*Original Article*

# The Prevention of Development of Colorectal Cancer by Colonoscopy after Positive Fecal Occult Blood Test

Rakchob T, MD[1], Supsamutchai C, MD[2], Teerapradith J, MD[2], Promboon T, MD[2], Chiemsombat P, MD[2], Choikrua P, BSc[3], Jirasiritham J, MD[2]

[1] Department of Surgery, Buriram Hospital, Buriram, Thailand
[2] Department of Surgery, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
[3] Surgical Research Unit, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

***Background:*** Fecal occult blood tests (FOBTs) have been known as a colorectal cancer (CRC) screening tool for 30 years. Because of the reasonable price and simplicity, the test is used to the present. However, fecal occult blood tests have low specificity to the human blood and colonoscopy is superior in colorectal cancer screening. Now, the use of fecal occult blood tests as screening tool has been questioned.

***Objective:*** To demonstrate that FOBTs have a role in improving diagnostic performance in colorectal cancer screening.

***Materials and Methods:*** Retrospective chart review of patients who were screening for colorectal cancer by FOBT and colonoscopy was performed from January 2006 to December 2015 in Ramathibodi Hospital. Patients with a history of CRC, incomplete colonoscopy and inflammatory bowel disease were excluded. Result of FOBT and colonoscopy were collected including pathological finding, size and location of the lesion.

***Results:*** 2,043 patients were included in this study. FOBT positive rate was 48.89% and cancer was found in this group 99 of 999 patients (9.9%). Positive predictive value (PPV), negative predictive value (NPV) and sensitivity of positive FOBTs for the cancer were 10 (8.2 to 12), 98.3 (97.3 to 99) and 84.6% (76.8 to 90.6), respectively. Positive predictive value (PPV), negative predictive value (NPV) and sensitivity of positive FOBTs for advanced adenoma and cancer were 12.5 (10.5 to 14.7), 96.6 (95.4 to 97.7) and 78.1% (70.9 to 84.3), respectively. Sensitivity was increased with the larger size and number of polyps; moreover sensitivity was highest in the left side colon (53.6%).

***Conclusion:*** In our study showed positive FOBTs has high sensitivity for colorectal cancer screening (84.6%) with acceptable PPV (10). With the advantage of the FOBTs, non-invasive, low cost and easy-to-used method, FOBTs should be considered for first step CRC screening. However, the high false positive rate of this test must be made aware.

***Keywords:*** Colorectal cancer screening, Colorectal polyp, Fecal occult blood test

**J Med Assoc Thai 2019;102(Suppl.2): S18-23**
**Website:** http://www.jmatonline.com

Colorectal cancer (CRC) is known as the third most common cancer in the world[1]. Most cases of CRC are sporadic and evolved from removable pre-cancerous lesions (adenomas) and also curable in early stage of cancer[2], so screening for CRC has a high potential for reducing morbidity and mortality.

Around 30 years ago, guaiac-based fecal occult blood tests (G-FOBT), used for colorectal cancer (CRC) screening, were introduced[3,4]. A G-FOBT is relatively inexpensive, easy to use and can be carried out at home[5]. However, G-FOBTs are not specific for human blood and quality control in the evaluation of the tests is hardly possible[6]. Despite these disadvantages, the G-FOBT is still the most implemented test for CRC screening for a long period[7-12].

Nowadays, colonoscopy is the most complete test for CRC and colorectal adenomas[13,14], but there has been low participation rate in population screening[15,16]. CT colonography (CTC) has been proposed as a screening test for CRC[17], but the cost effectiveness when compared with conventional colonoscopy is still in a doubt.

Colorectal cancer (CRC) screening is usually undertaken as a one step or two-step process depending on whether colonoscopy is used as the solo test or after the FOBT has been confirmed[18]. Anyway, FOBT has been used as the traditional first-step test in almost every screening programs[19].

The objective of this study was to demonstrate

**Correspondence to:**

Supsamutchai C.

Department of Surgery, Faculty of Medicine Ramathibodi Hospital, 270 Rama 6 Road, Ratchathewi, Bangkok 10400, Thailand.

