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Follow-up After Polypectomy: Consensus?

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Patients who have had a colorectal adenoma resected have an increased risk of subsequent cancer and may benefit from follow-up surveillance. Surveillance strategies should be tailored to the assessed risk of each individual patient. A number of long-term follow-up studies indicate that the risk of metachronous neoplasia is higher if on index colonoscopy there were multiple (≥2) adenomas, or if any adenoma was large (≥1 cm), contained villous tissue or severe dysplasia, or if the patient had a family history of colorectal neoplasia. Data from the U.S. National Polyp Study indicate that polyp resection and follow-up surveillance greatly reduces the incidence of metachronous cancer, and that the first follow-up colonoscopy does not need to be performed for 3 years. Current data have been incorporated into a comprehensive consensus practice guideline.

Key words: colorectal adenoma, polyp, carcinoma, follow-up, surveillance, colonoscopy, polypectomy
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INTRODUCTION

PATIENTS WHO have had colonoscopic resection of one or more colorectal adenomas have an increased risk of subsequent cancer, and may benefit from long-term follow-up surveillance. In the past, experts have debated how to perform this surveillance without the support of good scientific data. Clinicians have generally resorted to a rather nonselective routine approach to their polyp patients, rather than trying to assess each individual's risk of future cancer and tailor follow-up strategies to the unique features of each case. After years of outcome analysis and the performance of a few quality prospective trials, we now have substantial consensus on how to conduct cost-effective post-polypectomy surveillance [1].

The importance of performing proper surveillance is obvious. In the U.S.A., nearly 160 000 individuals are diagnosed with cancer each year. In 1993, over 2.5 million colonoscopies were performed, and over 650 000 patients underwent colonoscopic polypectomy [2]. If we err on the frequency or type of surveillance, it can either place patients at excessive risk for colorectal cancer, or can waste considerable health care resources.

OBJECTIVES OF SURVEILLANCE

The single most important objective of postpolypectomy surveillance is to reduce the chance of a patient developing and dying from colorectal cancer [3]. Efforts should focus on cancer prevention rather than just the detection and resection of benign, clinically insignificant recurrent polyps, *per se*. The clinician should carefully assess the risk of each individual patient, and tailor follow-up selectively to the specific features of each case. Both polyp and patient characteristics should be considered when prescribing a follow-up programme [4].

KEY QUESTIONS

The two key questions that must be addressed when designing surveillance strategies are: (a) what is the risk of colorectal cancer after resection of one or more benign adenomas; and (b) will postpolypectomy surveillance substantially reduce or eliminate that risk?

Related questions include:

1. What is the incidence of undetected synchronous adenomas and subsequent metachronous adenomas?
2. What factors are predictive of adenoma recurrence and subsequent cancer?
3. How should surveillance be performed? How frequently?
4. Does finding and removing colorectal adenomas prevent cancer?
5. What factors influence compliance and cost of postpolypectomy surveillance?

SURVEILLANCE METHODS

Colonoscopy is the procedure of choice for postpolypectomy surveillance [5]. It is more accurate than double-contrast barium enema for the detection of small polypoid lesions. Since the prime immediate objective is to detect developing adenomas that can be colonoscopically resected before cancer develops, this advantage is an important consideration. A controlled, single-blinded comparison study of double-contrast barium enema and colonoscopy performed by expert examiners reported an accuracy of 94% and 67% for diagnosing polyps for colonoscopy and radiographic studies, respectively [6]. In a more recent similarly controlled investigation, tandem colonoscopy performed by two experienced examiners on 96 patients indicated a miss rate of 14.7% for polyps measuring 8 mm in diameter or less, but no polyps larger than this remained undetected by the first examination [7]. Experienced, well-trained colonoscopists are able to examine the entire colon in over 95% of patients, and can resect most polyps that are detected with very low risk of complications [8].

Major complications of bleeding or perforation occur in 0.1–0.2% of patients undergoing diagnostic colonoscopy [9]. Major complications are substantially reduced with barium enema (0.02%) and flexible sigmoidoscopy (0.01–0.04%)

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[10, 11]. In the U.S.A. the cost of colonoscopy exceeds that of barium enema plus flexible sigmoidoscopy by 40–60%. However, because 30–40% of patients undergoing barium enema examination for the purpose of detecting recurrent polyps will be found to have abnormalities requiring the subsequent performance of colonoscopy, the average cost of the two alternative surveillance methods are nearly equal [12].

