**Name of Journal:** *World Journal of Gastrointestinal Surgery*

**Manuscript NO:** 81622

**Manuscript Type:** MINIREVIEWS

**Surveillance strategies following curative resection and non-operative approach of rectal cancer: How and how long? Review of current recommendations**

Lauretta A *et al.* Rectal cancer follow-up strategies

Andrea Lauretta, Giulia Montori, Gian Piero Guerrini

**Andrea Lauretta,** Department of Surgical Oncology, Centro di Riferimento Oncologico di Aviano IRCCS, Aviano 33081, Italy

**Giulia Montori,** Department of General Surgery, Vittorio Veneto Hospital, ULSS 2 Marca Trevigiana, Vittorio Veneto 31029, Italy

**Gian Piero Guerrini,** Hepato-Pancreato-Biliary Surgical Oncology and Liver Transplantation Unit, Policlinico-AUO Modena, Modena 41124, Italy

**Author contributions:** Lauretta A and Guerrini GP developed the project; Lauretta A and Montori G reviewed the literature; Lauretta A, Montori G, and Guerrini GP drafted and revised the manuscript, and are accountable for all aspects of the work; All authors read and approved the final manuscript.

**Corresponding author: Andrea Lauretta, MD, Chief Doctor, Surgeon, Surgical Oncologist,** Department of Surgical Oncology, Centro di Riferimento Oncologico di Aviano IRCCS, Via Franco Gallini 2, Aviano 33081, Italy. andrea.lauretta@cro.it

**Received:** November 23, 2022

**Revised:** December 30, 2022

**Accepted:** January 17, 2023

**Published online:** February 27, 2023

**Abstract**

Different follow-up strategies are available for patients with rectal cancer following curative treatment. A combination of biochemical testing and imaging investigation, associated with physical examination are commonly used. However, there is currently no consensus about the types of tests to perform, the timing of the testing, and even the need for follow-up at all has been questioned. The aim of this study was to review the evidence of the impact of different follow-up tests and programs in patients with non-metastatic disease after definitive treatment of the primary. A literature review was performed of studies published on MEDLINE, EMBASE, the Cochrane Library and Web of Science up to November 2022. Current published guidelines from the most authoritative specialty societies were also reviewed. According to the follow-up strategies available, the office visit is not efficient but represents the only way to maintain direct contact with the patient and is recommended by all authoritative specialty societies. In colorectal cancer surveillance, carcinoembryonic antigen represents the only established tumor marker. Abdominal and chest computed tomography scan is recommended considering that the liver and lungs are the most common sites of recurrence. Since local relapse in rectal cancer is higher than in colon cancer, endoscopic surveillance is mandatory. Different follow-up regimens have been published but randomized comparisons and meta-analyses do not allow to determine whether intensive or less intensive follow-up had any significant influence on survival and recurrence detection rate. The available data do not allow the drawing of final conclusions on the ideal surveillance methods and the frequency with which they should be applied. It is very useful and urgent for clinicians to identify a cost-effective strategy that allows early identification of recurrence with a special focus for high-risk patients and patients undergoing a “watch and wait” approach.

**Key Words:** Rectal cancer; Follow-up; Surveillance; Recurrence; Carcinoembryonic antigen; Computed tomography

**©The Author(s) 2023.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** Lauretta A, Montori G, Guerrini GP. Surveillance strategies following curative resection and non-operative approach of rectal cancer: How and how long? Review of current recommendations. *World J Gastrointest Surg* 2023; 15(2): 177-192

**URL:** https://www.wjgnet.com/1948-9366/full/v15/i2/177.htm

**DOI:** https://dx.doi.org/10.4240/wjgs.v15.i2.177

**Core Tip:** Follow-up programs following rectal cancer curative treatment are widely accepted as an integrated part of the therapeutic pathway, but there is still no consensus regarding which test should be performed, the time schedule, the frequency and the duration of surveillance. The impact on survival has also been questioned with recurrence detection not necessarily associated with curative surgery. The aim of this review was to provide an overview of recommendations on this topic with supporting evidence.

**INTRODUCTION**

Currently, the treatment of rectal cancer is based on a multimodal approach that involves not only the surgeon but other specialists such as gastroenterologists, radiotherapists, and oncologists. Due to the wide range of circumstances in the initial stage and responsivity to neoadjuvant treatments, many therapeutic pathways are available that may lead to different follow-up plans and open the door to the debate. There is currently no consensus about the types of tests to perform, the timing of the testing, and even the need for follow-up at all has been questioned. Only patients treated radically for the primary tumor with non-metastatic disease are eligible for post-operative follow-up. Although at the time of diagnosis, approximately 70% of patients affected by colorectal cancer will be treated surgically with curative intent[1], recurrence occurs in about 30% to 50% of patients undergoing curative treatments, including both local relapse and distant metastasis[2]. Therefore, surveillance programs following radical rectal cancer resection are an integral part of the therapeutic pathway. The most common sites of distant metastasis are the liver followed by the lungs; however, rectal cancer is correlated more often to local failure than colon cancer, carrying a significantly higher risk of local recurrence. Specifically, anastomotic recurrence is recorded in 5% to 15% of patients[3], although it should be noted that the recurrence more frequently grows extraluminally, generally in the pre-sacral area and less often in the anastomosis site[4]. The rate of distant metastasis in colon and rectal cancer is similar instead[5]. Treatment with curative intent of recurrence is feasible, and this increases prognosis and overall survival. Given the great risk of relapse, to improve prognosis of patients with disease recurrence, follow-up regimens should detect cancer recurrence early. The key point is to find the best surveillance programs that allow the early detection of recurrent cancer when it is still responsive to curative treatment. Follow-up programs have strategic importance only in this setting. Finally, we should consider two more aspects related to surveillance programs. Follow-up has an important psychological impact indeed: on the one hand it may provide comfort, reassuring the cancer survivor that there is no evidence of recurrence; on the other hand, it may induce negative effects such as stress and anxiety due to the intensive testing the patient is forced to go through. Finally, follow-up tests are costly and bring the inevitable risk of false positives, leading to pointless procedures and potential complications. In light of the clear benefits and potential risks of follow-up programs, it is urgent to establish a cost-effective strategy to guarantee early recognition of disease relapse and reduce potential shortcomings, narrowing surveillance to the highest-risk patients.

The aim of this study was to review the evidence of the impact of different follow-up tests and programs in patients with non-metastatic disease following surgery of the primary tumor. Current published guidelines from the most authoritative specialty societies were also reviewed and presented.

**Risk assessment**

Recurrence could be local or distant and numerous risk factors have been related to cancer relapse including tumor stage, grading, circumferential margin, location, obstruction, perforation, type and adequacy of resection, lympho-vascular invasion, blood transfusions, anastomotic leak, patient constitution and sex, and last but not least, the surgeon’s know-how and expertise leading to the saying “colorectal surgeons do it better”[6-9]. Nonetheless, the critical factor related to the risk of recurrence is the original histopathological cancer stage with an increased risk associated with advanced primary American Joint Committee on Cancer (AJCC) staging. Therefore, the follow-up strategy involves patients affected by early-stage disease, focusing especially on those belonging to stage II and III according to AJCC regarded as the highest risk patients. Patients affected by stage 0 neoplasia (carcinoma in situ without extension into the submucosa), patients operated with no curative intent and patients with major comorbidities that even in case of recurrence would be excluded from any active treatment, should not be followed-up. Finally, both locoregional and distant recurrences occur in most cases within 3 years of surgery, highlighting the importance of intensive early testing and suggesting a limited impact of longer follow-up[10].

**Follow-up tests**

Taking into account the different types of metastases, more than one surveillance test is usually performed to evaluate the different possible sites of recurrence. A combination of biochemical tests and imaging investigations are associated with physical examination to identify locoregional and distant metastases at an early stage. The most used tools to perform a complete surveillance include medical history and physical examinations, serial measurement of carcinoembryonic antigen (CEA), liver function tests, endoscopy, liver imaging and chest imaging and possibly, positron emission tomography (PET) scanning.

**Medical history and physical examinations**

Anamnesis and clinical examination are the first approach for any patient with rectal cancer history and are recommended by all scientific societies as an integral part of surveillance programs[4,11-15]. However, the value and role of the office visit are not still clear. The lack of specific symptoms makes diagnosis complicated and often delayed, and only 1.7% to 7% of patients with symptoms caused by recurrence have resectable disease[16-18]. Furthermore, about one-quarter of patients, even though within an intensive surveillance program, delay reporting symptoms until their next clinic visit[19]. The digital rectal examination (DRE) has progressively lost importance for the early detection of local recurrence and nowadays office evaluation remains key only for maintaining direct contact with patients, better planning surveillance tests and coordinating with different figures to avoid useless diagnostic procedures and pointless anxiety[15].

