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Post-Polypectomy Surveillance— Who and How



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Colorectal adenomas are the most frequent neoplastic lesions found during screening. Their presence signifies a possible increased risk for future colorectal neoplasia. In past decades it has been common practice to perform annual surveillance but this creates a huge burden on medical resources. High quality baseline colonoscopy with excellent preparation, adequate examination and complete polypectomy will reduce miss rates and should be the basis of any program. Findings at baseline colonoscopy can be used to predict future risk and surveillance intervals. High-risk adenomas characterised by size ≥ 1 cm, villous change, high-grade dysplasia or multiplicity (3) are found in approximately one-quarter of cases and justify a surveillance interval of three years. For those with one or two tubular adenomas (< 1 cm), an interval of 5–10 years is adequate. Hyperplastic polyps warrant only an average-risk screening program. Adoption of such guidelines will result in a freeing up of procedures to support screening.

INTRODUCTION

Colorectal adenomas are the most frequent neoplastic lesions found during screening and their removal reduces risk of future colonic neoplasia (1). A colonic adenomatous polyp is important not only in itself, but also because it signifies the potential for development of neoplasia anywhere in the colorectum at a future time. As a consequence, postpolypectomy surveillance consumes a significant amount of colonoscopic capacity in practice.

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Guidelines established in various countries, e.g. the US Multi-Society Task Force on Colorectal Cancer, the American Cancer Society and the National Health and Medical Research Council of Australia (2,3) make the point that in past decades it has been common practice to perform annual surveillance with a view to detect new (metachronous) or missed lesions. But since the 1970s, guidelines have progressively lengthened the interval, and focused on quality of procedure as the most appropriate way to deal with the huge burden on medical resources created by repeated surveillance colonoscopy, thus freeing procedures to support screening and timely diagnosis.

Several factors determine whether surveillance is appropriate and how it might be conducted. These

include: the nature of the polyp and predictors of new future adenomas, natural history of adenomas, quality of the colonoscopy and polypectomy at baseline, and outcomes of polyp surveillance programs.

NATURE OF A POLYP

A polyp is a localized epithelial protuberance. The principal types found in the large bowel are (4):

- adenoma or neoplastic polyp
- hyperplastic polyp
- hamartoma (juvenile and Peutz-Jeghers)
- inflammatory.

The term “polyp” is not synonymous with adenoma and they should not be used interchangeably. Hyperplastic polyps may co-exist with adenomas in an individual and were considered early on to be markers of more proximal adenomas but better-quality studies have not confirmed this.

Adenomas are subclassified according to histological findings as tubular, tubulovillous or villous according to the degree of villous change. Size is also an important feature, usually being described as diminutive (1–4 mm in largest diameter), small (5–9 mm) or large (10 mm or more). Adenomas are characterized by dysplastic change and further sub-classified according to the grade of dysplasia, preferably by a two-tier system of low- and high-grade dysplasia (4). “Severe” or “high-grade” dysplasia are terms used in preference to “carcinoma-in-situ,” which has aggressive connotations that are unwarranted. The label “carcinoma” or “malignant” in the context of an adenoma should be reserved for those adenomatous polyps where invasion is evident.

Adenomatous polyps are of concern because of their documented precancerous nature and because they may reflect a broader precancerous tendency in the remaining colon.

NATURAL HISTORY OF ADENOMATOUS POLYPS

On the basis of prevalence studies of adenomas obtained from autopsy examinations and the lifetime cumulative incidence of colorectal cancer, it appears probable that within an average lifetime, only about 5%–10% of adenomas become carcinomas. This has immediate impli-

cations for surveillance programs because it implies that adenomas fall into high-risk and lower-risk categories and by more accurately identifying those that confer a higher risk, unnecessary colonoscopies plus the associated risks and costs can be minimized (2).

Furthermore, most adenomas appear to grow slowly. Small polyps have been observed to grow very slowly and particularly those measuring 5 mm or less may remain the same size for years or even regress. Even with larger adenomas, the cumulative risk for developing a cancer in such polyps has been estimated to be about 1% per year (5).

The clinical context is also relevant to progression. Those in people with hereditary non-polyposis colorectal cancer characteristically show an accelerated evolution. Serrated adenomas, a particular mix of hyperplastic and adenomatous features in the one polyp, may evolve more rapidly to cancer (6). People with familial adenomatous polyposis or hyperplastic polyposis clearly warrant individualized surveillance as well. This review will not discuss these particular syndromes.

QUALITY OF COLONOSCOPY AND POLYPECTOMY

An extensive review of the most recent literature has shown that quality of baseline colonoscopy is critical because findings from the baseline colonoscopy—histopathology, number and adequacy of removal—are important predictors for subsequent neoplasia. Failure to adequately clear lesions or to remove an adenoma increases risk for subsequent lesions (2).

