Recommended Colorectal Cancer Surveillance Guidelines by the American Society of Clinical Oncology

By Christopher E. Desch, Al B. Benson III, Thomas J. Smith, Patrick J. Flynn, Carol Krause, Charles L. Loprinzi, Bruce D. Minsky, Nicholas J. Petrelli, David G. Pfister, and Mark R. Somerfield

**Objective:** To determine the most effective, evidence-based, postoperative surveillance strategy for the detection of recurrent colon and rectal cancer. Tests are to be recommended only if they have an impact on the outcomes listed below.

**Potential Intervention:** All tests described in the literature for postoperative monitoring were considered. In addition, the data were critically evaluated to determine the optimal frequency of monitoring.

**Outcomes:** Outcomes of interest included overall and disease-free survival, quality of life, toxicity reduction, and cost-effectiveness. The American Society of Clinical Oncology (ASCO) Colorectal Cancer Surveillance Expert Panel was guided by the principle of cost minimization, i.e., when two strategies were believed to be equally effective, the least expensive test was recommended.

**Evidence:** A complete MEDLINE search was performed of the last 20 years of the medical literature. Keywords included colorectal cancer, follow-up, and carcinoembryonic antigen, as well as the names of the specific tests. The search was broadened by articles from the tumor marker ASCO panel literature search, as well as from bibliographies of selected articles.

**Validation:** Five outside reviewers, the ASCO Health Services Research Committee, and the ASCO Board of Directors examined this document.

**Sponsor:** American Society of Clinical Oncology.


Because metastatic disease is usually fatal, there has been a tremendous amount of effort focused on finding recurrent colon and rectal cancers before symptoms develop, at a stage when another curative resection is still possible. Carcinoembryonic antigen (CEA) tests, colonoscopies, chest x-rays (CXRs), liver function tests (LFTs), complete blood cell counts (CBCs), fecal occult blood tests (FOBTs), computerized tomography (CT), and ultrasonography were all evaluated in this setting in the hopes of reducing the incidence of incurable metastatic disease.

The findings from studies of postoperative monitoring in colorectal cancer have varied widely. As a result of this uncertainty, there is considerable variation in follow-up practice. The variation in practice has resulted in wide variation in follow-up costs. For example, the differences between Medicare-allowed charges differed 28-fold (from $561 to $16,492 over a 5-year period). As a result of these differences in patterns, costs, and reported outcomes, the American Society of Clinical Oncology (ASCO) convened an expert panel to address the issue of colorectal cancer-related surveillance.

**PRACTICE GUIDELINES**

"Practice guidelines are systematically developed strategies to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."
Attributes of good guidelines include validity, reliability, reproducibility, clinical applicability, clinical flexibility, clarity, multidisciplinary process, review of evidence, and documentation. Guidelines may be useful in producing better care and decreasing its cost. Specifically, utilization of clinical guidelines may provide the following: (1) improvements in outcomes, (2) improvements in medical practice, (3) a means for minimizing inappropriate practice variation, (4) decision support tools for practitioners, (5) points of reference for medical orientation and education, (6) criteria for self-evaluation, (7) indicators and criteria for external quality review, (8) assistance with reimbursement and coverage decisions, and (9) criteria for use in credentialing decisions.

In formulating recommendations for colorectal cancer surveillance, ASCO considered these tenets of guideline development, emphasizing review of data from controlled clinical trials. However, it is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same results. Accordingly, ASCO considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient’s individual circumstances. In addition, these guidelines describe administration of therapies in clinical practice; they cannot be assumed to apply to interventions performed in the context of clinical trials, given that clinical studies are designed to test innovative and novel therapies in a disease for which better therapy is sorely needed. In that guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions for further research and those settings in which investigational therapy should be considered.

**METHODS**

A methodology similar to that applied in prior ASCO practice guidelines was used and is described in more detail below.

**Panel Composition**

The panel was composed of experts in clinical medicine, clinical research, outcomes/health services research, and related disciplines (medical decision making, health economics, and quality of life) and medical ethics, with a focus on expertise in colon and rectal cancer. A patient representative was also included on the panel. The clinical experts represented all relevant medical disciplines, including medical oncology, radiation oncology, and surgical oncology. Both academic and community practitioners were included. A steering committee under the auspices of the Health Services Research Committee chose panel participants for the clinical practice guideline development process. Panel participants are listed in the Appendix.

**Process Overview**

In evaluating the evidence regarding surveillance after primary treatment of colorectal cancer, the panel followed a process for guideline development established by the American College of Chest Physicians. The process included a systematic weighting of the level of the evidence and a systematic grading of the evidence for making a recommendation (Table 1).

