The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surveillance and Survivorship Care of Patients After Curative Treatment of Colon and Rectal Cancer

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STATEMENT OF THE PROBLEM

More than 140,000 people in the United States are diagnosed annually with colorectal cancer (CRC), and 5% to 40% of patients treated with curative intent develop a recurrence, typically within 5 years.[1–3] The optimal strategy for detecting recurrence would minimize cost and harm, such as psychosocial stress and unnecessary testing, and maximize survival and quality of life (QoL). Although surveillance recommendations include periodically taking a history, performing a physical examination, and evaluating laboratory blood testing, imaging studies, and endoscopy, surveillance approaches should be tailored, to a degree, by recurrence risk, incorporating clinicopathologic factors like disease stage, treatment regimen, and patient factors.[4]

CRC survivors compose the second largest group of cancer survivors, with ≈1.5 million survivors living in the United States.[5] The number of CRC survivors is increasing, in part because of the rising incidence of early onset CRC.[6] The optimal follow-up care for this growing population of posttreatment cancer survivors is unclear.[7–10] Depending on the definition used, an individual may be considered a cancer survivor from the time of diagnosis, during and immediately after treatment, and for the rest of his or her life. Recognizing that CRC treatment has multiple potential late and long-term consequences, survivors should be assessed for these sequelas and treated to improve their QoL. In 2006, the Institute of Medicine released a report highlighting the need to improve the care provided to cancer survivors and increasing awareness regarding the medical, functional, and psychosocial needs related to survivorship.[11,12] Although it is important to formalize CRC survivorship care and improve the transition from treatment to survivorship, the scientific evidence specific to CRC remains limited, and recommendations are often extrapolated from research regarding other cancer populations. However, generalizing survivorship goals and management strategies across heterogeneous groups of cancer survivors may result in inferior management of CRC-specific treatment-related effects.

Physical and psychosocial treatment effects that impact QoL are among the long-term challenges faced by CRC survivors, and recognizing and addressing these forms the basis for tailored CRC-specific survivorship care models. The American College of Surgeons Commission on Cancer, updated in 2020, includes standards for survivorship care as part of their cancer center accreditation.[13] In addition, the National Comprehensive Cancer Network (NCCN) now has a comprehensive guideline for survivorship care, which encompasses assessment and treatment of late and long-term effects of cancer therapy, as well as

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These guidelines should not be deemed inclusive of all proper methods of care nor exclusive of methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of all of the circumstances presented by the individual patient.

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guidelines regarding appropriate preventive health recommendations for patients with cancer.[10] Acknowledging the increasing importance of cancer survivorship care, a section dedicated to survivorship was added to this update of the previously published surveillance practice guideline.

Methodology

These guidelines were built in part on the American Society of Colon and Rectal Surgeons (ASCRS) *Practice Guideline for the Surveillance of Patients After Curative Treatment of Colon and Rectal Cancer* published in 2015.[14] A systematic, organized search of MEDLINE, PubMed, EMBASE, and the Cochrane Database of Collected Reviews was performed restricted to the English language. Because the past parameter included information on risk and surveillance, searches related to these topics were limited to the interval January 1, 2014, to October 6, 2020. Searches related to survivorship included articles published January 1, 1950, to October 6, 2020, because this topic was not included in the previous guideline (Fig. 1). Search terms regarding risk assessment included key words: *colorectal cancer*, *recurrence*, *risk colon cancer*, *rectal cancer*, *colorectal neoplasm*, *surveillance*, *strategies*, *intensity*, *cure*, *CEA*, *CT*, *colonoscopy*, *endoscopy*, *proctoscopy*, *ERUS*, and *follow-up*. Medical Subject Headings included *colorectal neoplasms*, *colonic neoplasms*, *rectal neoplasms*, *neoplasm recurrence, local*, *neoplasms, second primary*, and *neoplasm metastasis*. Search terms regarding surveillance included *colon cancer*, *rectal cancer*, *colorectal neoplasm*, *surveillance*, *strategies*, *intensity*, *cure*, *CEA*, *CT*, *colonoscopy*, *endoscopy*, *proctoscopy*, *ERUS*, *follow-up*, *colorectal neoplasms*, *colonic neoplasms*, *rectal neoplasms*, *neoplasm recurrence, local*, *neoplasms, second primary*, and *neoplasm metastasis*. Search terms regarding survivorship included key words *colon cancer*, *rectal cancer*, *colorectal cancer*, *quality of life*, *HRQOL*, *well being*, *wellbeing*, *satisfaction*, *life satisfaction*, *personal satisfaction*, *Health-Related Quality of Life*, *satisfaction*, *life satisfaction*, *personal satisfaction*, *fatigue*, *neuropathy*, *bowel dysfunction*, *sexual dysfunction*, *urinary dysfunction*, and *symptoms*.

Directed searches using embedded references from primary articles and existing guidelines were performed in selected circumstances. The 2860 screened articles were evaluated for their level of evidence, favoring clinical trials,

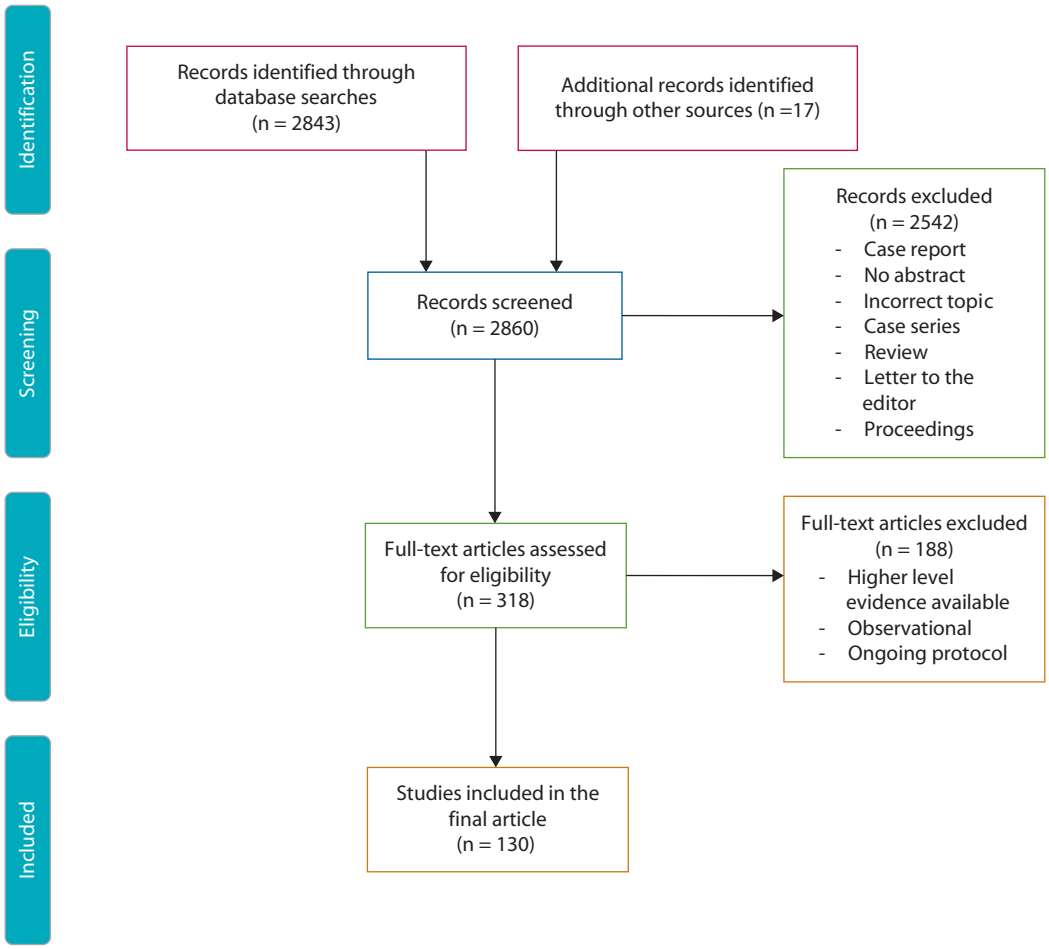

FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses literature search flow sheet.

