Diseases of the Colon & Rectum

Practice Parameters

Practice Parameters for the Surveillance and Follow-Up of Patients With Colon and Rectal Cancer

Prepared by
The Standards Practice Task Force
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The American Society of Colon and Rectal Surgeons is dedicated to assuring high quality patient care by advancing the science, prevention, and management of disorders and diseases of the colon, rectum, and anus. The Standards Committee is composed of Society members who are chosen because they have demonstrated expertise in the specialty of colon and rectal surgery. This Committee was created to lead international efforts in defining quality care for conditions related to the colon, rectum, and anus. This is accompanied by developing Clinical Practice Guidelines based on the best available evidence. These guidelines are inclusive, and not prescriptive. Their purpose is to provide information on which decisions can be made, rather that dictate a specific form of treatment. These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information about the management of the conditions addressed by the topics covered in these guidelines. It should be recognized that these guidelines should not be deemed inclusive of all proper methods of care or exclusive of methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of all of the circumstances presented by the individual patient.

INTRODUCTION FOR CLINICAL PRACTICE GUIDELINES

Each year approximately 148,000 new cases of colon and rectal cancer are diagnosed in the United States.[1] Of these cases, approximately 75 percent had disease that was entirely removed at the initial operation; therefore, approximately 110,000 patients per year will be eligible for postoperative follow-up. The types of tests to incorporate, the timing of these tests, and even whether to consider follow-up are all controversial issues.

The potential benefits of follow-up after colon and rectal cancer include improved overall survival, better monitoring of outcome, identification of other treat-

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able diseases found during follow-up, and greater psychologic support. These benefits must be carefully weighed against the potential negative physical, financial, and psychologic consequences of follow-up.

The following document examines the available literature and provides evidence-supported guidelines for colorectal cancer follow-up for physicians engaged in the care of patients with colorectal cancer. The source of the supporting literature was a Medline search (1966 through May 2002; parameters: human, English language; search terms: colon cancer, rectal cancer, or colorectal neoplasm and surveillance or follow-up). This search resulted in 2,599 articles. The titles of these articles were screened for relevance. Prospective, randomized, controlled trials, meta-analyses, and retrospective evaluations of randomized, controlled trials were given preference in developing these guidelines when such information was available.

Recommendation: Offering Follow-Up for Patients With Completely Resected Colorectal Cancer Is Justified (Evidence Level = I; Grade B)

There have been five single-institution, prospective, randomized, clinical trials of follow-up for patients with colon and rectal cancer (Table 1).[2–6] All of these studies compared intensive follow-up with a less intense strategy; in one case, the intense group was compared with almost no follow-up.[2] Two of these studies have examined the role of adding more tests while maintaining the same timing of follow-up visits.[4,5] Two studies have performed the same tests at differing intervals.[3,6] One study varied both timing and tests performed.[2] All five trials considered overall survival as the main outcome measure. The trials that considered the use of additional tests did not find an overall survival benefit for the group followed with the greater number of tests.[4,5] One of the two studies of timing found a survival advantage associated with more frequent follow-up.[6] The fifth trial considering both additional tests and more frequent timing did not identify a survival advantage for intense follow-up.[2] The majority of these trials seem to indicate no benefit for intensive follow-up; however, there are significant power and sample size issues with each of these studies.

Four meta-analyses have been performed that address the relationship between intensive follow-up and survival followed after resection for colorectal cancer (Table 2).[7–10] This method overcomes concerns raised in the individual studies regarding sample size and power, but raises new concerns about combining dissimilar follow-up programs into just two categories: intense or less intense. For example, the less intense follow-up program of the one study[5] would be considered an intense form of follow-up in another study.[3] In two of the meta-analyses, because of the paucity of randomized trials at the time of these studies, the authors chose to include nonrandomized studies. In the recent studies by Jeffery *et al.*[10] and Renehan *et al.*,[8] all five of the currently published randomized, controlled trials were included. Despite methodologic differences in each meta-analysis, all have identified a survival advantage for patients followed more intensely.[7–10]

The weight of these studies taken in aggregate supports a small but significant survival advantage for colorectal cancer follow-up. A number of additional factors will determine the appropriateness of follow-up in individual circumstances (*i.e.,* age, comorbidity, patient logistics, quality of life, and other factors).

