THE AMERICAN JOURNAL OF GASTROENTEROLOGY
Vol. 95, No. 11, 2000

ISSN 0002-9270/00/$20.00
Published by Elsevier Science Inc.
PII S0002-9270(00)02227-9

PRACTICE GUIDELINES

Polyp Guideline: Diagnosis, Treatment, and Surveillance for Patients With Colorectal Polyps*

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PREAMBLE

This guideline is a revision of a guideline originally developed and published in 1993 (1). It is intended to indicate preferable approaches to the management of patients with colorectal polyps based on available scientific evidence. It does not deal with colorectal neoplasia screening, a topic that has been addressed in three recent evidence-based guidelines (2–4). It also does not deal with patients with known colon cancer, hereditary nonpolyposis colorectal cancer syndrome, or familial polyposis.

Guidelines for clinical practice are intended to suggest preferable approaches to particular medical problems, as established by interpretation and collation of scientifically valid research derived from extensive review of the published literature. When data are not available that will withstand objective scrutiny, a recommendation may be made based on a consensus of experts. Guidelines are intended to apply to the clinical situation for all physicians without regard to specialty. Guidelines are intended to be flexible, not necessarily indicating the only acceptable approach, and should be distinguished from standards of care that are inflexible and rarely violated. Given the wide range of choices in any health care problem, the physician should select the course best suited to the individual patient and the clinical situation presented. These guidelines are developed under the auspices of the American College of Gastroenterology and its Practice Parameters Committee. These guidelines are also approved by the governing boards of the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy, and the American Association for the Study of Liver Diseases. Expert opinion is solicited from the onset for the document. Guidelines are reviewed in depth by the Committee, with participation from experienced clinicians and others in related fields. The final recommendations are based on the data available at the time of the production of the document and may be updated with pertinent scientific developments at a later time. The following guidelines are intended for *adults* and not for pediatric patients.

*This guideline is an official statement of the American College of Gastroenterology. It also has been endorsed by the American Society for Gastrointestinal Endoscopy and the American Gastroenterological Association.

DEFINITION AND CLINICAL CONSIDERATIONS

Colorectal polyps are classified histologically as neoplastic or nonneoplastic. Most colorectal cancers arise from neoplastic adenomatous polyps (adenomas). Adenomas are monoclonal derivatives of a mutated epithelial stem cell. Simple small (<1 cm) tubular adenomas are extremely common and have a low risk of becoming malignant. Only a few acquire the additional genetic alterations that make them grow, develop advanced histological features, and turn to cancer. Advanced adenomas are those that are larger (≥1 cm) or that contain appreciable villous tissue or high-grade dysplasia. Efforts to control colon cancer now focus mainly on strategies to reliably detect and resect advanced adenomas before they become malignant.

Grossly, a polyp is classified as pedunculated or sessile depending on whether it contains a discrete stalk. Polyps occasionally cause gross rectal bleeding or, very rarely, symptoms of partial bowel obstruction. Most polyps are asymptomatic lesions detected by screening or diagnostic studies performed for other reasons. Colorectal polyps are extremely common in Western countries; they are found in >30% of autopsies performed in people aged >60 yr (5, 6).

The main importance of polyps is their well recognized relationship to colorectal cancer (7). It now is generally accepted that most (>95%) colorectal cancers arise from benign, neoplastic adenomatous polyps (adenomas). Although this adenoma–carcinoma sequence can probably never be proved directly, persuasive data exist indicating that colorectal neoplasia progresses through a continuous process from normal mucosa, to benign adenoma, to carcinoma.

Histologically, polyps are classified as neoplastic (adenomas) or nonneoplastic (8, 9). Nonneoplastic polyps have no malignant potential and include hyperplastic polyps, hamartomas, lymphoid aggregates, and inflammatory polyps. Neoplastic polyps or adenomas have malignant potential and are classified according to the World Health Organization as tubular, tubulovillous, or villous adenomas, depending on the presence and volume of villous tissue (10). Tubular adenomas are composed of straight or branched tubules of dysplastic tissue; villous adenomas contain fingerlike projections of dysplastic epithelium. Approximately 70% of polyps removed at colonoscopy are adenomas (11).

From 70% to 85% of these are classified as tubular (0–25%, villous tissue), 10–25% are tubulovillous (25–75%, villous tissue), and <5% are villous adenomas (75%–100%, villous tissue).

Some degree of dysplasia exists in all adenomas. Most authorities recommend that dysplasia be classified as low- and high-grade, because this classification reduces the problem of interobserver variation (12). High-grade dysplasia includes the histological changes previously called "carcinoma in situ," "intramucosal carcinoma," or "focal carcinoma." Abandonment of these terms is recommended because of concern for misinterpretation of the clinical significance that might lead to overtreatment, and thus they will not be used in this guideline. Approximately 5–7% of patients with adenomas have high-grade dysplasia, and 3–5% have invasive carcinoma at the time of diagnosis. Increasing dysplasia and, presumably, malignant potential correlate with increasing adenoma size, villous component, and patient age (12). The likelihood of invasive carcinoma also increases with increasing polyp size (9).