meta-analysis/systematic reviews, comparative studies, and large registry retrospective studies over single institutional series, retrospective reviews, and peer-reviewed observational studies. Peer-reviewed observational studies and retrospective studies were included when higher-quality evidence was insufficient. A final list of 130 sources was evaluated for methodologic quality, the evidence base was examined, and a treatment guideline was formulated by the subcommittee for this guideline. The final grade of recommendation and level of evidence for each statement were determined using the Grades of Recommendation, Assessment, Development, and Evaluation system (Table 1).[15] When agreement was incomplete regarding the evidence base or treatment guideline, consensus from the committee chair, vice chair, and 2 assigned reviewers determined the outcome. Members of the ASCRS Clinical Practice Guidelines Committee worked in joint production of these guidelines from inception to final publication. Recommendations formulated by the subcommittee were reviewed by the entire Clinical Practice Guidelines Committee. Reflecting the evidence presented and notwithstanding the significant differences between colon cancer and rectal cancer, the term *colorectal cancer* (*CRC*) appears throughout these guidelines; when the literature specifically relates to *colon cancer* or *rectal cancer*, these terms were used.

The guideline was peer reviewed by *Diseases of the Colon & Rectum*, and the final guideline was approved by the ASCRS Executive Council. In general, each ASCRS Clinical Practice Guideline is updated every 5 years. This guideline conforms to the Appraisal of Guidelines Research and Evaluation checklist.

A. Risk Assessment and Stratification

1. Surveillance after resection of nonmetastatic colon or rectal cancer should be tailored to the relative risk of recurrence based on clinical and pathologic prognostic indicators. Grade of recommendation: Weak recommendation based on low-quality evidence, 2C.

There is a growing body of evidence linking poor oncologic outcomes like increased recurrence risk and worse overall survival (OS) and disease-free survival (DFS) to particular pathologic and molecular CRC features. Consideration of additional surveillance beyond what is typically advised based on stage alone may be justified in patients with signet ring cell adenocarcinoma (SRCC), negative nodes but with lymphovascular invasion (LVI), perineural invasion or tumor budding, a poorly differentiated tumor, or elevated CEA. Although there is evidence demonstrating that these features are associated with worse outcomes, suggesting that increased surveillance may improve outcomes under these circumstances, there are limited data supporting which specific strategy should be used or whether increased surveillance will actually impact outcomes for these patients.

Secco et al[16] reported a study that stratified 358 patients based on risk factors for CRC recurrence and randomly assigned patients to surveillance based on risk versus minimal surveillance. The strategies and definitions of

TABLE 1. The GRADE system: grading recommendations

Grade	*Description*	*Benefit vs risk and burdens*	*Methodologic quality of supporting evidence*	*Implications*
1A	Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C	Strong recommendation, low- or very-low quality evidence	Benefits clearly outweigh risk and burdens or vice versa	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
2A	Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B	Weak recommendations, moderate-quality evidence	Benefits closely balanced with risks and burdens	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C	Weak recommendation, low- or very-low quality evidence	Uncertainty in the estimates of benefits, risks and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted with permission from Chest. 2006;129:174-181.
GRADE = Grades of Recommendation, Assessment, Development, and Evaluation; RCT = randomized controlled trial.

risk from this 2002 publication are outdated now, but the authors demonstrated that high-risk patients who underwent more intensive follow-up underwent more curative metastasectomies and that patients who underwent "risk-adapted" surveillance had better 5-year survival than those who had minimal surveillance (50% vs 32%; $p < 0.01$). In this study, *intensive follow-up* was defined as office visits and CEA testing every 3 months for 2 years, every 4 months in year 3, and every 6 months in years 4 and 5, whereas abdominal and pelvic ultrasounds were performed every 6 months for 3 years and then yearly in years 4 and 5, and chest x-rays were performed yearly. Since this study, minimal follow-up groups have not been included in trials evaluating surveillance strategies for CRC.

Patients with primary colorectal SRCC adenocarcinomas or mucinous adenocarcinomas (MAC) have inferior survival rates and higher rates of recurrence in comparison with non-SRCC, non-MAC patients.[17] In a series of 22 patients with SRCC, 20 patients (91%) presented with stage III or IV disease.[18] The mean survival time was 52.7 ± 11.0 months (95% CI, 31.2–74.2 mo) in patients who underwent an R0 resection (n = 11) and 18.0 ± 6.7 months (95% CI, 4.8–31.2 mo) in the others (n = 11). In the 15 patients who died during the follow-up period, the mean progression-free survival was only 11.8 ± 3.5 months (95% CI, 4.9–18.7 mo).

One recent study of 8005 patients with colon cancer treated with resection between 2007 and 2015 compared outcomes between 7502 patients with classic adenocarcinoma, 428 patients with MAC, and 75 patients with SRCC. The 5-year OS for patients with classic adenocarcinoma, MAC, and SRCC was 82.0%, 64.2%, and 64.2% ($p < 0.001$), whereas the 5-year DFS was 71.6%, 64.3%, and 54.4% ($p < 0.001$), demonstrating that MAC and SRCC both convey a higher risk of recurrence.[19] Reported recurrences occurred most commonly in the liver, lungs, and peritoneum.

Patients with LVI and/or perineural invasion are at increased risk for local and distant recurrence after resection for CRC. In a data set of 126 patients who underwent resection of a T4 rectal cancer, extramural vascular invasion was associated with reduced OS ($p = 0.007$) and DFS ($p = 0.002$).[20] In addition, in a single-institution cohort of 860 patients with resected stage I CRC, LVI was an independent risk factor for reduced recurrence-free survival (HR = 2.6 (95% CI, 1.097–6.531); $p = 0.03$).[21] Poor differentiation on pathologic evaluation of a patient's tumor is also a negative prognostic factor. Cao et al[22] assessed prognostic features across 1412 CRCs and identified that poor differentiation, as well as perineural invasion and *BRAF* mutation, were independent prognostic factors for OS on Cox regression analysis.

