# COLORECTAL CANCER: SURGICAL MANAGEMENT OF RECURRENT AND METASTATIC DISEASE

John S. Bolton, MD, Jean-Nicolas Vauthey, MD, and Edward R. Sauter, MD
New Orleans, Louisiana

**The surgeon's responsibility to patients with colorectal cancer does not end with resection of the primary locoregional disease. The surgeon has a role to play in (1) designing and implementing strategies aimed at preventing recurrence, (2) early detection of recurrent disease, and (3) resective therapy of recurrent disease in selected instances, either with curative intent or for palliation. To perform these roles, the surgeon must have a thorough knowledge of catheter techniques for regional drug delivery, resective techniques for metastatic or locally recurrent disease, and combined surgical and radiotherapy approaches.**

Some 140,000 people in the United States will develop colorectal cancer in 1987 and approximately 50 percent will die of recurrent cancer within five years of the initial presentation.[1] Recurrent disease most often involves the liver and locoregional sites. Peritoneal implantation is slightly less common, and distant (extra-abdominal) metastatic disease occurs much less commonly. Combinations of recurrence in several of the above locations are also common.

Although the surgeon's primary responsibilities are to perform endoscopic surveillance, to provide tissue diagnosis, and to perform resection of locoregional disease, the surgeon's role does not stop with the operation. Additional responsibilities include (1) efforts at prevention of recurrent disease through postoperative adjuvant programs, (2) postoperative monitoring for recurrent disease, and (3) potentially curative or palliative surgical management of recurrent disease. Each of these roles will be discussed separately.

## PREVENTION OF RECURRENCE

Major efforts are being made to identify effective postoperative adjuvant therapies. Progress has been hampered by the resistance of most colorectal cancers to available chemotherapy, though modest improvements in survival with postoperative systemic drug therapy have been reported recently by several cooperative groups.[2,3] Of particular interest to the surgeon is the demonstration by Taylor et al[4] that short-term postoperative portal vein infusion of 5-fluorouracil can reduce dramatically the development of liver metastases and improve significantly the survival of patients undergoing curative resection for carcinoma of the colon or rectum. Confirmatory trials are being conducted by the National Surgical Adjuvant Breast Project and the North Central Cancer Treatment Group in the United States, and one additional trial is under way in Europe. If these trials confirm Taylor's findings, this relatively simple technique can be adopted by surgeons at the time of resection of the primary locoregional disease. The tech-

nique involves placement of a catheter into a peripheral radical of the portal venous system, through which 5-fluorouracil in standard doses is given as a continuous infusion for five to seven days postoperatively. Toxicity to date has been low, but further evolution of current prospective randomized trials is necessary before this can be recommended as a routine procedure.

## POSTOPERATIVE FOLLOW-UP

In most instances, the surgeon will carry out the postoperative follow-up program. Uncertainties exist as to (1) the contribution of follow-up visits to health maintenance, (2) the psychological effect of follow-up testing on the patient, and (3) the optimal frequency of postoperative diagnostic testing. Because metachronous, potentially curable cancer of the colon may develop, and because a small number of patients with recurrent cancer may be cured by aggressive surgical approaches, follow-up is warranted. Serial carcinoembryonic antigen determination is the least costly, most sensitive, and most specific diagnostic test for recurrent colon cancer.[5] Thus, a simple and relatively economical follow-up program for the first several years postoperatively should incorporate serial carcinoembryonic antigen determinations every six weeks, follow-up clinic visits with careful review of systems and physical examination four times per year, and examination of the anastomosis and any remaining colonic epithelium by endoscopy six months postoperatively and then on a yearly basis. More extensive workup is triggered by the development of symptoms or by a serial rise in carcinoembryonic antigen in an otherwise asymptomatic patient.

According to a series of asymptomatic, "second-look" operations carried out in the 1950s, and two more recent carcinoembryonic antigen-directed second-look series, most patients having resectable, potentially curable recurrences will have the recurrent disease confined to the liver or the primary surgical site.[6-8] Thus, when the carcinoembryonic antigen level is rising in an asymptomatic patient, the most valuable tests are colonoscopy and computed tomography (CT) scanning of the abdomen and pelvis. If potentially resectable disease is identified on these examinations, extra-abdominal workup, including chest CT scan and bone scan, is indicated prior to reoperation.