**CEA**

CEA is the most used tumor marker and hematic test in colorectal cancer follow-up. Its role has been extensively evaluated and it has been used in colorectal cancer for more than 40 years. CEA has not as much specificity and sensibility as a screening test, but is often the first indicator of relapse even in the case of cancers without CEA elevation prior to surgery[20]. CEA level is reported as being elevated in up to 75% of patients with colorectal cancer recurrence[21]. The reported sensitivity of CEA varies respectively from 44% to 89%, while specificity ranges from 42% to 98%[22-32]. The sensitivity and specificity of CEA for detecting recurrence depends on the cut-off value considered: a CEA cutoff of 10 µg/L is associated with sensitivity of 68% and specificity of 97%, while a cutoff of 2.5 µg/L has a sensitivity of 82% and a specificity of 80%[33]. Thus, a lower threshold level has resulted in increased sensitivity but reduced specificity. It has been reported that only 22.9% (range between 7.5% and 33%) of recurrences, identified by CEA elevation, are resectable at the time of diagnosis[10]. Recently, the follow-up after colorectal surgery (FACS) trial randomly assigned 1202 patients to four different types of follow-up. The authors report that CEA screening alone detected 6.7% of resectable metastases, compared with 8% in the computed tomography (CT) alone group and 6.6% in the group with association of CEA and CT. Thus, the rates of surgical treatment of recurrences were similar in the CEA alone group and CT alone group, without advantages in combination of CEA and CT[34]. CEA remains the most cost-effective method of identification of recurrence, although the curative rate of surgery in this scenario remains low. It should be noted that the possibility of false-positive CEA rising is real. The false-positive rate for CEA can be as high as 16%, especially in smokers[28]. For this reason, it is a common opinion to wait for a second CEA level to confirm an elevation trend and in the case of rising CEA on sequential measurements it is suggested to embark on more specific diagnostic tools. This attitude was recently confirmed by the CEA watch trial from the Netherlands that compared usual follow-up care with an intensified follow-up schedule performed with CEA measurements every 2 months and imaging in the case of two CEA rises. Intensive CEA surveillance protocol resulted in higher recurrence detection and more recurrence suitable for curative treatment. The time of detection of recurrent disease was shorter as well[35]. Rising CEA should be managed by investigating the possible recurrence site and even the employment of a PET or PET/CT is justified if the localization of the relapse is not clear[14,36]. Finally, CEA represents the only established tumor marker in colorectal cancer follow-up programs and is strongly recommended by all major scientific societies[4,11-15].

**Liver Imaging**

The most used imaging means of studying liver parenchyma are ultrasonography (US) and CT. US is operator dependent and has lower sensitivity than CT scans, but both may detect liver recurrence early. However, the real benefit of early recurrence detection in terms of curative resection is still controversial. Mäkelä *et al*[37] reported only 6 of 22 (27%) liver metastases identified by either ultrasound (4 cases) or CT scan (2 cases), prior to elevation of CEA. This was not associated with any resection. Schoemaker *et al*[38] demonstrated a significant identification rate of asymptomatic liver metastasis by CT scan, but these figures were not associated with increased hepatic resection rates (3 resections in the intensive surveillance group and 4 in the standard arm). The tests used in the standard arm (CEA and liver function tests) allowed identification of resectable liver recurrences with CT scans not adding any substantial advantages. More recently, the results of the FACS trial were similar: liver metastases were detected both by scheduled CEA only or scheduled CT only. No advantages were reported in combining CEA and CT. CEA is evidently more cost-effective, even though CT is crucial for confirming and localizing the recurrence[34].Only in the randomized controlled trial (RCT) from Rodríguez-Moranta *et al*[39] either abdominal CT or US were able to detect 10 (28.5%) distant metastases, 4 of which were resectable (40%). Indeed, there is an overlap between liver imaging and CEA, suggesting that isolated liver imagines in routine follow-up programs are not so useful. Nevertheless, liver imaging is recommended almost annually by all specialty societies[4,11-15].

**Chest Imaging**

Rectal cancer, more than colon cancer, frequently recurs in the lung given its particular venous drainage to the caval system, with an incidence of isolated lung metastasis of 2-10% of cases[40,41]. Unfortunately, as reported by a multicenter retrospective study, only 38% of those patients are eligible for curative metastasectomy and undergo surgical resection[42]. Mitry *et al*[43] reported even worse figures: only 4% of patients with synchronous pulmonary metastases and 14% of patients with metachronous pulmonary metastases are curatively resected. Lung recurrences may be detected by conventional chest radiography (CXR) or CT scan. The role of CXR has been evaluated, especially in the case of colon cancer follow-up, suggesting that it is not a valuable method for detecting resectable disease. Considering trials including both colon and rectal cancers, CXR was able to identify lung resectable recurrence in 1.8% to 12% of patients, which did not substantially modify survival[37,38,44]. Similarly, Rodríguez-Moranta *et al*[39] more recently reported that CXR was the first method indicating lung tumor recurrence in 3 patients (9%) in the intensive strategy group. However, only two recurrences were resectable (11%), and just one (25%) considering recurrence related to rectal cancer. These figures look similar to those published previously but highlight how the performance of CXR as a diagnostic tool is better if we consider only the patients affected by rectal cancer. However, even though CXR is not costly, a very low number of patients can benefit from scheduled CXR, and its role remains marginal in surveillance programs. Chest CT scan appears to be the only reliable method for investigating the lungs and it is suggested by all the specialty societies, at the expense of CXR[4,11-15].

**Endoscopy**

The role of colonoscopy and rectosigmoidoscopy after curative resection is crucial and is a very important tool for identifying anastomotic recurrence and metachronous colorectal cancers. In rectal cancer, especially in patients who did not receive any neoadjuvant treatment, about 3% to 50% of cases show a locoregional recurrence, including anastomotic recurrences, that is more frequent than in colon cancers[45]. Patients affected by rectal cancer have a lifetime risk of developing a metachronous tumor in the residual viscera that ranges from 1.1% to 6.3%[20], while the risk of developing a metachronous adenoma is up to 56%[46].Taking into account the reported figures of metachronous lesions, the role of colonoscopy is undisputed despite the invasiveness and the risk of possible complications, such as bleeding or perforation. Two studies[38,47] reported complications related to colonoscopy surveillance in only seven cases (three perforations and four hemorrhages out of 2112 colonoscopies: 0.4%). Eight RCTs included colonoscopy and proctoscopy as a part of intensive surveillance programs, compared either with less frequent or even no endoluminal testing[16,37-39,44,47-49]. These trials, except those reported by Rodríguez-Moranta *et al*[39] and Wang *et al*[47], suggest only a marginal benefit from colonoscopy. Instead, Rodríguez-Moranta *et al*[39] and Wang *et al*[47] reported a significant identification of local relapses that can be treated with salvage surgery, leading to significantly longer survival in patients undergoing intensive colonoscopic surveillance. However, the bad results of six RCTs[16,37,38,44,48,49] adopting intensive colonoscopy programs were probably due to the short median observation period reported by each study, which was less than 5 years. The reality is that patients treated for colon and rectal cancers have a life-long and cumulative risk of developing bowel cancer again and therefore the recommendation to perform a colonoscopy over a longer period is warranted and may prove more beneficial. The major scientific societies suggest colonoscopy as a follow-up modality for removing early adenomatous polyps and detecting metachronous cancer[4,11,13,14]. The American Society of Colon and Rectal Surgeon (ASCRS)[4], The Association of Coloproctology of Great Britain and Ireland (ACPGBI)[11], The American Society of Clinical Oncology (ASCO)[13] and The National Comprehensive Cancer Network (NCCN)[14], actually suggest colonoscopy at 1 year, and subsequently according to findings. Furthermore, the ASCRS[4], ASCO[13], and NCCN[14] recommend surveillance rectosigmoidoscopy even more frequently (every 3 to 6 months for 5 years) in the presence of local recurrence risk factors and consider transanal local excision and absence of neoadjuvant radiation a risk factor *per se*. However, colonoscopy is not able to detect extra-luminal recurrent disease, which is more frequent than intraluminal recurrence in the case of rectal cancer. More often a positive circumferential margin at the time of original resection results in an extra-parietal recurrence, usually in the pre-sacral site. Endorectal ultrasound (ERUS) may overcome this limit, giving an accurate imaging of surrounding pelvic tissues. The role of ERUS for the diagnosis of local recurrence after local excision and radical surgery for rectal cancer was evaluated by de Anda *et al*[50]. The authors reported that asymptomatic local recurrences are identified by ERUS in 30% of cases and these recurrences were actually missed by digital examination or proctoscopic examination. However, only 44% of cases were amenable to salvage surgery and the impact of earlier diagnosis was not significant in terms of patient survival. Larger, multi-institutional RCTs are needed to confirm the real role and effectiveness of ERUS. Considering the lack of clear data, the ASCR and NCCN recommend surveillance endoscopy “with or without” ERUS, or alternatively magnetic resonance imaging (MRI) in surveillance programs[4,14].

