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Colorectal Cancer: Surveillance After Curative-Intent Therapy

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Key Concepts

- Liver metastases and locoregional recurrence are more likely to be amenable to curative-intent salvage resection when detected in asymptomatic patients. Therefore, active surveillance is indicated for patients who are candidates for liver and/or intestinal resection.
- Use of carcinoembryonic antigen testing and computed tomography (CT) scans is associated with increased detection of asymptomatic recurrence after curative resection for colorectal cancer. There is no evidence to support the use of any other laboratory testing or positron emission tomography (PET) scans in routine surveillance.
- Patients with advanced age and comorbidity, who would not be fit to undergo therapy for recurrence, should not be subjected to active surveillance. They should, however, receive evaluation and treatment for symptoms suggestive of recurrence.
- Patients with resected rectal cancers are at greater risk for locoregional recurrence. This risk is increased by omission of chemoradiotherapy for locally advanced tumors, close or positive margins, T4 and N2 histology. Consideration should therefore be given to local pelvic surveillance both endoluminally and extraluminally in these patients at highest risk.
- Surveillance after resection of Stage I colorectal cancer remains controversial. While the recurrence rates are low, in general, there are markers of relatively greater risk, including margin positivity, unknown lymph node status (e.g., local excision), inadequate lymph node sampling, lymphovascular invasion, poorly differentiated histology, and/or T2 disease. Active surveillance may be considered for patients with one or more of these risk factors.

Introduction

With improvements in screening, diagnosis, surgical technique, and adjuvant therapy for colon and rectal cancers, nearly two-thirds of patients who undergo surgical resection survive 5 years or more [1]. As a result, there is a rapidly growing population of colorectal cancer survivors, exceeding 1.2 million in the United States alone [2]. These individuals face varying risk for subsequent colorectal cancer throughout their lifetime, yet there is little consensus on optimal regimens for surveillance and survivorship care [3, 4].

The primary goal of colorectal cancer surveillance is to detect treatable recurrent, metastatic or metachronous colorectal malignancy and optimize the opportunities for potentially curative intervention. Thus, surveillance strategies must include not only evaluation for local recurrence and distant metastasis from the treated cancer, but also the increased personal risk for subsequent primary colorectal cancers. For patients with suspected or known genetic colorectal cancer syndromes, these strategies must also take into account the risk of other associated cancers, and the screening needs of potentially affected family members [5]. Ultimately, the success of colorectal cancer surveillance may be measured by improvements in overall survival, cancer-specific survival, disability or quality of life. Some studies have evaluated proxy measures, such as the rate of curative-intent metastasectomy or resection of colorectal neoplasia, but it is not clear to what degree these additional interventions benefit colorectal cancer survivors more broadly.

In order to demonstrate benefits from active surveillance, there must be evidence of improved detection of recurrence in patients amenable to curative-intent salvage therapy that itself is efficacious in improving outcome after recurrence. It has proven challenging to support with real data each of the steps in this chain of logic [6]. In addition, interpretation and synthesis of

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findings of published studies are complicated by the heterogeneity of the interventions and comparisons—the surveillance intervention in one trial may be no more intensive than the control group regimen of another—and the challenges of obtaining adequate power to detect meaningful differences in survival and other objective oncologic outcomes in such studies.

It is also important to consider the appropriateness of surveillance for patients who might not be eligible for, or willing to undergo, treatment for recurrence. Recognizing that older adults account for the majority of colorectal cancer patients [7], patient preferences, age, comorbidities, and functional status must all contribute to the decision to pursue active surveillance. There is little need, for example, to conduct surveillance for asymptomatic liver metastases for a patient unwilling or unable to undergo hepatic resection and/or chemotherapy. For such patients, symptom-driven evaluations may suffice.

At the same time, the landscape around both the detection and treatment of recurrence continues to evolve. Compared with two decades ago, when some of the first randomized trials of intensive surveillance were conducted, the sensitivity of radiographic surveillance has increased severalfold, allowing detection of earlier metastatic disease in the liver and lungs. The advent of pelvic and liver MRI, endorectal ultrasound, and PET scanning offers new modalities for the detection of recurrent disease. Meanwhile, second- and third-line chemotherapeutic regimens, and ablative techniques for liver and lung metastases, have increased the options for both curative-intent and palliative-intent therapy for recurrent disease. More than a third of patients with recurrence undergo salvage resection, with median survival among these highly selected patients in excess of 3–5 years [8–11].

Timing and Choice of Surveillance Modalities

Intensity of Surveillance

There are various clinical, laboratory, radiographic, and endoscopic methods available for surveillance after treatment of colorectal cancer. Recommendations regarding their application and frequency of use vary between agencies involved in scripting guidelines for colorectal cancer care, and are summarized in Table 34-1. Most guidelines include more intensive early surveillance, with diminishing frequency after 2–5 years, due to the recognition that 80% of recurrences are detected within 3 years after initial curative-intent surgical therapy, and at least 95% are evident within 5 years [10, 12–14]. After 3 years without evidence of disease, cancer-specific mortality declines significantly and conditional survival thereafter is very high [15].

There have been eight prospective randomized trials addressing outcomes of surveillance after curative resection [16–23]. Overall, there is a lack of high-level evidence to support specific choices among surveillance regimens [24], but their interpretation is complicated by the heterogeneity of surveillance regimens, changes in diagnostic and therapeutic technologies available at the times they were conducted, and limitations of sample size and duration of follow-up [25].

Older trials, without intensive radiographic surveillance, have tended to show less benefit. For example, Ohlsson et al. [16] randomized 107 patients from 1983 to 1986 to either no follow-up or a surveillance regimen including CEA, colonoscopy, and chest X-rays, and found no meaningful differences in survival or recurrence patterns. Makela et al. [17] randomized 54 patients from 1988 to 1990 to yearly barium enema versus endoscopic surveillance plus liver ultrasonography and annual CT, with both groups receiving CEA testing and chest X-rays. In the intervention group, recurrences were found earlier (median 10 vs. 15 months, $p=0.002$), but patients were not significantly more likely to undergo salvage resection (19% vs. 14%, $p=0.67$) and 5-year overall survival was not significantly different (54% vs. 59%, $p=0.50$). In study of nearly 600 patients from 1983 to 1994, Kjeldsen et al. [18] applied the same modalities (clinical examination, colonoscopy, chest X-ray, hemoglobin, sedimentation rate, and liver enzymes) to the treatment and control arms, but varied the frequency of exams (every 6 months versus every 5 years). Recurrences in the every 6 months group were more likely to be asymptomatic (50% vs. 16%, $p=0.02$), and were subjected to more salvage resections (22% vs. 7%, $p=0.15$), but there was no difference in overall survival (70% vs. 68%, $p=0.48$) or cancer-specific survival (79% vs. 79%, $p=0.9$) between groups. And Schoemaker [19] et al. randomized 325 patients to clinical evaluation only versus additional chest X-ray, liver CT, and colonoscopy annually, and found only three resectable, asymptomatic recurrences (one each in the colon, liver and lung), without significant improvement in 5-year survival ($p=0.20$).

In contrast, more recent trials, incorporating more frequent endoscopy and modern imaging techniques, have been more likely to demonstrate benefit. In a study of 259 patients between 1997 and 2001, Rodriguez-Moranta et al. [20] compared routine clinical examination, colonoscopy, and CEA alone versus intensive surveillance with the addition of semi-annual abdominal CT or ultrasound, annual chest X-ray, and annual colonoscopy. They found improved survival for patients with Stage II cancers and rectal lesions, primarily due to the detection of resectable metachronous and locally-recurrent tumors. Pietra et al. [21] compared a regimen of annual CEA, ultrasound, chest X-ray, and colonoscopy against more frequent CEA and ultrasound, annual chest X-ray and colonoscopy, and the addition of annual abdominal CT. They found no difference in recurrence rates, but a significantly higher rate of salvage resection in the intensive surveillance group (65% vs. 10%, $p<0.01$), which translated into improved survival at 5 years (73% vs. 58%, $p=0.02$), particularly among those with recurrence (38% vs. 0%, $p<0.01$). Secco et al. [22] stratified patients into high and low risk of recurrence (based on primary tumor location, T stage, differentiation histology, and preoperative CEA level) then randomized to minimal surveillance versus active surveillance, with frequency of abdominopelvic ultrasound,

