

COLORECTAL CANCER

Interval faecal occult blood testing in a colonoscopy based screening programme detects additional pathology

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Background: Colonoscopic based surveillance is recommended for patients at increased risk of colorectal cancer. The appropriate interval between surveillance colonoscopies remains in debate, as is the “miss rate” for colorectal cancer within such screening programmes.

Aims: The main aim of this study was to determine whether a one-off interval faecal occult blood test (FOBT) facilitates the detection of significant neoplasia within a colonoscopic based surveillance programme. Secondary aims were to determine if invitees were interested in participating in interval screening, and to determine whether interval lesions were missed or whether they developed rapidly since the previous colonoscopy

Patients: Patients enrolled in a colonoscopic based screening programme due to a personal history of colorectal neoplasia or a significant family history.

Methods: Patients within the screening programme were invited to perform an immunochemical FOBT (Inform). A positive result was followed by colonoscopy; significant neoplasia was defined as colorectal cancer, adenomas either ≥ 10 mm or with a villous component, high grade dysplasia, or multiplicity (≥ 3 adenomas). Participation rates were determined for age, sex, and socioeconomic subgroups. Colonoscopy recall databases were examined to determine the interval between previous colonoscopy and FOBT offer, and correlations between lesion characteristics and interval time were determined.

Results: A total of 785 of 1641 patients invited (47.8%) completed an Inform kit. A positive result was recorded for 57 (7.3%). Fifty two of the 57 test positive patients completed colonoscopy; 14 (1.8% of those completing the FOBT) had a significant neoplastic lesion. These consisted of six colorectal cancers and eight significant adenomas.

Conclusions: A one off immunochemical faecal occult blood test within a colonoscopy based surveillance programme had a participation rate of nearly 50% and appeared to detect additional pathology, especially in patients with a past history of colonic neoplasia.

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Patients with a significant family history of colorectal cancer (two or more relatives affected, or one first degree relative under the age of 55 years) and those with a personal history of colorectal neoplasia are recommended to have colonoscopic surveillance.¹ There is significant debate over the recommended interval between colonoscopies within surveillance programmes. The American Polyp Study has demonstrated that post polypectomy colonoscopy at one and three years has a similar yield, leading to recommendations that post polypectomy colonoscopy can be delayed for 3–5 years, depending on histology.² However, in clinical practice, actual intervals vary widely and colonoscopy is often performed more frequently than this, presumably because of concerns of missed lesions and lesions with a more rapidly evolving biology.³ While a miss rate of lesions ≥ 10 mm in size has been quoted as up to 8%,⁴ it is doubtful that this justifies a repeat colonoscopy at one or even two years as the majority of sporadic adenomas do not appear to progress to cancer within that time frame.⁵

One way to manage the possibilities of missed or rapidly progressive lesions and give added reassurance to both clinician and the person under surveillance is to perform a faecal occult blood test (FOBT) in the interval (“interval FOBT”) between colonoscopies, so as to aid detection of such lesions.

The aims of this study were therefore to determine whether individuals at increased risk for colorectal cancer and registered in a colonoscopic surveillance programme would participate in interval FOBT, and whether this would result in detection of significant lesions.

METHODS

Individuals within a colonoscopy based surveillance programme were invited by mail to perform an interval FOBT. The surveillance programme at Flinders Medical Centre (FMC) and the Repatriation General Hospital Daw Park (RGHDP) follows the guidelines recommended by the Australian National Health and Medical Research Council.¹ These guidelines were the result of an evidence based medicine review, with colonoscopic surveillance being recommended for those individuals with a significant increase in risk of colorectal cancer, specifically those with a family history of two or more first or second degree relatives affected with colorectal cancer, or one relative affected under the age of 55 years. In those with previous colonic polyps, recommended post polypectomy colonoscopy intervals are: (a) three years for tubulovillous or villous adenomas or tubular adenomas ≥ 10 mm, or for more than two adenomas of any size, and (b) five years for single or two tubular adenomas < 10 mm. Patients with a previous colorectal cancer would have a repeat colonoscopy at 3–5 yearly intervals.