**Phone & Fax:** +66-2-2011304

**E-mail:** pogeneral2007@hotmail.com

**How to cite this article:** Supsamutchai C, Teerapradith J, Jirasiritham J, Promboon T, Chiemsombat P, Choikrua P. The Prevention of Development of Colorectal Cancer by Colonoscopy after Positive Fecal Occult Blood Test. J Med Assoc Thai 2019;102;Suppl.2: S18-23.

that FOBTs have a role in improving diagnostic performance; the tests were compared with no FOBTs in patients at Ramathibodi Hospital.

## Materials and Methods

Ethical approval was obtained from Ramathibodi Hospital, Mahidol university review board. The chart records in Ramathibodi Hospital from January 2006 to December 2015 were reviewed and 2,043 patients were identified. The inclusion criteria are patients with more than 20 years old, Patients with result of FOBT and colonoscopy at Ramathibodi Hospital and Patients who have not been screening CRC. The exclusion criteria are patients with known or symptomatic CRC, patients with a history of CRC, patients who underwent incomplete colonoscopy and inflammatory bowel disease as shown in the diagram below.

The most commonly implemented FOBT, Hemoccult II (Beckman Coulter) was used in this study. All patients underwent colonoscopy which performed by experienced gastroenterologists, general surgeons and surgical oncologists under conscious sedation technique (using midazolam and pethidine). Occasionally a computed tomographic colonoscopy was performed followed by a second colonoscopy, if necessary. Suspected neoplastic polyps were removed, and other abnormal lesions were biopsied. Lesions were classified as any adenoma (pedunculated or sessile polyps), carcinoma, or other and recorded in number, size (<10 mm, or ≥10 mm), and location (proximal [cecum to splenic flexure] or distal [descending colon] or rectum)[22]. Histology was evaluated by an experienced pathologist and graded as carcinoma, tubular adenoma, tubulovillous adenoma, villous adenoma, serrated adenoma, hyperplastic polyp, or miscellaneous. Polyp size was measured by the endoscopist. Advanced adenomas were defined as adenomas >10 mm, with high-grade dysplasia or with a villous component >20%[20].

### *Statistical analysis*

Univariable analyses were conducted using the $X^2$ test. A *p*-value of less than 0.05 was considered significant. Positive predictive values are calculated using the number of individuals with the relevant test result who underwent colonoscopy as the denominator. Rates and rate differences of participation, positivity, detection, PPV, and specificity

