Flexible sigmoidoscopy or colonoscopy as a screening modality for colorectal adenomas in older age groups? Findings in a cohort of the normal population aged 63–72 years

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Abstract

***Background*—Most cases of colorectal cancer originate from adenomas. Removing adenomas has been shown to reduce the incidence of colorectal cancer. The design of cost effective endoscopic screening programmes requires a knowledge of the distribution of adenomas in different age groups.**

***Aim*—To investigate the distribution of colorectal adenomas in older age groups in the normal population.**

***Method*—A total of 356 men and women selected randomly from the population register were offered a colonoscopic screening examination to detect and remove polyps.**

***Results*—In all, 241(68%) subjects, mean age 67.4 years (range 62–73), attended. The caecum was intubated in 193 (80%), and in this group 32 (38%) women and 51 (47%) men had adenomas. One hundred and ten (54%) of the adenomas and 11 (39%) of the "high risk adenomas" (adenomas larger than 10 mm in diameter, adenomas containing villous components, and adenomas with severe dysplasia) were found proximal to the sigmoid colon. In 36 (43%) of the subjects with adenomas, the adenomas were only found proximal to the sigmoid colon. Twenty two (11%) subjects had more than two adenomas. Of 203 adenomas discovered, 189 (93%) were less than 10 mm in diameter.**

***Conclusion*—More than half of the adenomas were localised proximal to the sigmoid colon, and, in nearly half of the adenoma bearing subjects examined, the adenoma was proximal to the descending colon. This indicates that a sigmoidoscopic screening examination in this age group would miss a substantial number of adenomas, but this may be acceptable as the vast majority of proximal adenomas do not progress to clinical cancer within the life expectancy of this age group.**

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Keywords: adenoma; colon; colorectal neoplasms; endoscopy; epidemiology; polyps

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Colorectal cancer is one of the leading causes of death from malignant disease in the western world. As many as 60–90% of cases of colorectal cancer are believed to develop from colorectal adenomas.[1–4] The average time for malignant transformation of an adenoma is estimated to be 10–15 years.[1 5] It should therefore be possible to remove an adenoma before it develops into overt cancer. Adenomas seldom give rise to symptoms and most of them are incidental findings during a clinical investigation or screening procedure. Endoscopic screening of asymptomatic persons has therefore been advocated as a means of reducing the incidence of colorectal cancer. Several screening modalities exist. Colonoscopy is the ideal, but it is expensive, time consuming, and requires highly trained endoscopists. Sigmoidoscopy is cheaper, better tolerated, and can be performed by specially trained technicians.[6–8] Uncontrolled cohort and case-control studies indicate that endoscopy screening and polypectomy may reduce the incidence of colorectal cancer by 76–90%.[5 9–11] Which screening modality to choose depends on the distribution of adenomas in the colon of the population to be screened as well as acceptability (safety, compliance, cost, and availability of trained personnel). Most of our knowledge of adenoma distribution is based on autopsy studies[12–15] and studies on subjects being examined because of symptoms or as part of a health care programme.[16–19] Autopsy studies have shown that the distribution of adenomas changes from predominantly left sided (distal) to right sided (proximal) localisation with increasing age,[13–15 20] indicating that sigmoidoscopy may not be an ideal screening modality for older age groups.

This study was performed to examine whether a screening programme based on sigmoidoscopy would discover the majority of adenomas in a normal population, aged 63 to 72 years, randomly selected from the population register.

Attendees and methods

ATTENDEES

In 1983 a randomised controlled prospective study of the effect of polypectomy on the incidence of colorectal cancer was started in the county of Telemark, Norway.[21] Four hundred men and women were selected from the population register and offered a flexible sigmoidoscopy screening examination. A further 399 subjects were drawn from the same register and enrolled as a control group. These subjects were not given any attention until 1996, when all survivors in both the screening group and the control group were invited to have an endoscopic examination with polypectomy on detection of polyps.[11] A press conference,

which resulted in much publicity, was held before a letter of invitation was mailed to enrolled participants. One reminding letter was sent to those who did not respond. Only subjects from the control group in whom the caecum was successfully intubated were subjected to analysis in this paper.