Patients registered on a colonoscopy recall database, who were not scheduled for colonoscopy in the study year, were invited by mail to participate in FOBT based surveillance screening. In the first and second years of the study (2000 and 2001), only patients enrolled in the FMC programme were invited. In the next year (2002) the study was extended

Abbreviations: FOBT, faecal occult blood test; FMC, Flinders Medical Centre; RGHDP, Repatriation General Hospital Daw Park

Table 1 Programme participation and positivity rates

	Invitation round (institution, year)				Total
	FMC 2000	FMC 2001	RGHDP 2002	FMC 2002	
Invited (n)	672	421	181	367	1641
Returned valid test	330 (49.1%)	201 (47.7%)	91 (50.3%)	163 (44.4%)	785 (47.8%)
Tested positive (n)	21 (6.4%)	15 (7.5%)	13 (14.3%)	8 (4.9%)	57 (7.3%)

FMC, Flinders Medical Centre; RGHDP, Repatriation General Hospital Daw Park.

to include those enrolled at RGHDP as well as FMC. Patients on the recall database were divided into two groups—either those who had entered the database purely due to a family history or those who had a personal history of colorectal neoplasia, irrespective of whether they also had a family history.

Individuals who were invited to participate received an immunochemical FOBT (Inform OBT; Enterix Pty Ltd, Sydney, Australia). Participation in FOBT was defined as return of correctly completed sample cards within 12 weeks of mailing out the invitations. The Inform samples were developed at the Enterix laboratory (North Ryde, NSW, Australia).⁶ Only FOBT sample cards that were correctly completed by participants were included for the purposes of this analysis.

Individuals who returned any positive result had their planned colonoscopy brought forward. If colonoscopy was judged to be incomplete by the proceduralist, then a radiological examination of the colon was also undertaken. Colonoscopic diagnoses were determined on the basis of the examination and from any pathology specimens. Significant colorectal neoplasia was defined as a carcinoma or adenomas with any of the following characteristics: ≥ 10 mm villous change, high grade dysplasia, or multiple (≥ 3) adenomas.

Demographic characteristics of the invited population (sex, age structure, and socioeconomic status) using the Socioeconomic Index for Areas (SEIFA, postcode based, Australian Bureau of Statistics) were extracted from the colonoscopy recall databases (SCOOP database (Department of Gastroenterology, Flinders University, Australia) and Kintrak database (Pecol Software, Adelaide, Australia)). Demographic characteristics of participants and non-participants were similarly determined and compared using the χ^2 test and by Wilcoxon sum of ranks analyses. The time between previous colonoscopy and FOBT was calculated from the recall databases and participants were allocated to one of two groups (≤ 2 years, > 2 years). Significant pathology was compared for the two groups using χ^2 analysis.

The study was approved by the Flinders Medical Centre Clinical Research Ethics Committee.

RESULTS

FOBT participation and positivity rates (tables 1, 2)

A total of 1641 patients were invited for the first time to participate in interval screening, comprising 672 from FMC in 2000, 421 from FMC in 2001, 367 from FMC in 2002, and 181 from RGHDP in 2002 (table 1).

A total of 792 patients responded to the invitation and participated in FOBT screening; in seven cases the FOB kits had been incorrectly completed, leaving 785 valid kits. In 1558 patients where the initial reason for entering the colonoscopic surveillance programme was well documented, 1033 were entered due to a personal history of colonic neoplasia, of which 538 (52%) participated—a significantly greater participation than those who has entered the programme due to family history alone (219/525 (42%); $p = 0.0001$). In total, 57 of the 785 participants returned a positive result (7.3%). A FOBT positive result was more likely in the group who had a personal history of colorectal neoplasia (51/538 (9.5%)) than those who entered the programme due to family history alone (6/219 (2.7%); $p = 0.0001$). Participants did not differ significantly from non-participants for age, sex, or socioeconomic status (table 2).

Pathology findings (tables 3, 4)

Fifty seven patients had a positive FOBT result; 16% had significant colorectal neoplasia detected (six colorectal cancers and eight significant adenomatous polyps) (table 3). This represents a prevalence of FOBT detectable significant pathology of 1.8% (14/785) in those who participated in the FOBT screening.

Those patients who were enrolled into the screening programme because of a personal history of neoplasia were more likely to have a cancer or advanced adenoma (11/538 (2%)) than those enrolled because of a family history (1/219 (0.05%); $p = 0.0024$).

