Colon Cancer

Elizabeth Hechenbleikner, MD, and Elizabeth Wick, MD, FACS

BACKGROUND AND EPIDEMIOLOGY

Colorectal cancer arises from the epithelial lining of the colon or rectum, with roughly 75% of cases occurring in the colon and 25% in the rectum. Colon cancer is one of the most commonly diagnosed cancers and a leading cause of cancer death in the United States. There is considerable geographic variation in colon cancer incidence, both within the United States and across the world, with increased incidence associated with developed and developing countries. Differences in diet, physical activity, and access to healthcare services are some of the proposed reasons for this regional variation. Most colon cancers are sporadic adenocarcinomas diagnosed in adults over the age of 50 years. In the United States, over the past decade, a consistent decline has been seen in colon cancer incidence rate in adults greater than 50 years old; however, in adults under the age of 50 years, the incidence rate has been rising nearly every year since 1992. Colon cancer mortality has also been decreasing in the United States, but disproportionately fewer white patients die from colon cancer as compared with African American patients, regardless of cancer stage. Because screening colonoscopy is not recommended until 50 years of age for individuals at average risk, colon cancers in younger patients generally present later, when symptoms such as abdominal pain or bloating develop. Timely screening colonoscopy is paramount for the early detection and potentially curative treatment for premalignant (adenomatous) and malignant lesions.

SCREENING RECOMMENDATIONS

Colonoscopy is considered the gold standard among colon cancer screening techniques because it is highly sensitive and allows for biopsy of abnormal areas and polyp removal. Overall screening colonoscopy rates are improving but continue to fall short of recommended levels in the United States, with cost and fear of the procedure and bowel preparation the major barriers to widespread adoption. Key goals during colonoscopy are to visualize the entire colon, including adequate cecal inspection, and to identify and remove all polyps. Two common screening tests that are less expensive than colonoscopy are the fecal occult blood test (FOBT) and flexible sigmoidoscopy. FOBT is less sensitive than colonoscopy, and sigmoidoscopy only visualizes the lower one third of the colon; however, decreased colon cancer mortality has been associated with regular use of FOBT and one-time screening sigmoidoscopy in select patients. Another test that has been available since the 1990s is computed tomographic colonography (CTC) or virtual colonoscopy. CTC, which still requires a bowel preparation, has been shown in some settings to be as effective as colonoscopy for detection of tumors 1 cm in size or larger.

Screening recommendations are based on one's lifetime risk of development of colon cancer. Most individuals have no identifiable risk factors and are considered average risk, with a 5% to 6% lifetime risk of colon cancer. In patients at average risk who are 50 years of age or older, the 2008 joint guidelines from the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology recommend: (1) annual FOBT; (2) flexible sigmoidoscopy every 5 years; (3) flexible sigmoidoscopy every 5 years with annual FOBT; (4) colonoscopy every 10 years; or (5) double-contrast barium enema every 5 years. In the 2008 joint guidelines, CTC was endorsed as a suitable screening option for those who decline or cannot tolerate colonoscopy, but the timing of repeat examinations is still uncertain. Moreover, a positive finding on FOBT, sigmoidoscopy, double-contrast barium enema, or CTC mandates follow-up colonoscopy.

About 25% of the population is at increased or moderate risk of development of colon cancer because of a personal or family history of colon cancer or adenomatous polyps. In this group, timing of colonoscopy screening examinations varies based on the individual's clinical situation. For example, patients with three to 10 adenomas or one adenoma larger than 1 cm or with high-grade dysplasia should have all lesions removed at initial colonoscopy, with a repeat examination within 3 years. In individuals with first-degree relatives with colon cancer diagnosed before the age of 60 years, colonoscopy should begin either at age 40 years or 10 years before the youngest diagnosed family member, with follow-up colonoscopy every 5 years.