TABLE 34-1. Summary of surveillance guidelines

Modality	American Society of Colon and Rectal Surgeons [37]	National Comprehensive Cancer Network [48, 49]	American Cancer Society, US Multisociety Task Force on Colorectal Cancer [70]	American Society of Clinical Oncology [55]	Cancer Care Ontario [51]	European Society of Medical Oncology [52, 79]	British Society of Gastroenterology, Association of Coloproctology for Great Britain and Ireland [72, 73]
History and physical exam	Every 3–6 months for 2 years, then every 6 months to 5 years	Every 3–6 months for 2 years, then every 6 months to 5 years	Not addressed	Every 3–6 months for 5 years	Every 6 months for 5 years	Every 3–6 months for 3 years, then every 6 months to 5 years	Not addressed
CEA	Every 3–6 months for 2 years, then every 6 months to 5 years	Every 3–6 months for 2 years, then every 6 months to 5 years	Not addressed	Every 3–6 months for 5 years	Every 6 months for 5 years	Every 3–6 months for 3 years, then every 6 months to 5 years	"Role of CEA is uncertain"
Other laboratory testing	Not recommended	Not recommended	Not addressed	Not recommended	Not recommended	Not recommended	Not recommended
Abdominal Imaging	CT scan annually for 5 years. Consider more frequent for highest risk[a]	CT scan annually for 5 years	Not addressed	CT scan annually for 3 years. Consider 6–12 months for high risk	CT scan annually for 3 years. US every 6–12 months may be substituted	CT scan or contrast-enhanced ultrasound every 6–12 months for 3 years for patients at higher risk of recurrence	"Reasonable to offer" CT of the liver within 2 years of resection
Pelvic imaging	CT scan annually for 5 years. Consider more frequent for highest risk[a]	CT scan annually for 5 years	Not addressed	CT scans every 6–12 months for 2–3 years, then annually up to 5 years	CT scan annually for 3 years for rectal cancers only	Not specifically recommended	Not specifically recommended
Chest imaging	CT scan annually for 5 years. Consider more frequent for highest risk[a]	CT scan annually for 5 years	Not addressed	CT scan annually for 3 years. Consider 6–12 months for high risk	CT scan annually for 3 years. CXR every 6–12 months may be substituted	CT scan every 6–12 months for 3 years for patients at higher risk of recurrence	Not specifically recommended
PET scan	Not recommended for routine surveillance	Not recommended for routine surveillance	Not addressed	Not recommended for routine surveillance	Not recommended for routine surveillance	Not recommended for routine surveillance	Not recommended
Colonoscopy	1 Year after resection (or within 6 months if previously incomplete). If normal, repeat in 3 years. If adenomas, repeat in 1 year. Annual colonoscopy for patients with suspected familial syndromes who have not undergone proctocolectomy	1 Year after resection (or within 6 months if previously incomplete). If normal, repeat in 3 years, then 5 years. If advanced adenoma, repeat in 1 year. Annual colonoscopy for patients with suspected familial syndromes who have not undergone proctocolectomy	1 Year after resection (or 1 year after colonoscopy that cleared synchronous disease before primary treatment). If normal, repeat in 3 years, then 5 years. More frequent if high-risk adenoma (s) or suspicion for Lynch syndrome	1 Year after resection, or upon completion of adjuvant therapy if previously incomplete. If normal, repeat in 5 years. Otherwise, according to endoscopic findings	1 Year after resection (or within 6 months if previously incomplete). If normal, repeat in 5 years	1 Year after resection, then every 3–5 years thereafter	Every 5 years after resection, until benefits outweighed by comorbidity

(continued)

TABLE 34-1. (continued)

Modality	American Society of Colon and Rectal Surgeons [37]	National Comprehensive Cancer Network [48, 49]	American Cancer Society, US Multisociety Task Force on Colorectal Cancer [70]	American Society of Clinical Oncology [55]	Cancer Care Ontario [51]	European Society of Medical Oncology [52, 79]	British Society of Gastroenterology, Association of Coloproctology for Great Britain and Ireland [72, 73]
Stage-specific recommendations	Stage 1: high risk only[b] Stage 2: all Stage 3: all Stage 4: when metastases are resected for cure	Stage 1: colonoscopic surveillance only Stage 2: all Stage 3: all Stage 4: when metastases are resected for cure, CT scan every 3–6 months for 2 years, then every 6–12 months to 5 years	Not addressed	Recommendations apply to Stage II and III disease only. Insufficient data to make recommendations for Stage I	Recommendations apply to Stage II and III disease only	Not addressed	Not addressed
Rectal surveillance	Proctoscopy every 6–12 months for patients with anastomosis, every 6 months after local excision, for 3–5 years. Endorectal ultrasound for high risk[c]	No additional testing specifically recommended	Proctoscopy, flexible sigmoidoscopy or endorectal ultrasound every 3–6 months for patients with anastomosis	Proctosigmoidoscopy every 6 months for 2–5 years for patients who did not receive radiotherapy, those with T4 or N2 tumors. Pelvic imaging for rectal tumors only	Proctosigmoidoscopy every 6 months for 2–5 years for patients who did not receive radiotherapy. Pelvic imaging for rectal tumors only	No additional testing specifically recommended	Not addressed

CEA Carcinoembryonic antigen, *CT* Computed tomography, *PET* Positron emission tomography

[a]Highest risk for systemic recurrence includes patients with N2 disease or after curative-intent metastasectomy

[b]High risk of recurrence in Stage I disease is to be defined by provider(s) according to features such as margin positivity, unknown lymph node status (e.g., local excision), inadequate lymph node sampling, lymphovascular invasion, poorly differentiated histology, and/or T2 disease

[c]High risk for local recurrence include local excisions with poor histology (T2+, poorly differentiated), positive margins, T4 or N2 disease

chest X-ray, and proctoscopy (for rectal cancers only) adapted to risk class. Recurrence rates were similar between regimens, but the likelihood of salvage reoperation for recurrence was higher with active surveillance among the high-risk (34% vs. 12%, $p<0.01$) but not low-risk (22% vs. 24%) patients. Survival at 5 years was improved with surveillance in both risk groups (both $p<0.01$, proportions were not presented in the manuscript).

In the Follow-up After Colorectal Surgery (FACS) trial, the only factorial-design randomized study to evaluate the role of CT scans of the chest, abdomen, and pelvis, Primrose et al. [23] compared four groups: minimum follow-up, CEA only (every 3 months for 2 years, then semiannually to 5 years), CT only (every 6 months for 2 years, then annually to 5 years), and both CEA and CT. Colonoscopy was performed at 5 years in the non-CT groups, and at 2 and 5 years in the CT groups. Between 2003 and 2009, they randomized over 1200 patients in 39 hospitals in the United Kingdom. Again, more curative-intent salvage operations were performed in the active surveillance groups (6.7% CEA alone, 8.0% CT alone, 6.6% CEA + CT) than the minimal follow-up group (2.3%, $p=0.02$), but there was no difference in survival (82% active vs. 84% minimal), and the addition of CT to CEA did not increase the detection of resectable recurrences.

Several meta-analyses have attempted to synthesize these and other non-randomized trials and have generally corroborated the findings of the trials described above. Tjandra and Chan [26] analyzed the seven pre-FACS studies above [16–20, 22, 27] and interim data from an ongoing study [4] and found that intensive surveillance resulted in more frequent and earlier detection of asymptomatic, resectable recurrence, with a small but statistically significant improvement in survival during follow-up (78% vs. 74%, $p=0.01$). Pita-Fernández et al. [28] evaluated 11 trials, including more than 4000 patients, randomized according to a variety of different protocols and regimens, and found a small improvement in overall survival with more intensive surveillance (74% vs. 71%, p value not reported). Survival was significantly improved among patients subjected to colonoscopy, chest X-ray, liver ultrasonography, CT, and clinical assessment. There was also improvement in survival associated with increased frequency of CEA testing, liver ultrasonography, and clinical assessment. Findings and conclusions were similar in a meta-analysis by Renehan et al. [29]. Further, a Cochrane Collaborative meta-analysis of the pre-FACS trials found that intensive surveillance more than doubled the odds of salvage surgery and was associated with approximately 27% reduced odds of mortality. Particular benefit was found in trails that increased frequency of testing and use liver imaging [25].

There are two ongoing randomized trials whose results have not yet been reported. The COLOFOL trial [30] in Denmark, Sweden, Poland, Ireland, and Uruguay is comparing semiannual CT or MRI against imaging performed at 12 and 36 months after resection. And the GILDA trial [4], in Italy, Spain, and the United States, evaluates increased frequency of colonoscopy, chest X-ray, liver ultrasound, and abdominopelvic CT (for rectal cancers only). As of 2004, GILDA had enrolled nearly 1000 patients and interim results demonstrated no improvement in mortality (7% in the intensive arms, 5% in the minimal surveillance arm).

Ultimately, high-level evidence to support each component of any of the guidelines included herein is lacking. Nevertheless, we can likely conclude that more frequent testing and the use of advanced imaging will result in more potentially curative surgery for recurrence and a measurable, but small, improvement in survival.

Physical Examination

Most of the major societies' guidelines include periodic clinical evaluation, including assessment of symptoms and physical examination. Findings suggestive of disease recurrence may include weight loss, fatigue, anemia, cough, abdominal pain, rectal bleeding, or changes in bowel habits. Physical examination should focus on the abdomen, including evaluation for wound implants, lymph nodes, and rectal exam (or perineal wound exam after abdominoperineal resection).

In addition to their role in colorectal cancer surveillance, these visits also serve an important survivorship role in overall health maintenance and management of physical and psychosocial function after colorectal resections. More than half of rectal cancer patients who undergo low anterior resection suffer bowel dysfunction [31, 32]. And high rates of depression persist among colorectal cancer survivors even more than 5 years beyond their diagnosis [33]. Additionally, health behavior promotion can improve cancer outcomes as well. High intake of red meat and saturated fat has been associated with worse survival after treatment of colorectal cancer [34, 35], whereas regular weekly exercise is associated with significantly increased disease-free survival [36]. Interventions to improve these preventive health-related behaviors may thus improve outcomes from both the cancer and comorbid disease.

American Society of Colon and Rectal Surgeons (ASCRS) recommends visits every 3–6 months for 2 years, followed by every 6 months until 5 years [37]. Recognizing that many patients who present with recurrence are symptomatic [18, 38], a detailed history and physical examination may be sufficient to detect recurrent disease in many instances. Symptomatic recurrences, however, are far less likely to be amenable to curative-intent therapy [38, 39].

Laboratory Testing

None of the major guidelines currently endorse the routine evaluation of complete blood count, liver function tests, fecal occult blood testing, or blood chemistries. However, most recommend checking levels of carcinoembryonic

antigen (CEA), an oncofetal protein that may be elevated in patients with recurrent colorectal cancer. CEA detects only about 30–60% of recurrences [10, 38, 40–43], the positive predictive value of CEA is only about 65% [44], and more than 15% of patients in surveillance have falsely elevated CEA in the absence of recurrence [40]. Yet, elevations in CEA may precede symptomatic presentation of metastasis [45], and the trials showing greatest benefit to intensive surveillance [21, 23] have included regular CEA evaluations. CEA elevations identify disease in the absence of abnormal imaging in up to 23% of patients with recurrent colorectal cancer [46], but may be more commonly elevated with metachronous liver metastases than with pulmonary metastases, luminal or locoregional recurrences [40, 42]. About a third of colorectal cancers do not produce CEA [47], but the significance of CEA elevation during surveillance seems to be independent of the preoperative CEA level [45]. Still, no studies have formally addressed the accuracy of surveillance CEA testing among patients with normal CEA at time of diagnosis.

