ORIGINAL ARTICLE

Colonoscopic Prioritization in Colorectal Carcinoma Screening Using Quantitative Immunochemical Faecal Occult Blood Test: A Pilot Study

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SUMMARY

Background: Screening for colorectal cancer (CRC) improves outcomes and reduces its incidence. However, population-based screening in Malaysia continues to be a challenge, in view of cost and limited availability of colonoscopic skills and facilities. Conventional qualitative faecal occult blood tests help to prioritize those who require earlier colonoscopies, but cannot distinguish between benign and malignant causes. Recently, quantitative immunochemical faecal occult blood tests (qFOBT) have demonstrated some discriminatory ability in distinguishing benign and malignant causes. We aim to assess feasibility of qFOBT as a tool for stratification of colonoscopic priority in asymptomatic patients.

Methods: A health awareness exhibition was held in a major shopping complex in Kuala Lumpur on 6 and 7 Feb 2010. All asymptomatic individuals > 40 years, and those < 40 with family history of CRC, were invited to participate. Eligible participants were given a questionnaire and screened using a qFOBT. A faecal haemoglobin level of 100 - 199 ng/mL was considered moderately positive, while a level of 200 ng/mL or more was strongly positive. Participants with a strongly positive qFOBT result were scheduled for a colonoscopy within the month, while those who were moderately positive were scheduled within 3 months.

Results: A total of 125 (82%) participants returned the qFOBT kit, of which 70 (56%) were male. The median age was 54 years. Majority of the participants were Chinese (60%), followed by Malay (25%), Indian (12%) and others (3%). Twelve (10%) participants were tested positive and were advised to undergo colonoscopy but 9 (75%) declined colonoscopy and further investigations citing lack of time as the reason. Of the 3 participants (all in the moderately positive group) who underwent colonoscopy, 2 had a family history of CRC. Colonoscopic findings revealed haemorrhoids in one participant and two participants had histologically proven benign sigmoid colonic polyps.

Conclusion: The use of qFOBT as a tool to screen and prioritize asymptomatic patients for early colonoscopy in CRC screening is logistically feasible. However, in order for it to be effective, measures to improve compliance to colonoscopy need to be taken

KEY WORDS:
Colorectal cancer screening, colonoscopy, quantitative faecal occult blood test

INTRODUCTION

In Malaysia, colorectal cancer (CRC) is the commonest cancer among men and the second most common cancer among women [1]. It is the third commonest cause of cancer-related mortality [1]. One of the main reasons for the high mortality is the high proportion of advanced stage at presentation. Most of the patients are usually symptomatic on presentation. Data from University of Malaya Medical Centre (UMMC) showed that 15% of patients presented with Dukes C and 39% with Dukes D disease respectively [2]. Population-based screening in Malaysia continues to be a challenge, in view of cost and limited availability of colonoscopic skills and facilities. For example, the colonoscopy waiting list for asymptomatic patients in UMMC is six months to a year, causing a delay in diagnosis and management of those in the asymptomatic stages of colorectal carcinoma.

Current recommended screening-tools in an average-risk population include yearly faecal-occult blood test (FOBT), five-yearly flexible sigmoidoscopy and ten-yearly colonoscopy [3]. Of all the recommended screening tools, FOBT is the least expensive and simplest test to perform. It has been shown to reduce mortality by 15-33% [4-6]. However, these results are based on studies using the guaiac-based FOBT, which requires dietary restriction and has a low specificity and a wide range of sensitivities. It is reported that the sensitivity for identifying neoplasia is from 12.9% to 78.6% while it is from 10.8% to 41.3% for advanced adenoma [7-9].

Improved test sensitivity has been achieved by the automated quantitative immunochemical faecal occult blood test (qFOBT). This test uses antibodies that specifically detect human haemoglobin (Hb) in stools, obviating the need for dietary restriction. It is more accurate in the detection of CRC and significant adenomas with higher sensitivity and specificity [10-12]. This test has now replaced the guaiac-based FOBT as a screening tool in certain countries [12-16]. Furthermore, qFOBT allows for the selection of a threshold for colonoscopy, making it an excellent tool for screening. A Hb threshold of 100 ng/mL has been shown to offer high sensitivity (61.5–76.5%), specificity (93.4–95.3%), and

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Fig. 1: qFOBT sampling kit (OC-Sensor μ, Eiken Chemical, Japan).

negative predictive values for significant colorectal neoplasia[13]. Using this level as the selection criterion for colonoscopic screening should therefore decrease the number of unnecessary colonoscopies while maintaining cancer detection rates.

The aim of this study is to assess feasibility of qFOBT as a tool for stratification of colonoscopic priority in asymptomatic patients.