In a single-institution retrospective review, Hogan et al[23] evaluated 379 patients who underwent segmental resection for colonic adenocarcinoma and 148 patients who underwent operations for rectal adenocarcinoma. On multivariable analysis, patients with colon cancer with LVI were at higher risk for local recurrence (HR = 1.9; $p = 0.002$), and patients with rectal cancer with LVI had a higher incidence of systemic recurrence (HR = 2.57; $p = 0.002$) and reduced OS (HR = 2.32; $p = 0.04$). LVI was also associated with reduced DFS after both colon and rectal resections (HR = 1.49; $p = 0.02$ and HR = 2.69; $p < 0.001$). In another single-institution retrospective series of 1437 consecutive patients who underwent resection for stage II or III CRC, LVI and perineural invasion were each associated with diminished OS and DFS.[24]

Elevated CEA levels before or after CRC resection are also predictive of a poor prognosis. A post hoc analysis of 3769 resected stage III CRC patients from the Multicenter International Study of Oxaliplatin/5-Fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) and Pan-European Trials in Alimentary Tract Cancer-8 revealed that postoperative CEA levels ≥5.0 ng/mL were associated with reduced DFS and OS.[25] In this analysis, the median time between surgery and postoperative CEA measurement was 4.3 weeks. In a series of 572 patients who underwent colon cancer resection for node-negative disease between 1985 and 1993 at a single institution, an elevated preoperative CEA was a significant predictor of worse survival at a median follow-up of 35 months.[26] Similarly, in a larger retrospective cohort of 965 patients who underwent resection for stage III CRC, a preoperative CEA level >3.0 ng/mL was associated with reduced DFS (HR = 4.6 (95% CI, 2.0–10.4)) and reduced OS (HR = 3.9 (95% CI, 1.1–13.8)).[27]

High-grade tumor budding is predictive of a poor prognosis in the setting of stage II colon adenocarcinoma, suggesting that patients with this poor prognostic indicator may also benefit from increased surveillance. In a single-institution retrospective series, 200 patients who underwent resection for stage II colon adenocarcinoma were divided into low-grade (n = 131) and high-grade (n = 69) tumor budding based on histopathology assessment using hematoxylin and eosin staining.[28] Overall recurrence rates were significantly lower in patients with low-grade tumor budding compared with high-grade tumor budding (10% vs 41%; $p < 0.001$). High-grade tumor budding was also associated with developing liver metastasis and peritoneal metastasis ($p < 0.001$ and $p = 0.003$). Five- and ten-year survival rates differed significantly between patients with low-grade tumor budding (93.9% and 90.6%) and those with high-grade tumor budding (73.9% and 67.8%). Further demonstrating the deleterious effect of aggressive tumor budding, the stage II patients with high-grade tumor budding had similar survival rates when compared with a cohort of 226 patients with stage III colon cancer (including high and low tumor budding) from the same institution.

In another series of 138 patients with stage II colon cancer evaluated retrospectively, T3 tumors were divided

into no or minimal tumor budding (BD-1, n = 111) and moderate or severe tumor budding (BD-2, n = 27).[29] The recurrence rates in the BD-1 and BD-2 groups were 4.5% and 48.0% ($p < 0.001$), and the 5-year disease-specific survival rates were 98.0% and 74.0% ($p < 0.001$). A recent prospective multicenter study evaluating the prognostic impact of tumor budding in stage II colon cancer enrolled 991 patients from 123 institutions and categorized patients by tumor budding grade (BD-1, n = 376; BD-2, n = 331; BD-3, n = 284).[30] Higher (ie, worse) BD classification was predictive of decreased relapse-free survival (BD-1, BD-2, and BD-3 survival rates were 90.9%, 85.1%, and 74.4%; $p < 0.001$) and significantly correlated with recurrence in liver, lungs, and peritoneum.

Patients with rectal cancer with risk factors such as positive distal or circumferential margins, poor response to neoadjuvant chemoradiotherapy, or positive lymph nodes also have a higher risk of recurrence and should typically be considered for increased surveillance.[31–33] Baik et al,[31] in a retrospective review of patients with rectal cancer, compared 460 patients with a negative circumferential margin with 44 patients with a positive margin and found that a positive margin was an independent risk factor for reduced, cancer-specific, 5-year survival (72.5% vs 26.9%; $p < 0.001$). In addition, Shiraishi et al,[33] in a retrospective review of 102 patients who underwent neoadjuvant chemotherapy for rectal cancer, found that 5-year recurrence-free survival was 81.1% in those who responded well to neoadjuvant therapy (>60% reduction in tumor volume measured by MRI) and 49.0% in poor responders ($p = 0.001$).

Based on the aforementioned studies, there are multiple, definable factors that increase a given patient's risk of recurrence. Whether more intensive surveillance in the subset of patients with increased risk of recurrence translates into improved survival is not known; thus, additional research, ideally with randomized controlled trials, is needed.

2. A risk-adapted surveillance strategy should be considered for patients with nonmetastatic colon or rectal cancer who did not receive guideline-recommended cancer treatment. Grade of recommendation: Weak recommendation based on moderate quality evidence, 2B.

Patients who receive guideline-based cancer care should typically undergo recommended protocolized surveillance. Meanwhile, patients in whom care guidelines were not followed have an increased risk of recurrence and may benefit from increased surveillance, but this concept has not been well-studied.

Inadequate lymph node retrieval (<12) after segmental colectomy for colon adenocarcinoma is associated with an increased likelihood of recurrence and should be considered a high-risk marker. In a secondary analysis of 1585 patients enrolled in the Intergroup Trial INT0089 evaluating adjuvant chemotherapy in patients with high-risk stage II/III colon cancer, mathematical modeling was used to determine the number of lymph nodes needed to be truly predictive of lymph node negativity and predicted a <25% probability of node positivity if >18 nodes are examined for T1/T2 tumors or if >10 nodes are examined for T3/T4 tumors.[34,35] A more mature analysis of the same trial but with 3411 patients with colon cancer reaffirmed that the number of retrieved lymph nodes is of prognostic significance.[36] Similarly, an analysis of the Veterans Affairs Central Cancer Registry database consisting of 5823 patients with stage I to III colon cancer revealed that OS increased with the number of lymph nodes harvested.[37] A retrospective analysis of the National Cancer Database including 35,787 patients with T3N0 resected colon cancers from 1985 to 1991 compared 5-year survival rates stratified by the number of examined lymph nodes and found that survival was 49.8% for patients with 1 to 7 lymph nodes, 56.2% for patients with 8 to 12 lymph nodes, and 63.4% for patients with ≥13 lymph nodes ($p < 0.001$).[38] Whether the survival difference was attributable to surgical, pathologic, or patient-related factors is not known. Given these data, patients with colon cancer with inadequate nodal sampling are at risk for worse survival and may benefit from increased surveillance.

Omitting chemotherapy or radiotherapy in situations where it would have been recommended according to established, stage-based guidelines or not completing chemotherapy or radiotherapy (eg, because of treatment toxicity) may also justify altering a patient's surveillance strategy.[39,40] The MOSAIC trial, a multicenter study of 2246 patients with stage II and III colon cancer published in 2009, randomized stage III patients to adjuvant 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) or leucovorin and 5-fluorouracil, and the FOLFOX group had significantly improved 5-year DFS (73.3% vs 67.4%) and 10-year OS (67.1% vs 59.0%).[41,42] Given that the control arm received demonstrably inferior chemotherapy and experienced decreased survival supports the recommendation to consider increased surveillance in patients who receive less than the recommended chemotherapy.

