*Original Article*

# Is Single Stool Occult Blood Test or Serum CEA Level Valuable in Health Check Up?

Ming-Chang Li
Jen-Kou Lin
Tzu-Chen Lin
Wei-Shone Chen
Jeng-Kae Jiang
Shung-Haur Yang
Huann-Sheng Wang
Shih-Ching Chang

*Division of Colorectal Surgery, Department of Surgery, Taipei Veterans General Hospital,*
*National Yang-Ming University, Taipei, Taiwan, R.O.C.*

***Key Words***
Fecal occult blood tests;
Serum CEA level;
Colorectal cancer;
Physical check-up;
Colonoscopy

***Purpose.*** Stool occult blood tests and serum CEA level examinations are widely used at health check-up of detecting colorectal lesions. The aim of this study is to evaluate the effectiveness of using single stool occult blood tests or serum CEA levels in routine health check up.
***Methods.*** We examined 1404 patients who came for health check up at Veterans General Hospital, Taipei, Taiwan from April 2004 to May 2005. They were all underwent single stool occult blood test, serum CEA level and complete colonoscopy during the check up.
***Results.*** There were patients with colorectal cancers in 9 (0.6%), polyps in 268 (19.1%) (Significant polyps in 95), diverticulum in 86 (6.1%) and other lesions in 9 (0.6%). Positive stool occult blood tests were noted in 97 patients (6.9%). The sensitivity, specificity, false positive rate and false negative rate of stool occult blood test to detect significant colorectal neoplasm were 14.4%, 93.1%, 6.9% and 85.6% respectively. There were 39 (2.8%) patients showed elevated serum CEA level with the cut-off value of 6.0 ng/mL. The sensitivity, specificity, false positive rate and false negative rate of elevated CEA level to detect colorectal tumor was 15.4%, 92.8%, 7.2% and 84.6% respectively. The distributions of colorectal cancers and polyps were 26.5% proximal and 73.5% distal to the descending colon. Among the patients with colorectal cancers, only one who came for health check-up was completely free of gastrointestinal symptoms.
***Conclusions.*** Single stool occult blood test and serum CEA level were failed to effectiveness in health check up due to very low sensitivity and unacceptable high false-negative rates, the routine fibro-sigmoidoscopic examination of 60cm in check up was not enough for complete detection of colorectal cancer and polyp because there were still one fourth lesions distributed proximal to the upper limit of flexible sigmoidoscopic examinations. The most effective ways to detect colorectal lesions were complete colonoscopy and the awareness of the early symptoms of the cancer. Complete colonoscopy should be recommended in patients asking for health checkup. [*J Soc Colon Rectal Surgeon* (*Taiwan*) *2006;17:71-78*]

Many organizations and expert panels recommend colorectal cancer screening in average-risk asymptomatic persons older than 50 years of age. Randomized, controlled trials show that screening with fecal occult blood tests (FOBTs) can reduce both death from colorectal cancer and subsequent incidence of new cancer. In recent years, Fecal occult blood tests (FOBT) and serum CEA level examinations are commonly included in the program of health check-up in Taiwan.

Recent studies have found that primary care providers use FOBT as primary screening test, how-

Received: April 28, 2006. Accepted: July 2, 2006.
Correspondence to: Dr. Jen-Kou Lin, Division of Colon and Rectal Surgery, Taipei Veterans General Hospital, No. 201, Shih-Pai Road, Sec. 2, Taipei 112, Taiwan. Tel: +886-2-2875-7544 ext. 110, Fax: +886-2-2875-7639, E-mail: jklin@vghtpe.gov.tw

ever, the methods used to obtain stool samples vary greatly. In 24% to 64% of practices, a single digital rectal examination plus single FOBT is performed in the office as the primary method. The presumed rationale for using an office-based test is to improve patient adherence. Previous studies have found that the sensitivity and specificity of an office-based FOBT is similar to that of the standard 6-sample home test.[1,2] There are no data evaluating the sensitivity and specificity of single FOBT or its effect on mortality reduction in colorectal cancer. No previous reports studied the colonoscopic findings in patients with negative single FOBT. Therefore, negative results on digital FOBT may falsely reassure both patients and physicians. If a single FOBT is commonly used for colorectal cancer screening or health check up, it is important to understand the sensitivity and specificity of this strategy.[3]

CEA has been used extensively in clinical practice. Its utility for colorectal cancer has been documented not only for monitoring recurrence of disease but also evaluating the effectiveness of chemotherapy and as a prognostic factor. Increasing serum levels of CEA indicate tumor recurrence and may have a lead time up to 23 months.[25] Compared to colonoscopy, chest x-ray, or physical examination, CEA measurements were found to be the most cost-effective test in detecting potentially curable recurrent disease. However, the predictive value of elevated serum CEA level in the early diagnosis of colorectal cancer is still controversial.

