RESEARCH

Surveillance colonoscopy in low-risk postpolypectomy patients: Is it necessary?

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ABSTRACT

Aim Patients who have had colorectal adenomas removed are at increased risk of developing colorectal cancer in the future. We sought to determine whether surveillance colonoscopy at 5 years in low-risk postpolypectomy patients is necessary and effective.

Method UK multicentre retrospective study. Patients diagnosed with 'low-risk' colorectal adenomas between April 2004 and April 2007 were identified and results of all subsequent lower gastrointestinal (GI) endoscopies were noted. Where no colonoscopy had been done at or after 5 years from the index investigation, patient details were cross-checked against hospital colorectal multidisciplinary team databases to ensure no colorectal cancer had been detected in the meantime.

Results 641 patients were included. 131 patients (20.4%) had a 'per protocol' surveillance colonoscopy at 5 years. Of these, no patients were found to have colorectal cancer, 10 patients (7.6%) had advanced adenomas, 26 patients (19.8%) had non-advanced adenomas and 95 patients (72.5%) had no further adenomas. 510 patients (79.6%) did not have a surveillance colonoscopy at 5 years. Of these, 110 patients (17.2%) developed lower GI symptoms within 5 years of their index endoscopy and underwent a further lower GI endoscopy to investigate these symptoms. 3 colorectal cancers in 3 patients were found during these endoscopies and two further colorectal cancers were found at symptomatic colonoscopies at or after 5 years from index.

Conclusions Patients with low-risk adenomas should be risk profiled. Those with risk factors, such as two adenomas, male sex and advanced adenomas at index procedure should be offered 5-year surveillance colonoscopy.

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of death from cancer in the

UK and the USA.^{1 2} In the UK, over 41 000 people are diagnosed with, and over 16 000 people die from, CRC each year. That equates to someone dying every 30 min as a result of this disease. The concept that most cancers arise from pre-existing polyps is widely accepted.³ Although not all colonic polyps are neoplastic, adenomatous polyps have malignant potential. Adenomas are usually asymptomatic and discovered incidentally. The lead time for progression of an adenoma to cancer has been found in one study to be 26 years for diminutive adenomas (<5 mm), 8 years for small adenomas (6–10 mm) and 5 years for large adenomas (≥10 mm).⁴

There are recognised risk factors for colonic cancer. These include a family history of CRC, genetic disorders such as familial adenomatous polyposis and hereditary non-polyposis colon cancer,^{5–8} acromegaly,⁹ longstanding inflammatory bowel disease of the colon,^{10–12} diets that are high in red and processed meat,^{13 14} and prior colorectal adenomas. Strong evidence suggests that detecting and removing colonic adenomas reduces the risk of CRC.¹⁵ Nevertheless, high detection rates of colorectal adenomas at follow-up (30%–50%) after a complete clearance colonoscopy have been reported.^{16–20} Patients who have had adenomas removed are at increased risk of developing CRC in the future and, therefore, may benefit from endoscopic surveillance.²¹

Colonoscopic surveillance in people at high risk of developing CRC can detect precancerous changes and potentially prevent progression to CRC. It can also identify cancer at an early stage when it is much more likely to be endoscopically or

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surgically treatable. Patients who are diagnosed at an early stage have a much better prognosis than those who present with more extensive disease: over 93% of patients diagnosed with Dukes stage A cancer survive 5 years compared with <7% of patients with advanced disease (modified Dukes stage D).²²

However, while colonoscopy is largely a safe procedure, it is important to appreciate that it is invasive with some associated morbidity. In a recent comprehensive, multicentre UK audit of colonoscopy undertaken over a 2-week period between 28 February 2011 and 11 March 2011, and including data on 20 085 colonoscopies, there were 29 admissions or episodes of unplanned care (0.14% or 1:693) for any reason following colonoscopy. A total of eight perforations (0.04% or 1:2511 procedures) and 52 haemorrhages (0.26% or 1:386 procedures), of which 11 required admission to hospital, were reported.²³ Furthermore, the prevalence of colonic adenomas is estimated to be 30%–40% at age 60 years;^{24–26} however, the lifetime cumulative incidence of CRC is only 5.5%, therefore many colonic adenomas do not progress to cancer. Small adenomas are rarely malignant; however, the malignant potential increases with increasing size.²⁷

