Guidelines for Colonoscopy Surveillance after Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society* †

Sidney J. Winawer, MD; Ann G. Zauber, PhD; Robert H. Fletcher, MD, MSc; Jonathon S. Stillman, MD; Michael J. O’Brien, MD, MPH; Bernard Levin, MD; Robert A. Smith, PhD; David A. Lieberman, MD; Randall W. Burt, MD; Theodore R. Levin, MD; John H. Bond, MD; Durado Brooks, MD, MPH; Tim Byers, MD, MPH; Neil Hyman, MD; Lynne Kirk, MD; Alan Thorson, MD; Clifford Simmang, MD; David Johnson, MD; Douglas K. Rex, MD

ABSTRACT Adenomatous polyps are the most common neoplastic findings uncovered in people who undergo colorectal screening or have a diagnostic workup for symptoms. It was common practice in the 1970s for these patients to have annual follow-up surveillance examinations to detect additional new adenomas as well as missed synchronous adenomas. As a result of the National Polyp Study report in 1993, which demonstrated clearly in a randomized design that the first postpolypectomy examination could be deferred for 3 years, guidelines published by a gastrointestinal consortium in 1997 recommended that the first follow-up surveillance be 3 years after polypectomy for most patients. In 2003, these guidelines were updated, colonoscopy was recommended as the only follow-up examination, and stratification at baseline into lower and higher risk for subsequent adenomas was suggested. The 1997 and 2003 guidelines dealt with both screening and surveillance. However, it has become increasingly clear that postpolypectomy surveillance is now a large part of endoscopic practice, draining resources from screening and diagnosis. In addition, surveys have demonstrated that a large proportion of endoscopists are conducting surveillance examinations at shorter intervals than recommended in the guidelines. In the present paper, a careful analytic approach was designed addressing all evidence available in the literature to delineate predictors of advanced pathology, both cancer and advanced adenomas, so that patients can be more definitely stratified at their baseline colonoscopy into those at lower or increased risk for a subsequent advanced neoplasia. People at increased risk have either three or more adenomas, or high-grade dysplasia, or villous features, or an adenoma ≥1 cm in size. It is recommended that they have a 3-year follow-up colonoscopy. People at lower risk who have one or two small (<1 cm) adenomas are recommended for a 3-year follow-up colonoscopy.

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INTRODUCTION

Adenomatous polyps are the most frequent neoplasm found during colorectal screening.1–4 Removal of these lesions has been shown to reduce the risk of future colorectal cancer and advanced adenomas.5–12 To further minimize the risk of colorectal cancer, patients with adenomas are usually placed into a surveillance program of periodic colonoscopy to remove missed synchronous and new metachronous adenomas and cancers.13–16 A large number of patients with adenomas are now being uncovered as a result of the increased utilization of colorectal cancer screening, particularly the dramatic increase in screening colonoscopy, which places a huge burden on medical resources applied to surveillance.17–19 Therefore, there is a need for increased efficiency of surveillance colonoscopy practices to decrease the cost, risk, and overutilization of resources for unnecessary examinations.

Therefore, the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society (ACS) have decided to issue updated joint guidelines on postpolypectomy surveillance. These guidelines differ from the earlier guidelines in several specific ways (Table 1):13–16; we offer a consensus statement that strengthens the guidelines; we specifically examined predictors of advanced adenomas and incorporated them into the guidelines; and we emphasize the quality of baseline colonoscopy and its impact on detection of postpolypectomy colorectal cancer.5,20,21 We reviewed recent evidence, particularly as it pertains to stratifying patients for future risk of advanced adenomas.

Risk stratification could markedly reduce the intensity of follow up in a substantial proportion of patients, so that colonoscopy resources could be shifted from surveillance to screening and diagnosis. Risk stratification could also reduce the small, but finite, screening colonoscopy complication rate.22 This set of guidelines is the latest in a series begun in 1997, updated in 2003, and built on the concept of change consistent with new evidence.13–16 It incorporates the American College of Gastroenterology polyp guidelines from 2000.23 Before the above guidelines, physicians had minimal guidance in managing postpolypectomy patients. Our goal is to provide a continuing basis for recommendations to guide postpolypectomy follow up.

These guidelines (Tables 2 and 3) have been endorsed by the Colorectal Cancer Advisory Committee of the ACS and by the governing boards of the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy.

METHODOLOGY AND LITERATURE REVIEW

We performed a Medline search of the post-polypectomy literature under the subject headings colonoscopy and adenoma, polypectomy...
TABLE 1 Differences from Prior Postpolypectomy Guidelines

1. The overall goal of these guidelines is to identify predictors of subsequent advanced adenomas and cancers to stratify patients into lower- and higher-risk groups.
2. These guidelines focus on the above risk stratification to encourage a shift from intense surveillance to surveillance based on risk. This would free up endoscopic resources for screening, diagnosis, and appropriate surveillance.
3. High-quality baseline colonoscopy is emphasized as critical for effectively reducing colon cancer risk.
4. Completeness of polypectomy at baseline is emphasized, particularly in the setting of piecemeal removal of large sessile polyps.
5. Follow-up surveillance of hyperplastic polyps is discouraged, except in the case of hyperplastic polyposis.
6. The importance of increasing awareness of hyperplastic polyposis is discussed.
7. The use of fecal occult blood testing during surveillance is discouraged at present but requires further study.
8. Follow-up intervals after removal of one or two small (<1 cm) adenomas have been lengthened (5 to 10 years or average risk screening options), and within this range, left to the clinician’s judgment and the patient’s preference.
9. Evolving technologies such as chromoendoscopy, magnification endoscopy, and CT colonography (virtual colonoscopy) are not yet established as surveillance modalities.

