Surgical and Ablative Modalities for the Treatment of Colorectal Cancer Metastatic to the Liver

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Annually, 147,500 people are diagnosed with colorectal cancer in the United States, and at least 50,000 of these people will develop liver metastases (Blumgart & Fong, 1995; Jemal et al., 2003; Wingo, Tong, & Bolden, 1995). The liver is the most common and often the only site of metastatic disease because it is the first major organ reached by venous blood draining from the intestinal tract (Fong, 1999; Fong, Fortner, Sun, Brennan, & Blumgart, 1999; Fong & Salo, 1999). When the liver is the only site of metastatic disease and all tumors can be safely removed, resection is appropriate therapy. For metastatic colorectal cancer (MCR) to the liver that is unresectable, chemotherapy offers disease control, with median survival being 12–16 months (Fong, 2000). Untreated hepatic colorectal metastases typically result in death in approximately 5–10 months, depending on extent of disease (Bengmark & Hafstrom, 1969; Oxley & Ellis, 1969; Wood, Gillis, & Blumgart, 1976).

A preoperative scoring system for patients being considered for resection has been developed in an attempt to predict patient outcome. The clinical risk score is calculated from five criteria: node-positive disease (from primary colon tumor), disease-free interval less than 12 months, number of liver tumors greater than one, size of largest tumor greater than 5 cm, and carcinoembryonic antigen (CEA) greater than 200 ng/ml. A point is assigned for each criterion. Patients with up to two criteria are more likely to benefit following hepatic resection alone, whereas patients with a higher score should be considered for stratification for adjuvant clinical trials because their disease is more likely to recur (Fong et al., 1999).

Colorectal cancer is the second leading cause of mortality from cancer in the United States. Death from colorectal cancer usually results from metastatic disease to the liver. Complete surgical resection is the only potentially curative treatment option for metastatic colorectal cancer to the liver, with a five-year survival rate of approximately 30%–40%. The addition of adjuvant systemic or hepatic intra-arterial pump chemotherapy appears to improve survival. Treatment options for unresectable disease in the liver are cryosurgery (intraoperative freezing of tumors), radiofrequency ablation (intraoperative or percutaneous heating of tumors), hepatic intra-arterial infusion pump chemotherapy (regional chemotherapy), and systemic chemotherapy. This article describes metastatic colorectal cancer disease presentation, extent of disease evaluation, and nonchemotherapeutic treatment options, including surgical and ablative therapies. The nurse’s role in caring for this population also will be discussed.

Key Words: colorectal neoplasms; digestive system surgical procedures; catheter ablation; infusions, intra-arterial

Clinical Evaluation

Clinical evaluation consists of diagnostic studies to determine the extent of disease; if the liver is found to be resectable, patients’ medical fitness to undergo surgical or ablative treatment also is determined. Imaging studies are essential in evaluating the location of the tumor and the extent of disease. Preoperative imaging plays a crucial role in patient selection. Accurate imaging is imperative to avoid surgery for patients whose disease may not be technically amenable to hepatic resection and to assist the surgeon in planning the appropriate operation. Radiologic preoperative workups have two objectives: to (a) exclude extrahepatic disease and (b) evaluate the number and size of tumors and proximity to the major vessels. The results of these studies are crucial in determining whether surgical resection is the appropriate course of treatment (DeMatteo & Fong, 1999; Fong, 1999, 2000; Fong & Salo, 1999; Jarnagin et al., 1999; Saini, 1997).

The test or combination of tests that are used are dependent on the plan of treatment (Rychcik, 2000). The following imaging

Symptoms and Clinical Presentation

Most patients with MCR to the liver are asymptomatic. In most cases, elevated CEA and liver function tests are found on routine follow-up (Fong, Kemeny, Paty, Blumgart, & Cohen, 1996). This warrants further investigation with radiologic tests.

Submitted September 2002. Accepted for publication October 12, 2002. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society.)

Digital Object Identifier: 10.1188/03.CJON.178-184
modalities are the ones most commonly used for assessing resectability.

**Chest radiography or chest computed tomography (CT):** The most common extra abdominal site of metastases from colorectal cancer is the lung. One or both of these tests must be obtained to rule out pulmonary metastases as part of the extent of disease evaluation. Often, a CT of the chest is performed if suspicious nodules are apparent on chest x-ray (Fong, 1999).

