Post-treatment surveillance after colorectal cancer treatment

AUTHORS: Beverly Moy, MD, MPH, Brian C Jacobson, MD, MPH
SECTION EDITORS: Kenneth K Tanabe, MD, Richard M Goldberg, MD
DEPUTY EDITOR: Sonali M Shah, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Sep 2023.**
This topic last updated: **Apr 24, 2023.**

INTRODUCTION

Colorectal cancer (CRC) is a common malignancy. Despite receiving potentially curative primary therapy, more than 40 percent of patients who present with stage II or III disease (table 1) will experience disease recurrence. (See "Adjuvant therapy for resected stage III (node-positive) colon cancer" and "Adjuvant therapy for resected rectal adenocarcinoma in patients not receiving neoadjuvant therapy" and "Neoadjuvant therapy for rectal adenocarcinoma".)

There has been and continues to be considerable variability among physicians in the use of follow-up studies after potentially curative resection of CRC and in the guidelines from major societies and expert groups. Multiple surveillance strategies have been published at costs ranging from a few hundred to several thousand dollars per patient.

Intensive postoperative surveillance programs have been justified in the hope that early detection of asymptomatic recurrences will increase the proportion of patients who are potentially eligible for curative therapy. A survival benefit from such an approach has in fact been shown in several meta-analyses. Furthermore, periodic imaging can detect early, potentially resectable recurrences.

This topic review will cover the rationale for intensive post-treatment surveillance in the first five years after treatment, data on the effectiveness of various surveillance strategies, and current recommendations for post-treatment surveillance in patients with resected CRC, including

recommendations from expert groups. Recommendations for secondary prevention (dietary modification, exercise, use of aspirin and other nonsteroidal anti-inflammatory drugs) and management of long-term CRC survivors are discussed separately. (See "The roles of diet, physical activity, and body weight in cancer survivors" and "Adjunctive therapy for patients with resected early stage colorectal cancer: Diet, exercise, NSAIDs, and vitamin D", section on 'Aspirin and other NSAIDs' and "Approach to the long-term survivor of colorectal cancer" and "Adjuvant therapy for resected stage III (node-positive) colon cancer", section on 'Adjunctive therapy' and "Adjunctive therapy for patients with resected early stage colorectal cancer: Diet, exercise, NSAIDs, and vitamin D".)

STAGE II AND III DISEASE

The vast majority of studies exploring the benefits of post-treatment surveillance have been conducted in patients with resected stage II or III disease. We recommend intensive postoperative surveillance for patients with resected stage II or III colorectal cancer (CRC) (table 1) who would be considered candidates for aggressive treatment, including curative-intent surgery:

- A clinical encounter with a physician every three to six months for the first three years and every six months during years 4 and 5.
- Serum carcinoembryonic antigen (CEA) level at each follow-up visit for at least the first three years.
- Annual computed tomography (CT) of the chest, abdomen, and pelvis for at least three years.
- Perioperative full colonoscopy to detect synchronous lesions, then a repeat colonoscopy one year later to exclude new lesions, and if normal, subsequent follow-up intervals of three to five years depending on the results of the prior colonoscopy.
- For patients with rectal cancer who have undergone low anterior resection and who have not received pelvic radiation therapy (RT), we suggest flexible proctosigmoidoscopy every six months for three to five years.

Rationale for intensive surveillance — The purpose of surveillance after definitive therapy of colon and rectal cancer is early identification of those patients who might potentially be cured by further surgical intervention and to screen for second primary cancers and polyps.

Increasing amounts of data support the view that early diagnosis of recurrent disease results in a more favorable outcome.

Intensive postoperative surveillance programs have been justified in the hope that early detection of asymptomatic recurrences will increase the proportion of patients who are potentially eligible for curative therapy. Although individual randomized trials do not demonstrate a survival benefit, meta-analyses suggest a modest but significant survival benefit from intensive surveillance after resection of CRC.

Does early detection of recurrent disease improve survival? — An important clinical question that arises when considering the debate over appropriate surveillance after treatment of primary CRC is whether early detection of recurrent disease improves survival. Reresection can cure some patients who have a limited localized recurrence. (See "Treatment of locally recurrent rectal adenocarcinoma" and "Overview of the management of primary colon cancer", section on 'Management of locally recurrent disease' and "Surgical resection of primary colon cancer", section on 'Locoregional recurrence'.)

Surgery has curative potential for some patients with limited sites of metastatic disease, particularly involving the liver and lung. Five-year survival rates approaching 40 percent have been reported in patients undergoing partial hepatectomy for limited hepatic metastases (table 2). (See "Potentially resectable colorectal cancer liver metastases: Integration of surgery and chemotherapy".)

Although isolated lung metastases are less common than liver involvement, metastasectomy has also been used to treat carefully selected patients with lung metastases, with five-year survival rates of 35 to 45 percent. (See "Surgical resection of pulmonary metastases: Outcomes by histology" and "Surgical resection of pulmonary metastases: Benefits, indications, preoperative evaluation, and techniques".)

Studies show that patients with asymptomatic rather than symptomatic recurrences are more likely to be eligible for potentially curative resection, they are more likely to have completely resected disease at re-exploration, and they have significantly better progression-free and overall survival rates after such surgery [1-4]. This was shown in a meta-analysis that included 4055 patients with resected stage I, II, or III CRC who were enrolled in 11 trials comparing intensive follow-up (history and physical examination with serum, radiologic, and endoscopic tests; the intensive group) with minimal/no follow-up (the control group) [4]. Intense follow-up was associated with a significantly higher probability of detecting asymptomatic disease recurrence (RR 2.59, 95% CI 1.66-4.06), of curative-intent surgery at recurrence (RR 1.98, 95% CI 1.51-2.60), and of all-cause (but not disease specific) survival after tumor relapse (RR 2.13, 95%

CI 1.24-3.69). Issues surrounding post-treatment surveillance for patients with resected stage I disease are discussed below. (See 'Stage I disease' below.)

However, it must be emphasized that symptomatic recurrences are not necessarily beyond the potential for curative treatment. In a review of the Eastern Cooperative Oncology Group's experience with recurrent colon cancer, 25 percent of ultimately resectable recurrences were symptomatic at presentation [5].

Intensive versus less intense surveillance strategies — We recommend intensive postoperative surveillance for most patients with resected stage II or III CRC (table 1) who would be considered candidates for curative-intent surgery. This recommendation is consistent with current published guidelines for post-treatment surveillance from most expert groups, including the American Society of Clinical Oncology (ASCO), Cancer Care Ontario, the European Society for Medical Oncology (ESMO), and the National Comprehensive Cancer Network (NCCN) (table 3) [6]. However, new data may lead to updated recommendations from various professional organizations supporting less intense surveillance.

The benefit of a more intensive, versus less intensive, post-treatment surveillance strategy continues to be debated. Overall, 6 of 13 randomized trials [7-19] support a modest but significant overall survival benefit for intensive post-treatment surveillance following potentially curative resection of CRC.

Multiple meta-analyses have addressed the role of more, versus less, intense surveillance after CRC resection [4,20-26]. The most recent Cochrane analysis on this issue [25] found that salvage surgery with curative intent was more frequent with intensive surveillance (risk ratio 1.98, 95% CI 1.53-2.56), but this did not appear to translate into a survival advantage. However, intensive surveillance was defined in various ways among the studies included in the Cochrane analysis, and some of the less intensive protocols were completely in line with the current guidelines and recommendations discussed herein. As an example, annual colonoscopy for five years was considered intensive, while colonoscopy at one and four years postresection was considered less intensive. Likewise, measurement of CEA every two months for three years, followed by every three months for two years, was considered intensive, while measurement of CEA every three to six months for three years, followed by every 12 months for two years, was considered less intensive. Moreover, the authors of the Cochrane review concluded that ongoing studies are still needed, owing to the ongoing advances in imaging and surgical technique, and the evolving use of adjuvant therapies.

The specific follow-up strategy — The best follow-up strategy (specific tests and inter-test interval) is not established, in part because of the wide variation in follow-up programs in the

randomized trials [27]. Furthermore, many studies included patients with stage I disease whose outcome is extremely favorable, further limiting the ability to detect a difference in outcome between the more and less intensively followed groups.

Nevertheless, the available guidelines suggest using serial CEA assay and periodic CT scanning for three to five years after resection:

- The contributions of serial CEA assay and periodic CT scanning were addressed in a trial conducted in the United Kingdom in which 1202 patients with stages I, II, or III resected CRC were randomly assigned to post-treatment follow-up with CEA "alone" (every three months for the first two years then every six months for three years, combined with a single CT scan at 18 months), CT alone (every six months for two years, then annually for three years), both tests, or minimal follow-up (follow-up testing only for symptoms) [16]. With a mean follow-up period of 4.4 years, two-thirds of recurrences were detected by a scheduled follow-up investigation. Of the 71 patients with a recurrence that was surgically treated with curative intent (5.9 percent of the total), rates were three to four times higher in each of the three more intensive surveillance groups (6.7, 8.0, and 6.6 percent, respectively for CEA "alone," CT alone, and a combined approach), compared with only 2.3 percent in the minimum follow-up group. There was no evidence for an additive effect of combined CEA assay and CT scanning, although patients in the CEA "only" arm also received a single CT scan at 18 months. Despite the higher rates of potentially curative surgery for recurrent disease, the number of deaths was not significantly different in the intense monitoring group versus the minimal follow-up group (18.2 versus 15.9 percent, respectively, difference 2.3 percent, 95% CI -2.6 to 7.1 percent).

- The cost-effectiveness of intensive surveillance using CEA and CT scanning was addressed in 2004 analysis in which the adjusted cost per year of life saved for intensive surveillance was US $5884 [28]. Interventions that yield a cost-effectiveness ratio of fewer than $50,000 to $100,000 per quality-adjusted life year gained have been considered to have an acceptable cost-effectiveness ratio in the United States and several other countries. (See "A short primer on cost-effectiveness analysis".)

The optimal frequency of post-treatment surveillance testing using CEA and CT scanning has been addressed in two analyses:

- The multicenter COLOFOL trial compared a high-intensity surveillance strategy (CEA testing and CT of the abdomen and chest at 6, 12, 18, 24, and 36 months) with a low-intensity surveillance strategy (CEA and CT at 12 and 36 months only) in 2555 patients following surgery and adjuvant therapy for stage II or III colon cancer [19]. There were no

significant differences between the groups in overall or cancer-specific mortality at five years or in the incidence of recurrence detection. Higher intensity surveillance was no more effective among patients with higher risk stage III disease or those with rectal cancer. Whether high-intensity surveillance resulted in more potentially curable recurrences was not addressed.

- A similar finding was noted in an analysis of data from the National Cancer Database (NCDB; a registry of incident cancer cases treated at more than 1500 Commission on Cancer [CoC]-accredited programs in the United States); investigators augmented the NCDB data with primary data collected by cancer registrars on surveillance testing, recurrence, and treatment of recurrence for 10 randomly selected patients treated between 2006 and 2007 at each CoC-accredited facility [29]. Facility-level testing patterns were used to define a high-intensity and a low-intensity group. Patients treated at high-intensity facilities underwent a mean of 2.9 imaging scans and 4.3 CEA tests over a three-year period, while those treated in the low-intensity facilities underwent a mean of 1.6 imaging scans and 1.6 CEA tests over three years.

  As in the COLOFOL trial, there was no significant difference in any key outcome (time to detection of recurrence, overall survival, likelihood of undergoing surgical resection for recurrence) for patients treated at high- versus low-intensity imaging facilities or high- versus low-intensity CEA facilities. However, the study was limited by a very small difference in mean testing frequency between the low- and high-intensity groups (a mean difference of 1.23 imaging tests and 2.68 CEA tests over three years).

Nonetheless, taken together, these studies suggest that imaging and CEA testing more often than yearly do little to improve survival, and this may result in a change in the management guidelines from the various professional organizations. Until then, we still follow the published guidelines from ASCO, Cancer Care Ontario, the NCCN, ESMO, and the American Cancer Society (ACS), which all suggest monitoring CEA every three to six months, at least for the first two to three years, and annual cross-sectional imaging for three to five years (table 3). These guidelines all predate the publication of the COLOFOL and NCDB studies.

Effectiveness of individual tests — An appropriate surveillance strategy should consider the temporal pattern and location of recurrent disease. The overwhelming majority of tumor recurrences develop within the first five years, most within the first two to three years after surgery. (See "Overview of the management of primary colon cancer", section on 'Prognosis'.)