Our primary aim is to evaluate the effectiveness of using single fecal occult blood tests or serum CEA levels in routine health check up. Besides, the value of flexible sigmoidoscopic examinations in detecting active colorectal lesions is also assessed in this article.

# Material and Methods

## Patient Selection

Patients were concecutively recruited from health check-up department from April 2004 and May 2005. Patients were excluded if they reported symptoms of lower gastrointestinal tract disease, including rectal bleeding for more than 1 occasion in the previous 6 months, a marked change in bowel habits, or lower abdominal pain that would normally require a medical evaluation. Other exclusion criteria included any previous disease of the colon, structural examinations of the colon within the previous 10 years, and serious comorbid conditions that would increase the risk for colonoscopy. All patients underwent single FOBT, serum CEA examination, and complete colonoscopy during the 1 or 2-day course of health check-up.[4]

## Procedures

Eligible patients had a complete physical examination by the study physician that included a rectodigital examination to identify rectal masses. FOBT was performed on a single sample by using guaiac-impregnated cards (Hemoccult II, SmithKline Beckman, Palo Alto, California).[5,6] They also received a sheet of written dietary instructions advising them to restrict consumption of red meat, vitamin C, and aspirin before obtaining the samples. Patients who did not have a completed digital FOBT or who did not submit test cards were excluded from this analysis. One adequate amount of stool sample was applied to the cards and they were returned on the day of the colonoscopy. Adequate amount of blood samples were also collected for complete blood tests including serum CEA level. The cut-off value of CEA level was 6.0 ng/mL. All patients had complete colonoscopy to the cecum, And in all cases, the endoscopists were not aware of the results of either FOBT or CEA levels.[2,5,7]

## Histologic Evaluation

At colonoscopy, all visible polypoid lesions were removed or biopsied and sent to pathology laboratories for processing. Results were interpreted by two central pathologists, and, when there was disagreement, a third reviewing pathologist. None of the pathologists were aware of the other test results or interpretations. Patients were classified on the basis of the most advanced lesion detected during colonoscopy. The term significant neoplasm (SN) was defined as adenoma with a di-

ameter ≥ 10 mm, adenoma with high-grade dysplasia, multiple adenoma (≥ 2) or colorectal cancer.[6,8,9]

### Statistical Analysis

The statistical analysis detailed here is based primarily on descriptive statistics, including means and standard errors for continuous variables as well as the calculation of rates and proportions for categorical data. The performance characteristics of the diagnostic screening strategies were evaluated by calculating sensitivity and specificity according to the standard definition, along with corresponding 95% confidence intervals (CIs). We also included positive and negative predictive values and likelihood ratios with corresponding 95% confidence intervals (CIs) for both positive and negative FOBT results. The $\chi^2$ test was used to calculated odds ratios and 95% confidence intervals (CIs) for the association between FOBT results, elevated serum CEA levels and the positive colonoscopic findings. p values of ≤ 0.05 were considered statistically significant. SPSS® software, version 12, (SPSS Inc., Chicago, IL) was used to analyze the data.

## Results

Of 1458 persons who were screened for inclusion of the study, 1404 met the criteria for enrollment. The mean age (± SE) of the study group was 63.1 ± 0.1 years; 872 patients (62.1%) were men. The number of patients with positive FOBT and elevated serum CEA levels were 97 (6.2%) and 39 (2.7%) respectively. There were 372 patients who had active lesions found in colonoscopic examinations (Table 1).

Of the 372 patients, 9 had colorectal cancer and 268 had colorectal polyps, and the positive FOBT rates among these patients were 55.5% and 5.1% (Table 2). The common benign lesion found was adenoma, diverticulum, and hyperplastic polyp. The correlation of FOBT results and colonoscopic findings is shown in Table 3. Among the 97 patients with single FOBT positive results, positive colonoscopic finding was seen in

**Table1. Characteristics of Included Patients**

| | |
|---|---|
| Mean age ± SE (range), year | 63.1 ± 0.1 (47-88) |
| Male : Female, n (%) | 872 : 532 (62.1 :37.9) |
| Variable | n (%) |
| Positive FOBT | 97 (6.9) |
| Elevated CEA | 39 (2.7) |
| Positive colonoscopic finding | 372 (26.5) |
| Colorectal Cancer | 9 (0.6) |
| Significant polyp | 95 (6.8) |
| Non-significant polyp | 173 (12.3) |
| Diverticulum | 86 (6.1) |
| Angiodysplasia | 9 (0.6) |