It is not possible to determine the histological type of a polyp by endoscopic inspection although magnifying endoscopy combined with dye spraying or narrow band imaging might facilitate classification of polyp type. Small and diminutive polyps cannot be distinguished as hyperplastic or adenomatous. Even for large polyps, the occasional hyperplastic polyp might mimic an adenoma. For these reasons, all polyps should be considered for removal and surveillance not planned until the type of adenoma is determined.

The appropriate approach to polypectomy has been reviewed elsewhere (3). Adequacy of removal is particularly important for several reasons:

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- A. the possibility of cancer within a polyp—the so-called “malignant polyp.” Four key factors are linked to favourable outcome and are accepted as indicating that polypectomy is adequate treatment:
- A clear margin of excision, normally at least 2 mm beyond the margin of the malignant change.
 - A well differentiated cancer.
 - Absence of invasion, particularly into lymphatics or veins.
 - Confidence that the lesion has been totally removed.
- B. the possibility that adenomas will be missed and progress to cancer before the next surveillance lesion.

PRACTICE RECOMMENDATION 1

On the basis of a range of studies, unfortunately in the absence of randomized controlled trials (2,3), the following are recommended:

- All polyps seen at colonoscopy should be removed or at least sampled.
- Early (that is within 3 to 12 months) review colonoscopy should be considered in the following situations:
 1. Piecemeal polypectomy of a large adenoma.
 2. Difficult polypectomy where neither the colonoscopist nor the histopathologist could be certain that the polyp had been completely removed.
 3. Removal of malignant polyp where the adequacy of the margin is uncertain. Under such circumstances, consideration should have been given to surgical resection.
 4. Inadequate mucosal views, for example as a result of incomplete bowel preparation, especially in the context of a patient where multiple adenomas have been identified and where the colonoscopist is not confident that the colon has been adequately cleared of all polyps.

ONCE AN ADENOMA IS DIAGNOSED

In practice, three key questions arise once an adenoma is diagnosed:

1. Given that an adenoma has been removed at colonoscopy and histologically classified, what characteristics justify surveillance and how should it be done?
2. Having decided to undertake surveillance, what is the appropriate interval to the next colonoscopy?

3. At subsequent colonoscopic examinations where the surveillance was initiated because of an adenoma, how do the findings influence subsequent intervals?

There has been no study which ideally addresses question 1. The ideal design would be one where complete colonoscopy was undertaken, adenoma status clearly defined, and patients then left without subsequent surveillance colonoscopies so as to determine what adenoma characteristics predicted those most likely to develop cancer. Such a study is now clearly unethical and the general consensus is that surveillance is justified whenever an adenoma is identified, although we will see that the recommendation might be no more than that appropriate for the general population.

Guidance for answering these questions come from existing literature. A recent comprehensive and structured review identified 47 articles of relevance (2). Before synthesizing a set of recommendations, several key studies will be commented on in relation to identified key risk factors.

ADENOMA MULTIPLICITY AND RISK FOR METACHRONOUS LESIONS

A large British cohort study of 1,618 patients who were initially treated for rectosigmoid adenomas in the pre-colonoscopy era using rigid sigmoidoscopy, does provide some insight into the risk factors for developing colorectal cancer (7). Average duration of follow-up was 14 years. The standardized incidence ratio for colon cancer was 6.6 for subjects who had multiple (≥ 3) adenomas in the rectosigmoid region.

The US National Polyp Study (8) and a pooled analysis of chemoprevention studies (2) generally show a significant association between multiplicity (≥ 3) adenomas at baseline colonoscopy and subsequent adenoma or cancer at follow-up.

ADENOMA SIZE AND RISK FOR METACHRONOUS LESIONS

Size ≥ 1 cm has generally been found across a range of studies, including the US National Polyp Study (8), to be a predictor of metachronous lesions (2). In the British cohort study, the risk ratio was 3.6 in subjects with large adenomas (7).

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Table 1
Characterization of risk status from baseline colonoscopic findings matched to surveillance interval

| <i>Risk status</i> | <i>Characteristics at Baseline Colonoscopy</i> | <i>Recommended Interval to Surveillance Colonoscopy</i> |
|---|---|--|
| High-risk adenoma (27% of diagnosed cases) | Multiplicity ≥ 3 adenomas (any size) Large size (≥ 1 cm) Villous change High-grade dysplasia Serrated adenoma (probable) | Three years |
| Low-risk adenoma (majority of diagnosed cases) | 1–2 tubular adenomas < 1 cm in size and not showing high-grade dysplasia or villous change. | A minimum five-year interval. Probably ten years is adequate. |

ADENOMA HISTOLOGY AND RISK FOR METACHRONOUS LESIONS

Degree of villous change is somewhat subjective and complicates its use as a predictor. The British study found that tubulovillous or villous histology significantly increased risk in the order of 3.8 to 5-fold (7). Other studies support the significance of such for risk (2).

High-grade dysplasia relates to both size and villous change and has been an important predictor in cohort studies in the order of 3-6 fold (2).