In general, liver metastases predominate overall, while lung metastases occur more commonly in patients with distal rectal cancers since the venous and lymphatic drainage of the distal

rectum bypass the liver.

History and physical examination — We suggest that patients have a clinical encounter with a physician every three to six months for the first three years and every six months during years 4 and 5. Most recurrences develop within the first three years, although failure beyond three years is not uncommon, particularly in patients treated for locally advanced rectal cancer. A history should be obtained at each visit, aimed at highlighting symptoms that could suggest cancer recurrence. The physical examination should include a rectal examination for those patients who have undergone low anterior resection or transanal excision for rectal cancer. Post-treatment surveillance guidelines from most expert groups, including ASCO, Cancer Care Ontario, ESMO, the New Zealand Ministry of Health, and the NCCN all recommend periodic history and physical examination (H&P) (table 3) [6,30-33].

Detection rates for recurrent disease based strictly on the H&P are between 15 and 41 percent [1,8,34,35]. Although the available data are limited, routine periodic H&Ps do not appear to influence the detection of resectable recurrences [5,35]. One reason may be that a significant number of recurrences are heralded by symptoms that occur between physician visits and are thus not affected by the performance of the H&P [3,7]. Additionally, liver and lung metastases are unlikely to be symptomatic early in their natural history.

The lack of contribution of routine physical examination to the outcome of surveillance was shown in a series of 1356 patients with stage II or III colon cancer who were followed according to a prescribed set of protocol guidelines after treatment on the multicenter adjuvant chemotherapy protocol Intergroup 0089 [5]. Of the 421 patients who developed recurrent disease, 96 underwent surgical resection with curative intent. In this group, the first indication of recurrent disease was elevated CEA, symptoms, chest radiograph (CXR), or colonoscopy in 31, 25, 12.5, and 15 percent, respectively. Routine physical examination failed to identify a single resectable recurrence.

A history should be obtained at each visit, aimed at highlighting symptoms that could suggest cancer recurrence. The physical examination should include a rectal examination for those patients who have undergone low anterior resection or transanal excision for rectal cancer.

Laboratory testing — The only laboratory test routinely recommended for CRC surveillance is serum CEA.

Carcinoembryonic antigen — We suggest obtaining serum CEA levels at each follow-up visit in patients with colon or rectal cancer for at least the first three years after primary resection, even if preoperative CEA levels were normal, as long as the patient would be considered a candidate for aggressive therapy, including surgery. This recommendation is

consistent with guidelines from most expert groups, including ASCO, the NCCN, the British Columbia Medical Association, Cancer Care Ontario, and ESMO (table 3) [6,30-33,36].

CEA is an oncofetal protein that is elevated in the serum of patients with a variety of cancers, including CRC [37]. Because it lacks both sensitivity and specificity, serum CEA is not a useful screening tool for CRC. However, in patients with established disease, the absolute level of the serum CEA correlates with disease burden and is of prognostic value [38,39]. Furthermore, elevated preoperative levels of CEA should return to baseline after complete resection; residual disease should be suspected if they do not [40].

The role of CEA testing as a component of post-treatment surveillance in patients with resected primary CRC has been extensively evaluated. The estimated sensitivity of CEA to detect disease relapse in patients with completely resected CRC depends on the threshold value used. In a Cochrane review, the pooled sensitivity for a cutoff value of 2.5 mcg/L was 82 percent, but specificity was only 80 percent [41]. Sensitivity was lower for a threshold of 10 mcg/L (68 percent), but specificity was higher (97 percent), reflecting fewer false positives. For a cutoff of 5 mcg/L, sensitivity and specificity rates were 71 and 88 percent, respectively. Serial measurement of CEA can detect disease recurrence even among patients with an initially normal CEA level, although the sensitivity is lower (between 27 and 50 percent in four separate studies [42-45]). Thus, a postoperative CEA elevation indicates recurrence with high probability, but a normal postoperative CEA level (even if it was initially elevated) is not useful for excluding a disease recurrence.

Despite its widespread use in follow-up strategies, the utility of serial CEA testing has been questioned.

Arguments in favor of carcinoembryonic antigen testing — The strongest argument put forth by advocates of serial CEA testing is that resection of limited metastases, particularly involving the liver, leads to long-term relapse-free survival in as many as 40 percent of patients who undergo an attempted resection. As noted previously, the detection of asymptomatic recurrences, particularly by CEA testing, increases the likelihood of a complete resection, which in turn is associated with better long-term outcome.

Studies have demonstrated a lead time of 1.5 to 6 months between elevation of serum CEA levels and detection of recurrent disease by other means [46-49]. Whether this lead time actually improves overall survival remains a point of controversy. However, as noted previously, at least one meta-analysis supports a significantly increased survival among patients who undergo intensive as compared with routine surveillance, as long as CEA testing is a component of follow-up [50]. (See 'Intensive versus less intense surveillance strategies' above.)

Finally, although systemic chemotherapy for metastatic CRC has not significantly improved five-year survival rates, it has produced meaningful improvements in median and progression-free survival. These benefits are most pronounced with regimens containing irinotecan or oxaliplatin in combination with fluorouracil (FU); median overall survival durations consistently approach 20 months, and in some studies, as high as 24 months. By contrast, among patients receiving supportive care alone for metastatic disease, median survival durations are five to six months. (See "Systemic therapy for metastatic colorectal cancer: General principles", section on 'Systemic therapy versus supportive care' and "Systemic therapy for nonoperable metastatic colorectal cancer: Selecting the initial therapeutic approach", section on 'Overview of the therapeutic approach'.)

Arguments against serial carcinoembryonic antigen testing — Opponents of serial CEA testing make the following arguments:

- 30 to 40 percent of all CRC recurrences are not associated with measurable elevations in serum CEA [51].
- The benefit of CEA monitoring is limited to a small number of patients with recurrent CRC and is not cost-effective.
- There are no data showing that CEA testing improves survival [23,52] or quality of life. The issue of cost-effectiveness is debated. One cost-effectiveness study examined the benefit of CEA monitoring on the life expectancy of patients with colon cancer using decision analysis [53]. The influence of CEA monitoring on quality adjusted life expectancy varied from an average increase of seven days (+0.3 percent) to an average decrease of five days (-0.09 percent). Cost-effectiveness of CEA testing ranged from $22,963 to $4,888,208 per quality adjusted life year (QALY) saved.

These results contrast with a simple cost analysis from the Eastern Cooperative Oncology Group database, in which the cost per resectable recurrence was only $5696 based on 1995 Medicare reimbursement guidelines [5]. CEA measurement was the most cost-effective test for detecting potentially curable recurrent disease. The contrast with the quality of life study exemplifies the tremendous difference between the cost per quality of life gained by treating a recurrence and the cost for simply finding the recurrence. (See "A short primer on cost-effectiveness analysis" and "Decision analysis".)

Frequency of testing — The optimal frequency of CEA measurements is unclear. Although one study suggests better disease-free survival in patients who have a CEA level checked every one or two months compared with less frequent intervals [46], these results have

not been confirmed by others [19], and no study has shown a survival benefit for any CEA testing frequency [19,29]. (See 'Intensive versus less intense surveillance strategies' above.)

Nevertheless, most published guidelines, including those from the NCCN [6], the ACS, an expert panel on tumor markers convened by ASCO, and the ESMO, recommend testing every three to six months for at least the first two to three years. (See 'Recommendations from major groups' below.)

If CEA monitoring is undertaken, an elevated CEA should be confirmed by retesting. False-positive elevations in CEA are common, especially when the level is between 5 and 10 ng/mL. A single institution retrospective review included 728 patients who had undergone resection for locoregional CRC over a nine-year period, had a perioperative CEA level of <5 ng/mL, and who developed an elevated CEA during subsequent follow-up [54]. Results were considered false positive if the CEA level exceeded 5 ng/mL and there was no evidence of disease recurrence on imaging or other diagnostic procedures with a follow-up of at least one year, or if the CEA elevation was followed by spontaneous normalization on at least two consecutive measurements. Overall, 358 of 728 eligible patients had at least one false-positive CEA elevation (49 percent), 370 (51 percent) had a true-positive CEA elevation, 35 of which were associated with a new cancer other than CRC. Among the patients with a false-positive CEA elevation, 111 had only one level that subsequently normalized; 93 percent of these were between 5 and 10 ng/mL. For the remaining 247 patients with a false-positive CEA, the peak was between 5 and 10 ng/mL in 91 percent. By contrast, no confirmed elevation of CEA >35 ng/mL was found to be a false-positive result, and false-positive elevations between 20 and 35 ng/mL were rare (3 of 358 patients).

One potential cause for a falsely elevated CEA level is adjuvant therapy with a FU-based regimen, possibly because of treatment-related changes in liver function [55]. Thus, waiting until adjuvant treatment is completed to initiate CEA surveillance is advisable [30].

In addition, CEA levels are significantly higher in cigarette smokers, and normal values of up to 10 ng/mL may be seen [56,57].

For a progressively rising CEA that is confirmed on retesting, further evaluation is necessary to identify the site of metastatic/recurrent disease. Testing may include abdominal and pelvic CT, chest CT, positron emission tomography (PET) scanning, and in some cases, colonoscopy. Surgical exploration in the setting of an elevated CEA level without a radiographic or endoscopic study localizing the area of disease recurrence is not warranted. (See 'Positron emission tomography scanning' below.)

Other tumor markers — The utility of other tumor markers, including CA 19-9 [58-60], DR-70 [61-63], soluble CD26 [64,65], and a blood test for detecting DNA from two methylated genes (branched-chain amino acid transaminase 1 [*BCAT1*] and IKAROS family zinc finger protein 1 [*IKZF1*]) that can differentiate adenoma and adenocarcinoma tissues from normal colorectal epithelium and benign pathologies [66], is unclear. Although one of these assays (the DR-70 [FDP] enzyme-linked immunosorbent assay [ELISA] test [Onko-Sure]) is approved in the United States in conjunction with other clinical modalities for serial monitoring after treatment of CRC and in other countries (Europe, India, Taiwan, Korea, and Vietnam) as a blood test for cancer detection, it is not clear that detection accuracy is improved over CEA alone [62,63]. In one study of 112 individuals with previously treated CRC, rates of sensitivity and specificity for the DR-70 assay in detecting clinical disease progression were 65 and 67 percent, respectively, and not better than CEA alone (sensitivity and specificity 65 and 73 percent, respectively) [62]. Among patients with disease progression, there was a suggestion that DR-70 was more effective at monitoring patients whose CEA values were <30 ng/mL, but the specific data were not provided.

Thus, use of the Onko-Sure assay could be considered for patients with initially low CEA levels. One of the advantages of the DR-70 assay, which measures fibrin and fibrinogen degradation products (collectively referred to as FDP) in the serum, is that the antigen is freely diffusible in the blood compared with CEA, which is normally attached to cancer cells due to its role as an adhesion molecule.

However, as with CEA, an elevated DR-70 assay value should not be interpreted as absolute evidence for the presence of disease recurrence, since a small percentage of healthy individuals as well as those with non-malignant conditions (pancreatic disease, heart disease, coagulation disorders, acute infection, or trauma) and malignancy at other sites have elevations in DR-70.

Circulating tumor DNA — Circulating tumor DNA (ctDNA) is the fraction of circulating DNA that is derived from a patient's cancer. CRCs shed DNA into the blood, and interest in using ctDNA as a sensitive indicator of relapse risk has grown as techniques to detect and quantify such DNA have improved:

- An early report of 27 patients surgically treated for CRC revealed ctDNA postoperatively in all 14 relapsing patients but not in any of the nonrelapsing patients [67]. Of the 21 patients treated for localized disease, all 6 who had ctDNA detected within three months after surgery relapsed, compared with only 4 of the remaining 15 patients who had no detection of ctDNA at three months postoperatively. The six with a ctDNA relapse had significantly shorter relapse-free and overall survivals than did those with no ctDNA detected. On average, relapses were detected after 8.2 months by ctDNA, 12.3 months by CEA, and 16.9 months by CT.

- Another study included 58 patients with resected stage I, II, or III CRC who underwent assay for ctDNA one month postoperatively and then at three- to six-month intervals using the safe-sequencing system (Safe-SeqS), an extremely sensitive mutation detection method that enables the detection of tumoral mutations in the peripheral circulation at low frequency [68]. The recurrence rate among those with positive ctDNA was 77 percent (10 of 13), and positive ctDNA preceded radiographic recurrence by a median of four months (range 2 to 31). Of the 45 patients with absent ctDNA, none relapsed at a median follow-up of 49 months. Three of the nonrelapsing patients had a positive ctDNA result, which eventually became undetectable with additional follow-up.

