RESEARCH COMMUNICATION

Colorectal Cancer Screening: Yield of Faecal Occult Blood Testing

Mei Lin Teoh[1]*, R Puvan[1], PY Cheah[2], Y Yuen[1]

Abstract

The incidence of colorectal cancer is rising and increasing public awareness of this condition has stimulated interest in screening tests. Colorectal cancer is treatable and curable in its early stages and clear benefits are present if the cancer can be detected in its early stages. Sensitivity of the faecal occult blood test (FOBT) by immunochemical techniques for colorectal (CRC) cancer screening has been reported as 67% to 89% in certain population screening programs. Although much work has been done to address screening of colorectal cancer in the community, not much has been done to establish what the expected outcomes of screening are in a cohort of voluntary asymptomatic individuals. This paper retrospectively reviews the findings in such a cohort who sought health assessment (including a FOBT) at a Health Screening Centre in a tertiary hospital in Singapore over the period of 2002 to 2007. The outcomes are discussed together with references to other relevant studies on faecal occult blood test screening of CRC.

Key Words: Colorectal cancer - faecal occult blood test - health assessment

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Introduction

Colorectal cancer (CRC) is the highest occurring cancer in men (17.8%) and second highest in women (14.5%) in Singapore (Lee, 2009). This condition alone accounts for over 7,277 cases in the period 2003 to 2007 in Singapore compared to 5,696 lung cancer cases in the same period. The incidence of colorectal cancer has also been on the increase (Seow et al., 2004). Increasing public awareness of this condition has stimulated interest in screening tests. Colorectal cancer is treatable and curable in its early stages and clear benefits are present if the cancer can be detected in its early stages. The faecal occult blood test (FOBT) is a simple and inexpensive as well as non-invasive screening tool. By immunochemical techniques, its sensitivity was reported as 67 to 89% in certain population screening programs (Saito, 2000).

Although much work has been done to address screening of colorectal cancer in the community and understanding its outcomes, not much has been done to establish what the expected outcomes of screening in a cohort of voluntary asymptomatic individuals. This is of relevance to practicing physicians since the outcomes would significantly impact on population screening practices. The predictive value of a faecal occult blood test helps the physician in guiding his patient in making an informed decision for further investigation and follow up. This paper retrospectively reviews the findings in a cohort of asymptomatic individuals who sought voluntary health assessment (including a FOBT) at a Health Screening Centre in a tertiary hospital in Singapore over the period of 2002 to 2007. The outcomes are discussed together with references to other relevant studies on faecal occult blood test screening of CRC (Fu et al., 2009).

Materials and Methods

Consecutive patients attending the Health Screening Centre (from 1st January 2002 to 31st Dec 2007) for voluntary health assessment were routinely offered a faecal occult blood test. The latter is a qualitative test using the immunochromatographic technique producing a qualitative result (positive or negative). Its sensitivity is 50ngHb/ml of buffer and only detects human hemoglobin. Patients who underwent a repeat health check within a year were excluded.

Patient dermographics, and FOBT results were obtained from the laboratory database. Results of faecal occult blood test and hemoglobin tests were not segregated into gender and age groups in the analysis. Colonoscopy outcomes and histopathological diagnoses were obtained from the database in the department of colorectal surgery. Detailed patient records were individually traced to obtain data of clinical history and treatment modalities.

The total sample size was 7,715. This excluded patients with repeat visits within a 12 month period to avoid double counting of subjects. Females made up 57% (n=4,398). Males made up 43% of cases (n=3,317). Mean age was 48 with a range from 13 to 91 years. A faecal occult blood test was offered to all patients.

[1]Department of Family Medicine and Continuing Care, [2]Department of Colorectal Surgery, Singapore General Hospital, Singapore
**For Correspondence: teoh.mei.lin@sgh.com.sg, mei_wes@yahoo.com.sg*

Table 1. Colonoscopy Outcome of Subjects with Positive FOBT

Findings	Frequency	Percentage	Cumulative %
Colorectal cancer	6	4	4
Benign polyps	34	23	27
Normal findings	109	73	100
Total	149	100	

Those who had positive faecal occult blood test were offered a repeat faecal occult blood test, in line with the routine clinical practice at our center. Only those with a second positive test were classified under the positive faecal occult blood study group. A negative second faecal occult blood test would classify the subject under the negative faecal occult blood study group. All repeat faecal occult blood tests were performed within 6 months of the first test. Those who had an initial positive faecal occult blood test but did not perform a repeat test within 6 months were also classified as positive.

Results

Of 7,715 cases, 7.2% (n=558) were positive on FOBT. These 558 subjects were offered colonoscopy as part of the assessment. Out these, only 149 proceeded with the procedure after consultation with the managing physician. Possible reasons for relatively low take up rate include the cost of colonoscopy, seeking colonoscopy in other clinics or hospitals of the patients'choice.