ENDOSCOPIC EXAMINATION

The attendees were given the choice of a flexible sigmoidoscopic examination or a full colonoscopic examination, the latter being recommended. All examinations except one were performed by the same endoscopist (E T-E). The bowel was cleansed by intake of only transparent liquids on the day before the examination, followed by 4 litres of a polyethylene glycol solution taken orally in the afternoon on the day before the examination. For those preferring sigmoidoscopy, bowel cleansing was limited to a single 240 ml sorbitol enema (Klyx) given 30 minutes before the endoscopic examination. A full medical and family history was recorded. A polyp was defined as a macroscopically elevated lesion of the mucosa irrespective of size, and was measured either by a scaled probe introduced through the biopsy channel of the endoscope, or with the biopsy forceps with the fully opened instrument equivalent to 9 mm. Polyps measuring 4–5 mm or more in diameter were subjected to polypectomy by diathermy snare whereas tissue specimens from smaller polyps were obtained with cold biopsy forceps. When more than 5–10 small polyps (1–2 mm) were found in the rectum, we aimed to sample at least two thirds of them. The localisation of each polyp was registered in centimetres from the anal verge for those in the rectum and sigmoid colon, and in colonic segments proximal to this. A proximal lesion was defined as a lesion proximal to the sigmoid/descending colonic junction. This definition was chosen because this is an anatomical landmark usually recognisable at a sigmoidoscopic examination, and this area is also usually cleansed after a small enema given immediately before the examination. No sedation or analgesia was used except for in one participant who insisted and was given 3 mg midazolam intravenously as premedication.

BIOLOGICAL MATERIAL

Polyps were fixed in formaldehyde for routine histological examination. All polyps were examined by the same experienced pathologist (B M), using the WHO classification.[22] Dysplasia was graded as mild, moderate, or severe. Adenomas containing more than 25% villous structures were defined as adenomas with villous components. Non-neoplastic polyps included hyperplastic polyps and mucosal tags.[12] Adenomas of particularly high risk of malignant transformation[1 3 23] were termed "high risk adenomas". They included those that were larger than 10 mm in diameter, those containing villous structures, and adenomas with severe dysplasia. A "significant finding" was defined as the discovery of a high risk adenoma and/or three or more adenomas irrespective of size or dysplasia or without villous components.

STATISTICAL ANALYSIS

Yates χ^2 test was used to determine statistical significance of differences between proportions in frequency tables. Fisher's exact test was used when the expected frequencies were small. The Mann-Whitney test was used to compare means in demographic data. Medians are given with interquartile ranges (range comprising 50% of the observations, from the 25th centile to the 75th centile). A two sided p value less than 0.05 was considered statistically significant. NCSS-97 and SPSS-8.0 statistical software was used for analysis of the data.

ETHICS

The study was approved by the regional ethics committee and performed in accordance with the Helsinki Declaration.

Results

Of the 399 people enrolled as a control group in 1983, 358 were still alive in 1996. All but two, who had emigrated, were invited to an endoscopic examination. In all, 241 (68%) attended; 19 (8%) of the attendees preferred sigmoidoscopy. Polyps were found in 180 (75%) subjects, and adenomas in 102 (42%). The cleansing was regarded as satisfactory in 234 subjects (97%). The caecum was intubated in 109 (84%) men and 84 (76%) women, 193 (80%) subjects in all. The following sections present the results from the group of 193 attendees in whom the caecum was successfully intubated. In table 1 demographic data for this group are compared with the data for the group of attendees in whom the caecum

Table 1 Characteristics of subjects screened for colorectal polyps (n=241)

