Outcomes after 10 years of a community-based flexible sigmoidoscopy screening program for colorectal carcinoma

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ABSTRACT

Objective: To evaluate the outcomes 10 years after a flexible sigmoidoscopy colorectal cancer (CRC) screening program in asymptomatic average-risk individuals.

Design, setting and patients: In 1995, a program of flexible sigmoidoscopy-based screening of asymptomatic average-risk individuals aged 55–64 years was established at Fremantle Hospital, Western Australia. Insertion depths, pathological findings and subject-rated pain scores have been prospectively recorded. A follow-up flexible sigmoidoscopy examination was offered to attendees 5 years after the initial screening. Post-screening malignancies were determined by linkage with the Western Australian Cancer Registry in September 2006.

Main outcome measures: Yield of neoplasia at initial and follow-up sigmoidoscopy, and the incidence of CRC detected after screening.

Results: Between 1995 and 2005, 3402 people underwent an initial flexible sigmoidoscopy screening examination (mean age, 60 years; women, 41%) and 1025 had a 5-year recall examination. Mean insertion depth was greater in men than women (60 cm v 52 cm, $P < 0.001$). The insertion depth in women was more likely to be < 40 cm (17% v 6%, $P < 0.001$). Mean pain score was 2.9 for men and 4.0 for women ($P < 0.001$). Fourteen per cent of initial screenings detected at least one adenoma. Over a mean follow-up time of 8 years, invasive CRC was detected by flexible sigmoidoscopy screening in 0.4% of participants; 0.7% of those with a normal result of screening later developed CRC, with 75% of these found proximal to the splenic flexure.

Conclusions: Flexible sigmoidoscopy is a viable screening method, with well defined utility and limitations, for CRC screening of asymptomatic people with average risk.

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Colorectal cancer is the second leading cause of cancer death in Australia.[1] Evidence from large, randomised controlled studies of biennial guaiac-based faecal occult blood testing (FOBT) indicates that this screening method can reduce colorectal cancer (CRC) mortality by up to 21%.[2]

While the use of FOBT is supported by Level I evidence, other screening methods, such as flexible sigmoidoscopy and colonoscopy, are the subject of ongoing evaluation, and it remains to be seen whether they will be shown to be superior to FOBT. The National Health and Medical Research Council currently includes 5-yearly flexible sigmoidoscopy as an alternative screening method.[3] Case–control studies have shown that sigmoidoscopy screening can reduce the risk of subsequent fatal distal CRC by up to 60%, and reduce by approximately 30% overall CRC mortality.[4,5] Randomised controlled trials currently underway will provide evidence of the magnitude of benefit of flexible sigmoidoscopy screening.[6-8]

Fremantle Hospital, in Western Australia, has been conducting a community-based screening program for CRC using flexible sigmoidoscopy since 1995. Here, we review the 10-year outcomes of the screening program, assessing in particular CRC detected and incidence of later malignancy.

METHODS

Patients and methods

In 1995, a flexible sigmoidoscopy-based CRC screening program for asymptomatic, average-risk individuals aged 55–64 years was established at Fremantle Hospital. Letters of invitation were sent to eligible people identified from the Western Australian Electoral Roll. Participation from volunteers was also accepted. The methods and progress results of the screening program have been reported previously.[9,10] Our study includes participant data up to the end of July 2005.

Outpatient flexible sigmoidoscopy screening was performed, without sedation, after phosphate enema. The procedures were performed by gastroenterologists and surgeons, or by supervised registrars and general practitioners, using a standard colonoscope, with air or carbon dioxide insufflation. Participants were asked to rate the pain experienced during the procedure on a visual analogue scale of increasing pain from 0 to 10.

Biopsies were taken of polyps identified by sigmoidoscopy, and patients with proven adenomas were advised to have a colonoscopy. An advanced lesion was defined as (i) any adenoma > 10 mm in size; (ii) any adenoma with villous histological features; or (iii) high-grade dysplasia or invasive CRC. Colonoscopy was arranged after liaison with the general practitioner, and the results of these procedures were obtained for most patients.