**Duplex ultrasound:** Duplex ultrasound or sonogram is a noninvasive test that uses sound waves to determine the overall extent of disease in the liver. Ultrasound is operator dependent and requires technical expertise. This test often can differentiate benign disease (e.g., cysts, hemangiomas, adenoma) from solid, malignant tumors. Duplex ultrasound evaluates the hepatic and portal vessels in the liver and vena cava. Tumor involvement or proximity to these vessels can be determined by duplex ultrasound. For the evaluation of hepatic metastases, this is the least invasive and least expensive test, but it usually is unable to assess extrahepatic disease (DeMatteo & Fong, 1999; Fong & Salo, 1999).

**Abdominal and pelvic CT:** CT uses a computer to produce cross-sectional images of the area of the body being studied. Oral and IV contrast dyes are used to enhance the images. A CT scan of the abdomen and pelvis usually is performed for patients who are being considered for surgical resection of liver metastases (Fong, 1999; Fong & Salo, 1999). Benefits of CT scanning are that it is widely available and relatively inexpensive. CT allows for a more comprehensive evaluation of both intrahepatic and extrahepatic sites of disease than ultrasound (Fong, 2000; Fong & Salo, 1999; McCarter & Fong, 2000; Saini, 1997). CT scan also can visualize lymph node enlargement and pelvic disease recurrence. These findings would warrant further workup and may preclude patients from surgical resection.

**Angiography:** Angiography of the liver, performed either with a traditional transfemoral approach or noninvasively using specialized three-dimensional reconstruction of CT images, is recommended for patients who will undergo hepatic artery infusion (HAI) pump placement. This technique provides information on the hepatic arterial anatomy and other vessels (DeMatteo & Fong, 1999).

**CT portography:** In this test, contrast dye is injected directly into the superior mesenteric artery through a transfemoral catheter. After the dye is injected, the portal venous structures are visualized by CT. CT portography is very sensitive in detecting colorectal metastases in the liver and is the best test to evaluate patients with numerous small lesions who are being evaluated for resection. Disadvantages of CT portography are its invasive nature and expense (Fong, 1999; Fong & Salo, 1999; McCarter & Fong, 2000). With recent advances in noninvasive CT angiography, many physicians no longer use this procedure (Fong, 2000; Povoski et al., 1998).

**Magnetic resonance imaging (MRI):** MRI uses a magnet to produce images of the area being studied. MRI is often the test of choice when attempting to differentiate between metastatic and benign tumors of the liver as part of patients’ workups. MRI is the best test for patients who are allergic to or unable to tolerate the contrast dye administered with CT scans. A drawback to MRI is its expense (DeMatteo & Fong, 1999; Fong, 1999, 2000; Fong & Salo, 1999; McCarter & Fong, 2000; Saini, 1997).

**Positron emission tomography (PET):** PET scan is a nuclear medicine study that uses 18FDG, a glucose analog, to assess the presence of metastatic disease. The rationale is that malignant cells have higher glucose metabolism than nonmalignant cells. The 18FDG is injected via IV, and patients are scanned to detect any areas with increased uptake. Increased uptake of 18FDG often represents a tumor, but areas of inflammation also will result in a positive test result. The usefulness and accuracy of this test for MCR currently is under investigation (DeMatteo & Fong, 1999; Fong, 1999, 2000; Fong & Salo, 1999; McCarter & Fong, 2000).

In addition to the radiologic workup, patients should have a recent colonoscopy (within the past year) to rule out recurrence at the anastomosis or another primary tumor (Jarnagin et al., 1999). When considering patients’ suitability for resection, other factors, such as age and comorbidities, also are taken into account. Hepatic resection is a complex operation and requires three to six hours of anesthesia. If patients are elderly or have any cardiopulmonary impairment, determining their cardiopulmonary function is essential. Cardiologists must evaluate and clear these patients for surgery, and appropriate tests such as thallium stress tests or pulmonary function tests must be performed.

**Treatment Criteria**

Treatment is based on the location and extent of the tumor and presence of distant disease. Other factors, such as comorbidity and the presence of cirrhosis, also are considered.