Colorectal adenomas are monoclonal derivatives of a mutated epithelial stem cell (13). Advanced adenomas, defined by the National Polyp Study as being ≥1 cm in diameter or containing appreciable villous tissue or high-grade dysplasia, result from a nonlinear, multistep accumulation of a number of genetic mutations and chromosomal deletions occurring over several years (12, 14). Environmental carcinogenic factors seem to interact with inherited and/or acquired genetic changes that may eventually produce a malignant phenotype. This model of molecular genesis helps to explain the clinical observation that most simple small tubular adenomas remain static or may actually regress with time, whereas only a few grow and develop villous changes, high-grade dysplasia, and invasive carcinoma (15, 16). Most small (<1 cm) tubular adenomas contain only the earliest occurring genetic alterations, and only a few of these develop the additional genetic changes necessary to stimulate accelerated cellular division and growth. A large body of recent scientific data discussed in this guideline indicate that clinicians should increasingly shift their focus away from simply detecting and harvesting large numbers of small, simple tubular adenomas toward strategies that allow the reliable detection of most advanced adenomas.

DIAGNOSIS AND TREATMENT

Colorectal polyps can be diagnosed by endoscopy or barium radiography. When there is an indication to examine the entire large bowel, colonoscopy is the diagnostic procedure of choice. It is the most accurate method of detecting polyps of all sizes and it allows immediate biopsy or polypectomy. Most polyps found during colonoscopy can be completely and safely resected, usually using electrocautery techniques. Scientific studies now conclusively show that resecting adenomatous polyps prevents colorectal cancer.

Colonic polyps can be diagnosed either by endoscopy or barium radiography. Because most polyps are asymptomatic, they are usually found incidentally or as the result of screening. Colonoscopy is the procedure of choice for diagnosing colorectal polyps. It is the most accurate method for detecting polyps of all sizes, and it allows biopsy of lesions and resection of most polyps (17, 18). An earlier controlled, single-blinded comparison study of colonoscopy and double-contrast barium enema performed by expert examiners reported an accuracy of 94% and 67% for diagnosing polyps for colonoscopy and radiographic studies, respectively (19). More recently, the National Polyp Study reported the results of a similar controlled comparison of colonoscopy and double-contrast barium enema performed in a large cohort of patients undergoing postpolypectomy surveillance. The barium enema study missed 52% of polyps that were ≥1 cm (20). In two other recently controlled investigations, tandem colonoscopies performed by two experienced examiners indicated an appreciable miss rate for polyps measuring <10 mm in diameter, but very few polyps ≥10 mm were undetected by the first examination (21, 22). Most polyps found during colonoscopy can be completely and safely removed by electrocautery (23, 24).

Despite its advantages for the diagnosis and treatment of polyps, colonoscopy has some limitations. Areas adjacent to acute angulations or flexures and the ileocecal valve may be difficult to observe. Furthermore, in 5–10% of patients, usually those with diverticulosis or previous pelvic surgery, the endoscopist may not be able to pass the instrument comfortably and safely to the cecum (25).

The single-contrast barium enema examination is an inaccurate method for detecting polyps in most patients. In one large screening study, single-contrast barium enemas found only 40% of neoplastic polyps detected on subsequent colonoscopy (26). Double-contrast techniques greatly improve the accuracy of radiological methods for detecting polyps (27). However, even when double-contrast methods are employed, barium enema examinations as they are currently performed in most community hospitals are insufficiently sensitive for the reliable detection of colorectal polyps (28). The other main limitations of barium enema is that it does not allow biopsy or polypectomy, and it has relatively low specificity (many false-positives) for polyps.

The most common use of flexible sigmoidoscopy is for screening asymptomatic average-risk persons for colonic neoplasms. Sensitivity and specificity are very high because few polyps within reach of the instrument are missed, and the false-positive rate is negligible. Although, theoretically, flexible sigmoidoscopy might diagnose the 70% of colorectal neoplasms that arise distal to the splenic flexure, in actual practice, because of some incomplete examinations, only 50–60% of all polyps and cancers are diagnosed (3). The combination of a double-contrast barium enema and flexible sigmoidoscopy has been promoted as an acceptable alternative to colonoscopy for patients requiring a complete examination of the large bowel in whom colonoscopy is

incomplete or unacceptable. When a barium enema is used for diagnosis or surveillance, flexible proctosigmoidoscopy usually should be done to ensure an adequate examination of the rectum. Flexible sigmoidoscopy also provides a more accurate examination of the sigmoid colon, which is often a difficult area for the radiologist to examine. Double-contrast barium enema seems to be more accurate in the proximal colon than in the distal colon (29). Although flexible sigmoidoscopy allows biopsy of lesions, it should not be used for electrosurgical polypectomy unless the entire colon is prepared, to eliminate the risk for electrocautery-induced explosion (30). Furthermore, detection of a neoplastic polyp by screening flexible sigmoidoscopy is usually an indication for colonoscopy, at which time the polyp can be resected and a search made for synchronous neoplasia.