THE RISK OF COLORECTAL CANCER FOLLOWING RESECTION OF SMALL POLYPS

Two studies from the Mayo Clinic, U.S.A. estimated the risk of cancer following polypectomy. Spencer and associates followed 751 patients for a total of 10000 person-years after proctosigmoidoscopic fulguration of single, small (≤1 cm) rectosigmoid polyps [13]. There was no apparent increased incidence of subsequent cancer in this group. In contrast, the same investigators reported that patients with larger adenomas had a risk of metachronous cancer that was 2.7 times greater than expected, and those with multiple polyps had a relative risk of five times greater than predicted [14]. Atkin and colleagues followed a group of 1618 patients for a mean of 14 years after polyps were detected and resected during rigid proctosigmoidoscopy [15]. Patients with index adenomas that contained villous tissue or were large (≥1 cm) had a 3.6-fold increased risk of subsequent cancer, while those with only smaller tubular adenomas had a subsequent incidence of cancer that was no greater than that of the average-risk population.

These investigators concluded that follow-up surveillance is indicated for patients with advanced adenomas which are large or contain appreciable villous changes, especially if these adenomas are also multiple. However, in patients with only small tubular adenomas, surveillance may not be warranted because the risk of subsequent cancer is no greater than that of the average-risk population. Follow-up for patients with small tubular adenomas should be individualised. It might be offered to younger healthy patients in high-incidence countries, such as the U.S.A., in order to reduce the risk of cancer below that of the average-risk population [5].

THE RISK OF COLORECTAL CANCER AFTER RESECTION OF LARGE ADENOMAS

Eide found that the risk of developing carcinoma in a 1 cm adenoma was 3%/year in a Norwegian population [16]. The U.S. National Polyp Study found a strong relationship between adenoma size and both the fraction of villous tissue and the incidence of high-grade dysplasia. The odds ratio for high-grade dysplasia in a large polyp was 20.3 compared to a small adenoma (≤5 mm) [17].

In an earlier Mayo Clinic study, Stryker and associates performed a retrospective analysis of 226 patients with large polyps (≥1 cm) detected by barium enema before the availability of colonoscopy [18]. Follow-up of these untreated patients showed that 37% of the polyps enlarged, 21 invasive carcinomas developed at a polyp site, and 11 carcinomas developed at another site. The cumulative risk of cancer at 5, 10, and 20 years was 2.5, 8 and 24%, respectively. This study also supports the need for periodic surveillance to identify metachronous neoplasms at a site in the colon remote from the index polyp.

A prospective study by Grossman and associates reported that patients with a single tubular adenoma <10 mm who had no first-degree relatives with colorectal cancer, had only a 3% prevalence of clinically significant metachronous neoplasms on follow-up colonoscopy [19]. Subgroups with advanced adenomas (≥10 mm, tubulovillous or villous, severely dysplastic, or invasive carcinoma) had a prevalence of subsequent adenomas of 8–18%. They also concluded that for persons whose only risk factor is a single small tubular adenoma, surveillance practices should be carefully individualised.

THE EFFECT OF POLYPECTOMY ON CANCER INCIDENCE

Colonoscopy has not been available long enough to prove that resecting all adenomas from a given population will reduce mortality from colorectal cancer. The uncontrolled series of Gilbertsen and Nelms and the case–control studies of Selby and associates and Newcomb and associates indicate that resection of rectosigmoid polyps during screening proctosigmoidoscopy will reduce mortality from distal cancer [20–22].

A recent landmark report from the U.S. National Polyp Study addressed the hypothesis that resecting all polyps in the colon of a well-defined population would reduce the total incidence of colorectal cancer [23]. The pooled study cohort of 1418 patients, who had had a complete clearing colonoscopy during which one or more adenomas were resected, underwent periodic follow-up surveillance colonoscopy for a mean of 5.9 years (8401 person-years). Five early asymptomatic cancers were detected by colonoscopy during this follow-up period, an incidence of cancer which was only 10–24% of that predicted by comparison with three selected reference groups.

FREQUENCY OF SURVEILLANCE

In terms of overall cost of postpolypectomy surveillance, the most important consideration, other than who should have surveillance, is how frequently it should be carried out. To answer this critical question, the U.S. National Polyp Study was designed in 1978 by a joint committee of the American Society for Gastrointestinal Endoscopy (ASGE), American Gastroenterological Association (AGA), and American College of Gastroenterology (ACG) [24]. This study, funded by the U.S. National Cancer Institute, was a prospective, multicentre, randomised trial with wide geographical representation enrolling patients with newly detected adenomas. The main objective of the study was to determine if follow-up colonic examinations performed at 3 years after initial polypectomy was as effective in detecting clinically significant neoplasms as performing evaluations at 1–3 years. All follow-up colonoscopies were performed by experienced study co-investigators.