MATERIALS AND METHODS

Ethics approval was obtained from our institutional Medical Ethics Committee prior to commencement of this study.

A health awareness exhibition was held in a major shopping complex in Kuala Lumpur on the 6th and 7th of February 2010. Based on previous health awareness programs conducted by our institution; attendance was estimated to reach approximately 200 participants. Given the predicted positive rate for qFOBT of 6%, we felt that sufficient numbers would be obtained with this sample size to pilot the feasibility of this protocol.

All voluntary participants were screened for eligibility by doctors via a questionnaire. The inclusion criteria included all asymptomatic participants who were ≥ 40 years of age and those who were asymptomatic and < 40 years old but with positive family history of colorectal cancer. The age of 40 is chosen as previous local data showed that the Malays and the indigenous community tend to get colorectal cancer at a younger age[27]. Participants who had symptoms of per rectal bleeding, abdominal pain, a change in bowel habits, and loss of weight were excluded from the screening test.

Eligible participants were given a qFOBT sampling kit (OC-Sensor μ, Eiken Chemical, Japan) (Figure 1) together with an illustrated instruction sheet. Stool samples were collected either on site by digital rectal examinations performed by the doctors or by the participants themselves at home. They were instructed to insert the sampling probe into different areas of the stool and placed in the tube container. The probe tip with the faecal sample was suspended in a standard volume of a Hb-stabilising buffer. No dietary restriction or medication

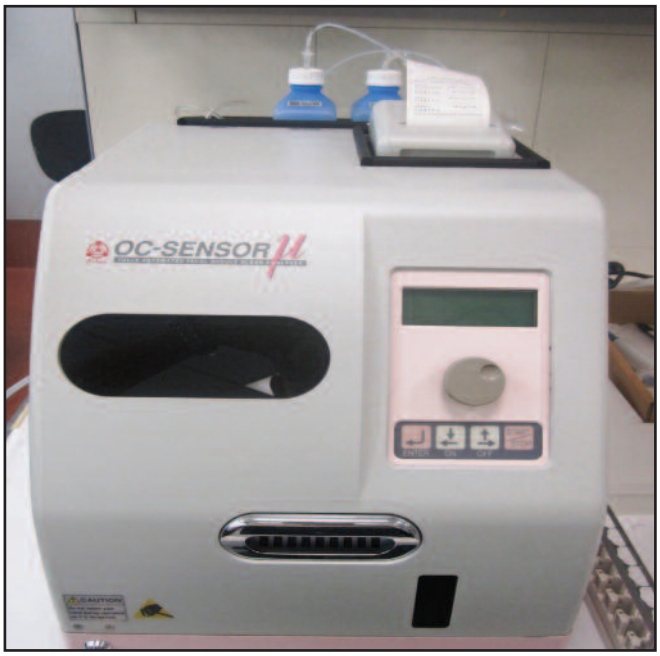

Fig. 2: OC-Sensor μ instrument (Eiken Chemical, Japan).

restriction was needed. Participants were encouraged to return the samples to University Malaya Medical Center within two days of stool collection. Further information on the significance of a positive test as well as the possible need and implications for colonoscopy was explained to each patient individually by doctors at the event.

The stool samples were then analysed by using the OC-Sensor μ instrument (Eiken Chemical, Japan) (Figure 2). Based on the manufacturer's recommendations, a faecal blood level of ≥ 100 ng Hb/ml was taken as a positive result. Participants with positive stool samples were contacted by doctors via phone with advice to return for medical evaluation and colonoscopy screening, which would be arranged by the doctors concerned.

Participants with a faecal blood level of ≥ 200 ng Hb/ml were considered as strongly positive and were scheduled an elective colonoscopy appointment within one month and those with a faecal blood level between 100 to 199 ng Hb/ml were given a colonoscopy date within 3 months' time. Participants with a negative result were advised to undergo yearly qFOBT screening.

RESULTS

One hundred and twenty five (82%) participants returned the qFOBT kit for analysis, of which 70 (56%) were male and 55 (44%) were female. The median age of the participants was 54 years (range 21 to 80). The majority of the participants were Chinese (60%), followed by Malay (25%), Indian (12%) and others (3%). Seventy four percent of the participants had a family history of colorectal cancer.

Twelve (10%) participants (7 males, 5 females) tested positive. Out of these twelve participants, eleven were in the strongly

Table I: Demographics and clinicopathological characteristics of participants with a quantitative faecal occult blood test (qFOBT) positive test

Factor / Category	No. (%) of patients
Positivity	
• Strongly positive	11 (92)
• Moderately positive	1 (8)
Gender	
• Male	7 (58)
• Female	5 (42)
Race	
• Chinese	6 (50)
• Malay	4 (33)
• Indian	2 (17)
Family history of colorectal cancer	
• Yes	5 (42)
• No	7 (58)
Colonoscopy Findings	
• Polyps	2 (17)
• Haemorrhoids	1 (8)
• Refused colonoscopy	9 (75)

positive group whereas one participant was in the moderately positive group. In this cohort, 50% were Chinese, followed by Malays (33%) and Indians (17%). The median age was 50 (range 25 to 64) years. Five (42%) participants had a family history of colorectal cancer (Table I).