**PET scanning**

PET with the use of radio-labeled glucose analogue 18F-fluorodeoxyglucose (FDG) and PET associated with a CT scan (FDG PET/CT) are metabolic imaging that highlight lesions with higher glucose metabolism. Malignant lesions have higher glucose metabolism and thus a higher uptake of FDG. The use of PET/CT in colorectal cancer follow-up is currently controversial. A review and meta-analysis[51] evaluating the performance of FDG-PET or PET/CT to detect recurrences of colorectal cancer in patients with raised CEA, identifies 11 studies with a total of 510 patients. In the case of an increase in CEA, one hundred and six patients (106/510: 20.8%) had a true-negative FDG-PET/ or PET/CT. Thus, both imaging modalities ruled out 20% of false positive elevations of CEA. Moreover, the diagnostic accuracy of these techniques was 88.6% and allows a differentiation of an inflammatory process from a recurrence. PET and PET/CT had a sensitivity of 90.3% and 94.1% and a specificity of 80% and 77.2% respectively. Similarly, both modalities had good accuracy (89.03% and 92.38% respectively). Supplementary analysis showed that PET and PET/CT gave a significantly higher diagnostic performance than CT scans. Sanli *et al*[52] reported that colorectal cancer relapse was accurately detected also in the case of normal CEA rates. The NCCN[14] suggests PET/CT scans in the case of an increasing CEA, even with negative CT scans. Recently, a novel hybrid technique was introduced in the oncological field matching PET and MRI in one examination: FDG-PET/MRI. Hybrid PET/MRI combines metabolic imaging of PET with excellent soft tissue morphology of MRI[53]. The accuracy of FDG-PET/MRI is apparently superior to MRI alone in restaging after neoadjuvant chemoradiation (naCRT). The study from Crimì *et al*[54] showed that in patients with locally advanced rectal cancer undergoing restaging following preoperative chemoradiotherapy, FDG-PET/MRI was more accurate and sensitive than MRI alone both for residual cancer and regional lymph nodes (respectively ypT accuracy 92% *vs* 89%; ypN accuracy 92% *vs* 86%). Two recent studies investigated the role of FDG-PET/MRI in pelvic recurrence of rectal cancer[55,56]. The first paper from Plodeck *et al*[55] was a retrospective, single reader study, assessing the performance of FDG-PET/MRI without any comparison to MRI alone: sensitivity, specificity and accuracy were 94%. The same group published a retrospective evaluation of diagnostic performance of PET/MRI compared to MRI alone in the diagnosis of pelvic recurrence of rectal cancer: sensitivity and accuracy of PET/MRI were respectively 94% and 93% compared to 88% sensitivity and 85% accuracy of MRI in detecting recurrence. Both imaging modalities are accurate in this setting even though PET/MRI increases confidence in diagnosis or exclusion of local recurrence and reduces the number of equivocal cases[56]. We can conclude that both PET and PET/CT provide useful information about sites of recurrence, especially extra-hepatic lesions, and possible metachronous tumors contributing substantially to patient management. Patients with a suspected recurrence, based on clinical findings or rising CEA, might benefit from a PET/CT as a first line imaging modality, since a negative CT scan does not definitively exclude a recurrence and will be followed by a PET/CT anyhow. PET/MRI is a promising imaging modality combining functional imaging and soft tissue contrast leading to more accurate evaluation of pelvic recurrence. Unfortunately, no prospective studies have evaluated the role of PET imaging in any colorectal cancer surveillance program. Indeed, the main limits of PET, PET/CTand PET/MRI are its limited availability and high cost: these drawbacks limit its use in follow-up programs and make PET imaging not realistic as a routine diagnostic method.

**Intensive *vs* Less Intensive Follow-up**

Different follow-up regimens have been studied in RCTs and non-randomized studies, meta-analysis and systematic review, that aimed to elucidate the impact of different surveillance programs and schedule in terms of survival, recurrence detection rate and the ability to offer salvage surgery in the case of recurrence. Intensive, less intensive or even no surveillance has been proposed and the influence on cancer related outcomes has been analyzed. We identified 17 RCTs[16,34-39,44,47-49,57-63] and 8 meta-analyses[19,64-70], evaluating different follow-up strategies during surveillance programs after curative colorectal cancer surgery. Results of RCTs and meta-analyses are summarized respectively in Tables 1 and 2. Three trials[58,60,61] comparing different settings of monitoring did not show any differences in terms of recurrence detection rates and time to detection between a hospital/specialist setting and a general practice setting. Medical safety was uncompromised even if the follow-up was performed by a trained nurse. Eight trials did not show any significant differences in survival between intensive and less intensive surveillance[16,34,37,38,44,49,62,63]. The trial by Ohlsson *et al*[44] did not show any survival improvement even comparing intense follow-up with no follow-up. On the other hand, in six trials, intensive follow-up was associated with an improved overall survival, instead[35,39,47,48,57,59]. Six meta-analyses showed that, in patients with colorectal cancer followed after curative resection, an intensive follow-up program improves overall survival, detection of asymptomatic relapses and reoperation with curative intent[19,64-68]. On the other hand, there are two more recent meta-analyses that were not able to demonstrate any significant benefit from an intensification of surveillance programs[69,70]. It should be noted that the recent COLOFOL trial[63] is not included in any published meta-analyses. This trial randomized 2509 patients with stage II or III colorectal cancer to either low frequency follow-up regimens (CEA and chest/abdomen CT scan at 12 and 26 months) or high frequency follow-up regimens (CEA and CT scan at 6-12-18-24-36 months) with patients undergoing the same kind of tests. No significant advantage of the high frequency follow-up testing, both in 5-year overall mortality and colorectal cancer-specific mortality was recorded[63]. Furthermore, Renehan *et al*[64] in their meta-analysis showed that intensive surveillance leads to a 10% decrease in 5-year mortality, however only in 2% of cases salvage surgery was possible. The authors suggested that intensive follow-up programs can ameliorate psychosocial support and well-being, alter dietary and lifestyle factors and finally improve treatment of coincidental diseases leading to survival benefits. However, Baca *et al*[10] suggested that meta-analytic techniques could not be appropriate to evaluate results because of the inadequacy of sample sizes and the high heterogeneity in surveillance programs considered in the different RCTs. Finally, it has been suggested that a structured follow-up should be performed only in patients who can benefit from further treatments[15].

**Cost of follow-up**

The pressure of rising health care costs has forced clinicians to review surveillance protocols to make them more effective and cheaper, trying to save unnecessary tests. Economic analysis of eleven different 5-year postoperative follow-up programs based on Medicare-allowed charges showed a wide range of costs: from $910 to $26717. Despite these significant disparities, no clear benefits were found in higher cost strategies in terms of quality of life and survival rate[71]. In the same year, Kievit *et al*[72] presented the results of a cost-effectiveness analysis comparing the results of three different policies comparing no follow-up, selective follow-up and intensive follow-up. In most cases, follow-up will only increase costs significantly without an increase in life expectancy and the author concluded that colorectal cancer follow-up is not “evidence-based medicine.” A Markov model was used to simulate follow-up over a 7-year period in patients who had undergone curative resection of colorectal cancer[73]. The influence of follow-up on the quality-adjusted life expectancy of patients who had Duke's stage A and B colorectal cancer was marginal, while it ameliorated the survival in Duke's stage C patients. Graham *et al*[17] analyzed the cost of the single diagnostic method per resectable recurrence: CEA was the most cost-effective method, costing $5696 per recurrence, while CXR and colonoscopy cost $10078 and $45810 per recurrence respectively. A risk adjusted follow-up policy, considering that older age and favorable cancer stage decrease cost-effectiveness, should focus solely on high-risk patients for the first 2-3 years using the most cost-effective test to increase benefits. On the other hand, a prospective, multicenter, RCT comparing a simple surveillance program including just clinical evaluation and CEA with an intensive strategy with abdominal-pelvic CT, CXR, and colonoscopy, found that, even though the overall cost of an intensive surveillance program was higher (€300315 *vs* €188630), the intensive follow-up was more cost-effective when resectability of recurrent disease was considered. In fact, the cost per resectable recurrence was €16684 in the intensive surveillance group, compared with €18863 in the simple follow-up strategy[39]. Therefore, justification of a surveillance strategy should be fundamentally based on evidence of clinical value allowing identification of recurrence at the point where a cure is still possible. Finally, the study from Augestad *et al*[61] demonstrated that a general practitioner’s organized follow-up was cost-effective compared with surgeon’s organized follow-up (£8233 *vs* £9889). Delegating follow-up can be effective but also safe with no harm for patients, but probably a precise algorithm of surveillance programs is the only way to help clinicians in charge for surveillance.

**Current guidelines and recommendations**

Published guidelines from the most authoritative specialty societies indicate different protocols including medical history and physical examination, CEA levels, abdominal-pelvic and chest imaging and endoscopy. Follow-up recommendations from ASCO[13], ASCRS[4], European Society of Medical Oncology (ESMO)[12], ACPGBI[11], NCCN[14] and European Society of Coloproctology (ESCP)[15] are summarized in Table 3. In 2013, ASCO[13] endorsed the Cancer Care Ontario guidelines on follow-up care and added some statements[74]. The guidelines are primarily for patients with stage II and III disease, while stage I patients and patients resected for metastatic disease should be monitored according to the discretion of the health care provider. The suggested surveillance program considers, in the first 2-4 years, more intensive testing since 80% of recurrences occur in the first 2-2.5 years from surgery[13]. NCCN[14] and ESMO[12] guidelines actually suggest semi-annual to annual abdomen and chest CT scans for 5 years considering that up to 10% of recurrences occur after 3 years[75]. The ASCRS guidelines[4] are very similar to the previous recommendations but support the advantage of follow-up in terms of survival in patients with stage I disease. The ASCRS[4] and NCCN[14] recommend a more intensive approach for patients treated by transanal excision, while ASCO[13] suggests the same intensive approach for patients not having received radiotherapy. In NCCN guidelines[14], surveillance programs are a little more frequent than other programs. The ESMO[12] and ACPGBI[11] recommendations suggest slightly less intensive testing with a minimum of two CT scans of the chest, abdomen and pelvis associated with regular serum CEA tests in the first 3 years. The ESCP[15] recommendations are actually an overview of national and international clinical practice guidelines. Interestingly, colonoscopy and endoscopic inspection of anastomosis are recommended but the optimum time schedule and duration of surveillance are not specified since the analyzed guidelines were not all concordant[15]. A different issue is represented by the significant variation in adhesion and compliance both of members of scientific societies and patients with the recommended follow-up tests. A postal survey was mailed to active members of ASCRS in 2000 assessing the methods and frequency of follow-up. The most used tests were colonoscopy and CEA but there was wide variation in the frequency of follow-up and the diagnostic modalities employed. More interestingly, only 50% of surgeons followed the recommended guidelines of the ASCRS to whom they belonged[76]. It is clear that specialty society’s recommendations differ and health care providers may find it difficult to choose the ones which are most appropriate. This may explain the low percentage of surgeons adhering to the recommended guidelines. It appears more sensible to adopt the follow-up scheme according to available manpower and local facilities.

