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

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ABSTRACT Patients with resected colorectal cancer are at risk for recurrent cancer and metachronous neoplasms in the colon. This joint update of guidelines by the American Cancer Society (ACS) and US Multi-Society Task Force on Colorectal Cancer addresses only the use of endoscopy in the surveillance of these patients. Patients with endoscopically resected Stage I colorectal cancer, surgically resected Stage II and III cancers, and Stage IV cancer resected for cure (isolated hepatic or pulmonary metastasis) are candidates for endoscopic surveillance. The colorectum should be carefully cleared of synchronous neoplasia in the perioperative period. In nonobstructed colons, colonoscopy should be performed preoperatively. In obstructed colons, double contrast barium enema or computed tomography colonography should be done preoperatively, and colonoscopy should be performed 3 to 6 months after surgery. These steps complete the process of clearing synchronous disease. After clearing for synchronous disease, another colonoscopy should be performed in 1 year to look for metachronous lesions. This recommendation is based on reports of a high incidence of apparently metachronous second cancers in the first 2 years after resection. If the examination at 1 year is normal, then the interval before the next subsequent examination should be 3 years. If that colonoscopy is normal, then the interval before the next subsequent examination should be 5 years. Shorter intervals may be indicated by associated adenoma findings (see Postpolypectomy Surveillance Guideline). Shorter intervals are also indicated if the patient's age, family history, or tumor testing indicate definite or probable hereditary nonpolyposis colorectal cancer. Patients undergoing low anterior resection of rectal cancer generally have higher rates of local cancer recurrence, compared with those with colon cancer. Although effectiveness is not proven, performance of endoscopic ultrasound or flexible sigmoidoscopy at 3- to 6-month intervals for the first 2 years after resection can be considered for the purpose of detecting a surgically curable recurrence of the original rectal cancer. (*CA Cancer J Clin 2006;56:160–167.*) *© American Cancer Society, Inc., 2006.*

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INTRODUCTION

Recommendations (Table 1) on the use of surveillance colonoscopy after resection of colorectal cancer were produced jointly by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society (ACS). They constitute the updated recommendations of both organizations. The rationale for combined guidelines by organizations is discussed in the accompanying joint recommendations on postpolypectomy surveillance. These guidelines were 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.

Table 2 summarizes the differences in these guidelines from previous guidelines on postcancer resection surveillance colonoscopy.

METHODOLOGY AND LITERATURE SEARCH

The literature search sought to identify randomized controlled trials and cohort studies in which patients with resected colorectal cancer and perioperative clearing of synchronous neoplasia by colonoscopy were followed to detect recurrent and/or metachronous neoplasms.

We searched the medical literature using MEDLINE (1966-January 17, 2005), the Cochrane Database of Systematic Reviews (fourth quarter 2004 update), and the Database of Abstracts of Reviews of Effects (fourth quarter 2004 update). In MEDLINE, subject headings for colorectal neoplasms were combined with subheadings and keywords for "surgery," "resection," "colonoscopy," "surveillance," and "follow-up" to identify relevant citations. Only studies published in the English language were included. Surveillance studies in patients with inflammatory bowel disease or hereditary nonpolyposis colorectal cancer (HNPCC) were specifically excluded. Keyword searches were also performed in the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects to identify any additional systematic reviews. In addition, a manual search was performed using references from retrieved reports, review articles, guidelines, meta-analyses, editorials, and textbooks of gastroenterology.