All the twelve participants were advised to undergo colonoscopy but nine of them (75%) declined colonoscopy and further investigations. Those who declined understood the implications of their decision (as reinforced by the contacting doctors) but gave lack of time to undergo the procedure as the reason. None cited lack of finances as a reason for defaulting.

Of the three participants (all of whom were in the moderately positive group) who underwent colonoscopy, two had a family history of colorectal cancer. Colonoscopic findings revealed haemorrhoids in one participant and two participants had histologically proven benign sigmoid colonic polyps.

DISCUSSION

This is a pilot study in Malaysia using the qFOBT. The positivity rate (10%) of our study was comparable with the results reported by WP Fu *et al* (2009) from Singapore [17]. However, our results are slightly higher compared to large scale studies conducted on the average-risk screening population. Ciatto S *et al* [16] reported a positivity rate of 3.7% in the Florence screening programme using the same qFOBT kit while Morikawa *et al* [12] and Guittet *et al* [18] reported positivity rates of 5.6% and 6.8% respectively using a different qFOBT kit.

A positive qFOBT determines who is more likely to have colorectal neoplasia and should be given priority for an early colonoscopy date. It is an excellent screening tool as it is simple, convenient and a non-invasive way to attract a healthy asymptomatic population into a screening programme. It focuses colonoscopy resources onto those more likely to have neoplasia, thus reducing healthcare costs. It also helps to reduce unnecessary colonoscopy appointments thereby reducing waiting time and exposure to colonoscopy risks.

However, the disadvantages of qFOBT include the psychosocial consequences of receiving false-positive results as well as false-negative results. It is reported that less than 10% of people with positive stool occult blood will actually have CRC [19] and those with non-bleeding CRC will not be detected by qFOBT.

Unfortunately, in our study, we were unable to produce the detection rates and the positive predictive values (PPVs) for cancer using the qFOBT as the compliance rate for colonoscopy was very low (25%). However, WP Fu *et al* from Singapore [17] reported that 6% of the positive qFOBT participants were found to have cancer and 23% had advanced polyps. Similar results were published from the Florence screening programme [16] which has 7.3% invasive cancer and 25.8% advanced adenoma out of 2,597 FOBT-positive participants. Guittet *et al.* [18] reported a PPV of 26.4% (3.3% invasive cancer and 23.1% advanced adenoma), while Morikawa *et al.* [12] reported a lower PPV of 20.2% (4.2% invasive cancer; 16.0% advanced adenoma). We believe that the results will be similar in our local settings.

Based on the recent evidence, qFOBT makes an excellent screening tool for CRC, as it not only has a higher detection rate, it also encourages a better participation rate [20] as it does not require any diet restrictions. In this study, 12 patients (10%) were found to have a positive qFOBT. As the colonoscopy list in our center is available three times per week, the addition of one qFOBT positive patient per list would be sufficient to meet the targeted screening time based on risk stratification.

The main challenge of CRC screening in our population is compliance with colonoscopy. It is the most critical aspect of any FOBT-based CRC screening campaign because those with a positive FOBT result must undergo full colonoscopy to ensure the efficacy of the programme. Published rates of colonoscopy among those with a positive FOBT result in both randomized and non-randomized studies are between 76% and 92% [21-25]. In this study, individuals with a positive result were telephoned directly by a surgeon who explained the significance of the test result, and invited them to the colorectal surgical clinic for a consultation and subsequent colonoscopy. In spite of this, participants still refused further colonoscopy, citing busy schedules. It is noted that those with a positive family history of CRC are more likely to undergo colonoscopy.

Therefore, we need to look at other underlying reasons for the poor compliance rate, which might not be overtly stated by patients. Denberg D *et al.* (2005) [26] reported that reasons affecting patients' compliance for colonoscopy include concerns about modesty, fear of pain, and lack of perceived risk for a condition that would warrant an invasive procedure. Future strategies should therefore also allay fears regarding colonoscopy in addition to emphasizing its importance for screening of CRC.

CONCLUSION

The use of qFOBT as a tool to screen and prioritize asymptomatic patients for early colonoscopy in colorectal carcinoma screening is logistically feasible. However, in order for it to be effective, measures to improve compliance to colonoscopy need to be taken.

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