

Chapter 12

Follow-Up in Patient's After Curative Resection for Colon Cancer Surveillance for Colon Cancer

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PICO table

Pt Population	Intervention	Comparators	Outcomes studied
Pts after curative resection of colorectal cancer	Intensive follow up	Clinical followup	Early detection of recurrence, salvage rates, cost

Introduction

According to the American Cancer Society, 134,490 new cases of colon and rectal cancer will be diagnosed in 2016. The effect is nearly equal between men and women, with 70,820 diagnosed in men, and 63,670 diagnosed in women [1]. Colon and rectal cancer is the fourth most common cancer, however it is the second most common cause of cancer deaths [1]. At least, one third (25–49% reported) of patients treated with stage II or stage III colon cancer will experience a recurrence, and this has remained fairly steady over the past 20 years [1–3].

The purpose of surveillance following potentially curative surgery for colorectal cancer, is the early identification of recurrent cancer in those patients who might potentially be cured by secondary surgical intervention. Secondly, surveillance also enables screening for metachronous primary cancers and polyps. The diagnosis of an asymptomatic recurrence is more likely to result in attempts at curative reoperation [4]. Even with an intensive investigative program, up to 50% of asymptomatic recurrences may not be detected [4]. Several studies have also demonstrated that asymptomatic recurrences of colorectal cancer are more amenable to a surgical resection with negative margins (R0) [5].

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Table 12.1 Surveillance recommendations-curative colon and rectal cancer

Intervention	Frequency		
	1–2 years	3–5 years	>5 years
H & P	3–6 months	6 months	Annual
CEA	3–6 months	6 months	None
Colonoscopy	1 year ^a	3 years ^b	5 years ^c
Flexible Sigmoidoscopy rectal cancer	6–12 months	Annual	None ^d
CT scan	Annual	Annual	Annual

^a3–6 months if not cleared at surgery

^bContinue at 3 years if adenoma is identified

^cIf cleared at 3 years

^dFollow colonoscopy

Although there is extensive literature of evaluating the benefit of surveillance strategies for colorectal cancer, there remains ongoing debate. The cost of intensive follow-up is unclear but remains central to the discussion [5].

Search Strategy

An electronic search of the PubMed database was performed from 1996 to 2016. This search terms included “cancer follow-up”, “colon surgery” and “postoperative surveillance for colon cancer” with 444 matches. The National Comprehensive Cancer Network (NCCN) [6], along with society guidelines from the American Society of Colorectal Surgeons (ASCRS), American Cancer Society of Clinical Oncology (ASCO) were reviewed. In addition the search included the Cochrane database, Google search and the Ontario evidence based series 26–2 on follow-up care surveillance protocol and secondary measures for survivors of colorectal cancer.

Results

Guidelines

The vast majority of studies exploring the benefits of surveillance have been conducted on patients with resected stage II or stage III disease. Intensive postoperative surveillance programs have been justified in the hope that early detection of asymptomatic recurrences will increase the proportion of patients potentially eligible for curative therapy [7]. Although individual randomized trials have not demonstrate a survival benefit, meta-analyses suggest a modest but significant survival benefit from intensive surveillance after resection of colorectal cancer [8–13]. It does seem clear patients with a recurrence detected by more intense surveillance are more

likely to undergo curative resection, whereas the actual reported survival advantage is more variable.

For a starting template, we began with the National Comprehensive Cancer Network guidelines version 2.2015(6) which recommend;

1. History and physical every 3–6 months for 2 years and then every 6 months for a total of 5 years
2. CEA every 3–6 months for 2 years, then every 6 months for a total of 5 years
3. CT scan of the chest, abdominal and pelvis annually up to 5 years, especially for patient's at high risk for recurrence. High risk patients would include those with lymphatic, venous or perineural invasion, with poorly differentiated tumors, or patients presenting with obstruction or perforation.
4. Colonoscopy at 1 year when the colon was cleared prior to or at the time of surgery – repeat in 3 years and then every 5 years.
5. If colonoscopy not performed at the time of surgery, then colonoscopy in 3–6 months.
6. PET CT scan is not routinely recommended

Most guidelines are based on the above recommendations. We will now review each of the recommendations.

History and physical examination – low quality evidence – strong recommendation

Recommendation – Office visit with history and physical every 3–6 months for 2 years and every 6 months for a total of 5 years

While the benefit of office visits has not been well established, up to one-half of symptomatic patients may not report their symptom(s) until it is time for the visit with her physician [14, 15]. In addition, this provides an opportunity to discuss the results of surveillance testing. The evidence is limited to suggest that the physician visits provide psychological support and reassurance for patients three, but is a good time to reinforce healthy behaviors such as physical activity.

CEA testing –moderate quality evidence – strong recommendation

Recommendation – CEA every 3–6 months for 2 years and then every 6 months for a total of 5 years- should correlate with the office visit

The use of CEA has been extensively studied. The rationale for postoperative CEA monitoring is to detect an asymptomatic recurrence. Its greatest use has been in patients that have an elevated CEA before surgery which returns to normal after surgery. The strongest argument in favor of CEA testing is that resection of limited metastases, particularly involving the liver, leads to long-term relapse free survival in as many as 40% of patients that undergo an attempted resection [7].