The future risk of developing CRC or advanced adenomas (≥ 1 cm in size, high-grade dysplasia or villous morphology) after polypectomy varies according to the number and size of the adenomas removed at baseline colonoscopy. According to the British Society of Gastroenterology (BSG) guidelines, patients are divided into low-risk, intermediate-risk and high-risk groups, and the interval to the first follow-up examination varies accordingly. Patients with only one or two small (<1 cm) adenomas are at low risk^{28–31} and need no colonoscopic surveillance or 5-yearly until one negative examination, then cease surveillance. There is no guidance as to which of these two options to choose, and it is interesting to note that the English Bowel Cancer Screening Programme (BCSP) opts not to offer surveillance to this cohort of patients. Patients with three or four small adenomas or at least one adenoma ≥ 1 cm are at intermediate risk^{17 19} and should be screened 3-yearly until two consecutive examinations are negative. If either of the following is detected at any single examination (at baseline or follow-up), five or more adenomas, or three or more adenomas at least one of which is ≥ 1 cm, the patient is at high risk^{17 30 32} and an extra examination should be undertaken at 12 months before returning to 3-yearly surveillance.

To date, there has been no assessment of the efficacy or necessity of the BSG guidelines for low-risk adenoma surveillance.

Objective

The primary aim of the study was to determine whether surveillance colonoscopy at 5 years in

low-risk postpolypectomy patients is necessary and effective by analysing CRC incidence and advanced/non-advanced adenoma rates.

The secondary aim was to identify patient characteristics within this cohort, such as age or gender, which may help to select those that should be referred for a surveillance colonoscopy after 5 years, and those who could be considered for no follow-up.

Design and setting

This UK multicentre retrospective study was carried out in the gastroenterology departments at University Hospital of North Tees, University Hospital of Hartlepool, South Tyneside District Hospital, Leeds General Infirmary and St James's University Hospital, Leeds. Using histology databases a list of all patients diagnosed with colorectal adenomas between April 2004 and April 2007 was obtained. The histology and endoscopy reports were reviewed and patients other than those fulfilling 'low-risk' criteria, in view of the number or size of any adenomas removed, were excluded. 'Low risk' was defined in accordance with the BSG guidelines: one or two adenomas of less than a centimetre in size. Patients whose endoscopy report was missing were excluded. Patients with known inflammatory bowel disease, previous colorectal polyps and previous CRC were also excluded.

Patient details were noted, including age and gender. The date and findings of the index investigation were recorded, including number, size, histological architecture and grade of dysplasia of adenomas detected, polypectomy technique, quality of bowel preparation and the presence of diverticulosis. The nature of the index investigation (i.e. full colonoscopy or flexible sigmoidoscopy) was noted, and any patient in whom the caecum was not intubated was excluded. Patients who had a flexible sigmoidoscopy as their index investigation were included only if they had a completion test in addition, such as a full colonoscopy, barium enema or CT colonography. If the patient had two procedures as their index investigation, e.g. a flexible sigmoidoscopy followed by a completion colonoscopy, the date of the first polypectomy was taken as the date of the index investigation.

For all patients included in the study, the details and results of all subsequent lower gastrointestinal (GI) endoscopies were noted. Details included date, indication for procedure (i.e. whether for investigation of symptoms or surveillance), quality of bowel preparation and whether the caecum was reached. Findings included the total number of adenomas detected, the largest size, highest level of architecture (villous>tubulovillous>tubular>serrated) and highest grade of dysplasia of adenomas detected, and whether cancer was found.

Where no colonoscopy had been done at or after 5 years from the index investigation, patient details

were cross-checked against hospital colorectal multi-disciplinary team (MDT) databases to ensure no CRC had been detected in the meantime.

If a polyp had been detected, removed but not retrieved for histological analysis during index or subsequent endoscopies, it was treated as an adenoma in this study. Wherever possible the histological size was used in preference to the endoscopic size; however, if the pathologist had not reported on the size of the adenoma, the endoscopist's estimation was used. Advanced adenomas were defined as adenomas 1 cm or greater in size, or with villous components (tubulovillous or villous), or with high-grade or severe dysplasia. Adenomas not meeting these criteria were defined as non-advanced.