	Caecum intubated (n=193)	*Caecum not intubated (n=48)*	*p Value*
Mean (range) age (y)	67 (63–72)	64.4 (63–72)	1.0
Men	109 (56)	21 (44)	0.2
Women	84 (44)	27 (56)	
Median (range) body mass index (kg/m^2)	25 (16–36)	24.2 (16–36)	0.03
Atherosclerotic disease*	31 (16)	8 (17)	0.9
Diabetes mellitus	7 (4)	1 (2)	0.9
Inflammatory bowel disease	4 (2)	0	0.7
Previously diagnosed CRC	4 (2)	1 (2)	1.0
Previously diagnosed non-colorectal cancer	5 (3)	0	0.6
Current smoker	44 (23)	17 (35)	0.1
Past smoker	62 (32)	10 (21)	0.2
First degree relative with CRC	14 (7)	3 (6)	1.0
Abdominal complaints†	47 (24)	10 (21)	0.7
Previous non-study colonoscopy	27 (14)	8 (16)	0.8

Data for those in whom the caecum was successfully intubated during the examination are compared with the data for those in whom the caecum was not intubated. Numbers represent subjects (%) if nothing else stated.
*Includes coronary heart disease, intermittent claudication, and cerebrovascular accidents.
†Includes constipation, irritable bowel syndrome, loose stools, diarrhoea, pain, flatulence, haemorrhoids, mucus in the stools, and anal pruritus, either isolated or in combination.
CRC, colorectal cancer.

Table 2 Findings of polyps of all types, adenomas and high risk adenomas in subjects in whom the caecum was intubated at screening colonoscopy

	Women (n=84)	*Men (n=109)*	*Total (n=193)*
Polyps*	56 (67)	86 (79)	142 (74)
Adenomas	32 (38)	51 (47)	83 (43)
High risk adenomas†	12 (14)	13 (12)	25 (13)
Significant finding‡	16 (19)	20 (18)	36 (19)

Values represent number of subjects (%).
*Including adenomas, hyperplastic polyps, mucosal tags, one carcinoid, and one angiolipoma.
†Adenoma ⩾10 mm in diameter and/or villous components and/or severe dysplasia.
‡High risk adenoma and/or three or more adenomas irrespective of size, dysplasia or villous components.

Table 3 Distribution of polyps in the segments of colon in individuals in whom the caecum was intubated at screening colonoscopy

	Rectum	*Sigmoid colon*	*Descending colon*	*Transverse colon*	*Ascending colon*	*Caecum*	*Total*
Adenomas							
Total	56 (28)	37 (18)	33 (16)	38 (19)	26 (13)	13 (6)	203 (100)
<5mm	46 (33)	14 (10)	22 (16)	27 (20)	21 (15)	10 (7)	140 (100)
5–9mm	6 (12)	19 (40)	8 (16)	10 (20)	4 (8)	2 (4)	49 (100)
⩾10mm	4 (29)	4 (29)	3 (21)	1 (7)	1 (7)	1 (7)	14 (100)
Moderate dysplasia	6 (15)	8 (20)	9 (22)	13 (32)	2 (5)	3 (7)	41 (100)
Severe dysplasia	0	3 (60)	2 (40)	0	0	0	5 (100)
Villous components	3 (18)	7 (41)	2 (12)	3 (18)	1 (6)	1 (6)	17 (100)
High risk adenoma*	5 (18)	12 (43)	5 (18)	3 (11)	1 (4)	2 (7)	28 (100)
Hyperplastic polyps	233 (78)	28 (9)	3 (1)	20 (7)	10 (3)	5 (2)	299 (100)
Mucosal tags	108 (73)	14 (10)	9 (6)	12 (8)	2 (1)	3 (2)	148 (100)
Histology unknown†	20 (83)	2 (8)	1 (4)	1(4)	0	0	24 (100)
Total no of polyps	417 (62)	81 (12)	46 (7)	71 (11)	38 (6)	21 (3)	674(100)

Adenomas are subdivided according to size, dysplasia and presence of villous components. Values represent numbers (%).
*Adenoma ⩾10 mm in diameter and/or villous components and/or severe dysplasia.
†No biological material obtained at biopsy.

was not intubated (n = 48). The only statistically significant difference between the two groups was in body mass index (kg/m^2), with a slightly lower median value in the group in whom the caecum was not intubated.