TABLE 2 Surveillance Recommendations

1. Patients with small rectal hyperplastic polyps should be considered to have normal colonoscopies, and therefore the interval before the subsequent colonoscopy should be 10 years. An exception is patients with a hyperplastic polyposis syndrome. They are at increased risk for adenomas and colorectal cancer and need to be identified for more intensive follow up.
2. Patients with only one or two small (<1 cm) tubular adenomas with only low-grade dysplasia should have their next follow-up colonoscopy in 5 to 10 years. The precise timing within this interval should be based on other clinical factors (such as prior colonoscopy findings, family history, and the preferences of the patient and judgment of the physician).
3. Patients with 3 to 10 adenomas, or any adenoma > 1 cm, or any adenoma with villous features, or high-grade dysplasia should have their next follow-up colonoscopy in 3 years providing that piecemeal removal has not been done and the adenoma(s) are completely removed. If the follow-up colonoscopy is normal or shows only one or two small tubular adenomas with low-grade dysplasia, then the interval for the subsequent examination should be 5 years.
4. Patients who have more than 10 adenomas at one examination should be examined at a shorter (<3 years) interval established by clinical judgment, and the clinician should consider the possibility of an underlying familial syndrome.
5. Patients with sessile adenomas that are removed piecemeal should be considered for follow up at short intervals (2 to 6 months) to verify complete removal. Once complete removal has been established, subsequent surveillance needs to be individualized based on the endoscopist’s judgment. Completeness of removal should be based on both endoscopic and pathologic assessments.
6. More intensive surveillance is indicated when the family history may indicate hereditary nonpolyposis colorectal cancer.

TABLE 3 Additional Surveillance Considerations

1. The present recommendations assume that colonoscopy is complete to the cecum and that bowel preparation is adequate. A repeat examination should be done if the bowel preparation is not adequate before planning a long-term surveillance program.
2. There is clear evidence that the quality of examinations is highly variable. A continuous quality improvement process is critical to the effective application of colonoscopy in colorectal cancer prevention.
3. A repeat examination is warranted if there is a concern that the polyp is incompletely removed, particularly if it shows high-grade dysplasia.
4. Endoscopists should make clear recommendations to primary care physicians about when the next colonoscopy is indicated.
5. Given the evolving nature of guidelines, it is important that physicians and patients should remain in contact so that surveillance recommendations reflect changes in guidelines.
6. Pending further investigation, performance of fecal occult blood test is discouraged in patients undergoing colonoscopic surveillance.
7. Discontinuation of surveillance colonoscopy should be considered in persons with serious comorbidities with less than 10 years of life expectancy, according to the clinician’s judgment.
8. Surveillance guidelines are intended for asymptomatic people. New symptoms may need diagnostic workup.
9. The application of evolving technologies such as chromoendoscopy, magnification endoscopy, narrow-band imaging, and computed tomography colonography are not established for postpolypectomy surveillance at this time.

surveillance, and adenoma surveillance, limited to English language from 1990 to 2005. This search identified 35 articles based on inclusion of data pertaining to baseline colonoscopy characteristics, advanced adenoma detection during follow-up surveillance, and advanced adenoma characteristics. Subsequently, we identified 12 additional articles from references of reviewed articles. Of these 47 articles, we considered 13 to be relevant studies according to the following criteria: 1) colonoscopy studies specifically addressing the relationship between baseline examination findings and detection of advanced adenoma or of any adenoma during follow-up colonoscopy; or 2) sigmoidoscopy studies, with large cohorts and follow up.
greater than 10 years, specifically addressing the association between baseline examination findings and detection of advanced adenomas during follow up. After the initial review of published data, we added one relevant abstract and a newly published article to the review. These were studies that were identified by members of the guideline committee and for which the data were available to the committee. We excluded studies that included patients with inflammatory bowel disease, prior history of colorectal cancer, and familial syndromes. Our final review was based on 15 studies that met the inclusion criteria.\textsuperscript{5,7,12,20,21,24–35} The most recent publication for the outcome of interest (adenomas and advanced neoplasia) was used for studies with more than one publication. We gave separate listings to the St. Mark’s study by Atkin\textsuperscript{7} for the outcomes for colon cancer and for rectal cancer. Two studies reported only on risk factors for adenomas rather than for advanced adenomas at surveillance.\textsuperscript{32,34}

The literature review was conducted by two independent authors (SJW and JSS). A third author (AGZ) created the evidence table, which was circulated among members of the US Multi-Society Task Force on Colorectal Cancer and the ACS’s Colorectal Cancer Advisory Committee. Recommendations in this report were based on the review of the evidence and the discussions at the combined meeting.

The evidence table (accessible at http://caonline.amcancersoc.org/content/vol56/issue3/) was organized to include the elements of study design. Ideally, the best study design would fulfill the following criteria: (1) be a randomized controlled trial or an observational cohort study of patients with adenoma(s) at baseline that were cleared by colonoscopy, after excluding people at high risk (such as familial syndromes); (2) consider all the candidate risk factors; (3) have sufficient follow-up time for adenomas to develop, with few dropouts; (4) have planned colonoscopic assessment for recurrence in all patients in the cohort; (5) have enough outcome events for reasonable statistical precision and sufficient statistical power to detect associations between baseline characteristics and adenoma outcomes; and (6) present the analyses that include adjustment for multiple risk factors and consider what the independent effects are.