An asymptomatic elevation of the CEA increases the likelihood of a complete resection and will be associated with better long-term outcomes. Of note, approximately 30% of all colorectal cancer recurrences are not associated with a CEA elevation. A false-negative CEA result is more commonly observed in poorly

differentiated tumors. Even in patients with a normal preoperative CEA, there may be an elevated CEA in over 40% of recurrences.

When an elevated CEA is detected, it should be confirmed by retesting. False positive elevations are seen in up to 50% of patients at some time during their surveillance and follow-up. Also the CEA level is elevated in cigarette smokers. However a progressively rising CEA confirmed on retesting is indicative of metastatic or recurrent disease. These patients need to undergo further evaluation and testing.

Colonoscopy – High quality evidence – strong recommendation Recommendation –

Colonoscopy at 1 year when the colon was cleared prior to or at the time of surgery – repeat in 3 years and then every 5 years thereafter.

If colonoscopy not performed prior to or at the time of surgery, for instance due to an obstructing lesion, perform a clearing colonoscopy at 3–6 months after surgery.

Flexible sigmoidoscopy or proctoscopy may be performed every 6 months for the first 2 years and annually for up to 5 years, following resection for rectal cancer. When poor prognostic factors are present suggesting a higher risk of local recurrence, proctosigmoidoscopy may be considered every 6 months for 3–5 years.

Synchronous colon cancers occur in 2–5% of patients with colorectal cancer [16]. Further, all patients with a history of colorectal cancer are at increased risk for developing adenomatous polyps. The National Polyp Study demonstrated a 76–90% reduction incidence of colorectal cancer when surveillance colonoscopy was used in the setting of adenomatous polyps.

Periodic colonoscopy then enables detection of metachronous cancers at a more favorable stage and even better, the prevention of metachronous cancers by identifying and removing adenomatous polyps. In an analysis of 9029 patients performed by the American Cancer Society-Multi Society Taskforce for Colorectal Cancer, 137 (1.5%) developed metachronous cancers detected by colonoscopy. This incidence compares favorably with screening colonoscopy.

The guidelines on the frequency for endoscopic surveillance following rectal cancer was traditionally based on a high pelvic recurrence rate. The use of more uniform surgical techniques including total mesorectal excision and the use of neoadjuvant therapy have resulted in local recurrence rates of less than 10%. The American Society of Clinical Oncology, the American Cancer Society and the US Multisociety Taskforce all have issued different recommendations. The American Society for Clinical Oncology, for example, no longer recommends proctosigmoidoscopy every 6 months in patients treated with adjuvant radiation for rectal cancer, but does recommend proctosigmoidoscopy every 6 months for 2–5 years for patients with rectal cancer not treated with radiation.

CT scan – medium quality evidence – strong recommendation**Recommendation – CT scan of the chest, abdomen and pelvis yearly for 5 years**

The current recommendation for CT scan of the chest, abdomen and pelvis has evolved over the past several years. Much of the data has come from surveillance studies where patients underwent more intense versus less intensive follow-up. In one meta-analysis [9], the survival benefit was most significant in patients that had had undergone both CT imaging and CEA measurement.

The most common sites for systemic recurrence for colorectal cancer are the liver and the lungs. 80% of recurrences will develop in the first 2–3 years. No study has directly compared the evidence regarding the benefit of CT scans every 6 months versus annually. Very high risk patients, such as those with prior liver metastases, N2 disease, or an indeterminate lesion on prior imaging may be imaged every 6 months [3].

There is less evidence for chest surveillance than for abdominal (liver) imaging. However in one European trial, there were seven asymptomatic patients with normal CEA levels [17] who had their pulmonary recurrences diagnosed only by CT scan, and therefore would have gone undetected without surveillance chest CT. The CT detected group had a significantly longer median survival from time of recurrence compared with their symptomatic counterparts (26.4 versus 12.6 months), but not significantly longer than the CEA detected group (19.2 months). The largest proportion of resectable recurrences were found using chest CT, even though a larger proportion of recurrences was found with abdominal imaging.

MRI and PET Scans

These imaging modalities are not routinely recommended. MRI may be considered in a patient that has a contraindication to intravenous contrast. Both MRI and PET scanning may be indicated for an equivocal abnormality found on a CT scan (Table 12.1).

Overall Utility

Many have questioned the cost-effectiveness of surveillance programs. A Cochrane systematic review revealed no effect on overall survival, no difference in disease specific survival as well and no difference in detection of recurrence [18]. The cost has been reported anywhere from \$1–\$4 million for life saved. On the other hand, the data described above clearly suggests that those patients who have a recurrence detected prior to symptoms have a higher resectability rate for cure with an associated higher 5 year survival rate

Personal Review of the Data

We believe that surveillance gives patients the best opportunity to detect a recurrence while it is still curable. In our practice, we generally follow the guidelines as outlined above. A careful, individualized evaluation of the patient's risks for recurrence as well as their comorbidities/ability to tolerate additional treatment will impact the recommendation for surveillance.

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