Perforation as the result of diagnostic colonoscopy has been reported in <0.1% of cases performed by experienced endoscopists (31). Perforation and clinically significant bleeding occur after colonoscopic polypectomy in about 0.2% and 1% of cases, respectively. Major complications occur less frequently during barium enema (0.02%) and flexible sigmoidoscopy (0.01–0.04%) (32, 33). The cost of colonoscopy exceeds that of barium enema plus flexible sigmoidoscopy by 40–60% in most centers. However, because 30–40% of patients undergoing barium enema examination for the purpose of detecting neoplasia will be found to have abnormalities requiring the subsequent performance of colonoscopy, the average costs of the two alternative diagnostic strategies are approximately the same (34).

Cohort and case-control studies suggest that endoscopic polypectomy reduces the subsequent incidence and mortality of colorectal cancer. Years ago, Gilbertsen and Nelms reported that annual screening rigid proctosigmoidoscopy reduced the incidence of rectal cancer by 85% (35). Three case-control studies performed by Selby *et al*., Newcomb *et al*., and Muller and Sonnenberg, respectively, indicated that endoscopic polypectomy reduced mortality from cancer in the part of the colon examined by 50–79% (36–38). Most convincing is a report from the National Polyp Study in which 1418 patients underwent a clearing colonoscopy with removal of at least one adenomatous polyp (39). After an average follow-up of 5.9 yr, the incidence of colorectal cancer was 76–90% lower than expected compared to three reference groups. Although these studies strongly suggest the effectiveness of polypectomy, no randomized trial has yet proved that resecting adenomas reduces colorectal mortality. Given the quality of available evidence, many now believe that such a trial would neither be feasible nor ethical to perform.

INITIAL MANAGEMENT OF POLYPS

Most patients with polyps detected by barium enema or flexible sigmoidoscopy, especially if the polyps are multiple or large, should undergo colonoscopy to excise the polyp and search for additional neoplasms. The decision whether to perform colonoscopy for patients with polyps <1 cm in diameter must be individualized depending on the patient's age, comorbidity, and past or family history of colorectal neoplasia. Complete clearing colonoscopy should be done at the time of every initial polypectomy to detect and resect all synchronous adenomas. Additional clearing examinations may be required after resection of large sessile adenomas or if, because of multiple adenomas or other technical reasons, the colonoscopist is not reasonably confident that all adenomas have been found and resected. Additional specific situations are discussed below.

Because of the adenoma–cancer relationship and the mounting evidence that resecting adenomas prevents cancer, most patients with polyps detected by barium enema or flexible sigmoidoscopy should undergo colonoscopy to excise the polyp and search for additional neoplasms. The incidence of synchronous adenomas in a patient with one known adenoma is 30–50% (40–42). Most polyps diagnosed during colonoscopy can be completely removed by electrocautery techniques. Surgical resection of a polyp is indicated only when an experienced endoscopist is unable to resect an advanced adenoma safely or when a malignant polyp requires colonic resection (28, 29). Most pedunculated polyps are resected by snare-polypectomy and the entire specimen is submitted for pathological evaluation. A total excisional biopsy is desirable so that the polyp can be properly classified and the presence or absence of malignancy determined; and so that, for malignant polyps, the grade, vascular and lymphatic involvement, and proximity to the margin of resection of the cancer can be assessed. Large sessile polyps usually require piecemeal snare resection; but, again, every effort is made to retrieve all resected tissue for pathological analysis. Injection of saline into the submucosa under a large or flat sessile polyp (saline-assisted polypectomy) may increase the ease and safety of snare-resection, especially in the right colon (43).

MANAGEMENT OF SMALL POLYPS

Small polyps (<1 cm) encountered during colonoscopy are usually resected using one of a number of different techniques, with and without electrocautery. The monopolar hot biopsy forceps has limitations and risks that need to be carefully considered. Representative biopsies should be obtained when small polyps are numerous. When a small polyp is encountered during screening flexible sigmoidoscopy, it should be biopsied to determine whether it is an adenoma and, thus, may be an indication for colonoscopy. Current evidence supports the recommendation that a hyperplastic polyp found during flexible sigmoidoscopy is not, by itself, an indication for colonoscopy. Data are conflicting as to whether small distal adenomas predict the presence of proximal clinically significant adenomas; therefore, the decision to do colonoscopy must be individualized.

Small sessile polyps are resected using several different techniques including hot and cold biopsy (with and without

cautery), hot or cold minisnare, or cold biopsy followed by fulgeration with a monopolar or bipolar electrode (44). The monopolar hot biopsy forceps should be used with great caution in the thin-walled right colon. There have been reported perforations and a relatively high rate of delayed bleeding using this device (45). When using any type of cautery probe in the right colon, it is important to apply low-power cautery cautiously without pressing the tip of the probe into the bowel wall. Even modest pressure can thin out the wall and increase the chance of perforation. A study of different methods of resecting diminutive polyps found a high rate (29%) of incomplete resection using the hot biopsy forceps (46). Thus, this device not only has been associated with more complications, it frequently fails to eradicate all neoplastic tissue.