Approximately 6% to 8% of the population is at high risk of development of colon cancer because of a hereditary syndrome like familial adenomatous polyposis (FAP) or hereditary nonpolyposis colon cancer (HNPCC) or a chronic medical condition like inflammatory bowel disease (IBD). Patients with suspected hereditary colon cancer should undergo genetic testing and counseling. Individuals with known or suspected FAP should undergo yearly flexible sigmoidoscopy or colonoscopy starting in childhood (age 10 to 12 years) until prophylactic or therapeutic total colectomy or proctocolectomy is deemed appropriate. Patients with HNPCC should have screening colonoscopies every 1 to 2 years starting in early adulthood (age 20 to 25 years) or 10 years before the youngest immediate family member with colon cancer. Patients with IBD should undergo screening colonoscopies with biopsies for dysplasia every 1 to 2 years after 8 years of pancolitis or 12 to 15 years of left-sided colitis.

PRESENTATION, DIAGNOSIS, AND WORKUP

Early colon cancer typically has no symptoms but may be discovered with a positive FOBT and subsequent colonoscopy. As the primary lesion enlarges, a change in bowel habits may be seen, such as decreasing stool caliber or rectal bleeding. Patients with late or advanced colon cancer often present with fatigue, weight loss, iron-deficiency anemia, or abdominal pain. Presenting symptoms may differ in patients with early or advanced colon cancer based on the location of the tumor. Right-sided tumors have a tendency to present with anemia; left-sided lesions are more likely to cause abdominal pain, obstruction, or rectal bleeding. Interestingly, various studies since the 1980s have reported an increasing percentage of right-sided colon cancers, perhaps in part because of increased colonoscopy utilization and different tumor biology and environmental factors that are currently under investigation.

When a patient is diagnosed with colon cancer, a thorough evaluation is required to establish the proper treatment. Medical comorbidities should be identified as should pertinent family history to rule out hereditary cancer syndromes. Complete colonoscopy with biopsies must be performed to confirm and tattoo the primary lesion along with any synchronous lesions. When a sporadic colon cancer is diagnosed, there is a 6% to 8% chance of having a synchronous lesion. Computerized tomographic (CT) scan of the abdomen and pelvis is done to evaluate the presence of metastases and adjacent organ invasion from the primary tumor. Chest x-rays should also be performed, and abnormal findings usually require chest CT scanning. Approximately 20% of patients in the United States present with metastatic disease, with the liver, lung, and peritoneum as the most common sites. Currently, the National Comprehensive Cancer Network (NCCN) does not recommend positron emission

tomography with CT scan for the initial staging of a primary colon cancer intended for surgical resection. Regarding laboratory data, a baseline serum carcinoembryonic antigen (CEA) level should be measured before treatment, particularly surgical resection. After surgical resection, CEA levels that do not normalize or subsequently become elevated indicate inadequate tumor resection, recurrence, or progression of disease and require further evaluation. Serum electrolytes, liver function tests, and a complete blood count are part of a standard workup, along with a proper nutrition assessment, and should be optimized before surgery whenever possible.

SURGICAL RESECTION AND STAGING

Surgical resection is the foundation of curative treatment for localized colon cancer and select patients with limited metastatic disease. Approximately 75% of patients are candidates for potentially curative surgical resection at the time of diagnosis. Ten percent to 25% of patients with isolated liver metastases are operative candidates. The goal of surgery is to achieve an appropriate oncologic resection, ideally an R0 resection, while minimizing complications like infection, hemorrhage, and sexual or urinary dysfunction. The abdomen should be thoroughly explored and any extracolonic tumor spread to the liver, omentum, hemidiaphragm, abdominal wall, or pelvis identified, along with careful palpation of the entire large bowel. The involved colonic segment should be completely removed with a 2-cm to 5-cm margin and en bloc resection of any local structures or organs invaded by the primary tumor. The major vascular pedicle and lymphatic drainage basins of the involved colonic segment should be removed in a curative resection. Per NCCN guidelines, a minimum of 12 lymph nodes are required for accurate assessment of nodal involvement. Bowel continuity should be restored when possible with a well-vascularized, tension-free anastomosis.

