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Colorectal Cancer Surveillance

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The majority of colorectal cancers are resected for cure, leaving many patients eligible for ongoing surveillance. The best schema for clinically useful and cost-effective follow-up is still controversial, but the goals are clear. Rational follow-up should detect treatable recurrent cancers, identify and remove metachronous polyps, and identify possible hereditary influences in development of a colorectal cancer. In theory, such follow-up will increase the survival of patients with cancer and improve their quality of life by successfully treating recurrences, preventing metachronous cancers of the colon or rectum, as well as preventing subsequent hereditary cancers from developing in the patient and/or their family members. How to accomplish this is still controversial, but it is clear that accurate risk stratification and patient selection are central to any program of surveillance. The intensity of surveillance should be proportional to the patient's risk of recurrence, and those patients unfit for further surgery because of age or comorbidity may be best served by colonoscopic follow-up only.

Types of Surveillance

Metachronous Colorectal Neoplasms

Those patients who have undergone successful treatment of a colorectal malignancy have an increased risk of developing subsequent polyps or cancers compared with the rate at which an age-matched control population would develop their first colorectal neoplasm. The period of risk for the development of metachronous disease seems to be lifelong and cumulative. The risk of developing metachronous polyps ranges between 30% and 56%, and the risk of a second cancer is 2%–8%.[1–3] Because these cancers arise from adenomatous polyps, periodic colonoscopy with polypectomy should prevent the development of subsequent cancers. The starting point and appropriate interval for surveillance colonoscopy in the population of patients undergoing follow-up for colorectal cancer are controversial and poorly studied. In the past, most clinicians advocated colonoscopic follow-up 1 year after surgery to visualize the anastomosis and look for missed synchronous lesions. Recently, the utility of early follow-up colonoscopy 1 year after surgery compared with delaying colonoscopy until 3 years after surgery has been questioned. The Standards Task Force of the American Society of Colon and Rectal Surgeons (ASCRS) has recommended colonoscopy surveillance to begin 3 years after surgery assuming preoperative or intraoperative clearance was done and was negative.[4] If preoperative or intraoperative clearance examination could not be done, postoperative colonoscopy within 6 months of surgery is recommended. If multiple synchronous polyps are identified, during the clearance examination, it may be reasonable to do the first surveillance examination at 1 year. Otherwise, posttreatment colonoscopy should be performed at 3-year intervals. Follow-up surveillance colonoscopy every 3 years can be continued for the duration of an individual's active life. It is also acceptable to extend follow-up colonoscopy to every 5 years after a negative colonoscopy at 3 years. Once the patient is older than age 80, further examinations may be of limited usefulness although exceptions can be made for individuals who are healthy and active despite their advanced age.

Recurrent Cancer

The term "recurrent cancer" is a misnomer because the cancer does not disappear and then return. It simply progresses in sites not clinically detectable at the time of the original surgery. Locoregional recurrences are more common in cases of rectal cancer, and may represent inadequate tumor clearance at the time of surgery. Distant disease, typically in the liver or lungs, usually does not cause symptoms until the situation is quite advanced. Options for the detection of asymptomatic recurrences include physical examination, carcinoembryonic antigen (CEA) monitoring, colonoscopy, chest X-ray, (CXR), and various scans. In this high technology era, careful attention to new symptoms such as abdominal pain, change in

bowel habits, weight loss, or anorexia is often lacking, but such symptoms are the first sign of recurrence in many cases. When present, a meticulous physical examination is conducted. This should include a digital rectal and vaginal examination for patients with rectal cancer. CEA testing is most useful in cases in which the level was increased preoperatively but decreased to normal levels after resection. Even in cases in which the preoperative CEA level is normal, serial CEA testing is often the first indication a patient has recurrent disease. Although CEA testing is controversial, the Standards Practice Task Force of the ASCRS recently recommended that CEA testing should be used as a part of follow-up for patients with colorectal cancer. This may be justified if its use is restricted to those who would tolerate reoperation if a recurrence were identified. Endoscopic follow-up is of limited usefulness in looking for recurrences because only 2% of recurrences are visible at colonoscopy. This is especially true for colonic anastomoses where recurrence is rare as compared with rectal anastomoses where mucosal recurrences are more likely to develop. Rigid proctoscopy is an alternative and, some suggest, superior way to assess a rectal anastomosis for recurrence. Patients with rectal cancer, especially those treated with transanal excision, should undergo endorectal ultrasound surveillance (usually every 3 months for the first year). There are currently insufficient data to recommend for or against routine use of CXR to identify an asymptomatic pulmonary metastasis. Its use should be restricted to patients who would tolerate a pulmonary resection. Computerized tomography (CT) and magnetic resonance imaging (MRI) scanning are very sensitive ways to detect liver and lung metastases, but are not recommended as a routine screening procedure. Positron emission tomography (PET) scanning may become the most sensitive way to detect recurrences, but although it is becoming more widely available, data supporting its use are still lacking. Although PET scanning is limited in its usefulness in detecting recurrence, it has been helpful in identifying patients with recurrence who have too many areas of distant recurrence to warrant operative therapy to remove the local, liver, or lung recurrence detected initially. Patients with isolated metastatic disease (fewer than eight liver metastases or 1 or 2 lobe lung involvement) may be candidates for operative treatment (see Chapter 34). As chemotherapy improves, operative therapy to resect residual disease may be more important to extract a cure.