The evidence table (accessible at http://caonline.amcancersoc.org/content/vol56/issue3/) includes classification of the type of design (randomized controlled trials [RCTs] or observational cohort studies), the number at risk, the follow-up intervals recommended, and the time followed. We also list the variables considered as risk factors and the effect of these factors on incidence of subsequent adenomas or on advanced neoplasia. The multivariate estimate of the relative risk is presented whenever available. The definition of an advanced neoplasm is given for each study and varies considerably by study. Summary comments on each study are also included.

Review of the evidence was confounded by variations in definitions, design of studies, timing and multiplicity of surveillance intervals, and quality of baseline colonoscopy (evidence tables accessible at http://caonline.amcancersoc.org/content/vol56/issue3/). Due to these variations, the review of the literature cited was descriptive rather than a single summary value of risk (ie, meta-analysis) for all studies. The literature cited is grouped by type of study design: (1) RCTs, where the surveillance interval is set and maintained as much as possible though eligibility requirements may vary; or (2) observational cohort studies, which are primarily registry studies with more passive recruitment for surveillance. The RCTs provide stronger evidence for the timing of follow-up examinations because those who received surveillance colonoscopy were not a special subset of all enrolled. As noted above, relative risks (RR) or odds ratios (OR) from multivariate analysis were presented in the evidence table whenever available. For two studies,\textsuperscript{7,21} the measure of risk was the standardized incidence ratio (SIR) with adjustment for age and sex rather than a relative risk. In one study,\textsuperscript{12} the hazard ratio (HR) is given as the measure of the effect. A descriptive graphical presentation was given with point estimates and confidence intervals for the relative risk for adenomas and advanced neoplasia by baseline adenoma characteristics of multiplicity, size, histology, high-grade
dysplasia, and location. These descriptive plots (Figure 1) of the measure of the effect for various risk factors provide a summary of the number of studies reporting a measure of effect for a given risk factor and the consistency and magnitude of this factor on adenoma and advanced neoplasia recurrence. The review of evidence assessed the risk factors for adenomas as well as for advanced adenomas, but the discussion concentrated on the factors affecting advanced adenomas. The definition of advanced adenoma differs from study to study. The most encompassing definition included any adenoma ≥1.0 cm, any villous component (ie, nontubular), or high-grade dysplasia, or invasive cancer.

Given the concern in detecting colorectal cancers at surveillance, the number of colorectal cancers detected by time under surveillance is cited whenever these data are included in the published study. Special characteristics of the study population and selection for the cohort were also noted in the evidence tables (accessible at http://caonline.amcancersoc.org/content/vol56/issue3/).

RESULTS OF THE LITERATURE REVIEW AND RATIONALE FOR THE GUIDELINES

Certain characteristics of colorectal adenomas at baseline colonoscopy are associated with the rate of adenoma detection and the histologic severity of subsequent adenomas. These data can be used as the basis for decisions about safe and effective postpolypectomy surveillance intervals by stratifying patients into lower- and higher-risk groups for future advanced adenomas. The available body of evidence is the basis for these recommendations.

Quality of Baseline Colonoscopy

Baseline adenoma characteristics play a major role in determining appropriate postpolypectomy surveillance intervals. Characteristics of the baseline colonoscopy are also an important predictor for subsequent neoplasia. The baseline colonoscopy needs to be of high quality for the baseline adenoma characteristics to be used for planning surveillance intervals. As defined by the US Multi-Society Task Force, a high quality colonoscopy reaches the cecum, has little fecal residue, and has a minimum time of withdrawal from the cecum of 6 to 10 minutes. Baseline colonoscopy without a good clearing of the colon places the patient at increased risk for subsequent neoplastic findings. Adenomas, advanced adenomas, and cancers are missed by colonoscopy. Sensitivity could be increased by continuing quality improvement programs for the performance of colonoscopy. Trials designed specifically to evaluate surveillance, in which colonoscopy is performed by experienced endoscopists, such as the National Polyp Study (NPS), have demonstrated that a low incidence of cancer can be achieved in postpolypectomy patients. The NPS required meticulous clearing at the initial baseline with repeat colonoscopy if this was not achieved with high confidence.