Selection of the appropriate surgical procedure is based on the location of the primary tumor and the presence of synchronous lesions or a hereditary cancer syndrome. The vascular supply to the involved colonic segment dictates the extent of resection. Removal of the appropriate vascular supply should ensure adequate lymphadenectomy. A right colectomy is performed for cancers of the cecum, ascending colon, and hepatic flexure. In this procedure, the ileocolic artery is ligated, as is the right colic artery if present, and the terminal ileum is transected roughly 10 to 15 cm proximal to the ileocecal valve (Figure 1). The transverse colon is divided proximal to the right branch of the middle colic artery (MCA), which can be ligated if necessary. An extended right or, in some instances, transverse colectomy can be performed for tumors in the mid transverse colon. For an extended right colectomy, the ileocolic and MCA are ligated at their origin; for a transverse colectomy, only the MCA is ligated. In this case, an anastomosis is created between either the ileum (extended right colectomy) or the ascending (transverse colectomy) and distal transverse colon. A transverse colectomy requires mobilization of both the hepatic and the splenic flexure to allow for adequate reach and a tension-free anastomosis. Splenic flexure tumors can be treated with either a subtotal colectomy or, if adequate mobility is present, a left colectomy. Descending colon cancers and select proximal sigmoid colon cancers are managed with a left colectomy with a descending to sigmoid or rectal anastomosis. With a left colectomy, the inferior mesenteric artery (IMA) should be ligated high near the aorta to allow for a tension-free anastomosis. The inferior mesenteric vein can be ligated just below the duodenum if additional mobility is needed. Sigmoid cancers are treated with a sigmoid colectomy and high ligation of the IMA (see Figure 1).The splenic flexure should be mobilized for left colon resections to ensure creation of a tension-free anastomosis. In the case of patients with synchronous colon cancers or a hereditary cancer syndrome, a total abdominal colectomy with ileorectal anastomosis may be warranted.

The most important prognostic factor after surgical resection is the pathologic stage. The tumor node metastasis (TNM) classification system developed and maintained by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) is the most universally used staging system for colon and rectal malignant diseases. Table 1 includes the most updated TNM staging for colorectal cancer. Colon cancer is localized to the bowel wall in stage I and II, regionally spread in stage III (i.e., lymph node involvement), and distantly spread or metastatic in stage IV. The 5-year survival rate decreases with stage progression: (1) stage I, 70% to 95%; (2) stage II, 54% to 65%; (3) stage III, 39% to 60%; and (4) stage IV, 0 to 16%. The risk of regional lymph node spread correlates with bowel wall penetration by the primary tumor (T status). Primary tumors limited to the submucosa have a 10% risk of regional spread, whereas those penetrating to the subserosa have a 45% risk. Extent of nodal metastases (N status) is the most important determinant for long-term survival and treatment planning. Inadequate lymphadenectomy is a poor prognostic indicator in localized and regionally spread colon cancers. Lymph node retrieval can be difficult but is facilitated by high ligation of vasculature. Too few lymph nodes can lead to understaging and thus inappropriate adjuvant treatment. Moreover, accurate histologic assessment of lymph nodes can vary markedly based on the pathologist's technique and skill.

OPEN VERSUS LAPAROSCOPIC COLECTOMY

Open colectomies are typically performed through a midline incision with the patient supine for right colon resections and in modified lithotomy position for left colon resections. The right or left colon is mobilized off the retroperitoneum via a lateral-to-medial approach. This approach begins in an avascular plane known as the white line of Toldt (the lateral reflection of parietal peritoneum). Peritoneal attachments at the hepatic or splenic flexure are taken with electrocautery, clipping, or suture ligation with care to avoid undue traction, which can cause avulsion injuries. The transverse colon is mobilized as far as required for an adequate oncologic resection and to facilitate bowel anastomosis, and a portion of the omentum near the tumor is removed with the specimen. The vascular supply is divided and ligated at the base of the mesentery based on tumor location as previously described. A hand-sewn or stapled bowel anastomosis is performed per surgeon preference with no significant difference in complications or outcomes. For transverse colectomy, the greater omentum is removed with the specimen.