Recommendations for management of asymptomatic CEA elevation are outlined in guidelines from both NCCN [48, 49] and ASCRS [37]. After confirmation of serial elevation in CEA level, a complete physical examination, endoscopy, and CT imaging of the chest, abdomen, and pelvis are performed. If these are all negative, consideration is given to PET-CT and/or repeat imaging every 3 months until levels decline or recurrence is detected.

Abdominal Imaging

The most common site of metachronous metastatic colorectal cancer is the liver [50]. Recommendations for routine imaging to detect liver metastases have, therefore, broadened substantially in the past decade. The Cochrane Collaborative meta-analysis [25] concluded that there was a survival benefit associated with liver imaging, with hazard ratio for mortality of 0.64 (95% confidence interval 0.49–0.85). This conclusion was derived from the results of five randomized trials [16, 17, 19–21], which used varying combinations of liver ultrasonography, abdominal CT, or both.

Observational studies have strongly supported the use of more frequent advanced liver imaging due to increased detection of resectable metastases. In a single-institution study, Fora et al. [14] reported results from their practice of CEA testing plus chest and abdominopelvic CTs every 6 months for the first 2 years, then annually to 5 years for patients with resected Stage II and III colorectal cancer. Among the 44 of 177 (25%) patients diagnosed with recurrence, CT detected the recurrence in 30 (68%). Half of patients diagnosed with recurrence had elevated CEA, but CEA was responsible for the diagnosis in only 8 (18%), and symptoms preceded diagnosis in only 3 patients (7%). Curative-intent salvage surgery was undertaken for 25 of the 44 recurrences (57%). Likewise, Arriola et al. [9] found that recurrences diagnosed by CT were far more likely to undergo curative-intent resection than those detected by CEA alone. In a meta-analysis of five surveillance trials, Renehan et al. [29] concluded that the regimens most consistently associated with improved survival included both CT scanning and frequent CEA testing.

Canadian [51] and European [52] guidelines provide the option of either CT or ultrasound, and as recently as 2004, ASCRS practice parameters for colorectal cancer [53] surveillance did not recommend routine liver imaging, because of the unclear survival benefit associated with salvage resection, the lack of evidence for incremental benefit of imaging in patients undergoing CEA testing, and the cost of CT. Since then, however, improvements in the detection and management of hepatic and pulmonary metastases have altered this calculus [54], and the current ASCRS practice parameter [37] and recommendations from other US-based agencies [48, 49, 55] recommend routine CT imaging, due to increased sensitivity for identifying early liver lesions, and the opportunity to evaluate the remainder of the abdomen and pelvis for other sites of metastasis (such as retroperitoneal lymph nodes and ovaries), and to identify local recurrence in the resection bed [37]. Despite a lack of controlled studies comparing different imaging intervals, the ASCRS guideline suggests consideration of semiannual imaging for patients at highest risk of recurrence, including those with resected N2 or Stage IV disease.

There is currently no organization that endorses routine use of PET-CT scans or liver MRI. One randomized trial compared addition of PET to a surveillance regimen including CTs at 9 and 15 months after surgery, and found shorter time to diagnosis (12.1 vs. 15.4 months, $p=0.01$) and a higher rate of resection for recurrence (44% vs. 10%, $p<0.01$) in the PET+CT group [56]. Nevertheless, a meta-analysis of the use of PET in surveillance regimens noted inadequate evidence to support its use in routine surveillance [57]. In the evaluation of unexplained CEA elevation, observational studies find that PET and PET-CT have sensitivity for detecting metastasis in excess of 90% despite somewhat lower specificity, from 70 to 80%, due to false positive findings [58–63]. In routine surveillance, however, PET does not improve sensitivity over CT due to its lower spatial resolution and the use of non-diagnostic quality CT imaging without contrast enhancement in combined PET-CT exams.

Chest Imaging

Whereas plain radiography was the mainstay of surveillance for pulmonary metastasis in the past, most of the major guidelines now recommend the use of cross-sectional thoracic imaging at least annually. This change has come with the recognition that pulmonary metastasis may present as a solitary site of disease recurrence [8, 50, 64, 65], and may

even represent the most common site of distant metastasis for distal rectal cancers [66, 67]. Unfortunately, among the published randomized studies, only the FACS trial [23] has included chest CT scans in the regimen, and this study did not find a statistically significant incremental benefit to CT scan over CEA alone (though the study was not powered to examine this comparison). In an observational study of 530 patients with resected Stage II or III colorectal cancers, Chau et al. [38] found that chest CT was responsible for 35% of the diagnosed metastases, and 73% of patients found to have isolated pulmonary recurrence underwent curative-intent resection. Thus, for now, chest imaging is recommended in spite of a lack of high-level evidence to support its effectiveness in practice.

Colonoscopy

Surveillance endoscopy after colorectal cancer resection can serve three important purposes: clearance of remaining colon when preoperative colonoscopy was incomplete, anastomotic surveillance for detection of local luminal recurrence, and detection of metachronous neoplasia. For patients who did not have complete colonoscopy before resection of the primary tumor (because of an obstructing tumor for example) complete colonoscopy should be performed within 3–6 months after surgery [37], because the estimated incidence of synchronous neoplasia exceeds 30% [68–70]. Anastomotic recurrence after resection of colon cancers is rare [29, 71], representing only about 4% of recurrences [65]. On the other hand, local recurrence is a common concern after low anterior rectal resections—local surveillance for rectal cancer is discussed in more detail below.

For patients who had complete colon evaluation before their primary resection, the primary goal of surveillance colonoscopy is the detection of metachronous neoplasia, or polyps that were missed on the preoperative evaluation. The BSG/ACPGBI guidelines suggest waiting until 5 years after resection [72, 73], whereas all of the other guidelines include a complete colonoscopy at 1 year, though the rate of clinically significant findings may be quite low. In a meta-analysis of 17 studies including nearly 8000 patients followed after curative colorectal cancer resections, there were only 57 metachronous cancers found with the first 2 years—an incidence of 0.7% [70], consistent with the incidence in other studies [74–76]. In a recent single-institution study, Cone et al. [71] found that 15% of patients had polyps on their 1-year colonoscopy, but only 3% of these were greater than 1 cm in diameter. Nevertheless, these detection rates, both for malignancy and for high-risk adenomas, are at least as high as those of average-risk screening exams. Combined with the recognition that more than half of metachronous cancers are detected in the first 2 years after resection [77, 78], these data have been considered reasonable justification for the recommendation for colonoscopy at 1 year in most guidelines [37, 48, 51, 52, 55, 70, 79, 80].

In a randomized trial, Wang et al. [75] evaluated even more frequent colonoscopy, comparing a regimen of exams every 3 months for 1 year, then every 6 months for 2 more years, then yearly to 5 years versus colonoscopy at 6, 30, and 60 months only. The overall incidence of anastomotic recurrence was 6.9% and metachronous cancers were found in 2.8%. There was a higher rate of asymptomatic recurrences and curative-intent salvage operations in the more frequent group, but no statistically significant difference in 5-year survival (77% vs. 72%, $p=0.25$). Likewise, in their meta-analysis of surveillance trials, Tjandra and Chan [26] concluded that there was an increase in the curative reoperation rate among studies with increased frequency of colonoscopy, but a mortality benefit to colonoscopy only when compared against no surveillance at all.

After the initial 1-year colonoscopy, patients with a personal history of colorectal cancer remain at increased risk for metachronous neoplasia for the rest of their lives. The annual incidence of a second primary colorectal cancer is about 0.3%, resulting in an incidence of 1.5–3.1% within 5–10 years [74, 78, 81, 82]. Up to half of patients develop metachronous polyps after resection of a primary colorectal cancer [83]. Thus, even after the first year, patients with a personal history of colorectal cancer still require more frequent endoscopic surveillance than average-risk individuals or those with a history of adenomas alone. The ASCRS guideline [37] recommends that the subsequent colonoscopy schedule be tailored to the findings at the 1-year examination, and to other patient specific risk factors and circumstances. Patients with high-risk adenomas (high-grade dysplasia, size greater than 1 cm or more than three adenomas) and those with a diagnosed or suspected hereditary colorectal cancer syndrome may require annual colonoscopy for more intensive surveillance [5]. On the other hand, patients with limited life expectancy are unlikely to benefit from the detection of an asymptomatic cancer, and may be selected for less frequent, or no, endoscopic surveillance [84–86].

Other methods of luminal surveillance are not formally recommended at this time. Air-contrast barium enema is a less effective means of surveillance after colonoscopic polypectomy [87], and would be expected to compare similarly among patients after cancer resections. CT colonography has been advocated elsewhere as a technique for simultaneous assessment of both luminal and distant disease [88, 89], but it has not been satisfactorily evaluated in the setting of colorectal cancer surveillance, and its sensitivity has not been satisfactory to replace optical colonoscopy in this setting [70, 90].