Only colonoscopic data from the department of Colorectal surgery at Singapore General Hospital were available. All procedures were performed within 6 months of referral.

Colonoscopy findings of the 149 patients showed 6 patients with colorectal cancer (with histopathology confirmation), 34 patients with benign polyps or varying sizes, and 109 had normal findings (see Table 1). The predictive value of positive FOBT for colorectal cancer is 4 % (6/149) in these 149 subjects who underwent colonoscopy.

In this study, we focus on the outcomes of the 149 patients that underwent colonoscopy because these have definitive outcomes that we can draw on for discussion (see Table 2). The negative faecal occult blood test group consists of 7,157 cases, for which no colonoscopy was performed.

Discussion

Of the 7,715 patients screened in our centre over the study period, 558 had positive FOBT outcomes. All patients were reviewed by doctors after their history taking, physical examinations and investigations. Of those who tested positive on faecal occult blood test, 149 underwent colonoscopic examination at the Singapore General Hospital. In this study, we focus our analysis on the 149 (27%) patients whom we have definitive outcomes and pathological results. The assumption here is that those who did not have colonoscopy (409 patients) were equally at risk of cancer but because the numbers without scope is large (much larger than the number who had scopes done), our results may be significantly skewed. We attempted to identify the reasons for the large number of subjects who did not proceed further but this information was not available from the database and casenotes. The postulated reasons are discussed below. Of the 149 subjects that underwent colonoscopy, 6 were diagnosed with colorectal cancer (see Table 2). Our positive predictive value for cancer colorectal is 4% (6/149).

Only 27% (149 out of 558) proceeded with a colonoscopic examination at the Singapore General Hospital. This is rather low an uptake as compared to a recent community screening during a cancer- awareness exhibition[4] which reported a colonoscopy uptake of 91% (52 out of 57 with positive FOBT proceeded to colonoscopy). The procedures were performed free of charge while in our cohort, the cost of all tests and procedures were fully borne by the patients. Some patients may also have had their colonoscopy done in other hospitals or centers for various reasons including convenience or accessibility. It is possible that the yield of colorectal cancer could have been different if all those with colonoscopy done in other centres were included in

Table 2. Summary of Details of Six Cases of Colorectal Cancer Detected by the Faecal Occult Blood Test

Patient	Diagnosis	Histology	Treatment	Subsequent follow up
55 yo male	Rectosigmoid cancer	Mod diff adenocarcinoma	Duke C1T3N1M0 adjuvant chemotherapy	Colonoscopy 2 years later showed normal bowel findings
68 yo Chinese female	Ascending colon cancer	Mod diff adenocarcinoma	Duke C2T3N2M0 right hemicolectomy	Follow up sigmidoscopy 6 years later showed normal findings
74 yo Chinese male	Sigmoid colon cancer	Mod diff adenocarcinoma	Dukes' T2N0 M0 high anterior resection Adjuvant chemo	A year later, CT scan showed interval development of liver lesions,confirmed to be metastases, Follow up colonoscopy 2 years after liver resection showed normal
70 yo Chinese female	Hepatic flexure cancer	Well diff adenocarcinoma	Dukes T3N1M0 right hemicolectomy Adjuvant chemotherapy	colonoscopy 3 years later was normal
55 yo Chinese female	Sigmoid colon cancer	Mod diff adenocarcinoma	Laparoscopic high anterior resection	Follow up colonoscopy 2 years later was normal
60 yo Chinese female	Ulcerating tumor in the splenic flexure	Well diff adenocarcinoma	Dukes BT3N0 M0 right hemicolectomy	Follow up colonoscopy 2 years later showed normal findings

the study.

The median age of our study subjects was 56 years which was similar to that in Fu's study (53 years) (Fu et al., 2009) derived from data in a colorectal awareness exhibition in a shopping mall. The predictive value of FOBT for colorectal cancer in our study was 4% (6 out of 149), slightly lower compared to that in Fu's study (6%, 3 out of 52). In the latter's study, subjects who tested once or twice positive with the FOBT (threshold fecal hemoglobin 100ng/ml) were further evaluated with colonoscopy tests. The slightly higher predictive value may also be contributed by a smaller sample size. Also, possible patient selection biases may be another factor. However, both studies were similar in that they involved asymptomatic subjects. .

A British study involving 21 community-based practices in the UK (Hamilton, 2005) showed a predictive faecal occult blood test value of 7.1% for CRC screening. This was a retrospective study involving over 60,000 subjects and detected 349 cases of CRC. This is one of the largest studies involving FOBT.