As discussed in the next section, the decision as to whether to perform colonoscopy for patients with polyps measuring <1 cm in diameter must be individualized depending on the patient's age, comorbidity, and past or family history of colonic neoplasia. Most small polyps are adenomas with some malignant potential, although the likelihood of cancer already existing in a polyp this size is small (<1%) (47, 48). Small polyps encountered during colonoscopy are usually resected. Representative biopsies should be obtained when these small lesions are numerous.

A Small Polyp Found During Screening Flexible Sigmoidoscopy

When a polyp less than about 8 mm in size is detected during screening flexible sigmoidoscopy, a biopsy usually should be done to determine whether it is an adenoma. Hyperplastic polyps, which are common in the lower left colon, have no malignant potential, and several prospective studies now have shown that they do not predict an increased prevalence of adenomas in the proximal colon (42, 49, 50). Therefore, if the only abnormality found during screening sigmoidoscopy is a hyperplastic polyp, no further evaluation or follow-up is indicated. Most larger polyps (>0.7 cm) are adenomas; therefore, there is usually no need to do a biopsy during screening sigmoidoscopy, with its added expense and delay.

Several studies have addressed the clinical importance of finding one or two small tubular adenomas (<1 cm) at proctosigmoidoscopy. Earlier studies by Spencer *et al*. from the Mayo Clinic and by Atkin *et al*. from St. Mark's Hospital, London, indicated that patients who had one or two small polyps, most of which were simple tubular adenomas, had no increase in their subsequent risk of colorectal cancer compared to that of the average age-matched population (51, 52).

A related question is, What is the prevalence of right-sided advanced adenomas in patients found to have small adenomas at screening flexible sigmoidoscopy? Recent studies provide conflicting answers to this important question (53–57). Zarchy and Ershoff found that patients with small (<1 cm) tubular adenoma(s) on sigmoidoscopy had <1% occurrence of a proximal synchronous advanced adenoma (≥1 cm, or with villous or high-grade dysplastic histology) (53). Patients with advanced lesions on sigmoidoscopy had a >10% prevalence of proximal advanced lesions on colonoscopy. In contrast, Read *et al*., in a similar study, reported that proximal adenomas were found in 29% of patients with diminutive adenomas (≤5 mm), in 29% of patients with small adenomas (6–9 mm), and in 57% of patients with advanced adenomas at sigmoidoscopy (54). Advanced proximal adenomas were found in 7% of patients with distal adenomas that were <1 cm in diameter.

The reasons for these conflicting results are unclear. A paper published last year by Wallace *et al*. from Boston seems to confirm the findings of Zarchy and Ershoff (55). Of 90 patients with a single tubular adenoma 1–5 mm in the distal colon, 0% had an advanced proximal adenoma, compared with 5.4% of those who had multiple distal adenomas and 7.9% of those who had advanced distal polyps. These authors concluded that patients undergoing screening sigmoidoscopy who are found to have a single tubular adenoma of ≤5 mm may not benefit from colonoscopy.

In summary, the management of a patient found to have small tubular adenomas at flexible sigmoidoscopy must be individualized. Colonoscopy to look for synchronous adenomas, or for follow-up to search for metachronous neoplasia, may be of little benefit to most patients with only one or two small (<1-cm) tubular adenomas. Younger, healthy individuals may wish to have colonoscopy to reduce their risk of cancer even below that of the average-risk population. Older patients, especially those with significant comorbidity, may not benefit from an intensive evaluation or follow-up.

The Small Flat Adenoma

Many recent papers describe small flat colorectal adenomas with a purportedly high malignant potential (58). These reports suggest that such lesions are common, may be missed during conventional colonoscopy, and frequently and rapidly degenerate into small flat cancers. Most, but not all, of the papers reporting these lesions have come from Japan and other Eastern countries. They stress the need for special techniques employing dye-staining chromoendoscopy, with or without magnification, to accurately detect these lesions.

For three reasons, small flat adenomas with a high malignant potential seem to be rare in Western countries, and there is little evidence that they are being overlooked by experienced Western endoscopists. First, several large series of diminutive polyps in the United States report a uniformly low prevalence of high-grade dysplasia (59). For example, a careful pathological analysis of 572 adenomas ≤5 mm in diameter removed by expert colonoscopist investigators in the US National Polyp Study showed that only 0.9% contained high-grade dysplasia (60).

Second, in Western countries, the finding of a small adenoma does not identify patients with an increased risk of

metachronous cancer. Long-term follow-up of patients who had small polyps resected at proctosigmoidoscopy at both the Mayo Clinic and St. Mark's Hospital, London, showed that a patient with only a small tubular adenoma had no subsequent increased risk of colorectal cancer (51, 52). Lastly, the most compelling evidence that premalignant flat adenomas are not frequently overlooked in Western countries was reported by the US National Polyp Study (39). During 8400 person-years of follow-up after colonoscopic polypectomy, only five new cancers were detected in a group of 1418 adenoma patients. All five of the cancers were early invasive carcinomas in a polypoid adenoma. If small flat adenomas with appreciable malignant potential had been missed during colonoscopy, small flat cancers without associated benign adenomatous tissue should have been detected during this careful follow-up surveillance.