Stage I Disease

Most of the major guidelines for and studies of colorectal cancer surveillance pertain primarily to Stage II–III disease, and to Stage IV tumors that have been resected with curative intent. Stage I patients have been largely excluded from many of the randomized trials. As a *result*, there remains controversy regarding approaches to the surveillance of resected Stage I colon cancers (see Table 34-1). Several of the guidelines specifically recommend against routine imaging. For example, NCCN [48] and ASCO [55] recommend only endoscopic surveillance for anastomotic recurrence or metachronous cancers. Further, there is presumed to be low incidence of systemic recurrence, as 5-year colon cancer survival rates exceed 90%, and very few operations for metachronous metastatic recurrence occur in patients who initially presented with a Stage I tumor [91]. Thus, there is concern that surveillance will identify more incidental findings than treatable recurrences. Chao and Gibbs [92] estimated it would take nearly 200 patients with Stage I disease in surveillance to detect each curable metastasis, and cautioned against over-testing in this setting.

On the other hand, in a secondary analysis [8] of the Clinical Outcomes of Surgical Therapy trial [93], which compared laparoscopic and open colectomy for colon cancer, the 5-year recurrence rate was 9.5% for early stage patients (including Stage I and IIa), occurring at a median of 1.8 years after primary resection. More than a third of patients with recurrence underwent salvage resection, with no difference in salvage rates between initially early and late stage patients. Median survival after salvage surgery for early stage patients was 51 months. Finding equivalent rates of salvage and better survival for recurrences after resection of early stage disease, Tsikitis et al. [8] recommended active survival for these patients, though they did not distinguish between Stage I (T1-2, N0) and Stage 2a (T3N0) in the study. Accordingly, the most recent ASCRS [37] Practice Guideline recommends consideration of active surveillance for Stage I patients, but limits the recommendation to those designated at higher risk—for example, close or positive margins, unknown lymph node status (e.g., local or endoscopic excision), inadequate lymph node sampling, lymphovascular invasion, poorly differentiated histology, and/or T2 disease.

Local Surveillance for Rectal Cancer

Additional surveillance recommendations for rectal cancer are predicated on the greater risk of locoregional recurrence, compared with colon cancers [70], due to both anatomic and biologic differences between the tumors [94–96]. Locoregional recurrence of rectal cancer can occur either intraluminally, typically at the site of anastomosis, or extraluminally, likely associated with residual lymphatic disease, close radial margins, or tumor shed during resection. Although the use of total mesorectal excision (TME) and chemoradiotherapy for locally advanced rectal cancers have substantially reduced local failure after primary resection [97–100], between 4 and 22% of patients still experience local recurrence [98, 99, 101–103]. The resulting downstaging that may occur with the use of preoperative therapy for rectal cancer also may creates confusion about how to classify future risk of recurrence. In the ASCRS practice guidelines, it is recommended that pretreatment clinical staging be used to guide surveillance intensity unless the pathologic staging exceeds the preoperative assessment [37].

Early identification of local recurrence may offer the opportunity for curative-intent salvage resection. Therefore, surveillance of colorectal anastomoses and pelvic imaging are recommended beyond what is performed for colon cancer surveillance. Physical assessment including meticulous pelvic and groin examinations should be performed every 6 months. For patients with a low anastomosis or distal tumor with local excision or non-operative management, digital exam of the anastomosis or tumor site should be included. For patients who have undergone abdominoperineal resection (APR), careful palpation of the perineum and, in women, the posterior wall of the vagina is recommended. Special attention should be paid to areas of nodularity or changes over time. Any suspicious lesions should undergo biopsy as local recurrences after APR are frequently perineal or pre-sacral [100].

Proctosigmoidoscopy is recommended in the most recent ASCRS practice parameters [37] every 6–12 months for 3–5 years for those who have undergone a low anterior resection with anastomosis, and more frequently for those considered to be at higher risk of local recurrence. These higher risk patients and tumors might include men, distal lesions, close margins, incomplete TME, positive lymph nodes, lack of treatment response, lymphovascular invasion, and/or poor differentiation [98, 103–108]. On the other hand, in recognition of the substantially lower recurrence rate associated with TME and chemoradiotherapy, some guidelines have suggested limiting additional endoscopic surveillance only to patients who did not receive guideline-concordant multimodality therapy [51, 55]. To date, however, there have been no high-quality trials evaluating the effect of proctosigmoidoscopy on detection of recurrence, salvage resection, or survival after low anterior resection.

Recognizing that proctosigmoidoscopy only evaluates endoluminal surfaces, and thus may not detect early disease in residual mesorectum or other extraluminal tissues, the most recent ASCRS [37] and ACS/MSTF [70] guidelines also suggest consideration of endorectal ultrasonography (ERUS) for patients considered to be at high-risk for local recurrence. In three studies, ERUS identified asymptomatic rectal cancer recurrence that was otherwise undetected by digital exam, endoscopy, CT, or CEA in about 30% of cases [109–111]. Surgically resectable recurrences were more common in the ERUS-detected group, suggesting it may identify earlier

recurrent disease [111]. Further, ERUS-guided biopsy may provide the best opportunity to obtain histologic evaluation of extraluminal abnormalities [112–114]. Extraluminal pelvic disease may otherwise be evaluated by cross-sectional imaging. ASCO [55] and CCO [51] both recommend pelvic CT imaging for rectal cancers only, as a means of detection of local recurrence. MRI of the pelvis can also be used and is highly accurate for the diagnosis of pelvic recurrence [115], but its use in routine surveillance did not improve the detection of resectable recurrence in a single trial [116], and its cost-effectiveness has not been evaluated.

For rectal cancers treated by local excision, rather than radical resection, particular attention must be paid to both endoluminal and mesorectal surveillance. Even among the best candidates—those with T1 cancers and no high-risk histologic features—there is a significantly higher risk of local recurrence compared with resection with TME, ranging from 4 to 33% [117–119]. Outcomes of local excision for higher stage tumors are even worse [120]. Thus, at least semiannual endoscopic surveillance after local excision is highly recommended, and consideration may be given to the use of ERUS for these patients, especially.

As there is increasing interest in and application of non-operative approaches for patients who experience complete clinical response after chemoradiotherapy [121, 122], surveillance regimens for these patients will need to be defined as well. Because non-operative treatment is currently limited to clinical trials [123], none of the guidelines include formal recommendations for such patients. However, the non-operative trials reported to date have employed remarkably intensive surveillance, including very frequent physical examination, endoscopy, and imaging, often with pelvic MRI [122–125].

Compliance with Guidelines

Despite published recommendations for surveillance after resection for colorectal cancer, compliance with surveillance remains challenging both for patients and their physicians. There is evidence that patients who adhere to recommended surveillance have a greater likelihood of curative-intent reoperation for recurrence and improved overall and disease-specific 5-year survival [126, 127]. Yet anywhere from 25 to 42% of patients have poor completion of recommended surveillance, and 11–21% have no surveillance at all [126–129]. Studies in Canada [130], the Netherlands [131, 132], and Norway [133] have found substantial differences in the surveillance patterns between providers, and noted that routines are commonly inconsistent with published guidelines. Among US Medicare beneficiaries, there is substantial geographic variation in the intensity of surveillance, with about 60% of patients failing to complete recommended testing, while 23% undergo testing more intensive than recommended by guidelines [134]. Similarly, a survey of ASCRS membership revealed that colon and rectal surgeons employ a wide variety of surveillance approaches, and only 30% performed surveillance in accordance with a formal national or local guideline [135].

There is also little consensus regarding who should manage cancer surveillance—the operating surgeon, medical oncologist, gastroenterologist, or primary care doctor. This ambiguity may contribute to nonadherence in many patients, as responsibility for ordering and managing testing can be undefined [136]. In a survey of Canadian colorectal cancer specialists, Earle et al. found high levels of endorsement of recommended surveillance, and a belief that specialty physicians are more capable of effective surveillance. Similarly, in a Texas study, patients who saw a medical oncologist as part of surveillance were significantly more likely to exhibit compliance with minimal recommendations for office visits, CEA testing, and colonoscopy [128]. Two randomized trials have compared surveillance by general practitioners and surgeons. In both studies, surveillance by surgeons was associated with more costly and intensive diagnostic testing, but no difference in recurrence rates, time to diagnosis, survival, or quality of life [137, 138] Patients seeing general practitioners received more fecal occult blood testing, whereas those followed by surgeons had more ultrasounds and colonoscopies [137]. Patients followed by primary care doctors report that greater attention is paid to preventive health maintenance for comorbidities [139].

In a single-institution study, Standeven et al. [140] found that, compared with community-based primary care follow-up, the establishment of a formal surveillance program in a referral center improved adherence to surveillance guidelines. Strand et al. [141] trained specialty nurses to conduct surveillance and found similar patient satisfaction and detection of recurrence among patients randomized patients to visits with either the nurse or a surgeon. It remains unclear, however, whether such a model—a multidisciplinary team with a clinic dedicated to colorectal cancer surveillance—could be replicated more widely.

Quality of Life

Apart from the cancer-specific outcomes of surveillance, an essential question is the effect of intensive surveillance on psychological health and quality of life. While reassuring surveillance examinations may allay fears of cancer recurrence for some patients, there could be others for whom surveillance examinations create additional unwarranted worry and result in investigations for false positive or incidental findings.

Most patients in surveillance report, however, that these anxieties and inconveniences are outweighed by the reassurance and optimism imparted by negative results [142]. In the randomized trial by Kjeldsen et al. [143] patients randomized to more frequent evaluations reported greater confidence in

the surveillance process, and somewhat less worry about test results, even in this trial which showed no effect of surveillance intensity on survival. Likewise, Stiggelbout et al. [144] interviewed more than 212 patients undergoing surveillance for colorectal cancer and found generally positive attitudes toward surveillance, with relatively little worry regarding testing. Even when asked to consider the possibility that testing would not improve the detection of recurrence, 64% of patients in that study still expressed a preference for active surveillance.

Cost

As recommendations for surveillance imaging have expanded in recent guidelines, another important consideration will be the costs of surveillance. Total costs of the surveillance regimens in published studies vary 28-fold [145], without a clear correlation between cost and efficacy. Meanwhile, between 1999 and 2006, the use of CT and MRI scans in the follow-up of patients with colorectal cancer increased at an annual rate of more than 5%, and the use of PET scans more than tripled [146].