**Surgery**

**Hepatic resection:** Surgery is the only treatment modality that offers a potential for a cure and has a five-year survival rate of 30%–40%. The treatment goal of surgery is complete excision of the tumor with negative histologic margins while leaving enough normal liver tissue to regenerate and sustain life (DeMatteo, Palese, et al., 2000; Gazelle & Haaga, 1992). The only contraindication in otherwise fit candidates is extrahepatic metastases and the inability to remove all of the disease (DeMatteo, Palese, et al.; Fong, 1999; Fong et al., 1999; Fong & Salo, 1999; Jarnagin et al., 1999; McCarter & Fong, 2000). As a result of improved patient selection and refined operating techniques that have decreased the need for blood transfusion, hepatic resection has been documented to be safe, with a mortality rate of less than 5% at major centers (Fong, 1999).

The liver is divided into hemi-livers (the right and left lobes) and is additionally subdivided into eight segments (the anatomical segments of Couinaud; see Figure 1) (Gazelle & Haaga, 1992). In a healthy liver, up to 80% or six of the eight segments, may be removed with the expectation that the liver remnant will regenerate sufficiently for survival. The piece of liver that is left behind grows until the liver reaches its original volume. It takes approximately three weeks for the liver to regenerate to its original size (Blumgart, Leach & Karran, 1971). By six weeks, normal liver function is restored. Two-thirds of resections involve removing more than half the liver (Fong, 1999, 2000).

Prior to resection, surgeons may perform an exploratory laparoscopy before proceeding to laparotomy. The purpose of laparoscopy is to assess for extrahepatic or additional hepatic disease not seen on the imaging studies. Patients whose extrhepatic disease is found on laparoscopy will avoid unnecessary laparotomies (Fong, 2000; Jarnagin et al., 2000). If no additional disease is noted on laparoscopy, surgeons will proceed with an exploratory laparotomy.
of the abdomen to assess for extrahepatic disease (Jarnagin et al., 1999). In one study, 22% of patients had extrahepatic disease discovered on laparoscopy or laparotomy that was not noted on the imaging studies (Jarnagin et al., 1999). A high bilateral subcostal incision is made for the operation. If extrahepatic disease is noted during the laparotomy, the resection is abandoned. If no extrahepatic disease is discovered, surgeons proceed to intraoperative ultrasound of the liver to assess all tumors in the liver and identify the lesions’ relationships to the major vascular structures (Fong et al., 1996).

The type of operation performed is dependent on the number, size, and location of the tumors; the amount of normal liver tissue that can be safely removed; and the margin of normal tissue that is desired. Types of resection include wedge resections, right and left lobectomies, and various segmental hepatectomies (DeMatteo, Palese, et al., 2000).

**Wedge resections** involve removing only the tumor and a small amount of the surrounding liver tissue (Gazelle & Haaga, 1992). In the past, wedge resections commonly were used to remove tumors that did not require lobar resection (DeMatteo, Palese, et al., 2000). Studies have shown that patients who undergo wedge resections have a high incidence of positive surgical margins and often recur at this site (DeMatteo, Palese, et al.).

**Segmental hepatectomy** is based on the Couinaud segmental classification of the liver. Any segments containing the tumor are completely removed. Up to six segments of the liver can safely be removed (Fong, 2000). Blood loss is minimized by first dividing the pedicle or segmental blood supply. This technique allows for the surgeon to have better control of the liver and results in a lower rate of positive surgical margins (DeMatteo, Fong, Jarnagin, & Blumgart, 2000; DeMatteo, Palese, et al., 2000).

More extensive operations include right and left hepatectomies, extended right hepatic lobectomy (right trisegmentectomy), left lateral segmentectomy, and extended left hepatectomy (left trisegmentectomy) (Fong et al., 1996) (see Figure 2). Up to 80% of the liver can be removed with full regeneration expected. Figure 3 illustrates liver regeneration following hepatic resection visualized on postoperative CT scans.