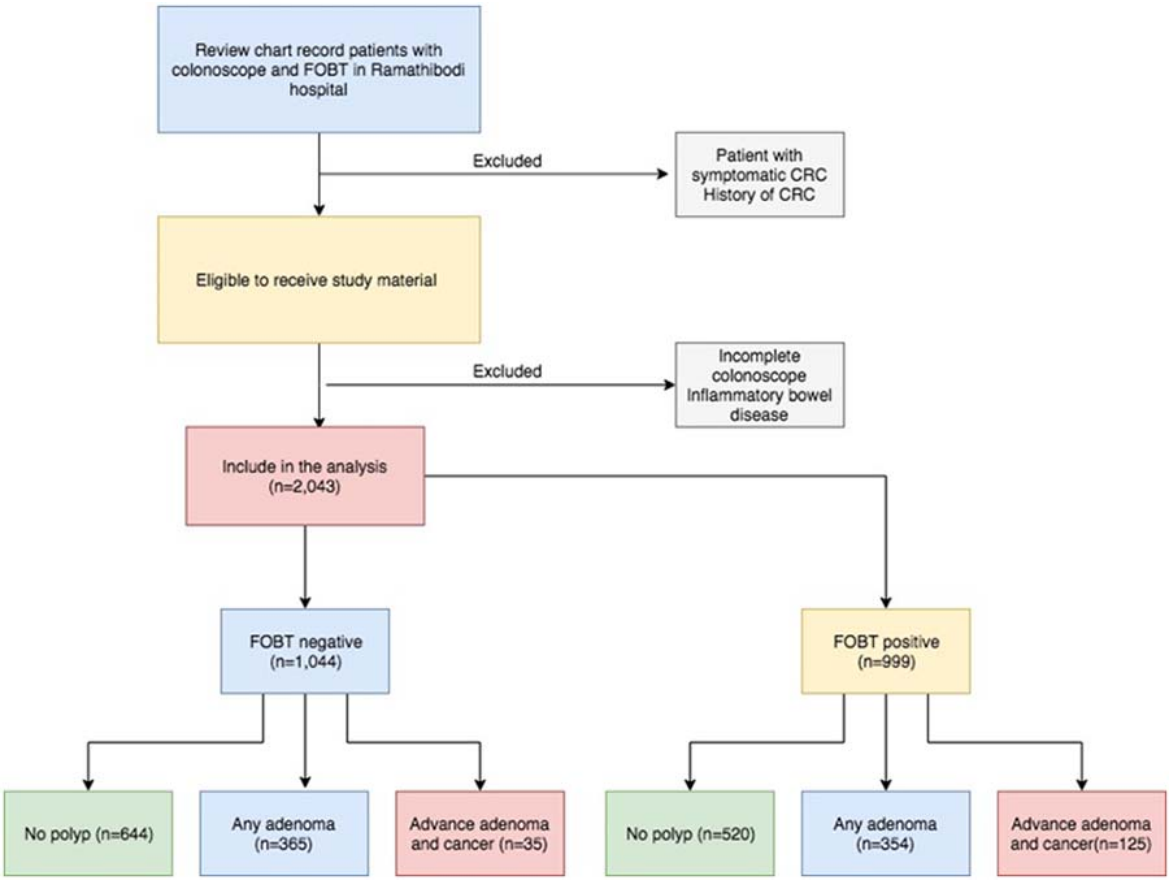


**Figure 1.** Study flow diagram.

were calculated and all percentages were reported with 95% confidence intervals (95% CI). Rate differences are statistically significant if the confidence interval does not include zero. Data were analyzed using STATA V.14 (StataCorp LP 4905 Lakeway Drive College Station, Texas 77845-4512 USA).

If >1 lesion was present, a patient was classified by the most advanced lesion from more to less severe: from carcinoma, to ≥1 adenoma ≥10 mm, to high-grade dysplasia, to villous component >20%, to minor neoplasia.

Statistically significant differences are supplemented with *p*-values. In the tables, statistically significant differences are bolded.

## Results

We included 2,043 patients who underwent a colorectal screening program in our hospital between January 2006 and December 2015. FOBT was performed in all included patients. FOBT positivity rate was 48.89%. A total of 2,043 patients were referred for colonoscopy. Colorectal cancer was detected in 99 of 999 (9.9%) patients with positive FOBT (Table 1).

Adenomas were detected in 824 of 2,043 individuals (40.33%). All 824 Polyps were classified into 6 pathologic subgroups. 56 of 824 polyps were classified as 'advance adenoma' (6.79%).

The positive predictive values (PPV) and negative predictive values (NPPV) of a positive FOBT result for cancer are 10 (8.2 to 12) and 98.3 (97.3 to 99), respectively, with sensitivity for the detection of colorectal cancer is 84.6% (76.8 to 90.6, 95% CI).

Table 2 shows sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPPV) stratified by type, location, number, and size of adenoma.

The sensitivity and negative predictive values (NPPV) of a positive FOBT result for advanced adenomas and cancer are 8.1% and 96.6 (95.4 to 97.7, 95% CI) respectively.

Sensitivity for detecting colonic polyp is highest in left-sided colon (53.6%) and sensitivity increased with greater number and size of adenomas. Higher Negative predictive value was observed for the rectum than for right and left side adenomas.

Result shows that significant rate of positive FOBT is higher in older age group (>50 year) ($p = 0.008$). The rates of positive results increased with age. At age more than 50 years FOBT have highest likelihood ratio of positive result (OR = 1.36, 1.08 to 1.71, 95% CI).

## Discussion

Stool occult blood has a role as an alternative tool for screening colorectal cancer, whereas colonoscopy has more precision on advance adenomatous polyp and cancer detection and also can perform tissue-biopsy for diagnosis confirmation. Moreover, colonoscopy can treat some advance polyps but these cost more and considered as invasive procedures which have risks of complications for example: abdominal bloating, colonic perforation or post-polypectpmy bleeding. According to standard recommendations, all patients who had CRC risks should go for colonoscopy, but this is hardly possible in the real world practice because of the lack of resources or even endoscopists. In order to fill this gap, the use of FOBT for screening CRC has many benefits; to decrease workload; costs less resources, reduces complication after colonoscopy, can be used on a routine basis and more practical for patients to perform by themselves. It represents a significant cost savings compared to solo colonoscopy. From the results, precision and performances in FOBT positive from advance adenoma and cancer groups were statistically significant for truly positive finding from tests. Besides, our characteristic data show this study has more female patients than males; this may be because, naturally, females are more concerned about heath and screening themselves than male patients.