Among a cohort of Italian patients undergoing surveillance with clinical examination, CEA, abdominal ultrasonography, chest X-ray, and colonoscopy, the 5-year cost of surveillance averaged $5400 per patient, but more than $100,000 per detected case of potentially curable recurrence [147]. Similarly, in a meta-analysis of five randomized trials [16–19, 21], Renehan et al. [148] estimated the average costs of surveillance at almost £2500 per patient, or about £3000 per year of life saved—within the range of acceptable cost-effectiveness for the UK's National Health Service. And a comparative study in France estimated that intensive surveillance cost an additional 3144€ per quality-adjusted life year gained over a minimal surveillance strategy [149].

We can conclude from these limited data that the cost-effectiveness of colorectal cancer surveillance is likely to be within the range of other interventions considered acceptably costly. Caution must be taken, however, if an increase in the cost, complexity, and frequency of recommended testing is contemplated.

Conclusions

There continues to be substantial uncertainty about the magnitude of benefits from active surveillance and the content of optimal surveillance regimens after curative resection for colorectal cancer. With improved imaging technology and a growing array of management options for recurrence, however, active surveillance is recommended for patients eligible for treatment of recurrent disease. Although there is likely great value to standardization of surveillance regimens, optimal approaches will require tailoring of surveillance strategies to individual patient risk factors. Perhaps the introduction of biomarkers [150] or simulation models [151, 152] to estimate individual risk will inform choices about surveillance modalities in the future [153]. In coming years, the GILDA [4, 154] and COLOFOL [30] trials should contribute important data on the cancer-related outcomes of surveillance and will also report on health-related quality of life and the cost-effectiveness of intensive surveillance. For now, however, decisions must be based largely on clinicopathologic risk factors, preferences for intensity of testing, and willingness to pursue further investigation and active treatment for abnormalities detected by testing.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013;63(1):11–30. http://www.ncbi.nlm.nih.gov/pubmed/23335087.
2. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin. 2014;64(4):252–71. http://www.ncbi.nlm.nih.gov/pubmed/24890451.
3. Vernava III A, Longo W, Virgo K, Coplin M, Wade T, Johnson F. Current follow-up strategies after resection of colon cancer. Dis Colon Rectum. 1994;37(6):573–83. doi:10.1007/BF02050993.
4. Grossmann EM, Johnson FE, Virgo KS, Longo WE, Fossati R. Follow-up of colorectal cancer patients after resection with curative intent—the GILDA trial. Surg Oncol. 2004;13(2–3):119–24.
5. NCCN Clinical Practice Guidelines in Oncology—Genetic/familial high-risk assessment: colorectal, Version 2.2014. 2014. http://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf. Accessed 24 Apr 2015.
6. Fahy BN. Follow-up after curative resection of colorectal cancer. Ann Surg Oncol. 2014;21(3):738–46. http://www.ncbi.nlm.nih.gov/pubmed/24271157.
7. Cancer of the colon and rectum—SEER stat fact sheets. http://seer.cancer.gov/statfacts/html/colorect.html. Accessed 2 Apr 2015.
8. Tsikitis VL, Malireddy K, Green EA, Christensen B, Whelan R, Hyder J, 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(22):3671–6. http://jco.ascopubs.org/content/27/22/3671.abstract.
9. Arriola E, Navarro M, Parés D, Muñoz M, Pareja L, Figueras J, et al. Imaging techniques contribute to increased surgical rescue of relapse in the follow-up of colorectal cancer. Dis Colon Rectum. 2006;49(4):478–84. doi:10.1007/s10350-005-0280-9.
10. Kobayashi H, Mochizuki H, Sugihara K, Morita T, Kotake K, Teramoto T, et al. Characteristics of recurrence and surveillance tools after curative resection for colorectal cancer: a multicenter study. Surgery. 2007;141(1):67–75.
11. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. Ann Surg. 1999;230(3):309–18. discussion 318–21.