From the year 2000 onwards, participants with initially normal results (normal or hyperplastic polyps only) of the examination have been recalled after 5 years. Participants were sent invitations for a follow-up flexible sigmoidoscopy screening, and phone contact was made to confirm continued eligibility for screening. Follow-up procedures were performed by the same staff and using the same methods as for the initial examinations.

Cancer outcomes

Linkage of the screening cohort to the Western Australian Cancer Registry was performed in September 2006, with approval of the South Metropolitan Health Service Human Research Ethics Committee. Date of diagnosis with CRC and location of the cancer were obtained. A proximal CRC was defined as being proximal to or including the splenic flexure, and a distal one as being located in the rectum, sigmoid or descending colon. Only CRC data coded as invasive and based on histological verification were included.

Statistical analysis

Our findings are presented descriptively with analysis of univariate factors performed by χ^2 testing for categorical variables and analysis of variance (ANOVA) (SPSS, version 11.0, SPSS Inc, Chicago, Ill, USA). Risk ratios were calculated comparing the pathological findings at the initial and follow-up sigmoidoscopy screening. To examine variables predicting adenoma detection at the initial or follow-up screening, a multinomial

1 Summary of the findings of the initial and follow-up flexible sigmoidoscopy examinations

	Men	Women	Total	*P**
Initial sigmoidoscopy	*n* = 1992	*n* = 1410	*n* = 3402	
Mean insertion depth (cm)	60	52	57	< 0.001
Mean pain score (scale of 0–10)	2.9	4.0	3.4	< 0.001
Proportion with:†				
Normal findings	61%	75%	67%	< 0.001
Any neoplasia	17%	10%	14%	< 0.001
Advanced neoplasia	6.4%	3%	5%	< 0.001
Invasive colorectal cancer‡	0.6%	0.1%	0.4%	0.09
5-year follow-up sigmoidoscopy	*n* = 639	*n* = 386	*n* = 1025	
Mean insertion depth (cm)	62	52	58	< 0.001
Proportion with:†				
Normal findings	65%	75%	70%	0.001
Any neoplasia	14%	6.5%	11%	< 0.001
Advanced neoplasia	2.8%	1.0%	2.1%	0.07
Invasive colorectal cancer	0	0	0	0

* For difference between the sexes. † Percentages do not equal 100%, as some cases with minor histological abnormalities are not included. ‡ After follow-up colonoscopy. ◆

regression model was constructed using the variables: age, sex, insertion depth, pain score, proceduralist seniority and training background, bowel preparation quality, and findings at initial sigmoidoscopy. Variables with a bivariate association at $P < 0.2$ were selected for inclusion in the model. Similarly, a model was constructed to examine factors predictive of diagnosis of later CRC, if sigmoidoscopy results were normal.

RESULTS

Initial screening

Between July 1995 and July 2005, 3402 initial flexible sigmoidoscopy screening examinations were performed. The mean age of participants was 60 years (range, 53–70 years) and 41% were women. The response rate in the first 5 years (initial phase) of the program was estimated at 23%.[10] Volunteers accounted for 43% of those attending initial screening.

Mean sigmoidoscope insertion depth for men was 60 cm compared with 52 cm for women ($P < 0.001$). Compared with men, the insertion depth for women was more likely to be less than 40 cm (17% v 6%, $P < 0.001$), and women were less likely to have an insertion depth of 50 cm or greater (63% v 80%, $P < 0.001$). The mean pain score was 2.9 for men and 4.0 for women ($P < 0.001$). Satisfactory bowel preparation was reported in 93% of men and 92% of women. A summary of the findings is given in Box 1. No cases of significant bleeding or perforation were reported during the screening period.

Overall, the adenoma detection rate was 14%. Advanced adenomas were detected in 5% of procedures. Men were significantly more likely to have a lesion detected than women. Invasive CRC was ultimately diagnosed in 11/1992 men (0.6%) and 1/1410 women (0.1%) ($P = 0.09$).