Laparoscopic colectomy offers many advantages over traditional open surgery. Postoperative pain and length of hospital stay are significantly reduced, but oncologic outcomes remain similar for localized colon cancer. Correct patient positioning is an integral part of successful laparoscopic colectomy. The patient is secured supine for right colectomies and in the modified lithotomy position with minimal hip flexion and legs in padded stirrups for left colectomies. The patient must be secured to the bed with a strap to prevent the patient from slipping because the bed is frequently repositioned to facilitate laparoscopic dissection. For right colectomy via a lateral-to-medial approach, four basic ports can be placed as follows: an umbilical camera port and three working ports in the left upper quadrant, left lower quadrant, and suprapubic midline (Figure 2, *A*). Similarly for left colectomy, a four-trocar technique can be set up as follows: an umbilical camera port and three working ports in the right upper quadrant, right lower quadrant, and suprapubic midline (Figure 2, *B*). Additional ports can be placed to optimize exposure based on surgeon preference.

Passive exposure of the colon is achieved with steep Trendelburg's positioning and rotating the table away from the anatomic location of the tumor. The small bowel and omentum are moved into the upper abdomen. The colon can be mobilized via a lateral-to-medial or medial-to-lateral approach. In the latter, the main vascular pedicles are divided first followed by complete mobilization and transection of the involved colonic segment. The colon can then exteriorized