The date of colonoscopy prior to FOBT was known for 764/785 patients (97.3%). A total of 549 had previously had a colonoscopy within two years of the FOBT; in this group, 11 (2%) had significant colorectal neoplastic lesions. A total of 215 patients had a colonoscopy more than two years prior to

Table 2 Demographic characteristics of the invited, participating, and non-participating populations

Characteristic	Invited	Participating	Non-participating	Participating v non-participating
Sex (% female)	53.4	53.4	53.4	NS (χ^2)
Age (y) (at invitation) (median [range] (mean))	61 [23–95] (60.1)	63 [28–89] (61.9)	58 [23–95] (58.6)	NS (Wilcoxon)
Median SES indicator (SEIFA rank)	57	54	61	NS (Wilcoxon)
Reason for colorectal surveillance*				
Personal history	1033	538	495	0.0001
Family history	525	219	306	χ^2

SEIFA, Socioeconomic indicator for areas, Australian Bureau of Statistics (NB only first time offers included).

*Reason for initial inclusion not clear in 83 patients.

Table 3 Results of follow up and pathology found

Outcome	Personal history of adenomatous polyps or cancer	Significant family history of colorectal cancer	Total
FOBT positive	51	6	57
Colonoscopy completed	46	5	51
Cancer or polyps detected*	25	3	28
Other pathology detected†	11	1	11
Normal	10	1	12
Pathology reports available	25	3	28
Cancer‡	6	0	6
Adenoma advanced§	5	1	6
Adenoma not advanced¶	11	2	13
Hyperplastic polyp	3	0	3

FOBT, faecal occult blood test.

*Includes all patients with either cancer or polyps (including hyperplastic), with or without other non-neoplastic pathologies.

†Includes patients where the only pathology was non-neoplastic (that is, diverticulosis, colitis, haemorrhoids, etc).

‡Includes two intramucosal carcinomas; T is lesions according to the WHO classification.¹⁷

§Includes adenomas with any of the following characteristics: ≥ 10 mm, with villous change, high grade dysplasia, or multiple (≥ 3).

¶Includes all adenomas excluding advanced or hyperplastic.

their FOBT. Two significant colorectal neoplastic lesions were found in this group (0.9%; NS) (table 4).

DISCUSSION

This study demonstrates that additional pathology is found when interval FOBT is incorporated into colonoscopic based screening for individuals with past colonic neoplasia or significant family history. In our study, a first time immunochemical interval FOBT detected significant neoplasia (colorectal cancer, adenomas ≥ 10 mm, with villous change, with high grade dysplasia, or multiple (≥ 3) adenomas) in 1.8% of subjects who participated in screening. Six cancers were identified (0.8% of those completing the FOBT), two of which were advanced (Dukes' C).

The participation rate of 47.8% was perhaps a little disappointing as these were high risk patients who were on an established screening programme. While significant interval neoplasia is detected in 1.8% of participants, this is reduced to 0.9% of all those within the surveillance programme given the non-participation rate. Participation in interval faecal occult blood testing needs to be improved to maximise the effect of this intervention. It could be improved by telephoning patients to encourage their participation and notifying patients' general practitioners that the patient is due for a faecal occult blood test (this is done for the surveillance colonoscopies in the programme).

It is possible that patients, having performed an interval FOBT, might be reassured by a normal result and not participate in their colonoscopy screening. We examined our participation rate for screening colonoscopies due in 2003. We found that of 283 patients due, 30 (11%) did not participate for legitimate reasons (unwell, deceased, or age

related), with 221 of the remaining 257 (87%) participating. We felt this represented a fairly high participation rate, suggesting that participation in interval faecal occult blood testing does not adversely affect participation in screening colonoscopy.