Statistical methods

Continuous variables were assessed for normality by visual inspection of the histogram. Descriptive statistics were used to characterise the patient sample, using proportions, means with SDs and medians with IQRs where appropriate. Bivariate comparisons were performed for no further adenomas at surveillance and further adenomas at surveillance, as well as no advanced adenomas at surveillance and advanced adenomas at surveillance using χ^2 test for categorical variables and Student t test for parametric data. A two-sided p value <0.05 was taken as statistically significant.

RESULTS

In total, 820 patients met the inclusion criteria between April 2004 and April 2007. Although the timeframes varied between hospitals, for logistical reasons, in each hospital cases were chronological. From 820 patients, 179 were excluded and therefore, overall 641 patients were included for analysis in this study and followed up for a total of 3525 years.

Patient characteristics are presented in [table 1](#).

The findings at further lower GI endoscopy are presented in [figure 1](#).

Patients who had a 'per protocol' surveillance colonoscopy

In total, 131 patients (20.4%) had a 'per protocol' surveillance colonoscopy at 5 years (± 6 months). There were no cancers found in this group. Ten patients (7.6%) were found to have advanced adenomas (see [table 2](#)). Twenty-six patients (19.8%) were found to have non-advanced adenomas, but the majority, 95 patients (72.5%), had no further adenomas found at surveillance.

Patients who did not have a 'per protocol' surveillance colonoscopy

In total, 510 patients (79.6%) did not have a surveillance colonoscopy at 5 years. These patients were followed up for a median of 90 months (range 67–

Table 1 Demographic characteristics of all enrolled patients

Age in years, mean/median/range	63.4/65/25–91
Men, n (%)	361 (56.3)
Index investigation, n (%)	
Full colonoscopy	545 (85.0)
Flexible sigmoidoscopy+completion colonoscopy	41 (6.4)
Flexible sigmoidoscopy+barium enema	49 (7.6)
Flexible sigmoidoscopy+CT colonography	6 (0.9)
Diverticular disease at index investigation, n (%)	175 (27.3)
Bowel preparation, n (%)	
Good/satisfactory	574 (89.5)
Poor	27 (4.2)
Not stated	40 (6.2)
Number of adenomas at index investigation, n (%)	
1	517 (80.7)
2	124 (19.3)
Size of adenomas at index investigation, n (%)	
Diminutive (≤ 5 mm) adenoma(s) only	366 (57.1)
At least one adenoma between 6 and 9 mm	275 (42.9)
Polypectomy technique, n (%)	
Hot biopsy	356 (55.5)
Cold biopsy	50 (7.8)
Cold snare	182 (28.4)
Hot snare	9 (1.4)
Not recorded	44 (6.9)
Histological architecture of adenomas at index, n (%)	
Tubular	639 (83.5)
Tubulovillous	104 (13.6)
Villous	3 (0.4)
Serrated	15 (2.0)
Not retrieved	4 (0.5)
Grade of dysplasia of adenomas at index, n (%)	
Low grade	749 (97.9)
High grade	12 (1.6)
Not retrieved	4 (0.5)
Patients with high-grade dysplasia, tubulovillous or villous morphology at index, n (%)	106 (16.5)

108 months). Records of all further lower GI endoscopies performed after their index procedure were reviewed and patient details were checked against local colorectal MDT databases to ensure they had not been diagnosed with CRC via a route other than endoscopy. In total, 110 patients (17.2%) developed lower GI symptoms within 5 years of their index endoscopy and, therefore, underwent a further lower GI endoscopy to investigate these symptoms. The mean and median time to next endoscopy in these patients was 33.6 and 34 months, respectively (range 1–59 months). Three CRCs in 3 patients were found during these endoscopies. Two further CRCs were found at symptomatic colonoscopies at or after 5 years from index, thus a total of 5 CRCs in 5 patients were diagnosed (see [table 3](#)).