**Review of Available Data**

Pertinent information from the published literature as of July 1998 was retrieved and reviewed for the creation of these guidelines. Searches of MEDLINE (National Library of Medicine, Bethesda, MD) and other databases for pertinent articles were performed. Search words included colon cancer, rectal cancer, follow-up, each specific test considered, cost-effectiveness, and clinical trials. Directed searches were made of the primary articles. In addition, certain authors/investigators were contacted to obtain more recent, unpublished information. Much of the literature on CEA testing examined by the ASCO Tumor Marker Guidelines Panel was also relevant. The panel did not review the evidence on CEA testing, and instead used the guideline already developed by the ASCO Expert Panel on Tumor Marker Recommendations. Each other follow-up test, including the history and physical examination, was discussed based on the evidence in the literature. More weight was given to publications that described randomized trials. The guidelines were reviewed by three outside experts in gastroenterology, an expert in surgical oncology, and an outside health service researcher.

The panel considered colon and rectal cancer as different tumors where appropriate. However, for most issues, the follow-up is similar. When possible, the tests with the greatest potential to detect recurrence were considered, but alternatives were provided when cost or patient comfort was a major issue.

<table>
<thead>
<tr>
<th>Table 1. Levels of Evidence and Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>V</td>
</tr>
</tbody>
</table>

**Grade** | **Grade of Recommendation** |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>There is evidence of type I or consistent findings from multiple studies of type II, III, or IV.</td>
</tr>
<tr>
<td>B</td>
<td>There is evidence of type II, III, or IV and findings are generally consistent.</td>
</tr>
<tr>
<td>C</td>
<td>There is evidence of type II, III, or IV but findings are inconsistent.</td>
</tr>
<tr>
<td>D</td>
<td>There is little or no systematic empirical evidence.</td>
</tr>
</tbody>
</table>
The following outcomes were considered in determining the optimal
tests and frequency of postoperative colorectal cancer monitoring:
survival, disease-free survival, quality of life, reduction in toxicity, and
cost-effectiveness. However, these outcomes were difficult to apply in
many situations because of the lack of clinical trials addressing specific
tests.

The panel addressed the success of surgery for isolated metastatic
disease. Several published studies show a 20% to 30% long-term
survival rate in selected patients undergoing resection for isolated
hepatic or pulmonary metastases. Therefore, the panel also ad-
dressed whether any of the tests clearly identified resectable (hepatic,
pulmonary, and local) disease before symptoms developed.

Until there is better therapy for metastatic disease, extending the lead
time (ie, the interval between when the test is positive and when
symptoms begin) by frequent testing is unlikely to prolong survival or
quality of life. The data are clear, however, that chemotherapy of
asymptomatic colorectal cancer can improve short-term survival and often
improve the quality of life. Furthermore, there is some evidence that
treatment of patients with asymptomatic metastatic colorectal cancer
may yield better results than treatment of those patients only once they
come symptomatic. The Nordic Gastrointestinal Tumor Adjuvant
Therapy Group found that patients treated while asymptomatic had 6
months better average survival, although randomized cohorts were
imbalanced in terms of risk. Allen-Mersh et al found improved
survival of 6 months in a group of patients who had received palliative
hepatic artery embolization compared with those who had not. The
National Cancer Institute of Canada is coordinating a confirmatory
randomized phase III trial (CAN-NCIC-C010, NCI-V94-0463) to
evaluate immediate versus delayed fluorouracil and leucovorin for
asymptomatic advanced colorectal cancer patients. Expected accrual
would include 180 patients. The trial is designed to determine whether
there are survival and quality-of-life differences for asymptomatic
patients who receive chemotherapy before the onset of symptoms from
advanced disease compared with those who are treated with chemotherapy
only when symptoms develop.

The panel focused on the ability to detect those patients with
asymptomatic metastatic colorectal cancer and recommended tests that
are able to discover a recurrence before symptoms develop and that
have been shown consistently in the literature to be the first test to
document an isolated metastasis. Because resection of an isolated
metastasis seems to be the only way to improve long-term survival for
patients with colorectal cancer, most of the commonly available
surveillance tests could be justified only in those patients who would be
willing and able (ie, lacking significant comorbidity) to undergo a
hepatic, pulmonary, or anastomotic resection.

The panel limited its attention to sporadic cases of colon and rectal
cancer. Patients with hereditary cancers may need more frequent
attention: guidelines for screening this population are addressed in the
World Health Organization (WHO) publication on the prevention of
colorectal cancer.

Consensus Development Based on Evidence

The panel identified topics to be addressed by the guideline,
developed a strategy for completion of the guideline, and reviewed the
literature. The panel examined both retrospective and prospective
studies that evaluated the effectiveness of surveillance testing in
detecting recurrence earlier and positively affecting survival. The
recommendations made by the expert panel are based on current
methods of detecting the recurrence of colorectal cancer. The guidelines
were circulated in draft form through several iterations, and all
members of the panel had an opportunity to comment on the recommenda-
tions.