The lower yield of CRC from FOBT screening in our study may be also be contributed by selection bias as the individuals attending the health asssessment centre could possibly be more health conscious and may practice healthier lifestyle habits that may reduce their risk of colorectal cancers.

Newer methods of colorectal cancer screening are still being explored. A study by the Colorectal Cancer Study Group (involving 4404 subjects) demonstrated that faecal DNA was four times more sensitive than the Hemoccult II for invasive CRC. It detected 16 out of 31 invasive cancers compared to 4 out of 31 in the latter ($p<0.005$). The DNA panel was also more than twice as sensitive as Hemoccult II for adenomas containing high grade dysplasia ($p<0.001$) (Imperiale and Ranosohoff, 2004). In another study, similar findings were obtained with a sensitivity rate of 64% for colorectal cancers and 57% for advanced adenomas (Tagore and Lawson, 2003). Ahliquist however reported faecal DNA screening for CRC at 90% and 82 % for advanced polyps (Ahliquist and Skoletsky, 2000). This study was performed on archived stool specimens and many subjects had advanced disease.

CT colonography is a non invasive imaging test that combines multiple helical CT scans to create a 3 D image of the colon (Mandel, 2008). Patients found to have significant lesions have to be referred for a colonoscopy. In 1 study, Sensitivity was reported at 93.8% for polyps 10mm or larger, 93.9% for those at least 8mm, and 88.7 % for at least 6mm. Specificities were reported as 96.0%, 92.2% and 79.6% respectively (Pickhardt and Choi, 2003). These rather high rates were obtained when the tests were performed under optimal conditions. Another study by Cotton showed sensitivities of 39% and 59% and specificities 90.5% and 96% (Cotton and Durkalski, 2004) polyps at least 6mm and 10mm respectively. Results vary if the CT colonographic screening was performed under different set of conditions ie ideal conditions compared to general practice conditions. Ideal conditions include complete cleansing of the colon and experienced and skilled readers of the CT images (which involves proper training, consistent standardized interpretation) (Rockey, 2009). A meta analysis of 4181 patients found high and consistent sensitivities and specificities for polyps 1 cm or larger, but lower values for smaller polyps (Halligan et al., 2005). Another meta analysis of studies involving 6000 patients showed wide variation in sensitivity among studies particularly related to polyp size (Mulhall and Veerapan, 2005). This led authors to conclude that the variability in sensitivity rates need to be resolved before CT colonography can be recommended as a screening tool. Another metanalysis of 30 colonography studies showed that sensitivity is higher for larger polyps, and 2-D and 3-D CT colonography performed equally well (Rosman and Korsten, 2007). CT colonography thus performed well for lesions 1 cm and larger, reasonably well for those 0.6 cm and larger. This level of performance is perhaps sufficient because these polyps may be clinically more significant (Kim and Pickhardt, 2007).

Capsule endoscopy (CE) involves the use of a wireless capsule containing a miniaturized camera, light source and a wireless circuit for acquiring and transmitting signals. It provides up to 2 pictures per second for 8 hours after swallowing, as it traverses the digestive tract. [9]. It is mainly used for small intestine examination, usually after upper and lower endoscopies do not reveal a cause of gastrointestinal bleeding. This modality has also been studied for colorectal cancer screening. A pilot study of 41 patients was done to evaluate colonoscopy and CE for screening or evaluation of symptoms. CE identified 19 out of 25 positive findings, and 10 out of 13 with significant polyps (polyp > 6mm size). It picked out lesions in 7 people who had a negative colonoscopy. The sensitivity and specificity are 77% and 70% respectively and its PPV was 59 %. These results do suggest some promise for CE use but further studies are required (Schoofs and Deviere, 2007).

Benefits of performing flexible sigmoidoscopy for cancer screening have largely come from case control studies (Mandel, 2008). Reduction in rates of distal colon cancer screening is variable but the concern of cancers in the proximal colon will largely be missed if flexible sigmoidoscopy was to be used alone for screening. No RCTs have analyzed colorectal cancer mortality reduction from flexible sigmoidoscopy combined with FOBT.

Double contrast barium enema usage for colorectal cancer screening has come mostly from observational studies. Sensitivity was 32% for polyps <0.5 cm, 53% for polyps 0.6 to 1.0 cm and 48% for polyps > 1cm, when compared to colonoscopy. It is used in situations where colonoscopy is unavailable or contraindicated.

In conclusion, FOBT by immunochemical methods has value in screening of colorectal cancer in asymptomatic individuals, although more studies are needed to establish its value in screening of large populations and reducing CRC mortality. More cohesive follow-up of patients should be considered in the planning of health assessment programmes especially after the detection of abnormal results. Other new modalities for CRC screening are available and may be considered for certain subgroups of patients.

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