- A third analysis included 125 patients with stage I, II, or III CRC who had assessment of ctDNA by multiplex, polymerase chain reaction (PCR)-based next-generation sequencing that targeted 16 mutations and was personalized for each patient based on whole-exome sequencing of each patient's tumor and matched germline DNA; assessments were performed prior to surgery, one month postoperatively, and every third month for up to three years [69]. Following definitive therapy, ctDNA-positive patients were 40 times more likely to experience a disease recurrence (hazard ratio [HR] 43.5, 95% CI 9.8-193.5), and in all multivariate analyses, ctDNA status was independently associated with relapse after adjusting for known clinicopathologic risk factors. Of the 58 patients with post-adjuvant-chemotherapy blood samples, all 7 who were ctDNA positive relapsed, compared with 7 of the 51 who were ctDNA negative (100 versus 14 percent).

In none of these studies is it clear that earlier detection resulted in a significantly greater opportunity for potentially curative treatment at the time of relapse.

While these results are promising, a year 2018 joint review of the utility of ctDNA analysis in patients with cancer by ASCO and the College of American Pathologists (CAP) concluded that there is no evidence of clinical utility and little evidence of clinical validity for ctDNA assays in early stage cancer for post-treatment monitoring or detection of residual disease [70]. A phase II/III trial (NRG GI-005) in North America is planned for patients with resected stage II colon cancer [71]. In addition to assessing ctDNA clearance with adjuvant chemotherapy and outcomes for patients with detectable levels of ctDNA receiving adjuvant chemotherapy, another objective is to evaluate the cost-effectiveness of ctDNA monitoring as compared with currently accepted practices in the long-term surveillance of resected CRC.

Liver function tests — Current evidence does not support routine assay of liver function tests (LFTs) for surveillance after treatment of CRC since they lack sensitivity to detect early recurrences. In one retrospective cohort study, for example, only 2 of 109 patients (2 percent) undergoing curative-intent salvage surgery for recurrence first presented with non-CEA-related

laboratory abnormalities [1]. None of the guidelines from expert groups recommends the use of follow-up LFTs [30,31,72,73].

Complete blood count — No portion of the complete blood count (CBC) can accurately predict recurrence of CRC, and routine monitoring of the CBC is not recommended in guidelines from expert groups [30,31,72,73].

Fecal occult blood testing — Given the recommendation from most expert groups that patients who have CRC undergo surveillance colonoscopy, routine fecal occult blood testing (FOBT) adds little to the surveillance strategy and is not recommended in any post-treatment surveillance guidelines from expert groups [30,31,72,73]. (See 'Postoperative endoscopic surveillance' below.)

A number of studies support the use of FOBT as a screening tool to detect primary CRC. (See "Tests for screening for colorectal cancer".)

The data regarding use of this test to detect disease recurrence are not as strong. The goal of FOBT after initial treatment is to detect anastomotic recurrences, new polyps, or metachronous cancers. However, FOBT is inferior to colonoscopy for this purpose since it has a low sensitivity and specificity [74-77]. In one study, for example, FOBT was performed before 1244 colonoscopies in patients with previous cancer [76]. FOBT was positive in only three of nine patients with local recurrence and 2 of 13 with a metachronous cancer. Studies of FOBT using new fecal immunohistochemical tests, instead of the older guaiac-based tests, in this scenario are lacking.

Radiographic imaging

Chest radiograph — Annual CXR is not recommended as a component of post-treatment surveillance in guidelines from any major group, including NCCN guidelines [6,30,31,36,72,73,78].

CXR is a noninvasive, relatively inexpensive test that may be used to detect pulmonary metastases [7,10,79]. However, the greater sensitivity and widespread availability of chest CT for the detection of intrathoracic metastases has rendered the discussion of CXR irrelevant. (See 'Computed tomography scans' below.)

Computed tomography scans — For patients with resected stage II or III colon or rectal cancer, we suggest annual surveillance CT scans of the chest and abdomen for at least three years if the patient would be eligible for aggressive therapy, including curative-intent surgery. For patients with rectal cancer, we suggest an annual pelvic CT if pelvic radiation therapy was

not administered. These recommendations are consistent with guidelines from ASCO [30], the NCCN [6], and others (table 3).

The role of routine postoperative follow-up CT scans has evolved over the past few years. As noted previously, systematic reviews and meta-analyses support a survival advantage for patients undergoing intensive as compared with nonintensive follow-up. However, the tests that were considered part of intensive follow-up differed in the five randomized trials included in these meta-analyses [7-10,13], particularly with regard to CT scanning. In some cases, CT was performed of liver only, or pelvis only, and all studies used chest radiography alone to evaluate for pulmonary metastases. Furthermore, patients with any stage disease were included, and adjuvant chemotherapy was not always administered. Nevertheless, in one meta-analysis, the survival benefit from intensive surveillance was most pronounced in trials that used both CT imaging (every 3 to 12 months) and frequent measurement of CEA [21]. Two other meta-analyses reported a survival benefit specifically with liver imaging [22,80]. (See 'Intensive versus less intense surveillance strategies' above.)

Other data to support the utility of CT scanning come from studies evaluating surveillance policies in patients participating in adjuvant chemotherapy trials [1,5,79,81,82]. In both United States Intergroup studies for colon cancer, CT was not mandated in the follow-up policy [1,5], while two European trials did include routine postoperative CT scanning [79,82]. In the European studies, 32 and 44 percent of relapses were detected by imaging, respectively, and 38 and 46 percent of these patients proceeded to potentially curative resection, respectively. Only between 20 and 22 percent of all relapsed patients in both United States trials underwent potentially curative resection. Thus, routine rather than directed (ie, for evaluation of symptoms) postoperative CT scans are more likely to detect patients with isolated potentially resectable hepatic metastases [82,83].

There is less evidence for chest surveillance than for liver imaging, and none of the meta-analyses addressed thoracic imaging specifically. However, in one of the European trials, all seven patients with CT-detected pulmonary relapses who underwent potentially curable resection were asymptomatic with normal CEA levels and would otherwise have been undetected [82]. The CT-detected group had a significantly longer median survival from the time of relapse as compared with the symptomatic group (26.4 versus 12.6 months), but not the CEA-detected group (19.2 months). While the greatest number of recurrences was found with abdominal CT scanning, the largest proportion of resectable recurrences was found using thoracic CT scan.

An important point is that when planning the post-treatment surveillance strategy, care should be taken to limit the number of unnecessary CT scans, particularly in younger individuals, given

concerns about radiation exposure and the risk for second malignancies. (See "Radiation-related risks of imaging".)

Positron emission tomography scanning — PET scans have no role in routine surveillance, and their use is specifically discouraged in guidelines from expert groups, including ASCO [30] and the NCCN [6].

The role of PET in the detection of recurrence after potentially curative surgery is uncertain. Although early recurrences (and unexpected second primary tumors) may be found in some patients, these benefits are counterbalanced by false-positive and false-negative results, and uncertainty as to the survival impact of adding PET to the postoperative surveillance strategy.

These issues were illustrated in a trial that randomly assigned 130 patients undergoing potentially curative resection of colon or rectum cancer to conventional surveillance (periodic serum tumor markers, ultrasound, CXR, and CT at 9 and 15 months) with or without a PET scan at 9 and 15 months [84]. Because of missing data, primary analyses were performed with 125 patients (60 in the PET group versus 65 in the conventional group). The number of patients with a suspected recurrence was 44 (23 in the PET group and 21 in the conventional group), and recurrence was confirmed by biopsy or surgery in 15 patients in the PET group versus 12 in the conventional group (25 versus 18.5 percent), a difference that was not statistically significant. The PET group had a significantly shorter time to recurrence (12 versus 15 months), and recurrences were also more frequently cured by surgery in this group (10 versus 2). PET also detected three unsuspected second primary tumors (one gastric gastrointestinal stromal tumor and two primary lung cancers); three patients had a false-positive result, and 2 of 25 patients with a recurrence had a false-negative result.

Until further data are available, PET scans should not be used as a component of routine surveillance. On the other hand, for patients with a persistently elevated serum CEA and unrevealing conventional diagnostic studies, PET scanning may reveal occult metastatic disease and potentially alter patient management. This topic is discussed in detail elsewhere. (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Clinical staging evaluation'.)

Diagnosing second cancers and polyps — Endoscopy is the only means to directly visualize intraluminal CRC and is the mainstay of surveillance techniques to diagnose a metachronous CRC or polyps.

Perioperative colonoscopy — Synchronous colon cancers, defined as two or more distinct primary tumors separated by normal bowel and not due to direct extension or metastasis, occur in 2 to 5 percent of patients with CRC [85,86]. All patients treated for a primary

CRC should undergo colonoscopy to exclude synchronous malignancy and non-malignant polyps. CT colography or double contrast barium enema can be performed preoperatively in patients with obstructing tumors. If colonoscopy cannot be performed preoperatively (for example, in a patient with an obstructing cancer), it should be done following recovery from surgery (usually within six months postoperatively) [87].

Postoperative endoscopic surveillance — Although the question of a survival benefit is unsettled, periodic post-treatment endoscopic surveillance is endorsed by major groups, including ASCO, ESMO, Cancer Care Ontario, the NCCN [6], the ACS, and the joint ACS/United States Multisociety Task Force on Colorectal Cancer [30-33]. (See 'Guidelines from major groups' below.)

The goals of surveillance colonoscopy are twofold: to detect metachronous CRCs and polyps (nonanastomotic new tumors developing at least six months after the initial diagnosis), and detection of anastomotic recurrences of the initial primary cancer at a stage that would allow curative treatment:

- Metachronous lesions develop in 1.5 to 3 percent of patients, most of which develop in the first 36 months postoperatively (rate 0.35 to 0.5 percent per year) [10,50,85,88-94]; however, risk remains elevated for up to 10 years in some patients [85]. Over one-half of these "metachronous" lesions arise within 24 months of the initial resection and may represent synchronous cancers that were missed initially; others represent early anastomotic recurrences [10,89,91,95]. The high yield of CRC at surveillance colonoscopy at one year [95] is the reason that most expert guidelines, including those of ASCO and the United States Multisociety Task Force on Colorectal Cancer, recommend a colonoscopy one year after resection [30,31,73,78,87].

- Anastomotic recurrences occur in 2 to 4 percent of patients with colon cancer; rates are higher in patients with rectal cancer, particularly in patients who have not undergone a total mesorectal excision and/or pelvic radiation therapy [8-10,13,35,89,94,96]. Approximately 90 percent of anastomotic recurrences are detected within three years of the primary resection [89,90,94].

The benefits [7,10,97,98] and optimal frequency of postoperative colonoscopic surveillance have been debated. Observational studies utilizing large administrative databases [97-99] and meta-analyses of randomized controlled trials [4,24] show that patients who undergo surveillance colonoscopy after CRC resection have lower overall, but not disease-specific, mortality. Furthermore, neither randomized trials [7,8,10] nor meta-analyses [80] have shown a survival

benefit by performing colonoscopy at annual or shorter intervals as compared with less frequent intervals (three or five years).

The inability to detect a disease-specific survival benefit from early detection of anastomotic recurrences may be related to the fact that the overwhelming majority of patients with endoscopically detected anastomotic recurrences are unresectable for cure. Because local recurrence rates for rectal cancer are generally higher than those seen in colon cancer, and early detection may lead to successful retreatment, there is a rationale for performing periodic examinations of the rectum by rigid or flexible proctoscopy sigmoidoscopy. (See 'Proctosigmoidoscopy' below.)

On the other hand, periodic colonoscopy is of clear benefit for detecting metachronous cancers at a surgically curable stage as well as the prevention of metachronous cancers via identification and removal of adenomatous polyps. The following represents the available data:

- In an analysis performed by the ACS/United States Multisociety Task Force on Colorectal Cancer of 23 randomized trials and cohort studies in which patients with resected CRC underwent perioperative clearing by colonoscopy, there were 9029 patients in whom 137 apparently metachronous cancers developed [100]. Among three studies in which the number of colonoscopies performed could be determined, 157 colonoscopies were performed per metachronous cancer detected, a rate that compares favorably with the rate of prevalent cancer detected during screening colonoscopy [101-103]. Where reported, 69 of 106 metachronous cancers (65 percent) were node negative, 29 of 52 (56 percent) were asymptomatic, and 62 of 71 (87 percent) were operated for cure.