Our data show that the rates of positive FOBT result is higher than previous studies from Allison and teams[18] in 8,000 average risk patients without symptoms (48.63% vs. 2.5%). Also Sensitivity of FOBT test to detect

**Table 1.** Show sample characteristic data

| Characteristics | Total n = 2,043 | FOBT negative n (%) | FOBT positive n (%) | *p*-value |
|---|---|---|---|---|
| Age (year) | | | | |
| <50 | 355 (17.38) | 204 (19.54) | 151 (15.12) | 0.008 |
| ≥50 | 1,688 (82.62) | 840 (80.46) | 848 (84.88) | |
| Sex | | | | |
| Male | 823 (40.28) | 394 (37.74) | 429 (42.94) | 0.017 |
| Female | 1,220 (59.72) | 650 (62.26) | 570 (57.06) | |
| FH colorectal cancer | | | | |
| No | 1,960 (95.94) | 992 (95.02) | 968 (96.90) | 0.032 |
| Yes | 83 (4.06) | 52 (4.98) | 31 (3.10) | |
| Cancer | | | | |
| No | 1,921 (94.26) | 1,026 (98.28) | 895 (90.04) | 0.000 |
| Yes | 117 (5.74) | 18 (1.72) | 99 (9.96) | |

**Table 2.** Show test result polyp and cancer performance

| Polyp and cancer performance characteristic | FOBT | | Sensitivity percentage (95% CI) | Specificity percentage (95% CI) | Positive predictive value percentage (95% CI) | Negative predictive value percentage (95% CI) |
|---|---|---|---|---|---|---|
| | n, positive | n, negative | | | | |
| Polyp | | | | | | |
| No polyp | 520 | 644 | 44.7 (41.8 to 47.6) | 45.5 (42.2 to 48.9) | 52.1 (48.9 to 55.2) | 38.3 (35.4 to 41.3) |
| Any adenoma | | | | | | |
| Age total | 354 | 365 | 49.2 (45.5 to 53) | 51.3 (48.6 to 54) | 35.4 (32.5 to 38.5) | 65 (62.1 to 67.9) |
| Age <50 | 34 | 39 | 46.6 (34.8 to 58.6) | 58.5 (52.5 to 64.3) | 22.5 (16.1 to 30) | 80.9 (74.8 to 86) |
| Age ≥50 | 320 | 326 | 49.5 (45.6 to 53.5) | 49.3 (46.3 to 52.4) | 37.7 (34.5 to 41.1) | 61.2 (57.8 to 64.5) |
| Advance adenoma + cancer | | | | | | |
| Age total | 125 | 35 | 78.1 (70.9 to 84.3) | 53.6 (51.3 to 55.9) | 12.5 (10.5 to 14.7) | 96.6 (95.4 to 97.7) |
| Age <50 | 6 | 2 | 75 (34.9 to 96.8) | 58.2 (52.8 to 63.5) | 4.0 (1.5 to 8.4) | 99 (96.5 to 99.9) |
| Age ≥50 | 119 | 33 | 78.3 (70.9 to 84.6) | 52.5 (50 to 55.15) | 14 (11.8 to 16.6) | 96.1 (94.5 to 97.3) |
| Cancer | 99 | 18 | 84.6 (76.8 to 90.6) | 53.4 (51.1 to 55.6) | 10 (8.2 to 12) | 98.3 (97.3 to 99) |
| Location | | | | | | |
| Left side colon | 268 | 232 | 53.6 (49.1 to 58.0) | 52.6 (50.1 to 55.1) | 26.8 (24.1 to 29.7) | 77.8 (75.1 to 80.3) |
| Right side colon | 187 | 188 | 49.9 (44.7 to 55) | 48.1 (44.3 to 51.9) | 34.3 (30.3 to 38.5) | 63.8 (59.6 to 68) |
| Rectum | 89 | 98 | 47.6 (40.3 to 55) | 51 (48.7 to 53.3) | 8.9 (7.2 to 10.8) | 90.6 (88.7 to 92.3) |
| Number | | | | | | |
| 1 | 229 | 299 | 43.4 (39.1 to 47.7) | 49.3 (46.7 to 51.8) | 23 (20.4 to 25.8) | 71.3 (68.5 to 74.1) |
| 2 | 164 | 120 | 57.7 (51.8 to 63.6) | 52.6 (50.3 to 55) | 16.5 (14.2 to 18.9) | 88.5 (86.4 to 90.4) |
| ≥3 | 164 | 114 | 59 (53 to 64.8) | 52.8 (50.4 to 55.1) | 16.5 (14.2 to 18.9) | 89.1 (87 to 90.9) |
| Diameter | | | | | | |
| <1 cm | 414 | 463 | 47.2 (43.9 to 50.6) | 49.8 (46.9 to 52.7) | 41.4 (38.3 to 44.5) | 55.7 (52.6 to 58.7) |
| ≥1 cm | 106 | 45 | 70.2 (62.2 to 77.4) | 52.8 (50.5 to 55) | 10.6 (8.8 to 12.7) | 95.7 (94.3 to 96.8) |