## TABLE 1. SITES OF RECURRENCE AFTER RESECTION OF DISEASE METASTATIC TO THE LIVER

| Site | Percent Recurrence |
|------|---------------------|
| Liver only | 14 |
| Liver and peritoneum | 7 |
| Liver and all other | 21 |
| Lung only | 42 |
| Lung and other | 7 |
| Other | 7 |

## SURGICAL MANAGEMENT

The survival rate following reoperation for resection of recurrent colorectal cancer is a function of the follow-up method and the factors used to select patients for reoperation. Overall, probably not more than 5 percent of patients with recurrent colorectal cancer can be cured be secondary resective procedures; therefore, careful selection is paramount to avoid needless reoperation in patients with little or no prospect for cure. Most patients who enjoy long-term survival after secondary resective procedures will have metastatic disease of limited extent that is confined to the liver. Multiple retrospective series attest to a 20 to 25 percent five-year survival rate after resection of colorectal cancer metastatic to the liver, provided that careful selection factors are used (Table 1).[9-11]

Resection techniques for disease metastatic to the liver include wedge resection, segmentectomy (most commonly of segments II and III), left lobectomy, right lobectomy, and right trisegmentectomy. These techniques have been well standardized and postoperative mortality is less than 5 percent when operations are performed by experienced surgeons. Problems with intraoperative blood loss and postoperative metabolic derangements are minimal in most cases. Technical details, which require the close attention of the surgeon, are the delineation of the hepatic arterial and hepatic venous anatomy and the recognition of aberrant right hepatic segmental ductal drainage into the left hepatic duct in 15 percent of patients, an anomaly of major importance in patients undergoing left hepatic lobectomy.[12] Surgical principles of safe resection include (1) preliminary hilar dissection when major lobar resections are planned, carefully preserving arterial and portal venous inflow to nonresected segments, (2) careful preservation of hepatic

venous drainage of nonresected segments, (3) expeditious technique to minimize blood loss, (4) provisions for rapid blood replacement made in advance of transsection of the liver substance, (5) good control of transsected biliary radicals at the line of resection, and (6) closed-suction drainage.

Several prognostic factors have been recognized that aid in patient selection for attempts at resection of liver metastases. The presence of extrahepatic metastases is an absolute contraindication to liver resection. It has been observed by the authors that patients whose initial lesion was staged as Dukes' B (as opposed to Dukes' C) primary lesion are more likely to have a favorable outcome. This trend has been observed by others as well.[11,13,14] The presence of multiple liver metastases, provided they are resectable, has not had a deleterious effect on survival.[10,11,13] In view of this, a slightly more aggressive attitude has been adopted toward resection of multiple, even bilobar, metastases. Technical difficulties, however, usually preclude the resection of more than two or three lesions, and it must be stressed that patients with multiple lesions undergoing resection require very careful selection. DNA histograms (as determined by flow cytometry) have not been found to be useful prognostic indicators. Nor has the timing of presentation of the liver metastases (synchronous vs metachronous) or the size of the metastatic lesions been helpful.

While others have advocated "neoadjuvant" hepatic arterial, portovenous, or intraperitoneal infusion chemotherapy after resection of metastatic disease to the liver, it has been the experience of the authors that the pattern of failure after resection of hepatic metastases has been distant in most cases (Table 1). Thus, postoperative adjuvant therapy after resection of liver metastases has not been used as a treatment modality herein.

The Cavitron ultrasonic surgical aspirator (CUSA) has been advocated for liver resection, but it has been found cumbersome and not useful for routine lobectomies. It can, however, be quite helpful for large wedge resections adjacent to the hilus of the liver (segments IV or V) or adjacent to the major hepatic venous drainage. In these situations, the more precise dissection afforded by the CUSA can aid in the identification of important anatomical structures.

For large tumors that are approximated closely to the inferior vena cava or major hepatic venous drainage, magnetic-resonance imaging is helpful preoper-

**TABLE 2. NORTHERN CALIFORNIA ONCOLOGY GROUP\* TRIAL OF HEPATIC ARTERIAL INFUSION VS INTRAVENOUS INFUSION OF 5-FLUOROURACIL FOR UNRESECTABLE METASTATIC DISEASE CONFINED TO THE LIVER**

| Infusion Technique | Percent Major Response | Median Time to Hepatic Progression |
|---|---|---|
| Hepatic artery infusion 0.2 mg/kg/d × 14 days every 28 days | 37 | 658 days |
| Intravenous infusion 0.075 mg/kg/d × 14 days every 28 days | 10 | 203 days |

\* From Hohn D et al[17]

atively in predicting resectability; however, it is not used routinely. Intraoperative ultrasound may identify small, additional metastatic deposits not identified by manual palpation of the liver.[15,16] Identification of these lesions will often permit their resection and may help to prevent early recurrence in the liver. Intraoperative ultrasound, therefore, should be used whenever possible.

For patients with unresectable metastases confined to the liver, hepatic arterial-infusion chemotherapy has been widely used. This form of therapy is attractive from a theorectical and practical standpoint; however, the Infusaid pump is expensive and requires a major surgical procedure for implantation.

