study have a significant implication for CRC screening. A number of studies showed that early detection based on fecal occult blood test helped decrease CRC mortality by 15%-25%[4,7,36]. Mandel *et al*[7,37] found that screening once every year or once every two years with g-FOBT or IFOTB can decrease the mortality of CRC and CRC related diseases, compared to no screening. In our test, for 65 subjects, IFOBT showed negative result while Tf were positive. Hence, Tf is appropriate for the screening of CRC and precancerous lesions. Positive likelihood ratio, which involves both sensitivity and specificity of screening, can fully evaluate the diagnosing value of screening. It is very stable and not subject to morbidity. Results of our study demonstrated that the positive likelihood ratio of Tf detecting CRC was similar with that of IFOBT in various populations, which indicates that Tf has a similar value with IFOBT and is fit for the CRC screening in an average- risk population. Further, the findings of the analysis suggest that a combination of Tf, IFOBT and g-FOBT enables compensation of the inadequacy of single tests, which will reduce false negative rate and improve the positive ratio. So, in order to enhance the sensitivities of detecting CRC and precancerous lesions, all three methods should be used simultaneously.

Our study does have some limitations, and the first is its study subject. The sensitivity and specificity of Tf had been calculated in this study, those of that in an average-risk group are yet to be further determined. Prospective studies in an average-risk group are needed to validate these results. Nevertheless, hardly everyone at average-risk group can undergo colonoscopy, leading that the specificities of fecal occult blood tests can not be evaluated. We prepare to apply computed tomographic virtual

colonoscopy to screen patients who are at average-risk for CRC. The second is the range of age in this study is very wide. The third major limitation of our study is that the three stool occult blood tests were all qualitative and certain amount of deviation was existed compared to quantitative test.

In conclusion, Tf dipstick test can be applied to screen for CRC and precancerous lesions and the efficacy is approximately the same as that of IFOBT in high risk cohort. By combining g-FOBT, Tf and IFOBT, the sensitivity can be improved significantly while the specificity is sacrificed. Large-scale and prospective clinical studies will be needed to determine whether Tf dipstick test can be used as a screening method for CRC and precancerous lesions in different screening population.

COMMENTS

Background
Fecal occult blood test (FOBT) is a simple and convenient tool for colorectal cancer (CRC) screening. Immuno fecal occult blood test (IFOBT) has limited sensitivities and specificities for detecting CRC and precancerous lesions.

Research frontiers
FOBT, a non-invasive method, can reduce CRC incidence and mortality rate. However, hemoglobin (Hb) is unstable in feces because it can be degraded by bacteria. Furthermore, Hb can not be used to detect lesions that are not accompanied by bleeding. Transferrin (Tf), which is present in plasma by the release of neutrophil-specific granules, is undetectable in normal human gastrointestinal tract. Tf can resist degradation caused by digestive enzymes and bacteria, and is more stable than hemoglobin in stool.

Innovations and breakthroughs
Tf dipstick test was found to be as sensitive and specific as IFOBT in the detection of CRC and precancerous lesions in high-risk cohort. Combining guaiac fecal occult blood test, IFOBT and Tf enhanced the sensitivity.

Applications
Tf dipstick test can be applied to screen for CRC and precancerous lesions and the efficacy is approximately the same as that of IFOBT in high risk cohort.

Terminology
Transferin (Tf), a type of β1 globulin with a molecular weight of 77 KD, transports extracellular iron into cells through membrane receptor-mediated endocytosis. Detection of Tf in feces or contents in the stomach indicates bleeding in gastrointestinal tract.

Peer review
The study seeks to evaluate biomarkers for colorectal cancer screening. To develop non-invasive method such as fecal test for cancer screening is clinically relevant. The study has tested a reasonable size of cohorts and found combined test of several markers let to significantly increased sensitivity of detecting cancerous lesions compared to the commonly used method. The results suggest that the transferrin dipstick test might be used as an additional tool for colorectal cancer and precancerous lesions screening in a high-risk cohort.

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