In summary, there is little evidence that early colonic cancer is a frequently overlooked entity in Western countries, provided that patients undergo colonoscopy by well trained, experienced endoscopists. Modern high-resolution video endoscopy seems to detect most clinically significant lesions without the need for special techniques such as chromoendoscopy with or without magnification. It is possible that early, *de novo* flat cancers are more prevalent in Eastern countries, where there is an appreciably lower incidence of colorectal neoplasia and a different combination of familial and environmental factors causing the disease. Also, a recent controlled study demonstrated that Eastern and Western expert pathologists use different histological criteria to diagnose invasive colorectal carcinoma (61).

MANAGEMENT OF LARGE SESSILE POLYPS

A patient who has had successful colonoscopic excision of a large sessile polyp (>2 cm) usually should undergo follow-up colonoscopy in 3–6 months to determine whether resection was complete. If residual polyp is present, it should be resected and the completeness of resection documented within another 3–6-month interval. If complete resection is not possible after two or three examinations, the good-risk patient should usually be referred for surgical therapy.

Large sessile polyps (>2 cm) usually contain villous tissue with a high malignant potential and tend to recur locally after resection (62). For technical reasons, many such lesions cannot be completely or safely excised during colonoscopy, and the patient should be referred for primary surgical resection. A patient who has had successful colonoscopic excision of a large sessile polyp usually should undergo follow-up colonoscopy 3–6 months later to determine whether resection was complete (63). If residual polyp is present, it should be removed and the completeness of resection documented within another 3–6-month interval. If complete resection is not possible after 2–3 examinations, the patient should usually be referred for surgical therapy.

MALIGNANT POLYPS

No further treatment is indicated after colonoscopic resection of a malignant polyp (an adenomatous polyp with cancer invading the submucosa) if the endoscopic and pathological criteria listed below are fulfilled. Patients with malignant sessile polyps with favorable prognostic criteria should have follow-up in about 3 months to check for residual abnormal tissue at the polypectomy site. After one negative result examination, the clinician can revert to standard surveillance as performed for patients with benign adenomas.

When a patient's malignant polyp has poor prognostic features, the relative risks of surgical resection should be weighed against the risk of death from metastatic cancer. The patient at high risk for morbidity and mortality from surgery probably should not have surgical resection. If a malignant polyp is located in that part of the lower rectum that would require an abdominal–perineal resection, local excision rather than a standard cancer resection usually is justified. Rectal ultrasound studies may assist in determining correct treatment. During colonoscopic excision of a large sessile polyp that may require subsequent surgical resection, it may be useful to mark the polypectomy site with India ink.

A malignant polyp is a neoplasm that contains cancer cells that have penetrated through the muscularis mucosal layer into the submucosa (64). Usually the term is used to describe an endoscopically resected polyp that initially seems benign but that, on histological analysis, contains invasive carcinoma. Questions that must be addressed when dealing with these lesions are: Does the patient require cancer surgery, or is colonoscopic polypectomy adequate treatment? Is the risk for local recurrence or lymph node metastasis greater than that of partial colectomy, or is it so small that no further treatment is indicated?

The risk for lymphatic spread from a malignant polyp has been estimated by histological study of resected specimens. Because lymphatics do not penetrate much beyond the muscularis mucosae, focal cancer that has not invaded through this layer seems to have little or no risk for lymph node spread (65). Prospective studies of patients with resected polyps containing such superficial carcinomas confirm that colonoscopic polypectomy is definitive therapy for these lesions (66). In one large series, lymph node metastasis occurred in about 10% of cases in which adenocarcinoma penetrated the muscularis mucosae into the submucosa layers (67). However, all of these cancers involving lymph nodes were poorly differentiated. Only 5–10% of all colorectal carcinomas are poorly differentiated.

In a large series of cases with malignant polyps, 60 patients were followed a minimum of 5 yr after resection or until death (68). Two patients with incompletely excised polyps developed local recurrence, and one patient with a poorly differentiated carcinoma developed lymph node metastasis. Therefore, if there is no evidence of high-grade

malignancy or incomplete excision in a properly processed specimen, simple polypectomy seems to be adequate treatment. A number of smaller series confirm these criteria (69–73). Some of these add the stipulation that lymphatic or vascular invasion in the polyp also requires surgery for definitive treatment. These series also indicate that cancer invasion of the stalk of a pedunculated polyp is not, by itself, a predictor of recurrent cancer as long as the margin of resection is not involved.

The risk for death from elective colonic resection averages about 2% and varies from 0.2% in young, healthy persons to >5% in elderly patients (74–76). An analysis of published series of malignant polyps estimated that the risk of residual cancer or nodal metastases from endoscopically resected pedunculated and sessile malignant polyps with favorable criteria was 0.3% and 1.5%, respectively (77). Another review of endoscopically resected polyps with poor prognostic factors (poorly differentiated cancer, margin involvement, or presence of lymphatic or vascular invasion) reported residual cancer in 8.5% and 14.4%, for patients with pedunculated and sessile malignant polyps, respectively (78).