On the other hand, studies designed for other purposes, such as the pooled chemoprevention studies reported by Robertson et al, and community studies clearly show that higher miss rates commonly occur. Incomplete removal of large sessile polyps, particularly by piecemeal polypectomy, could contribute to a higher subsequent incidence of a colon cancer as in the chemoprevention trials. Atkin also demonstrated that inadequate removal of sessile rectosigmoid adenomas at baseline was associated with a marked increase in risk for rectal cancer. The NPS exclusion of patients with sessile adenomas larger than 3.0 cm and provision for individualized follow up for these patients could be another factor that contributed to the low incidence of cancer at follow up in this study. Loeve assessed colorectal cancer incidence after adenoma detection in Holland based on 78,473 patients and found that colorectal cancer incidence was not greatly reduced until 5 to 6 years after the initial diagnosis and attributed the lack of earlier effect to inadequate removal of adenomas when initially diagnosed. It is therefore important to consider early and late appearing cancers separately in postpolypectomy trials to separate true incidence reduction from missed cancers. This point is illustrated in the chemoprevention trials, in which a
FIGURE 1  Associations between Adenoma Characteristics at Baseline and Subsequent Risk of Adenomas and of Advanced Adenomas or Colorectal Cancer. The dotted line separates the results from the randomized controlled trials of surveillance and chemoprevention from the results of the observational cohort studies. Within the two groupings, the studies are listed by year published. Graphs are presented for the baseline risk factors of adenoma multiplicity (≥3), adenoma size (≥1.0 cm), and adenoma histology (tubulovillous or villous) in A, and for high grade dysplasia and for proximal location in B. The left column is for the risk with respect to adenomas at surveillance, and the right column is for risk with respect to advanced neoplasia. The studies differ with respect to the classification levels of the risk factors and on the definition of advanced neoplasia. The specification of each study is given in the evidence tables accessible at http://caonline.amcancersoc.org/content/vol56/issue3/. The studies also cover different periods of follow up and use different measures of effect, such as odds ratios (OR), relative risks (RR), hazard ratios (HR), and standardized incidence ratios (SIR), as noted in the evidence tables accessible at http://caonline.amcancersoc.org/content/vol56/issue3/. RR is used on the horizontal axis to represent these different measures of effect. The referent category for the ORs, RRs, and HRs is the lowest risk category. These estimates are denoted by circles. Multivariate estimates are used when available. In two studies,7,21 SIRs were reported and are denoted by squares. The referent category for the SIR is the general population. Note: Avidan34 and Noshirwani31 used number of adenomas, not ≥3 adenomas. RR represents OR, RR, or HR, or standardized incidence ratio as summarized for each study in the evidence tables accessible at http://caonline.amcancersoc.org/content/vol56/issue3/. CC = colon cancer; RC = rectal cancer.
large proportion of cancers were found early; this was probably due in part to inadequate removal of large adenomatous polyps. For example, nine of 19 cancers in the study of Robertson et al were found within 26 months of the initial colonoscopy.\(^{20}\)

**Characteristics of Baseline Adenomas as Predictors of Subsequent Advanced Adenomas**

See evidence table (accessible at http://caonline.amcancersoc.org/content/vol56/issue3/) and Figure 1.

**Multiplicity**

Multiplicity at baseline has been shown to predict subsequent detection of advanced adenomas. Of the RCTs, the National Polyp Study,\(^{25}\) the European fiber and calcium study,\(^{29}\) and the pooled analysis of chemoprevention studies\(^{30}\) showed that multiplicity conferred an increased risk for advanced neoplasia at surveillance. The pooled analysis did not report odds ratios but did report a significant difference in mean number of prior lifetime adenomas at baseline in those with and without advanced neoplasia at surveillance. Neither the wheat bran study described by Martinez\(^{28}\) nor the chemoprevention study presented by van Stolk\(^{27}\) noted a significant association between baseline multiplicity and detection of advanced adenoma at follow up. However, 35% of subjects in Martinez’s study\(^{28}\) had prior adenomas, so that prior colonoscopies may have reduced the number of adenomas detected at the index colonoscopy for study accrual. Van Stolk\(^{27}\) showed that individuals with three or more adenomas at baseline were more likely than those with one or two adenomas at baseline to have an adenoma detected at surveillance (OR = 2.25; 95% CI: 1.20 to 4.21), but found no adenoma characteristic predictive of advanced adenomas at surveillance. She noted, however, that her study had limited power to detect risk factors for advanced neoplasia.

The observational cohort studies also showed that multiplicity was a risk factor for subsequent advanced adenomas and cancer. Atkin followed a cohort of patients that initially had had rectosigmoid adenomas removed but with no further intervention in the colon for an average of 13.8 years. She showed that having two or more rectosigmoid adenomas, compared to one rectosigmoid adenoma at baseline, was associated with an increased risk for subsequent colon cancer but not for subsequent rectal cancer.\(^{7}\) Noshirwani, et al. reported that the number of adenomas at baseline was related to an increased risk (OR = 1.25; 95% CI: 1.13 to 1.38) for advanced adenomas at surveillance in a cohort from the Cleveland Clinic.\(^{31}\)

**Size**

Adenoma size greater than 1 cm also was shown to predict metachronous advanced adenomas in the wheat bran study.\(^{28}\) However the other four RCTs did not find adenoma size at baseline to be an independent predictor of advanced neoplasia at surveillance. Adenoma size was important in seven of eight of the observational cohort studies assessing advanced neoplasia. Loeve did not present data on adenoma size.\(^{21}\) In a rigid sigmoidoscopy study, Atkin reported that there was a significant trend (\(P < 0.002\)) for increased risk of subsequent colon cancer with increasing size of the rectosigmoid adenoma at baseline.\(^{7}\) The SIR for colon cancer was 1.5 (95% CI: 0.8 to 2.4) in patients with baseline adenomas less than 1 cm in size, increased to SIR = 2.2 (95% CI: 1.1 to 4.0) for 1 to 2 cm adenomas and further increased to SIR = 5.9 (95% CI: 2.8 to 10.6) for adenomas larger than 2 cm. Increasing size of the rectosigmoid adenomas at baseline also showed a significantly increasing trend of an increase in standardized incidence ratio for rectal cancer even though the individual standardized incidence ratios for rectal cancer by adenoma size were not statistically different from the general population risk. Yang, et al., also in a sigmoidoscopy study, demonstrated that larger adenoma size was related to subsequent risk of advanced neoplasia at surveillance with RR = 2.4 (95% CI: 1.3 to 4.6) for size 0.6 to 1.0 compared with size ≤0.5 cm and RR = 4.4 (95% CI: 1.9 to 10.2) for size greater than 1.0 cm at baseline.\(^{30}\) Noshirwani, et al. demonstrated that a baseline adenoma ≥1 cm compared with less than 1 cm conferred an OR
of 3.68 for subsequent advanced neoplasia. Bertario, et al. found that patients with adenomas greater than 2 cm compared with ≤2 cm at baseline had a hazard ratio of 4.0 (95% CI: 1.1 to 14.4) for the development of follow-up advanced adenomas. Lieberman, et al., in 5-year follow-up results from the VA Cooperative Study 380, found that the percentage of patients with advanced neoplasia was higher in those with baseline adenomas ≥1.0 cm (2.6%) compared with less than 1.0 cm (0.4%) over 5 years surveillance. Although the majority of studies reported size to be a significant factor, some did not. Neither van Stolk nor Bonithon-Kopp found size to be a significant predictor of metachronous advanced adenomas. Incomplete removal of large polyps identified at baseline could be a reason that larger size was a strong predictor of subsequent advanced neoplasia in these studies.