The panel did not attempt to codify established practice. The experts
reviewed the available evidence and added their best clinical judgment
to make final recommendations, using standardized language to charac-
terize the strength of the evidence. In accordance with the ASCO Health
Services Research Policies and Procedures for guidelines, “recommend-
dation” was used when there was level I or II evidence and panel
consensus. “Suggestion” was used when there was level III, IV, or V
evidence and panel consensus. “No guideline possible” was used when
there were no data or the panel could not reach consensus.

Guideline and Conflict of Interest

The content of the guidelines and the draft manuscript were reviewed
and approved by the Health Services Research Committee and by the
ASCO Board of Directors before dissemination. All members of the
expert panel complied with ASCO policy on conflict of interest, which
requires disclosure of any financial or other interest that might be
construed as constituting an actual, potential, or apparent conflict.
Members of the expert panel completed ASCO’s disclosure form and
were asked to reveal ties to companies developing products that might
potentially be affected by promulgation of the guidelines. Information
was requested regarding employment, consultancies, stock ownership,
honoraria, research funding, expert testimony, and membership on
company advisory committees. The panel made decisions on a case-by-
case basis as to whether an individual’s role should be limited as a result
of a conflict.

Revision Dates

At annual intervals, the panel chairpersons and two panel members
designated by the chairpersons will determine the need for revisions to
the guidelines, on the basis of an examination of current literature. The
entire panel will be reconvened every 3 years to discuss potential
changes or more frequently if new information suggests that more
timely modifications may be warranted. When appropriate, the panel
will recommend revised guidelines to the Health Services Research
Committee and the ASCO Board for review and approval.

Review of Available Data

The results of postoperative monitoring in colorectal cancer have
varied widely. The most comprehensive study of follow-up care was
done in Australia with 325 patients at several centers. The randomized
study design tested the addition of a yearly colonoscopy, CT scan of the
liver, and CXR to a regular schedule of physician or nurse examination,
CBCs, LFTs, FOBT, and CEA testing (n = 167 for intensive follow-up v
n = 158 for standard follow-up; the results of this trial are summarized
in Table 2). Of note, patients on the standard arm underwent colonos-
copy, CT scan, and CXR after completing 5 years of follow-up. This
study was designed to detect a 15% difference in survival between the
two groups. Overall, there was a 6% to 7% advantage at 5 years in
overall survival rates for the intensively screened group; however, this
difference did not reach statistical significance by the design of the trial
(P = .07 on univariate Cox regression; P = .1986 when joint effects of
significant variables were considered).

Yearly colonoscopy detected no asymptomatic local recurrences;
only one asymptomatic second primary colon cancer was found. Yearly
CT scans detected asymptomatic liver-only metastases much more
frequently than the standard screening strategy (10/14 v 0/12, respec-
tively, P = .0002). However, the resection rate of the discovered liver
metastases was not significantly different between the two arms (three v four), and only one of these patients has subsequently remained disease-free (intensive arm). The patients allocated to the intensely monitored arm underwent an extra 608 CT scans.

The CXR was not very effective at detecting recurrences. Only 5% of patients had asymptomatic lung metastases found by annual CXR, with three patients resectable and only one patient remaining disease-free long term. In the annual screening group, 633 more CXRs were obtained every 3 months (rectal cancer only) and a yearly colonoscopy. In addition, intensive surveillance patients underwent liver ultrasonography every 3 months (rectal cancer only) and a yearly abdominal CT scan. Again, recurrence rates were nearly the same in the "intensified follow-up" and control groups (42%, or 22/52, and 39%, or 21/54, respectively). Attempts at curative resections of recurrence were possible in five patients (29%) in the experimental group and in three patients (17%) in the control group. Less than one third of patients with recurring disease, even in the intensely followed group, had a chance of long-term survival with a high-intensity follow-up strategy. salvage therapy seemed successful in two of five patients in the intensive group (v none of the three patients in the control arm), which is a net 4% of the original population. Intensive surveillance resulted in only a slight improvement in the cancer-specific (78% v 71%) and overall (75% v 67%) 5-year survival rates. Neither of these differences was statistically significant, although the power of the comparisons was limited.

In the other prospective randomized trial performed by Makela et al,21 all individuals underwent similar testing with history and physical examination, CEA testing, and CXR. The standard surveillance group underwent rigid sigmoidoscopy (rectal cancer only) and a yearly barium enema. The intensive surveillance group received a flexible sigmoidoscopy every 3 months (rectal cancer only) and a yearly colonoscopy. In addition, intensive surveillance patients underwent liver ultrasonography every 6 months and a yearly abdominal CT scan. Again, recurrence rates were nearly the same in the "intensified follow-up" and control groups (42%, or 22/52, and 39%, or 21/54, respectively). Attempts at curative resection were possible in 22% and 14%, respectively. The results of such surgery were not reported, however. The cancer-specific survival rates at 5 years were not reported, but overall survival rates were not statistically different (59% v 54%). However, as with the study by Ohlsson et al,20 the sample size in the trial reported by Makela et al was relatively small, increasing the chance of a false-negative result. Indeed, there was not enough statistical power in either study to detect a small survival benefit (< 15%) for monitoring.