OTHER RISK FACTORS FOR METACHRONOUS LESIONS

Location in the colorectum has not been consistently associated with risk. Age, sex and family history are variably associated with some risk or no risk. Family history of cancer plus age > 60 y has, together with diagnosis of adenoma, been shown to increase risk almost 5-fold (8).

SUMMARY OF BASELINE COLONOSCOPY RISK PREDICTORS

The totality of evidence is summarized in Table 1.

The British study (7) has given some insight into the risk of colon cancer based on rectal adenoma features. Interestingly, in those subjects with small tubular adenomas, the incidence ratio was not increased (at 0.5).

SURVEILLANCE INTERVALS

Several studies have given information as to what con-

stitutes an appropriate surveillance interval. The most informative of these has been the US National Polyp Study (8), a properly designed randomized trial to test the question. Importantly, that study examined the value of a one-year-versus a three-year surveillance interval following complete clearance of the colon of polyps, including early review colonoscopy if necessary. They observed that the adenoma recurrence rates were no higher when the surveillance interval was three years compared to one year, even in people with high-risk adenomas at baseline. Consequently most national guidelines project that apparently low-risk adenoma patients can wait five and possibly ten years for the surveillance colonoscopy. Indeed, entering such people into a general population average-risk program might be sufficient.

What should happen based on the findings at a subsequent, i.e. surveillance, colonoscopy has hardly been studied. A rational approach would seem to be to reset the interval to the next procedure according to the findings at that procedure, except of course in the polyposis syndromes where the program must be highly personalized. If no adenomas are found at a surveillance colonoscopy, it is generally considered appropriate to move to the next longest interval, either five to six years or ten years as the case might be.

OTHER TESTS: CT COLONOGRAPHY AND FOBT

Because sampling, by polypectomy or biopsy, is critical for appropriate assessment of people known to have colonic adenomas, surveillance by alternative procedures such as CT colonography do not feature in

recommendations for surveillance, particularly for those with high-risk adenomas.

Because surveillance intervals have lengthened and occasional patients might rapidly develop new lesions, or lesions might have been missed, there is some evidence for the value of using fecal occult blood tests in the interval between colonoscopies (9). The new fecal immunochemical test technology (FIT) is considerably more sensitive for adenomas than the older guaiac tests (10). However, there might not be a need for this if the initial procedure is of high quality and risk-profiling is otherwise undertaken carefully.

PRACTICE RECOMMENDATIONS FOR SURVEILLANCE

Collating this information, and considering the published professional consensus statements, the following recommendations are made (see also Table 1):

1. High-risk adenoma patients where the colon has been adequately cleared—a three year interval is appropriate. These high-risk predictors account for approximately 27% of people with adenomas (11).
2. Low-risk adenoma patients where the colon has been adequately cleared—a minimum five-year interval is appropriate. Some national recommendations are now proposing that these people be considered in the average risk group, but this is in countries where colonoscopy at ten year intervals is part of the recommendations for average risk. Few are willing to suggest that these people be removed from any form of colonoscopic surveillance.
3. Polyposis syndromes require an individualized program.
4. Small hyperplastic polyps not constituting the hyperplastic polyposis syndromes do not warrant surveillance.

These findings are summarized in the broader clinical algorithm presented in Figure 1. ■

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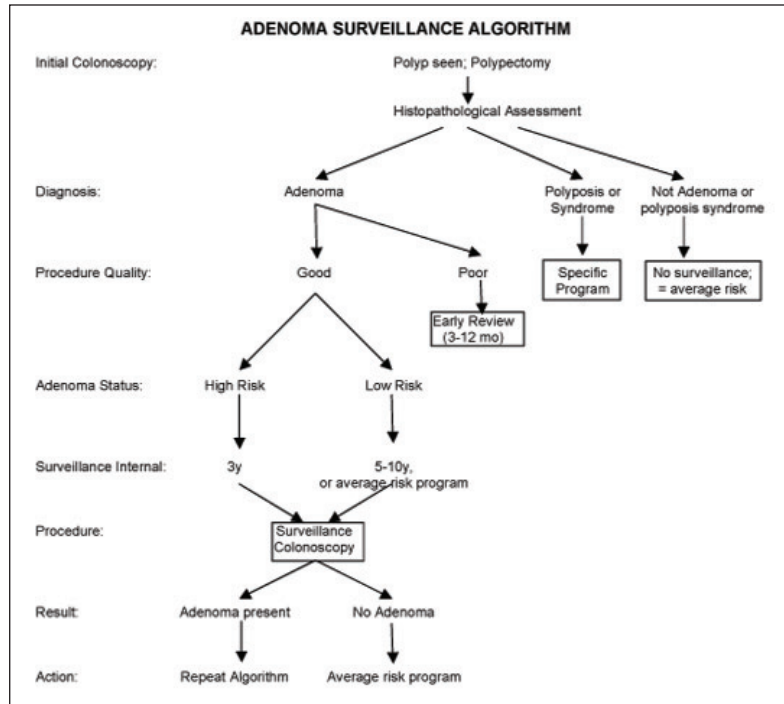


Figure 1.

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