POLYP DISTRIBUTION

In the group of 193 subjects in whom the caecum was intubated, polyps were found in 142 (74%) and adenomas in 83 (43%) (table 2). Table 3 shows the distribution of polyps in the segments of the colon. An abundance of small polyps (1–2 mm) was found in the rectum. A total of 205 (74%) of these were sampled; 16 (8%) were adenomas, 108 (53%) were hyperplastic polyps, and 73 (36%) were mucosal tags. Colorectal cancer was discovered in two subjects. About half of the adenomas were found in the rectum and sigmoid colon (table 3). Two thirds of high risk adenomas were also found at this location (table 3). Most of the adenomas detected (189; 93%) were less than 10 mm in diameter (tables 3 and 4). Moderate or severe dysplasia was found in 46 (23%) and villous components in 17 (8%) of the adenomas (tables 3 and 4). Adenomas were exclusively localised in the rectum and sigmoid colon in 28 subjects (15% of all with caecum intubated). In 36 (19% of all with caecum intubated), the adenomas were exclusively localised proximal to the sigmoid colon, and, in eight of this group (4% of all with caecum intubated), high risk adenomas were discovered. Of these subjects, only one had a first degree relative with colorectal cancer. Only 22 (27%) of adenoma bearers had more than two adenomas (range 1–22) (fig 1). Fifteen (8% of all with caecum intubated) had adenomas solely proximal to the splenic flexure; in three of these (2% of all with caecum intubated), high risk adenomas were detected.

Table 4 Size, presence of dysplasia and number of adenomas found in subjects in whom the caecum was intubated at screening colonoscopy (% of total number of adenomas)

	Women (n=84)	*Men (n=109)*	*Total (n=193)*
Number of adenomas	93	110	203
Median (interquartile range) number of adenomas per adenoma bearing subject	2 (1–3)	1 (1–2)	1 (1–3)
Median (interquartile range) size of adenomas (mm)	4 (3–5)	3 (3–5)	4 (3–5)
Adenomas			
<5mm	62 (67)	78 (72)	140 (69)
5–9 mm	24 (26)	25 (23)	49 (24)
⩾10 mm	7 (8)	7 (6)	14 (7)
Moderate dysplasia	19 (20)	22 (20)	41 (20)
Severe dysplasia	2 (2)	3 (3)	5 (2)
Villous components	10 (11)	7 (6)	17 (8)
High risk adenomas*	15 (16)	13 (12)	28 (14)

*Adenomas ⩾10 mm in diameter and/or villous components and/or severe dysplasia.

ADENOMAS LOCALISED IN THE PROXIMAL COLON COMPARED WITH THE DISTAL COLON

Table 5 gives the number of adenomas found in the proximal colon in relation to the number of polyps found in the rectosigmoid colon. Forty seven subjects had adenomas in the rectosigmoid colon; 19 (40%) of these had proximal adenomas, compared with 36 (25%) subjects with proximal adenomas in the group of 146 with no distal adenoma. This gives a relative risk (RR) of 1.6 (95% confidence interval 2.6 to 1.0) (p = 0.06) of finding a proximal adenoma when a distal adenoma is present compared with finding a proximal adenoma with no distal adenoma detected. The relative risk of having proximal adenomas for subjects with distal adenomas larger than 5 mm compared with those with distal adenomas smaller than 5 mm was 1.5 (3.8 to 0.6) (p = 0.5). The relative risk of having a proximal adenoma with a distal adenoma of any size compared with having a proximal adenoma and a distal polyp of any kind was 1.3 (2.1 to 0.8) (p = 0.3). Nine (31%) of 29 men with adenomas in the rectosigmoid colon had adenomas in the proximal colon, whereas 22

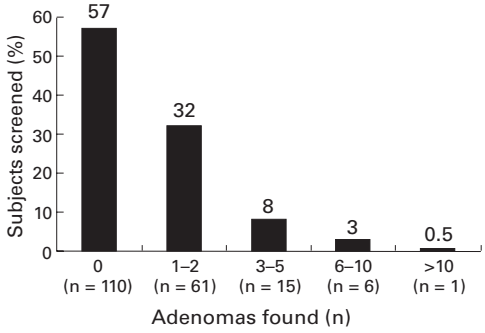

Figure 1 Percentage distribution of subjects with caecum intubated categorised according to number of adenomas found (none, 1–2, 3–5, 6–10 and more than 10). Total number of individuals in each category is given under the bars, which express percentage of individuals in each category.