**Histology**

Histologic type of adenoma at baseline was not a significant predictor of advanced neoplasia in the randomized trials but was for several of the observational cohorts. Histology is a particularly difficult predictor to evaluate because of the somewhat subjective nature of classifying tubular, tubulovillous, and villous adenomas. Atkin, et al., in a rigid sigmoidoscopy study, demonstrated that tubulovillous histology at baseline was associated with an SIR = 3.8 (95% CI: 2.2 to 6.0), and villous histology had an SIR = 5.0 (95% CI: 2.2 to 9.9) for the detection of subsequent colon cancer. Histology at baseline was also an important predictor for subsequent rectal cancer risk in this study. In another sigmoidoscopy study, Yang, et al. reported that villous or tubulovillous histology at baseline conferred a relative risk of 8.34 (95% CI: 3 to 16.0) for the detection of advanced neoplasms (rectal cancer, or adenoma with severe dysplasia) at follow up. Loeve reported a significant trend for increasing risk of colorectal cancer at surveillance in relationship to increasing villous component or carcinoma in situ compared with tubular histology.

High-grade dysplasia is related to larger adenoma size and villous component at baseline and is an important predictor for subsequent advanced neoplasia in three of the observational cohort studies. By definition, all adenomas have some level of dysplasia. In the past, dysplasia has been classified as mild, moderate, severe, or carcinoma in situ. Currently, severe dysplasia or carcinoma in situ are considered the equivalent of high-grade dysplasia, and mild or moderate dysplasia are considered the equivalent of low-grade dysplasia. For the purposes of this analysis, wherever possible, the risks are assessed for high-grade and low-grade dysplasia. Atkin, et al. found increasing degree of dysplasia was associated with an increasing risk of subsequent colon cancer with a standardized incidence ratio of 3.3 (95% CI: 1.1 to 8.0) for severe dysplasia in baseline adenomas. Yang reported odds ratios of 5.9 (95% CI: 2.6 to 13.5) and 14.4 (95% CI: 5.0 to 41.4), respectively, for the development of subsequent advanced neoplasia (rectal cancer or severe dysplasia) in patients with moderate and severe dysplasia at baseline. Lieberman, et al., in the VA Cooperative Study, determined that 10.9% of patients with high-grade dysplasia in adenomas of any size at baseline had advanced neoplasia over the 5-year surveillance period compared with 0.6% in those with tubular adenomas less than 1.0 cm lacking high-grade dysplasia.

**Location**

Martinez, et al. reported that a proximal adenoma at baseline was associated with an increased risk of subsequent advanced adenomas. The odds ratio was 1.65 (95% CI: 1.02 to 2.67) for baseline proximal adenomas only versus distal adenomas only, and OR = 2.69 (95% CI: 1.34 to 5.42) for proximal and distal adenomas versus distal adenomas only at baseline. Similarly, Bonithon-Kopp, et al. reported an odds ratio of 2.63 (90% CI: 1.31 to 5.3) for subsequent advanced neoplasia for patients with proximal compared with no proximal location of baseline adenomas. In the observational cohort study of Loeve using large registry databases, the risk of colorectal...
cancer at surveillance was slightly lower for patients with colon adenomas at baseline than rectal adenomas.

**Other Risk Factors: Patient Age, Sex, History of Polyps, and Family History of Colorectal Carcinoma**

In their RCTs, Martinez and Bonithon-Kopp reported an increasing risk of subsequent neoplasia with increasing age. Age was frequently employed as a control variable in the analyses without an explicit risk factor presented for the age effect. Martinez and Bonithon-Kopp reported an increased risk for men for advanced neoplasia at surveillance. Sex was also frequently employed as a control variable in the analyses without an explicit risk factor presented for the sex effect.

Both Martinez and Bonithon-Kopp noted that a history of polyps before the baseline adenoma was associated with an increased risk for advanced neoplasia at surveillance. Although it is not always possible to determine whether prior polyps are adenomatous polyps, the presence of prior polyps can be considered as an additional risk factor. The effect of prior adenomas or other polyps on subsequent risk was not considered in all studies. When noted in the reviewed studies, the percentage of patients in a study with prior adenomas or other prior polyps is included in the evidence table (accessible at http://caonline.amcancersoc.org/content/vol56/issue3/).

