

ORIGINAL ARTICLE

## Attendance at surveillance endoscopy of patients with adenoma or colorectal cancer

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### Abstract

**Objective.** Surveillance of patients treated for adenoma or colorectal cancer (CRC) is intended to reduce the incidence of CRC. Responsibility for the adherence to surveillance advice is often left to the patients and family physician. It is not known whether this type of passive policy affects the efficacy of surveillance. The aim of this study was to determine the yield of surveillance without active invitation to follow-up endoscopy. **Material and methods.** The study comprised a cohort follow-up of patients under 75 years of age with adenomas or CRC at index endoscopy in the period 1997–99. Adherence and intervals of follow-up endoscopy were determined up to December 2004. **Results.** During the inclusion period 2946 patients underwent lower endoscopy. In total, 393 patients were newly diagnosed with colorectal polyps ( $n = 280$ ) or CRC ( $n = 113$ ). Polyps were classified as adenomas in 167/280 (61%) patients. Forty-five (27%) of the adenoma patients underwent surveillance endoscopy within the guideline interval, 63 (38%) underwent delayed endoscopy, and 59 (35%) did not have any follow-up at all. CRC was diagnosed in 113 patients. Thirty-six patients who died during the first year or were diagnosed with metastases were excluded from the analysis. Twenty-three (30%) of the remaining 77 patients underwent endoscopic surveillance according to the guidelines, 40 (52%) had delayed surveillance endoscopy, and 14/77 (18%) did not undergo surveillance endoscopy at all. **Conclusions.** In surveillance for colorectal neoplasia, active follow-up invitation is important. Given the low follow-up rate in our series, passive follow-up policies may lead to underperformance of surveillance programs. An active and controlled follow-up is advisable.

**Key Words:** Adenomatous polyps, colonic polyps, colorectal neoplasm, follow-up after polypectomy, practice guidelines

### Introduction

Colorectal cancer (CRC) is the second most common cause of death from malignant disease in the Western world. This disease is the result of a multistep adenoma–carcinoma sequence [1–4]. In a study of the natural history of colorectal adenomas it is reported that the cumulative risk of malignant transformation of adenomas with a diameter of at least 1 cm was 2.5%, 8% and 24%, respectively, after 5, 10 and 20 years of follow-up [5].

Several studies have shown that repeated endoscopic screening with removal of adenomas reduces the incidence of CRC [6–8]. The rationale for colonoscopic surveillance is based on the 30–50%

detection rate of recurrent adenomas at follow-up [2]. Consequently, a well-planned and evidence-based scheme for follow-up is mandatory in order to detect advanced colorectal neoplasia at an early stage, and to prevent the development of CRC.

Until 2001 the Dutch guidelines recommended a first surveillance endoscopy one year after removal of an adenoma, followed by further colonoscopy at 5-year intervals when none or one adenoma was encountered and at 3-year intervals when two or more adenomas were found at follow-up [9].

During the time frame of this study, there was no clear consensus on guidelines regarding endoscopic follow-up after colorectal resection in patients diagnosed with CRC. As a result, follow-up programs for

CRC used in Dutch hospitals varied considerably [10]. One work group recommended that the entire colon should be visualized by colonoscopy before or shortly after CRC resection, followed by surveillance colonoscopy one year after resection, to detect metachronous carcinoma. Further surveillance endoscopies should be performed at 3- to 5-year intervals when no new neoplasias were encountered [11]. Our local guidelines recommended colonoscopic surveillance one year after colorectal surgery for CRC.

In most Dutch clinical practices, removal of adenomas or CRC is followed by documented advice to both the patient and general practitioner (GP) for follow-up surveillance, but does not include active invitation when the screening interval has passed. The GP thus serves as the central manager of care, as is common in many countries. To what extent this policy showing a passive role of the hospital affects the efficacy of surveillance is unknown.

The aim of this study was to assess the yield of surveillance without an active hospital-initiated invitation for follow-up endoscopy.