Other potential end points for follow-up have been less extensively studied. Although several studies have attempted to address the issue of cost of follow-up, cost effectiveness has not been examined in the context of a prospective, randomized trial. Graham *et al.*11reported on the cost per resectable recurrence identified using 1995 Medicare reimbursement costs. They found that CEA was the cheapest option, costing $5,696 per recurrence; CXR cost $10,078 and colonoscopy $45,810 per recurrence. Similarly, Virgo and colleagues[12] reported on the potential variation in cost associated with follow-up as a function of the variability of follow-up intensity. Norum and Olsen[13] performed a theoretical cost-effectiveness analysis based on the recommended Norwegian Gastrointestinal Cancer Groups preferred follow-up strategy. This analysis found that the program was cost effective over a wide range of assumptions. It is unclear whether this analysis is generalizable to other economic situations or other follow-up strategies.

Little data exists concerning the effect of follow-up on patient health-related quality of life (HRQL) or the related topic of patient preference for follow-up. It has been suggested that follow-up may provide reassurance or provoke anxiety. Stiggelbout *et al.*[14] have attempted to address this question. They identified a cohort of patients and randomly interviewed patients one week before scheduled follow-up, two weeks

Table 1.
Prospective, Randomized Trials of Colorectal Cancer

Study	N	Stratification	Standard Arm	Study Arm[a]	Length of Follow-Up (yr)	Five-Year Survival (Study *vs.* Standard Arm)
Ohlsson *et al.*, 1995[2]	107	No	Written recommendations to leave fecal hemoglobin every third month for two years and then yearly, return for symptoms	**3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48, 60: Physical examination, rigid proctoscopy, CEA, AP, GGT, fecal hemoglobin, CXR; additionally endoscopy of anastomosis at 9, 21, 42, Complete colonoscopy at 3, 15, 30, 60, CT pelvis at 3, 6, 12, 18, 24**	6.8	75% *vs.* 67%
Makela *et al.*, 1995[4]	106	No	Follow-up office visits every three months for two years, then every six months for next three years, CBC, Hemoccult, CEA, CXR, and rigid proctoscopy at each visit if sigmoid or rectal tumor, barium enema each year	Follow-up office visits every three months for two years, then every six months for next three years; CBC, Hemoccult, CEA, CXR, and **flex sigmoidoscopy** at each visit if sigmoid or rectal tumor; **ultrasound every six months, CT and colonoscopy each year**	>5	59% *vs.* 54%
Kjeldsen *et al.*, 1997[3]	597	Dukes stage and tumor location (rectum, sigmoid, other)	60-, 120-, 180-month follow-up: history, examination, DRE, gynecologic examination, Hemoccult II, colonoscopy, CXR, hemoglobin, erythrocyte sedimentation rate, LFTS	Same tests at **6, 12, 18, 24, 30, 36, 48**, 60, 120, **150**, 180 months	310 patients >5	70% *vs.* 68%
Schoemaker *et al.*, 1998[5]	325	Dukes stage and location in the colon or rectum	Follow-up every three months for two years, thereafter every six months for five years; at each visit structured interview, CBC, LFTs, CEA, Hemoccult II	Follow-up every three months for two years, thereafter every six months for five years; at each visit structured interview, CBC, LFTs, CEA, Hemoccult II; **yearly CXR, CT scan, colonoscopy**	>5	78% *vs.* 72%
Pietra *et al.*, 1998[6]	207	No	Six-month interval for first year, then once a year; ultrasound, CEA at each visit, CXR, colonoscopy yearly	**Three-month interval for first two years, six-month intervals for three years,** yearly thereafter; ultrasound, CEA at each visit; CXR, colonoscopy and **CT yearly**	**Not stated**	**73% *vs.* 58%[b]**

CEA = carcinoembryonic antigen; AP = alkaline phosphatase; GGT = gamma glutamyl transpeptidase; CXR = chest x-ray; CT = computerized tomography; CBC = complete blood count; DRE = digital rectal examination; LFTs = liver function tests.

[a]Bold = differences between Standard Arm and Study Arm.

[b]$P < 0.02$.