FOBT screening has been shown to be able to detect colorectal cancer in this setting. Skaife *et al* performed immunochemical FOB testing (using the same test as in this study) on samples obtained on digital rectal examination, prior to planned colonoscopy, in patients in a surveillance programme because of a past history of colorectal cancer. In 611 patients there was a 9.7% positivity rate, with nine cancers being detected in the FOBT positive group and none in those who were FOBT negative. In four cases the cancer was a local recurrence and in five it was a metachronous cancer.⁷

The lesions that we detected may have been missed or may have been rapidly developing lesions. A miss rate for significant adenomas (polyps ≥ 10 mm) has been demonstrated to be as high as 8%, and up to 15% for adenomas greater than 5 mm.⁴ If the lesions we detected were new rapidly developing lesions, we might have expected a greater proportion in the group that had their prior colonoscopy 3–5 years earlier rather than 1–2 years earlier. The converse appeared to be true, with 34% of test positives in the group with recent colonoscopy having significant neoplasia versus 10% in the group with a colonoscopy greater than two years previously. This may imply that the lesions were missed, rather than rapidly developing, but the numbers are small and the difference did not reach statistical significance. This could reflect poor colonoscopy technique, although when we audited all colonoscopies performed for screening in 2000

Table 4 Relationship between date of colonoscopy prior to faecal occult blood test (FOBT) and pathology found

	Time between FOBT and prior colonoscopy (y)	
	≤ 2 years	> 2 years
Completed FOBT and previous colonoscopy date known	549	215
FOBT positive	36 (6.6%)	20 (9.3%)
Completed follow up	32	19
Significant pathology	11 (2.0% of participants, 34.4% of test positives)	2 (0.9% of participants, 10% of test positives)
Cancer	4 (0.7% of participants, 11.1% of test positives)	1 (0.5% of participants, 5.0% of test positives)

and 2001 we demonstrated an acceptable standard, with a 97% caecal intubation rate.⁸ We have now also introduced colonic extubation time to our audit as another measure of colonoscopy quality.

The rate of interval neoplasia was higher than we expected. It may be that patients with minimal symptoms that might reflect neoplastic change were more likely to participate in the study than those with no symptoms, although only three cancers (Dukes' B and above) would be expected to cause symptoms.

Addition of interval FOB testing to a colonoscopic based screening regimen does add cost to the surveillance programme. The positivity rate was relatively high, at 7.3%, although this is within the range seen when an immunochemical FOBT was performed in a population based screening setting (which varied from 2.5% to 7.5%⁹⁻¹²). The rate of cancers found (of 0.8%) was similar to that seen in some population based studies of screening guaiac-FOBT.⁹⁻¹¹ FOBT in this latter setting is felt to be appropriate and cost effective.¹³ It is possible that a delay in detection of the interval neoplastic lesions until the next surveillance colonoscopy was due would not have affected the outcome, but this is not the case in all, especially the cancers, and possibly the advanced adenomas which constituted the majority of the interval neoplastic lesions detected. Given that the positivity rate and yield are similar when comparing our group having colonoscopic surveillance to the population studies, it seems reasonable to add in at least one interval FOBT between colonoscopies, especially in those patients enrolled in a screening colonoscopy programme because of a personal history of colorectal neoplasia.

The next issue to resolve is whether interval FOBT repeated at annual or other intervals would give a further increase in yield compared with a one-off interval FOBT. If the majority of lesions being detected are those that have been missed at the preceding colonoscopy, and given the sensitivities of a one-off immunological FOBT of 68.8–84.6% depending on test type,^{14,15} it could be argued that a one-off FOBT performed just once between surveillance colonoscopies is sufficient. While repeated FOBT improves sensitivity in population screening,¹⁶ whether or not this is efficient or worthwhile in colonoscopic surveillance programmes where most lesions will have been removed by colonoscopy is uncertain and would need a very large ongoing study to demonstrate its value.

In conclusion, individuals in a high risk colonoscopic surveillance programme are willing to perform interval FOBT, confirming its feasibility. The participation was lower than hoped but a first time FOBT detected significant neoplasia in 1.8% of patients who participated. It must be remembered that faecal occult blood testing has a false negative rate, and so the rate of interval neoplasia would be expected to be higher than this. While it is possible that repeated interval FOBT within such colonoscopic surveillance programmes may decrease this false negative rate, our data certainly suggest that at least one FOBT should be considered in the

interval between surveillance colonoscopies, particularly in those patients who have a past history of colorectal neoplasia (that is, either adenoma or cancer), in which interval faecal occult blood testing has a higher yield for additional pathology than those who have a family history alone.

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