**Table 2. Results of Colonoscopic Findings and FOBT**

| Colonoscopic Findings | Patients, n | Single FOBT (+), n (%) |
|---|---|---|
| Total Patients | 372 | 29 (7.8) |
| CRC | 9 | 5 (55.5) |
| Polyps | 268 | 13 (5.1) |
| Tubular Adenoma | 169 | 11 (6.5) |
| Villous Adenoma | 11 | 0 (0) |
| Tubulovillous Adenoma | 17 | 1 (5.9) |
| Hyperplastic Polyp | 46 | 1 (2.4) |
| Chronic Inflammation | 25 | 0 (0) |
| Significant polyps | 95 | 9 (5.3) |
| Non-significant. polyps | 173 | 4 (2.3) |
| Diverticulum | 86 | 11 (12.8) |
| Angiodysplasia | 9 | 0 (0) |

**Table 3. Correlation of FOBT and Colonoscopic Findings**

| Results | FOBT (+), n (%) N = 97 | FOBT (-), n (%) N = 1307 | Odds Ratio, (95% CIs) | *p |
|---|---|---|---|---|
| Patient with positive colonoscopic findings | 29 (29.9) | 343 (26.2) | 1.20 (0.76-1.90) | 0.43 |
| CRC | 5 (5.0) | 4 (0.3) | 17.70 (4.67-67.05) | < 0.001 |
| Significant polyps | 9 (9.2) | 86 (6.6) | 1.45 (0.71-2.98) | 0.30 |
| Non-significant polyps | 5 (5.0) | 168 (12.8) | 0.37 (0.15-0.92) | 0.026 |
| Diverticulum | 10 (10.3) | 76 (5.8) | 1.86 (0.93-3.73) | 0.075 |
| Angiodysplasia | 0 (0) | 9 (0.7) | – – | 0.412 |

*: The $\chi^2$ test, CRC: colorectal cancers, CIs: confidence intervals.

**Table 4. Correlation of CEA level and Colonoscopic Findings**

| Results | CEA = 6 ng/mL, n (%), N=39 | CEA<6 ng/mL, n (%), N=1365 | Odds Ratio (95% CIs) | *p |
|---|---|---|---|---|
| Patient with positive colonoscopic findings | 10 (25.6) | 362 (26.5) | 1.35 (0.56-1.88) | 0.90 |
| CRC | 3 (7.6) | 6 (0.4) | 18.88 (4.54-78.47) | <0.001 |
| Significant polyps | 3 (7.6) | 92 (6.7) | 1.15 (0.35-3.82) | 0.815 |
| Non-significant polyps | 4 (10.4) | 169 (12.4) | 0.81 (0.28-2.30) | 0.691 |
| Diverticulum | 0 (0) | 86 (6.3) | – – | 0.106 |
| Angiodysplasia | 0 (0) | 9 (0.7) | – – | 0.611 |
| Mean CEA ± SE (Range) | | 2.5 ± 0.2 (0.98 – 33.37) | | |

*: The $\chi^2$ test, CRC: colorectal cancer, CIs: confidence intervals.

29 (29.9%) patients. In these 5 (5.0%) patients were colorectal cancer, 9 (9.2%) were significant polyps and 10 (10.3%) were diverticulum. The correlation of CEA level and neoplastic lesions is shown in Table 4. There were 39 patients who had elevated serum CEA levels, and 10 (25.6%) of these 39 patients had positive colonoscopic findings. When the patients had positive FOBT result, the risk of colorectal cancer was significantly higher than the patients who had negative FOBT result (5.0% vs 0.3%, ORs: 17.70, $p < 0.001$), and the risk of non-significant polyp was significantly lower than the negative FOBT patients (5.0% vs 12.8%, ORs: 0.37, $p = 0.026$). Among the 10 patients combined with serum CEA level greater than 6 ng/mL and positive colonoscopic findings, 3 (7.6%) patients had colorectal cancer, 3 (7.6%) had significant polyp, and 4 (10.4%) had non-significant polyp. When the patients had elevated serum CEA levels, the risk of colorectal cancer was significantly higher than the patients without elevated serum CEA levels (7.6% vs 0.4%, ORs: 18.88, $p < 0.001$).

The distribution of active colorectal lesions is shown in Table 5. Three quarters of the active lesions were distributed at a location distal to descending colon ($n = 274$, 73.5%), which was the usual upper limit of a 60cm sigmoidofibroscopy reached.