Goldberg et al22 reported on 1,247 patients enrolled in the North American Gastrointestinal Intergroup adjuvant colon cancer clinical trial and followed according to protocol. History and physical examination, CXRs, LFTs, and CEA testing were performed and hemograms were obtained every 3 months × 4, every 4 months × 3, then every 6 months for a total of 5 years. Proctoscopy and barium enema or colonoscopy were routinely performed at 24 and 40 weeks, then annually. CEA tests were performed on 827 patients. CT scans were not mandated. Of 1,247 patients, 548 (44%) experienced recurrence and 222 (18%) had "curative intent surgery" (CIS) attempted. In 109 patients (9%), CIS could actually be completed. The 5-year disease-free survival rate of the patients who completed CIS was 23%. CIS was possible in 75% of patients detected by surveillance tests, and in only 30% whose recurrence was first signaled by symptoms. For all the surveillance tests performed on 1,247 patients, 28 patients were alive at 5 years after a curative resection of recurrent disease and 12 patients were alive after CIS for a second cancer. The authors wrote that this was a multimillion dollar investment in surveillance and that efforts should be directed toward increasing effectiveness and reducing costs. Full results and motivating factors for CIS are listed in Table 3.

Numerous case series and a quantitative review of nonrandomized trials have suggested that postoperative monitoring affords either a small survival benefit or a more favorable distribution of second curative resections.23-28 However, these studies are plagued by selection bias and a differential intensity of follow-up between the control and intervention groups. None of the studies in the quantitative review was randomized and no specific test was thoroughly examined. Finally,
many of the publications addressing the usefulness of a specific test predated the era of adjuvant therapy. Recurrences after adjuvant therapy are less common and perhaps less amenable to treatment (eg, local recurrence of rectal cancer after surgery, chemotherapy, and radiation), which further reduces the “payoff” of surveillance. Understanding the limitations in the scientific data available to address the issue at hand, the following guidelines are presented (Table 4).

**Table 4. Summary of Colorectal Cancer Surveillance Guidelines**

1. **Carcinoembryonic Antigen**
   - **Note:** Adapted from the ASCO Clinical Practice Guidelines for the Use of Tumor Markers in Breast and Colon Cancer. If resection of liver metastases would be clinically indicated, it is recommended that postoperative serum CEA testing be performed every 2 to 3 months in patients with stage II or III disease for ≤ 2 years after diagnosis.
   - An elevated CEA level, if confirmed by retesting, warrants further evaluation for metastatic disease but does not justify the institution of systemic therapy for presumed metastatic disease.

2. **History and Physical Examination**
   - There are no data that directly address the contribution of the history and physical examination to outcomes of colorectal cancer surveillance. However, it is the consensus of the expert panel to suggest that a clinical history and pertinent physical examination should be performed every 3 to 6 months for the first 3 years and annually thereafter.

3. **Liver Function Tests**
   - The data are sufficient to suggest against the regular monitoring of any LFTs after primary therapy for colon and rectal cancer.

4. **Fecal Occult Blood Test (FOBT)**
   - The data are sufficient to recommend against periodic FOBTs in surveillance for colorectal cancer recurrence.

5. **Computed Tomography**
   - The data are sufficient to recommend against routine CT scanning in the follow-up of colorectal cancer.

6. **Chest X-Ray**
   - Data are sufficient to suggest against routine yearly CXRs in the follow-up of colorectal cancer. CXRs may be ordered to diagnose abnormalities prompted by elevated CEA levels or for patients who have symptoms suggestive of a pulmonary metastasis.

7. **Colonoscopy**
   - All patients should have a colonoscopy for the pre- or perioperative documentation of a cancer- and polyp-free colon. The data are sufficient to recommend colonoscopy every 3 to 5 years to detect new cancers and polyps. Routine annual colonoscopies are not recommended for all patients. The follow-up schema for colorectal screening guidelines outlined by the W HO panel is recommended.

8. **Flexible Proctosigmoidoscopy (rectal cancer)**
   - Combined chemotherapy and pelvic radiation represent the standard treatment for patients with stage I and stage III rectal cancer. For patients who have not received pelvic radiation, either because they could not or because they refused such treatment, direct imaging of the rectum at periodic intervals is suggested. For patients who have received pelvic radiation, direct imaging of the rectum (except colonoscopy at 3 to 5 years) is not suggested. All patients with rectal cancer should have a colonoscopy for the pre- or perioperative documentation of a cancer- and polyp-free colon.

9. **Pelvic Imaging**
   - Data are sufficient to suggest against routine pelvic imaging in asymptomatic patients who have received surgical resection and radiation for rectal cancer.

10. **Complete Blood Cell Count**
    - The expert panel recommends against routine monitoring of the CBC for colorectal cancer surveillance.