Family history of colorectal cancer and adenomas at a young age is an established risk factor for the development of colorectal cancer. However, few studies have specifically addressed the relationship between family history and metachronous advanced adenomas in postpolypectomy patients. The National Polyp Study demonstrated that a family history of colorectal cancer in patients ≥60 years of age predicted a 4.8-fold increased risk of advanced adenomas at follow up. Fossi noted family history of colorectal cancer in a first-degree relative as a risk factor for adenomas at surveillance, but the study did not report on risk factors for advanced adenomas at surveillance. As noted above, Martinez and Bonithon-Kopp both reported proximal adenomas at baseline as predictors of subsequent advanced neoplasia. Proximal adenomas are associated with family history of colorectal cancer. It is possible that these studies might also have had an increased risk for advanced adenoma because of the association of family history of colorectal carcinoma with proximal adenomas.

**SUMMARY OF BASELINE PREDICTORS**

The totality of evidence suggests that multiplicity (≥3 adenomas), size (≥1 cm), villous features, and high-grade dysplasia are predictors of future advanced adenomas or cancers. Family history and proximal location may also predict metachronous advanced adenomas but have not been well studied. Analysis of the relative importance of each of these predictors is complicated by their interrelationships. Consequently, multivariate analysis for some studies may find that size and histology are the most important, whereas others may report that multiplicity is the most important.

There is a consensus among many of the studies that the group at lower risk for subsequent advanced adenomas has only one or two adenomas, all less than 1 cm in size, with no high-grade dysplasia or villous features. Risk for colon cancer in such low-risk patients, over an average of 14 years, has been shown in a rigid sigmoidoscopy polypectomy study to be similar to the average risk population.7 In colonoscopy studies, patients have been followed only 5 to 6 years after colonoscopic polypectomy to assess their subsequent risk for neoplasia. Sigmoidoscopic polypectomy without colonoscopic assessment is insufficient to establish colonoscopic surveillance intervals. In the Atkin study, colon risk was assessed in an anatomic area where polypectomy was not performed (ie, above the rectosigmoid). Post-polypectomy surveillance guidelines should ideally be based on colonoscopic follow up of patients who have had colonoscopic polypectomy. Based on the available evidence, we can project that apparently low-risk patients can wait 5 and possibly 10 years for repeat colonos-
copy. However, further evaluation of this low-risk group is required to confirm the safety of these intervals.

For rarer events, such as colorectal cancer at surveillance and even for adenomas in the smaller studies, the confidence intervals on colorectal cancer or advanced neoplasia may be relatively wide. Consequently, a nonstatistically significant result does not rule out that this factor has no impact on risk for surveillance findings.

**DISCUSSION**

These guidelines are based on all of the available evidence, clinical experience, knowledge of the adenoma-carcinoma sequence, and expert opinion. They are intended to be used by clinicians as a guide in their approach to postpolypectomy surveillance, taking into consideration clinical judgment in patient comorbidities, patient preferences, and family history. The differences between these guidelines and prior ones are shown in Table 1. The detailed evidence for these guidelines is presented in the literature review summarized by the evidence tables accessible at http://caonline.amcancersoc.org/content/vol56/issue3/ and in Figure 1.

There is strong evidence that the adenoma cohort can be stratified according to the risk of development of subsequent advanced adenomas. Recommendations for surveillance intervals in persons with multiple adenomas and those with advanced adenomas are based primarily on the National Polyp Study,25 a randomized controlled trial, and observational cohort studies. Recommendations in the low-risk group of one to two small tubular adenomas are based on the low incidence of advanced adenomas in observational cohort studies and the National Polyp Study over 3- to 6-year intervals and the observation by Atkin, et al. that persons with small tubular adenomas are not at increased risk of developing colorectal cancer. In the opinion of the panel, the data from observation of cohort studies supports an interval of at least 5 years in this low-risk group; however, the panel reasoned that based on the Atkin data, informed physicans and their patients could conclude that a 10-year interval, similar to that used in the average-risk population, would also be acceptable. The recommendation to perform short interval follow up in patients with 10 or more adenomas is based on the increased probability of missed lesions in patients with numerous adenomas. The recommendation to perform very short interval follow up in patients with large sessile polyps removed piecemeal is the repeated observation that a significant fraction of these polyps are incompletely removed by the initial polypectomy. Recommended intervals in HNPCC are based on the known rapid transformation through the adenoma carcinoma sequence in these patients.

The present collaborative effort between the US Multi-Society Task Force on Colorectal Cancer and the ACS was based on several considerations. The gradual increase in screening and the marked increase in screening colonoscopy are producing a large subset of the population that requires surveillance based on adenoma detection. Both societies felt the need to update the guidelines for the follow up of these patients, according to the latest evidence. Recent surveys have shown that 50% of endoscopists are not following previously published guidelines for postpolypectomy surveillance.51,52 It was felt that a consensus by the two organizations would strengthen the recommendations and increase their utilization.

From the 1970s to the 1990s, annual follow-up colonoscopy was common practice after polypectomy, and there were no guidelines available addressing how clinicians should best follow these patients. In 1993, a report from the National Polyp Study demonstrated that it was safe to defer the first follow-up examination for 3 years.25 This evidence, along with the knowledge of the long natural history of the adenoma-carcinoma progression, led to guidelines in 1997 that recommended a 3-year interval for the first follow-up examination after removal of adenomas.15,16 Practice began to evolve along the lines of this evidence. Guidelines have been used in the courts of law as indicating the standard of practice.