All patients referred for colonoscopy to the seven participating centres who did not have a personal or family history of familial polyposis, inflammatory bowel disease, or a past history of polypectomy or colorectal cancer, were eligible for the study. From this group, patients were invited to enrol in the investigation if they had one or more adenomas resected which were <3 cm in diameter and did not contain invasive carcinoma, and if the colonoscopist believed that all polyps had been resected. Study patients were randomly assigned to have follow-up examinations either at 1 and 3 years, or only at 3 years after the initial clearing examination. A total of 1418 patients were randomised to the two follow-up groups. The percentage of patients who had adenomas on follow-up was 41.7% in the group examined at 1 and 3 years, and 32.0% in the group examined only at 3 years [25]. However, the number of patients who had advanced adenomas (>1 cm in diameter, high-grade dysplasia, or invasive carcinoma) was the same in both groups (3.3%). The study concluded that colonoscopy performed 3 years after colonoscopic polypectomy detects important colonic lesions as effectively as

colonoscopy conducted at both 1 and 3 years. Therefore, an interval of at least 3 years is recommended before the first surveillance colonoscopy is performed after resection of colorectal adenomas.

The U.S. National Polyp Study has reported several additional observations that assist in the design of surveillance strategies for individual polyp patients. Recurrence of clinically significant adenomas was more likely if the index polyps contained villous tissue, were multiple, or if the patients were older, male, or had a family history of colorectal neoplasia. Therefore, these features are predictors of recurrence and need to be considered as we instruct our patients on follow-up. In addition, a cross-section analysis of all patients colonoscoped at the study centres indicates that it takes an average of approximately 10 years for a neoplastic polyp to develop in a "clean" colon, grow to significant size, and degenerate into a cancer. These data also support the recommendations of the study that follow-up examinations to detect metachronous neoplasia do not need to be frequent if accurate methods are employed [26].

CONSENSUS RECOMMENDATIONS

A comprehensive practice guideline based on available scientific data and expert consensus was recently developed and published by the American College of Gastroenterology [1]. A committee of experts drafted this document after a careful review of the findings of the U.S. National Polyp Study and other long-term investigations of postpolypectomy surveillance. This guideline, "Diagnosis, treatment and surveillance for patients with nonfamilial colorectal polyps," was also reviewed by a selected group of 15 gastroenterology, pathology, and oncology consultants, and was reviewed and endorsed by the American Gastroenterological Association and the American Society for Gastrointestinal Endoscopy. Widespread adoption of these recommendations should substantially reduce the cost of postpolypectomy surveillance, while at the same time providing adequate protection for this high-risk group. The recommendations are as follows:

1. Complete colonoscopy should be performed at the time of polypectomy to detect and resect all synchronous adenomas. Additional clearing examinations may be required after resections of a large sessile adenoma or of multiple adenomas to ensure complete resection.
2. Repeat colonoscopy to check for missed synchronous and for metachronous adenomas is performed in 3 years for most patients with a single, or only a few adenomas, provided they have a high quality initial examination.
3. Selected patients with multiple adenomas or those who have had a suboptimal initial clearing examination might require colonoscopy at 1 and 4 years.
4. After one negative 3-year follow-up examination, subsequent surveillance intervals may be increased to 5 years.
5. The presence of severe or high-grade dysplasia in a resected polyp does not, *per se*, modify recommendations 1–4.
6. If complete colonoscopy is not possible, flexible sigmoidoscopy plus double-contrast barium enema is an acceptable alternative.
7. Since patients undergoing resection of a single small tubular adenoma (<1 cm) do not have an increased subsequent risk of cancer, follow-up surveillance may not be indicated.
8. Surveillance should be individualised according to the age and comorbidity of the patient, and should be discontinued when it appears unlikely that continued follow-up is capable of prolonging life quality or life expectancy.

COST–BENEFIT CONSIDERATIONS

Many practitioners in the U.S.A. still perform follow-up colonoscopy 1 year after polypectomy. Extending this interval to 3 years as recommended in the ACG guideline will result in considerable cost savings.

Ransohoff and Lang have pointed out that the resection of small adenomas is unlikely to significantly reduce colorectal cancer morbidity or mortality [27]. They argue that since 30–50% of persons over age 50 years have small adenomas, yet few of these persons will ever develop colon cancer, the current practice to perform periodic surveillance colonoscopy following removal of small adenomas detected during screening should be re-examined. In addition, they performed a cost-effectiveness analysis of available data, and concluded that the cost of surveillance of individuals with a low subsequent risk of death from colorectal cancer, such as those with a single small adenoma, is prohibitive [28]. Based on his assumptions, it would cost $80 000–$300 000 per life saved for a surveillance programme of colonoscopy every 3 years for all 50-year-old polyp patients followed for 30 years.

The cost of postpolypectomy surveillance represents a significant "hidden cost" of screening of the average-risk population for colorectal cancer using faecal occult blood tests and flexible sigmoidoscopy. A sizable minority of patients with a positive screening test will be found to have one or more adenomas. In order to ensure that screening is carried out in a cost-effective manner, it is imperative, therefore, that surveillance for patients with polyps is performed correctly.

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