cancer and large adenoma (≥1 cm) in our study is higher. Allison et al observed sensitivity for cancer and large adenoma of 37% and 30.8%, respectively, for Hemoccult II. They concluded that sensitivity of one FOBT test is too low to use as single screening test.

PPV of CRC detection and Adenomas detection in our study is lower compared with the UK National Health Service Bowel Cancer Screening Program (BCSP)[19]. In this study, PPV of 'Abnormal' FOBT test results for bowel cancer and adenomas were 10 and 35.4 respectively. As a screening test for CRC, our study showed that with high sensitivity and acceptable PPV, Single FOBT test may be used. If patients have positive FOBT results, colonoscopy is suggested.

In many literatures, sigmoidoscopy examination was involved in the protocol for the early detection of colorectal cancer. Sung JJ et al[14] in 2003, screening 505 patients by 3 techniques, consist of FOBT, flexible sigmoidoscopy and colonoscopy. The study shows a significant number of colorectal neoplasm have been under diagnosed with FOBT alone or FOBT plus flexible sigmoidoscopy, because FOBT has high false-positive rates and hence more frequent unnecessary colonoscopy. Even combining FOBT with flexible sigmoidoscopy, 19% of lesions still are missed in proximal colon.

However, another multicenter study from Italy, Segnan N et al[15] in 2007, 18,447 patients, comparing the 3 techniques for screening CRC found that the detection rate of advanced neoplasia in distal colon was the same for sigmoidoscopy and colonoscopy. They found in average risk population had 2.8% prevalence of advanced neoplasia in proximal colon among subjects examined with colonoscopy. Therefore, the data from average risk group of their study show the same prevalence of advance adenoma in colonoscopy group (7.1%) and in the sigmoidoscopy group (5.2%).

Some randomized studies support screening by FOBT, Kronborg et al[10] reported in 1996. The enrolled 14,203 participants underwent complete screening protocol compared with control participants group. Data indicate that every 2 years screening by FOBT can reduce colorectal cancer mortality over 10 years 18%, when compared with control group. But annual or biennial FOBT screening might reduce the present high rate of interval cancer; it would increase costs and the proportion of false-positive FOBT results. Nevertheless, even if they used annual screening, they found an increased rate of colonoscopy from 4.3% to 8.6%.

Limitation of this study is the selection bias from population and small sample size. Another limitation of this study is the FOBT itself that might yield false negative results if the specimen is of poor qualify or there was inadequate preparation due to diet or other medications confusion.

In conclusion, FOBT can be used as an option for screening colorectal cancer. It is non-invasive, low cost and easy to use for screening but its high false-positive rates may increase the number unnecessary colonoscopy. Further study is needed to demonstrate benefits of FOBT over other aspects such as post-treatment surveillance programs, cancer recurrence detection or specific population screening protocols. Because even in a rural or small hospital settings, this FOBT could be run, and is thus a test most suitable for a developing country such as Thailand.

## What is already known on this topic?

Fecal occult blood tests are used for screening tool for colorectal cancer. They can detect and reduce colorectal cancer mortality by 10. In another study, 18 showed that the test had low sensitivity and suggested not to use FOBTs as the single screening test. However, FOBTs use is still remains the screening tool for first step screening[19].