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TABLE 1 Postcancer Resection Surveillance Colonoscopy Recommendations

1. **Patients with colon and rectal cancer should undergo high quality perioperative clearing.** In the case of nonobstructing tumors, this can be done by preoperative colonoscopy. In the case of obstructing colon cancers, computed tomography colonography with intravenous contrast or double contrast barium enema can be used to detect neoplasms in the proximal colon. In these cases, a colonoscopy to clear the colon of synchronous disease should be considered 3 to 6 months after the resection if no unresectable metastases are found during surgery. Alternatively, colonoscopy can be performed intraoperatively.
2. **Patients undergoing curative resection for colon or rectal cancer should undergo a colonoscopy 1 year after the resection (or 1 year following the performance of the colonoscopy that was performed to clear the colon of synchronous disease).** This colonoscopy at 1 year is in addition to the perioperative colonoscopy for synchronous tumors.
3. **If the examination performed at 1 year is normal, then the interval before the next subsequent examination should be 3 years.** If that colonoscopy is normal, then the interval before the next subsequent examination should be 5 years.
4. **Following the examination at 1 year, the intervals before subsequent examinations may be shortened if there is evidence of hereditary nonpolyposis colorectal cancer or if adenoma findings warrant earlier colonoscopy.**[1]
5. **Periodic examination of the rectum for the purpose of identifying local recurrence, usually performed at 3- to 6-month intervals for the first 2 or 3 years, may be considered after low anterior resection of rectal cancer.** The techniques utilized are typically rigid proctoscopy, flexible proctoscopy, or rectal endoscopic ultrasound. These examinations are independent of the colonoscopic examinations described above for detection of metachronous disease.

TABLE 2 Differences between Current and Previous Guidelines on Postcancer Resection Surveillance Colonoscopy

In addition to careful perioperative clearing of the colorectum for synchronous lesions, a colonoscopy is recommended 1 year after surgical resection because of high yields of detecting early second, apparently metachronous cancers.
Clinicians can consider periodic examination of the rectum for the purpose of identifying local recurrence after low anterior resection of rectal cancer.

We excluded articles if there was no evidence of perioperative colonoscopic clearing or if a modality other than colonoscopy (flexible sigmoidoscopy, barium enema) was used for perioperative clearing.

A total of 66 studies were retrieved for detailed evaluation, and 43 were excluded: 26 because of incomplete perioperative colonoscopic clearing or because this was accomplished with modalities other than colonoscopy, 13 did not pertain to the focus of our paper, three were reports of work in progress that were published in final form in other studies included in our analysis, and one reported the preliminary results of an ongoing trial. The remaining 23 studies were included in our analysis.[2–24]

Evidence tables were created to summarize the studies and were circulated to members of the US Multi-Society Task Force and the ACS Colorectal Cancer Advisory Committee. The evidence was reviewed and recommendations developed at a joint meeting.

DISCUSSION OF EVIDENCE AND RATIONALE FOR THE RECOMMENDATIONS

Limitations in the Selected Studies

Some limitations were identified in interpreting the selected studies on postcancer surveillance colonoscopy literature.[2–24] For example, the term "metachronous cancer" had variable definitions. In some instances, it was based on the site of tumor appearance within the colon, and in others it was based on time after resection of the initial primary. Many studies made no mention of whether patients may have had hereditary nonpolyposis colorectal cancer. In some cohorts, there was incomplete follow up of patients. Surveillance intervals were different across studies. Some studies did not clearly separate metachronous tumors from anastomotic recurrences or anastomotic from local or regional recurrences. In some cases, there was also failure to report the stage of metachronous cancers and whether or not they were resectable for cure at the time they were diagnosed. In some studies, it was not clear whether colonoscopies were routine procedures in asymptomatic surveillance patients versus diagnostic procedures based on symptoms or laboratory findings. Colonoscopy completion rates and complication rates were commonly not reported, and there was also frequently lack of information on mortality rates. Despite these limitations, a number of clinically relevant trends are evident regarding colorectal cancer recurrence, metachronous cancer, and the utility of surveillance procedures in patients with resected colorectal cancer.

Candidates for Postcancer Resection Surveillance Colonoscopy

In general, patients who undergo surgical resection of Stage I, II, or III colon and rectal cancers, or curative-intent resection of Stage IV cancers are candidates for surveillance colonoscopy. Patients who undergo curative endoscopic resection of Stage I colon cancers are also candidates for surveillance colonoscopy. Patients with Stage IV colon or rectal cancer that is unresectable for cure are generally not candidates for surveillance colonoscopy because their chance of survival from their primary cancer is low, and the risks of surveillance outweigh any potential benefit.