---

**COLORECTAL CANCER SURVEILLANCE GUIDELINES**

1. **Carcinoembryonic Antigen**
   - **Guideline:** Note: This guideline was adapted from the ASCO Clinical Practice Guidelines for the Use of Tumor Markers in Breast and Colon Cancer. If resection of liver metastases would be clinically indicated, it is recommended that postoperative serum CEA testing be performed every 2 to 3 months in patients with stage II or III disease for ≤ 2 years after diagnosis. An elevated CEA level, if confirmed by retesting, warrants further evaluation for metastatic disease but does not justify the institution of systemic therapy for presumed metastatic disease.
   - **Level of Evidence:** II.
   - **Grade of Recommendation:** C.

   CEA has been studied extensively, as reported in the literature. The ASCO tumor marker panel guidelines discuss the rationale for postoperative CEA monitoring to detect asymptomatic recurrences, and this subject will not be further reviewed here. Of note, approximately 30% of all colorectal cancer recurrences do not produce CEA; a false-negative CEA test result is more common in poorly differentiated tumors, and patients with a normal preoperative CEA level may have an elevated CEA level at recurrence (44% in one series).

2. **History and Physical Examination**
   - **Guideline:** There are no data that directly address the contribution of the history and physical examination to outcomes of colorectal cancer surveillance. However, it is the consensus of the expert panel that a clinical history and pertinent physical examination should be performed every 3 to 6 months for the first 3 years and annually thereafter.
   - **Level of Evidence:** V.
   - **Grade of Recommendation:** Panel Consensus.

   No formal examination of the contribution of the physician’s history and physical examination to the health outcomes of the colorectal cancer patient has been performed. Data from the largest study of surveillance to date showed that nearly 80% of recurrences were found by CEA testing, with only 20% found by a routine history and physical examination done at the same time interval. Other studies have confirmed that the history and physical examination added little to the regular laboratory/imaging testing program. Several studies have shown that 45% or more of the recurrences within the first 3 years are prompted by symptoms that occur between physician visits and diagnostic tests. In these studies, regular testing was performed every 3 to 4 months.

   Although the above-mentioned studies suggest that regular physician visits have only a small direct effect on patient outcomes (ie, recurrences are occasionally detected this way,
and some are potentially resectable), these data fail to address other potential benefits of the physician-patient encounter. For example, patients require coordinated care, including scheduling and interpretation of their examination and test results. The physician visit provides an opportunity to provide reassurance and discuss prevention, dietary advice, new therapy, genetic information, and other health concerns.

The panel thus suggests clinical follow-up every 3 to 6 months for the first 3 years, then annually. After that, medical follow-up should be driven by symptoms or the need for age-related periodic health maintenance. Current practice is that over 90% of colorectal surgeons follow patients every 3 to 6 months for the first 3 years, and over 80% continue to follow their patients at least yearly.2

3. Liver Function Tests

**Guideline:** The data are sufficient to suggest against the regular monitoring of any LFTs after primary therapy for colon and rectal cancer.

**Level of Evidence:** IV.

**Grade of Recommendation:** D. Panel Consensus.

Most strategies for colorectal cancer follow-up have included LFTs. However, no studies have shown any outcome improvement for the routine monitoring of any of the liver functions. One study clearly shows that results of other blood and radiologic tests become positive well before LFT results do.28 Therefore, the panel agreed that there was no evidence to support the regular monitoring of liver function.

4. Fecal Occult Blood Test

**Guideline:** The data are sufficient to recommend against periodic FOBTs in surveillance for colorectal cancer recurrence.

**Level of Evidence:** II.

**Grade of Recommendation:** C.

The usefulness of FOBTs for detecting colon cancer recurrence after colon cancer surgery has been compared with the usefulness of structural colorectal evaluation. In the study by Ohlsson et al.,20 three recurrences were first found by fecal hemoglobin assay. Two of those recurrences were also discovered during proctosigmoidoscopy.20 Safi and Beyer29 showed that only 12% of recurrences had mucosal disruption and that the fecal hemoglobin assay was therefore a low-yield test. A trial of serial FOBTs in 1,217 colon cancer survivors demonstrated poor sensitivity and specificity of FOBTs for detecting recurrent cancers or polyps.32 As colonoscopy is recommended by the panel as part of regularly scheduled examinations, according to WHO guidelines,18 the use of FOBTs probably adds little to postoperative monitoring.