Similarly, multiple trials show that radiation improves local recurrence rates for stage II and III rectal cancer.[43,44] For example, in the Dutch Colorectal Cancer Group trial, 1861 patients were randomly assigned to total mesorectal excision (TME) alone or TME plus preoperative radiation, and at 10 years, the patients who received TME alone had a local recurrence rate of 11%, whereas the patients who had TME and radiation had a local recurrence rate of 5%.[43] Patients in whom preoperative or postoperative radiation in the setting of stage II or III rectal cancer was indicated but omitted are at increased risk of recurrence, particularly local recurrence, which may justify increased surveillance in these patients. Increased surveillance may also be considered in patients whose rectal cancer treatment did not

include a high-quality TME given the data showing that complete TME decreases local recurrence.[45,46] In addition, modification of standard surveillance is recommended for patients with rectal cancer treated nonoperatively who are being surveyed as clinical complete responders.[47]

Incorporating the above-mentioned factors into decision-making regarding recurrence risk and intensity of surveillance can be challenging for clinicians. Tools are being created to improve physicians' and patients' understanding of the implications of risk factors on recurrence. For example, Zafar et al,[48] using data from 8249 patients with CRC, developed an online risk calculator to estimate the risk of recurrence 1 year after surgery considering patient demographics, stage, histology, and treatment factors.

B. Surveillance

3. Surveillance is recommended for patients with stage II and III colon or rectal cancer who have undergone resection with curative intent. Grade of recommendation: Strong recommendation based on high-quality evidence, 1A.

The main purpose of surveillance is to improve survival through early detection of treatable recurrences. There have now been 13 randomized controlled trials evaluating the importance of surveillance for patients after undergoing resection of colon and rectal cancer and assessing the use of various versions of follow-up in this setting. One early study that attributed a survival benefit to surveillance was reported by Secco et al,[16] discussed above in statement 1 and published in 2002, randomized 358 CRC patients to risk-adapted follow-up based on prognostic risk factors or minimal follow-up and demonstrated improved survival in high-risk patients who underwent intensive rather than minimal follow-up (50% survival for high-risk patients who underwent intensive follow-up vs 32% survival for those who underwent minimal follow-up; $p < 0.01$).[16] Notably, the study by Secco et al[16] was completed before the routine use of CT in follow-up protocols.

Another study demonstrating a survival benefit attributed to enhanced surveillance, published in 2006 by Rodríguez-Moranta et al,[49] was a multicenter trial that randomized 259 patients with resected stage II or III CRC to either simple or intensive surveillance. Simple surveillance patients underwent blood work (CEA, liver function tests, and complete blood cell count) and clinical evaluations every 3 months in years 1 and 2, then every 6 months in years 3 to 5, as well as a colonoscopy at years 1 and 3. The enhanced surveillance patients had blood work and clinical evaluations on the same schedule but had colonoscopy yearly, abdominal CT or liver ultrasound every 6 months in years 1 and 2 and annually in years 3 to 5, and chest x-ray annually for 5 years. Although OS and tumor recurrence were not different between the 2 study groups, subgroup analysis that was not explicitly powered to assess these outcomes showed improved survival in patients with stage II CRC (HR = 0.34 (95% CI, 0.12–0.98); $p = 0.04$) and in patients with rectal cancer (HR = 0.09 (95% CI, 0.01–0.81); $p = 0.03$) related to intensive surveillance.

More recent randomized controlled trials assessing various surveillance schedules have not demonstrated significant differences in survival related to intensive follow-up compared with less intensive strategies. However, comparing outcomes between trials is challenging because study regimens vary substantially such that, in older studies, the protocols for more intensive follow-up groups are often equivalent to the less intensive follow-up groups in more recent trials. The COLOFOL and Gruppo Italiano di Lavoro per la Diagnosi Anticipata (GILDA) trials, the most recent, relevant trials assessing what should be included in surveillance and at what intervals, were published since the last ASCRS Surveillance Clinical Practice Guidelines (CPG) and are discussed in detail in statement 6 (Table 2).[50,51]

During the course of surveillance, the development of suspicious symptoms should prompt investigation, because these may be the first sign of CRC recurrence. In randomized studies, 16% to 66% of patients with CRC were symptomatic at the time of their diagnosis of recurrence.[52–54] Although investigating symptoms can determine whether a cancer has recurred, <7% of patients with symptomatic CRC recurrence have resectable disease.[53,55] The definition of suspicious symptoms varies between studies but commonly includes new-onset abdominal pain, change in bowel habits, blood in stool, abdominal mass, weight loss, and obstructive symptoms. Patients should be counseled regarding the nature of symptoms concerning for potential recurrence and instructed to represent should these symptoms develop.

4. Surveillance is recommended for patients with stage IV colon or rectal cancer who have undergone therapy with curative intent. Grade of recommendation: Strong recommendation based on low-quality evidence, 1C.

The role of surveillance in stage IV patients remains controversial, because most studies regarding follow-up and surveillance for survivors of colon or rectal cancer exclude patients with stage IV disease. Meanwhile, the potential for long-term survival after curative intent therapy under these circumstances, in properly selected patients, is well documented, especially in patients with isolated or oligometastatic disease.[34,35,56,57] The optimal timing and specifics of surveillance for these patients remain unclear and may mimic the recommended surveillance for stage III patients while considering the risk profile and performance status of the individual patient. (Table 3)

5. After treatment for stage I colon or rectal cancer, selected patients should be considered for surveillance.

TABLE 2. Summary of findings of the COLOFOL and GILDA trials comparing high- versus low-intensity surveillance

Number of Patients	*Trial*	
	COLOFOL (N = 2509)	*GILDA (N = 1228)*
Low intensity:	Colon	Colon
Blood work	CEA: 12, 36	CEA: 4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Office visits	12, 36	4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Imaging	CT: 12, 36	liver US: 4, 16
Colonoscopy	[a]	12 and 48
High intensity:	Colon	Colon
Blood work[b]	CEA: 6, 12, 18, 24, 36	4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Office visits	6, 12, 18, 24, 36	4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Imaging	CT: 6, 12, 18, 24, 36	Liver US: 4, 8, 12,16, 24, 36, 48, 60 and cxr: 12, 24, 36, 48, 60
Colonoscopy	[a]	12, 24, 36, 48, 60
Low intensity:	Rectal	Rectal[c]
Blood work	CEA: 12, 36	CEA: 4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Office visits	12, 36	4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Imaging	CT: 12, 36	Liver US: 8, 16 and cxr: 12
Colonoscopy/procto	[a]	Colonoscopy: 12 and 48; Procto: 4
High intensity:	Rectal	Rectal[c]
Blood work[b]	CEA: 6, 12, 18, 24, 36	4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Office visits	6, 12, 18, 24, 36	4, 8, 12, 16, 20, 24, 30, 36, 42, 48, 60
Imaging	CT: 6, 12, 18, 24, 36	liver US: 4, 8, 12,16, 24, 36, 48, 60 and cxr: 12, 24, 36, 48, 60 and CT: 4, 12, 24, 48
Colonoscopy/procto	[a]	Colonoscopy: 12, 24, 36, 48, 60; Procto: 4, 8
Results		
Disease-free survival	No difference	High-intensity diagnosed recurrences a mean of 5.9 mo earlier
Overall survival	No difference	No difference

All intervals are in months.
CT = CT scan of chest, abdomen and pelvis (the GILDA trial obtained abdominopelvic studies); CXR = chest radiograph; US = ultrasound; procto = proctoscopy; GILDA = Gruppo Italiano di Lavoro per la Diagnosi Anticipata.
[a]Colonoscopy was allowed in COLOFOL but intervals were not dictated by the trial.
[b]Blood work for the GILDA trial in the high-intensity group included CEA, complete blood cell count, and carbohydrate antigen 19-9
[c]Patients with rectal cancer in GILDA underwent digital rectal exam at office visits.