Goals of Surveillance: Detection of Recurrent Cancer versus Metachronous Cancers and Adenomas

There are two fundamental goals of surveillance of patients with resected colon or rectal cancer. One goal is the detection of early recurrences of the initial primary cancer at a stage that would allow curative treatment. The second goal is detection of metachronous colorectal neoplasms. In regard to detection of recurrences of the initial primary cancer, serial measurements of carcinoembryonic antigen are widely used.[25] In addition, recent meta-analyses of randomized controlled trials suggest that annual chest x-rays and computed tomography (CT) scans of the liver can improve survival from the original primary cancer by early detection of surgically curable recurrences.[26] The roles of serial performance of serum carcinoembryonic antigen measurements, serial chest x-rays,

and CT scans of the liver are not reviewed here. Neither individual randomized controlled trials of intensive surveillance with colonoscopy[20] nor meta-analyses of these trials[26] have demonstrated a survival benefit from the original primary tumor by performing colonoscopy at annual or shorter intervals. The failure of surveillance endoscopic exams to improve survival from recurrent colorectal cancer appears to result from relatively low rates of anastomotic or intraluminal recurrence and the observation that anastomotic or intraluminal recurrences are generally associated with intraabdominal or pelvic disease that is unresectable for cure.[2–24,26,27] In summary, performance of annual colonoscopy for the purpose of detecting recurrent disease does not have an established survival benefit for patients with colorectal cancer. (However, as noted below, there is a rationale for surveillance of the rectum after resection of rectal cancer for the detection of local recurrence.) The primary goal of surveillance colonoscopy after resection of colorectal cancer is detection of metachronous neoplasms.

Distinguishing Rectal Cancer versus Colon Cancer Follow Up

Although there is no established benefit from endoscopic surveillance for the purpose of detecting early recurrences of the original cancer, in clinical practice many clinicians distinguish between rectal and colon cancer in this regard. The distinction is based on differences in the rates of local recurrence of rectal versus colon cancer. Specifically, in the case of colon cancer, recurrence at the anastomosis occurs in only 2% to 4% of patients.[2–24] Because the overwhelming majority of patients with endoscopically detected anastomotic recurrences in the colon are unresectable for cure, surveillance colonoscopy for this purpose generally should not be undertaken. On the other hand, local recurrence rates of rectal cancer can be 10 or more times higher.[28–33]

High recurrence rates of rectal cancer are partly a function of surgical technique and volume.[28–33] Specifically, recurrence rates below 10% have been consistently reported when patients are operated on by a technique called total mesorectal excision.[34–36] This technique involves sharp dissection of the rectum and its surrounding adventitia along the first plane outside the adventitia (the mesorectal fascia).[35,36] The technique can be performed using either an open or laparoscopic-assisted approach[37–40] and has been reported to allow higher rates of successful low anterior resection[40] and lower rates of postoperative sexual dysfunction in men.[41]

Local recurrence rates of rectal cancer can also be reduced by administration of chemotherapy and radiation therapy,[34] which have been most effectively administered in the neoadjuvant (preoperative) setting to patients with locally advanced disease. Patients with rectal cancer typically undergo preoperative staging, either by endoscopic ultrasound[42–44] or magnetic resonance imaging,[45–48] followed by neoadjuvant chemoradiation in selected patients.[49] The combination of neoadjuvant chemoradiation and resection by surgeons trained in total mesorectal excision has resulted in very low recurrence rates for rectal cancer.[34] Because local recurrence rates for rectal cancer across the United States are generally higher than those achieved in series utilizing total mesorectal excision, there is a rationale for performing periodic examinations of the rectum by rigid or flexible proctoscopy or endoscopic ultrasound. These techniques have not been shown to improve survival, and the only rationale for their use is high rates of local recurrence.