**Follow-up following a complete response after chemoradiation**

Locally invasive rectal cancer is currently managed by neoadjuvant combined modality therapy (chemoradiation or even radiation alone regimens) followed by total mesorectal excision. The benefit of neoadjuvant therapy is not only the long-term local disease control, but also tumor regression. naCRT induces tumor regression (downsizing) and eventually lymph node sterilization (downstaging). After naCRT, up to 25% of patients have complete pathological tumor regression with no residual viable tumor cells at the time of surgery[77-80]. These patients have the so called “pathologic complete response (pCR)”. A pCR is defined as an absence of viable tumor on histologic examination of the resection specimen and is reported as ypT0N0[81]. In a systematic review, the finding of pCR was associated with local recurrence rate and distant metastasis respectively of 0.7% and 8.7%. The 5-year overall survival rate was 90.2%, the disease-free survival (DFS) rate 87%[82]. These surprising results in patients with pCR have changed the role of standard surgery, especially considering morbidity and mortality associated with rectal surgery. Habr-Gama *et al*[83] from Brazil firstly proposed a non-operative approach for patients with significant or complete tumor regression. This alternative approach is also described as “organ-sparing treatment”, “rectal preservation” or the “watch and wait” strategy. Patients with apparent clinical complete response (cCR) after naCRT are ideal candidates for conservative strategy. cCR is usually described as absence of tumor according to clinical, radiological and endoscopic investigations; however, the description cannot be as clear as pCR. Although the definition of cCR remains an active question and there is no uniform consensus, the absence of any palpable tumor at DRE and no visible lesion (flat scar, whitening of the mucosa or teleangiectasia) at endoscopy are widely accepted as main criteria to define cCR. The clinical criteria are normally complemented by the absence of residual tumor and metastatic lymph nodes on MRI[84].The landmark paper based on this approach was firstly published in 2004 and since that time the San Paolo group has regularly updated their work[83,85]. Over 18 years, 67 (39%) patients were considered to have cCR after being reassessed following completion of radiotherapy at least 8 weeks later. At a mean follow-up of more than 5 years, overall survival reached 96% and DFS was 72% in nonoperative patients. Local recurrence (only endoluminal) and distant metastasis were observed in 11% and 10% respectively. All local recurrences were responsive to salvage therapy: 4 patients underwent radical surgery, 3 local excision and 1 additional endorectal brachytherapy[85]. Similar results have been reported by different authors in smaller studies[86,87], but these surprising results have not been repeated by other studies with an 80% relapse rate following cCRs within 10 months of observation[88,89].The data from the International Watch and Wait Database, including more than one-thousand patients managed by watch and wait strategy, showed a local regrowth rate of 25% and 8% distant metastasis at 3 years[90]. More recently, a total neoadjuvant therapy (TNT) has also been adopted with application of both radiation and full systemic chemotherapy before surgery leading to even better results in terms of tumor response[91]. In the prospective, randomized phase II trial from Garcia-Aguilar *et al*[91] the 3-year DFS was 76% and organ preservation was achievable in up to 53% of patients treated with TNT. Considering all these figures, the watch and wait strategy sounds promising and appealing since it avoids the significant morbidity related to surgery. Patients with a complete clinical response may achieve similar overall survival and local cancer control of patients undergoing standard surgery. The main challenge to a non-operative approach of locally advanced rectal cancer is the identification of patients with a true complete tumor regression since there is a real risk of leaving occult residual disease within the rectum or perirectal nodes. Thus, patients reported to have a cCR may bear microscopical disease with a high risk of early recurrence. These considerations are crucial for determining what kind of surveillance protocols should be adopted especially in this particular subset of patients. Again, the Brazil group[92] suggests a strict follow-up program including DRE, rigid proctoscopy with biopsy of suspicious lesions and CEA levels every 1-2 months for the first year, every 6 months in the second year and yearly thereafter. Chest X-ray and abdominal CT scans are recommended at 6 months and 12 months and yearly thereafter. The recently published RESARCH study[84] also adopts a strict follow-up strategy in patients who undergo a rectal sparing approach following neoadjuvant therapy: physical examination including digital rectal exploration, CEA levels and proctoscopy every 3 months for 2 years and subsequently every 6 months for 3 years. Chest and abdomen CT scans are recommended annually, while MRI of the pelvis is performed every 6 months for 2 years and yearly thereafter. Colonoscopy is performed at 1 year and 4 years following surgery[84]. Even though it is not suggested by the Habr-Gama *et al*[92] and the RESARCH study[84], FDG-PET and PET-CT may play an important role for surveying non-operative patients, considering that these imaging modalities are the most accurate and may help to distinguish fibrosis from viable tumor cells. Recently it has been suggested that FDG-PET/MRI may improve accuracy in restaging patients deemed to have a cCR. FDG-PET/MRI evaluating residual disease at restaging following TNT had an accuracy of 100% compared to 71% of MRI alone, adding value in restaging and surveillance programs of patients enrolled in non-operative management[93]. Finally, patients elected for this novel approach must be committed to an intensive follow-up regimen until the natural history of the non-operative approach is definitively clarified. The watch and wait strategy can only be offered to patients who will be compliant with frequent clinical and radiological evaluation. However, the key point of this novel approach remains to identify a true pCR without a resection and through targeted follow-up. Achieving the equivalence between cCR and pCR represents the crossroads to avoid either useless major resections or the risk of early local recurrence or, more correctly, tumor persistence.

**CONCLUSION**

Follow-up programs after rectal cancer resection are intuitively beneficial and appealing even though there is no clear evidence of benefits in terms of earlier detection of recurrence, surgical resections with curative intent and improved overall survival. The literature does not agree with the type of ideal surveillance methods and the timeframe with which they should be applied. Moreover, the cost-effectiveness of various surveillance strategies, the quality-of-life implications and the role of different surveillance techniques have not yet been clearly evaluated. In this difficult age for healthcare economies, the optimization of resources and therefore also of surveillance programs is necessary. The improvement of recurrence risk stratification, the identification of the patient population that will truly benefit from follow-up and avoid unnecessary examination in low-risk patients should be the main goal in designing a value-based follow-up strategy. The main purpose of a surveillance program must be early identification of a recurrence when curative interventions are still possible.

**REFERENCES**

1 **Jemal A**, Murray T, Samuels A, Ghafoor A, Ward E, Thun MJ. Cancer statistics, 2003. *CA Cancer J Clin* 2003; **53**: 5-26 [PMID: 12568441 DOI: 10.3322/canjclin.53.1.5]

2 **Böhm B**, Schwenk W, Hucke HP, Stock W. Does methodic long-term follow-up affect survival after curative resection of colorectal carcinoma? *Dis Colon Rectum*1993; **36**: 280-286 [PMID: 8449134 DOI: 10.1007/BF02053511]

3 **Heald RJ**, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986; **1**: 1479-1482 [PMID: 2425199 DOI: 10.1016/s0140-6736(86)91510-2]

4 **Hardiman KM**, Felder SI, Friedman G, Migaly J, Paquette IM, Feingold DL; Prepared on behalf of the Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surveillance and Survivorship Care of Patients After Curative Treatment of Colon and Rectal Cancer. *Dis Colon Rectum* 2021; **64**: 517-533 [PMID: 33591043 DOI: 10.1097/DCR.0000000000001984]

5 **Asgeirsson T**, Zhang S, Senagore AJ. Optimal follow-up to curative colon and rectal cancer surgery: how and for how long? *Surg Oncol Clin N Am* 2010; **19**: 861-873 [PMID: 20883959 DOI: 10.1016/j.soc.2010.06.003]

6 **Mirnezami A**, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. *Ann Surg* 2011; **253**: 890-899 [PMID: 21394013 DOI: 10.1097/SLA.0b013e3182128929]

7 **Obrand DI**, Gordon PH. Incidence and patterns of recurrence following curative resection for colorectal carcinoma. *Dis Colon Rectum* 1997; **40**: 15-24 [PMID: 9102255 DOI: 10.1007/BF02055676]

8 **Phillips RK**, Hittinger R, Blesovsky L, Fry JS, Fielding LP. Local recurrence following 'curative' surgery for large bowel cancer: I. The overall picture. *Br J Surg*1984; **71**: 12-16 [PMID: 6689962 DOI: 10.1002/bjs.1800710104]

9 **Heald RJ**, Moran BJ, Ryall RD, Sexton R, MacFarlane JK. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978-1997. *Arch Surg* 1998; **133**: 894-899 [PMID: 9711965 DOI: 10.1001/archsurg.133.8.894]

10 **Baca B**, Beart RW Jr, Etzioni DA. Surveillance after colorectal cancer resection: a systematic review. *Dis Colon Rectum* 2011; **54**: 1036-1048 [PMID: 21730795 DOI: 10.1007/DCR.0b013e31820db364]

11 **Leong K**, Hartley J, Karandikar S. Association of Coloproctology of Great Britain & Ireland (ACPGBI): Guidelines for the Management of Cancer of the Colon, Rectum and Anus (2017) - Follow Up, Lifestyle and Survivorship. *Colorectal Dis* 2017; **19 Suppl 1**: 67-70 [PMID: 28632315 DOI: 10.1111/codi.13706]

12 **Glynne-Jones R**, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A, Arnold D; ESMO Guidelines Committee. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2017; **28**: iv22-iv40 [PMID: 28881920 DOI: 10.1093/annonc/mdx224]