Table 5 Findings in proximal colon (caecum to and including the descending colon) in subjects in whom the caecum was intubated in the following categories according to findings in the rectosigmoid colon: those with their largest adenoma less than 5 mm, those with their largest adenoma 5–9 mm, those with the largest adenoma >9 mm, those with no adenoma, those with no polyp of any kind and those with polyps of any kind

Findings in rectosigmoid colon	*Adenoma in the proximal colon*	*High risk adenoma* in the proximal colon*	*Significant finding† in the proximal colon*
No polyp (n=77)	20 (26)	5 (6)	9 (11)
No adenoma (n=146)	36 (25)	8 (5)	11 (8)
Adenoma <5 mm (n=19)	6 (32)	0	2 (11)
Adenoma 5–9 mm (n=17)	8 (47)	2 (12)	4 (24)
Adenoma ⩾10 mm (n=11)	5 (45)	1 (9)	1 (9)
Adenoma any size (n=47)	19 (40)	3 (6)	7 (15)
Polyp of any kind (n=116)	35 (30)	8 (7)	13 (11)

Values represent subjects (%).
*Adenoma ⩾10 mm in diameter and/or villous components and/or severe dysplasia.
†High risk adenoma and/or three or more adenomas of any size, grade of dysplasia, or with or without villous components.

(28%) of 80 men with no adenomas in the rectosigmoid colon had adenomas in the proximal colon (RR 1.1 (2.2 to 0.5); p = 0.9). For women, the same figures were 10 (56%) of 18 and 14 (21%) of 66 (RR 2.6 (4.8 to 1.2); p = 0.01).

POSSIBLE MARKERS FOR ADENOMA PREVALENCE

We did not find any associations between the presence of hyperplastic polyps and adenomas; 46 (42%) of those without adenomas in their colon, 40 (48%) of those with adenomas, and 13 (36%) of those with only proximal adenomas had distal hyperplastic polyps (p = 0.4–0.6). No relations were found between having only proximally located adenomas and gender (p = 0.5), body mass index (over or under the 50 percentile) (p = 0.2), age group (below or over 68 years) (p = 0.5), smokers versus non-smokers (p = 0.1), or having first degree relatives with colorectal cancer (p = 0.7).

Twenty eight (15%) of the group of 193 subjects in whom the caecum was intubated had had an endoscopic large bowel examination other than the screening examination. Four subjects had had a total of eight adenomas removed during these examinations, the largest 7 mm in diameter, none of them showing more than moderate dysplasia. In all four, distal adenomas were detected at the screening.

Discussion

This study showed that almost half of the study population, 63–72 years of age, had adenomas, and that a substantial proportion had adenomas only proximal to the sigmoid colon. Autopsy studies have reported that 32–50% of women and 40–62% of men in the age group 60–80 years have adenomas.[12 14 15 20] Colonoscopic studies on age groups comparable with this study population found adenomas in 26% of women[16] and 25–45% of men.[16–19 24] The percentage of subjects with only proximal adenomas compares with previous endoscopic studies, which have shown that 13–70% of adenoma bearers have no distal adenoma.[3 17–19 24–26] The discrepancy in figures between autopsy studies and previous endoscopic studies may be partly due to autopsy study selection bias, as adenomas are associated with certain risk factors, such as atherosclerosis, that predispose for early death.[27] The use of a magnifying lens at autopsy and insufflation with air, stretching the mucosa and making minor lesions invisible at colonoscopy, may contribute to a higher pick up rate of minor lesions in autopsy studies. The bowel cleansing was good in almost all attendees, but even under these circumstances it has been estimated that 16–27% of polyps smaller than 5 mm and 5–17% of polyps 6–9 mm in size will be missed at a single endoscopic examination.[28–30] This is a further indication that the true number of adenomas in a live normal population may indeed be higher than recorded in endoscopy studies and closer to the prevalence reported in autopsy studies.