Grade of recommendation: Weak recommendation based on low-quality evidence, 2C.

After curative intent resection, most patients with stage I colon or rectal cancer do not require surveillance beyond interval colonoscopy to assess for recurrent cancer or a second primary tumor.[39,40] Although controversy remains regarding the role of surveillance for selected patients with stage I colon or rectal cancer because of the lack of high-quality data regarding its effectiveness, recurrences do occur in this subgroup, and surveillance-based detection for recurrent disease may be associated with potential clinical salvage. A strategy for identifying selected higher-risk stage I patients is recommended, and providers are encouraged to consider, discuss, and implement surveillance schedules with these patients. Higher-risk stage I patients include those with high-risk features on pathology (reviewed in statement 1), patients with rectal cancer treated with transanal excision, patients with colon cancer treated with endoscopic resection without subsequent segmental colectomy, and stage I patients who did not undergo guideline-based treatment.[58–60] Patients who have had resection for stage I disease and are assigned to surveillance typically follow the strategy used for stage II patients (Table 3).

Stage I patients who had transanal excision of rectal cancer or endoscopic excision of colon cancer deserve special consideration. Patients with stage I rectal cancer who undergo transanal excision are at increased risk for local recurrence compared with stage-matched patients who undergo proctectomy and should undergo surveillance.[40] In a recent retrospective review by Hwang et al,[58] of 268 patients with T1 rectal cancer (26% underwent transanal excision and the rest underwent TME), all 12 patients who had a local recurrence were in the transanal excision group. Similar considerations are germane to patients with malignant colon polyps (eg, T1 adenocarcinoma arising in a pedunculated polyp) treated with polypectomy alone who forgo segmental resection; under these circumstances, surveillance is not well described. Patients who undergo endoscopic excision alone for T1 colon cancer may have recurrence rates as high as 20%.[59,60] Yoshi et al[59] retrospectively reviewed 184 patients with T1 CRC who underwent endoscopic excision alone and compared their outcomes with 205 patients who underwent endoscopic excision followed by radical resection and found that patients with LVI, poor differentiation, or high-grade tumor budding had a recurrence rate of 20.1% after endoscopic excision versus 3.7% in the surgery group ($p = 0.001$). Patients without these features who underwent

TABLE 3. Recommended schedule of surveillance for patients with colon and rectal cancer with high-risk stage I,[a] stage II, and III or stage IV disease treated with curative intent

Colon	*Rectum*[b]
Office visit and CEA Every 3-12 mo for first 2 y Every 6-12 mo for the next 3 y CT chest/abdomen/pelvis[c] 2 times in 5 y or up to annually for 5 y[d] Colonoscopy 1 y after treatment (or 1–6 mo after surgery if colonoscopy not adequate preoperatively)[d] and depending on findings repeat in 3 y repeat every 5 y or more frequently if indicated	Office visit and CEA Every 3-12 mo for first 2 y Every 6-12 mo for the next 3 y CT chest/abdomen/pelvis[c] 2 times in 5 y or up to annually for 5 y[d] Colonoscopy 1 y after preoperative colonoscopy (or 1–6 mo after surgery if colonoscopy not adequate preoperatively)[e] and depending on findings repeat in 3 y repeat every 5 u or more frequently if indicated Proctoscopy (±ERUS) Every 6–12 mo[f] for patients who underwent resection with anastomosis or every 6 mo for patients who underwent local excision for 3–5 y

Surveillance is limited to 5-year duration.
ERUS = endorectal ultrasound.
[a]High risk of recurrence as determined by the treating provider. High-risk factors may include locally excised rectal cancer, margin ≤1 mm, or malignant polyps treated with excision.
[b]For patients who receive neoadjuvant therapy, these guidelines refer to clinical rather than pathologic stage.
[c]Positron emission tomography (PET)-CT is not typically recommended, although PET-CT or MRI might be considered for imaging in a patient with contraindication to intravenous contrast-enhanced CT scanning or to follow-up abnormalities seen on CT scans.
[d]Evidence supports imaging at 12 and 36 months but can be done up to annually; more frequent imaging may be considered for patients at particularly high risk for recurrence, including those with N2 disease, previous liver resection for metastasis, and so forth.
[e]Further colonoscopy frequency depends on the results of the 1-year colonoscopy and patient factors.
[f]Patients at higher risk for local recurrence may be considered for more frequent intervals and for ERUS in addition to proctoscopy. Higher-risk patients may include those who underwent local excision with T2, poor differentiation, margins ≤1 mm, or patients who underwent resection of T4 or N2 rectal cancer.

endoscopic excision alone had a recurrence rate of 3.4%. The retrospective review by Belderbos et al[60] reviewed 370 patients with T1 CRC who underwent endoscopic excision alone and found a low risk of recurrence (6.2%), although there was no stratification based on histopathology. Although supporting evidence is limited, surveillance should typically be considered for patients who do not proceed with segmental resection in the setting of higher-risk malignant polyps (eg, tumors with LVI, higher tumor grade, tumor budding, inadequate margin, or a sessile morphology).[39,40]

6. After completing treatment for stage II/III colon or rectal cancer, regularly scheduled office visits and CEA testing should typically be included as a part of a comprehensive surveillance strategy. Grade of recommendation: Strong recommendation based on high-quality evidence, 1A.

The optimal intervals for surveillance and what specifically should be included in a surveillance protocol have not been determined, but CEA is an important marker of recurrence. For stage II and III colon or rectal cancer, the NCCN guidelines still recommend a history and physical examination with CEA every 3 to 6 months for 2 years and then every 6 months for 3 more years.[39,40] Three randomized controlled trials with different intensities of follow-up, including varying schedules for checking CEA levels and imaging, were published since the last ASCRS Surveillance CPG was published.[50,51,61] Given the evidence currently available, the grade of statement 6 has been changed from 1B in the last ASCRS Surveillance CPG to 1A.

The COLOFOL and GILDA trials compared various surveillance strategies with different intensities for patients with stage II and III colon or rectal cancer after undergoing therapy with curative intent (Table 2).[50,51] Although the follow-up regimens differed significantly between the 2 studies, both were adequately powered, with large numbers of patients (2509 for COLOFOL and 1228 for GILDA) and had similar findings. In the COLOFOL trial, there were no differences in detection of recurrence (21.6% (95% CI, 19.4%–24.0%) for high-intensity surveillance vs 19.4% (95% CI, 17.3%–21.8%) in the low-intensity group; $p = 0.15$) or 5-year overall mortality between groups (13.0% (95% CI, 11.3%–15.1%) for the high-intensity group vs 14.1% (95% CI, 12.3%–16.2%) for the low-intensity group). In the GILDA trial, recurrence rates were comparable between the 2 groups: 22% in the intensive surveillance group versus 18.8% in the minimal surveillance group. In addition, although the intensive group in the GILDA trial detected cancer recurrence a mean of 5.9 months earlier (95% CI, 2.71–9.11 mo), there were no significant differences in DFS or OS. According to the a priori analysis plans, the comparisons were not adjusted for tumor characteristics, but there were no baseline differences between groups in terms of stage, sex, tumor location, or treatment received.