## Material and methods

### *Patient selection:*

In a prospective study we evaluated the follow-up of all patients under 75 years of age who were diagnosed between January 1997 and December 1999 with CRC or adenomas during colonoscopy or sigmoidoscopy. The study was performed in a single general hospital in The Netherlands with a large gastroenterology practice covering both urban and rural regions of the South West Netherlands. Patients were identified by a database search of the endoscopic report system Endobase<sup>®</sup>. This report system is used in 40% of Dutch hospitals. The reports are based on text blocks, which are coded with the GET-C coding system, an extension of the ICD-10 coding system. All endoscopy reports are stored in the Endobase<sup>®</sup> database and can be used for analyses [12,13].

The following identifiers were used: polyp, adenoma and colorectal cancer. Patients known to have familial adenomatous polyposis, hereditary non-polyposis CRC, inflammatory bowel disease or with a prior history of CRC or adenomas were excluded.

### *Data collection*

The interval of follow-up endoscopy was determined from index endoscopy in the period 1997–99, until December 2004. Endoscopies performed in subjects who had no previous records of CRC or adenomas

were labeled as index endoscopy. There were various reasons for colonoscopy, ranging from abdominal pain and diarrhea to rectal blood loss and changed bowel habit. On the day before colonoscopy, patients received 4 l polyethylene glycole-based electrolyte solution for bowel preparation, in accordance with the instructions for use. Midazolam was administered intravenously before the endoscopic procedure. When a colonoscopy was performed within 3 months of the prior endoscopy, this was reported as one procedure when the repeated endoscopy was performed in order to complete the previous endoscopic procedure.

After the initial procedure, patients were advised about the interval for follow-up endoscopy. GPs were informed about the recommended follow-up interval through the endoscopic report.

For accurate follow-up data, it was verified whether patients had been alive and eligible for surveillance at the time of the intended follow-up visit by checking their records or contacting their GP. Furthermore, endoscopies that were performed because of abdominal complaints were not counted as surveillance endoscopies.

The following data were collected: demographic information (date of birth, gender, patient identification, etc.), date of index endoscopy, diagnosis at index endoscopy including number and site of the neoplastic lesions, surveillance endoscopies until December 2004, time of interval between the subsequent endoscopies, therapy, double-contrast barium enema, and metastasis at time of diagnosis or follow-up.

The histology results, i.e. type of polyp or tumor and grade of dysplasia or differentiation, were obtained from the PALGA database. This database is a national archive containing the abstracts and diagnostic codes of all histopathology and cytopathology reports in The Netherlands since 1991 [14]. Patients were classified on the basis of their most advanced lesion in order to determine the prevalence of pathological features. Patients with intramucosal carcinoma or carcinoma *in situ* were classified as having an adenoma with high-grade dysplasia. Cancer was defined as the invasion of malignant cells beyond the muscularis mucosa [15,16]. Only patients diagnosed with adenocarcinoma were included in the CRC group. Patients with other lesions, such as carcinoid, lymphomas, sarcoma, leiomyoma, lymphangioma, and hemangioma, were excluded because of the different follow-up approaches used compared with that for adenocarcinoma [15].

Polypoid lesions were classified as adenomatous and non-adenomatous polyps. Non-adenomatous polyps included hyperplastic polyps, hamartomas,

lymphoid aggregates and inflammatory polyps. Adenomatous polyps were classified according to the World Health Organization as tubular, tubulovillous and villous, depending on the presence and volume of villous tissue [16]. The grade of dysplasia was classified as low, intermediate, or high-grade.

#### Statistical analysis

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) for Windows version 12.0. Descriptive statistics were used to analyze and report the data. Differences in outcome between groups of patients were calculated by means of Student's *t*-test or the chi-square/Fisher exact test, when appropriate. To correct for multiple testing, the Bonferroni correction was used when appropriate.