Recent guidelines have introduced the concept of risk stratification of patients at the time
of polypectomy into those more likely or less likely to develop subsequent serious neoplasia. In addition, the concept of the advanced adenoma as a surrogate biological indicator of cancer risk has been adopted. Colorectal cancer would be a more ideal outcome measure. However, the advanced adenoma was adopted as an early outcome measure of efficacy because a much longer period of time would be required for conclusions to be drawn if cancer were used as the outcome measure. This reasoning is supported by several studies that have demonstrated the relationship between advanced adenomas and cancer. A uniform definition of the advanced adenoma has not yet been clearly established, but most include adenomas with size ≥1 cm, any villous histology, or high-grade dysplasia.

Several studies have examined factors that could predict future risk of advanced adenomas, including number, size, histology, and location of baseline adenomas, as well as patient age and family history of colorectal cancer. Most of the studies that assessed risk factors for advanced adenomas at surveillance were either randomized controlled trials of surveillance, chemoprevention trials, or registry-based observational cohort studies of patients returning for surveillance with less structured follow up outside the context of a clinical trial. The most consistent evidence for predicting subsequent advanced adenomas indicates that multiplicity, size, villous histology, and high-grade dysplasia are the important factors at baseline. Based on these factors, patients can be stratified at the time of colonoscopy into lower or higher risk for subsequent advanced adenomas. The strongest studies for evaluating predictive factors for future neoplasia after polypectomy are those specifically designed as postpolypectomy surveillance studies such as the National Polyp Study. Chemoprevention randomized trials were designed to assess the drug intervention effect with less of an emphasis on determining optimal surveillance intervals.

Patients who have had a polypectomy and long-term surveillance have been shown to have a reduced incidence of colorectal cancer. When one separates out the effect of initial polypectomy from the subsequent surveillance, modeling has demonstrated that more than 90% of the reduced incidence over the first 5 to 6 years is the result of the initial polypectomy. However, there is a subgroup that can be identified as having a higher risk of subsequent cancer by using the advanced adenoma as a surrogate marker. These observations support the concept of stratifying patients by baseline factors so that the group at increased risk can be identified for more intensive surveillance and the group at lower risk can be identified for less intensive surveillance. Reduction in the intensity of surveillance could free up endoscopic resources that could be shifted to screening and diagnosis, thereby increasing the benefit and reducing the procedural risk.

Use of fecal occult blood testing (FOBT) after colonoscopy in postpolypectomy patients has been reported to be a widespread practice (38% of patients had FOBT after adenoma removal at colonoscopy). The National Polyp Study has demonstrated that use of FOBT after colonoscopy results in a substantial number of unnecessary colonoscopies: 77% of colonoscopies performed to evaluate positive surveillance FOBT results detected no advanced adenomas or cancer (ie, the positive predictive value was 23%). In a recent report by Bampton, et al. of 785 patients having had a recent surveillance colonoscopy, the positive predictive value for an immunochemical FOBT was 27%. This was in a high-risk cohort comprised of patients with history of colonic neoplasia or with strong family history. A lower positive predictive value would be expected in a lower-risk population. The possible benefit of FOBT in patients having surveillance colonoscopies needs further study, but with the present available evidence this should be discouraged.

In the present guidelines, recommendations for the lower-risk group are intentionally flexible because follow-up colonoscopy studies are limited to 5 to 6 years. Some physicians and patients may elect to have a follow-up colonoscopy at 5 years because they wish to be assured that future risk has been reduced below that of the average-risk population. Others may
feel confident that this risk has already been reduced below that of the general population by adequate clearing of the colon and would be satisfied with either a 10-year follow-up colonoscopy or choosing other screening options currently recommended for individuals at average risk.14

Risk stratification and recommended follow-up intervals are based on the presumption that a high-quality colonoscopy was performed at baseline. However, variable colonoscopic miss rates for adenomas and cancer have been shown.5,20,39-42,60-62

This variability in colonoscopic baseline quality could translate into either a lower rate of subsequent cancers detected during surveillance as in the National Polyp Study5,62 or a higher rate as seen by Robertson, et al. and others.20,39,61 For example, in the NPS, if the baseline colonoscopy did not clear the colon with high confidence (excellent preparation, complete polypectomy), the exam was repeated before entering the patient into the surveillance program. Repeat exams were required in 13% of the cases.25 Such rigor contributed to a marked reduction in colorectal cancer incidence in the NPS, which was not observed in other studies.20,39,61 In the Australian and Japanese studies,50,62 the low miss rates were calculated only from cases in which the cecum was intubated. In one study of “missed cancers,”39 failure to intubate the cecum accounted for some undetected cancers.

The quality of the baseline examination can be evaluated to some extent by the number of cancers detected earlier versus later in a surveillance program. Thus, the major benefit of the baseline colonoscopic polypectomy rests on the quality of that examination.37,38 The concern by clinicians of missed cancers can be assuaged by high-quality baseline performance of colonoscopy. Protection can never be 100%, but it is high (76% to 90% colorectal cancer incidence reduction) with high confidence examination.5,63

There was insufficient evidence to include family history in the guidelines as a predictor of metachronous advanced adenomas. Clearly, however, family history of colorectal cancer in a close relative does increase the risk of colorectal cancer in other relatives and needs further study in the postpolypectomy setting.47-49

Issues such as this must be considered on an individual basis when clinicians are determining appropriate follow up.