- All patients with a history of CRC are at risk for developing adenomatous polyps, the precursor of most invasive cancers. The National Polyp Study revealed a 76 to 90 percent reduction in the incidence of CRC when surveillance colonoscopy was used in the setting of polyps [104]. Performing colonoscopy at three-year intervals is as effective as one-year intervals for detecting new polyps [105]. This subject is discussed in detail elsewhere. (See "Overview of colon polyps".)

Guidelines from major groups — Although all guidelines recommended periodic colonoscopy after treatment of CRC (table 3), the frequency and management of patients with abnormal findings one-year post-treatment are slightly different.

We suggest that if the one-year colonoscopy is normal that subsequent colonoscopies be undertaken once every three to five years, depending on the results of the prior colonoscopy. Shorter endoscopic testing intervals may be indicated if the patient's age, family history, or tumor testing suggest the possibility of definite or probable hereditary nonpolyposis CRC (Lynch

syndrome) or the serrated polyposis syndrome [106]. (See 'Assessing genetic susceptibility' below and "Overview of colon polyps", section on 'Serrated polyposis syndrome'.)

Links to these and other society guidelines can be found elsewhere. (See 'Society guideline links' below.)

Older adults — Expert guidelines for post-treatment surveillance of patients with treated CRC do not specifically address when, if ever, post-treatment surveillance endoscopy should be stopped. Few studies have addressed surveillance colonoscopy in the elderly [107-110]. The decision to stop surveillance endoscopy should depend on whether an individual patient's life expectancy and the likelihood of finding an advanced adenoma or second CRC justifies the risk and inconvenience of periodic endoscopy. At least some retrospective data suggest a low incidence of CRC detection and a relatively high rate of postprocedure hospitalization among elderly patients compared with younger individuals. In a retrospective cohort study of 27,763 patients ≥50 years of age (4834 ≥75 years of age) undergoing surveillance colonoscopy for a history of CRC or adenomatous polyps at a single integrated California health system, CRC incidence among elderly patients was significantly lower than that of younger individuals (0.24 versus 3.61 per 1000 person-years) [107]. Furthermore, after adjusting for comorbid illness, sex, and race/ethnicity, older age was independently associated with a significantly higher risk of postprocedure hospitalization (adjusted odds ratio [OR] 1.28, 95% CI 1.07-1.53), as was the presence of a Charlson comorbidity score of 2 (table 4) (adjusted OR 2.54, 95% CI 2.06-3.14) or higher. However, that study failed to account for the protective effect of prior colonoscopy (ie, that the older patients had likely undergone more surveillance colonoscopies with the potential for removal of precancerous lesions).

Recommendations for ongoing surveillance in elderly individuals with a treated CRC are complicated by other factors such as how much residual colon is present after surgery, and how many (if any) adenomas were found in the previous one or two surveillance colonoscopies. Nevertheless, the higher risk for postprocedure hospitalization and the impact of comorbidity should be taken into account when assessing the relative risks and benefits of periodic surveillance colonoscopy.

Proctosigmoidoscopy — We suggest that patients who have undergone limited surgery (eg, transanal excision) or a low anterior resection for rectal cancer and have not received radiation therapy (RT) undergo flexible proctosigmoidoscopy, with or without endoscopic ultrasound (EUS), every six months for two to five years. In our view, EUS adds very little time, has the same prep as the sigmoidoscopy itself (ie, just enemas), and does not add a sedation requirement, and often the recurrence is a focus in the perirectal fat that would be missed by standard endoscopy.

This recommendation is consistent with guidelines from ASCO (table 3) [30]; however, it differs from the guidelines of other groups.

- Guidelines from the NCCN recommend flexible proctosigmoidoscopy with EUS or magnetic resonance imaging (MRI) every three to six months for the first two years, then at six-month intervals for a total of five years for patients with rectal cancer who were treated only with transanal excision [6].

- Guidelines from ESMO do not address the role of post-treatment proctosigmoidoscopy after treatment for rectal cancer, stating only that full colonoscopy should be performed within one year of resection if it was not initially performed, then follow-up colonoscopy every five years up to age 75 [33].

- On the other hand, New Zealand guidelines include proctoscopy or sigmoidoscopy at 3, 6, 12, and 24 months postsurgery for all individuals with rectal cancer [78].

- Updated guidelines from the United States Multisociety Task Force on Colorectal Cancer suggest local surveillance with flexible sigmoidoscopy (or endoscopic ultrasound [EUS]) every three to six months for the first two to three years after surgery for the following groups, who are at increased risk of a local recurrence [87]:

    - Patients with localized rectal cancer who have undergone surgery without total mesorectal excision (TME)
    - Patients who have undergone transanal local excision or endoscopic submucosal dissection alone
    - Patients with locally advanced rectal cancer who did not receive neoadjuvant chemoradiotherapy and then a TME

Proctosigmoidoscopy is less expensive, less time consuming, and safer than colonoscopy. It has a role in patients with rectal cancer, since anastomotic recurrence is more likely in this setting than in cancer of the colon [90]. However, the effectiveness of proctosigmoidoscopy is no better established than colonoscopy for the detection of curable anastomotic recurrences.

Patients with rectal cancer who have undergone pelvic RT are substantially less likely to develop cancer recurrence than those who did not receive it [86]. This is the reason why ASCO guidelines recommend surveillance with proctosigmoidoscopy only for patients who have not received pelvic RT (table 3) [30].

Transrectal endoscopic ultrasound — Following therapy of rectal cancer, transrectal EUS (TEUS) may be more accurate than other radiographic imaging modalities for early detection of

local recurrence. However, the optimal selection criteria for patients who would benefit from the addition of TEUS to the post-treatment surveillance strategy are unclear, as is the optimal timing and frequency of study. The updated guidelines from the United States Multisociety Task Force on Colorectal Cancer now include EUS as an alternative to sigmoidoscopy in the recommended testing strategy for those at high risk of recurrence [87], while the NCCN includes EUS as an alternative to flexible sigmoidoscopy for patients with rectal cancer undergoing transanal excision only (table 3). The role of TEUS in individuals with rectal cancer is discussed in detail elsewhere. (See "Endoscopic ultrasound for evaluating patients with rectal cancer", section on 'Surveillance after surgical resection'.)

Contrast-enhanced ultrasound — Used mainly in Europe, contrast-enhanced ultrasound (CEUS) using SonoVue (sulphur hexafluoride microbubbles) provides similar diagnostic performances to other imaging modalities (contrast-enhanced CT or magnetic resonance imaging [MRI]) for the assessment of focal liver lesions [111]. It is a cost-effective alternative for the detection of liver metastases, but utility for detection of recurrent CRC outside of the liver is not well studied [112]. CEUS is not included in any expert guideline. (See "Contrast-enhanced ultrasound for the evaluation of liver lesions", section on 'Indications'.)

STAGE I DISEASE

There are no data available to guide recommendations for post-treatment surveillance in patients with resected stage I colon or rectal cancer (table 1), and the recommendations of expert groups are variable (table 3). Consistent with updated American Society of Clinical Oncology (ASCO) guidelines [30], we suggest not pursuing any post-treatment surveillance strategy for most asymptomatic patients with resected stage I colorectal cancer (CRC), with the exception of interval colonoscopy. However, some of these patients have higher-risk disease (eg, rectal cancer treated with endoscopic or transanal excision, colon cancers treated with endoscopic resection alone, and patients who did not undergo guideline-based treatment) for whom surveillance-based detection as is used for higher-stage disease might reveal a potentially salvageable recurrence.

As noted above, the emerging consensus as to the best surveillance strategy for patients with resected CRC has focused mainly on stage II and III disease. In general, aggressive surveillance other than colonoscopy has generally not been recommended in patients with resected stage I tumors, since over 95 percent are cured by surgery alone.

However, newer data are challenging this viewpoint. A secondary analysis of data from the Clinical Outcomes of Surgical Therapy (COST) trial (laparoscopic versus open colectomy for colon

cancer) included 527 patients with stages I (n = 265) or IIA disease and 254 patients with stage IIB or III disease (as defined by the 2002 American Joint Committee on Cancer [AJCC] staging criteria) [113]. The post-treatment surveillance strategy consisted of carcinoembryonic antigen (CEA) testing every three months for the first year, and then every six months for five years; chest radiograph every six months for two years then annually, and colonoscopy at one year, and then every three years if the colon was free of neoplasia; CT scans were performed for symptoms, physical findings, or an increased CEA.

Five-year recurrence rates were higher in patients with later stage disease (36 versus 10 percent). However, patients with earlier stage disease experienced similar benefits from postoperative surveillance as did those with later stage disease (salvage rate 36 and 37 percent), and the method of first detection of recurrence was not significantly different: CEA, 29 versus 37 percent; chest radiograph, 7 versus 12 percent; colonoscopy, 13 versus 9 percent.

The authors concluded that implementation of surveillance guidelines for patients with stage I disease was appropriate. However, the number of patients who can be cured as a result of routine periodic CEA and imaging surveillance is very small: less than 1 percent [114].

There is no consensus on this point, and guidelines from expert groups are mixed:

- Guidelines from ASCO [30], Cancer Care Ontario [31], the British Columbia Medical Association [36], and the National Comprehensive Cancer Network (NCCN) do not recommend surveillance for treated stage I colon cancer beyond routine colonoscopy [6]. However, NCCN guidelines do suggest that patients with stage I rectal cancer be followed in a similar manner to those with stage II or III disease, with periodic history and physical examination and CEA levels, periodic CT scanning for those who are candidates for resection of isolated metastases, and proctoscopy with EUS or MRI every three to six months for the first two years, then every six months for a total of five years for those who have undergone transanal excision only (table 3) [6].

We also agree with Clinical Practice Guidelines from the American Society of Colon and Rectal Surgeons, which states that higher-risk patients with stage I disease (eg, rectal cancer treated with endoscopic or transanal excision, colon cancers treated with endoscopic resection alone, and patients who did not undergo guideline-based treatment) follow the recommended guidance for post-treatment surveillance for more advanced disease following potentially curative therapy (table 3) [115].

- The European Society for Medical Oncology (ESMO) guidelines for post-treatment surveillance after treatment of localized colon cancer are the same for stage I, II, and III disease; in contrast, the guidelines for rectal cancer do not state whether or not the post-

treatment surveillance guidelines apply to stage I as well as stage II or III rectal tumors [33,73].

- Guidelines from the New Zealand Ministry of Health include stage I colon and rectal cancer in the surveillance strategy, but include different recommendations for high-risk (stage IIB, III) and low-risk (stage I, IIA) tumors [78].

RESECTED STAGE IV DISEASE

Given the high risk for recurrence, more frequent post-treatment assessment may be warranted for patients with resected metastatic disease, at least in the first three years. There are no data to guide recommendations for surveillance in patients with resected metastatic CRC, and in the absence of data, the post-treatment surveillance strategy for this group should be individualized.

Some patients with stage IV colorectal cancer are amenable to potentially curative metastasectomy; five-year survival rates of approximately 40 percent are reported, particularly for isolated liver metastases. (See "Hepatic resection for colorectal cancer liver metastasis", section on 'Oncologic'.)

There are no data for surveillance in this group, and the optimal post-treatment surveillance strategy is unknown. Whether recommendations for post-treatment surveillance in patients with resected stage II or III disease (table 1) can be extrapolated to a patient with metastatic colorectal cancer who underwent metastasectomy and is currently without evidence of disease is unclear. However, following the same rationale as for stages II and III disease, early detection of asymptomatic recurrences may increase the proportion of patients who are potentially eligible for additional curative therapy. (See "Hepatic resection for colorectal cancer liver metastasis", section on 'Repeat resection for colorectal liver metastases'.)

Guidelines are not available from the American Society of Clinical Oncology (ASCO) [30], Cancer Care Ontario [31], the British Columbia Medical Association, or the New Zealand Ministry of Health [36]. The National Comprehensive Cancer Network (NCCN) guidelines suggest following the same surveillance strategy as for resected stage II or III disease, but also recommend more frequent computed tomography (CT) scanning (table 3) [6]. ESMO guidelines also suggest more intense follow-up in patients who underwent a complete resection of metastatic disease, repeating CEA levels and CT scans at intervals of three to six months during the first three years [116].

In the absence of data, the post-treatment surveillance strategy for this group should be individualized.