### Results

From January 1997 to December 1999, a total of 2946 patients under 75 years of age underwent colonoscopy ( $n=1932$ ) or sigmoidoscopy ( $n=1014$ ), 46% of them were men (M/F 1355/1591). During the study period, polyps were newly diagnosed in 280 (10%) patients and CRC in 113 (4%). For these patients the endoscopy was defined as the index endoscopy.

Among all patients who underwent colonoscopy, significantly more male patients had neoplastic lesions in comparison with female patients (230/1355 versus 163/1591,  $p < 0.01$ ). Table I shows the characteristics of patients diagnosed with polyps or CRC. The median age of patients diagnosed with CRC was significantly higher than that of patients with polyps; 65 versus 60 years of age ( $p < 0.001$ ).

#### Polypoid lesions

In total, 280 patients were diagnosed with polypoid lesions and classified according to their most advanced lesion. Adenomas were present in 167/280 (60%) patients and only hyperplastic polyps in 26/280 (9%). No histological evaluation was performed in 77 (28%) patients (Table II). Six patients diagnosed with inflammatory polyps, as well as four patients diagnosed with hamartomas and lipomas were excluded from further analysis.

#### Adenomatous polyps at index endoscopy

The histological examination of the adenomas showed tubular adenomas in 70/167 (42%) patients, tubulovillous in 20/167 (12%), villous in 18/167 (11%) and adenomas without further specification in 59/167 (35%) patients.

During follow-up at least one surveillance endoscopy was performed in 65% (108/167) of the patients (Table II). This was performed within one year in 27% (45/167), in accordance with the then prevailing guidelines. Sixty-three (38%) adenoma patients underwent a delayed surveillance endoscopy, and 59 (35%) did not have any follow-up at all. At first surveillance endoscopy, CRC was diagnosed in 1/108 patients (interval 3 years) and adenomas in 7/108 (6%) patients. Of the 59 patients who did not undergo surveillance, 4 (7%) died within one year of the index endoscopy as a result of other illnesses.

#### Other polypoid lesions

Even though the guidelines advised against surveillance endoscopy in patients diagnosed with hyperplastic polyps only, 8 (31%) of the 26 patients in this category underwent a surveillance endoscopy. Among those 8 patients, 1 patient was diagnosed

Table I. Gender and age of patients diagnosed with polyps or colorectal cancer (CRC) in the period 1997–99.

Characteristic	All polyps <i>n</i> (%)	Adenomatous polyps <i>n</i> (%)	CRC <i>n</i> (%)
Gender			
Male	165/280 (59)	99/167 (59)	65/113 (58)
Female	115/280 (41)	68/167 (41)	48/113 (42)
Age group (years)			
<40	14/280 (5)	6/167 (4)	3/113 (3)
40–49	29/280 (11)	19/167 (11)	4/113 (4)
50–59	85/280 (30)	50/167 (30)	24/113 (21)
60–69	106/280 (38)	61/167 (36)	42/113 (37)
70–75	46/280 (16)	31/167 (19)	40/113 (35)
Age (years)			
Median (range)	60 (22–75)	61 (22–75)	65 (26–75)

Table II. Number of patients undergoing surveillance endoscopy in relation to baseline histology, interval at first endoscopy and findings at surveillance endoscopy.

	Polyps			
	No histology <i>n</i> = 77	Hyperplastic <i>n</i> = 26	Adenomatous <i>n</i> = 167	CRC <i>n</i> = 113
No of pts with SE <sup>1</sup> (% of cases, 95% CI)	21/77 (27%, 17–37)	8/26 (31%, 13–49)	108/167 (65%, 57–72)	63/77 <sup>2</sup> (82%, 73–90)
Interval of first SE				
Median in years (range)	1 year (0.5–3.5)	1.5 years (1–6)	1 year (0.3–6)	1 year (0.3–5.5)
<b>0–1 year</b>				
9/77		2/26	45/167	23/77
(% of cases)	(12%)	(8%)	(27%)	(30%)
Findings				
Polyp <sup>3</sup>	3		9	
Adenoma	2	1	3	3
CRC	1			
<b>&gt; 1–3 years</b>				
10/77		5/26	50/167	31/77
(% of cases)	(13%)	(19%)	(30%)	(40%)
Findings				
Polyp	3	1	16	
Adenoma			4	5
CRC			1	1
<b>&gt; 3–6 years</b>				
2/77		1/26	13/167	9/77
(% of cases)	(2%)	(4%)	(8%)	(12%)
Findings		No neoplasia		No neoplasia
Polyp			2	
Adenoma	1			
CRC				

Abbreviation: CRC = colorectal cancer.