In some cases, tumors can be technically resectable but the future remnant liver is too small to sustain life. Some patients with small remnant livers postresection are at a higher risk for liver failure. To address this potential problem, an investigational procedure called preoperative portal vein embolization (PVE) is being used to increase the size of the future remnant liver prior to an operation. PVE is performed percutaneously under CT or ultrasound guidance by an interventional radiologist. During PVE, the portal vein branch of the side of the liver to be resected is occluded, causing compensatory hypertrophy of the opposite side (remnant) of the liver (Makuuchi & Takayama, 2000). A CT scan is performed three to six weeks after PVE to assess response, and if the future remnant liver has grown sufficiently, patients will have better capacity to regenerate and an operation is scheduled (Abdalla, Hicks, & Vauthey, 2001; Azoulay et al., 2000; Brown, Brody, Decorato, & Getrajdman, 2001; Wakabayashi et al., 2002). The efficacy and usefulness of PVE currently are under investigation.
Complications of Surgery

Although complications are reported in 20%–50% of patients who undergo liver resection, the mortality rate remains low at 2%–4% at major centers; in these cases, death usually results from liver failure or hemorrhaging. Other complications include biliary leak or fistula, reported in 3%–4% of cases, and perihepatic abscess, found in 1%–9% of cases. Patients who undergo hepatic resection are at risk for pulmonary complications because of the high transverse incision that is necessary to safely access liver tumors. The incision is associated with postoperative discomfort and increased respiratory effort. In addition, most patients develop a sympathetic right pleural effusion postoperatively that can contribute to pulmonary compromise (Fong, 1999; Fong & Salo, 1999). Sympathetic pleural effusion requiring tube thoracotomy occurs in 5%–10% of patients. Cardiopulmonary complications include pneumonia (5%–22%), myocardial infarction (1%), and pulmonary embolism (1%). The average length of stay for patients after liver resection is 10 days (Fong, 1999, 2000; Fong, Blumgart, Fortner, & Brennan, 1995; Scheele, Stangl, Altendorf-Hofmann, & Gall, 1991).

Ablative Treatment Modalities

Cryoablation and radiofrequency ablation are used to treat liver tumors; however, they are unlikely to be curative. These procedures can be performed laparoscopically or percutaneously during open operations. Useful roles for ablation techniques include treatment of small lesions in patients with medical contradictions to liver resection, small unresectable recurrences after previous liver resection, and scattered unresectable bilobar cancer (Dale, Souza, & Brewer, 1998; Fong & Salo, 1999). The use of these ablative therapies in conjunction with liver resection in cases where complete resection is not possible is under investigation (Dale et al.; Fong & Salo). Clinical trials are under way using multiple modalities to treat patients in an effort to improve patient outcomes.

Cryoablation: Cryoablation kills tumors by freezing and thawing tissues and results in tumor cell death (Fong, 1999). A special vacuum-insulated cryoprobe that uses liquid nitrogen as a cooling agent is inserted directly into the tumor to freeze the tumor cells (Fong et al., 1996; Polk, Fong, Karpeh, & Blumgart, 1995). A margin of normal tissue around the tumor is frozen to ensure adequate treatment. Each tumor takes between 30–40 minutes to freeze. This procedure can be performed even on tumors deep inside the liver with the assistance of ultrasound guidance (Blumgart & Fong, 1995; Fong, 1999). When cryosurgery has been used alone, a 75% relapse of preoperative CEA levels has been observed within six months, suggesting recurrent disease in the liver (Seifert & Morris, 1999). An average of 45% of patients undergoing cryoablation will experience complications, including pleural effusions, hemorrhage, biliary fistulation, hepatic abscess, and renal failure (Seifert & Morris). At centers where aggressive cryoablation is performed, mortality rates are comparable to hepatic resection and less than 4% (Fong, 1999; Fong & Salo, 1999).

Radiofrequency ablation (RFA): RFA is a technique that uses heat to kill tumors. A radiofrequency electrode is inserted into the tumor by ultrasound, CT, or MRI guidance. This technique is effective only in tumors that are 3 cm or smaller with the RFA probes that currently are available (Fong, 1999, 2000; McCarter & Fong, 2000; Prime, 2002). The size of lesions amenable to treatment may increase in the near future with the development of new equipment. Patients tolerate radiofrequency reasonably well with minimal side effects (Fong, 2000; Wood et al., 2000). Reported side effects include fever, pain, third-degree skin burn, intrahepatic abscesses, and biliary fistulas. Complications have been reported in less than 8% of patients treated with RFA (Curley, 2001; Wood et al., 2000).