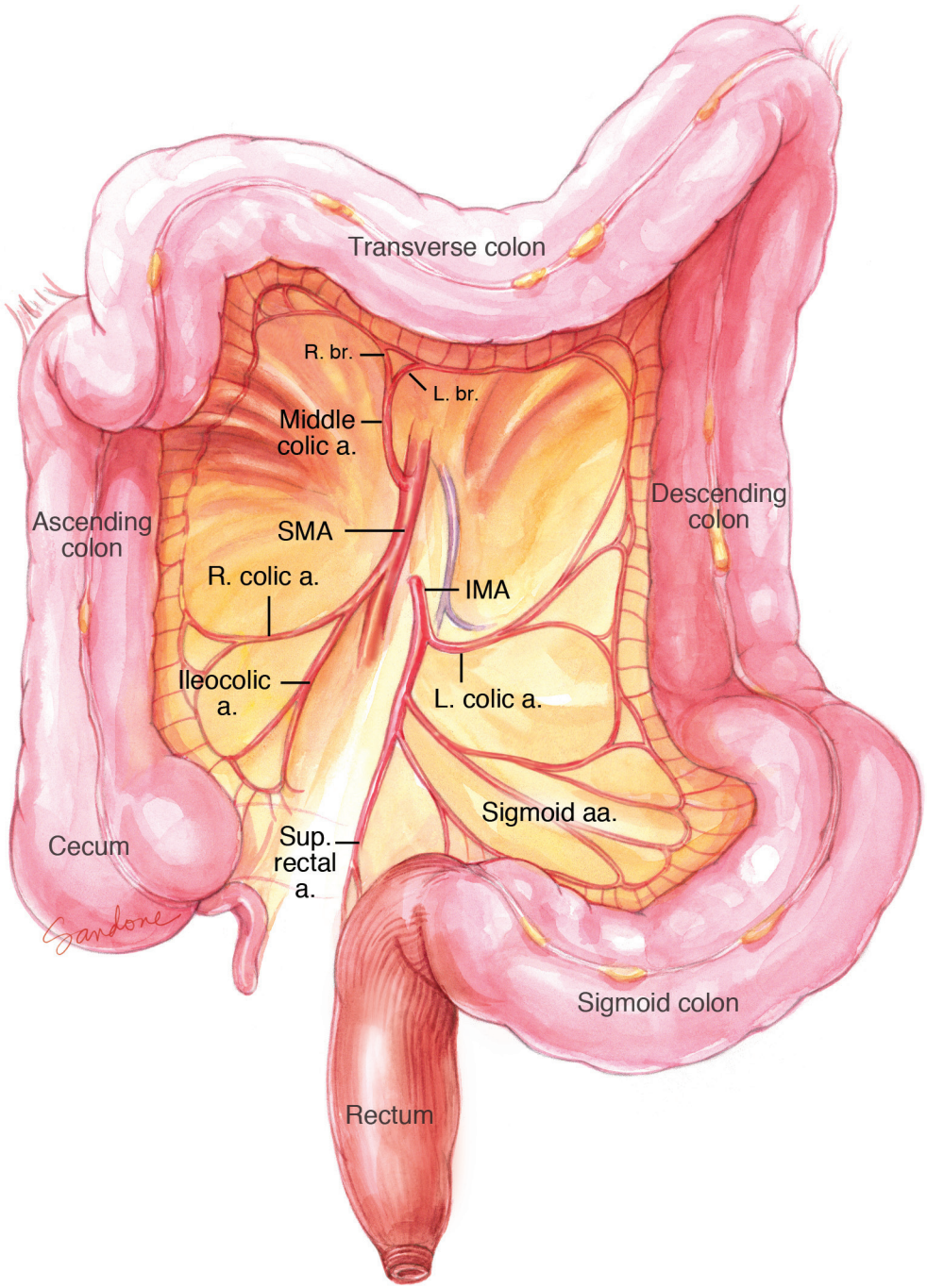

FIGURE 1 Different segments of the colon with the corresponding vascular supply. *a.,* Artery; *aa.,* arteries; *IMA,* inferior mesenteric artery; *L.,* left; *R.,* right; *R. br.,* right branch of middle colic artery; *L. br.,* left branch of middle colic artery; *SMA,* superior mesenteric artery; *Sup. Rectal,* superior rectal. *(Illustration used with permission from Cameron JL, Sandone C:* Atlas of gastrointestinal surgery, *ed 2, vol II, 2012, Shelton, CT, PMPH-USA.)*

through either an enlarged trocar incision or a separate incision followed by extracorporeal anastomosis. Hand-assist ports can also be used for bulky tumors or difficult patient anatomy. Hallmark anatomic complications include injury to the ureters (right and left colectomy), duodenum (right colectomy), and spleen (left colectomy). When recognized during surgery, all injuries should be repaired immediately with conversion to an open procedure as necessary. Roughly 30% of ureteral injuries involve the distal ureter, and most can be repaired with ureteroneocystostomy and stent placement. Iatrogenic splenic injury is uncommon and usually involves a capsular tear from excessive traction. Splenic salvage should be attempted with packing, topical hemostatic agents, or suture repair. If bleeding persists and is uncontrollable, splenectomy is required.

CHALLENGING AND COMPLICATED CASES

The location of the primary tumor predisposes patients to specific complications like malignant duodenocolic fistula in the setting of transverse colon cancers. If the cancer is localized, surgical management includes a right hemicolectomy and pancreaticoduodenectomy

TABLE 1: Tumor node metastasis (TNM) staging system for colorectal cancer

Anatomic stage/prognostic groups					
Stage	*T*	*N*	*M*	*Dukes**	*MAC**
0	Tis	N0	M0	—	—
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1-T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3-T4a	N1/N1c	M0	C	C2
	T2-T3	N2a	M0	C	C1/C2
	T1-T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3-T4	N2b	M0	C	C2
	T4b	N1-N2	M0	C	C3
IVA	Any T	Any N	M1a	—	—
IVB	Any T	Any N	M1b	—	—

Note: *cTNM* is the clinical classification, and *pTNM* is the pathologic classification. The *y* prefix is used for those cancers that are classified after neoadjuvant pretreatment (e.g., ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to stage group 0 or 1. The *r* prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).

*Dukes *B* is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes *C* (and TN1 M0 and any T N2 M0). MAC is the modified Astler-Coller classification.

Primary tumor (T): *T0,* no evidence of primary tumor; *Tis,* carcinoma in situ: intraepithelial or invasion of lamina propria; *T1,* tumor invades submucosa; *T2,* tumor invades muscularis propria; *T3,* tumor invades through muscular propria into pericolorectal tissues; *T4a,* tumor penetrates to the surface of the visceral peritoneum; *T4b,* tumor directly invades or is adherent to other organs or structures.

Regional lymph nodes (N): *N0,* no regional lymph node metastasis; *N1,* metastasis in one to three regional lymph nodes; *Nla,* metastasis in one regional lymph node; *Nlb,* metastasis in two to three regional lymph nodes; *Nlc,* tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis; *N2,* metastasis in four or more regional lymph nodes; *N2a,* metastasis in four to six regional lymph nodes; *N2b,* metastasis in seven or more regional lymph nodes.