Robertson *et al*³³ developed an algorithm to assign a presumptive explanation for interval CRCs soon after a colonoscopy. To be adjudicated as a 'new

Figure 1 Flow chart of patients included in the study and their outcomes including findings at further lower gastrointestinal endoscopy. AA, advanced adenoma(s); CRC, colorectal cancer; MDT, multidisciplinary team; NAA, non-advanced adenoma(s); No As, no adenomas.

cancer', three or more years must have passed between the prior colonoscopy and the exam diagnosing cancer, and there must have been no significant adenoma detected in the same segment of the

Table 2 Description of each case of advanced neoplasia in patients who underwent 'per protocol' surveillance colonoscopy

Patient	Site	Adenoma size (mm)	Histological architecture	Grade of dysplasia
1	Rectum	7	Tubulovillous	Low
2	Rectum	3	Tubulovillous	Low
3	Descending	7	Tubulovillous	Low
4	Sigmoid	7	Tubulovillous	Low
5	Sigmoid	10	Tubulovillous	Low
6	Distal transverse	10	Tubular	Low
7	Rectum	11	Tubulovillous	High
8	Splenic flexure	10	Tubular	Low
9	Sigmoid	7	Tubulovillous	Low
10	Sigmoid	11	Tubular	Low

colorectum on the prior exam, as described below. Similarly, cancers were assigned as 'missed lesions' if they were found within 3 years of the prior colonoscopy and there was no evidence of a significant adenoma in the same segment at that exam. To ascribe a case as 'incomplete adenoma resection', there had to be a 'significant' adenoma resected from the same segment of the colon during the prior colonoscopy. Given that adenomatous polyps increase in size over time, the definition of what constituted a

Table 3 Description of each case of colorectal cancer

Patient	Age	Site of cancer	Time lapse from index investigation (months)
1	79	Sigmoid-descending junction	55
2	72	Rectum	37
3	76	Caecum	69
4	78	Caecum	62
5	73	Ascending	57

significant adenoma varied based upon on the time since last colonoscopy. Specifically, if three or more years had passed since the last colonoscopy, then an adenoma ≥ 5 mm in size or with villous histology or with high-grade dysplasia was considered significant. If fewer than 3 years had passed, then an adenoma ≥ 1 cm in size or with villous histology or with high-grade dysplasia was considered significant.

According to the algorithm in our cohort, all 5 CRCs would be classed as 'new'.

A further 54 patients (8.4%) had a surveillance colonoscopy that was not 'per protocol', i.e. it was done prior to 5 years from the index procedure. This was usually because the time interval between index and surveillance procedures had been calculated at the time of the index procedure prior to histology results being known: some polyps that were assumed to be adenomas were actually hyperplastic, which would have downgraded these patients from moderate or high risk to low risk.

Of the 133 patients in this cohort who were above the age of 75 years at the time of their index procedure, 13 (9.8%) underwent a surveillance colonoscopy. The mean and median time interval between the index investigation and surveillance colonoscopy was 50.7 and 60 months, respectively (range 6–62 months).

Results of all further lower GI endoscopies

Overall, 301 patients (47.0%) had at least one further lower GI endoscopy following their index investigation. A total of 377 further lower GI endoscopies were performed in these 301 patients, of which 322 (85.4%) were full colonoscopies to the caecum and

55 (14.6%) were flexible sigmoidoscopies or incomplete colonoscopies. In 31 (8.2%) of these procedures, the bowel prep was poor, in 296 (78.5%) the bowel prep was good or satisfactory and in 50 (13.3%) the quality of bowel prep was not recorded.

Of the 301 patients who had a further lower GI endoscopy after their index procedure, 20 (6.6%) were found to have advanced neoplasia. This included 5 patients (1.7%) with CRCs and 15 patients (4.9%) with advanced adenomas (i.e. villous or tubulovillous histology or high-grade dysplasia or tubular adenoma ≥ 1 cm). All CRCs were found in patients whose further colonoscopy was to investigate GI symptoms or signs, such as per rectal bleeding or iron deficiency anaemia. A total of 144 'symptomatic colonoscopies' were performed postindex investigation, giving a symptomatic colonoscopy CRC rate of 3.5%. No CRCs were found during surveillance colonoscopies (0%); however, it is interesting to note that four of the five CRCs were diagnosed at the 5-year 'per protocol' time frame (i.e. 5 years $\pm$ 6 months) or later. In total, 63 patients (20.9%) were found to have non-advanced adenomas and 218 patients (72.4%) had no further neoplastic lesions identified.