Table 2.
Meta-Analyses of Follow-Up Studies

Study	Numbers and Types of Studies Included	N	Major Finding
Bruinvels *et al.*, 1993[9]	7 nonrandomized trials	3,283	+9.1% risk difference in favor of intense f/u when CEA used
Rosen *et al.*, 1998[7]	2 RCTs; 3 comparative cohort studies	2,005	1.16 relative survival rate at five years when Hx, PE, and CEA performed at least three times per year for first two years
	14 single-cohort studies	6,641	1.13 relative survival rate at five years when Hx, PE, and CEA performed at least three times per year for first two years
Jeffery *et al.*, 2002[10]	5 RCTs	1,342	OR = 0.67 for intensive f/u compared with less intense
Renehan *et al.*, 2002[8]	5 RCTs	1,342	Combined risk ratio 0.81 in favor of intensive follow-up

RCT = randomized, controlled trial; CEA = carcinoembryonic antigen; Hx = history; PE= physical examination; OR = odds ratio.

after the visit, or in the middle of two visits. Using a generic survey instrument (SF-20) they found no differences in HRQL based on the timing of these interviews. They also found patients had a strong preference for follow-up.[14] A second study reported by Kjeldsen *et al.*,[15] of a cohort from within a prospective, randomized trial, again found insignificant differences in HRQL based on intensity of follow-up. Patients who were followed more intensely had a greater confidence in the utility of follow-up.

Recommendation: Routine Office Visits Should Be Part of a Follow-Up Program for Patients Who Have Completed Treatment for Colon and Rectal Cancer (Level II, Grade A)

Symptoms are the first sign of recurrence for many patients with colorectal cancer. Even within carefully performed, randomized trials, 16 to 66 percent of patients were symptomatic at the time of the diagnosis of disease recurrence.[3,4] The lack of specific symptoms results in delays in evaluation and results in many of these patients having unresectable disease at the time of diagnosis. Studies suggest that despite the frequency with which symptomatic patients are identified, the minority of symptomatic patients have resectable disease: approximately 1.7 to 7 percent of all patients in follow-up have resectable disease identified on the basis of symptoms.[3,11,16] However, if routine office visits are given credit for the identification of these patients, the office visit becomes one of the single best means of identification of patients with resectable disease.

Data suggest that routine physical examination of the asymptomatic patient is rarely informative with respect to identification of resectable disease.[2,11,17] However, this is not the only potential role of physical examination of these individuals. Several studies have suggested an increased susceptibility to second neoplasms in patients surviving colorectal carcinoma.[18,19] The physician may take this as an opportunity to ensure that adequate screening for the most common secondary malignancies (breast, prostate, thyroid) also is performed.

Recommendation: Serum Hemoglobin, Hemoccult II, and Liver Function Tests (Hepatic Enzymes Tests) Should Not Be Routine Components of a Follow-Up Program (Level II, Grade A)

Few studies have specifically addressed the role of serum hemoglobin in the follow-up of patients with colorectal cancer. Graffner *et al.*[20] reported a series of 190 patients collected prospectively, 47 of whom developed recurrences, and in no case was recurrence identified by hemoglobin alone. Similarly, Peethambaram *et al.*[17] reported a series of 316 patients treated on various North Central Cancer Treatment Group adjuvant therapy protocols at the Mayo Clinic. Ninety-eight patients developed recurrences; only one of these was identified by an abnormal hemoglobin value (1 percent of recurrences or 0.3 percent of entire cohort). Although hemoglobin evaluations also were part of the follow-up strategy for the three randomized trials,[3–5] only in one study was the timing of hemoglobin studies different between the intense fol-

low-up and standard arms of the study. In this study, there was no difference in overall survival between the two follow-up strategies.[3]

The possible role of liver function tests (LFTs) in follow-up has been extensively studied. Several studies have identified the test characteristics of LFTs in this role; most have found positive predictive values of <10 percent.[20] In most series, gamma glutamyltranspeptidase (GGT) seems marginally more sensitive than alkaline phosphatase.[2,21,22] However, regardless of which enzyme was chosen this was still a poor test for identification of resectable disease; several series that have directly examined the role of LFTs in follow-up have found that far <10 percent of recurrences were identified by an elevated LFT and most commonly <1 percent.[2,16,17,23] The only randomized, controlled trial, in which LFTs were included in the intensive follow-up strategy and omitted in the comparison group, did not show an improvement in survival with intensive follow-up.[2] Based on the data currently available, only 2 to 3 patients per 1,000 followed will have potentially resectable disease identified by an elevation in LFTs.[16,17]