RECOMMENDATIONS FROM MAJOR GROUPS

Several organizations, including the American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology (ESMO), and the National Comprehensive Cancer Network (NCCN) have published guidelines for post-therapy surveillance of patients with resected colorectal cancer (CRC), several of which are compared and contrasted in the table (table 3) [6,30,31,33,36,73,78,116,117]. In 2013, ASCO updated its prior 2005 recommendations for follow-up care, surveillance protocols, and secondary prevention measures for survivors of CRC [30], endorsing the previously published recommendations of Cancer Care Ontario [31]. The key recommendations included the following:

- Surveillance should be guided by presumed risk of recurrence and functional status of the patient. Patients at higher risk should be considered for more frequent testing. If the patient is not a surgical candidate or a candidate for systemic therapy because of severe comorbid conditions, surveillance tests should not be performed.
- Surveillance is especially important in the first two to four years after surgery, when the risk of recurrence is greatest.
- Specific recommendations for the elements of the surveillance strategy are outlined in the table, which also contrasts the ASCO recommendations with those of other expert groups (table 3).
- A treatment plan from the specialist should be sent to the patient's other providers, particularly the primary care physician, and it should have clear directions for appropriate follow-up.
- Despite the lack of high-quality evidence on secondary prevention in CRC survivors, it is reasonable to counsel patients on maintaining a healthy body weight, being physically active, and eating a healthy diet.

Links to these and other society guidelines can be found elsewhere. (See 'Society guideline links' below.)

PREVENTIVE CARE FOR LONG-TERM SURVIVORS

Little is known about the appropriate primary and preventive care of survivors as they transition from treatment into the period of active surveillance and then to long-term survivorship, or who should be responsible for providing that care. In the setting of breast cancer, randomized trial data provide evidence that primary care providers are able to monitor survivors for recurrence-related clinical events as well as cancer specialists, as long as they are advised of the appropriate surveillance and management strategy. (See "Overview of cancer survivorship care for primary care and oncology providers".)

Coordination of care — There are no data that address the utility of generalist versus specialist care in colorectal cancer (CRC) survivors. However, in general, CRC survivors who are followed by generalists tend to receive more preventive care than do patients who are seen primarily by oncologists, while on the other hand, cancer-related screening may decrease as oncologists become less involved in survivor care. In addition, because many CRC survivors are elderly, primary care providers may be better equipped to address comorbidities that are often neglected among cancer survivors. These results suggest a need for a shared survivorship care plan in which the roles of the primary care physician and oncology specialist are explicitly outlined. The updated 2013 American Society of Clinical Oncology (ASCO) guidelines for follow-up care for survivors of CRC explicitly state that a treatment plan from the specialist should be sent to the patient's other providers, especially the primary care physician, with clear directions on appropriate follow-up [30]. These issues are addressed in more detail elsewhere. (See "Overview of cancer survivorship care for primary care and oncology providers", section on 'Coordination of care'.)

Secondary prevention — There are emerging data on the role of various host factors, including diet and lifestyle, as secondary prevention for CRC survivors. While the available data are derived from prospective observational studies and lack confirmation from randomized clinical trials, the 2013 updated ASCO guidelines for post-treatment follow-up [30] endorsed the following Cancer Care Ontario recommendations for secondary prevention [31]:

- Patients should be advised to eat a healthy diet and seek to maintain a healthy body weight.
- Survivors should engage in a physically active lifestyle, seeking to engage in at least 150 minutes per week of moderate intensity, or 75 minutes per week of vigorous activity aerobic activity, as recommended by the American College of Sport Medicine [118].
- There remains uncertainty regarding the benefits of regular use of aspirin or a cyclooxygenase inhibitor and in which survivors; an ongoing Cancer and Leukemia

Group B (CALGB) study is evaluating whether celecoxib will improve outcomes in CRC survivors, and eligible patients should be encouraged to enroll.

These issues are all discussed in detail elsewhere. (See "The roles of diet, physical activity, and body weight in cancer survivors" and "Adjunctive therapy for patients with resected early stage colorectal cancer: Diet, exercise, NSAIDs, and vitamin D".)

SCREENING OF FAMILY MEMBERS

A positive family history for colorectal cancer (CRC), particularly in first degree relatives, increases the risk of developing CRC. Thus, when caring for a patient with CRC, the clinician should recommend screening of family members when appropriate. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors".)

Both the American Gastroenterological Association (AGA) and the American Cancer Society (ACS) recommend that first-degree relatives of patients with CRC be offered average-risk screening methods beginning at age 40 [119]. (See "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp".)

Assessing genetic susceptibility — Among the multiple cancer family syndromes, several are known to be associated with the development of colon cancer, including adenomatous and hamartomatous polyposis syndromes (eg, familial adenomatous polyposis [FAP], MUTYH-associated polyposis [MAP], juvenile polyposis, Peutz-Jeghers syndrome) and Lynch syndrome (hereditary nonpolyposis colorectal cancer [HNPCC]). (See "Familial adenomatous polyposis: Screening and management of patients and families" and "*MUTYH*-associated polyposis" and "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis" and "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Cancer screening and management" and "Juvenile polyposis syndrome".)

- Lynch syndrome is an inherited disorder associated with CRC. Its prevalence among patients with CRC is between 1 and 5 percent. The minimum diagnostic criteria to suspect Lynch syndrome are controversial, but the possibility should be considered in patients fulfilling the revised Bethesda guidelines for testing colorectal tumors for Lynch syndrome (table 5). However, the sensitivity of these criteria for capturing all cases of Lynch syndrome is limited. Increasingly, universal testing of all CRCs for Lynch syndrome by assessment of microsatellite instability (MSI) or absence of expression of a mismatch repair protein (MMR) is advocated by expert groups, including the American Society of

Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), and others [120-122].

High levels of microsatellite instability (MSI) are the biologic footprint of cells that have deficient DNA repair capacity that may be inherited (Lynch syndrome) or acquired (most often through hypermethylation of the promoter region preventing protein transcription). In either case, the end result is silencing of genes governing mismatch repair. Deficient mismatch repair is the genetic abnormality underlying Lynch syndrome and is present in both the tumor and in germline DNA. (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis" and "Molecular genetics of colorectal cancer", section on 'Mismatch repair genes'.)

- The other major inherited CRC syndrome is familial adenomatous polyposis (FAP). This disorder is much less common than Lynch syndrome and is characterized by multiple polyps throughout the colon. (See "Clinical manifestations and diagnosis of familial adenomatous polyposis".)

- The less common MAP is an autosomal recessive polyposis syndrome caused by biallelic mutations in the *MUTYH* gene [123]. MAP is currently the only known recessive hereditary colon cancer syndrome. The clinical phenotype is multiple polyps throughout the colon, but fewer than seen with FAP. (See "*MUTYH*-associated polyposis".)

Genetic testing for the responsible gene (the *APC* gene) in FAP, for germline mutations in mismatch repair genes in Lynch syndrome, and for the two most common *MUTYH* gene mutations (Y179C and G396D), is available, and patients with CRC who meet these diagnostic criteria should undergo genetic counseling to discuss genetic testing. The demonstration of a mutated gene can then be used to screen the remainder of the family and identify those members who need intensive monitoring. The topic of screening for Lynch syndrome, FAP, and MAP, as well as recommendations for cancer surveillance for individuals who are found to have one of these syndromes, is addressed elsewhere. (See "Familial adenomatous polyposis: Screening and management of patients and families" and "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Cancer screening and management".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Colorectal cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Colon and rectal cancer (The Basics)")
- Beyond the Basics topics (see "Patient education: Colon and rectal cancer (Beyond the Basics)" and "Patient education: Colorectal cancer treatment; metastatic cancer (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Rationale** – The purpose of surveillance after definitive therapy of colorectal cancer (CRC) is early identification of those patients who might potentially be cured by further surgical intervention and to screen for second primary cancers and polyps. Early diagnosis of an asymptomatic recurrence increases the likelihood of a complete surgical resection if potentially resectable recurrent disease is identified, and may improve survival. (See 'Does early detection of recurrent disease improve survival?' above and 'Diagnosing second cancers and polyps' above.)
- **Stage II and III disease**
  - We recommend intensive postoperative surveillance for most patients with resected stage II or III CRC (table 1) who would be considered candidates for aggressive treatment, including curative-intent surgery. However, new data may lead to updated recommendations from various professional organizations supporting less intense surveillance. (See 'Intensive versus less intense surveillance strategies' above.)

The following recommendations for the specific components of the post-treatment follow-up strategy of patients with resected stage II or III CRC (table 1) are consistent with guidelines from the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) (table 3).

- We suggest that patients have a clinical encounter with a physician every three to six months for the first three years and every six months during years 4 and 5. A history should be obtained at each visit, aimed at highlighting symptoms that could suggest cancer recurrence. The physical examination should include a rectal examination for those patients who have undergone low anterior resection or transanal excision for rectal cancer. (See 'History and physical examination' above.)

- We suggest obtaining serum carcinoembryonic antigen (CEA) levels at each follow-up visit for at least the first two to three years after primary resection, even if preoperative CEA levels were normal. It is reasonable to eliminate CEA testing from the surveillance strategy in patients who would not be potentially eligible for resection if an early recurrence were documented. (See 'Carcinoembryonic antigen' above.)

- We suggest that all patients undergo a complete colonoscopy either before surgical resection or (for those with initially obstructing tumors) within a few months after resection to exclude synchronous polyps and cancer. (See 'Perioperative colonoscopy' above.)

  We suggest a repeat colonoscopy one year after primary resection to exclude new lesions, and if normal, subsequent follow-up intervals of three to five years depending on the results of the prior colonoscopy. (See 'Postoperative endoscopic surveillance' above and 'Guidelines from major groups' above.)

  We also suggest that patients who have undergone low anterior resection for rectal cancer and who have not received radiation therapy undergo flexible proctosigmoidoscopy every six months for two to five years. This recommendation is controversial, however, and consensus-based guidelines from the NCCN no longer recommend surveillance proctosigmoidoscopy in this population (table 3) [6]. (See 'Proctosigmoidoscopy' above.)

- We also suggest annual surveillance computed tomography (CT) scans of the chest and abdomen for at least three years if the patient would be eligible for aggressive therapy, including curative-intent surgery. For patients with rectal cancer, we

suggest an annual pelvic CT if pelvic radiation therapy was not administered. (See 'Radiographic imaging' above.)

- Specific guidelines for post-treatment surveillance in patients who have more locally advanced rectal cancer, who achieve a clinical complete response to neoadjuvant therapy, and who are following an initial "wait and watch" nonoperative strategy, are addressed in detail elsewhere. (See "Neoadjuvant therapy for rectal adenocarcinoma", section on 'Tumor response assessment and follow-up'.)

- **Stage I disease**

  - After curative intent resection, most patients with stage I CRC do not require surveillance beyond interval colonoscopy to assess for recurrent cancer or a second primary cancer because the risk is very low.

  - However, for some patients with higher-risk disease (eg, rectal cancer treated with endoscopic or transanal excision, colon cancers treated with endoscopic resection alone, and patients who did not undergo guideline-based treatment) surveillance-based detection as is used for higher-stage disease, might reveal a potentially salvageable recurrence. (See "Overview of the management of rectal adenocarcinoma", section on 'Clinical/pathologic T1N0 amenable to endoscopic polypectomy or transanal excision' and "Overview of the management of primary colon cancer", section on 'Management of carcinoma in a polyp'.)

- **Resected stage IV disease**

  - Given the high risk for recurrence, most frequent post-treatment assessment may be warranted for individuals with resected metastatic disease.

  - There are no data to guide recommendations for surveillance in patients with resected metastatic CRC, and in the absence of data, the post-treatment surveillance strategy for this group should be individualized. (See 'Resected stage IV disease' above.)

ACKNOWLEDGMENT

The UpToDate editorial staff acknowledges Francis A Farraye, MD, MSc, who contributed to an earlier version of this topic review.