The Northern California Oncology Group study[17] suggested that the response rate of liver metastases is enhanced significantly by hepatic artery infusion as compared with intravenous infusion of 5-fluorouracil (Table 2). The development of extrahepatic metastases, however, is not affected in any way by hepatic artery infusion of 5-fluorouracil. In addition, biliary sclerosis is a limiting factor of hepatic artery infusion of 5-fluorouracil,[18] although it appears that the incidence of this serious complication can be decreased by a reduction of the 5-fluorouracil dose. No prospective, randomized, noncrossover trials have compared hepatic artery infusion to intravenous infusion of 5-fluorouracil, so that the impact, if any, of hepatic artery infusion therapy on survival is unknown. Unfortunately, no such study is likely to be performed in the near future, so conclusions about the worth of

hepatic artery-infusion chemotherapy are not possible at this time.

Local regional recurrences and, rarely, lung metastases may also be resected with curative intent and occasional long-term survival in carefully selected patients. The most favorable experience with resection of locoregional recurrence has been in conjunction with intraoperative radiation therapy.[19]

Finally, palliative resections of symptomatic lesions may provide beneficial relief to patients with incurable recurrent disease. For instance, intestinal obstruction that is caused by recurrent disease should be relieved surgically when the patient's overall condition permits and when survival of several months or more is otherwise anticipated. Surgical procedures to relieve obstructive jaundice caused by metastatic nodal involvement in the porta hepatis are occasionally of benefit; however, the development of percutaneous and endoscopic techniques for biliary decompression have lessened the need for surgical intervention. Metastatic lesions may occasionally be resected and will afford significant pain relief. Obviously, these procedures must be individualized in accordance with the particular circumstances of each case and with other available therapeutic options.

## Literature Cited

1. Cancer Statistics, 1987. CA 1987; 37:12–13.
2. Laurie J, Moertel C, Fleming T, et al. Surgical adjuvant therapy of poor prognosis colorectal cancer with levamisole alone or combined levamisole and 5-fluorouracil. Proc ASCO 1986; 5: 81.
3. Wolmark N, Fisher B, Rockette H, et al. Adjuvant therapy of carcinoma of the colon: Five-year results of NSABP protocol C-01. Proc ASCO 1987; 6:92.
4. Taylor I, Brooman P, Rowling JT. Adjuvant liver perfusion in colorectal cancer: Initial results of a clinical trial. Br Med J 1977; 2:1320–1322.
5. 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.
6. Griffin WO, Humphrey L, Sosin H. The prognosis and management of recurrent abdominal malignancies. Curr Probl Surg 1969; 30:4–43.
7. Martin EW, Minton JP, Carey LC: CEA-directed second-look surgery in the asymptomatic patient after primary resection of colorectal carcinoma. Ann Surg 1985; 202:310–317.
8. Minton JP, Hoehn JL, Gerber DM, et al. Results of a 400-patient carcinoembryonic antigen second-look colorectal cancer study. Cancer 1985; 55:1284–1290.
9. Foster JH, Berman MM. Solid liver tumors. In: Major Problems in Clinical Surgery, Vol. 22. Philadelphia: WB Saunders, 1977.
10. Nordlinger B, Quilichini MA, Parc R, et al. Hepatic resection for colorectal liver metastases: Influence on survival of preoperative factors and surgery for recurrences in 80 patients. Ann Surg 1987; 205:256–263.
11. Adson MA, Van Heerden JA, Adson MH, et al. Resection of hepatic metastases from colorectal cancer. Arch Surg 1984; 119:647–651.
12. Healey JE, Schroy PC. Anatomy of the biliary ducts within the human liver: Analysis of the prevailing pattern of branching and the major variations of the biliary ducts. Arch Surg 1953; 66:599.
13. Fortner JG, Silva JS, Golbey RB. Multivariate analysis of a personal series of 247 consecutive patients with liver metastases from colorectal cancer: I. Treatment of hepatic resection. Ann Surg 1984; 199:306–315.
14. Iwatsuki S, Esquivel CO, Gordon RD, Starzel TE. Liver resection for metastatic colorectal cancer. Surgery 1986; 100: 804–809.
15. Rifkin MD, Rosato FE, Branch HM. Intraoperative ultrasound of the liver: An important adjunctive tool for decision-making in the operating room. Ann Surg 1987; 205:466–471.
16. Machi J, Isomoto H, Yamashita Y. Intraoperative ultrasonography in screening for liver metastases from colorectal cancer: Comparative accuracy with traditional procedures. Surgery 1987; 101:678–683.
17. Hohn D, Stagg R, Friedman M, et al. The NCOG randomized trial of intravenous versus hepatic arterial FUDR for colorectal cancer metastatic to the liver. Proc ASCO 1987; 6:85.
18. Bolton JS, Bowen JC: Biliary sclerosis associated with hepatic artery infusion of floxuridine. Surgery 1986; 99:119–122.
19. Gunderson LL, Cohen AM, Dosoratz DE, et al. Residual unresectable or recurrent colorectal cancer: External beam irradiation and intraoperative electron beam boost plus or minus resection. Int J Radiat Oncol: Biol Phys 1983; 9:1597–1606.