The role of fecal occult blood testing also has been extensively evaluated in the follow-up of patients with colorectal cancer. Fecal occult blood testing with Hemoccult II was usually performed in the context of an office visit.[3–6,24,25] This test is potentially capable of identifying both local recurrences (if an intraluminal component exists) and metachronous disease. Studies have suggested that this test will be positive in approximately 10 to 30 percent of recurrences and a similar percentage of metachronous lesions.[20,24,25] Abnormalities in fecal hemoglobin are, however, infrequently an early sign of recurrent disease. Fecal hemoglobin testing results in the identification of a resectable recurrence in 0 to 9 per 1,000 patients followed with this test.[2,17,20,25]

Recommendation: Carcinoembryonic Antigen Should Be Used as a Part of Follow-Up for Colorectal Cancer; the Use of Other Tumor Markers Remains Experimental (Level II, Grade B)

Carcinoembryonic antigen (CEA) has been used in colorectal cancer follow-up for more than 30 years. More information exists concerning CEA than any other test used in follow-up. Most studies have indicated that a CEA level >5 ng/ml has a positive predictive value of 70 to 80 percent for recurrent disease.[20,26,27] Also, CEA often is the first indicator of disease recurrence. Most series suggest that CEA is the first abnormal test in 38 to 66 percent of disease recurrences.[2,4,11,20,26,27] The typical lead-time between CEA elevation and the identification by other tests is four to six months.[2,26,28,29] Lower cutoff points for beginning a diagnostic workup have resulted in increased sensitivity, but this comes at the expense of specificity.[27,30,31] Several articles have indicated that CEA sensitivity will vary with the site of disease recurrence.[20,26,27] Moertel *et al.*,[27] for example, has found CEA 78 percent sensitive for liver metastases, but only 42 and 45 percent sensitive for lung metastases and local recurrences respectively.

The optimal timing of CEA measurement has not been determined. One single institution study has suggested an increased disease-free survival from 10 to 33 percent if CEA was measured at 1-month to 2-month intervals compared with longer intervals.[32] These results have not been confirmed by other studies nor has any single study identified a survival advantage relative to the performance of CEA evaluation at any frequency. One randomized, controlled study has included CEA determination as a part of intense follow-up and not in the standard follow-up arm of the study. This study failed to show a survival advantage for the intensely monitored group.[2] However, three meta-analyses have suggested that intensive follow-up as defined by the frequency of follow-up visits and CEA determinations leads to a significant survival advantage.[7–9]

Although no study to date has shown a survival advantage attributable to CEA, examination of individual studies that have used follow-up records from large, multi-institutional, colon cancer adjuvant therapy trials as the source of data suggest that at least 3 to 5 per 100 patients subjected to follow-up will have resectable, recurrent disease identified through elevated CEA.[11,16,27] These numbers probably underestimate the potential benefit, because in each of these series, CEA was used in the follow-up of only 62 to 84 percent of patients.[11,16,27]

Few comparisons of differing algorithms to evaluate elevations in CEA have been performed to this point. Regardless of how often CEA is checked or the cutoff used to separate normal and abnormal values, once an elevation is identified expert opinion suggests that the first step should be confirmation of the elevation with a second level before embarking on a more intensive workup, because false-positive elevations have been reported in 7 to 16 percent.[26,27]

A large number of tumor markers in addition to CEA are currently undergoing evaluation. Although many have shown prognostic importance, none have been extensively evaluated enough in the context of follow-up to be recommended.[33,34] Therefore, use of additional tumor markers should be considered experimental at this time.

Recommendation: There Is Insufficient Data To Recommend for or Against CXR as Part of Routine Colorectal Cancer Follow-Up (Level II, Grade C)

The role of chest radiography (CXR) in the evaluation of patients after treatment for colon and rectal cancer has received a moderate amount of study. Three reviews of large series of colon adjuvant therapy trials have suggested that performance of CXR leads to the identification of resectable disease in 0.9 to 1.9 percent of those followed.[11,16,17] It must be emphasized that these trials included only patients with colon cancer. Similar series evaluating the role of CXR in patients with rectal cancer would likely result in a higher percentage of patients deriving benefit because of the higher likelihood of lung metastases in the population with rectal cancer. Three, prospective, randomized trials that included both colon and rectal cancer patients have suggested that resectable disease can be identified in 1.8 to 12 percent of patients through the use of CXR.[2,4,5] Although no study has compared differences in overall survival based on the use of CXR, it seems that there may be some benefit to its inclusion in follow-up. Further studies are needed to define the role of CXR in follow-up for colorectal cancer.