When colon or rectal cancer is resected endoscopically and surgical resection is not planned because of favorable histology[50] and/or increased surgical risk, a follow-up endoscopic examination to inspect and biopsy the resection site is reasonable.[51] The follow-up examination is considered standard in the case of a sessile malignant polyp removed by piecemeal resection.[1] These examinations are typically performed 3 to 6 months after the initial endoscopic resection.

Detection of Metachronous Neoplasms

A second potential benefit of surveillance colonoscopy is the detection of metachronous cancers at a surgically curable stage, as well as the prevention of metachronous cancers via

TABLE 3 Metachronous Cancers in Postcancer Resection Surveillance Colonoscopy Studies

Study	N	Colonoscopies	Metachronous CRCs (all)	Metachronous CRCs (within 24 months)	Dukes' A or B	Number Asymptomatic	Reoperation for Cure
Barillari[2]	481		12	6*	9	6†	7
Barrier[3]	61‡		0				
Carlsson[4]	129	546	1	0	NS	NS	NS
Castells[5]	199		0				
Chen[6]	231		4	0	NS	4	4
Eckardt[7]	212		0				
Granqvist[8]	390	600	12	7	5§	6§	10
Green[9]	3278		42	24	23	NS	NS
Juhl[10]	133	316	4	0	4	4	4
Khoury[11]	389	3889	2	1	NS	NS	NS
Kjeldsen[12]	597		10	NS	NS	8	8
Kronborg[13]	239	710	4	3	4	NS	4
Makela[14]	106		1	NS	NS	NS	1
McFarland[15]	74	237	0				
Obrand[16]	444		0				
Ohlsson[17]	53¶		0				
Patchett[18]	132		2	NS	NS	0	NS
Pietra[19]	207		1	NS	NS	NS	NS
Schoemaker[20]	325	733	8	5	5	1	NS
Skaife[21]	611	609**	5	1	NS	NS	NS
Stigliano[22]	322		5	0	NS	NS	NS
Togashi[23]	341	1570	22	9	17	NS	22
Weber[24]	75	197	2	1	2	NS	2
Total	9029	9407	137	57	69	29	62

*Paper states "more than one half" arose in first 24 months.
†Paper reports 46 combined local recurrences with metachronous tumors, of which 22 were asymptomatic; number calculated assumes similar proportion for metachronous cancers.
‡Subgroup who underwent perioperative colonoscopy.
§Paper reports 26 combined local recurrences with metachronous tumors, of which 10 were Dukes' A or B and 14 were asymptomatic; numbers calculated assume similar proportion for metachronous cancers.
¶Intensive surveillance subgroup (control group did not undergo routine colonoscopy).
**Two patients underwent barium enema for completion of incomplete colonoscopy.

identification and removal of adenomatous polyps. The incidence of metachronous cancers, the timing at which metachronous cancers occur, and the stage of these cancers at presentation or identification by surveillance colonoscopy should determine the optimal intervals for performance of surveillance colonoscopy directed toward metachronous disease. The evidence from published studies of postcancer resection surveillance in colonoscopy was reviewed to determine what these rates and timing of metachronous cancers are (Table 3). Limitations in interpretation of this literature were described above.

From 2% to 7% of patients with colorectal cancer have one or more synchronous cancers in the colon and rectum at the time of initial diagnosis.[3,4,13,24,52,53] From a practical perspective, it is impossible to differentiate whether apparent metachronous cancers appearing in the interval shortly after resection of colorectal cancer are true metachronous lesions or missed synchronous lesions. Provided that appropriate clearing of the colon is achieved in the perioperative period, all subsequently identified cancers are, for practical purposes, metachronous lesions.