Most endoscopic studies have recruited their subjects from health conscious groups such as doctors, dentists, and people attending special health care programmes. People with known colon pathology and gastrointestinal symptoms have been excluded. To preserve the status of being a random sample of the normal population, there were no exclusions from our study group. Thus several of the attendees had abdominal complaints, earlier diagnosed colorectal cancer, and first degree relatives with colorectal cancer (table 1). These risk factors may increase the prevalence of adenomas in our study group compared with other endoscopy studies.

The caecum was reached in 80% in our study. This is lower than reported in other studies, where the caecum was reached in 90–100%[31–34]; this may partly be explained by the facts that 8% preferred a sigmoidoscopic examination and sedation was not given routinely. The demographic data for those in whom the caecum was intubated are comparable with the data for those in whom the caecum was not intubated. The slight difference in body mass index in the two groups can hardly be of any clinical importance and may be coincidental. The caecum was intubated in a lower proportion of women than men. Other investigators have also reported a lower success rate for women,[34 35] and this may be due to a more tortuous sigmoid colon and the shape of the pelvic outlet in women. Only eight adenomas had been removed from the study population before the screening examination, and this number would not have any impact on our results. The attendance rate for the screening examination was 68%. Attendance for screening programmes is traditionally high in Norway, both mammography and cervical smear screening achieve 80% attendance rate in most counties. We do not know anything about those who declined to attend in our study. It has been shown that those who comply with screening examinations are a selected group of the population.[36–38] It is also known that subjects who refuse to attend may be those with the highest risk of general somatic morbidity and hence may harbour more adenomas than the attendees.[39] We were not able to find any factors (age, gender, smoking, atherosclerotic disease, or a first degree relative with colorectal cancer) predisposing to an adenoma distribution with only proximal adenomas. This may

be due to the small numbers in our study and hence lack of statistical power. The figures do, however, indicate that differences in risk are so small that these factors should be of hardly any clinical use in organised screening within the present age group.

We did not find any association between hyperplastic polyps and proximal adenomas. Other investigators have found such an association.[40–42] These studies have been criticised for their selection of study subjects and their retrospective design.[43] Other investigators have more recently been unable to confirm these findings.[43–46]

Autopsy studies have shown a proximal shift in the distribution of adenomas in the colon with advancing age, with most adenomas found distally at ages below 60 and most in the proximal colon at age 70 years or older.[13 14 20] This is compatible with our results. To achieve a high attendance rate for a flexible sigmoidoscopy screening examination, it is probably wise to limit bowel cleansing to a small enema, for example a 240 ml sorbitol enema, administered immediately before the examination. A flexible sigmoidoscopy examination immediately after a small enema may occasionally allow visualisation of the descending colon and even the transverse colon. One may therefore detect some of the adenomas proximal to the sigmoid/descending colonic junction.

In conclusion, this colonoscopic screening study of a normal population aged 63–72 years of age achieved a 68% attendance rate. With an adenoma prevalence of 43% and adenomas localised exclusively proximal to the sigmoid colon in 19% of attendees, endoscopic screening, if considered at all at this age, should probably be colonoscopy rather than flexible sigmoidoscopy. This would, however, require a high degree of acceptability in the population as in Telemark. An alternative strategy with flexible sigmoidoscopy and a baseline colonoscopy only in those who were found to have rectosigmoid adenomas would have missed eight subjects (4%) with high risk adenomas and 11 subjects (6%) with significant findings. This may be considered acceptable in populations with a low acceptance of colonoscopy, as the vast majority of proximal adenomas will not progress to clinical cancer within the life expectancy of this age group.

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