Table 4 shows the characteristics at index procedure for patients who were found to have further neoplastic lesions (advanced and non-advanced) at subsequent lower GI endoscopies. Table 5 shows the characteristics at index procedure for patients who were found to have advanced neoplastic lesions at subsequent lower GI endoscopies.

Of the 130 female patients who had further lower GI endoscopies after their index procedure, 27 (20.8%) had further adenomas (advanced and non-

Table 4 Characteristics at index procedure for patients who were found to have further neoplastic lesions

	No. of patients with further adenomas (advanced and non-advanced)	No. of patients with no further adenomas	p Value
Mean age, years (SD)	60.9 (12.4)	60.3 (12.3)	0.687
Gender			
Men	56	115	0.021
Women	27	103	
No. of adenomas at index			
1	61	172	0.316
2	22	46	
Size group of adenoma(s) at index			
Diminutive (≤ 5 mm)	41	127	0.167
Small (6–9 mm)	42	91	
Adenoma type (advanced=high-grade dysplasia, tubulovillous or villus morphology)			
Non-advanced	65	185	0.176
Advanced	18	33	

Table 5 Characteristics at index procedure for patients who were found to have further advanced neoplastic lesions

	No. of patients with advanced adenomas	No. of patients with no advanced adenomas	p Value
Mean age, years (SD)	64.7 (13.3)	60.1 (12.2)	0.115
Gender			
Male	13	158	0.444
Female	7	123	
No. of adenomas at index			
1	11	222	0.013
2	9	59	
Size group of adenoma(s) at index			
Diminutive (≤ 5 mm)	9	159	0.314
Small (6–9 mm)	11	122	
Adenoma type (advanced=high-grade dysplasia, tubulovillous or villus morphology)			
Non-advanced	12	238	0.004
Advanced	8	43	

advanced) detected compared with 56 (32.8%) of the 171 male patients who had further adenomas detected ($p=0.021$).

In total, 139 patients had only 1 diminutive adenoma found at their index investigation. Of this group, 37 patients (26.6%) had any further adenomas detected at subsequent endoscopies, and only 6 patients (4.3%) had advanced neoplastic lesions. In comparison, 39 patients had 2 small adenomas, of which at least one was larger than diminutive in size. Of this group, 18 patients (46.2%) had further adenomas detected at subsequent endoscopies and 6 patients (15.4%) had advanced neoplastic lesions.

DISCUSSION

As a consequence of the ever-increasing demand for colonoscopy, endoscopy units are under considerable pressure to meet the UK government's 18-week target time between patient referral and treatment. A 25% increase in demand was seen over 7 years prior to 2005.³⁴ Introduction of the National Health Service BCSP in April 2006 has resulted in a further increase in the volume of colonoscopy. Therefore, ensuring that surveillance colonoscopy is restricted to those who are most likely to benefit has assumed greater importance. It is interesting to note that while the BCSP has adopted the BSG guideline there has been a small modification in that it does not include an option for a 5-year follow-up colonoscopy in the low-risk group. Our study shows that a minority of 'low-risk' patients (20.4%) actually have a per protocol surveillance colonoscopy. In those that do, we have found that the majority (72.5%) have no further adenomas detected at their surveillance endoscopy and that the yield for detecting advanced neoplasia at the 5-year surveillance colonoscopy is low (7.6%). No cancers were found at surveillance.

A previous UK study found that patients from whom only small (<1 cm) tubular adenomas were removed had no increased risk of developing colon cancer long term and the risk of rectal cancer was profoundly decreased compared with the unexamined population.³⁵ These results were replicated by a similar study from the USA where no increased incidence of cancer was observed in 751 patients after removal of small (1 cm or less) colorectal polyps.³⁶ The results from our study confirm that the benefits compared with the risks of surveillance colonoscopy are likely to be small in patients with only one to two small adenomas, and that follow-up colonoscopy, if undertaken at all, should be delayed by at least 5 years. The advanced neoplasia rate, including CRC, in our entire cohort was 6.6%, and we conclude that it is sensible to offer additional colonoscopies in the interim if the patient has new colorectal symptoms.