In summary, the literature dealing with malignant polyps indicates a low risk for residual cancer when the criteria are favorable. Even with unfavorable criteria, the likelihood of death from cancer is low and must be weighed against the surgical risk of colectomy for each patient.

Recommendations for a Patient With a Malignant Polyp

Although these recommendations are not the result of controlled prospective trials, they are the product of considerable clinical experience and formal decision analysis. The risk for local recurrence or for lymph node metastasis from invasive carcinoma in a colonoscopically resected polyp is less than the risk for death from colonic surgery, and therefore the ACG recommends no further treatment if the following criteria are fulfilled:

1. The polyp is considered to be completely excised by the endoscopist and is submitted *in toto* for pathological examination.
2. In the pathology laboratory, the polyp is fixed and sectioned so that it is possible to accurately determine the depth of invasion, grade of differentiation, and completeness of excision of the carcinoma.
3. The cancer is not poorly differentiated.
4. There is no vascular or lymphatic involvement.
5. The margin of excision is not involved. Invasion of the stalk of a pedunculated polyp, by itself, is not an unfavorable prognostic finding, as long as the cancer does not extend to the margin of stalk resection.

Patients with malignant polyps with favorable prognostic criteria should have follow-up colonoscopy in 3 months to check for residual abnormal tissue at the polypectomy site if the polyp was sessile (79). After one negative follow-up examination, care can revert to standard surveillance as performed for patients with benign adenomas. Because the incidence of recurrent cancer is small, no other follow-up laboratory or imaging studies are indicated for these patients.

When a patient's malignant polyp has poor prognostic features, one should weigh the relative risks of surgical resection against the risk of death from metastatic cancer. The patient at high risk for morbidity and mortality from surgery should probably not have surgical resection. If a malignant polyp is located in that part of the low rectum that would require an abdominal-perineal resection, local excision rather than a standard cancer resection is usually justified. Rectal ultrasound may help to determine whether local excision is possible. Depending on the pathological features of the resected specimen, further treatment (for example, radiotherapy) may be indicated.

Tattooing the Polypectomy Site

When large sessile polyps are resected that may prove either not to be completely resectable colonoscopically or that might contain invasive carcinoma with unfavorable prognostic features, it is useful to mark the polypectomy site (80, 81). If surgery proves necessary, this tattooing procedure will assist the surgeon in locating the area to be resected. If surgery is to be performed employing laparoscopic techniques, such marking is essential unless the polyp is located in the cecum or rectum. Sterile carbon-particle India ink that does not contain excessive quantities of gelatin or preservatives, diluted 1:100 in normal saline, is injected through a long, stiff needle catheter. The injection usually is made tangentially at the base of a fold into the submucosa near the polypectomy site in at least two opposite quadrants. The stain is permanent and is easily identified by the surgeon from the serosal surface of the bowel.

PRIMARY PREVENTION OF COLORECTAL ADENOMAS

To prevent initial or recurrent colorectal adenomas, a diet that is low in fat and high in fruits, vegetables, and fiber is recommended. Normal body weight should be maintained, and smoking and excessive alcohol use should be avoided. Daily dietary supplementation with 3 g of calcium carbonate may reduce the recurrence of adenomas. Other chemopreventive measures (i.e., supplementation with aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), selenium, or folic acid), supported by indirect data, cannot yet be recommended pending the results of ongoing clinical trials showing both efficacy and a good risk–benefit ratio.

Patients who have had colonoscopic resection of a colorectal adenomatous polyp often ask if there is anything they can do to prevent recurrent polyps or cancer. Epidemiological and animal studies strongly implicate environmental factors, especially diet, as a cause of colorectal adenomatous polyps and cancer (82). Populations in high-incidence countries tend to consume a diet that is high in animal meat and total fat and is relatively low in fruits, vegetables, and fiber.

Excessive calorie intake leading to obesity also has been linked to the risk of developing colorectal neoplasia (83).

Evidence-based guidelines now recommend several primary preventive measures that an individual might take to improve health and reduce the risk of developing colorectal adenomas and cancer. The National Cancer Institute encourages Americans to eat a diet that is low in fat and high in fruits, vegetables, and fiber (84). Specifically, fat intake should not exceed 25–30% of total calories. The diet should contain both substantial varieties and amounts of fruits and vegetables (at least five servings per day). Total fiber intake by adults should equal 20–30 g per day. Although one recent long-term study employing dietary questionnaires in relatively young female nurses found no protective effect of total dietary fiber, a number of earlier studies suggest that regular consumption of wheat bran may be beneficial (85, 86). Total calorie intake should not exceed energy requirements so that normal body weight consistently is maintained.