Recommendation: Routine Use of Hepatic Imaging Studies in the Follow-Up of Colorectal Cancer Should Not Be Performed (Level II, Grade B)

Few studies have been performed that have evaluated the role of routine liver imaging in the follow-up of colon or rectal cancer. A recent prospective cohort study by Howell *et al.*[35] found that annual CT scan detected 21 of 24 liver metastases in the asymptomatic state. Unfortunately, this strategy led to resection of disease in only 2 of 157 (1.3 percent) patients followed in this manner. Two randomized trials that included abdominal CT or abdominal CT and ultrasound have been published. Makela and colleagues[4] reported 6 of 22 (27 percent) metastases in the group followed with intensive tests were identified by abdominal CT or ultrasound. However, this apparently did not lead to any attempted resections. Schoemaker and colleagues[5] found that routine abdominal CT led to a highly significant increase in the detection of asymptomatic recurrences (60 percent were identified by this technique in the asymptomatic state compared with none in the standard follow-up arm). Despite the marked difference in the rate of identification of asymptomatic liver metastases by CT scan, there was not a difference in hepatic resection rates between those undergoing routine CT and those not. In 3 of 167 patients (1.8 percent), CT scan led to the resection of asymptomatic liver disease, whereas 4 symptomatic patients in the standard arm underwent liver resection. This implies that the screening tests used in the standard follow-up arm collectively provided the same information as routine CT scan with respect to identifying resectable liver recurrences (these tests included CEA and LFTs).[5] Because of the cost of CT and the probable overlap with CEA, CT should not be used routinely in follow-up.

There is no data currently available that address the role of monoclonal antibody or positron emission tomography scans as first-line studies in the follow-up of colon and rectal cancer patients. Both of these studies have been extensively studied concerning their role in follow-up of other abnormal tests (usually CEA elevations; the source of which has eluded conventional work up).[36–39] Neither has, however, been evaluated as a first-line test for patients undergoing routine follow-up.

Recommendation: Periodic Anastomotic Evaluation Is Recommended for Patients Who Have Undergone Resection/ Anastomosis or Local Excision of Rectal Cancer (Level III, Grade B)

The rate of anastomotic recurrence after colon cancer resection is too low to justify routine visualization.[40] There have, however, been authors and expert panels who have suggested that surveillance may play a role in rectal cancers because of the higher rates of local recurrence associated with tumors in this location, especially in patients with AJCC II or III disease if combined chemotherapy and radiation therapy were not performed.[41,42] There have been two, prospective, randomized trials that have considered the role of anastomotic visualization/imaging after low

anterior resection. Ohlsson and colleagues[2] visualized the anastomosis of such patients at 9, 21, and 42 months postoperatively. In addition, full colonoscopy also was performed for these patients at 3, 15, 30, and 60 months. This combination of studies identified one anastomotic recurrence among 53 patients, 19 of who had rectal cancer.[2] Makela *et al.*[4] used flexible sigmoidoscopy at each office visit if the patient had rectal or sigmoid cancer in addition to yearly colonoscopy. They found 1 local recurrence of 52 patients (33 of whom had rectal or sigmoid cancers) by this combination of procedures.[4] In neither study were increased absolute numbers or increased percentage of resectable anastomotic recurrences identified through heightened surveillance. However, these studies are too small to definitively comment on the benefit of intraluminal surveillance.

Because most local recurrences occur as a result of positive circumferential margins at the time of the original resection, recurrent disease most often begins extraluminally, limiting the utility of routine intraluminal evaluation. Endorectal ultrasound (EUS), which can image the adjacent tissues in the pelvis, may be of greater benefit than traditional intraluminal evaluations. The role of EUS in the follow-up patients with colorectal/anal anastomosis is currently being evaluated in a number of centers.[43–45] Studies of the test characteristics of EUS taken collectively have suggested that EUS has a positive predictive value of 42 to 100 percent and negative predictive value of 90 to 99 percent.[43–45] One study has suggested that EUS identifies tumor recurrence at earlier points than is available with conventional imaging, leading to a greater percentage of resectable recurrences and increased survival compared with local recurrences found by conventional means.[43] These early results will need to be confirmed in larger multi-institutional clinical trials.