Hepatic Intra-Arterial Infusion Therapy

HAI pumps are used to deliver chemotherapy directly into the liver, a procedure known as regional chemotherapy. The pump is placed surgically under the skin in the left or right lower quadrant of the abdomen. A catheter connected to the pump delivers a continuous dose of chemotherapy directly into the hepatic artery and liver and is used most often in conjunction with systemic chemotherapy. Regional chemotherapy allows for the administration of a higher dose of chemotherapy directly into the liver (Fong et al., 1996). When used as adjuvant therapy, HAI has been documented to decrease the risk of recurrence of hepatic metastases (Kemeny et al., 1999). The use of regional chemotherapy alone or combined with ablative techniques is under investigation in clinical trials. Most complications from HAI chemotherapy are chemotherapy-toxicity related, the most common being hepatic toxicity manifested by hyperbilirubinemia. In most patients, the bilirubin returns to normal when HAI chemotherapy is stopped for a period of time and decadrone is infused via the pump (Fong et al., 1996; Kemeny et al.). Other less common complications include infection around the pump pocket; hepatic arterial thromboses, which render the pump unusable; dislodgment of the catheter; and perfusion of areas outside the liver (Kemeny et al.).

Prognosis

Patients who have undergone liver resection for MCR have a median survival of 30 months and a five-year survival of about 25%–40% (Fong, Blumgart, Cohen, Fortner & Brennan, 1994). Disease recurrence will occur in two-thirds of patients (Fong & Salo, 1999). Some patients may be candidates for...
TABLE 1. PREPROCEDURE AND PREOPERATIVE CARE

<table>
<thead>
<tr>
<th>ACTION</th>
<th>RATIONALE</th>
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<tr>
<td>Ambulatory initial assessment is performed.</td>
<td>Patients’ conditions are assessed. Assessment is necessary to maintain an ongoing record so that appropriate care is rendered (Knobf, 1998). Physical and psychosocial assessments are necessary so that a plan of care may be individually tailored to meet each patient’s needs (Burke, 1999). Interdisciplinary referrals to social work, chaplaincy, nutritional service, patient representatives, and integrative medicine are made as needed.</td>
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<tr>
<td>Preoperative or preprocedure teaching is begun. Educational materials at the authors’ institution and pertinent topics include</td>
<td>Patient education begins in the ambulatory care setting and is one of nurses’ most important roles (Lamkin, 1993). A combination of verbal teaching, written materials, and audiovisual guides facilitates the learning process (Burke, 1999; Mayer, 1998). In cases when patients will be participating in clinical trials, research nurses also participate in patient teaching and help meet patients’ educational needs (Nevidjon, 1993). Barriers to patient education and learning, including language differences, low literacy, and anxiety must be identified, and the teaching program must be developed to meet the special needs of patients. Benefits to patients from preoperative and preprocedure teaching include lower anxiety levels, fewer postoperative complications, and the ability to better participate in postoperative care (Burke, 1999).</td>
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<tr>
<td>– Preoperative CD-ROM: Liver Resection</td>
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<td>– Written educational material including</td>
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<tr>
<td>– Before, During and After Surgery: A Guide for Patients and Families</td>
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<tr>
<td>– Getting Ready for Surgery</td>
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<tr>
<td>– Liver Resection</td>
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<td>– Cryosurgery for Liver Tumors</td>
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<td>– Handling Fatigue During and After Cancer Treatment</td>
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<td>– Radiofrequency Ablation</td>
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<td>– The Implanted Liver Infusion Pump</td>
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<td>– Patient-Controlled Anesthesia</td>
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<td>– Common Medications Containing Aspirin</td>
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<td>– Bowel Preparation</td>
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<tr>
<td>Information from interactive CD-ROMs and booklets are reviewed with patients at the authors’ institution in person. Preoperative teaching includes preparation for surgery (including bowel preparation) and expectations for postoperative care. Questions are encouraged and answered. Medication history is reviewed. Patients are encouraged to call with any additional questions.</td>
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<tr>
<td>Emotional support is provided. Patients are encouraged to verbalize feelings.</td>
<td>Patients often are anxious during diagnoses and surgical and interventional treatments. Listening to patients and providing empathy can be valuable to patients and their families (Northouse &amp; Mellon, 1998).</td>
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<tr>
<td>Vital signs are monitored.</td>
<td>Increased temperature may indicate lung atelectasis, wound infection, biloma, or abscess (Burke, 1999; Rychcik, 2000).</td>
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<td>Aggressive chest physical therapy, including deep breathing exercises, is begun postoperation.</td>
<td>Risk of pneumonia is reduced. Patients who undergo hepatic resection are at risk for pulmonary complications because of the high transverse incision necessary to safely access liver tumors (Burke, 1999; Fong, 1999; Fong &amp; Salo, 1999; Tono, Hasuike, Ohzato, Takatsuka, &amp; Kikkawa, 2000).</td>
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<tr>
<td>Pain medication is administered via patient-controlled analgesia pump. Once oral intake is resumed, oral analgesics are administered.</td>
<td>Pain control enables patients to perform necessary recovery activities such as walking and deep breathing exercises (Burke, 1999).</td>
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<tr>
<td>Strict inputs and outputs</td>
<td>Fluid and electrolyte imbalances can indicate renal insufficiency resulting from liver failure or fluid overload. Measuring inputs and outputs and daily weights enable monitoring of the fluid balance and need for fluid replacement or diuretic therapy (Burke, 1999).</td>
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<tr>
<td>Daily weights</td>
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<td>Daily blood work, including complete blood count, comprehensive chemistry panel, and prothrombin time (PT)</td>
<td>Elevated serum bilirubin may indicate biloma, biliary obstruction, or liver failure. During liver regeneration, phosphorus frequently is decreased and PT often is increased. Phosphorus is replaced as needed. An elevated PT is managed with the administration of fresh, frozen plasma and vitamin K (Rychcik, 2000). Depending on intraoperative blood loss, transfusion therapy may be required (Burke, 1999).</td>
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<tr>
<td>Assess incision daily. It usually can be open to air on day two postoperation.</td>
<td>Early signs and symptoms of infections can be detected promptly (Burke, 1999).</td>
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<tr>
<td>Nurses contact patients at home postdischarge.</td>
<td>Assess condition over the phone and answer any questions that patients may have. Patients are instructed to report any signs and symptoms of infection or any other problems that may occur. A follow-up appointment is made for patients within two weeks of discharge.</td>
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Nursing Management