REFERENCES

1. Goldberg RM, Fleming TR, Tangen CM, et al. Surgery for recurrent colon cancer: strategies for identifying resectable recurrence and success rates after resection. Eastern Cooperative Oncology Group, the North Central Cancer Treatment Group, and the Southwest Oncology Group. Ann Intern Med 1998; 129:27.
2. Quentmeier A, Schlag P, Smok M, Herfarth C. Re-operation for recurrent colorectal cancer: the importance of early diagnosis for resectability and survival. Eur J Surg Oncol 1990; 16:319.
3. Ovaska J, Järvinen H, Kujari H, et al. Follow-up of patients operated on for colorectal carcinoma. Am J Surg 1990; 159:593.
4. Pita-Fernández S, Alhayek-Aí M, González-Martín C, et al. Intensive follow-up strategies improve outcomes in nonmetastatic colorectal cancer patients after curative surgery: a systematic review and meta-analysis. Ann Oncol 2015; 26:644.
5. Graham RA, Wang S, Catalano PJ, Haller DG. Postsurgical surveillance of colon cancer: preliminary cost analysis of physician examination, carcinoembryonic antigen testing, chest x-ray, and colonoscopy. Ann Surg 1998; 228:59.
6. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology. Available at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf (Accessed on July 25, 2023).
7. Ohlsson B, Breland U, Ekberg H, et al. Follow-up after curative surgery for colorectal carcinoma. Randomized comparison with no follow-up. Dis Colon Rectum 1995; 38:619.
8. Mäkelä JT, Laitinen SO, Kairaluoma MI. Five-year follow-up after radical surgery for colorectal cancer. Results of a prospective randomized trial. Arch Surg 1995; 130:1062.
9. Kjeldsen BJ, Kronborg O, Fenger C, Jørgensen OD. A prospective randomized study of follow-up after radical surgery for colorectal cancer. Br J Surg 1997; 84:666.
10. Schoemaker D, Black R, Giles L, Toouli J. Yearly colonoscopy, liver CT, and chest radiography do not influence 5-year survival of colorectal cancer patients. Gastroenterology 1998; 114:7.
11. Rodríguez-Moranta F, Saló J, Arcusa A, et al. Postoperative surveillance in patients with colorectal cancer who have undergone curative resection: a prospective, multicenter, randomized, controlled trial. J Clin Oncol 2006; 24:386.
12. Wang T, Cui Y, Huang WS, et al. The role of postoperative colonoscopic surveillance after radical surgery for colorectal cancer: a prospective, randomized clinical study. Gastrointest

Endosc 2009; 69:609.

13. Pietra N, Sarli L, Costi R, et al. Role of follow-up in management of local recurrences of colorectal cancer: a prospective, randomized study. Dis Colon Rectum 1998; 41:1127.
14. Secco GB, Fardelli R, Gianquinto D, et al. Efficacy and cost of risk-adapted follow-up in patients after colorectal cancer surgery: a prospective, randomized and controlled trial. Eur J Surg Oncol 2002; 28:418.
15. Grossmann EM, Johnson FE, Virgo KS, et al. Follow-up of colorectal cancer patients after resection with curative intent-the GILDA trial. Surg Oncol 2004; 13:119.
16. Primrose JN, Perera R, Gray A, et al. Effect of 3 to 5 years of scheduled CEA and CT follow-up to detect recurrence of colorectal cancer: the FACS randomized clinical trial. JAMA 2014; 311:263.
17. Wattchow DA, Weller DP, Esterman A, et al. General practice vs surgical-based follow-up for patients with colon cancer: randomised controlled trial. Br J Cancer 2006; 94:1116.
18. Rosati G, Ambrosini G, Barni S, et al. A randomized trial of intensive versus minimal surveillance of patients with resected Dukes B2-C colorectal carcinoma. Ann Oncol 2016; 27:274.
19. Wille-Jørgensen P, Syk I, Smedh K, et al. Effect of More vs Less Frequent Follow-up Testing on Overall and Colorectal Cancer-Specific Mortality in Patients With Stage II or III Colorectal Cancer: The COLOFOL Randomized Clinical Trial. JAMA 2018; 319:2095.
20. Mokhles S, Macbeth F, Farewell V, et al. Meta-analysis of colorectal cancer follow-up after potentially curative resection. Br J Surg 2016; 103:1259.
21. Renehan AG, Egger M, Saunders MP, O'Dwyer ST. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. BMJ 2002; 324:813.
22. Figueredo A, Rumble RB, Maroun J, et al. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. BMC Cancer 2003; 3:26.
23. Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2007; :CD002200.
24. Tjandra JJ, Chan MK. Follow-up after curative resection of colorectal cancer: a meta-analysis. Dis Colon Rectum 2007; 50:1783.
25. Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2019; 9:CD002200.
26. Jeffery M, Hickey BE, Hider PN, See AM. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2016; 11:CD002200.

27. Baca B, Beart RW Jr, Etzioni DA. Surveillance after colorectal cancer resection: a systematic review. Dis Colon Rectum 2011; 54:1036.

28. Renehan AG, O'Dwyer ST, Whynes DK. Cost effectiveness analysis of intensive versus conventional follow up after curative resection for colorectal cancer. BMJ 2004; 328:81.

29. Snyder RA, Hu CY, Cuddy A, et al. Association Between Intensity of Posttreatment Surveillance Testing and Detection of Recurrence in Patients With Colorectal Cancer. JAMA 2018; 319:2104.

30. Meyerhardt JA, Mangu PB, Flynn PJ, et al. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer: American Society of Clinical Oncology clinical practice guideline endorsement. J Clin Oncol 2013; 31:4465.

31. Earle C, Annis R, Sussman J, et al. Follow-up care, surveillance protocol, and secondary prev ention measures for survivors of colorectal cancer. Recommendations from cancer Care On tario (CCO) available online at https://www.cancercare.on.ca/cms/one.aspx?objectId=28072 1&contextId=1377 (Accessed on November 22, 2013).

32. Labianca R, Nordlinger B, Beretta GD, et al. Primary colon cancer: ESMO Clinical Practice Guidelines for diagnosis, adjuvant treatment and follow-up. Ann Oncol 2010; 21 Suppl 5:v70.

33. Glynne-Jones R, Wyrwicz L, Tiret E, et al. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28:iv22.

34. Törnqvist A, Ekelund G, Leandoer L. The value of intensive follow-up after curative resection for colorectal carcinoma. Br J Surg 1982; 69:725.

35. Castells A, Bessa X, Daniels M, et al. Value of postoperative surveillance after radical surgery for colorectal cancer: results of a cohort study. Dis Colon Rectum 1998; 41:714.

36. British Columbia MEdical Association Guidelines. Followup of colorectal polyps or cancer. ht tp://www.bcguidelines.ca/pdf/colorectal_followup.pdf (Accessed on November 26, 2013).

37. Fletcher RH. Carcinoembryonic antigen. Ann Intern Med 1986; 104:66.

38. Arnaud JP, Koehl C, Adloff M. Carcinoembryonic antigen (CEA) in diagnosis and prognosis of colorectal carcinoma. Dis Colon Rectum 1980; 23:141.

39. Clinical practice guidelines for the use of tumor markers in breast and colorectal cancer. Adopted on May 17, 1996 by the American Society of Clinical Oncology. J Clin Oncol 1996; 14:2843.

40. Goldstein MJ, Mitchell EP. Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer. Cancer Invest 2005; 23:338.

41. Nicholson BD, Shinkins B, Pathiraja I, et al. Blood CEA levels for detecting recurrent colorectal cancer. Cochrane Database Syst Rev 2015; :CD011134.
42. Hara M, Kanemitsu Y, Hirai T, et al. Negative serum carcinoembryonic antigen has insufficient accuracy for excluding recurrence from patients with Dukes C colorectal cancer: analysis with likelihood ratio and posttest probability in a follow-up study. Dis Colon Rectum 2008; 51:1675.
43. Zeng Z, Cohen AM, Urmacher C. Usefulness of carcinoembryonic antigen monitoring despite normal preoperative values in node-positive colon cancer patients. Dis Colon Rectum 1993; 36:1063.
44. Bhattacharjya S, Aggarwal R, Davidson BR. Intensive follow-up after liver resection for colorectal liver metastases: results of combined serial tumour marker estimations and computed tomography of the chest and abdomen - a prospective study. Br J Cancer 2006; 95:21.
45. Park IJ, Choi GS, Lim KH, et al. Serum carcinoembryonic antigen monitoring after curative resection for colorectal cancer: clinical significance of the preoperative level. Ann Surg Oncol 2009; 16:3087.
46. Minton JP, Hoehn JL, Gerber DM, et al. Results of a 400-patient carcinoembryonic antigen second-look colorectal cancer study. Cancer 1985; 55:1284.
47. McCall JL, Black RB, Rich CA, et al. The value of serum carcinoembryonic antigen in predicting recurrent disease following curative resection of colorectal cancer. Dis Colon Rectum 1994; 37:875.
48. Hine KR, Dykes PW. Serum CEA testing in the post-operative surveillance of colorectal carcinoma. Br J Cancer 1984; 49:689.
49. Martin EW Jr, Cooperman M, Carey LC, Minton JP. Sixty second-look procedures indicated primarily by rise in serial carcinoembryonic antigen. J Surg Res 1980; 28:389.
50. Bruinvels DJ, Stiggelbout AM, Kievit J, et al. Follow-up of patients with colorectal cancer. A meta-analysis. Ann Surg 1994; 219:174.
51. Benson AB 3rd, Desch CE, Flynn PJ, et al. 2000 update of American Society of Clinical Oncology colorectal cancer surveillance guidelines. J Clin Oncol 2000; 18:3586.
52. Treasure T, Monson K, Fiorentino F, Russell C. The CEA Second-Look Trial: a randomised controlled trial of carcinoembryonic antigen prompted reoperation for recurrent colorectal cancer. BMJ Open 2014; 4:e004385.
53. Kievit J, van de Velde CJ. Utility and cost of carcinoembryonic antigen monitoring in colon cancer follow-up evaluation. A Markov analysis. Cancer 1990; 65:2580.

54. Litvak A, Cercek A, Segal N, et al. False-positive elevations of carcinoembryonic antigen in patients with a history of resected colorectal cancer. J Natl Compr Canc Netw 2014; 12:907.

55. Moertel CG, Fleming TR, Macdonald JS, et al. An evaluation of the carcinoembryonic antigen (CEA) test for monitoring patients with resected colon cancer. JAMA 1993; 270:943.

56. Alexander JC, Silverman NA, Chretien PB. Effect of age and cigarette smoking on carcinoembryonic antigen levels. JAMA 1976; 235:1975.

57. Sajid KM, Parveen R, Durr-e-Sabih, et al. Carcinoembryonic antigen (CEA) levels in hookah smokers, cigarette smokers and non-smokers. J Pak Med Assoc 2007; 57:595.

58. Guadagni F, Roselli M, Cosimelli M, et al. TAG-72 (CA 72-4 assay) as a complementary serum tumor antigen to carcinoembryonic antigen in monitoring patients with colorectal cancer. Cancer 1993; 72:2098.

59. von Kleist S, Hesse Y, Kananeeh H. Comparative evaluation of four tumor markers, CA 242, CA 19/9, TPA and CEA in carcinomas of the colon. Anticancer Res 1996; 16:2325.

60. Carpelan-Holmström M, Louhimo J, Stenman UH, et al. Estimating the probability of cancer with several tumor markers in patients with colorectal disease. Oncology 2004; 66:296.

61. Kerber A, Trojan J, Herrlinger K, et al. The new DR-70 immunoassay detects cancer of the gastrointestinal tract: a validation study. Aliment Pharmacol Ther 2004; 20:983.

62. Small-Howard AL, Harris H. Advantages of the AMDL-ELISA DR-70 (FDP) assay over carcinoembryonic antigen (CEA) for monitoring colorectal cancer patients. J Immunoassay Immunochem 2010; 31:131.

63. Shimwell NJ, Wei W, Wilson S, et al. Assessment of novel combinations of biomarkers for the detection of colorectal cancer. Cancer Biomark 2010; 7:123.

64. Cordero OJ, Imbernon M, Chiara LD, et al. Potential of soluble CD26 as a serum marker for colorectal cancer detection. World J Clin Oncol 2011; 2:245.

65. Ayude D, Fernández-Rodríguez J, Rodríguez-Berrocal FJ, et al. Value of the serum alpha-L-fucosidase activity in the diagnosis of colorectal cancer. Oncology 2000; 59:310.

66. Young GP, Pedersen SK, Mansfield S, et al. A cross-sectional study comparing a blood test for methylated BCAT1 and IKZF1 tumor-derived DNA with CEA for detection of recurrent colorectal cancer. Cancer Med 2016; 5:2763.

67. Schøler LV, Reinert T, Ørntoft MW, et al. Clinical Implications of Monitoring Circulating Tumor DNA in Patients with Colorectal Cancer. Clin Cancer Res 2017; 23:5437.

68. Wang Y, Li L, Cohen JD, et al. Prognostic Potential of Circulating Tumor DNA Measurement in Postoperative Surveillance of Nonmetastatic Colorectal Cancer. JAMA Oncol 2019; 5:1118.