<sup>1</sup>SE: Surveillance endoscopy; <sup>2</sup>113 patients minus patients who died during the first year after diagnosis and those who were known to have metastases; <sup>3</sup>polyp: hyperplastic polyps and polyp without histological evaluation.

with a single adenoma. A second endoscopy was performed in 4 of the 26 patients for reasons other than surveillance.

Of the 77 patients in the group in whom polypoid lesions were removed without further histological evaluation, 21 (27%) received surveillance endoscopy. In this group, one patient was diagnosed with CRC at surveillance endoscopy after an interval of one year. Single adenomas were diagnosed in 3 patients, while no histologic evaluation was performed in 6 patients.

### CRC

At index endoscopy, CRC was diagnosed in 113/2946 (4%) of the patients. At the time of diagnosis metastases were found in 11 (10%) patients. In total, 102 patients (90%) underwent curative resection. In this group, metastases were diagnosed in 15/102 patients during the first year after diagnosis. Fifteen of the 113 patients died within one year after they were diagnosed with CRC, of whom 6 were known to have metastases and 9 died from complications of surgery, or from comorbidity.

Those patients who died during the first year after diagnosis or were known to have metastases were

excluded from further follow-up analysis. Furthermore, one patient moved to another city during the time of follow-up and was also excluded from the follow-up analysis.

The attendance rate at surveillance endoscopy was thus analyzed for 77 curatively treated patients. Sixty-three (82%) of them underwent surveillance endoscopy, 30% within one year according to the guidelines (Table II). No surveillance was performed in 14 (18%) of the 77 patients with at least 12 months' survival.

At first surveillance endoscopy, 1/63 patients was diagnosed with recurrent CRC at an interval of 1.5 years and 8/63 (13%) patients were diagnosed with adenomas during surveillance endoscopy. A double-contrast barium enema for surveillance was performed after 6 months in one of the 15 patients who had not undergone any surveillance endoscopy.

### Discussion

Colorectal neoplasia is a common disorder with a high tendency for metachronous recurrence. National and international guidelines therefore advise surveillance after endoscopic or surgical removal of colorectal adenomas and/or cancer. The

organization and quality control of surveillance differ between regions. In many countries it is common practice to rely on the patient and GP for adherence to follow-up and scheduling of surveillance endoscopy. Such a policy is also common practice in The Netherlands. The adherence to surveillance guidelines under such policies is, however, unknown.

Therefore, as the impact of surveillance protocols depends largely on adherence, the aim of this study was to provide data on the attendance rates for surveillance endoscopy. We show that despite unambiguous guidelines in a region with a well-organized health-care system with unrestricted access for all and full insurance coverage of costs, the majority of patients tend not to undergo adequate surveillance. Only 27% of the adenoma patients underwent a surveillance endoscopy within the recommended period, one-third underwent delayed surveillance, and 35% did not undergo surveillance endoscopy at all. Of the CRC patients, only 30% of the eligible patients had surveillance within the recommended 1-year interval. In addition to this undertreatment, overtreatment was also observed, as 31% of patients with solitary or a limited number of hyperplastic polyps and 27% of patients in whom polypoid lesions had been removed without further histological evaluation nevertheless underwent surveillance endoscopy.