13 **Meyerhardt JA**, Mangu PB, Flynn PJ, Korde L, Loprinzi CL, Minsky BD, Petrelli NJ, Ryan K, Schrag DH, Wong SL, Benson AB 3rd; American Society of Clinical Oncology. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer: American Society of Clinical Oncology clinical practice guideline endorsement. *J Clin Oncol* 2013; **31**: 4465-4470 [PMID: 24220554 DOI: 10.1200/JCO.2013.50.7442]

14 National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology. Rectal Cancer. Version 3.2022. 2022 Oct 27 [cited 31 October 2022]. Available at: https://www.nccn.org/professionals/physician\_gls/pdf/rectal.pdf

15 **Bastiaenen VP**, Hovdenak Jakobsen I, Labianca R, Martling A, Morton DG, Primrose JN, Tanis PJ, Laurberg S; Research Committee and the Guidelines Committee of the European Society of Coloproctology (ESCP). Consensus and controversies regarding follow-up after treatment with curative intent of nonmetastatic colorectal cancer: a synopsis of guidelines used in countries represented in the European Society of Coloproctology. *Colorectal Dis* 2019; **21**: 392-416 [PMID: 30506553 DOI: 10.1111/codi.14503]

16 **Kjeldsen BJ**, Kronborg O, Fenger C, Jørgensen OD. A prospective randomized study of follow-up after radical surgery for colorectal cancer. *Br J Surg* 1997; **84**: 666-669 [PMID: 9171758]

17 **Graham RA**, Wang S, Catalano PJ, Haller DG. Postsurgical surveillance of colon cancer: preliminary cost analysis of physician examination, carcinoembryonic antigen testing, chest x-ray, and colonoscopy. *Ann Surg* 1998; **228**: 59-63 [PMID: 9671067 DOI: 10.1097/00000658-199807000-00009]

18 **Goldberg RM**, Fleming TR, Tangen CM, Moertel CG, Macdonald JS, Haller DG, Laurie JA. Surgery for recurrent colon cancer: strategies for identifying resectable recurrence and success rates after resection. Eastern Cooperative Oncology Group, the North Central Cancer Treatment Group, and the Southwest Oncology Group. *Ann Intern Med* 1998; **129**: 27-35 [PMID: 9652996 DOI: 10.7326/0003-4819-129-1-199807010-00007]

19 **Bruinvels DJ**, Stiggelbout AM, Kievit J, van Houwelingen HC, Habbema JD, van de Velde CJ. Follow-up of patients with colorectal cancer. A meta-analysis. *Ann Surg* 1994; **219**: 174-182 [PMID: 8129488 DOI: 10.1097/00000658-199402000-00009]

20 **Meyerhardt JA**, Mayer RJ. Follow-up strategies after curative resection of colorectal cancer. *Semin Oncol* 2003; **30**: 349-360 [PMID: 12870136 DOI: 10.1016/s0093-7754(03)00095-2]

21 **Mayer RJ**, Garnick MB, Steele GD Jr, Zamcheck N. Carcinoembryonic antigen (CEA) as a monitor of chemotherapy in disseminated colorectal cancer. *Cancer*1978; **42**: 1428-1433 [PMID: 709511 DOI: 10.1002/1097-0142(197809)42:3+<1428::aid-cncr2820420808>3.0.co;2-h]

22 **Glover C**, Douse P, Kane P, Karani J, Meire H, Mohammadtaghi S, Allen-Mersh TG. Accuracy of investigations for asymptomatic colorectal liver metastases. *Dis Colon Rectum* 2002; **45**: 476-484 [PMID: 12006929 DOI: 10.1007/s10350-004-6224-y]

23 **Sugarbaker PH**, Gianola FJ, Dwyer A, Neuman NR. A simplified plan for follow-up of patients with colon and rectal cancer supported by prospective studies of laboratory and radiologic test results. *Surgery* 1987; **102**: 79-87 [PMID: 3589978]

24 **Wanebo HJ**, Llaneras M, Martin T, Kaiser D. Prospective monitoring trial for carcinoma of colon and rectum after surgical resection. *Surg Gynecol Obstet* 1989; **169**: 479-487 [PMID: 2683153]

25 **Minton JP**, Hoehn JL, Gerber DM, Horsley JS, Connolly DP, Salwan F, Fletcher WS, Cruz AB Jr, Gatchell FG, Oviedo M. Results of a 400-patient carcinoembryonic antigen second-look colorectal cancer study. *Cancer* 1985; **55**: 1284-1290 [PMID: 3971297 DOI: 10.1002/1097-0142(19850315)55:6<1284::aid-cncr2820550622>3.0.co;2-b]

26 **Tate H**. Plasma CEA in the post-surgical monitoring of colorectal carcinoma. *Br J Cancer* 1982; **46**: 323-330 [PMID: 7126423 DOI: 10.1038/bjc.1982.207]

27 **Boey J**, Cheung HC, Lai CK, Wong J. A prospective evaluation of serum carcinoembryonic antigen (CEA) levels in the management of colorectal carcinoma. *World J Surg* 1984; **8**: 279-286 [PMID: 6464483 DOI: 10.1007/BF01655052]

28 **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**: 943-947 [PMID: 8141873]

29 **McCall JL**, Black RB, Rich CA, Harvey JR, Baker RA, Watts JM, Toouli J. The value of serum carcinoembryonic antigen in predicting recurrent disease following curative resection of colorectal cancer. *Dis Colon Rectum* 1994; **37**: 875-881 [PMID: 8076486 DOI: 10.1007/BF02052591]

30 **Wang JY**, Tang R, Chiang JM. Value of carcinoembryonic antigen in the management of colorectal cancer. *Dis Colon Rectum* 1994; **37**: 272-277 [PMID: 8137675 DOI: 10.1007/BF02048166]

31 **Hine KR**, Dykes PW. Serum CEA testing in the post-operative surveillance of colorectal carcinoma. *Br J Cancer* 1984; **49**: 689-693 [PMID: 6733018 DOI: 10.1038/bjc.1984.109]

32 **Martin EW Jr**, Cooperman M, Carey LC, Minton JP. Sixty second-look procedures indicated primarily by rise in serial carcinoembryonic antigen. *J Surg Res* 1980; **28**: 389-394 [PMID: 7392594 DOI: 10.1016/0022-4804(80)90100-6]

33 **Nicholson BD**, Shinkins B, Mant D. Blood Measurement of Carcinoembryonic Antigen Level for Detecting Recurrence of Colorectal Cancer. *JAMA* 2016; **316**: 1310-1311 [PMID: 27673308 DOI: 10.1001/jama.2016.11212]

34 **Primrose JN**, Perera R, Gray A, Rose P, Fuller A, Corkhill A, George S, Mant D; FACS Trial Investigators. Effect of 3 to 5 years of scheduled CEA and CT follow-up to detect recurrence of colorectal cancer: the FACS randomized clinical trial. *JAMA* 2014; **311**: 263-270 [PMID: 24430319 DOI: 10.1001/jama.2013.285718]

35 **Verberne CJ**, Zhan Z, van den Heuvel E, Grossmann I, Doornbos PM, Havenga K, Manusama E, Klaase J, van der Mijle HC, Lamme B, Bosscha K, Baas P, van Ooijen B, Nieuwenhuijzen G, Marinelli A, van der Zaag E, Wasowicz D, de Bock GH, Wiggers T. Intensified follow-up in colorectal cancer patients using frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging: Results of the randomized "CEAwatch" trial. *Eur J Surg Oncol* 2015; **41**: 1188-1196 [PMID: 26184850 DOI: 10.1016/j.ejso.2015.06.008]

36 **Maas M**, Rutten IJ, Nelemans PJ, Lambregts DM, Cappendijk VC, Beets GL, Beets-Tan RG. What is the most accurate whole-body imaging modality for assessment of local and distant recurrent disease in colorectal cancer? A meta-analysis : imaging for recurrent colorectal cancer. *Eur J Nucl Med Mol Imaging* 2011; **38**: 1560-1571 [PMID: 21468765 DOI: 10.1007/s00259-011-1785-1]

37 **Mäkelä JT**, Laitinen SO, Kairaluoma MI. Five-year follow-up after radical surgery for colorectal cancer. Results of a prospective randomized trial. *Arch Surg*1995; **130**: 1062-1067 [PMID: 7575117 DOI: 10.1001/archsurg.1995.01430100040009]

38 **Schoemaker D**, Black R, Giles L, Toouli J. Yearly colonoscopy, liver CT, and chest radiography do not influence 5-year survival of colorectal cancer patients. *Gastroenterology* 1998; **114**: 7-14 [PMID: 9428212 DOI: 10.1016/s0016-5085(98)70626-2]

39 **Rodríguez-Moranta F**, Saló J, Arcusa A, Boadas J, Piñol V, Bessa X, Batiste-Alentorn E, Lacy AM, Delgado S, Maurel J, Piqué JM, Castells A. Postoperative surveillance in patients with colorectal cancer who have undergone curative resection: a prospective, multicenter, randomized, controlled trial. *J Clin Oncol* 2006; **24**: 386-393 [PMID: 16365182 DOI: 10.1200/JCO.2005.02.0826]

40 **McCormack PM**, Ginsberg RJ. Current management of colorectal metastases to lung. *Chest Surg Clin N Am* 1998; **8**: 119-126 [PMID: 9515176]

41 **Manfredi S**, Bouvier AM, Lepage C, Hatem C, Dancourt V, Faivre J. Incidence and patterns of recurrence after resection for cure of colonic cancer in a well defined population. *Br J Surg* 2006; **93**: 1115-1122 [PMID: 16804870 DOI: 10.1002/bjs.5349]