In the significant neoplasm group, the sensitivity of positive FOBT, elevated serum CEA level and either one of the examinations (positive FOBT or elevated serum CEA level) were 14.4%, 15.4% and 34.8% (Table 6). The specificity among them was 93.1%,

**Table 5. The Distribution of Active Colorectal Lesions Found in Colonoscopic Examinations**

| Location | n | (%) |
|---|---|---|
| Cecum | 16 | (4.2) |
| Ascending Colon | 34 | (9.3) |
| Hepatic Flexure | 10 | (2.8) |
| Transverse Colon | 29 | (7.8) |
| Splenic Flexure | 9 | (2.4) |
| Descending Colon | 25 | (6.6) |
| Sigmoid Colon | 127 | (34.2) |
| Rectum | 122 | (32.7) |
| Distal to Descending Colon | 274 | (73.5) |

**Table 6. Specificity, Sensitivity, False Positive and Negative Rates of FOBT and CEA Level for Colorectal Lesions**

| Variables | FOBT (+) %, (95% CI) | CEA ≥ 6ng/dl %, (95% CI) | FOBT (+) or CEA ≥ 6ng/dl %, (95% CI) |
|---|---|---|---|
| Sensitivity (SN) | 14.4 (9.9-17.5) | 15.4 (12.7-19.3) | 34.8 (25.1-39.5) |
| Spesificity (SN) | 93.1 (90.2-95.5) | 92.8 (88.1-97.6) | 95.0 (93.2-96.9) |
| FPR (SN) | 6.9 (3.2-9.8) | 7.2 (2.9-11.7) | 5.0 (2.2-7.7) |
| FNR (SN) | 85.6 (79.1-92.7) | 84.6 (76.1-94.7) | 65.2 (59.3-72.4) |
| Sensitivity (CRC) | 55.5 (31.6-72.4) | 33.3 (11.6-61.2) | 66.7 (31.3-81.2) |
| Specificity (CRC) | 93.4 (91.2-95.1) | 96.8 (93.3-97.2) | 92.4 (90.9-97.0) |
| FPR (CRC) | 6.6 (3.7-8.2) | 3.2 (1.9-5.6) | 7.6 (3.7-9.9) |
| FNR (CRC) | 44.5 (22.1-67.5) | 66.7 (41.4-88.2) | 33.3 (11.1-74.4) |

SN: significant neoplasm, CRC: colorectal cancer, FPR: false positive rate, FNR: false negative rate.

**Table 7. Detail of Patients with Screened Colorectal Cancer**

| | Gender | Age | Initial Symptoms | TNM | FOBT | CEA | Location |
|---|---|---|---|---|---|---|---|
| 1 | M | 82 | bloody stool | pT3N1M0 | 1+ | 2.68 | Rectum |
| 2 | F | 79 | Nil | PTisN0M0 | - | 1.81 | R-S |
| 3 | F | 68 | weakness | pT3N1M1 | - | 38.37 | T-colon |
| 4 | M | 82 | dizziness | pT3N0M0 | 2+ | 3.2 | S-colon |
| 5 | M | 78 | loss of body weight | pT3N0M0 | - | 6.05 | Rectum |
| 6 | M | 77 | loss of body weight | pT3N1M0 | 1+ | 2.47 | S-colon |
| 7 | F | 81 | diarrhea | pT3N0M0 | 1+ | 2.79 | A-colon |
| 8 | M | 79 | loss of body weight | pT2N0M0 | - | 11.96 | S-colon |
| 9 | M | 66 | weakness | pT3N2M0 | 1+ | 3.48 | Rectum |

CIS: carcinoma in situ, R-S: recto-sigmoid junction.

92.8% and 95.0%. The false positive rate and false negative rate were 6.9%, 85.6%: 7.2%, 84.6% and 5.0%, 65.2%, respectively. The sensitivity, specificity, false positive and negative rates among the colorectal cancer group were also shown in Table 6.

The details of the patients who had colorectal cancer found during this health checkup were mentioned in Table 7. Among the 9 patients with colorectal cancer, only 1 (No. 2) was completely free of symptoms after a more detailed retrospective history taking. Only 5 of these patients had positive FOBT and only 3 of these patients had serum CEA level higher than 6 ng/mL. All of the 9 patients were admitted to hospital, received complete survey of colorectal cancer, and radical surgery were all done smoothly. Five (No. 2, 4, 5, 7, 8) of them were TNM stage I or II. Two of the patients had tumor at a location proximal to splenic flexure.

