Hepatic Colorectal Metastasis: Current Status of Surgical Therapy

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Metastatic colorectal cancer to the liver develops in over 50,000 US patients each year and is rapidly fatal if untreated. Even the most active chemotherapeutic agents barely prolong survival for more than 3 years. Liver

Fong and Blumgart provide an excellent review of the current status of surgical therapy for metastases from colorectal carcinoma. This review summarizes the literature demonstrating the safety and efficacy of liver resection for colorectal metastases. It also documents the acceptance of surgical resection as the standard treatment for hepatic colorectal metastases, given that it is the only potentially curative modality.

Although most series report complication rates of hepatic resection in the range of 20% to 50%, Fong and Blumgart emphasize that this high complication rate does not translate into high mortality. Centers that have experience with liver resection for colorectal metastases report < 5% mortality. Also, surgical resection can provide long-term survival for patients with metastases from colorectal carcinoma. As summarized by the authors, 5-year survival rates range from 25% to 37% and, in selected series, can be as high as 44% when computed tomographic (CT) portography, intraoperative ultrasound, margin evaluation, and portal lymph node assessment are utilized to guide patient selection.[1]

**Ruling Out Extrahepatic Disease**

The ability to use present-day technology to select patients who are likely to do well following hepatic resection is important. This is especially true with respect to ruling out extrahepatic disease, which is the one contraindication for hepatic resection of colorectal metastases.

The assessment of extrahepatic disease is best performed intraoperatively by the surgeon. As shown by Fuhrman and associates,[1] evaluation of areas such as the porta hepatis is extremely important in ruling out lymph node metastases prior to performing hepatic resection. In their series of 151 patients undergoing operative exploration, 107 (71%) underwent hepatic resection with all margins negative for tumor. Of the 151 patients, 30 were determined to have extrahepatic disease at celiotomy. Fourteen patients (9.2%) had peritoneal tumor implants and 16 patients (10.6%) had periportal lymph node metastases confirmed by frozen section.

In our own series, thorough abdominal exploration revealed extrahepatic disease in 13 (21%) of 62 patients. Routine periportal/celiac lymph node biopsies revealed metastases in an additional 12 patients (19%), 7 (11%) of whom had periportal/celiac lymph node metastases alone.[2] These data emphasize that a meticulous abdominal exploration prior to hepatic resection for colorectal metastases is essential to identify extrahepatic disease. Periportal and celiac lymph nodes are commonly involved by tumor. Therefore, we recommend routine periportal/celiac lymph node biopsies in the absence of other sites of extrahepatic disease prior to hepatic resection.

There is no question that patients can be understaged at the time of potential hepatic resection because of unrecognized extrahepatic disease or additional intrahepatic metastases. Intraoperative ultrasound is the most sensitive test for the detection of hepatic metastases, with a reported sensitivity of 98% to 100%. Intraoperative ultrasound also establishes the relationship of tumors to critical vascular structures, such as the hepatic and portal veins. This technology has been reported to have changed management in 15% to 49% of patients with metastatic liver cancer.[3,4]

**Is Chest CT Necessary?**

As part of the preoperative evaluation, Fong and Blumgart recommend that patients undergo a chest CT scan prior to hepatic resection. To a certain degree, this recommendation is in conflict with their own data.[5] These data came from 100 consecutive patients who were thought to have potentially resectable metastatic colorectal cancer to the liver and were subjected to CT scan of the chest. Patients with a positive chest CT underwent thoracoscopy/thoracotomy prior to liver resection. Of
100 patients with a negative chest x-ray, 11 had a positive chest CT, and 4 of the 11 were found to have malignant lesions of the lung (3 metastatic colorectal cancers, 1 primary lung cancer) at thoracoscopy/thoracotomy prior to liver resection.

Blumgart and Fong concluded that the low overall positive yield, as well as low positive predictive value, of chest CT in the setting of a negative chest x-ray calls into question the utility of a routine chest CT as part of the evaluation prior to hepatic resection for colorectal metastases. At Roswell Park Cancer Institute, our policy is not to order a chest CT in the presence of a negative chest x-ray.

**Prognostic Variables**

Fong and Blumgart emphasize the use of prognostic variables in selecting patients for potentially curative hepatic resection of metastases from colorectal carcinoma. The authors state that these are prognostic factors and not contraindications to hepatic resection. These prognostic variables can be easily remembered by the pneumonic SINS, which stands for: stage of the primary colorectal tumor; interval between the diagnosis of the primary colorectal cancer and the development of hepatic metastases; number of metastases; and size of the hepatic metastases.

Size of hepatic metastases is especially important in determining the type of hepatic resection to be performed. In the registry of over 800 patients who underwent hepatic resection for colorectal carcinoma reported by Hughes and colleagues, an anatomic resection was performed in patients with metastasis > 4 cm in size for fear that a wedge resection might compromise the margin of resection.

The number of hepatic metastases is also an important prognostic factor. Most surgeons performing hepatic resection for colorectal carcinoma, after all other prognostic factors have been considered, would embark on resection in patients with one to four metastases. However, it is important not to become a cookbook surgeon for whom these numbers are written in stone. More than likely, patients with five, six, or seven metastases do poorly because of unrecognized extrahepatic disease or additional intrahepatic metastases.

**Follow-up Surveillance**

Fong and Blumgart also review postoperative surveillance following hepatic resection for colorectal metastases. Close follow-up is justified since re-resection of hepatic metastases or the subsequent resection of pulmonary metastases can be potentially curative. An increasing number of reports in the literature have examined the effectiveness of second resections as treatment for recurrent hepatic metastases from colorectal carcinoma. These studies demonstrate that repeat hepatic resection can be performed safely and for cure.

In general, the prognostic factors used for repeat resections are the same as those used when the patient presents initially (SINS). However, at the time of a repeat resection it is important for the surgeon to rule out extrahepatic intraabdominal metastases, especially in the porta hepatis and celiac lymph node basins.

**Role of Adjuvant Therapy**

As the authors report, the literature has demonstrated that, in the majority of patients, recurrences following hepatic resection occur most commonly in the liver and, secondarily, in the lung. Because of these patterns of recurrence, it is obvious that hepatic resection alone is insufficient therapy for the majority of patients. Hence, it is important to address the role of adjuvant therapy following resection.

As reported by Fong and Blumgart, none of the retrospective studies reported to date has answered the question concerning the role of adjuvant therapy. However, a national intergroup trial with Margaret Kemeny, MD, as principal investigator has reached its accrual goal, and results should be available in the next 2 to 3 years. This trial is randomizing patients, following resection of one to three hepatic metastases, to receive either no further therapy or adjuvant intraarterial 5-fluorouridine (FUDR) and systemic continuous-infusion fluorouracil. Investigators are anxiously awaiting the results of this important trial.

**Cryosurgery Still Experimental**

Finally, I agree with the authors that cryosurgery for hepatic metastases from colorectal carcinoma must still be regarded as an experimental modality and should be used only in the setting of a clinical trial. At Roswell Park Cancer Institute, we currently consider performing cryosurgery in patients with greater than four but no more than six metastases following complete evaluation both preoperatively with CT portography and intraoperatively with hepatic ultrasound and porta hepatis/ceeliac lymph node assessment. These metastases need to involve no more than 40% of the hepatic parenchyma because of concerns of hepatic failure following freezing.

*Cryosurgery is not an innocuous* procedure. As emphasized by Fong and Blumgart, it can have severe complications. Cryosurgery...
should be performed only by surgeons who have experience with hepatic resection. It also must be kept in mind that cryosurgery is a form of local therapy, and that, at present, hepatic resection remains the gold standard of local treatment.

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