42 **Kobayashi H**, Mochizuki H, Sugihara K, Morita T, Kotake K, Teramoto T, Kameoka S, Saito Y, Takahashi K, Hase K, Oya M, Maeda K, Hirai T, Kameyama M, Shirouzu K, Muto T. Characteristics of recurrence and surveillance tools after curative resection for colorectal cancer: a multicenter study. *Surgery* 2007; **141**: 67-75 [PMID: 17188169 DOI: 10.1016/j.surg.2006.07.020]

43 **Mitry E**, Guiu B, Cosconea S, Jooste V, Faivre J, Bouvier AM. Epidemiology, management and prognosis of colorectal cancer with lung metastases: a 30-year population-based study. *Gut* 2010; **59**: 1383-1388 [PMID: 20732912 DOI: 10.1136/gut.2010.211557]

44 **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**: 619-626 [PMID: 7774474 DOI: 10.1007/BF02054122]

45 **McCall JL**, Cox MR, Wattchow DA. Analysis of local recurrence rates after surgery alone for rectal cancer. *Int J Colorectal Dis* 1995; **10**: 126-132 [PMID: 7561427 DOI: 10.1007/BF00298532]

46 **Chen F**, Stuart M. Colonoscopic follow-up of colorectal carcinoma. *Dis Colon Rectum* 1994; **37**: 568-572 [PMID: 8200236 DOI: 10.1007/BF02050992]

47 **Wang T**, Cui Y, Huang WS, Deng YH, Gong W, Li CJ, Wang JP. The role of postoperative colonoscopic surveillance after radical surgery for colorectal cancer: a prospective, randomized clinical study. *Gastrointest Endosc* 2009; **69**: 609-615 [PMID: 19136105 DOI: 10.1016/j.gie.2008.05.017]

48 **Secco GB**, Fardelli R, Gianquinto D, Bonfante P, Baldi E, Ravera G, Derchi L, Ferraris R. Efficacy and cost of risk-adapted follow-up in patients after colorectal cancer surgery: a prospective, randomized and controlled trial. *Eur J Surg Oncol* 2002; **28**: 418-423 [PMID: 12099653 DOI: 10.1053/ejso.2001.1250]

49 **Rosati G**, Ambrosini G, Barni S, Andreoni B, Corradini G, Luchena G, Daniele B, Gaion F, Oliverio G, Duro M, Martignoni G, Pinna N, Sozzi P, Pancera G, Solina G, Pavia G, Pignata S, Johnson F, Labianca R, Apolone G, Zaniboni A, Monteforte M, Negri E, Torri V, Mosconi P, Fossati R; GILDA working group. A randomized trial of intensive versus minimal surveillance of patients with resected Dukes B2-C colorectal carcinoma. *Ann Oncol* 2016; **27**: 274-280 [PMID: 26578734 DOI: 10.1093/annonc/mdv541]

50 **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**: 818-824 [PMID: 15085436 DOI: 10.1007/s10350-004-0514-2]

51 **Lu YY**, Chen JH, Chien CR, Chen WT, Tsai SC, Lin WY, Kao CH. 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**: 1039-1047 [PMID: 23407908 DOI: 10.1007/s00384-013-1659-z]

52 **Sanli Y**, Kuyumcu S, Ozkan ZG, Kilic L, Balik E, Turkmen C, Has D, Isik G, Asoglu O, Kapran Y, Adalet I. The utility of FDG-PET/CT as an effective tool for detecting recurrent colorectal cancer regardless of serum CEA levels. *Ann Nucl Med* 2012; **26**: 551-558 [PMID: 22644560 DOI: 10.1007/s12149-012-0609-0]

53 **Lee DH**, Lee JM. Whole-body PET/MRI for colorectal cancer staging: Is it the way forward? *J Magn Reson Imaging* 2017; **45**: 21-35 [PMID: 27346172 DOI: 10.1002/jmri.25337]

54 **Crimì F**, Spolverato G, Lacognata C, Garieri M, Cecchin D, Urso ED, Zucchetta P, Pucciarelli S, Pomerri F. 18F-FDG PET/MRI for Rectal Cancer TNM Restaging After Preoperative Chemoradiotherapy: Initial Experience. *Dis Colon Rectum* 2020; **63**: 310-318 [PMID: 31842163 DOI: 10.1097/DCR.0000000000001568]

55 **Plodeck V**, Rahbari NN, Weitz J, Radosa CG, Laniado M, Hoffmann RT, Zöphel K, Beuthien-Baumann B, Kotzerke J, van den Hoff J, Platzek I. FDG-PET/MRI in patients with pelvic recurrence of rectal cancer: first clinical experiences. *Eur Radiol* 2019; **29**: 422-428 [PMID: 29980927 DOI: 10.1007/s00330-018-5589-6]

56 **Plodeck V**, Platzek I, Streitzig J, Nebelung H, Blum S, Kühn JP, Hoffmann RT, Laniado M, Michler E, Hoberück S, Zöphel K, Kotzerke J, Fritzmann J, Weitz J, Radosa CG. Diagnostic performance of (18)F-fluorodeoxyglucose-PET/MRI versus MRI alone in the diagnosis of pelvic recurrence of rectal cancer. *Abdom Radiol (NY)* 2021; **46**: 5086-5094 [PMID: 34402948 DOI: 10.1007/s00261-021-03224-3]

57 **Pietra N**, Sarli L, Costi R, Ouchemi C, Grattarola M, Peracchia A. Role of follow-up in management of local recurrences of colorectal cancer: a prospective, randomized study. *Dis Colon Rectum* 1998; **41**: 1127-1133 [PMID: 9749496 DOI: 10.1007/BF02239434]

58 **Wattchow DA**, Weller DP, Esterman A, Pilotto LS, McGorm K, Hammett Z, Platell C, Silagy C. General practice vs surgical-based follow-up for patients with colon cancer: randomised controlled trial. *Br J Cancer* 2006; **94**: 1116-1121 [PMID: 16622437 DOI: 10.1038/sj.bjc.6603052]

59 **Sobhani I**, Tiret E, Lebtahi R, Aparicio T, Itti E, Montravers F, Vaylet C, Rougier P, André T, Gornet JM, Cherqui D, Delbaldo C, Panis Y, Talbot JN, Meignan M, Le Guludec D. Early detection of recurrence by 18FDG-PET in the follow-up of patients with colorectal cancer. *Br J Cancer* 2008; **98**: 875-880 [PMID: 18301402 DOI: 10.1038/sj.bjc.6604263]

60 **Strand E**, Nygren I, Bergkvist L, Smedh K. Nurse or surgeon follow-up after rectal cancer: a randomized trial. *Colorectal Dis* 2011; **13**: 999-1003 [PMID: 20478003 DOI: 10.1111/j.1463-1318.2010.02317.x]

61 **Augestad KM**, Norum J, Dehof S, Aspevik R, Ringberg U, Nestvold T, Vonen B, Skrøvseth SO, Lindsetmo RO. Cost-effectiveness and quality of life in surgeon versus general practitioner-organised colon cancer surveillance: a randomised controlled trial. *BMJ Open* 2013; **3** [PMID: 23564936 DOI: 10.1136/bmjopen-2012-002391]

62 **Treasure T**, Monson K, Fiorentino F, Russell C. The CEA Second-Look Trial: a randomised controlled trial of carcinoembryonic antigen prompted reoperation for recurrent colorectal cancer. *BMJ Open* 2014; **4**: e004385 [PMID: 24823671 DOI: 10.1136/bmjopen-2013-004385]

63 **Wille-Jørgensen P**, Syk I, Smedh K, Laurberg S, Nielsen DT, Petersen SH, Renehan AG, Horváth-Puhó E, Påhlman L, Sørensen HT; COLOFOL Study Group. Effect of More vs Less Frequent Follow-up Testing on Overall and Colorectal Cancer-Specific Mortality in Patients With Stage II or III Colorectal Cancer: The COLOFOL Randomized Clinical Trial. *JAMA* 2018; **319**: 2095-2103 [PMID: 29800179 DOI: 10.1001/jama.2018.5623]

64 **Renehan AG**, Egger M, Saunders MP, O'Dwyer ST. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. *BMJ* 2002; **324**: 813 [PMID: 11934773 DOI: 10.1136/bmj.324.7341.813]

65 **Tjandra JJ**, Chan MK. Follow-up after curative resection of colorectal cancer: a meta-analysis. *Dis Colon Rectum* 2007; **50**: 1783-1799 [PMID: 17874269 DOI: 10.1007/s10350-007-9030-5]

66 **Pita-Fernández S**, Alhayek-Aí M, González-Martín C, López-Calviño B, Seoane-Pillado T, Pértega-Díaz 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**: 644-656 [PMID: 25411419 DOI: 10.1093/annonc/mdu543]

67 **Rosen M**, Chan L, Beart RW Jr, Vukasin P, Anthone G. Follow-up of colorectal cancer: a meta-analysis. *Dis Colon Rectum* 1998; **41**: 1116-1126 [PMID: 9749495 DOI: 10.1007/BF02239433]

68 **Figueredo A**, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, Zuraw L, Zwaal C; Gastrointestinal Cancer Disease Site Group of Cancer Care Ontario's Program in Evidence-based Care. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. *BMC Cancer* 2003; **3**: 26 [PMID: 14529575 DOI: 10.1186/1471-2407-3-26]

69 **Mokhles S**, Macbeth F, Farewell V, Fiorentino F, Williams NR, Younes RN, Takkenberg JJ, Treasure T. Meta-analysis of colorectal cancer follow-up after potentially curative resection. *Br J Surg* 2016; **103**: 1259-1268 [PMID: 27488593 DOI: 10.1002/bjs.10233]