5. Computed Tomography

**Guideline:** The data are sufficient to recommend against routine CT scanning in the follow-up of colorectal cancer.

**Level of Evidence:** II.

**Grade of Recommendation:** A.

Some published series of postoperative monitoring include abdominal CT or ultrasonography,21,23,26,27 but others do not.20,24,25,28 A large survey of surgical practice shows that approximately 25% of surgeons order a CT scan every 6 to 12 months for 5 years; the majority do not routinely order this test.2

Studies reporting the routine use of liver imaging have been unable to show that this test finds curable metastatic lesions before other tests. Schoemaker et al.19 showed that liver metastases were detected in 10 of 14 patients while they were asymptomatic but that only three patients could have curative resection and only one patient was alive at 20 months; these results are consistent with other studies. Makela et al.21 showed that CEA testing was the first method to document recurrence in the majority of patients after colorectal surgery. In this study, ultrasonography detected only four of 22 recurrences and CT scanning found two of 22 recurrences before CEA or other testing (which included a CXR, symptoms, endoscopy, and a FOBT). The meta-analysis of colon cancer follow-up showed that routine testing produced a survival benefit; some of the patients included in the analysis had undergone routine ultrasonography, but none had routine CT testing. Only strategies that included a CEA test showed a survival benefit, but the number of liver-imaging tests was small.23 Sugarbaker et al.27 examined a series of 66 consecutive patients and showed that liver imaging (including CT scans, liver-spleen scans, and ultrasonography) performed three times a year added little to the benefit of CEA monitoring. The recommended strategy after this study was to perform CEA testing and office visits alone. Deveney and Way26 noted that CT scanning showed the first evidence of recurrence in nine of 23 patients who experienced recurrence, of 65 patients followed. However, seven of the nine had concurrent elevations of their CEA levels. The false-negative rate for CT scanning was 39% and the sensitivity was 61%.

Periodic CT scanning has been proposed to detect CEA-negative recurrences. Approximately 30% of all colorectal cancer recurrences do not produce CEA,30 a false-negative CEA test result is more common in poorly differentiated tumors.33 However, the usefulness of CT scanning, even in this situation, is unproven. The panel determined that the role of CT scanning, ultrasonography, and magnetic resonance imaging is to diagnose abnormalities prompted by an abnormal CEA test result or clinical symptom. Future studies should directly compare serum CEA and radiologic
testing to determine whether there is a role for CT scanning in the asymptomatic, CEA-negative patient.

6. Chest X-Ray

**Guideline:** Note: There was not consensus among panel members on this guideline. One dissenting vote is noted here. Data are sufficient to advise against routine yearly CXRs in the follow-up of colorectal cancer. CXRs may be ordered to diagnose abnormalities prompted by elevated CEA levels or for patients who have symptoms suggestive of a pulmonary metastasis.

**Level of Evidence:** II.

**Grade of Recommendation:** B.

Most follow-up protocols in the literature have included routine CXRs every 6 to 12 months after curative surgery. In a trial that compared yearly CXRs to CXRs only when clinically indicated, 5% of patients had their first recurrence noted on CXRs. Only three of 157 patients could be surgically resected, and only one had long-term survival.

Most of the other relevant studies are case series (level IV) that did not include a comparison group. Rocklin et al28 showed the CXR was the first study documenting recurrence in five of 17 patients with recurrent disease (level IV). Eight other recurrences detected by CEA testing were located in the liver and pelvis. A randomized study that compared no follow-up with intensive testing, including a CXR, found that the CXR identified two of 17 recurrences in the monitored group and one of 18 in the control group (level II). None of the patients underwent a pulmonary resection. Tornqvist et al25 showed that 14 of 69 patients with recurrent disease had pulmonary metastases discovered by CXR only. Seven patients underwent resection and four are free of disease. Another study showed that 15 of 350 recurrences were discovered by yearly CXR.29 Seven patients were resected and only two are free of disease. A study reported that a surveillance CXR found three of 43 recurrences, but none occurred in a long-term survivor. Of recurrent disease patients followed at the National Institutes of Health, 21% had pulmonary metastases but only 3% of the recurrences were isolated in the lung.27

Despite the low false-positive rate and low cost of CXRs, the advantage in outcome has been small. Although it is the practice of some physicians and cooperative groups to obtain yearly CXRs, the absolute benefit is small (three of 157 screened patients resected, one of 157 alive at 48 months).19

7. Colonoscopy

**Guideline:** All patients should have a colonoscopy for the pre- or perioperative documentation of a cancer- and polyp-free colon. The data are sufficient to recommend colonoscopy every 3 to 5 years to detect new cancers and polyps. Routine annual colonoscopies are not recommended for all patients. The follow-up schema for colorectal screening guidelines, devised by the WHO panel for patients with adenomatous polyps, is recommended.18

**Level of Evidence:** I.

**Grade of Recommendation:** B.

At the time of the initial colorectal cancer diagnosis, all patients should have visualization of the entire large bowel to determine the presence of metachronous lesions. If colonoscopy of the entire bowel was not (or could not be) performed before resection, a postoperative colonoscopy is warranted.