12. Sargent D, Sobrero A, Grothey A, O'Connell MJ, Buyse M, Andre T, et al. Evidence for cure by adjuvant therapy in colon cancer: observations based on individual patient data from 20,898 patients on 18 randomized trials. J Clin Oncol. 2009;27(6):872–7. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738431/.
13. Seo SI, Lim S-B, Yoon YS, Kim CW, Yu CS, Kim TW, et al. Comparison of recurrence patterns between ≤5 years and >5 years after curative operations in colorectal cancer patients. J Surg Oncol. 2013;108(1):9–13. http://www.ncbi.nlm.nih.gov/pubmed/23754582.
14. Fora A, Patta A, Attwood K, Wilding G, Fakih M. Intensive radiographic and biomarker surveillance in stage II and III colorectal cancer. Oncology. 2012;82(1):41–7.
15. Sargent DJ, Patiyil S, Yothers G, Haller DG, Gray R, Benedetti J, et al. End points for colon cancer adjuvant trials: observations and recommendations based on individual patient data from 20,898 patients enrolled onto 18 randomized trials from the ACCENT group. J Clin Oncol. 2007;25(29):4569–74.
16. Ohlsson B, Breland U, Ekberg H, Graffner H, Tranberg KG. Follow-up after curative surgery for colorectal carcinoma. Randomized comparison with no follow-up. Dis Colon Rectum. 1995;38(6):619–26.
17. Makela 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(10):1062–7.
18. Kjeldsen BJ, Kronborg O, Fenger C, Jorgensen OD. A prospective randomized study of follow-up after radical surgery for colorectal cancer. Br J Surg. 1997;84(5):666–9. http://www.ncbi.nlm.nih.gov/pubmed/9171758.
19. 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(1):7–14. http://www.sciencedirect.com/science/article/pii/S0016508598706262.
20. Rodríguez-Moranta F, Saló J, Arcusa A, Boadas J, Piñol V, Bessa X, 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(3):386–93.
21. Pietra N, Sarli L, Costi R, Ouchemi C, Grattarola M, Peracchia A. Role of follow-up in management of local recurrences of colorectal cancer. Dis Colon Rectum. 1998;41(9):1127–33. doi:10.1007/BF02239434.
22. Secco GB, Fardelli R, Gianquinto D, Bonfante P, Baldi E, Ravera G, 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(4):418–23. http://www.sciencedirect.com/science/article/pii/S0748798301912508.
23. Primrose JN, Perera R, Gray A, Rose P, Fuller A, Corkhill 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(3):263–70. http://www.ncbi.nlm.nih.gov/pubmed/24430319.
24. Baca B, Beart RW, Etzioni DA. Surveillance after colorectal cancer resection: a systematic review. Dis Colon Rectum. 2011;54(8):1036–48.
25. Jeffery M, Hickey B, Hider P. Follow up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev. 2007;1, CD002200. http://espace.library.uq.edu.au/view/UQ:137177.
26. Tjandra J, Chan MY. Follow-up after curative resection of colorectal cancer: a meta-analysis. Dis Colon Rectum. 2007;50(11):1783–99. doi:10.1007/s10350-007-9030-5.
27. Jain N, Pietrobon R, Hocker S, Guller U, Shankar A, Higgins LD. The relationship between surgeon and hospital volume and outcomes for shoulder arthroplasty. J Bone Joint Surg Am. 2004;86-A(3):496–505.
28. Pita-Fernandez S, Alhayek-Ai M, Gonzalez-Martin C, Lopez-Calvino B, Seoane-Pillado T, Pertega-Diaz S. Intensive follow-up strategies improve outcomes in nonmetastatic colorectal cancer patients after curative surgery: a systematic review and meta-analysis. Ann Oncol. 2015;26(4):644–56. doi:10.1093/annonc/mdu543.
29. 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(7341):1–8.
30. Colofol—evaluation of the frequency of a surveillance program. http://www.colofol.com. Accessed 17 Apr 2015.
31. Juul T, Ahlberg M, Biondo S, Emmertsen KJ, Espin E, Jimenez LM, et al. International validation of the low anterior resection syndrome score. Ann Surg. 2014;259(4):728–34. http://www.ncbi.nlm.nih.gov/pubmed/23598379.
32. Peeters KCMJ, van de Velde CJH, Leer JWH, Martijn H, Junggeburt JMC, Kranenbarg EK, et al. Late side effects of short-course preoperative radiotherapy combined with total mesorectal excision for rectal cancer: increased bowel dysfunction in irradiated patients—a Dutch colorectal cancer group study. J Clin Oncol. 2005;23(25):6199–206.
33. Ramsey SD, Berry K, Moinpour C, Giedzinska A, Andersen MR. Quality of life in long term survivors of colorectal cancer. Am J Gastroenterol. 2002;97(5):1228–34.
34. Meyerhardt JA, Niedzwiecki D, Hollis D, Saltz LB, Hu FB, Mayer RJ, et al. Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer. JAMA. 2007;298(7):754–64.
35. McCullough ML, Gapstur SM, Shah R, Jacobs EJ, Campbell PT. Association between red and processed meat intake and mortality among colorectal cancer survivors. J Clin Oncol. 2013;31(22):2773–82.
36. Meyerhardt JA, Heseltine D, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol. 2006;24(22):3535–41. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16822843.
37. Steele SR, Chang G, Hendren S, Weiser MR, Irani J, Buie WD, et al. Practice guidelines for the surveillance of patients after curative treatment of colon and rectal cancer. Dis Colon Rectum. 2015;58(8):713–25.
38. Chau I, Allen MJ, Cunningham D, Norman AR, Brown G, Ford HER, 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(8):1420–9.
39. 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(1):59–63.
40. Moertel CG, Fleming TR, Macdonald JS, Haller DG, Laurie JA, Tangen C. An evaluation of the carcinoembryonic antigen (CEA) test for monitoring patients with resected colon cancer. JAMA. 1993;270(8):943–7.
41. Glover C, Douse P, Kane P, Karani J, Meire H, Mohammadtaghi S, et al. Accuracy of investigations for asymptomatic colorectal liver metastases. Dis Colon Rectum. 2002;45(4):476–84.
42. Carriquiry LA, Piñeyro A. Should carcinoembryonic antigen be used in the management of patients with colorectal cancer? Dis Colon Rectum. 1999;42(7):921–9.
43. Tan E, Gouvas N, Nicholls RJ, Ziprin P, Xynos E, Tekkis PP. Diagnostic precision of carcinoembryonic antigen in the detection of recurrence of colorectal cancer. Surg Oncol. 2009;18(1):15–24.
44. Metser U, You J, McSweeney S, Freeman M, Hendler A. Assessment of tumor recurrence in patients with colorectal cancer and elevated carcinoembryonic antigen level: FDG PET/CT versus contrast-enhanced 64-MDCT of the chest and abdomen. Am J Roentgenol. 2010;194(3):766–71.
45. Irvine T, Scott M, Clark CI. A small rise in CEA is sensitive for recurrence after surgery for colorectal cancer. Colorectal Dis. 2007;9(6):527–31.
46. Verberne C, Wiggers T, Vermeulen KM, de Jong KP. Detection of recurrences during follow-up after liver surgery for colorectal metastases: both Carcino-Embryonic Antigen (CEA) and imaging are important. Ann Surg Oncol. 2013;20:457–63.
47. Goslin R, O'Brien MJ, Steele G, Mayer R, Wilson R, Corson JM, et al. Correlation of plasma CEA and CEA tissue staining in poorly differentiated colorectal cancer. Am J Med. 1981;71(2):246–53.
48. NCCN Clinical Practice Guidelines in Oncology: colon cancer. http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed 14 Apr 2015.
49. NCCN Clinical Practice Guidelines in Oncology: rectal cancer. http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed 14 Apr 2015.
50. Kjeldsen BJ, Kronborg O, Fenger C, Jørgensen OD. The pattern of recurrent colorectal cancer in a prospective randomised study and the characteristics of diagnostic tests. Int J Color Dis. 1997;12(6):329–34.
51. Earle C, Annis R, Sussman J, Haynes AE, Vafaei A. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer. Toronto, ON; 2012. https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=124839.
52. Labianca R, Nordlinger B, Beretta GD, Mosconi S, Mandalà M, Cervantes A, et al. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 suppl 6:vi64–72. http://annonc.oxfordjournals.org/content/24/suppl_6/vi64.short.
53. Anthony T, Simmang C, Hyman N, Buie D, Kim D, Cataldo P, et al. Practice parameters for the surveillance and follow-up of patients with colon and rectal cancer. Dis Colon Rectum. 2004;47(6):807–17. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15108028.
54. Cummings LC, Payes JD, Cooper GS. Survival after hepatic resection in metastatic colorectal cancer: a population-based study. Cancer. 2007;109(4):718–26.
55. Meyerhardt JA, Mangu PB, Flynn PJ, Korde L, Loprinzi CL, Minsky BD, 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(35):4465–70. http://www.ncbi.nlm.nih.gov/pubmed/24220554.
56. Sobhani I, Tiret E, Lebtahi R, Aparicio T, Itti E, Montravers F, et al. Early detection of recurrence by 18FDG-PET in the follow-up of patients with colorectal cancer. Br J Cancer. 2008;98(5):875–80.
57. Patel K, Hadar N, Lee J, Siegel BA, Hillner BE, Lau J. The lack of evidence for PET or PET/CT surveillance of patients with treated lymphoma, colorectal cancer, and head and neck cancer: a systematic review. J Nucl Med. 2013;54(9):1518–27. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3980728&tool=pmcentrez&rendertype=abstract.
58. Flanagan FL, Dehdashti F, Ogunbiyi OA, Kodner IJ, Siegel BA. Utility of FDG-PET for investigating unexplained plasma CEA elevation in patients with colorectal cancer. Ann Surg. 1998;227(3):319–23.
59. Flamen P, Hoekstra OS, Homans F, Van Cutsem E, Maes A, Stroobants S, et al. Unexplained rising carcinoembryonic antigen (CEA) in the postoperative surveillance of colorectal cancer: the utility of positron emission tomography (PET). Eur J Cancer. 2001;37(7):862–9.
60. Shen Y-Y, Liang J-A, Chen Y-K, Tsai C-Y, Kao C-H. Clinical impact of 18F-FDG-PET in the suspicion of recurrent colorectal cancer based on asymptomatically elevated serum level of carcinoembryonic antigen (CEA) in Taiwan. Hepatogastroenterology. 2006;53(69):348–50.
61. Kyoto Y, Momose M, Kondo C, Itabashi M, Kameoka S, Kusakabe K. Ability of 18F-FDG PET/CT to diagnose recurrent colorectal cancer in patients with elevated CEA concentrations. Ann Nucl Med. 2010;24(5):395–401.
62. Lu YY, Chen JH, Chien CR, Chen WTL, Tsai SC, Lin WY, et al. Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: a systematic review and meta-analysis. Int J Colorectal Dis. 2013;28(8):1039–47.
63. Huebner RH, Park KC, Shepherd JE, Schwimmer J, Czernin J, Phelps ME, et al. A meta-analysis of the literature for whole-body FDG PET detection of recurrent colorectal cancer. J Nucl Med. 2000;41:1177–89. http://www.ncbi.nlm.nih.gov/pubmed/10914907.
64. Grossmann I, Doornbos PM, Klaase JM, de Bock GH, Wiggers T. Changing patterns of recurrent disease in colorectal cancer. Eur J Surg Oncol. 2014;40:234–9.
65. Ohlsson B, Pålsson B. Follow-up after colorectal cancer surgery. ActaOncol.2003;42(8):816–26.doi:10.1080/02841860310019016.
66. Ding P, Liska D, Tang P, Shia J, Saltz L, Goodman K, et al. Pulmonary recurrence predominates after combined modality therapy for rectal cancer. Ann Surg. 2012;256(1):111–6.
67. Nordholm-Carstensen A, Krarup P-M, Jorgensen LN, Wille-Jorgensen PA, Harling H. Occurrence and survival of synchronous pulmonary metastases in colorectal cancer: a nationwide cohort study. Eur J Cancer. 2014;50(2):447–56.
68. Piñol V, Andreu M, Castells A, Payá A, Bessa X, Jover R. Synchronous colorectal neoplasms in patients with colorectal cancer: predisposing individual and familial factors. Dis Colon Rectum. 2004;47(7):1192–200. doi:10.1007/s10350-004-0562-7.