70 **Jeffery M**, Hickey BE, Hider PN, See AM. Follow-up strategies for patients treated for non-metastatic colorectal cancer. *Cochrane Database Syst Rev* 2016; **11**: CD002200 [PMID: 27884041 DOI: 10.1002/14651858.CD002200.pub3]

71 **Virgo KS**, Vernava AM, Longo WE, McKirgan LW, Johnson FE. Cost of patient follow-up after potentially curative colorectal cancer treatment. *JAMA* 1995; **273**: 1837-1841 [PMID: 7776499]

72 **Kievit J**, Bruinvels DJ. Detection of recurrence after surgery for colorectal cancer. *Eur J Cancer* 1995; **31A**: 1222-1225 [PMID: 7577026 DOI: 10.1016/0959-8049(95)00155-c]

73 **Borie F**, Combescure C, Daurès JP, 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**: 563-569 [PMID: 15366746 DOI: 10.1007/s00268-004-7256-0]

74 **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): Cancer Care Ontario; 2012 Feb 3 [cited 31 October 2022]. In: Program in Evidence-based Care Evidence-Based Series No.: 26-2. Available at: https://old-prod.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/2012-cancer-care-ontario-survivors-colorectal-cancer.pdf

75 **Seo SI**, Lim SB, Yoon YS, Kim CW, Yu CS, Kim TW, Kim JH, Kim JC. Comparison of recurrence patterns between ≤5 years and >5 years after curative operations in colorectal cancer patients. *J Surg Oncol* 2013; **108**: 9-13 [PMID: 23754582 DOI: 10.1002/jso.23349]

76 **Giordano P**, Efron J, Vernava AM 3rd, 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**: 199-207 [PMID: 16969616 DOI: 10.1007/s10151-006-0280-3]

77 **Onaitis MW**, Noone RB, Fields R, Hurwitz H, Morse M, Jowell P, McGrath K, Lee C, Anscher MS, Clary B, Mantyh C, Pappas TN, Ludwig K, Seigler HF, Tyler DS. Complete response to neoadjuvant chemoradiation for rectal cancer does not influence survival. *Ann Surg Oncol* 2001; **8**: 801-806 [PMID: 11776494 DOI: 10.1007/s10434-001-0801-2]

78 **García-Aguilar J**, Hernandez de Anda E, Sirivongs P, Lee SH, Madoff RD, Rothenberger DA. A pathologic complete response to preoperative chemoradiation is associated with lower local recurrence and improved survival in rectal cancer patients treated by mesorectal excision. *Dis Colon Rectum* 2003; **46**: 298-304 [PMID: 12626903 DOI: 10.1007/s10350-004-6545-x]

79 **Stipa F**, Chessin DB, Shia J, Paty PB, Weiser M, Temple LK, Minsky BD, Wong WD, Guillem JG. A pathologic complete response of rectal cancer to preoperative combined-modality therapy results in improved oncological outcome compared with those who achieve no downstaging on the basis of preoperative endorectal ultrasonography. *Ann Surg Oncol* 2006; **13**: 1047-1053 [PMID: 16865595 DOI: 10.1245/ASO.2006.03.053]

80 **Kuo LJ**, Liu MC, Jian JJ, Horng CF, Cheng TI, Chen CM, Fang WT, Chung YL. Is final TNM staging a predictor for survival in locally advanced rectal cancer after preoperative chemoradiation therapy? *Ann Surg Oncol* 2007; **14**: 2766-2772 [PMID: 17551794 DOI: 10.1245/s10434-007-9471-z]

81 **Weiser MR**, Beets-Tan R, Beets G. Management of complete response after chemoradiation in rectal cancer. *Surg Oncol Clin N Am* 2014; **23**: 113-125 [PMID: 24267169 DOI: 10.1016/j.soc.2013.09.012]

82 **Martin ST**, Heneghan HM, Winter DC. Systematic review and meta-analysis of outcomes following pathological complete response to neoadjuvant chemoradiotherapy for rectal cancer. *Br J Surg* 2012; **99**: 918-928 [PMID: 22362002 DOI: 10.1002/bjs.8702]

83 **Habr-Gama A**, Perez RO, Nadalin W, Sabbaga J, Ribeiro U Jr, Silva e Sousa AH Jr, Campos FG, Kiss DR, Gama-Rodrigues J. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. *Ann Surg* 2004; **240**: 711-7; discussion 717-8 [PMID: 15383798 DOI: 10.1097/01.sla.0000141194.27992.32]

84 **Barina A**, De Paoli A, Delrio P, Guerrieri M, Muratore A, Bianco F, Vespa D, Asteria C, Morpurgo E, Restivo A, Coco C, Pace U, Belluco C, Aschele C, Lonardi S, Valentini V, Mantello G, Maretto I, Del Bianco P, Perin A, Pucciarelli S. Rectal sparing approach after preoperative radio- and/or chemotherapy (RESARCH) in patients with rectal cancer: a multicentre observational study. *Tech Coloproctol* 2017; **21**: 633-640 [PMID: 28755256 DOI: 10.1007/s10151-017-1665-1]

85 **Habr-Gama A**, Perez RO, São Julião GP, Proscurshim I, Gama-Rodrigues J. Nonoperative approaches to rectal cancer: a critical evaluation. *Semin Radiat Oncol*2011; **21**: 234-239 [PMID: 21645869 DOI: 10.1016/j.semradonc.2011.02.010]

86 **Smith JD**, Ruby JA, Goodman KA, Saltz LB, Guillem JG, Weiser MR, Temple LK, Nash GM, Paty PB. Nonoperative management of rectal cancer with complete clinical response after neoadjuvant therapy. *Ann Surg* 2012; **256**: 965-972 [PMID: 23154394 DOI: 10.1097/SLA.0b013e3182759f1c]

87 **Maas M**, Beets-Tan RG, Lambregts DM, Lammering G, Nelemans PJ, Engelen SM, van Dam RM, Jansen RL, Sosef M, Leijtens JW, Hulsewé KW, Buijsen J, Beets GL. Wait-and-see policy for clinical complete responders after chemoradiation for rectal cancer. *J Clin Oncol* 2011; **29**: 4633-4640 [PMID: 22067400 DOI: 10.1200/JCO.2011.37.7176]

88 **Rossi BM**, Nakagawa WT, Novaes PE, Filho WD, Lopes A. Radiation and chemotherapy instead of surgery for low infiltrative rectal adenocarcinoma: a prospective trial. *Ann Surg Oncol* 1998; **5**: 113-118 [PMID: 9527263 DOI: 10.1007/BF02303843]

89 **Nakagawa WT**, Rossi BM, de O Ferreira F, Ferrigno R, David Filho WJ, Nishimoto IN, Vieira RA, Lopes A. Chemoradiation instead of surgery to treat mid and low rectal tumors: is it safe? *Ann Surg Oncol* 2002; **9**: 568-573 [PMID: 12095973 DOI: 10.1007/BF02573893]

90 **van der Valk MJM**, Hilling DE, Bastiaannet E, Meershoek-Klein Kranenbarg E, Beets GL, Figueiredo NL, Habr-Gama A, Perez RO, Renehan AG, van de Velde CJH; IWWD Consortium. Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study. *Lancet* 2018; **391**: 2537-2545 [PMID: 29976470 DOI: 10.1016/S0140-6736(18)31078-X]

91 **Garcia-Aguilar J**, Patil S, Gollub MJ, Kim JK, Yuval JB, Thompson HM, Verheij FS, Omer DM, Lee M, Dunne RF, Marcet J, Cataldo P, Polite B, Herzig DO, Liska D, Oommen S, Friel CM, Ternent C, Coveler AL, Hunt S, Gregory A, Varma MG, Bello BL, Carmichael JC, Krauss J, Gleisner A, Paty PB, Weiser MR, Nash GM, Pappou E, Guillem JG, Temple L, Wei IH, Widmar M, Lin S, Segal NH, Cercek A, Yaeger R, Smith JJ, Goodman KA, Wu AJ, Saltz LB. Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy. *J Clin Oncol* 2022; **40**: 2546-2556 [PMID: 35483010 DOI: 10.1200/JCO.22.00032]

92 **Habr-Gama A**, Perez RO. Immediate surgery or clinical follow-up after a complete clinical response? *Recent Results Cancer Res* 2014; **203**: 203-210 [PMID: 25103007 DOI: 10.1007/978-3-319-08060-4\_14]

93 **Ince S**, Itani M, Henke LE, Smith RK, Wise PE, Mutch MG, Glasgow SC, Silviera ML, Pedersen KS, Hunt SR, Kim H, Fraum TJ. FDG-PET/MRI for Nonoperative Management of Rectal Cancer: A Prospective Pilot Study. *Tomography* 2022; **8**: 2723-2734 [PMID: 36412686 DOI: 10.3390/tomography8060227]

**Footnotes**

**Conflict-of-interest statement:** The authors have no conflicts of interest to declare.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** November 23, 2022

**First decision:** December 10, 2022

**Article in press:** January 17, 2023

**Specialty type:** Oncology

**Country/Territory of origin:** Italy

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): D

Grade E (Poor): 0

**P-Reviewer:** Chen N, China; Sun J, China; Tong WD, China **S-Editor:** Zhang H **L-Editor:** Filipodia **P-Editor:** Zhang H