These findings are similar to the results of the Follow-up After Colorectal Surgery (FACS) study from

2014, which randomly assigned 1202 patients with CRC from 39 hospitals to surveillance with CEA alone, CEA and CT, CT alone, or minimal follow-up. This trial did not identify a survival advantage for surveillance with CEA in combination with CT imaging versus CEA alone (absolute difference = 2.3% (95% CI, −2.6% to 7.1%)), although this was not the primary end point.[62] However, patients surveilled with CEA testing either alone or in combination with CT who were diagnosed with recurrent cancer were more likely to be treated with curative intent when compared with the minimal follow-up group (OR = 3.00 (95% CI, 1.23–7.33) and OR = 3.10 (95% CI, 1.12–8.71)). In terms of cost-effectiveness, a follow-up cost analysis using data from the FACS study was performed by Mant et al,[63] and showed that the additional cost per patient treated surgically with curative intent compared with minimal follow-up was 40,131 pounds for CEA testing, 43,392 pounds for the CT group, and 85,151 pounds for the combined group. The lack of an impact on survival meant that there was little difference in QoL-years saved between groups. Additional health economics analysis related to CRC surveillance is beyond the scope of this CPG.

Another recently reported trial that focused specifically on surveillance using CEA, the CEA Watch study, was a multicenter, crossover, cluster randomized trial in the Netherlands.[61] In the more intensive CEA group (ie, shorter follow-up intervals), CEA was measured every 2 months for 3 years and then every 3 months for the next 2 years. In the less intensive group, CEA was checked every 3 to 6 months for 3 years and then annually for 2 years. Although both groups underwent imaging, patients in the more intensive group had a yearly CT, and patients in the less intensive group had a liver ultrasound and a chest x-ray every 6 months. In this study, no significant differences were found between the surveillance groups in terms of OS or DFS; however, more intensive CEA surveillance identified significantly more recurrences (55.2% vs 41.9%; $p = 0.007$). In addition, the method of recurrence detection differed between the groups, whereby the proportion of patients with recurrence detected by imaging was similar in the 2 groups, and more recurrences were detected by CEA testing in the more intensive CEA group. Given the available evidence, a reasonable surveillance protocol for patients with colon or rectal cancer resected with curative intent is presented in Table 3.

In terms of potentially using other tumor markers or testing in CRC surveillance, the GILDA trial tested carbohydrate antigen 19-9 in addition to CEA for patients with colon and rectal cancer in the intensive follow-up group, but this testing did not improve outcomes. Furthermore, no randomized trial or meta-analysis has reported a significant effect on survival related to surveillance using other common tests, including serum hemoglobin, liver function studies, or fecal occult blood. Kjeldsen et al[64] assessed the use of blood testing other than CEA in a randomized controlled trial of 597 patients with CRC published in 1997 and found that serum hemoglobin and liver function tests had low sensitivities for detecting recurrence. Therefore, these tests are not typically recommended as part of a surveillance regimen. Similarly, the role of circulating DNA in the surveillance of patients with colon or rectal cancer treated with curable intent has not been established.[65]

7. After completing treatment for stage II/III colon or rectal cancer, radiographic surveillance should typically include cross-sectional chest and abdominopelvic CT imaging. Grade of recommendation: Strong recommendation based on high-quality evidence, 1A.

Given that the most common sites of systemic recurrence for CRC include the liver and the lung, surveillance imaging typically uses CT with intravenous and oral contrast or, for patients with certain contrast allergies, MRI. Although the previous surveillance ASCRS practice parameter recommended cross-sectional chest and abdominopelvic imaging annually for 5 years, the current NCCN guidelines recommend abdominopelvic imaging every 6 to 12 months for a total of 5 years with the caveat that obtaining imaging more frequently than yearly is a lower grade practice recommendation.[39,40] Recognizing the currently available evidence regarding imaging and surveillance, the grade of recommendation for statement 7 has been changed from 1B in the last ASCRS Surveillance CPG to 1A.

Although multiple meta-analyses have evaluated imaging in this setting, the Cochrane analysis of surveillance for patients treated for nonmetastatic CRC was updated in 2019 and included 19 studies with 13,216 patients.[66] This analysis included only randomized controlled trials comparing various follow-up strategies and found that intensive follow-up made little or no difference for OS (HR = 0.91 (95% CI, 0.80–1.04)) and probably did not affect CRC-specific survival (HR = 0.93 (95% CI, 0.81–1.07)) or relapse-free survival (HR = 1.05 (95% CI, 0.92–1.21)) but that symptomatic recurrences were less frequent in the intensive follow-up group (relative risk = 0.59 (95% CI, 0.41–0.86)) and that salvage surgery with curative intent was more frequent in patients with intensive follow-up (relative risk = 1.98 (95% CI, 1.53–2.56)). Of note, because of the differences in imaging intervals across the included studies, this meta-analysis does not offer much guidance regarding how often imaging should be performed under these circumstances.

The COLOFOL and GILDA randomized controlled trials provide additional guidance regarding the use of surveillance imaging (Table 2).[46,47] The combination of these 2 studies provides a relatively robust pooled intensive surveillance group and 2 true minimal surveillance groups, because imaging the liver either via ultrasound or CT twice in 60 months is significantly less frequent than

what was recommended in the last ASCRS Surveillance CPG. Both of these trials showed that liver imaging performed twice in a 60-month period, whether via CT or ultrasound, did not affect OS, but the more intensive group in the GILDA trial did have an improved DFS of 5.9 months (95% CI, 2.71–9.11).[47]

Another large retrospective study including 8529 patients with stage I to III CRC from the National Cancer Database corroborated these findings when it did not find an association between imaging surveillance intensity and the detection of recurrence, rate of resection of cancer recurrence, or OS.[67] In this study, patients at high-intensity follow-up institutions underwent a mean of 2.9 (95% CI, 2.8–2.9) imaging studies, and patients followed at low-intensity follow-up institutions underwent a mean of 1.6 (95% CI, 1.6–1.7; $p < 0.001$) imaging studies over 3 years. Median time to detection of recurrence for patients treated at facilities with high-intensity imaging surveillance (15.1 mo; interquartile range, 8.2–26.3 mo) was not different from patients treated with low-intensity imaging surveillance (16.0 mo; interquartile range, 7.9–27.2 mo; $p = 0.60$).

Given the differences in follow-up protocols between COLOFOL and GILDA, past studies with more intensive surveillance regimens, and the lack of a study comparing the recent NCCN recommended surveillance with a less intensive regimen, there is insufficient evidence to recommend one imaging follow-up regimen over another. Given the available data, cross-sectional chest and abdominopelvic imaging surveillance should typically be performed at least twice (at 12 and 36 mo in recent trials) in a 5-year follow-up period or more often based on the providers' judgment and patient risk factors (Table 3).

The evidence regarding positron emission tomography (PET) imaging for surveillance remains insufficient to alter recommendations from the previous ASCRS Surveillance CPG, which relegated PET to specific situations, such as identifying extrahepatic/extrapulmonary metastases or helping to differentiate benign from malignant lesions observed on CT imaging.[39,40] Both NCCN and American Society of Clinical Oncology recommend against the use of PET as part of routine surveillance for CRC patients.[39,40,68] Sobhani et al[69] reported a randomized, controlled, multicenter trial of 239 patients with CRC who compared surveillance with physical examination and CEA every 3 months and liver ultrasound and whole-body CT every 6 months to the same surveillance with the addition of PET every 6 months for 3 years. This study found no differences between the groups in terms of rates of unresectable recurrence or death and concluded that adding PET increased cost without improving outcomes.[69]

8. Surveillance colonoscopy is typically recommended 1 year after completing treatment for stage II/III colon or rectal cancer. In patients with an incomplete preoperative evaluation, completion colonoscopy should typically be performed within 6 months of resection or on the completion of adjuvant therapy. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.