Expert nursing management is essential in caring for patients undergoing treatment of MCR with surgical and ablative modalities. Preoperative and preprocedure nursing assessment and education are performed in the ambulatory care setting. The nursing management that is required postoperatively or postprocedure depends on the procedure performed. For example, patients undergoing liver resection will spend at least 24 hours in the postanesthesia care unit or surgical intensive care setting (Rychik, 2000). Patients who undergo percutaneous radiofrequency ablation in the interventional radiology suite will be monitored in the recovery area for several hours prior to going to the inpatient unit. After patients return to the surgical unit, they require careful observation and assessment for postoperative or postprocedure complications. Table 1 describes typical nursing management of this patient population.

Summary

The liver is the most common and often the only site of metastatic disease for patients with colorectal cancer. Complete resection remains the only potentially curative treatment option. When liver resection is not an option, ablative techniques may be useful. Ablative techniques such as cryosurgery and radiofrequency ablation are used in patients with medical contradictions to liver resection, small unresectable recurrences after previous resection, and bilobar unresectable cancers. Their efficacy is under investigation. In addition to investigational chemotherapy, many clinical trials for MCR are in progress or on the horizon, including epidermal growth factors, molecularly targeted therapies, and oncolytic viral therapies. For all patients with MCR, expert nursing care is necessary to provide patient education, emotional support, assessment, and management of potential complications. The large number of patients with hepatic metastases, in addition to the complex treatment options available, has increased the importance and challenges of the nursing role in caring for this patient population.

References


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Rapid Recap

Surgical and Ablative Modalities for the Treatment of Colorectal Cancer Metastatic to the Liver

- The liver is the most common and often the only site of metastatic disease for patients with colorectal cancer.
- Death from colorectal cancer usually results from metastatic disease to the liver.
- Complete surgical resection is the only potential cure for metastatic colorectal cancer (MCR) to the liver, with a five-year survival rate of approximately 30%-40%.
- Ablative therapies including cryosurgery and radiofrequency ablation may be useful in patients when complete resection is not an option.
- Expert nursing care of patients with MCR is necessary to provide patient education, emotional support, and assessment and management of potential complications.