Among 23 studies in which patients underwent perioperative clearing by colonoscopy, there were 9,029 patients in whom 137 apparent metachronous cancers developed.[2–24] Among studies in which the number of colonoscopies performed could be determined, 9,407 colonoscopies were performed to detect 60 metachronous cancers in 2,706 patients.[4,8,10,11,13,15,20,21,23,24] This is a rate of 157 colonoscopies per metachronous cancer detected, which compares favorably to the rate of prevalent cancers detected during screening colonoscopy. Thus, among four screening colonoscopy studies in patients age 50 and old-

TABLE **4** Additional Recommendations Regarding Postcancer Resection Surveillance Colonoscopy

1. These recommendations assume that colonoscopy is complete to the cecum and that bowel preparation is adequate.
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.[50]
3. Endoscopists should make clear recommendations to primary care physicians about when the next colonoscopy is indicated.
4. Performance of fecal occult blood test is discouraged in patients undergoing colonoscopic surveillance.
5. Discontinuation of surveillance colonoscopy should be considered in persons with advanced age or comorbidities (with less than 10 years of life expectancy), according to the clinician's judgment.
6. Surveillance guidelines are intended for asymptomatic people. New symptoms may need diagnostic workup.
7. Chromoendoscopy (dye-spraying) and magnification endoscopy are not established as essential to screening or surveillance.
8. Computed tomography colonography (virtual colonoscopy) is not established as a surveillance modality.

TABLE **5** Key Research Questions Regarding Surveillance of the Colorectum after Resection of Colorectal Cancer

1. What clinical, genetic, or biologic markers predict development of metachronous cancers (ie, stratify risk) in colorectal cancer patients without hereditary nonpolyposis colorectal cancer?
2. Are new colorectal cancers in the short-term interval after surgical resection true metachronous cancers or missed synchronous lesions?
3. Do follow-up procedures (flexible sigmoidoscopy, endoscopic ultrasound) after resection of rectal cancer improve any outcomes?
4. Should the treatment of rectal cancer (eg, neoadjuvant chemoradiation, total mesorectal excision) influence whether follow up for local recurrence is justified?
5. Should adjunctive testing (eg, immunochemical fecal occult blood testing) be added to colonoscopy in the surveillance of patients who have undergone resection of colorectal cancer?

er,[54–57] the number of colonoscopies needed to detect one invasive cancer was 135. Excluding reference 55, which was performed in male veterans, (a group expected to have higher prevalence of neoplasia), 156 colonoscopies were performed per invasive cancer detected in the remaining three studies.[54,56,57]

Among studies of post cancer resection surveillance colonoscopy, there were 57 metachronous cancers in the first 2 years after resection of the initial primary, with an incidence rate of 0.7% over this interval. This estimate is consistent with a review of tumor registries in Nebraska, which calculated an annual incidence for metachronous cancers of 0.35% per year.[58] When reported, 69 of 106 (65%) of metachronous cancers were Dukes' Stage A or B,[2,8–10,13,20,23,24] 29 of 52 (56%) were asymptomatic,[2,6,8,10,12,18,20] and 62 of 71 (87%) were operated for cure.[2,6,8,10,12–14,23,24] Taken together, these findings were considered sufficient to warrant a colonoscopy 1 year after resection or after the perioperative clearing colonoscopy for the purpose of identification of apparently metachronous colorectal neoplasms. The recommendation to perform a colonoscopy at 1 year does not diminish the need for high quality in the performance of the perioperative clearing examination(s) for synchronous neoplasms.

Alternatives to Colonoscopy for Surveillance

Colonoscopy is considered the test of choice for detection of metachronous neoplasms in the postcancer resection surveillance colonoscopy setting (Table 4). Double contrast barium enema was less sensitive than colonoscopy for large and small polyp detection after resection of adenomas.[59]

CT colonography has not been evaluated adequately in the surveillance setting, and results for polyp detection are quite mixed.[60–63] Guaiac-based fecal occult blood testing has been generally considered to have very low positive predictive value after clearing colonoscopy. This was confirmed for the first 5 years after colonoscopy in a recent large study.[64] Immunochemical fecal occult blood testing warrants additional evaluation as an adjunct to colonoscopy[65] in this setting. Fecal DNA testing[66] has not been evaluated for postcancer resection surveillance and is not recommended for this indication.

KEY RESEARCH QUESTIONS

There are a number of questions that cannot be fully addressed by currently available evidence. Some of these key research questions are listed in Table 5.

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