The purpose of subsequent colonoscopy in patients who have undergone CRC resection is to assess for intraluminal anastomotic recurrence and synchronous or metachronous polyps or cancers. Patients with CRC have a higher rate of developing metachronous cancer and adenomatous polyps compared with the general population or patients who had adenomatous polyps without cancer, and anastomotic recurrence occurs in ≈1% to 2% of patients with CRC.[64,70] Given the risk of future neoplasia, randomized trials evaluating surveillance protocols usually incorporate colonoscopy as part of a monitoring strategy, and because the majority of interval CRCs are thought to be attributed to missed adenomas, the first posttreatment colonoscopy is typically recommended at a 1-year interval.[34,35,54,55,71] The GILDA trial randomly assigned patients to either undergo colonoscopy at 1 and 4 years or yearly and did not find a difference in OS between the 2 groups.[50,51] In practice, after the first interval colonoscopy, subsequent colonoscopy should typically be performed every 3 to 5 years for purposes of neoplasia surveillance, and shorter intervals may be recommended depending on specific circumstances and endoscopic findings.[71,72] Patients at higher risk for neoplasia, such as those with a hereditary CRC syndrome, should typically follow more intensive endoscopic surveillance as delineated in other ASCRS guidelines.[73,74]

9. Surveillance proctosigmoidoscopy with or without endorectal ultrasound is recommended for patients with rectal cancer who have undergone local excision or resection with curative intent with an anastomosis. Grade of recommendation: Weak recommendation based on moderate-quality evidence, 2B

Surveillance proctosigmoidoscopy, in addition to interval colonoscopy, is typically recommended after proctectomy in patients with rectal cancer.[14] Given the currently available evidence regarding proctosigmoidoscopy under these circumstances, the grade for this statement was changed from 1C in the previous ASCRS Surveillance CPG to 2B. Until the GILDA trial, none of the randomized rectal cancer surveillance trials included proctoscopy or flexible sigmoidoscopy in addition to colonoscopy. In the GILDA trial, patients underwent proctoscopy either once at 4 months or twice at 4 months and 8 months with no differences in outcomes reported between these strategies.[51] Because the widespread implementation of improvements in surgical techniques for rectal cancer excision (eg, TME) and the use of neoadjuvant chemoradiation have resulted in local recurrence rates of <10%, some organizations, including the NCCN, no longer recommend proctoscopy

after proctectomy for rectal cancer.[40–43,69] However, the US Multi-Society Task Force continues to recommend sigmoidoscopy or endorectal ultrasound (in addition to scheduled surveillance colonoscopy) every 3 to 6 months for the first 2 to 3 years after rectal cancer surgery without TME or after TME in the setting of locally advanced rectal cancer without neoadjuvant chemoradiation.[71]

Proctosigmoidoscopy with or without endorectal ultrasound (which may increase sensitivity for detecting local recurrence) is also recommended after transanal excision of rectal cancer. Recognizing the high recurrence rate after transanal excision, the NCCN continues to recommend proctosigmoidoscopy every 6 months for 3 to 5 years in these patients.[40] There are no clear data quantifying the benefit of adding endorectal ultrasound to endoscopy, and endorectal ultrasound has not been investigated in a randomized fashion in this capacity. However, evidence suggests that endorectal ultrasound with fine-needle aspiration biopsy may help diagnose rectal cancer nodal metastases or pelvic recurrence.[75,76] Although surveillance of patients with rectal cancer using endorectal ultrasound may be more sensitive than digital examination or conventional endoscopy in detecting locoregional recurrence, whether this impacts OS is not known. In addition, there are no comparative studies assessing the role of MRI in surveillance after proctectomy or transanal excision. Additional considerations regarding watch-and-wait, nonresection based therapy for rectal cancer are beyond the scope of this guideline and are addressed in other ASCRS practice guidelines.[77]

C. Survivorship

10. A survivorship care plan is recommended for patients after colon or rectal cancer resection and should typically include a treatment summary, a plan for follow-up care, and information about common late and long-term adverse effects associated with the treatment received. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.

Patient perceptions of follow-up after CRC treatment are predominantly positive, although some survivor-specific priorities, like psychosocial, financial, and QoL concerns, often remain unmet.[78] Survivorship care plans (SCPs), designed to communicate information about late effects of treatment and align patient-centered priorities within otherwise routine CRC follow-up care, have been recommended by the Institute of Medicine since 2006 for patients with cancer treated with curative intent.[11] Core elements of an SCP include a summary explaining the treatment given for the patient's cancer, information on late and long-term adverse effects of the treatment received, and a plan for follow-up care. These elements are typically part of a written document that is given to the patient and their primary care provider by the treating physician (surgeon or medical oncologist) or by the survivorship program team. The 2020 American College of Surgeons Commission on Cancer updated its survivorship program requirements and now recommends SCPs as part of a formal survivorship program, whereas the 2016 standards document had required SCPs for 50% of survivors.[10,12]

Despite these reasonable ambitions, randomized studies of cancer survivors with a variety of primary cancers, not limited to CRC, have not demonstrated significant or sustained benefits in terms of QoL, quality of care, care coordination, or oncologic outcomes attributable to SCPs.[79–81] Meanwhile, in a retrospective study reported in 2015 that asked 832 colorectal or lung cancer survivors whether they had received a written treatment summary and/or information regarding who to see for cancer-related follow-up, only 25% received both, but those who did were more likely to have had cancer follow-up care (OR = 5.1 (95% CI, 3.3–8.0)).[82] Additional evidence supporting SCPs comes from a randomized controlled trial of 221 patients with CRC who were randomly assigned to usual care or usual care plus a supportive care pathway called Survivor Care, which provided patients with educational materials, an SCP, and a needs assessment and included 3 follow-up telephone calls.[82,83] In this study, the groups were compared at 2 and 6 months, and the Survivor Care group was found to be more satisfied with survivorship care as demonstrated by the results of a questionnaire related to care; however, the groups did not differ in terms of distress or QoL scores.

Although the evidence shows few measurable benefits related to SCPs, it remains unclear whether this may be because of insensitive outcome measures, variability in SCP content and delivery, incomplete representation of CRC survivor needs, or other factors. In addition, there is little research exploring the effects that SCPs may have on factors such as coordination of care, physician–patient communication, or use of health care services, which likely provide the mechanisms through which SCPs may actually benefit survivors.[82] The ideal format of a CRC-specific SCP and incorporating this into routine practice may also be hampered by logistical barriers, like limited resources, time constraints, and personnel, and require further investigation.

11. After completing treatment for colon or rectal cancer, patients should typically be assessed for psychosocial morbidity (eg, adverse lifestyle behaviors, cognitive dysfunction, or fear of recurrence causing distress) and offered appropriate treatment. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.