69. Reinert T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. JAMA Oncol 2019; 5:1124.

70. Merker JD, Oxnard GR, Compton C, et al. Circulating Tumor DNA Analysis in Patients With Cancer: American Society of Clinical Oncology and College of American Pathologists Joint Review. J Clin Oncol 2018; 36:1631.

71. Morris V, Dasari A, Kopetz S. Can Circulating Tumor DNA in Early-Stage Colorectal Cancer Be More Than a Prognostic Biomarker? JAMA Oncol 2019; 5:1101.

72. Glimelius B, Påhlman L, Cervantes A, ESMO Guidelines Working Group. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010; 21 Suppl 5:v82.

73. Argilés G, Tabernero J, Labianca R, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2020; 31:1291.

74. Graffner H, Hultberg B, Johansson B, et al. Detection of recurrent cancer of the colon and rectum. J Surg Oncol 1985; 28:156.

75. Peethambaram P, Weiss M, Loprinzi CL, et al. An evaluation of postoperative follow-up tests in colon cancer patients treated for cure. Oncology 1997; 54:287.

76. Jahn H, Joergensen OD, Kronborg O, Fenger C. Can Hemoccult-II replace colonoscopy in surveillance after radical surgery for colorectal cancer and after polypectomy? Dis Colon Rectum 1992; 35:253.

77. Ahlquist DA, Wieand HS, Moertel CG, et al. Accuracy of fecal occult blood screening for colorectal neoplasia. A prospective study using Hemoccult and HemoQuant tests. JAMA 1993; 269:1262.

78. New Zealand Guidelines Group: Guidance on surveillance for people at increased risk of col orectal cancer. http://www.health.govt.nz/publication/guidance-surveillance-people-increas ed-risk-colorectal-cancer (Accessed on November 22, 2013).

79. Bleeker WA, Mulder NH, Hermans J, et al. Value and cost of follow-up after adjuvant treatment of patients with Dukes' C colonic cancer. Br J Surg 2001; 88:101.

80. Jeffery GM, Hickey BE, Hider P. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2002; :CD002200.

81. Tepper JE, O'Connell M, Hollis D, et al. Analysis of surgical salvage after failure of primary therapy in rectal cancer: results from Intergroup Study 0114. J Clin Oncol 2003; 21:3623.

82. Chau I, Allen MJ, Cunningham D, et al. The value of routine serum carcino-embryonic antigen measurement and computed tomography in the surveillance of patients after adjuvant chemotherapy for colorectal cancer. J Clin Oncol 2004; 22:1420.

83. Mortazavi A, Shaukat A, Othman E, et al. Postoperative computed tomography scan surveillance for patients with stage II and III colorectal cancer: worthy of further study? Am J Clin Oncol 2005; 28:30.
84. Sobhani I, Tiret E, Lebtahi R, et al. Early detection of recurrence by 18FDG-PET in the follow-up of patients with colorectal cancer. Br J Cancer 2008; 98:875.
85. Ringland CL, Arkenau HT, O'Connell DL, Ward RL. Second primary colorectal cancers (SPCRCs): experiences from a large Australian Cancer Registry. Ann Oncol 2010; 21:92.
86. Passman MA, Pommier RF, Vetto JT. Synchronous colon primaries have the same prognosis as solitary colon cancers. Dis Colon Rectum 1996; 39:329.
87. Kahi CJ, Boland CR, Dominitz JA, et al. Colonoscopy Surveillance After Colorectal Cancer Resection: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2016; 150:758.
88. Safi F, Beyer HG. The value of follow-up after curative surgery of colorectal carcinoma. Cancer Detect Prev 1993; 17:417.
89. Barillari P, Ramacciato G, Manetti G, et al. Surveillance of colorectal cancer: effectiveness of early detection of intraluminal recurrences on prognosis and survival of patients treated for cure. Dis Colon Rectum 1996; 39:388.
90. Juhl G, Larson GM, Mullins R, et al. Six-year results of annual colonoscopy after resection of colorectal cancer. World J Surg 1990; 14:255.
91. Green RJ, Metlay JP, Propert K, et al. Surveillance for second primary colorectal cancer after adjuvant chemotherapy: an analysis of Intergroup 0089. Ann Intern Med 2002; 136:261.
92. Mulder SA, Kranse R, Damhuis RA, et al. The incidence and risk factors of metachronous colorectal cancer: an indication for follow-up. Dis Colon Rectum 2012; 55:522.
93. Cali RL, Pitsch RM, Thorson AG, et al. Cumulative incidence of metachronous colorectal cancer. Dis Colon Rectum 1993; 36:388.
94. Fuccio L, Rex D, Ponchon T, et al. New and Recurrent Colorectal Cancers After Resection: a Systematic Review and Meta-analysis of Endoscopic Surveillance Studies. Gastroenterology 2019; 156:1309.
95. van Lanschot MCJ, van Leerdam ME, Lansdorp-Vogelaar I, et al. Yield of Surveillance Colonoscopies 1 Year After Curative Surgical Colorectal Cancer Resections. Clin Gastroenterol Hepatol 2019; 17:2285.
96. Obrand DI, Gordon PH. Incidence and patterns of recurrence following curative resection for colorectal carcinoma. Dis Colon Rectum 1997; 40:15.

97. Ramsey SD, Howlader N, Etzioni R, et al. Surveillance endoscopy does not improve survival for patients with local and regional stage colorectal cancer. Cancer 2007; 109:2222.

98. Fisher DA, Jeffreys A, Grambow SC, Provenzale D. Mortality and follow-up colonoscopy after colorectal cancer. Am J Gastroenterol 2003; 98:901.

99. Rulyak SJ, Lieberman DA, Wagner EH, Mandelson MT. Outcome of follow-up colon examination among a population-based cohort of colorectal cancer patients. Clin Gastroenterol Hepatol 2007; 5:470.

100. Rex DK, Kahi CJ, Levin B, et al. Guidelines for colonoscopy surveillance after cancer resection: a consensus update by the American Cancer Society and the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2006; 130:1865.

101. Rex DK, Lehman GA, Ulbright TM, et al. Colonic neoplasia in asymptomatic persons with negative fecal occult blood tests: influence of age, gender, and family history. Am J Gastroenterol 1993; 88:825.

102. Imperiale TF, Wagner DR, Lin CY, et al. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. N Engl J Med 2000; 343:169.

103. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Fecal DNA versus fecal occult blood for colorectal-cancer screening in an average-risk population. N Engl J Med 2004; 351:2704.

104. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993; 329:1977.

105. Winawer SJ, Zauber AG, O'Brien MJ, et al. Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. The National Polyp Study Workgroup. N Engl J Med 1993; 328:901.

106. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013; 369:1095.

107. Tran AH, Man Ngor EW, Wu BU. Surveillance colonoscopy in elderly patients: a retrospective cohort study. JAMA Intern Med 2014; 174:1675.

108. Travis AC, Pievsky D, Saltzman JR. Endoscopy in the elderly. Am J Gastroenterol 2012; 107:1495.

109. Day LW, Walter LC, Velayos F. Colorectal cancer screening and surveillance in the elderly patient. Am J Gastroenterol 2011; 106:1197.

110. Wilson JA. Colon cancer screening in the elderly: when do we stop? Trans Am Clin Climatol Assoc 2010; 121:94.

111. Westwood M, Joore M, Grutters J, et al. Contrast-enhanced ultrasound using SonoVue® (sulphur hexafluoride microbubbles) compared with contrast-enhanced computed

tomography and contrast-enhanced magnetic resonance imaging for the characterisation of focal liver lesions and detection of liver metastases: a systematic review and cost-effectiveness analysis. Health Technol Assess 2013; 17:1.

112. Piscaglia F, Nolsøe C, Dietrich CF, et al. The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS): update 2011 on non-hepatic applications. Ultraschall Med 2012; 33:33.
113. Tsikitis VL, Malireddy K, Green EA, et al. Postoperative surveillance recommendations for early stage colon cancer based on results from the clinical outcomes of surgical therapy trial. J Clin Oncol 2009; 27:3671.
114. Chao M, Gibbs P. Caution is required before recommending routine carcinoembryonic antigen and imaging follow-up for patients with early-stage colon cancer. J Clin Oncol 2009; 27:e279.
115. Hardiman KM, Felder SI, Friedman G, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surveillance and Survivorship Care of Patients After Curative Treatment of Colon and Rectal Cancer. Dis Colon Rectum 2021; 64:517.
116. Van Cutsem E, Cervantes A, Nordlinger B, et al. Metastatic colorectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2014; 25 Suppl 3:iii1.
117. El-Shami K, Oeffinger KC, Erb NL, et al. American Cancer Society Colorectal Cancer Survivorship Care Guidelines. CA Cancer J Clin 2015; 65:428.
118. Schmitz KH, Courneya KS, Matthews C, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 2010; 42:1409.
119. Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology 2003; 124:544.
120. Stoffel EM, Mangu PB, Gruber SB, et al. Hereditary colorectal cancer syndromes: American Society of Clinical Oncology Clinical Practice Guideline endorsement of the familial risk-colorectal cancer: European Society for Medical Oncology Clinical Practice Guidelines. J Clin Oncol 2015; 33:209.
121. Giardiello FM, Allen JI, Axilbund JE, et al. Guidelines on genetic evaluation and management of Lynch syndrome: a consensus statement by the US Multi-Society Task Force on Colorectal Cancer. Dis Colon Rectum 2014; 57:1025.
122. Balmaña J, Balaguer F, Cervantes A, et al. Familial risk-colorectal cancer: ESMO Clinical Practice Guidelines. Ann Oncol 2013; 24 Suppl 6:vi73.
123. Sieber OM, Lipton L, Crabtree M, et al. Multiple colorectal adenomas, classic adenomatous polyposis, and germ-line mutations in MYH. N Engl J Med 2003; 348:791.

Topic 2493 Version 90.0

GRAPHICS

Colorectal cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)
T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscularis propria into pericolorectal tissues
T4	Tumor invades* the visceral peritoneum or invades or adheres¶ to adjacent organ or structure
T4a	Tumor invades* through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b	Tumor directly invades* or adheres¶ to adjacent organs or structures
* Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina). ¶ Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classification should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN prognostic factor should be used for perineural invasion.	
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis

N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
N1a	One regional lymph node is positive
N1b	Two or three regional lymph nodes are positive
N1c	No regional lymph nodes are positive, but there are tumor deposits in the: ▪ Subserosa ▪ Mesentery ▪ Nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	Four or more regional nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis by imaging, etc; no evidence of tumor in distant sites or organs. (This category is not assigned by pathologists.)
M1	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
M1a	Metastasis to one site or organ is identified without peritoneal metastasis
M1b	Metastasis to two or more sites or organs is identified without peritoneal metastasis
M1c	Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

Prognostic stage groups

When T is…	And N is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1, T2	N0	M0	I
T3	N0	M0	IIA
T4a	N0	M0	IIB
T4b	N0	M0	IIC
T1-T2	N1/N1c	M0	IIIA
T1	N2a	M0	IIIA
T3-T4a	N1/N1c	M0	IIIB

T2-T3	N2a	M0	IIIB
T1-T2	N2b	M0	IIIB
T4a	N2a	M0	IIIC
T3-T4a	N2b	M0	IIIC
T4b	N1-N2	M0	IIIC
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB
Any T	Any N	M1c	IVC

TNM: Tumor, Node, Metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. Corrected at 4th printing, 2018.

Graphic 111438 Version 10.0

Results of hepatic resection for metastatic colorectal cancer

Author and year	Number of patients	Five-year OS, percent	Median survival, months
Hughes KS; 1986	607	33	NR
Scheele J; 1995	434	33	40
Nordlinger B; 1996	1568	28	NR
Jamison RL; 1997	280	27	33
Fong Y; 1999	1001	37	42
Iwatsuki S; 1999	305	32	NR
Choti M; 2002	133	58	NR
Abdalla E; 2004	190	58	NR
Fernandez FG; 2004	100	58	NR
Wei AC; 2006	423	47	NR
Rees M; 2008	929	36	42.5
de Jong M; 2009	1669	47	36
Morris EJ; 2010	3116	44	NR

OS: overall survival; NR: not reported.