There are no data suggesting that colonoscopy reduces deaths from recurrent cancer. Despite this, direct visualization of the bowel is frequently performed for colon and rectal cancer follow-up. In fact, a survey of colorectal surgeons shows that almost 75% of physicians perform this test every 6 to 12 months for at least 5 years.2 Colonoscopy at 3-year intervals has been shown to have the same outcomes as yearly colonoscopy for patients with polyps.35

Studies on this issue show a wide variation in the results of periodic examinations. A study by Juhl et al36 followed 261 patients after curative surgery with a yearly colonoscopy or barium enema. Forty-four of 56 recurrences occurred within the first 2 years; only one recurrence was detected after 4 years. Most recurrences were in the liver, lung, or abdomen, but nine anastomotic recurrences were found within the first 30 months after surgery. All of these recurrences were in patients who had had a low anterior resection, and none of these patients had totally resectable disease. Four metachronous cancers (all stage A/B and resectable) and 160 polyps were discovered with this screening strategy. In a study by Rocklin et al,28 endoscopy showed the first recurrence in three of 65 patients (17 of the 65 experienced recurrence). In this study, 82% of all recurrences were found within 3 years of the original diagnosis.

Using colonoscopy every 6 months for 2 years and then yearly thereafter, Deveney and Way26 followed 65 patients after curative surgery. No recurrences were found solely on the basis of a barium enema, CXR, or colonoscopy. Thirty benign polyps were removed; there were no metachronous cancers. Similarly, another study that used several monitoring tests showed that colonoscopy did not find any of the 35 recurrences (among 107 patients) before some other test documented recurrence, and no metachronous lesions were found.20 In this study, most of the local recurrences were discovered because of symptoms and were located in the pelvis. The study by Tornqvist et al25 showed that only 3% of recurrences were first revealed by barium enema. A larger proportion of recurrences were discovered by proctoscopy (discussed in guideline 8, following). This study was not
able to demonstrate any difference in outcomes or resectability in an extremely intense versus less intense screening strategy. A randomized study showed that one of 21 recurrences in a minimal follow-up group, compared with two of 22 recurrences in a more intensely followed group, was discovered by endoscopy. At least two of these recurrences were in the pelvis.

A quantitative review of nonrandomized trials examined the detection of metachronous cancers in patients with minimal versus intense follow-up. There were 1.7% more cancers discovered in the intense follow-up group. However, the number of curative resections did not differ between the two groups. Unfortunately, the method used to detect the metachronous lesions was not identified.

Single- or double-contrast barium enemas are alternatives to colonoscopy. The double-contrast method has about a 10% greater positive predictive value over the single-contrast method. A prospective study by Norfleet et al. in 3,006 patients compared barium enema to colonoscopy in patients whose polyps were detected during a fiberoptic sigmoidoscopy. The sensitivities of the single- and double-contrast barium enemas were 13% and 26%, respectively; therefore, colonoscopy was the preferred test in this population. In another study that compared radiologic with direct visualization, the barium enema did not miss polyps, but the false-positive rate was approximately 2%. A combination of flexible sigmoidoscopy and double-contrast barium enema has a combined sensitivity of 94% and specificity of 99% for neoplasms.

8. Flexible Proctosigmoidoscopy (rectal cancer)

Guideline: Combined chemotherapy and pelvic radiation represent the standard treatment for patients with stage II and stage III rectal cancer. For patients who have not received pelvic radiation, either because they could not for medical reasons or because they refused such treatment, direct imaging of the rectum at periodic intervals is suggested. For patients who have received pelvic radiation, direct imaging of the rectum (except colonoscopy at 3 to 5 years) is not suggested. All patients with rectal cancer should have a colonoscopy for the pre- or perioperative documentation of a cancer- and polyp-free colon.

Level of Evidence: IV.

Grade of Recommendation: C, Panel Consensus.

Local (pelvic and anastomotic) recurrences are more common in patients with rectal cancer than in those with colon cancer; however, pre- or postoperative pelvic radiation has reduced the risk of local rectal recurrence to less than 10%. Juhl et al. showed that all nine anastomotic recurrences were found by endoscopy after a low anterior resection. Most patients reported symptoms before the test was performed, and the tests were not performed as regularly as the protocol suggested. None of the patients could be treated curatively for this problem.

Proctosigmoidoscopy was the first test to reveal recurrence in 7% of patients in the study by Tornqvist et al. In this series, 16 of 22 patients with anastomotic or pelvic recurrences died after the documentation of recurrence. Six of eight patients who were operated upon for cure underwent a successful resection, but the majority were ultimately not able to be treated for cure.

The outcomes of proctosigmoidoscopy on survival, quality of life, and costs have not been directly measured independently of other follow-up testing. However, the panel was convinced that successful surgery for an anastomotic recurrence for patients who had not received pelvic radiation would enhance survival and quality of life. Therefore, the panel suggests periodic direct examination of the rectum only for patients who have not received pelvic radiation. The panel underscores, however, that combined chemotherapy and pelvic radiation represent the standard treatment for patients with stage II and stage III rectal cancer. The WHO surveillance guidelines devised for patients with adenomatous polyps should be followed for patients who have received pelvic radiation.

9. Pelvic Imaging

Guideline: Data are sufficient to suggest against routine pelvic imaging in asymptomatic patients who have received surgical resection and radiation for rectal cancer.

Level of Evidence: IV.

Grade of Recommendation: D.