69. Van Leersum NJ, Aalbers AG, Snijders HS, Henneman D, Wouters MW, Tollenaar RA, et al. Synchronous colorectal carcinoma: a risk factor in colorectal cancer surgery. Dis Colon Rectum. 2014;57(4):460–6. http://journals.lww.com/dcrjournal/Fulltext/2014/04000/Synchronous_Colorectal_Carcinoma___A_Risk_Factor.8.aspx.
70. Rex DK, Kahi CJ, Levin B, Smith RA, Bond JH, Brooks D, 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(6):1865–71.
71. Cone MM, Beck DE, Hicks TE, Rea JD, Whitlow CB, Vargas HD, et al. Timing of colonoscopy after resection for colorectal cancer: are we looking too soon? Dis Colon Rectum. 2013;56(11):1233–6. http://journals.lww.com/dcrjournal/Fulltext/2013/11000/Timing_of_Colonoscopy_After_Resection_for.7.aspx.
72. Scholefield JH, Steele RJ. Guidelines for follow up after resection of colorectal cancer. Gut. 2002;51 suppl 5:v3–5. http://gut.bmj.com/content/51/suppl_5/v3.short.
73. Cairns SR, Scholefield JH, Steele RJ, Dunlop MG, Thomas HJW, Evans GD, et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut. 2010;59(5):666–89.
74. Cali RL, Pitsch RM, Thorson AG, Watson P, Tapia P, Blatchford GJ, et al. Cumulative incidence of metachronous colorectal cancer. Dis Colon Rectum. 1993;36(4):388–93.
75. Wang T, Cui Y, Huang W-S, Deng Y-H, Gong W, Li C, et al. The role of postoperative colonoscopic surveillance after radical surgery for colorectal cancer: a prospective, randomized clinical study. Gastrointest Endosc. 2009;69(3, Part 2):609–15. http://www.sciencedirect.com/science/article/pii/S0016510708018397.
76. Lan Y-T, Lin J-K, Li A-Y, Lin T-C, Chen W-S, Jiang J-K, et al. Metachronous colorectal cancer: necessity of post-operative colonoscopic surveillance. Int J Colorectal Dis. 2005;20(2):121–5. doi:10.1007/s00384-004-0635-z.
77. Barillari P, Ramacciato G, Manetti G, Bovino A, Sammartino P, Stipa V. 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(4):388–93. http://journals.lww.com/dcrjournal/Fulltext/1996/39040/Surveillance_of_colorectal_cancer__Effectiveness.5.aspx.
78. Green RJ, Metlay JP, Propert K, Catalano PJ, Macdonald JS, Mayer RJ, et al. Surveillance for second primary colorectal cancer after adjuvant chemotherapy: an analysis of intergroup 0089. Ann Intern Med. 2002;136(4):261–9. doi:10.7326/0003-4819-136-4-200202190-00005.
79. Glimelius B, Tiret E, Cervantes A, Arnold D, Group on behalf of the EGW. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 suppl 6:vi81–8. http://annonc.oxfordjournals.org/content/24/suppl_6/vi81.short.
80. Davila RE, Rajan E, Baron TH. ASGE guideline: colorectal cancer screening and surveillance. Gastrointest Endosc. 2006;63(4):546–57. http://www.ncbi.nlm.nih.gov/pubmed/16564851.
81. Mulder SA, Kranse R, Damhuis RA, Ouwendijk RJ, Kuipers EJ, van Leerdam ME. The incidence and risk factors of metachronous colorectal cancer: an indication for follow-up. Dis Colon Rectum. 2012;55(5):522–31. http://journals.lww.com/dcrjournal/Fulltext/2012/05000/The_Incidence_and_Risk_Factors_of_Metachronous.5.aspx.
82. Bouvier A-M, Latournerie M, Jooste V, Lepage C, Cottet V, Faivre J. The lifelong risk of metachronous colorectal cancer justifies long-term colonoscopic follow-up. Eur J Cancer. 2008;44(4):522–7. http://www.sciencedirect.com/science/article/pii/S0959804908000129.
83. Chen F, Stuart M. Colonoscopic follow-up of colorectal carcinoma. Dis Colon Rectum. 1994;37(6):568–72. doi:10.1007/BF02050992.
84. Battersby NJ, Coupland A, Bouliotis G, Mirza N, Williams JG. Metachronous colorectal cancer: a competing risks analysis with consideration for a stratified approach to surveillance colonoscopy. J Surg Oncol. 2014;109(5):445–50.
85. Day LW, Walter LC, Velayos F. Colorectal cancer screening and surveillance in the elderly patient. Am J Gastroenterol. 2011;106(7):1197–206. doi:10.1038/ajg.2011.128.
86. Tran AH, Man Ngor EW, Wu BU. Surveillance colonoscopy in elderly patients: a retrospective cohort study. JAMA. 2014;90027(10):1675–82. http://www.ncbi.nlm.nih.gov/pubmed/25111954.
87. Winawer SJ, Stewart ET, Zauber AG, Bond JH, Ansel H, Waye JD, et al. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. N Engl J Med. 2000;342(24):1766–72. doi:10.1056/NEJM200006153422401.
88. Choi YJ, Park SH, Lee SS, Choi EK, Yu CS, Kim HC, et al. CT colonography for follow-up after surgery for colorectal cancer. AJR Am J Roentgenol. 2007;189(2):283–9.
89. Kim HJ, Park SH, Pickhardt PJ, Yoon SN, Lee SS, Yee J, et al. CT colonography for combined colonic and extracolonic surveillance after curative resection of colorectal cancer. Radiology. 2010;257(3):697–704.
90. Cotton PB, Durkalski VL, Pineau BC, Palesch YY, Mauldin PD, Hoffman B, et al. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA. 2004;291(14):1713–9.
91. Zakaria S, Donohue JH, Que FG, Farnell MB, Schleck CD, Ilstrup DM, et al. Hepatic resection for colorectal metastases: value for risk scoring systems? Ann Surg. 2007;246(2):183–91.
92. 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(36):e279–80. http://jco.ascopubs.org/content/27/36/e279.long.
93. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med. 2004;350(20):2050–9. http://www.ncbi.nlm.nih.gov/pubmed/15141043
94. Cancer Genome Atlas Network. Comprehensive molecular characterization of human colon and rectal cancer. Nature. 2012;487(7407):330–7. http://www.ncbi.nlm.nih.gov/pubmed/22810696.
95. Zhuang C-L, Ye X-Z, Zhang X-D, Chen B-C, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. Dis Colon Rectum. 2013;56(5):667–78. doi:10.1097/DCR.0b013e3182812842.
96. Yamauchi M, Morikawa T, Kuchiba A, Imamura Y, Qian ZR, Nishihara R, et al. Assessment of colorectal cancer molecular

features along bowel subsites challenges the conception of distinct dichotomy of proximal versus distal colorectum. Gut. 2012;61(6):847–54. http://www.ncbi.nlm.nih.gov/pubmed/22427238.
97. Sauer R, Liersch T, Merkel S, Fietkau R, Hohenberger W, Hess C, et al. Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer: results of the German CAO/ARO/AIO-94 randomized phase III trial after a median follow-up of 11 years. J Clin Oncol. 2012;30(16):1926–33. http://www.ncbi.nlm.nih.gov/pubmed/22529255.
98. Quirke P, Steele R, Monson J, Grieve R, Khanna S, Couture J, et al. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. Lancet. 2009;373(9666):821–8. http://www.ncbi.nlm.nih.gov/pubmed/19269520.
99. Van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. Lancet Oncol. 2011;12(6):575–82. http://www.ncbi.nlm.nih.gov/pubmed/21596621.
100. Kusters M, Marijnen CA, van de Velde CJ, Rutten HJ, Lahaye MJ, Kim JH, et al. Patterns of local recurrence in rectal cancer; a study of the Dutch TME trial. Eur J Surg Oncol. 2010;36(5):470–6. http://www.ncbi.nlm.nih.gov/pubmed/20096534.
101. Rasanen M, Carpelan-Holmstrom M, Mustonen H, Renkonen-Sinisalo L, Lepisto A. Pattern of rectal cancer recurrence after curative surgery. Int J Colorectal Dis. 2015;30(6):775–85. http://www.ncbi.nlm.nih.gov/pubmed/25796493.
102. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. Lancet. 1993;341(8843):457–60. http://www.ncbi.nlm.nih.gov/pubmed/8094488.
103. Wibe A, Rendedal PR, Svensson E, Norstein J, Eide TJ, Myrvold HE, et al. Prognostic significance of the circumferential resection margin following total mesorectal excision for rectal cancer. Br J Surg. 2002;89(3):327–34. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11872058.
104. Nagtegaal ID, van de Velde CJ, van der Worp E, Kapiteijn E, Quirke P, van Krieken JH. Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. J Clin Oncol. 2002;20(7):1729–34. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11919228.
105. Patel SA, Chen Y-H, Hornick JL, Catalano P, Nowak JA, Zukerberg LR, et al. Early-stage rectal cancer: clinical and pathologic prognostic markers of time to local recurrence and overall survival after resection. Dis Colon Rectum. 2014;57(4):449–59. http://www.ncbi.nlm.nih.gov/pubmed/24608301.
106. Park IJ, You YN, Agarwal A, Skibber JM, Rodriguez-Bigas MA, Eng C, et al. Neoadjuvant treatment response as an early response indicator for patients with rectal cancer. J Clin Oncol. 2012;30(15):1770–6. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3383178&tool=pmcentrez&rendertype=abstract.
107. Trakarnsanga A, Gonen M, Shia J, Goodman KA, Nash GM, Temple LK, et al. What is the significance of the circumferential margin in locally advanced rectal cancer after neoadjuvant chemoradiotherapy? Ann Surg Oncol. 2013;20(4):1179–84. http://www.ncbi.nlm.nih.gov/pubmed/23328971.
108. Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? J Clin Oncol. 2008;26(2):303–12. http://www.ncbi.nlm.nih.gov/pubmed/18182672.
109. Lohnert MS, Doniec JM, Henne-Bruns D. Effectiveness of endoluminal sonography in the identification of occult local rectal cancer recurrences. Dis Colon Rectum. 2000;43(4):483–91. http://www.ncbi.nlm.nih.gov/pubmed/10789743.
110. De Anda EH, Lee SH, Finne CO, Rothenberger DA, Madoff RD, Garcia-Aguilar J. Endorectal ultrasound in the follow-up of rectal cancer patients treated by local excision or radical surgery. Dis Colon Rectum. 2004;47(6):818–24. http://www.ncbi.nlm.nih.gov/pubmed/15085436.
111. Ramirez JM, Mortensen NJ, Takeuchi N, Humphreys MM. Endoluminal ultrasonography in the follow-up of patients with rectal cancer. Br J Surg. 1994;81(5):692–4.
112. Morken JJ, Baxter NN, Madoff RD, Finne 3rd CO. Endorectal ultrasound-directed biopsy: a useful technique to detect local recurrence of rectal cancer. Int J Color Dis. 2006;21(3):258–64. http://www.ncbi.nlm.nih.gov/pubmed/15942740.
113. Gleeson FC, Larson DW, Dozois EJ, Boardman LA, Clain JE, Rajan E, et al. Local recurrence detection following transanal excision facilitated by EUS-FNA. Hepatogastroenterology. 2012;59(116):1102–7. http://www.ncbi.nlm.nih.gov/pubmed/22281976.
114. Maleki Z, Erozan Y, Geddes S, Li QK. Endorectal ultrasound-guided fine-needle aspiration: a useful diagnostic tool for perirectal and intraluminal lesions. Acta Cytol. 2013;57(1):9–18. doi:10.1159/000342919.
115. Lambregts DM, Cappendijk VC, Maas M, Beets GL, Beets-Tan RG. Value of MRI and diffusion-weighted MRI for the diagnosis of locally recurrent rectal cancer. Eur Radiol. 2011;21(6):1250–8. http://www.ncbi.nlm.nih.gov/pubmed/21240647.
116. Titu LV, Nicholson AA, Hartley JE, Breen DJ, Monson JR. Routine follow-up by magnetic resonance imaging does not improve detection of resectable local recurrences from colorectal cancer. Ann Surg. 2006;243(3):348–52. http://www.ncbi.nlm.nih.gov/pubmed/16495699.
117. Nash GM, Weiser MR, Guillem JG, Temple LK, Shia J, Gonen M, et al. Long-term survival after transanal excision of T1 rectal cancer. Dis Colon Rectum. 2009;52(4):577–82.
118. You YN, Baxter NN, Stewart A, Nelson H. Is the increasing rate of local excision for stage I rectal cancer in the United States justified? A nationwide cohort study from the National Cancer Database. Ann Surg. 2007;245(5):726–33.
119. Paty PB, Nash GM, Baron P, Zakowski M, Minsky BD, Blumberg D, et al. Long-term results of local excision for rectal cancer. Ann Surg. 2002;236(4):522–30.
120. Mellgren A, Sirivongs P, Rothenberger DA, Madoff RD, Garcia-Aguilar J. Is local excision adequate therapy for early rectal cancer? Dis Colon Rectum. 2000;43(8):1064. http://www.ncbi.nlm.nih.gov/pubmed/10950004.
121. Habr-Gama A, Perez RO, Sabbaga J, Nadalin W, São Julião GP, Gama-Rodrigues J. Increasing the rates of complete response to neoadjuvant chemoradiotherapy for distal rectal cancer: results of a prospective study using additional chemotherapy during the resting period. Dis Colon Rectum. 2009;52(12):1927–34.