Many CRC survivors experience deterioration in health-related QoL (HRQoL) in both early and late posttreatment phases, which is broadly influenced by and interrelated with physical, social, emotional, and cognitive factors.[84]

Reduction in HRQoL may negatively impact survival as shown by Ratjen et al,[84] in a prospective study of 1294 CRC survivors in Germany. Multivariable logistic regression analysis showed that a 10-point increase in the HRQoL score decreased the risk of death by 24% (HR = 0.76 (95% CI, 0.70–0.82)).

Meanwhile, physical activity (PA) and positive lifestyle behaviors have been associated with improved QoL after CRC treatment, yet many CRC survivors do not meet public health guidelines for health behaviors or engage in adverse lifestyle behaviors (eg, 60% are overweight and 62% are insufficiently active).[85–88] However, evidence supporting causality between PA and improved QoL in CRC survivors is limited. Potential difficulties demonstrating an association between PA and QoL include lack of objective activity measurement tools and standardized QoL instruments and issues with clarifying dose–response effects of PA in addition to issues accounting for patient-related variables (eg, location of primary tumor and time interval since treatment).[89–91] Two systematic reviews examining both short- and long-term CRC survivors reported a positive association between PA and QoL.[92,93] Although observational studies have also identified associations between PA and QoL, most randomized trials have failed to demonstrate that PA or exercise intervention improves QoL.[94–100] In contrast to these negative trials, Brown et al[101] showed that high-dose aerobic PA of 300 min/wk improved QoL outcomes in CRC survivors, suggesting a dose–response effect, and Hawkes et al[102] showed improvement in QoL mediated by a behavioral change intervention emphasizing exercise. Similarly, Greenlee et al[103] found that a telephone-based intervention to increase PA and improve diets in breast cancer and CRC survivors was more effective in breast cancer survivors, who were also more compliant with the program.

There is accumulating observational evidence that some modifiable lifestyle factors, such as PA, are inversely associated with CRC recurrence and OS and CRC-specific survival.[104] Meyerhardt et al[105,106] showed that patients with stage II to III colon cancer who participated in 18 metabolic equivalent task hours per week of PA reduced all-cause and cancer-specific mortality by ≈50%. Similarly, a reduction in CRC-specific mortality of 39% was reported in a meta-analysis of 7422 CRC survivors from 7 prospective studies controlling for PA.[107] In this study, each 10 metabolic equivalent task hours per week increase in postdiagnosis PA was associated with a 28% decreased mortality risk. Although additional randomized controlled trials are needed to evaluate the association between PA and improved CRC mortality and to establish evidence-based PA protocols, it is reasonable to recommend that survivors perform moderate levels of PA with the goal to gradually increase activity to the national recommendation of 150 minutes per week of moderate activity defined as any activity that increases the heart rate including performing activities that make the muscles work harder than usual at least 2 days per week (as per the US Department of Health and Human Services).[108] Additional recommendations regarding specific physical activities under these circumstances are beyond the scope of these guidelines.

In terms of psychosocial morbidity related to survivorship, a significant proportion of CRC survivors experience clinically meaningful levels of anxiety and depressive symptoms, and up to 45% of patients with nonmetastatic CRC experience cognitive impairment.[109] Despite pervasive psychologic effects, predictors of cancer-specific psychosocial distress (eg, fear of recurrence or abandonment, economic stressors) and broader mental health concerns and effective interventions have not been well established.[110–112] Several randomized trials composed of heterogeneous cancer survivors have reported improvements in mental health outcomes using cognitive behavior therapy and/or stress reduction strategies, although the long-term durability of these interventions and their applicability to CRC survivors are unclear.[113–115]

Psychosocial morbidity among CRC survivors encompasses a wide range of debilitating symptoms that are likely intimately connected to QoL, and identifying and effectively treating patients experiencing these issues largely remain unmet survivorship challenges; thus, it is reasonable for providers to assess for key psychiatric symptoms during the survivorship phase to facilitate appropriate referral to mental health experts, as needed. Patients with rectal cancer likely have increased psychosocial morbidity because of their increased functional difficulties with altered bowel, bladder, and sexual function and ostomies.[116] In addition, moderate or severe fatigue may effect up to 45% of patients across multiple common cancers, and the prevalence of fatigue may be affected by concomitant depression.[117] Recognizing symptoms of fatigue and depression and appropriately counseling patients may be beneficial in a survivorship program.

12. After completing treatment for colon or rectal cancer, patients should be assessed and treated for late and long-term treatment-related symptoms including functional impairment (eg, peripheral sensory neuropathy and bowel, urinary, and sexual dysfunction). Strong recommendation based on moderate-quality evidence, 1B.

The multimodal therapy used to treat many patients with CRC can cause late and long-term adverse effects.[116,118,119] These consequences are more common in patients with rectal cancer and in patients treated with multiple therapeutic modalities (eg, chemotherapy, radiotherapy, surgery).[118] Survivorship increasingly recognizes that these adverse effects exist and affect patients' QoL and recommends using validated measurement tools to facilitate diagnosis and treatment.

A common functional impairment related to CRC treatment is peripheral neuropathy attributed to oxaliplatin chemotherapy, which affects ≈40% of patients. This neuropathy can substantially affect QoL by causing pain and difficulty with activities of daily living and can be measured using validated scales (eg, total neuropathy score) to allow for comparing serial assessments.[120,121] In addition to requiring treatment in and of itself, peripheral neuropathy often requires alterations in other areas of survivorship care, like modifying PA and addressing stability, balance, and gait, typically with referrals for physical and/or occupational therapy. Painful chemotherapy-induced neuropathy can be treated with duloxetine based on the results of a multicenter, placebo-controlled, randomized trial showing that pain scores were improved significantly 5 weeks after initiation of treatment.[122] In addition, a secondary analysis of a multicenter, randomized controlled trial found that patients receiving chemotherapy for a variety of cancers who participated in a moderate-intensity, home-based exercise program had fewer neuropathy symptoms compared with the control group that did not exercise.[123] Other potential treatments for peripheral neuropathy related to chemotherapy, like tricyclic antidepressants, gabapentin, and topical treatments, do not have strong supporting data.[124]

Another common concern shared by patients after treatment for CRC is bowel dysfunction. Patients with an ostomy can experience a range of unique issues and should typically see an ostomy nurse periodically for stoma assessment and care and education regarding adapting to life with a stoma, as supported by multiple studies.[125] Patients without an ostomy, especially patients with a low anastomosis, may experience bowel dysfunction, including frequency, urgency, and clustering, which may be attributed to low anterior resection syndrome.[126] Up to 50% of patients with rectal cancer report bowel dysfunction, which should, ideally, be assessed using a validated scale such as the Memorial Sloan-Kettering Cancer Center Bowel Function Instrument or the low anterior resection syndrome score.[116,127,128] Treatment of bowel dysfunction under these circumstances is often empiric and may include fiber supplementation, antidiarrheals, and dietary adjustment.[10] A study comparing bowel symptoms in patients before and after a pilot intervention for bowel dysfunction using dietary modification through coaching demonstrated a clinical benefit, and a randomized, prospective trial evaluating this strategy is ongoing.[129]

In addition, 20% to 30% of patients with rectal cancer experience urinary and/or sexual dysfunction after completing their treatment.[118] Selected patients should typically be screened for urinary dysfunction, such as incontinence and retention, and sexual dysfunction, because these can negatively effect QoL.[130] Under these circumstances, patients should generally be referred to a specialist such as a urologist or urogynecologist for further assessment and care.

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