Some factors point towards higher risk of further adenomas and further advanced neoplasia. We found that male patients were significantly more likely to

have further adenomas on subsequent endoscopies compared with female patients. However, it should be noted that a study by Erichsen *et al*³⁷ found that in comparison with CRCs, interval cases were more likely to be women (54% vs 48%). We also found that patients with two small adenomas at index were significantly more likely to have advanced neoplasia at subsequent endoscopies compared with patients with only one small adenoma. Furthermore, we found that patients with advanced adenoma(s) at index (i.e. adenomas that had tubulovillous or villous histology or high-grade dysplasia) were significantly more likely to have advanced neoplasia found at subsequent endoscopies compared with patients with non-advanced small adenoma(s) at index.

Patients with low-risk adenomas should be risk profiled. Those with risk factors, such as two adenomas, male sex, advanced adenomas at index procedure or strong family history, as well as those falling outside the BCSP enrolment age or who want colonoscopy surveillance should be offered a surveillance procedure at 5 years provided they are fit for the procedure. Everyone else could be considered for discharge with advice to return if symptomatic and encouraged to participate in the 2-yearly national faecal occult blood screening programme.

It is interesting to note that hot biopsy was the preferred polypectomy technique in over 50% of the adenomas detected at index procedure in our cohort. The current vogue is to use cold snare rather than hot biopsy for removing small polyps, but at the time of audit (i.e. April 2004 to April 2007) hot biopsy was still a popular technique.

A limitation of this study is that it assumes colonoscopy is 100% sensitive. We know this is not the case, however, even when intubation to the caecum is achieved. Miss rates for small adenomas are in the order of 25%–50%.^{38–40} Furthermore, around 6%–12% of larger adenomas (≥ 1 cm)^{39–41} and around 4% of cancers are missed at colonoscopy.⁴² It is, therefore, possible that some of the neoplastic lesions detected at the endoscopies that followed the index procedure were missed lesions as opposed to new lesions. However, this would only support our recommendations above and instead of offering surveillance to all low-risk patients' endoscopists would be better concentrating on performing meticulous examinations of the colon at the index procedure.

In summary, a significant proportion of low-risk postpolypectomy patients develop lower GI symptoms that necessitate colonoscopic investigation within 5 years of their index procedure—in our study, this was 17.2% of patients. For the remainder, the yield of advanced neoplasia at surveillance endoscopy was very low, especially for patients with only one small tubular or serrated adenoma. Only a small percentage of adenomas found at index procedure in this cohort were sessile-serrated adenomas (2%). This probably

reflects the reduced awareness of the sessile-serrated adenoma at the period of the study. It is important to highlight that the current advice is that serrated polyps with dysplasia should be treated as high-risk lesions.⁴³

Significance of this study

What is already known about the subject?

Patients who have had colorectal adenomas removed are at increased risk of developing CRC in the future, and therefore may benefit from endoscopic surveillance which can detect precancerous changes and potentially prevent progression to CRC. The British Society of Gastroenterology guidelines suggest that patients with only one or two small adenomas are at low risk, and need no colonoscopic surveillance or 5-yearly until one negative examination then cease surveillance.

What are the new findings?

This study reports on the efficacy and necessity of the BSG guidelines for low risk adenoma surveillance, which has not been assessed previously. The yield of advanced neoplasia at surveillance endoscopy was very low. No cancers were found at surveillance.

How might this impact on clinical practice in the foreseeable future?

Patients with low risk adenomas should be risk profiled. Those with risk factors, such as two adenomas, male sex, advanced adenomas at index procedure or strong family history, as well as those falling outside the BCSP enrolment age or who want colonoscopy surveillance should be offered 5 year surveillance provided they are fit for the procedure. Everyone else could be discharged with advice to return if symptomatic and encouraged to participate in the 2 yearly national FOB screening programme.

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revising it critically for important intellectual content. BRH made substantial contributions to analysis and interpretation of the data for the work and revising it critically for important intellectual content. MDR made substantial contributions to the conception and design of the work and revising it critically for important intellectual content. All authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work.

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