Recall screening

From September 2000 to July 2005, follow-up screening was performed in 1025 people. The mean interval from the time of initial screening was 5.2 years. These results are also given in Box 1. Of the 2270 participants who had initial flexible sigmoidoscopy screening between 1995 and 1999 and were eligible for the 5-year follow-up screening, 958 (42%) attended after an invitation for follow-up screening. The relative risk (RR) of finding any neoplasia at the recall screening (compared with the initial screening) was reduced, but the difference was not significant (RR, 0.8; 95% CI, 0.6–1.0); the likelihood of finding advanced neoplasia was more substantially reduced (RR, 0.4; 95% CI, 0.3–0.6). Up to July 2005, no CRC was detected by routine follow-up screening.

Predictors of neoplasia at initial and follow-up screening

On multinomial regression analysis, age over 60 years (odds ratio [OR], 1.3; 95% CI, 1.1–1.6), male sex (OR, 2.0; 95% CI 1.6–2.6) and good bowel preparation (OR, 2.4; 95% CI, 1.6–4.1) were significant independent predictors of an adenoma. At the recall screening, only male sex was a significant predictor of adenoma (OR, 2.1; 95% CI 1.3–3.3).

Cancer findings

As a result of initial screening and subsequent colonoscopy, a total of 13 invasive malignancies (0.4% of participants) were diagnosed. Ten derived from a lesion identified by sigmoidoscopy, and two new rectal malignancies and one proximal malignancy were detected at follow-up colonoscopy. Thus, flexible sigmoidoscopy found the index lesions in 12 patients with advanced adenoma and one with multiple small adenomas. CRC staging data were available for all lesions, with nine being Stage I, three Stage III, and one Stage IV disease.

Linkage to the WA Cancer Registry in September 2006 gave a mean follow-up time of 8.2 years for the cohort. From the 2933 participants whose initial screening had not shown any colorectal neoplasia, invasive CRC had been recorded by the Registry in 20 of these patients (0.7%). Fifteen cancers appear to have been located proximal to the splenic flexure and five were distal. In men, the CRC incidence was 0.6% (0.4% proximal, 0.2% distal), and in women the incidence was 0.8% (0.6% proximal, 0.2% distal), although these sex differences were not statistically significant. Of these 20 patients, 18 had attended only the initial flexible sigmoidoscopy screening. Of the two who had also attended the 5-year follow-up sigmoidoscopy, one was a 62-year-old woman who had developed iron deficiency anaemia 12 months before the follow-up screening, but had not attended an arranged colonoscopy. CRC stage data were available for 11 patients, with two being Stage I, one Stage II, five Stage III, and three Stage IV disease.

The mean time from flexible sigmoidoscopy screening to later CRC diagnosis was 4.1 years (range, 0.2–8.6 years), and, as mentioned above, no CRC was found at routine follow-up sigmoidoscopy during the study period. Of five patients with distal malignancy, the mean time to CRC diagnosis after sigmoidoscopy was 2.7 years, with only one of these occurring within 2 years of

sigmoidoscopy. Mean time to diagnosis of proximal cancers was 4.4 years, with only two of the 15 diagnosed within 2 years. Data for these patients are summarised in Box 2.

When distal post-screening cancers only were assessed, then poor bowel preparation (compared with satisfactory preparation) was a significant predictor of CRC risk (OR, 7.2; 95% CI, 1.2–43.6). When proximal post-screening cancers only were considered, then an insertion depth of ⩽ 30 cm (compared with deeper insertion) showed a trend to greater risk of later CRC (OR, 3.5; 95% CI, 1.0–12.4). However, when post-screening cancers at all locations were considered, these associations were not present.

Combining data for cancers detected by sigmoidoscopy screening with those detected after screening allows estimation of the sensitivity and negative predictive value of flexible sigmoidoscopy (with follow-up of any adenoma) for detecting or predicting invasive CRC:

- for all patients with CRC diagnosed at flexible sigmoidoscopy or within 2 years of screening (by which time an invasive CRC should have become clinically apparent), sensitivity is 87% and negative predictive value is 99.9%;
- for a 5-year period after flexible sigmoidoscopy, the sensitivity of the test to identify patients "at risk" of CRC falls to 48% (75% for distal CRC; 9% for proximal CRC), with a negative predictive value of 99.6%.