## Discussion

Screening asymptomatic persons for colorectal cancer can reduce mortality rate among those who accept the test, but only if screening is performed with adequate quality. Judith reported that the sensitivity and specificity of single FOBT were 4.9%, 97.1% and of 6-sample FOBT were 23.9%, 93.9%. Despite low sensitivity of single FOBT, many clinicians still use single FOBT with rectodigital examinations for primary screening.[18] This approach may be attractive because the test can be completed during the office visit and does not depend on patient adherence in returning test cards. The guaiac-based FOBT was easy-to use and inexpensive. It is hypothesized that use of nonsteroidal anti-inflammatory drugs or lack of dietary restrictions could produce false-positive results on digital FOBT and lead to unnecessary colonoscopy. Compared to this study, Bini and colleagues[12] found similar rates of pathological findings in asymptomatic patients with positive single FOBT. The other small retrospective study also supported Bini and colleagues' findings.[16,17,18,19]

The major role of serum CEA levels is in the follow up of patients for relapse after intended curative treatment of colorectal cancer. When patients with a normal postoperative CEA level have serial elevation of serum CEA levels, recurrence of cancer should be suspected. However, the value of serum CEA levels in predicting colorectal cancer during screening is still questioning. Greg and colleagues[31] reported that fewer than 25% of patients with an early disease had an elevated CEA levels and claimed that CEA may not be useful in screening colorectal diseases. In this study, there were only 10 (2.7%) in 372 patients with colorectal neoplasm (cancer and polyp) and 3 of 9 colorectal caner patients had elevated CEA levels compatible with Greg's findings. It is obvious that an elevated serum CEA level is not an ideal indicator for predicting colorectal malignancy.

Specificity and sensitivity are important factors in selecting and appropriate screening strategy for colorectal cancer. Tests with low specificity are more likely to produce false positives and result in unnecessary, costly subsequent more confirmly examinations. These costs include time, patient anxiety, overuse of limited endoscopy resources, and money.[12,27,28] Tests

with low sensitivity are more likely to result in false negatives, or a missed diagnosis of a cancer. Early diagnosis and treatment are necessary for optimal survival rates. The single FOBT has a specificity for cancers of 96.8% to 98.9% and a wide range of reported sensitivities for cancers at 11% to 80.8% according to the Medicare 2003.[31] This blood-based test has a sensitivity for hemoglobin of 0.3 mg hemoglobin per gram of stool. The colon does have a small amount of normal blood loss, but 2 to 3 mL/day is considered the lower limit of GI tract pathology. According to the report of Beckman with the colleagues, all single FOBT will be positive with a blood loss of 10 mL/day. Testing of three or six consecutive stools is important because tumors may bleed in small amounts, intermittently, or not at all.[29,30]

Helm reported that as screening methods, the false negative rate must lower than 30%.[27] In our study, the highest false negative rate was up to 85.6%, which means that either single FOBT or serum CEA levels may not be an ideal methods in screening colorectal cancer.

In screening colorectal cancer, the American Cancer Society recommends five screening regimens for adults of average risk:[17,18,21] (1) Fecal occult blood test (FOBT) every one year, (2) Flexible sigmoidoscopy every 5 years, (3) FOBT every one year + sigmoidoscopy every 5 years, (4) Double-contrast barium enema every 5 years; and (5) Complete colonoscopy every 10 years. In our study, there were 26.5% of the lesions located proximal to descending colon, which means there were nearly one fourth of the lesion may be missed when flexible sigmoidoscopy was used for screening, and this screening method may not sufficient for moderate to high risk adults, especially for the old age patients asking for a complete health check up.

It is known that most screened colorectal cancers were early staged (Dukes' staging A or B). Hurlstone with colleagues reported that 50-80% of screened cancers were Dukes' stage A or B in the United Kingdom.[19] In our study, there were 5 (55.5%) of 9 patients of colorectal cancer found in health check up had Dukes'A or B tumors. After a more detailed retrospective history taking, we found that there was only 1 (11.1%) patients was actually free of symptoms before coming check-up in our study.

In conclusion, single FOBT and serum CEA level are poor screening tests for colorectal cancer and can not be used in patients asking for a health check up. Flexible sigmoidoscopic examination may not enough for detection of colorectal lesions because there were still one fourth lesions distributed proximal to the upper limit of Sigmoidoscopy. The most effective ways to detect colorectal lesions were complete colonoscopy and the awareness of the early symptoms of the cancer. Complete colonoscopy should be recommended in patients asking for health checkup.

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