Recommendation: Data Concerning Proper Timing of Office Visits, CEA, and CXR Is Insufficient To Recommend One Particular Schedule of Follow-Up Over Another; However, Office Visits and CEA Evaluations Should Be Performed at a Minimum of Three Times Per Year for the First Two Years of Follow-Up (Level II, Grade A)

The natural history concerning the timing of recurrent and metastatic disease has been well documented.[29,40] The majority of recurrences or metastases from colon and rectal cancer occur during the first two years of follow-up. Most follow-up strategies attempt to take advantage of this by planning more intensive follow-up during this period of maximal risk. This may represent a flawed strategy, because several trials have suggested lower resection and survival rates in patients whose disease is detected within the first year of follow-up.[16,17]

Two studies have directly attempted to address the question of frequency of follow-up. Tornqvist *et al.*[46] reported the results of two prospectively followed cohorts of patients, one whom was followed yearly and a second followed more often. In both cohorts, the same tests were used. They found no differences in detection rate or outcome based on timing.[46] A second, more recent trial was reported by Kjeldsen and colleagues.[3] In this prospective, randomized trial, patients were randomized to receive examination at 6-month intervals for 3 years and then 12-month intervals through Year 5 or just follow-up at 5 years. The tests performed at each visit were the same regardless of timing. This study found no difference in overall survival between these two strategies.[3] Notably, this study did not include CEA evaluations. Timing also has indirectly been evaluated in the context of a meta-analysis. Rosen and colleagues[7] found that when patients were seen at least three times per year for two years, with at least history, examination, and CEA, they had a statistically significant improvement in survival compared with patients followed less often or with other tests.[7]

The majority of studies reported have used a similar strategy with respect to timing with tests being performed every 3 months for the first 2 years followed by every 6 month testing through Years 3 and 4 and annually thereafter.[4,6] This also is the pattern most commonly used in practice across the United States.[47,48] Because of the lack of a direct comparison of this approach with any other, there is insufficient data to comment on whether this constitutes the optimal timing of follow-up visits and tests.

Recommendation: Complete Visualization of the Colon Should Be Performed if Practical in All Patients Being Considered for Colon or Rectal Cancer Resection; Posttreatment Colonoscopy Should Be Performed at Three-Year Intervals (Level III, Grade A)

Several studies have suggested that preoperative colonic clearance is preferable to postoperative clear-

ance.[41,49,50] However, if not performed preoperatively or intraoperatively because of obstruction, perforation, or other factors preclude complete evaluation of the colon, colonic evaluation should be performed within six months postoperatively.

The main goal of colonoscopy in colorectal cancer follow-up is to identify metachronous cancers and polyps. These are both difficult goals because the development of metachronous cancers and polyps may occur during an extended period of time. Goldberg *et al.*[16] reported on a large series of patients who had been accrued and followed in the context of Intergroup 0035 (a prospective, randomized, colon cancer adjuvant therapy trial). Endoscopic surveillance was to be performed *via* proctoscopy/barium enema or colonoscopy at 24 and 48 weeks and then annually. At a median follow-up of seven years, 24 patients (1.9 percent) had developed metachronous colorectal cancers. Routine bowel surveillance identified nine of these patients. Based on their retrospectively evaluated series of patients, Cali and colleagues[51] have estimated the risk of metachronous cancer development at 0.35 percent per year of follow-up. Metachronous polyp development may occur significantly more often and more rapidly; Chen and Stuart[52] reported a >50 percent rate of development of metachronous adenomas within five years of surgery.

Three, prospective, randomized trials have included regular colonoscopy as a part of intensive follow-up.[2,4,5] Ohlsson *et al.*[2] performed four colonoscopies during five years (at 3, 15, 30, and 60 months) for patients in the intensive surveillance arm of their study. At a median follow-up of 6.8 years, no patient in the intensive surveillance arm had developed metachronous cancer. Makela and colleagues[4] reported that after five years, among 52 patients undergoing yearly colonoscopy, one patient (1.9 percent) was diagnosed with metachronous cancer and nine patients (17 percent) developed adenomatous polyps. Schoemaker *et al.*[5] reported detection of three metachronous cancers among 167 patients (1.8 percent) followed for more than five years with yearly colonoscopy. Only one of these individuals was asymptomatic. This group also reported detection and removal of a greater number of adenomatous polyps in this same group of patients. The number of individual patients who developed polyps was not given.[5] These studies taken together suggest a limited benefit to colonoscopy within the first five to seven years after surgery with respect to the identification of metachronous cancer. Although these trials suggest a marginal benefit to the performance of colonoscopy, each of these studies addresses risk only during the study period. It is highly likely that the period of risk for the development of metachronous disease is lifelong and cumulative. Colonoscopy performed less frequently but during a longer period may prove more beneficial.