122. Smith JD, Ruby JA, Goodman KA, Saltz LB, Guillem JG, Weiser MR, et al. Nonoperative management of rectal cancer with complete clinical response after neoadjuvant therapy. Ann Surg. 2012;256(6):965–72. http://www.ncbi.nlm.nih.gov/pubmed/23154394.
123. Smith JJ, Chow OS, Eaton A, Widmar M, Nash GM, Temple LKF, et al. Organ preservation in patients with rectal cancer with clinical complete response after neoadjuvant therapy. J Clin Oncol. 2015;33(supp 3):a509. http://meetinglibrary.asco.org/content/140433-158.
124. Weiser MR, Beets-Tan R, Beets G. Management of complete response after chemoradiation in rectal cancer. Surg Oncol Clin N Am. 2014;23(1):113–25. http://www.ncbi.nlm.nih.gov/pubmed/24267169.
125. Habr-Gama A, Perez RO, Proscurshim I, Campos FG, Nadalin W, Kiss D, et al. Patterns of failure and survival for nonoperative treatment of stage c0 distal rectal cancer following neoadjuvant chemoradiation therapy. J Gastrointest Surg. 2006;10(10):1319. http://www.ncbi.nlm.nih.gov/pubmed/17175450.
126. Castells A, Bessa X, Daniels M, Ascaso C, Lacy AM, García-Valdecasas JC, et al. Value of postoperative surveillance after radical surgery for colorectal cancer: results of a cohort study. Dis Colon Rectum. 1998;41(6):714–23. discussion 723–4.
127. Laubert T, Bader FG, Oevermann E, Jungbluth T, Unger L, Roblick UJ, et al. Intensified surveillance after surgery for colorectal cancer significantly improves survival. Eur J Med Res. 2010;15(1):25–30.
128. Vargas GM, Sheffield KM, Parmar AD, Han Y, Brown KM, Riall TS. Physician follow-up and observation of guidelines in the post treatment surveillance of colorectal cancer. Surgery. 2013;154(2):244–55. doi:10.1016/j.surg.2013.04.013.
129. Sisler JJ, Seo B, Katz A, Shu E, Chateau D, Czaykowski P, et al. Concordance with ASCO guidelines for surveillance after colorectal cancer treatment: a population-based analysis. J Oncol Pract. 2012;8(4):e69–79. http://jop.ascopubs.org/content/8/4/e69.abstract.
130. Cheung WY, Pond GR, Rother M, Krzyzanowska MK, Swallow C, Brierley J, et al. Adherence to surveillance guidelines after curative resection for stage II/III colorectal cancer. Clin Colorectal Cancer. 2008;7(3):191–6. http://www.sciencedirect.com/science/article/pii/S1533002811704194.
131. Grossmann I, de Bock GH, van de Velde CJH, Kievit J, Wiggers T. Results of a national survey among Dutch surgeons treating patients with colorectal carcinoma. Current opinion about follow-up, treatment of metastasis, and reasons to revise follow-up practice. Colorectal Dis. 2007;9(9):787–92.
132. Van Steenbergen LN, de Hingh IHJT, Rutten HJT, Rijk MCM, Orsini RG, Coebergh JWW, et al. Large variation between hospitals in follow-up for colorectal cancer in southern Netherlands. Int J Colorectal Dis. 2013;28(9):1257–65. doi:10.1007/s00384-013-1693-x.
133. Søreide K, Træland JH, Stokkeland PJ, Glomsaker T, Søreide JA, Kørner H. Adherence to national guidelines for surveillance after curative resection of nonmetastatic colon and rectum cancer: a survey among Norwegian gastrointestinal surgeons. Colorectal Dis. 2012;14(3):320–4. doi:10.1111/j.1463-1318.2011.02631.x.
134. Cooper GS, Kou TD, Reynolds HL. Receipt of guideline-recommended follow-up in older colorectal cancer survivors. Cancer. 2008;113(8):2029–37. doi:10.1002/cncr.23823.
135. Giordano P, Efron J, Vernava AM, Weiss EG, Nogueras JJ, Wexner SD. Strategies of follow-up for colorectal cancer: a survey of the American society of colon and rectal surgeons. Tech Coloproctol. 2006;10(3):199–207.
136. Cardella J, Coburn NG, Gagliardi A, Maier B-A, Greco E, Last L, et al. Compliance, attitudes and barriers to post-operative colorectal cancer follow-up. J Eval Clin Pract. 2008;14(3):407–15. doi:10.1111/j.1365-2753.2007.00880.x.
137. Wattchow DA, Weller DP, Esterman AJ, Pilotto L. General practice vs. surgical-based follow-up for patients with colon cancer: randomised controlled trial. Br J Cancer. 2006;94(8):1116–21.
138. Augestad KM, Norum J, Dehof S, Aspevik R, Ringberg U, Nestvold T, et al. Cost-effectiveness and quality of life in surgeon versus general practitioner-organised colon cancer surveillance: a randomised controlled trial. BMJ Open. 2013;3(4):e002391. http://bmjopen.bmj.com/content/3/4/e002391.abstract.
139. Haggstrom D, Arora N, Helft P, Clayman M, Oakley-Girvan I. Follow-up care delivery among colorectal cancer survivors most often seen by primary and subspecialty care physicians. J Gen Intern Med. 2009;24(2):472–9. doi:10.1007/s11606-009-1017-6.
140. Standeven L, Price Hiller J, Mulder K, Zhu G, Ghosh S, Spratlin JL. Impact of a dedicated cancer center surveillance program on guideline adherence for patients with stage II and III colorectal cancer. Clin Colorectal Cancer. 2013;12(2):103–12. doi:10.1016/j.clcc.2012.09.006.
141. Strand E, Nygren I, Bergkvist L, Smedh K. Nurse or surgeon follow-up after rectal cancer: a randomized trial. Colorectal Dis. 2011;13(9):999–1003. doi:10.1111/j.1463-1318.2010.02317.x.
142. Papagrigoriadis S, Heyman B. Patients' views on follow up of colorectal cancer: implications for risk communication and decision making. Postgrad Med J. 2003;79(933):403–7. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1742752/.
143. Kjeldsen BJ, Thorsen H, Whalley D, Kronborg O. Influence of follow-up on health-related quality of life after radical surgery for colorectal cancer. Scand J Gastroenterol. 1999;34(5):509–15.
144. Stiggelbout AM, de Haes JC, Vree R, van de Velde CJ, Bruijninckx CM, van Groningen K, et al. Follow-up of colorectal cancer patients: quality of life and attitudes towards follow-up. Br J Cancer. 1997;75(6):914–20. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2063387/.
145. Virgo KS, Vernava AM, Longo WE, McKirgan LW, Johnson FE. Cost of patient follow-up after potentially curative colorectal cancer treatment. JAMA. 1995;273(23):1837–41.
146. Dinan MA, Curtis LH, Hammill BG, Patz EF, Abernethy AP, Shea AM, et al. Changes in the use and costs of diagnostic imaging among Medicare beneficiaries with cancer, 1999–2006. JAMA. 2010;303(16):1625–31.
147. Audisio R, Setti-Carraro P, Segala M, Capko D, Andreoni B, Tiberio G. Follow-up in colorectal cancer patients: a cost-benefit analysis. Ann Surg Oncol. 1996;3(4):349–57. doi:10.1007/BF02305664.
148. Renehan AG, O'Dwyer ST, Whynes DK, Renehan AG, O'Dwyer ST, Whynes DK. Cost effectiveness analysis of intensive versus conventional follow up after curative resection for colorectal cancer. BMJ Br Med J. 2004;328(7431):81. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC314047/.

149. Borie F, Combescure C, Daurès J-P, Trétarre B, Millat B. Cost-effectiveness of two follow-up strategies for curative resection of colorectal cancer: comparative study using a markov model. World J Surg. 2004;28(6):563–9. doi:10.1007/s00268-004-7256-0.
150. Longley DB, McDermott U, Johnston PG. Predictive markers for colorectal cancer: current status and future prospects. Clin Colorectal Cancer. 2003;2(4):223–30.
151. Rose J, Augestad K, Kong C, Meropol N, Kattan M, Hong Q, et al. A simulation model of colorectal cancer surveillance and recurrence. BMC Med Inform Decis Mak. 2014;14(1):1–13. doi:10.1186/1472-6947-14-29.
152. Radespiel-Tröger M, Hohenberger W, Reingruber B. Improved prediction of recurrence after curative resection of colon carcinoma using tree-based risk stratification. Cancer. 2004;100(5):958–67. doi:10.1002/cncr.20065.
153. Soreide K. Endoscopic surveillance after curative surgery for sporadic colorectal cancer: patient-tailored, tumor-targeted or biology-driven? Scand J Gastroenterol. 2010;45(10):1255–61.
154. Johnson FE, Virgo KS, Grossmann EM, Longo WE, Fossati R. Colorectal cancer patient follow-up following surgery with curative intent: the GILDA trial. J Clin Oncol. 2004;22(14 suppl):3645. http://hwmaint.meeting.ascopubs.org/cgi/content/abstract/22/14_suppl/3645.