**Figure Legends**

**Table 1 Randomized controlled trials: Different surveillance strategies following curative colorectal cancer resection**

|  |  |  |  |
| --- | --- | --- | --- |
| **Ref.** | **Surveillance strategy** | **No. of patients randomized** | **Significant benefit** |
| Ohlsson *et al*[44], 1995 | Total | 107 | No |
| None (FOBT) | 54 |
| Intensive follow-up: examinations, FOBT, CEA, endoscopy, CXR, CT | 53 |
| Mäkelä *et al*[37], 1995 | Total | 106 | No |
| Standard | 54 |
| More intensive examinations, FOBT, CEA, colonoscopy, CXR, liver US, CT | 52 |
| Kjeldsen *et al*[16], 1997 | Total | 597 | No |
| Standard | 307 |
| More intensive examinations, blood tests, FOBT, CXR, colonoscopy | 290 |
| Schoemaker *et al*[38], 1998 | Total | 325 | No |
| Standard: examinations, blood test, CEA, FOBT | 158 |
| Intensive: standard plus CXR, CT, colonoscopy | 167 |
| Pietra *et al*[57], 1998 | Total | 207 | Yes (increased curative reoperation; increased survival) |
| Standard | 103 |
| More intensive examinations, CEA, colonoscopy, CXR, liver US, CT | 104 |
| Secco *et al*[48], 2002 | Total | 358 (21 drop out) | Yes (increased curative reoperation; increased survival) |
| Minimal: examinations yearly and on demand | 145 |
| Risk-adapted | 192 |
| -Low risk: less frequent examinations, CEA, rectosigmoidoscopy, CXR, US | 84 |
| -High risk: more frequent examinations, CEA, rectosigmoidoscopy, CXR, US | 108 |
| Wattchow *et al*[58], 2006 | Different settings no different tests | 203 (46 lost fu) | No |
| General Practitioner | 81 |
| Surgeon visit | 76 |
| Rodríguez-Moranta *et al*[39], 2006 | Total | 259 | Yes (increased curative reoperation; increased survival only for stage II colon tumor and rectal tumor) |
| Standard: examinations, blood tests and CEA. Colonoscopy only if history of HNPCC and synchronous neoplasm | 127 |
| Intensive: standard plus annual colonoscopy, CXR, US and CT | 132 |
| Sobhani *et al*[59], 2008 | Total | 130 | Yes (increased curative reoperation; number of patients too small to evaluate survival) |
| Standard: examinations, CEA, CXR, US and CT | 65 |
| Intensive: standard plus 18FDG-PET | 65 |
| Wang *et al*[47], 2009 | Total | 326 | Yes (increased curative reoperation; no increased survival) |
| Standard: examinations, CEA, colonoscopy, CXR, liver US and CT | 161 |
| Intensive: standard plus more frequent colonoscopy | 165 |
| Strand *et al*[60], 2011 | Different settings no different tests | 110 | No |
| Nurse | 54 |
| Surgeon visit | 56 |
| Augestad *et al*[61], 2013 | Different settings no different tests | 110 | No |
| General Practitioner | 55 |
| Surgeon visit | 55 |
| Primrose *et al*[34] (FACS), 2014 | Total | 1202 | No |
| Minimal follow-up: no scheduled follow-up except a single CT scan at 12-18 mo | 301 |
| CEA follow-up: CEA every 3 mo for 2 yr, then every 6 mo for 3 yr, with a single CT scan at 12-18 mo | 300 |
| CT follow-up: CT scan every 6 mo for 2 yr, then annually for 3 yr | 299 |
| CEA and CT follow-up: combined CEA and CT imaging as above | 302 |
| Treasure *et al*[62] (the CEA Second-Look trial), 2014 | Total | Tot 216 | No |
| Standard: CEA monitoring with no further action even in case of CEA rising | 108 |
| Aggressive: CEA monitoring followed by second-look operation and possible resection in case of CEA rising | 108 |
| Verberne *et al*[35] (CEAwatch)1, 2015 | Total | 3223 | Yes (increased curative reoperation; no increased survival) |
| Standard: CEA every 3 mo, examinations, liver US and CXR every 6 mo | 1182 |
| Intensive: CEA every 2 mo, examinations and CT annually. If CEA rise, repeat CEA after 1 mo. If two consecutive CEA rise, CT scan | 316 |
| Standard and Intensive: patients participated both in the standard protocol and in the intensive protocol | 1725 |
| Rosati *et al*[49] (GILDA), 2016 | Total | 1228 | No |
| Standard: examinations, CEA, colonoscopy, CXR, liver imaging (US or CT scan) | 613 |
| Intensive: standard plus CA19-9, blood test, more frequent colonoscopy, CXR and liver imaging (US or CT), CT abdomen-pelvis | 615 |
| Wille-Jørgensen *et al*[63] (COLOFOL), 2018 | Total | 2509 | No |
| Standard: CEA, CT chest, abdomen and pelvis at 12 and 36 mo | 1256 |
| Intensive: CEA, CT chest, abdomen and pelvis every 6 mo for 2 yr, then at 36 mo | 1253 |

1During the study period, hospitals changed from a standard follow-up schedule to the intensive follow-up schedule every 3 months. CEA: Carcinoembryonic antigen; CT: Computed tomography; CXR: Conventional chest radiography; FOBT: Fecal occult blood test; HNPCC: Hereditary non-polyposis colorectal cancer; mo: months; US: Ultrasonography; yr: years.

**Table 2 Meta-analyses of follow-up studies with different surveillance strategies**

|  |  |  |
| --- | --- | --- |
| **Ref.** | **Studies included and number of patients** | **Benefit on survival** |
| Bruinvels *et al*[19], 1993 | 7 nonrandomized | Yes |
| 3283 patients |
| Rosen *et al*[67], 1998 | 2 RCTs, 3 nonrandomized | Yes |
| 2005 patients |
| Renehan *et al*[64], 2002 | 5 RCTs | Yes |
| 1342 patients |
| Figueredo *et al*[68], 2003 | 6 RCTs | Yes |
| 1679 patients |
| Tjandra *et al*[65], 2007 | 8 RCTs | Yes |
| 2923 patients |
| Pita-Fernández *et al*[66], 2015 | 11 RCTs | Yes |
| 4055 patients |
| Mokhles *et al*[69], 2016 | 11 RCTs | No |
| 4515 patients |
| Jeffery *et al*[70], 2016 | 15 RCTs | No |
| 5403 patients |

RCT: Randomized controlled trial.

**Table 3 Summary of current surveillance guidelines from specialty societies**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Guideline** | **MH & PE** | **CEA** | **Abdomen imaging** | **Chest imaging** | **Colonoscopy** |
| ASCO[13] | Every 3-6 mo for 5 yr | Every 3-6 mo for 5 yr | CT of abdomen and pelvis annually for 3 yr, for high-risk patients every 6-12 mo for 3 years and then annually for 2 yr | CT of chest annually for 3 yr, for high-risk patients every 6-12 mo for 3 yr | Colonoscopy at 1 yr, subsequently according findings and every 5 yr if normal. Rectosigmoidoscopy every 6 mo for 5 yr in rectal cancer not irradiated |
| ASCR[4] | Every 3-6 mo for 2 yr, then every 6 mo for 3 yr | Every 3-6 mo for 2 yr, then every 6 mo for 3 yr | CT of abdomen and pelvis 2 times in 5 yr, for high-risk patients annually for 5 yr | CT of chest 2 times in 5 yr, for high-risk patients annually for 5 yr | Colonoscopy at 1 yr, subsequently according findings and every 5 yr if normal. Rectosigmoidoscopy (+/- ERUS) every 6-12 mo for 3 to 5 yr for patients treated with TME; every 6 mo in patients treated with local excision |
| ESMO[12] | Every 6 mo for 2 yr | Every 6 mo for 3 yr | CT of abdomen and pelvis 2 times within 3 yr | CT of chest 2 times within 3 yr | Colonoscopy every 5 yr up to age 75 |
| ACPGI[11] | No recommendation for frequency | Every 6 mo for 3 yr | CT of abdomen and pelvis 2 times within 3 yr | CT of chest 2 times within 3 yr | Colonoscopy at 1 yr subsequently according findings and every 5 yr if normal |
| NCCN[14] | Every 3-6 mo for 2 yr, then every 6 mo for 3 yr for stage II or greater | Every 3-6 mo for 2 yr, then every 6 mo for 3 yr for stage II or greater | CT of abdomen and pelvis every 3-6 mo for 2 yr, then every 6-12 mo for 3 yr | CT of chest every 3-6 mo for 2 yr, then every 6-12 mo for 3 yr | Colonoscopy at 1 yr, repeat in 3 yr then every 5 yr, Proctoscopy (with ERUS or MRI) every 3-6 mo for 2 yr, then every 6 mo for 3 yr for patients treated with transanal excision |
| ESCP[15] | No recommendation for frequency. Until 5 yr after surgery with a more frequent regimen in the first 2 yr to 3 yr | Every 3–6 mo for 2–3 yr, then every 6-12 mo until 5 yr after surgery | CT abdomen alternating with US for at least 5 yr with a more frequent regimen in the first 2-3 yr | CT of chest alternating with CXR every 3-12 mo for at least 5 yr after surgery | No recommendation for colonoscopy and proctoscopy |

ACPGI: The association of Coloproctology of Great Britain and Ireland; ASCO: American Society of Oncology; ASCRS: American Society of Colon Rectal Surgeon; CEA: Carcinoembryonic antigen; CT: Computed tomography; CXR: Conventional chest radiography; ERUS: Endorectal ultrasound; ESMO: European Society for Medical Oncology; ESCP: European Society of Coloproctology; mo: months; MH & PE: Medical history and physical examination; MRI: Magnetic resonance imaging; NCCN: National Comprehensive Cancer Network; TME: Total mesorectal excision; US: Ultrasonography; yr: years.



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2023 Baishideng Publishing Group Inc. All rights reserved.**