The benefit of removing adenomatous polyps has been studied in the context of screening average risk populations and has been found to be worthwhile. The recommended interval for colonoscopy for purposes of screening is currently every ten years.[53] Patients who have previously been treated for colon or rectal cancers seem to be at higher risk for developing metachronous polyps and cancers and therefore would represent a population even more likely to benefit from colonoscopy than a screening population. Because of the increased rate of polyp formation in the posttreatment population, increasing the frequency of colonoscopy seems warranted. The National Polyp Study has suggested that a three-year interval between colonoscopies is as efficacious as a colonoscopy at both one-year and three years after removal of an adenomatous polyp.[54] Extrapolation of this data to subgroup of patients undergoing follow-up justifies colonoscopy at least at three-year intervals.

The utility of early follow-up colonoscopy one year after surgery compared with delaying colonoscopy until three years after surgery has not been defined. Identification of the starting point and most appropriate interval for the performance of colonoscopy in the population of patients undergoing follow-up for colorectal cancer remain important questions for future studies. Although controversial, follow-up for patients with completely resected colon or rectal cancer is justified based on small but significant survival advantages identified in meta-analysis of randomized, controlled trials. However, significant gaps in our knowledge exist, including the impact of follow-up on cost, quality of life, and patient satisfaction. Significant questions also remain concerning the proper tests to use, the timing of these tests, and how follow-up should be tailored to account for patient life expectancy, access, and comorbid issues. As diagnostic and treatment options for recurrent or metastatic disease multiply and improve, these questions will become increasingly important. Well-designed and executed, prospective, randomized, clinical trials are needed to further our knowledge in this field.

Appendix A.
Levels of Evidence

Level I:	Evidence from properly conducted randomized, controlled trials
Level II:	Evidence from controlled trials without randomization or Cohort or case-control studies or Multiple time series, dramatic uncontrolled experiments
Level III:	Descriptive case series, opinions of expert panels

Appendix B.
Scale Used for Evidence Grading

Grade	Explanation
A	High-level (level I or II), well-performed studies with uniform interpretation and conclusions by the expert panel.
B	High-level, well-performed studies with varying interpretations and conclusions by the expert panel.
C	Lower level evidence (level II or less) with inconsistent findings and/or varying interpretations or conclusions by the expert panel.

Appendix C.
Summary Guidelines for Posttreatment Follow-Up of Patients With Colorectal Cancer

Recommendation	Level of Evidence	Grade of Evidence
Offering follow-up for patients with completely resected colorectal cancer is justified.	Level I	Grade B
Routine office visits should be part of a follow-up program for patients who have completed treatment for colon and rectal cancer.	Level II	Grade A
Carcinoembryonic antigen should be used as a part of follow-up for colorectal cancer. The use of other tumor markers remains experimental.	Level II	Grade B
Periodic anastomotic evaluation is recommended for patients who have undergone either resection/anastomosis or local excision of rectal cancer.	Level III	Grade B
The data concerning proper timing of office visits, CEA, and anastomotic visualization for patients with rectal cancer, are insufficient to recommend one particular schedule of follow-up over another, however, office visits and CEA evaluations should be performed at a minimum of 3 times per year for the first two years of follow-up.	Level II	Grade B
Complete visualization of the colon should be performed if practical in all patients being considered for colon or rectal cancer resection Posttreatment colonoscopy should be performed at three-year intervals.	Level III	Grade A
There is insufficient data to recommend for or against CXR as part of routine colorectal cancer follow-up.	Level II	Grade C
Serum hemoglobin, Hemoccult II, and liver function tests (hepatic enzymes tests) should not be routine components of a follow-up program.	Level II	Grade A
Routine use of hepatic imaging studies in the follow-up of colorectal cancer should not be performed.	Level II	Grade B

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