Hereditary Cancer

Heredity is thought to be a major factor in 10%–25% of colorectal cancers. Patients who developed their cancer before age 50 years or who have first-degree relatives who developed colorectal or associated cancers such as endometrial, ovarian, ureteral, or bladder cancer or who have multiple family members with varying cancers especially if diagnosed before 50 years of age may have a hereditary cancer. Some inherited syndromes predispose the individual not only to development of young-age-of-onset colorectal cancer but also other organ cancers. Thus, in addition to informing family members of their risks and need for intensive surveillance, the patient's follow-up plan may need to incorporate surveillance of other potential sites of cancer. Sometimes, genetic counseling and testing is useful and prophylactic surgery may be considered as in the case of hereditary nonpolyposis colon cancer syndrome.

Risk of Recurrence/Pattern of Recurrence

The risk of recurrence is proportional to the stage of the original disease. Most Stage IV patients have undergone palliative treatment and are not candidates for surveillance unless they were treated by operative removal of metastatic disease. Patients with Stage I colon cancer treated by radical surgery have such a low chance of recurrent disease that routine surveillance may not be justified. However, Stage I rectal cancer patients treated by local therapy are at significant risk of local recurrence and may deserve close follow-up. Patients with Stage II or III disease would seem to benefit most from close surveillance. Other tumor or surgery related factors such as degree of differentiation, presence of lymph node metastases, iatrogenic perforation, and poor primary tumor clearance, influence the risk of recurrence, and could be used to more accurately predict an individual patient's risk of recurrence, and guide the development of a specific follow-up program. To date, there is no standardized formula for doing this but an experienced clinician can individualize follow-up based on the risk of recurrence, the patient's overall health status, the patient's willingness to undergo serial testing and the ability for the patient to undergo aggressive retreatment if recurrence is identified.

The patterns of recurrence reflect the location of the primary tumor.[5] Rectal cancers tend to recur locally in the pelvis, but this tendency has diminished recently with improved mesorectal clearance techniques and the use of neoadjuvant chemoradiation. All colorectal cancers metastasize hematogenously to the liver and lungs as well as to regional lymphatics, and these areas need to be evaluated when looking for recurrent disease.

It is well established that 60%–80% of recurrences occur within 2 years of surgery, and more than 90% of recurrences are found within 5 years. Therefore, follow-up protocols should be most intensive for the first 2 years, and then taper off in frequency of evaluations over the next 3 years. The exception to this timing of recurrence is the patient who has had pelvic radiation. In such cases, recurrence tends to occur later so intensive surveillance may need to extend to 5 or 6 years. Subsequent to that, the risk of recurrence is so low that colonoscopic surveillance for metachronous cancers is all that is warranted. The development of symptoms at any time during follow-up should prompt a thorough diagnostic work-up and specific treatment.

Surveillance Effectiveness

The utility of a surveillance program should be manifest in an improvement in survival or quality of life when compared with patients who have received little or no follow-up. Several variables confound our ability to evaluate the advantages derived from intensive efforts to detect recurrent cancer before it becomes evident clinically. The first is the lead time bias that results from detecting asymptomatic recurrences. Early detection of such a recurrence for which no effective treatment can be offered will still result in a measured prolongation of survival from the time of diagnosis of the recurrence when compared with those patients treated for symptomatic recurrences because they were identified earlier. Even if the treatment provided does impart some benefit, the bias between groups persists.

The identification of recurrent disease does not necessarily result in improved outcomes. Only about 10% of recurrences are resectable with curative intent and chemotherapy offers little chance of cure. Those patients who are fortunate to have a lesion amenable to surgery are often not suitable surgical candidates as a result of age or comorbidity, and should not be subjected to intense follow-up because any information obtained cannot be acted upon. There is a subset of patients with resectable disease, who may benefit from radical re-resection, with 5-year survivals of 25%–30% in most series. PET scanning can assist in identifying this small group of individuals.[6]

The results of intensive follow-up programs reported in the literature have been disappointing. A recent review summarized the results of the six randomized, prospective trials of high-intensity versus low-intensity follow-up after surgical resection with curative intent for colorectal cancer.[7–13] Recurrences were not more common in the closely monitored group, but they were found earlier and were more likely to result in reoperation with curative intent. Despite this, only two of the six studies demonstrated a statistically significant improvement in overall survival as a result of intensive surveillance.