Ohlsson et al. performed pelvic CT scanning on every patient at 3, 6, 12, 18, and 24 months after an anteroposterior resection. The pelvis was the initial site of relapse in four of six patients. However, all four patients were detected because of the appearance symptoms; the pelvic CT scan simply corroborated the recurrence and did not signal recurrent cancer. Makela et al. showed that CT scanning revealed the first abnormality in only two of the 19 patients with recurrence in the pelvis. In neither of these cases did the CT scan prompt a curative resection.

Pre- or postoperative pelvic radiation has reduced the risk of local recurrence to less than 10%. The panel recognizes the impact pelvic recurrences can have on quality of life. For instance, if further treatment were available in a patient who had not had surgery, radiation, and chemotherapy, detecting a recurrence before symptoms appear might result in a useful intervention. Therefore, the panel suggests CT imaging for patients who may benefit from a treatment that could provide a quantitative or qualitative benefit. The optimal duration of CT imaging in this situation has not been proven; the expert panel believes that for those patients who have
had local excision or resection without pelvic radiation, more than 80% of local recurrences would be detected within the first 36 months. If the patient has already received surgery, radiation, and chemotherapy, however, detecting a local recurrence before the appearance of symptoms is not likely to change outcome or treatment planning. Furthermore, it is often difficult to detect local recurrence by pelvic CT in patients who have had surgery and pelvic radiation.

10. Complete Blood Cell Count

*Guideline:* The expert panel advises against routine monitoring of CBC for colorectal cancer surveillance.

*Level of Evidence:* V.

*Grade of Recommendation:* Panel Consensus.

There was no formal literature comparing postoperative monitoring of any portion of the CBC to other methods of colorectal follow-up. Because other tests have greater sensitivity and specificity than the CBC for this function, and because there is no biologic relationship between hemoglobin levels and colorectal cancer recurrence, the panel agreed that there was no clinical indication to recommend this test in the absence of bleeding or infection.

**FUTURE DIRECTIONS**

A guideline should serve as an indicator of good practice as determined by the best evidence. It should not be used to codify current clinical practice or create new practice patterns without objective evidence. The guideline process should communicate that there is either sufficient evidence to either support or recommend against a particular posttreatment follow-up regimen, or communicate that no guideline is possible based on existing data. In the absence of published evidence, it is important to propose a research plan that would help determine what test(s) or procedure(s) can be objectively justified.

The quality of the cancer-related follow-up literature is poor. Good-quality clinical trials are desperately needed to sort out which tests make a difference in important outcomes. Most physicians and patients believe that follow-up will provide benefit and better outcomes. However, this issue needs rigorous study to separate wishful thinking from clinical fact. The panel believes that the most important area to study at this point is the usefulness of radiologic (CT) follow-up of colon and rectal cancer. A study that randomized patients with routine CEA testing to CT versus no CT to follow resectability and survival could clarify the impact of CT testing on patient outcomes and cost. The treatment of colorectal cancer is evolving, particularly with the introduction of new agents. Most of the studies that have failed to show a survival benefit with intensive surveillance were performed before the introduction of optimal biochemical modulation of fluorouracil therapy and before the introduction of irinotecan. More recent data confirm that chemotherapy in metastatic colorectal cancer can improve short-term survival and quality of life. Treatment of patients with asymptomatic colorectal cancer may yield better results than treatment of those patients only after they become symptomatic. Ongoing and future clinical trials will help determine which specific tests are optimal for the detection of early asymptomatic metastases.

**ACKNOWLEDGMENT**

The expert panel expresses its gratitude to Drs Daniel G. Haller, Robert J. Mayer, and Margaret A. Tempero for their thoughtful reviews of earlier versions of the guidelines.

**APPENDIX**

ASCO Expert Panel on Colorectal Cancer Surveillance

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al B. Benson III, MD, Co-Chair</td>
<td>Northwestern University, Chicago, IL</td>
</tr>
<tr>
<td>Christopher E. Desch, MD, Co-Chair</td>
<td>Medical Oncology</td>
</tr>
<tr>
<td>Patrick J. Flynn, MD</td>
<td>Medical Oncology/Hematology</td>
</tr>
<tr>
<td>Carol Krause</td>
<td>Minnesota Oncology Hematology, P.A., Minneapolis, MN</td>
</tr>
<tr>
<td>Charles L. Loprinzi, MD</td>
<td>Medical Oncology/Hematology</td>
</tr>
<tr>
<td>Bruce D. Minsky, MD</td>
<td>Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td>Nicholas J. Petrelli, MD</td>
<td>Memorial Sloan-Kettering Cancer Center, New York, NY</td>
</tr>
<tr>
<td>David G. Pfister, MD</td>
<td>Memorial Sloan-Kettering Cancer Center, New York, NY</td>
</tr>
<tr>
<td>Thomas J. Smith, MD</td>
<td>Massey Cancer Center, Virginia Commonwealth University, Richmond, VA</td>
</tr>
</tbody>
</table>