## What this study adds?

Fecal occult blood tests have high sensitivity and acceptable PPV for detecting advanced adenoma and cancer. FOBTs is still the acceptable screening tool for colorectal cancer although they produce high false positives, causing unnecessary colonoscopies.

## Potential conflicts of interest

The authors declare no conflict of interest.

## References


1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359-86.
2. Arnold CN, Goel A, Blum HE, Boland CR. Molecular pathogenesis of colorectal cancer: implications for molecular diagnosis. Cancer 2005;104:2035-47.
3. Stroehlein JR, Fairbanks VF, McGill DB, Go VL. Hemoccult detection of fecal occult blood quantitated by radioassay. Am J Dig Dis 1976;21:841-4.
4. Winawer SJ. Fecal occult blood testing. Am J Dig Dis 1976;21:885-8.
5. Guy GP, Jr., Richardson LC, Pignone MP, Plescia M. Costs and benefits of an organized fecal immunochemical test-based colorectal cancer screening program in the United States. Cancer 2014;120:2308-15.
6. Young GP, St John DJ, Winawer SJ, Rozen P. Choice of fecal occult blood tests for colorectal cancer screening: recommendations based on performance characteristics in population studies: a WHO (World Health Organization) and OMED (World Organization for Digestive Endoscopy) report. Am J Gastroenterol 2002;97:2499-507.
7. Cummings KM, Michalek A, Mettlin C, Mittelman A. Screening for colorectal cancer using the Hemoccult II stool guaiac slide test. Cancer 1984;53:2201-5.
8. Hardcastle JD, Armitage NC, Chamberlain J, Amar SS, James PD, Balfour TW. Fecal occult blood screening for colorectal cancer in the general population. Results of a controlled trial. Cancer 1986;58:397-403.
9. Faivre J, Arveux P, Milan C, Durand G, Lamour J, Bedenne L. Participation in mass screening for colorectal cancer: results of screening and rescreening from the

Burgundy study. Eur J Cancer Prev 1991;1:49-55.
10. Kronborg O, Fenger C, Olsen J, Jorgensen OD, Sondergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. Lancet 1996;348:1467-71.
11. Miller SF, Knight AR. The early detection of colorectal cancer. Cancer 1977;40:945-9.
12. Mandel JS, Church TR, Bond JH, Ederer F, Geisser MS, Mongin SJ, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med 2000;343:1603-7.
13. Lieberman DA, Weiss DG. One-time screening for colorectal cancer with combined fecal occult-blood testing and examination of the distal colon. N Engl J Med 2001;345:555-60.
14. Sung JJ, Chan FK, Leung WK, Wu JC, Lau JY, Ching J, et al. Screening for colorectal cancer in Chinese: comparison of fecal occult blood test, flexible sigmoidoscopy, and colonoscopy. Gastroenterology 2003;124:608-14.
15. Segnan N, Senore C, Andreoni B, Azzoni A, Bisanti L, Cardelli A, et al. Comparing attendance and detection rate of colonoscopy with sigmoidoscopy and FIT for colorectal cancer screening. Gastroenterology 2007;132:2304-12.
16. Lisi D, Hassan C, Crespi M. Participation in colorectal cancer screening with FOBT and colonoscopy: an Italian, multicentre, randomized population study. Dig Liver Dis 2010;42:371-6.
17. Levin B, Lieberman DA, McFarland B, Smith RA, Brooks D, Andrews KS, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin 2008;58:130-60.
18. Young GP, Macrae FA, St John DJB. Clinical methods of early detection: basis, use and evaluation. In: Young GP, Rozen P, Levin B, editors. Prevention and early detection of colorectal cancer. London: Saunders; 1996. p. 241-70.
19. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology 2003;124:544-60.
20. Winawer SJ, Zauber AG, Fletcher RH, Stillman JS, O'Brien MJ, Levin B, et al. Guidelines for colonoscopy surveillance after polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. Gastroenterology 2006;130:1872-85.
21. Brecht JG, Robra BP. A graphic method of estimating the specificity of screening programmes from incomplete follow-up data. Methods Inf Med 1987;26:53-8.
22. de Neree Tot Babberich MPM, Vermeer NCA, Wouters MWJM, van Grevenstein WMU, Peeters KCMJ, Dekker E, et al. Postoperative outcomes of screen-detected vs non-screen-detected colorectal cancer in the Netherlands. JAMA Surg 2018;153:e183567.