Patients with a family history indicating HNPCC require special screening and surveillance.13,15,49 HNPCC is an autosomal dominant inherited cancer syndrome which accounts for 1% to 5% of colorectal cancer cases and is caused by germline mutations in one of five mismatch repair genes. The mean age for colorectal cancer development in HNPCC is 44 years. Cancers tend to be right sided and often are poorly differentiated, mucus-producing tumors with intense lymphocytic infiltrates. Tumors demonstrate microsatellite instability (MSI) and immunostaining is often negative for one of the mismatch repair gene products. There are no clinical criteria that are perfectly sensitive for HNPCC. The modified Bethesda criteria perform best in this regard.64 HNPCC should be suspected when colorectal cancer or other tumors with relative specificity for HNPCC (endometrial, ovarian, small bowel, ureter, or renal pelvis) occur in younger people, when multiple relatives and generations are affected, or when tumor location and histology are suggestive. Potentially affected persons can be screened by testing their tumors for microsatellite instability or for mismatch repair gene products by immunostaining. Genetic testing is used when these screening tests are positive or when the clinical presentation and family history are very strongly suggestive. Tumors in HNPCC move through the adenoma-carcinoma sequence more rapidly than sporadic tumors.50 Definite or potential gene carriers are screened by colonoscopy every 2 years beginning at age 20 to 25 years until age 40 years, and then annually.13 Surveillance recommendations are essentially the same as screening. The colon must be carefully cleared and complete polypectomy is essential, particularly for advanced adenomas. Patients who develop advanced adenomas and proven gene carriers can be offered prophylactic
subtotal colectomy followed by annual proctoscopy and polypectomy.

Other issues evolving in the literature that require further study and may affect future guidelines as data matures include different recommendations for men and for women by age. Given the evolving nature of guidelines, it is important that physicians and patients remain in contact so that surveillance practices will reflect changes in guidelines.

Management of patients with hyperplastic polyps only was omitted from prior guidelines. There is no evidence that patients with small distally located hyperplastic polyps have an increased risk for colorectal cancer, and they should therefore be rescreened as appropriate for average-risk patients. The present guidelines state this explicitly. It has been shown recently, however, that hyperplastic polyps are not a homogenous histological category, and there is accumulating evidence from molecular genetic studies that some histological variants of hyperplastic polyps may evolve into a unique type of adenoma called a serrated adenoma that resembles a hyperplastic polyp with dysplasia. This type of adenoma has in turn been linked to the ultimate development of sporadic MSI adenocarcinoma. This form of colonic adenocarcinoma shares with HNPCC the genetic attribute (in this case, acquired) of microsatellite instability (sporadic MSI cancers) due to mismatch repair deficiency. Hyperplastic polyps at risk for such a progression exhibit atypical architectural and cytologic features, are often large and sessile, and are usually proximally located. Other terms for these hyperplastic polyp variants are sessile serrated adenoma or serrated polyp with abnormal proliferation. Some authors have suggested that complete removal and surveillance, as for typical adenomas, may be warranted in these cases.

All endoscopists must remain alert to the syndrome of hyperplastic polyposis. Hyperplastic polyposis was defined by Burt and Jass for the World Health Organization International Classification of Tumors as: (1) at least five histologically diagnosed hyperplastic polyps proximal to the sigmoid colon, of which two are greater than 1 cm in diameter; or (2) any number of hyperplastic polyps occurring proximal to the sigmoid colon in an individual who has a first-degree relative with hyperplastic polyposis; or (3) greater than 30 hyperplastic polyps of any size distributed throughout the colon. Studies have found an increased risk of colorectal cancer in these patients. The pathway may be through the serrated adenoma. The magnitude of the increased risk has not been determined. A recent case series of 15 patients found no cancer developed within 3 years of follow up. The optimal management of hyperplastic polyposis has not yet been defined and requires further study.

Technological advances such as computed tomography (CT) colonography (also known as virtual colonoscopy, which uses CT scan technology), chromoendoscopy (endoscopy with dye spraying of the mucosa), narrow-band imaging (a high-resolution endoscopic technique that enhances the fine structure of the mucosal surface without dye), and magnification endoscopy (real-time magnification of endoscopic images) may one day be shown to be important in postpolypectomy surveillance. Some of these techniques may have a special role in detecting flat adenomas. However, at this time there is insufficient evidence that any of these techniques should be part of routine postpolypectomy surveillance.

In summary, guidelines are dynamic and based on the evidence currently in the literature, understanding of the adenoma carcinoma sequence, and expert opinion. Guidelines must be updated as new evidence becomes available. The committee identified a number of areas of uncertainty and considers the following to be among the important questions for further study.

**QUESTIONS TO BE ADDRESSED**

1. What are the reasons that guidelines are not more widely followed?
2. How can adherence to quality control indicators at baseline colonoscopy be encouraged to reduce the miss rate of advanced adenomas and colorectal cancers?
3. Will emerging studies with longer colonoscopy follow up support the safety of lengthening surveillance intervals?
4. What is the appropriate management and surveillance of the hyperplastic polyposis syndrome?
5. What is the appropriate surveillance of patients who have had an adenoma removed in piecemeal fashion?
6. Which definition of advanced adenoma is most strongly associated with subsequent cancer?
7. In the setting of postpolypectomy surveillance, what is the role of family history in predicting advanced adenomas and colorectal cancer?
8. What roles will chromoendoscopy, magnification endoscopy, narrow-band imaging, and CT colonography play in postpolypectomy surveillance?
9. How can molecular genetic information help to stratify risk in patients with adenomatous polyps?

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