Graphic 74509 Version 7.0

Summary of professional guidelines regarding posttreatment surveillance for resected colon and rectal cancer

Organization	History and physical examination	CEA testing	CT scanning	Endoscopic surveillance	C
ASCO[1] and CCO[2]	Every 3 to 6 months for 5 years.	Every 3 to 6 months for 5 years.	Abdomen and chest annually for 3 years; pelvis: rectal cancer only, annually for 3 to 5 years.	Colonoscopy at 1 year*; subsequent studies dictated by prior findings. If negative, every 5 years. Proctosigmoidoscopy every 6 months for 2 to 5 years if rectal cancer and no pelvic RT.	Posttre surveill guided risk of functio recomm for rese III colo cancer. Recom provide stage I to lack recomm
American Cancer Society[3]	Every 3 to 6 months for the first 2 years, then every 6 months to 5 years.	Every 3 to 6 months for the first 2 years, then every 6 months to 5 years if the patient is a potential candidate for further intervention.	Abdomen/pelvis and chest every 12 months for 5 years for stage III and high-risk stage I/II disease.	Colonoscopy in year 1; if advanced adenoma, repeat in 1 year; otherwise, repeat in 3 years. If no advanced adenoma in year 4, repeat every 5 years.	High-ri disease
NCCN[4]	Every 3 to 6 months for 2 years, then every 6 months for 3 years.	Every 3 to 6 months for 2 years for ≥T2 disease, then every 6 months for 3 years. For resected metastatic disease, every 3 to 6	Colon: Abdomen/pelvis and chest every 6 to 12 months for up to 5 years for those at high risk of recurrence¶. For rectal cancer, CT chest/abdomen	Colonoscopy at 1 yearΔ; subsequent studies dictated by prior findings. If no advanced adenoma, repeat at 3 years, then every 5 years; if advanced adenoma at 1 year, repeat at 1 year.	Recom to stag resecte cancer, II, III, o IV recta

		months for 2 years, then every 6 months for 3 to 5 years.	and pelvis every 3 to 6 months for 2 years, then every 6 to 12 months for up to 5 years for those at high risk of recurrence¶. For resected metastatic disease, CT abdomen/pelvis and chest every 3 to 6 months for 2 years, then every 6 to 12 months up to a total of 5 years.	Flexible sigmoidoscopy with EUS or MRI every 3 to 6 months for 2 years, then every 6 months to complete 5 years for patients with rectal cancer undergoing transanal excision only.	
ESMO colon cancer[5]	Every 3 to 6 months for 3 years, then every 6 to 12 months for 2 more years.	Every 3 to 6 months for 3 years, then every 6 to 12 months for 2 years.	Abdomen, chest, and pelvis every 6 to 12 months for 3 years, then every 12 months for 2 more years.	Colonoscopy at 1 year; every 3 to 5 years thereafter.	Guideli localize do not applica stage I More ir surveill years f metast Refer t on "Sur colorec resecti
ESMO rectal cancer[7]	Every 6 months for 2 years◇.	Every 6 months for the first 3 years.	A minimum of 2 CT scans of the chest, abdomen, and pelvis in the first 3 years.	Colonoscopy every 5 years up to age 75.	High-ri circum resecti positive more p surveill recurre

					More ir surveill years f metast Refer t on "Sur colorec resecti
New Zealand[8]	Clinical assessment§ stratified according to risk of recurrence: ▪ *High-risk cancer (stage IIB, III):* Every 6 to 12 months for 3 years, then annually for 2 years. ▪ *Lower risk (stage I, IIA), or with comorbidities restricting future surgery:* Annual review for 5 years or when symptoms occur.	*For high-risk cancer (stage IIB, III):* Every 6 to 12 months for 3 years, then annually for 2 years. *For lower risk (stage I, IIA), or with comorbidities restricting future surgery:* Annually for 5 years.	All individuals with stages I to III colorectal cancer should have liver imaging between years 1 and 3.	Colonoscopy at 1 year¥; colonoscopy every 6 to 12 months for 3 years for high-risk patients (stages IIB, III), then annually for at least 5 years. For low-risk patients, colonoscopy every 3 to 5 years. For rectal cancer, proctoscopy or sigmoidoscopy at 3, 6, 12, and 24 months postsurgery; colonoscopy at 3- to 5-year intervals thereafter.	Recom stages colorec
US Multi-Society Task Force on Colorectal Cancer[9]				Colonoscopy 1 year after surgery (or 1 year after the clearing perioperative colonoscopy). The interval to the next colonoscopy should be 3 years and then 5 years. If neoplastic polyps are	

				detected, the intervals between colonoscopies should be shorter and in accordance with published guidelines for polyp surveillance intervals[10]. These intervals do not apply to patients with Lynch syndrome. For rectal cancer, flexible sigmoidoscopy or EUS every 3 to 6 months for the first 2 to 3 years after surgery for patients at high risk for local recurrence. Refer to UpToDate topic on "Surveillance after colorectal cancer resection."	
British Columbia Medical Association[11]	Every 3 to 6 months for 2 years, then every 6 months for 3 years.	Every 3 months for 3 years, then every 6 months for 2 years.	Liver ultrasound or CT scans (preferred) every 6 months for 3 years, then annually for 2 years. Annual chest CT for 3 years.	Colonoscopy at 1 year; if normal, repeat 3 years later and, if normal, every 5 years thereafter.	These g resecte colon a Patient comorb advanc 5-year are not surveill
American Society of Colon and Rectal Surgeons[12]	Every 3 to 12 months for 2 years, then every 6 to 12 months for 3 years.	Every 3 to 12 months for 2 years, then every 6 to 12 months for 3 years.	Twice in 5 years or up to annually for 5 years.	Colonoscopy at 1 year (or 1 to 6 months after surgery if inadequate colonoscopy preoperatively, and depending on findings, repeat at 3 years, then every 5 years or more	Recom to high (eg, rec posttra colorec endosc only, or based t stage I disease

				frequently as indicated). Proctoscopy ±endoscopic ultrasound every 6 to 12 months after rectal cancer resection with anastomosis (no RT), or every 6 months following local excision for 3 to 5 years.	curativ UpToD "Survei colorec resecti

CEA: carcinoembryonic antigen; CT: computed tomography; ASCO: American Society of Clinical Oncology; CCO: Cancer Care Ontario; RT: radiation therapy; NCCN: National Comprehensive Cancer Network; EUS: endoscopic ultrasound; MRI: magnetic resonance imaging; ESMO: European Society for Medical Oncology.

* Except if no preoperative colonoscopy because of obstructing lesion; do as soon as possible after completion of adjuvant chemotherapy rather than waiting until 1 year.

¶ Features suggesting a high risk of recurrence: poorly differentiated histology, lymphatic or venous invasion.

Δ Except if no preoperative colonoscopy because of obstructing lesion; recommend at 3 to 6 months rather than waiting until 1 year.

◇ Minimum provisional recommendation.

§ Clinical assessment for patients with colon cancer includes physical examination, CEA, chest/abdominal and pelvic CT scans, colonoscopy, and liver ultrasound. Clinical assessment for rectal cancer patients includes physical examination, CEA, chest/abdominal and pelvic CT scans, colonoscopy, and proctoscopy or sigmoidoscopy.

¥ If no complete colonoscopy before surgery, perform colonoscopy within 6 months.

References

1. *Meyerhardt JA, Mangu PB, Flynn PJ, et al. Follow-Up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer: American Society of Clinical Oncology Clinical Practice Guideline Endorsement. J Clin Oncol 2013; 31:4465.*
2. *Cancer Care Ontario. Available at: https://www.cancercareontario.ca/en/content/follow-care-surveillance-protocols-and-secondary-prevention-measures-survivors-colorectal-cancer.*
3. *American Cancer Society Colorectal Cancer Survivorship Care Guidelines. CA Cancer J Clin 2015; 65:427.*
4. *National Comprehensive Cancer Network. Available at: www.nccn.org.*
5. *Argiles G, Tabernero J, Labianca R, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. Ann Oncol 2020; 31:1291.*
6. *Van Cutsem E, Cervantes A, Nordlinger B, et al. Metastatic colorectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2014; 25 Suppl 3:iii1.*
7. *Glynne-Jones R, Wyrwicz L, Tiret E, et al. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (suppl 4):iv22.*

8. *Guidance on Surveillance for People at Increased Risk of Colorectal Cancer. Published by the New Zealand Guidelines Group for the Ministry of Health PO Box 10 665, Wellington 6143, New Zealand. Available at: www.health.govt.nz/publication/guidance-surveillance-people-increased-risk-colorectal-cancer.*
9. *Colonoscopy surveillance after colorectal cancer resection: Recommendations of the US Multi-Society Task Force on Colorectal Cancer (American Gastroenterological Association, American College of Gastroenterology, American Society for Gastrointestinal Endoscopy). Gastroenterology 2016; 150:758.*
10. *Guidelines for colonoscopy surveillance after screening and polypectomy from the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 20121; 143:844.*
11. *British Columbia Medial Association. Follow-up of Colorectal Polyps or Cancer (2013). Available at: www.bcguidelines.ca/pdf/colorectal_followup.pdf.*
12. *Hardiman KM, Felder SI, Friedman G, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surveillance and Survivorship care of patients after curative treatment of colon and rectal cancer. Dis Colon Rectum 2021; 64:517.*

Graphic 91618 Version 21.0

Charlson risk index

Condition	Assigned weights for diseases
Myocardial infarct	1
Heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Ulcer disease	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate or severe renal disease	2
Diabetes with end organ damage	2
Any tumor	2
Leukemia	2
Lymphoma	2
Moderate or severe liver disease	3
Metastatic solid tumor	6
AIDS	6
Weighted comorbidity classes	
Low	0 points
Medium	1 to 2 points
High	3 to 4 points
Very high	≥5 points

AIDS: acquired immunodeficiency syndrome.

Adapted from: Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40:373.

Graphic 72047 Version 4.0

The revised Bethesda guidelines for testing colorectal tumors for microsatellite instability (MSI)

Tumors from individuals should be tested for MSI in the following situations:
1. Colorectal cancer diagnosed in a patient who is less than 50 years of age.
2. Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors*, regardless of age.
3. Colorectal cancer with the MSI-H¶-like histologyΔ diagnosed in a patient who is less than 60 years of age◇.
4. Colorectal cancer diagnosed in a patient with one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years.
5. Colorectal cancer diagnosed in a patient with two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age.

HNPCC: hereditary nonpolyposis colorectal cancer; MSI-H: microsatellite instability-high.

* HNPCC-related tumors include colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain (usually glioblastoma as seen in Turcot syndrome) tumors, sebaceous gland adenomas and keratocanthomas in Muir-Torre syndrome, and carcinoma of the small bowel.

¶ MSI-H in tumors refers to changes in two or more of the five National Cancer Institute-recommended panels of microsatellite markers.

Δ Presence of tumor infiltrating lymphocytes. Crohn's-like lymphocytic reaction, mucinous/signet-ring differentiation, or medullary growth pattern.

◇ There was no consensus among the Workshop participants on whether to include the age criteria in guideline 3 above; participants voted to keep less than 60 years of age in the guidelines.

Graphic 72965 Version 5.0

Contributor Disclosures

Beverly Moy, MD, MPH No relevant financial relationship(s) with ineligible companies to disclose. **Brian C Jacobson, MD, MPH** No relevant financial relationship(s) with ineligible companies to disclose. **Kenneth K Tanabe, MD** Patent Holder: EGF SNP to determine risk for HCC [Cirrhosis, hepatocellular carcinoma]; Use of EGFR inhibitors to prevent HCC [Cirrhosis, hepatocellular carcinoma]. Consultant/Advisory Boards: Cancer Expert Now [GI cancers, melanoma]; GSK [GI Cancers]; Imvax [GI cancers]; Leidos [Melanoma, GI cancers]; Teledoc [GI cancers, melanoma]. Other Financial Interest: American Cancer Society [Honoraria as editor of Cancer]. All of the relevant financial relationships listed have been mitigated. **Richard M Goldberg, MD** Equity Ownership/Stock Options: Advanced Chemotec Inc [Pancreatic cancer]; Compass Therapeutics [Biliary tract and colorectal cancer]. Consultant/Advisory Boards: AbbVie [GI cancers]; Advanced Chemotherapy Technologies [GI cancer]; AstraZeneca [GI cancer]; Bayer [GI cancer]; Compass Therapeutics [GI cancer]; Eisai [GI cancer]; G1 Therapeutics [GI cancer]; GSK [Colorectal cancer]; Innovative Cellular Therapeutics [Colorectal cancer]; Inspirna [Colorectal cancer]; Merck [GI cancer]; Modulation Therapeutics [Lymphoma]; Novartis [GI cancer]; Sorrento Therapeutics [GI cancer]; Taiho [GI cancer]. Other Financial Interest: Taiho [Expert testimony GI cancer]. All of the relevant financial relationships listed have been mitigated. **Sonali M Shah, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→