Several factors may be responsible for the low attendance rate in eligible patients. First of all, the general follow-up policy in most clinical practices in The Netherlands is that after removal of adenomas or CRC both the patient and GP are advised to comply with follow-up endoscopy. This advice is not accompanied by a specific appointment, nor are reminders sent to either the patient or the GP by the end of the intended interval. Most hospitals do not keep track of their adenoma patients, and are thus also unable to send reminders when the surveillance interval has passed without control endoscopy. In The Netherlands only a few hospitals use an active invitation strategy, which may be an efficient way of improving guideline adherence. In the hospital in which this study was performed, an automatic recall system was developed in the beginning of 2005, using the Endobase report system for flexible endoscopies [12].

The poor adherence to follow-up guidelines may to some extent also be related to patients' lack of compliance. This may be due to the burden of bowel preparation or the endoscopic procedure itself, which is uncomfortable and inconvenient, and associated with a, albeit low, risk of complications [17,18]. Furthermore, lack of compliance may be caused by fear of recurrent pathology, as well as by ignorance and insufficient information about the

reasons for surveillance endoscopy [19]. This suggests that adherence to follow-up schedules might be improved by providing better information to patients.

Little is known about attendance at surveillance endoscopy in other countries. A survey study conducted by the National Cancer Institute in the United States among gastroenterologists and surgeons about their perceived need for the frequency of surveillance after polypectomy suggests considerable over-performance of surveillance colonoscopy, particularly for hyperplastic polyps and small adenomas, when compared with the published guidelines [20]. However, this study was based on physicians' self-reported practice patterns, and not on actual data of individual patients, which means that the results may not truly reflect the clinical practice of surveillance endoscopy.

During the time this study was performed, there was no consensus regarding the follow-up of patients with CRC in The Netherlands [10]. In our practice and that of most other gastroenterologists, patients were advised to undergo surveillance within one year after surgery, depending on their clinical condition. Only 30% of the eligible CRC patients underwent a surveillance endoscopy within one year.

Recent Dutch oncology guidelines recommend a surveillance colonoscopy 3 to 5 years after colorectal resection [21]. However, in clinical practice there is still wide variation in CRC follow-up programs used in the different hospitals in The Netherlands, among other things induced by differences in regional cancer-center guidelines [22]. In other countries there is also considerable controversy about how often patients should be seen and what tests should be performed for surveillance after treatment for CRC. It is nevertheless general practice to follow patients with CRC for several years after their surgery, resulting in an overall survival benefit [23]. Different studies claim that the most crucial phase of follow-up is the first two to three years after primary tumor resection, since during this time the vast majority of recurrences will become apparent [24,25]. We demonstrate in this study that 18% of the colon cancer patients with curative surgery did not undergo any surveillance endoscopy.

Our results are in line with data from an American database study, which reported that 17% of 52,283 patients did not undergo surveillance endoscopy after curative resection of CRC [26].

The results of this study were derived from one hospital covering both a city and a rural area of Southwest Netherlands. There are no data available on the application of the guidelines in other hospitals. However, approximately 60% of the endoscopy units in The Netherlands apply the same passive

follow-up policy, i.e. not sending invitational letters, as in the hospital connected with this study (data not published), so the current findings are likely to be representative of the situation in those gastroenterology practices, given the fact of the mixed catchment area. Furthermore, there is a long-standing excellent contact with the referring family physicians, and the gastroenterology practice has long been in the forefront of the development of endoscopy database applications.

In conclusion, in this study the majority of adenoma and CRC patients do not receive adequate surveillance endoscopy despite guidelines and documented written and oral follow-up advice to patients and GPs. It is important to take note of this low adherence to surveillance which shows that passive follow-up policies may lead to underperformance of surveillance programs. In view of the growing interest for colorectal screening, it is necessary to evaluate the efficacy of existing national surveillance programs. Implementing an active approach policy is important and should encourage physicians and patients to adhere to a surveillance protocol as well as improving attendance at surveillance endoscopy. The efficacy of such an alternative approach needs to be proven. We should invest in a regional or even national surveillance strategy including active invitation by means of combined endoscopy and histology database systems, as well as by increasing patients' awareness.

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