Chemoprevention of colorectal cancer is defined as the use of a specific chemical compound to prevent, inhibit, or reverse carcinogenesis. Epidemiological and animal studies suggest that a number of vitamins, minerals, and drugs may be protective (87). These include the antioxidant vitamins (A, E, and C), folic acid, vitamin D and calcium, selenium, aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs), and hormonal replacement in postmenopausal women.

Indirect studies of chemopreventive agents often have been contradictory or inconclusive, and some of these compounds have undesirable side effects. Therefore, few specific recommendations to supplement the diet with potentially protective vitamins, minerals, or drugs can be made at this time, pending the results of ongoing controlled chemoprevention trials designed to show their efficacy and risk–benefit ratios. One recently completed multicenter trial showed that after resection of one or more adenomas, 19% fewer patients who took 3 g of calcium carbonate (1.2 g calcium) a day over 4 yr developed recurrent adenomas (88). The total number of recurrent adenomas was reduced by 24%. As the toxicity of this inexpensive supplement is minimal, and as it also may reduce the risk of osteoporosis, it now can be recommended to individuals with resected adenomas who wish to try to decrease their risk of recurrence.

In an earlier study, the same consortium of university centers failed to demonstrate a protective effect of supplementation with the antioxidant vitamins, A, E, and C (89). Similar completed controlled trials are needed before dietary supplementation with folate, selenium, or NSAIDs can be recommended to the American public. Although some risk reduction seems to result from postmenopausal hormone replacement in women, the effect is modest and seems to require long-term use to be effective. Although this may prove to be an added benefit for women who choose long-term replacement, it does not seem to be, by itself, a strong indication for this option (90).

Regular exercise that helps to maintain normal body weight has a number of important health benefits, including a reduction in the risk of developing colorectal neoplasia. Smoking and excessive alcohol use also have been linked to a higher risk for this disease and should be avoided for the same reasons (87).

SURVEILLANCE OF FAMILIES OF PATIENTS WITH ADENOMAS

Colonoscopic surveillance should be considered for first-degree relatives of adenoma patients, particularly when the adenoma was advanced or diagnosed before age 60 yr, or, in the case of siblings, when a parent also had colorectal cancer diagnosed at any age. When indicated, surveillance should be initiated 5 yr younger than the age of initial adenoma diagnosis, or at age 40 yr (whichever occurs first), and then at intervals of 3–5 yr, depending on findings.

A family history of colorectal cancer or adenomas identifies individuals who are at increased risk for colorectal cancer. The familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer syndromes, which are not addressed in this guideline, account for about 1% and 6% of all colorectal cancers, respectively. Recent studies also indicate that a sizable fraction of "sporadic" cancers and adenomas may also have an underlying inherited genetic cause (91).

A recent analysis from the National Polyp Study shows that some first-degree relatives of patients with adenomas have a substantially increased risk of colorectal cancer and may benefit from special surveillance (92). Parents and siblings of patients with adenomas diagnosed at any age had a relative risk of colorectal cancer of 1.78 compared with spouse controls. The relative risk for siblings of patients in whom adenomas were diagnosed before age 60 yr was 2.59. The relative risk of siblings of patients with adenomas diagnosed at any age, who also had a parent with a history of colorectal cancer diagnosed at any age, was 3.25. These findings were confirmed by a recent large study involving three university-based colonoscopy practices in New York City (93). Based on these new data, colonoscopy surveillance should be considered for first-degree relatives of adenoma patients, particularly when the adenoma was diagnosed before the age of 60 yr, or, in the case of siblings, when a parent also had colorectal cancer. When colonoscopic surveillance is indicated, it should be performed 5 yr younger than the age of initial adenoma diagnosis, or age 40 yr (whichever occurs first), and then at an interval of 3–5 yr, depending on findings.

POSTPOLYPECTOMY SURVEILLANCE

Complete colonoscopy should be done at the time of initial polypectomy to detect and resect all synchronous adenomas. Additional clearing examinations may be required after resection of a large sessile adenoma, or if (because of multiple adenomas or other technical reasons) the colonos-

copist is not reasonably confident that all adenomas have been found and resected.

After a complete clearing colonoscopy has been accomplished after an initial polypectomy, repeat colonoscopy to check for metachronous adenomas should be performed in 3 yr for patients at high risk for developing metachronous advanced adenomas. This includes those who at baseline examination have multiple (>2) adenomas, a large (≥1 cm) adenoma, an adenoma with villous histology or high-grade dysplasia, or have a family history of colorectal cancer.

Repeat colonoscopy to check for metachronous adenomas should be performed in 5 yr for most patients at low risk for developing advanced adenomas. This includes those who at baseline examination have only one or two small tubular adenomas (<1 cm) and no family history of colorectal cancer. Selected patients at low risk for metachronous advanced adenomas may not require follow-up surveillance.

After one negative follow-up surveillance colonoscopy, subsequent surveillance intervals may be increased to 5 yr. If complete colonoscopy is not feasible, flexible sigmoidoscopy followed by a double-contrast barium enema is an acceptable alternative. Follow-up surveillance should be individualized according to the age and comorbidity of the patient, and should be discontinued when it seems unlikely that follow-up is capable of prolonging quality of life.