2 Patients diagnosed with colorectal cancer after normal results of flexible sigmoidoscopy (FS) screening

Proximal colorectal cancer	*n* = 15
Proportion men	47%
Mean (95% CI) insertion depth of initial FS (cm)	55 (41–69)
Mean (95% CI) time to colorectal cancer diagnosis (years)	4.4 (2.9–5.1)
Proportion with inadequate bowel preparation	7%
Distal colorectal cancer	*n* = 5
Proportion men	60%
Mean (95% CI) insertion depth of initial FS (cm)	66 (40–92)
Mean (95% CI) time to colorectal cancer diagnosis (years)	2.7 (1.5–3.9)
Proportion with inadequate bowel preparation	40%

DISCUSSION

In this long-term study of flexible sigmoidoscopy-based screening in average-risk people, 55–64 years of age, 14% of those attending the initial screening were diagnosed with neoplastic lesions and 0.4% were subsequently found to have invasive CRC. These data are consistent with reported baseline findings of other large flexible sigmoidoscopy screening trials.[6,7] In women, the sigmoidoscope insertion depth tends to be less than in men, overall pain scores are higher, and a lower rate of neoplasia is detected. The 23% uptake rate by those mailed invitations for flexible sigmoidoscopy screening in our study compares with the 14% uptake for sigmoidoscopy and FOBT screening in another Australian study,[11] and the 32% uptake in an Italian cohort also for FOBT–sigmoidoscopy screening.[12]

Cancers detected by screening tend to be at an early stage (nine of 13 were Stage I). While our data are incomplete, those diagnosed later after a normal flexible sigmoidoscopy result tended to be more advanced (73% Stage III or IV). This may reflect a greater burden of proximal and often asymptomatic cancer in this group. In a large colorectal cancer series of public hospital patients in WA, 16% overall presented as Stage I, while 48% presented as Stage III or IV.[13]

After an average of 8 years' follow-up, 0.7% of participants who had received a normal screening result were later diagnosed with CRC. Seventy-five per cent of these cancers were proximal. The potential miss rate of flexible sigmoidoscopy remains a contentious issue. Multiple studies support the likelihood that 2%–5% of asymptomatic individuals will have isolated proximal advanced neoplasia.[14-16] We found that invasive CRC at any site was unlikely within 2 years of a negative result of flexible sigmoidoscopy, with a sensitivity of 87% and a negative predictive value of 99.9% (which partly reflects that CRC is still uncommon in people aged 55–64 years). Sensitivity falls to 48% for identifying those at risk of CRC within 5 years. The sensitivity of one immunochemical FOBT for detecting current invasive CRC was 66% in a study in which all participants also received colonoscopy.[17] The negative predictive value for cancer in this study was 99.9%; that is, 0.1% of patients with a negative result of an FOBT actually had CRC.

While colonoscopy may be considered the "gold standard" for bowel examination, it too has a false negative rate. Several studies have documented CRC being diagnosed after colonoscopy.[18-20] A WA study of cancer after a negative colonoscopy result found a 0.5% incidence of CRC within 5 years.[21] As such, the incremental benefit of colonoscopy over flexible sigmoidoscopy may be smaller than anticipated.

Our data have some limitations. The screening group is a heterogeneous mix of people responding to a mailed invitation and a large contingent of volunteers from the community, and there is no prospectively recruited control group with which to compare outcomes. Modelling by the WA Cancer Registry based on age-specific rate data suggests that the expected incidence of CRC in an equivalently aged cohort over a similar time period would be 45 cases (compared with our total of 33).[22] Our cohort represents those at average CRC risk, whereas the general population contains a mix of average and above average risk (family history of CRC, etc).

The strengths of our study are in its use of biopsy to confirm whether polyps were neoplastic, and being able to reliably capture CRC outcomes by using the WA Cancer Registry and its data linkage capabilities.

In summary, our 10-year study of flexible sigmoidoscopy shows that this screening method remains a viable screening tool and provides important data for determining the utility and limitations of this technique in Australia.

COMPETING INTERESTS

None identified.

AUTHOR DETAILS

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