Because of the concern that inadequate sample size was in part responsible for the negative results encountered in the above studies, three separate metaanalyses have been conducted on these data.[6,14,15] Although this resulted in a more clearly discerned reduction in death from recurrent cancer, the reduction in absolute risk was only 7%.

Cost of Surveillance

Offsetting the survival benefits of an intensive surveillance program are the costs associated with such testing. Given the large number of patients involved, cost implications for Medicare and private insurers are significant. The heterogeneity of follow-up regimens results in 5-year Medicare-allowed charges of $910 to $26,717 per patient.[16] One of the above metaanalyses evaluated the cost-associated intensive follow-up in terms of cost per year of life gained and found it to be $6096.[17] Beart's hypothetical cost analysis of a program to closely follow Stage II and III patients resulted in a cost of $6558 per patient salvaged by resection.[18] Although these costs are significant, they seem to be below the accepted threshold of $30,000 per year of life gained.

Quality of Life

Intensive surveillance may have a negative impact on quality of life secondary to the anxiety, inconvenience, and cost associated with the testing. Conversely, intensive testing may be reassuring to patients and improve their quality of life. Investigators in Denmark found that although patients subjected to closer follow-up expressed greater confidence in their examinations, the increment in quality of life was marginal and did not justify the expense of follow-up.[19] Stiggelbout et al.[20] also showed no differences in health-related quality of life when different intervals of follow-up were studied but they did show patients had a strong preference for follow-up. Additional data are needed to determine methods and settings for follow-up that maximize both survival and the quality of life.

Recommendations

Recommendations for surveillance of patients who have undergone curative resection of colorectal cancer are as follows.

Virtually all patients can undergo follow-up studies that are focused on excluding hereditary cancer and on prevention of synchronous cancer by every 3- to 5-year surveillance colonoscopies to remove metachronous polyps. If hereditary cancer is likely, work-up appropriately and/or consider referral to experts in hereditary cancers. In addition to counseling the patient about their own risks for other sites of cancer development, the clinician must attempt to educate the patient's family members about their risks and surveillance or treatment options.

The search for treatable recurrent disease is more selective. It is helpful to first determine whether the patient has a significant risk of recurrence. If so, determine whether the patient prefers an aggressive approach to follow-up testing and whether the patient could tolerate retreatment if recurrence is identified. If there is a minimal risk of recurrence and/or the patient refuses or is not a candidate for aggressive follow-up, no additional testing is done. It is comforting for patients to know that should recurrence develop, you are available and palliative treatment can be instituted. Patients should still undergo routine colonoscopic surveillance every 5 years to detect metachronous polyps or cancer.

If there is a significant risk of recurrence and the patient wants aggressive follow-up and would tolerate retreatment,

follow-up will include the search for recurrent disease. Typically this includes: history, physical examination, and serial testing as noted below every 3–6 months for the first 3 years, and then every 6–12 months for an additional 2 years. If pelvic radiation was used for rectal cancer, the closer interval of follow-up may need to be extended to 5 or 6 years. Careful attention to new symptoms and physical finding should be made.

Complete colonoscopy before resection, followed by an examination 1–3 years after surgery and every 3–5 years thereafter for the duration of the patient's productive life.

Serial CEA testing every 3 months for the first postoperative year or two and every 6–12 months thereafter for patients who desire an aggressive follow-up protocol and would tolerate aggressive retreatment for locoregional disease or hepatic or pulmonary metastasis.

Serial CXR every 6–12 months for patients who desire an aggressive follow-up protocol and would tolerate pulmonary resection.

Serial proctoscopy and selective endorectal ultrasound for rectal cancer patients who desire an aggressive follow-up protocol and would tolerate aggressive radical pelvic surgery with or without additional radiation and chemotherapy.

Based on the available evidence, there is no role for the routine use of liver function tests, hemoglobin, CT scanning, MRI, or PET scanning in asymptomatic patients.[4,7]

Future studies may more clearly define the role of these and other surveillance modalities.

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Colorectal cancer (CRC) is the third most common cause of cancer death in the United States; an estimated 147,950 new cases are diagnosed each year, of which 10.Â There has been and continues to be considerable variability among physicians in the use of follow-up studies after potentially curative resection of CRC and in the guidelines from major societies and expert groups. Multiple surveillance strategies have been published at costs ranging from a few hundred to several thousand dollars per patient. Surveillance of colorectal cancer: effectiveness of early detection of intraluminal recurrences on prognosis and survival of patients treated for cure. Dis Colon Rectum 1996;39:388-93. 40. Barrier A, Houry S, Huguier M. The appropriate use of colonoscopy in the curative management of colorectal cancer. Colonoscopy surveillance plays an important role in colorectal cancer prevention by removal of the precursor lesions (adenomas) and early detection of cancer, resulting in improved survival rates. Therefore, Hodgkin lymphoma survivors treated with infradiaphragmatic radiotherapy and/or high-dose procarbazine could benefit from colonoscopy, or other surveillance modalities, which are expected to reduce colorectal cancer incidence and mortality.