In patients found to have a colorectal adenoma, the prevalence of synchronous polyps is 30–50% (40–42). Some of these polyps, especially those measuring <1 cm in diameter, will be missed on the initial colonoscopy (26, 27). Metachronous adenomas are reported in 20–50% of patients, depending on the follow-up surveillance interval used (94–98). The National Polyp Study found that the rate of adenoma detection 3 yr after initial adenoma resection was 32–42% (99). Recurrent adenomas were mostly small, tubular adenomas with low-grade dysplasia and therefore were of negligible immediate clinical significance. Only 3.3% of patients in each follow-up group had advanced adenomas (>1 cm, or with villous tissue or high-grade dysplasia) after 3 yr of follow-up.

A large series found no increased incidence of cancer in 751 patients after resection of small colorectal polyps (<1 cm) compared with that of the local community from which these cases originated (51). However, the relative risk for developing colon cancer was 2.7 times that of the average-risk population if the index polyps were ≥1 cm, and was increased 5-fold in patients who initially had multiple polyps (100). Another long-term follow-up study of 1618 postpolypectomy patients also found no increased risk for cancer in patients undergoing resection of single small (<1 cm) tubular adenomas, but an increased risk of 3.6 times in those with index adenomas that were large (≥1 cm) or contained villous tissue, and 6.6 times in patients with multiple adenomas on their original examinations compared with the known rates in the local community (52). Therefore, clearly some (but not all) patients with adenomas have a clinically significant risk for developing colorectal cancer and may benefit from postpolypectomy surveillance.

Most patients who have had resection of a colorectal adenoma, therefore, have some degree of increased risk for recurrent adenomas and subsequent cancer, and may benefit from long-term surveillance. The purpose of this surveillance is to detect and resect synchronous adenomas missed during the initial colonoscopy and all subsequent metachronous advanced adenomas, before they become malignant.

The appropriate frequency of surveillance was investigated by the National Polyp Study (99). Analysis of the age distribution and colonoscopic findings of patients evaluated for this study suggests that the average time it takes for an advanced adenoma to develop from a grossly normal-appearing colon is about 5 yr and for a gross cancer to develop is about 10 yr (6). This supports the concept of a long natural history of evolution of cancer through an intermediate adenoma stage and suggests that frequent surveillance is not necessary if accurate methods are used to detect developing neoplasia. In the National Polyp Study, colonoscopy performed 3 yr after initial colonoscopic removal of adenomatous polyps detected advanced adenomas as effectively as follow-up colonoscopy performed after both 1 and 3 yr. At 3 yr, only 3.3% of patients in each group had advanced adenomas.

Therefore, this landmark study initially recommended an interval of at least 3 yr before follow-up colonoscopy after resection of newly diagnosed adenomatous polyps. Further analysis of data from the National Polyp Study and data from more recent outcome studies of postpolypectomy surveillance, now indicate that it is possible to further stratify risk of recurrent advanced adenomas based on baseline features of each case (101–103). Patients with a relatively high risk of developing advanced adenomas during follow-up include those with multiple adenomas (>2), large adenomas (≥1 cm), or a first-degree relative with colorectal cancer. These patients still should undergo the first follow-up colonoscopy at 3 yr. Patients with a low risk of metachronous advanced adenomas include those with only one or two small adenomas (<1 cm) and no family history of colorectal cancer. For these patients, the first follow-up colonoscopy can be safely delayed until at least 5 yr. For older patients in the low risk category, especially those with substantial comorbidity, no follow-up may be indicated. Data from the National Polyp Study and from reported experiences with screening colonoscopy indicate that after a patient has had one negative follow-up colonoscopy, the subsequent surveillance intervals safely may be increased to 5 yr, or, for selected older patients with comorbid conditions, no further follow-up may be indicated (104, 105).

Cost Considerations

Because many clinicians perform postpolypectomy surveillance more frequently than needed, national adoption of these recommendations should reduce substantially the cost of postpolypectomy surveillance. Ransohoff *et al*. have es-

timated that resection of small tubular adenomas is unlikely to significantly reduce colorectal cancer morbidity or mortality (106). He 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 (<1 cm) tubular adenoma, is prohibitive. Based on his assumptions it would have cost, in 1991, $80,000–$300,000 per life saved for a surveillance program of colonoscopy every 3 yr for all 50-yr-old patients with small adenomas followed for 30 yr.

In a cost-effectiveness modeling analysis of colorectal cancer screening, Lieberman concluded that conventional postpolypectomy surveillance comprised 19–34% of the total cost of a screening program (107). According to his analysis, if surveillance focused only on the detection of advanced adenomas, this percentage cost could be reduced to 11–20%. One large practice in Minnesota consisting of 19 gastroenterologists tested this conclusion (108). Based on a comparison of 500 surveillance colonoscopies performed before and after implementation of a follow-up program designed to detect only advanced adenomas, they projected a substantial annual saving in facility and professional charges.

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Received and accepted July 26, 2000.

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