Distant metastasis (M): *M0,* no distant metastasis; *M1,* distant metastasis; *M1a,* metastasis confined to one organ or site (e.g., liver, lung, ovary, nonregional node); *M1b,* metastasis in more than one organ/site or the peritoneum.

American Joint Committee on Cancer: AJCC cancer staging manual, *ed 7, New York, 2010, Springer.*

or segmental duodenectomy (en bloc). Ascending colon cancers invading the right kidney require right hemicolectomy with en bloc partial or total nephrectomy. Malignant colovesical fistulae can occur in the setting of sigmoid colon cancers. Surgical management in this setting is often a sigmoid colectomy or Hartmann's procedure (rectosigmoid colon resection with rectal stump closure and end colostomy) with en bloc partial cystectomy, but total pelvic exenteration may be required for extensive tumors or those involving the prostate. Advanced colon cancers can also involve the ovaries. Oophorectomy is recommended during colon cancer resection if the ovaries look grossly abnormal, are invaded by the primary tumor, or have known metastases. Ovarian metastases develop in less than 15% of women with colon cancer, and prognosis is generally poor. Routine prophylactic oophorectomy is not recommended unless there are pertinent risk factors, such as a history of HNPCC or a breast cancer susceptibility (BRCA) gene mutation.

Although most colon cancer resections are elective, some patients present emergently if there is acute obstruction or perforation. Emergent surgery in this setting is associated with high morbidity and mortality. Surgical management is based on the location of the obstructing lesion. One-stage right hemicolectomy with primary anastomosis is the preferred approach for right-sided lesions. Left-sided colonic obstructions can be challenging to manage, and the optimal approach is somewhat controversial. The historically advocated three-stage approach is as follows: defunctioning colostomy (first stage), primary resection of colon tumor (second stage), and colostomy closure (third stage). Given the morbidity associated with three operations, this approach is now typically reserved for cases where neoadjuvant treatment is needed to facilitate an R0 resection. More recently, a Hartmann's procedure was the operation of choice for patients presenting with colorectal cancer (CRC) and acute obstruction, but now, surgeons favor resection with primary anastomosis with or without a diverting loop ileostomy for patients with hemodynamically stable conditions and acute presentations. Sometimes an on-table, intraoperative colonic lavage can be done to facilitate primary anastomosis in the patient with obstruction. When patients with left-sided colon cancers present with obstruction, the entire colon can be very dilated and the cecum, the area of the colon with the thinnest wall, can even perforate. In this case, a subtotal colectomy may be indicated. Colonic stents have been available since the 1990s and can be used when appropriately skilled endoscopists are available, usually for left-sided cancers. Stents are used for palliation in unresectable cases or as a temporizing measure to allow for proper staging workup so that a definitive treatment plan can be determined.

The role of surgery in metastatic colon cancer continues to evolve. Patients with liver-only metastasis should be offered surgical resection when feasible because this offers the greatest likelihood of cure. Five-year survival rates after surgical resection range from 24% to 58%, with median survival times averaging approximately 35 to 40 months. Resectability is defined as the ability to remove all macroscopic tumor tissue (R0 resection) while maintaining adequate inflow, outflow, and remnant liver parenchyma. High-quality cross-sectional CT imaging with three-dimensional volume rendering is routinely used to determine tumor resectability. When hepatic resection is not feasible, other nonextirpative treatment options include radiofrequency ablation (RFA), hepatic artery infusion (HAI) chemotherapy, transarterial chemoembolization (TACE), and transarterial brachytherapy. The integration of chemotherapy with liver surgery for the treatment of stage IV colon cancer has increased the complexity of patient treatment. Patients with initially resectable liver metastases may be given chemotherapy in the neoadjuvant or adjuvant setting with the goal of improving curability and survival by eliminating occult micrometastatic disease. Patients with initially unresectable liver disease are sometimes given neoadjuvant chemotherapy to convert metastases to resectable lesions. The timing of liver resection in patients with metastases is a controversial issue. A one-stage approach with combined colon and hepatic resection is a reasonable option for patients with low-volume liver metastases who can tolerate simultaneous procedures. Complications with the primary tumor such as perforation or bleeding take priority and delay liver resection until further workup is completed. Bilobar liver metastases or questionably resectable lesions should be managed

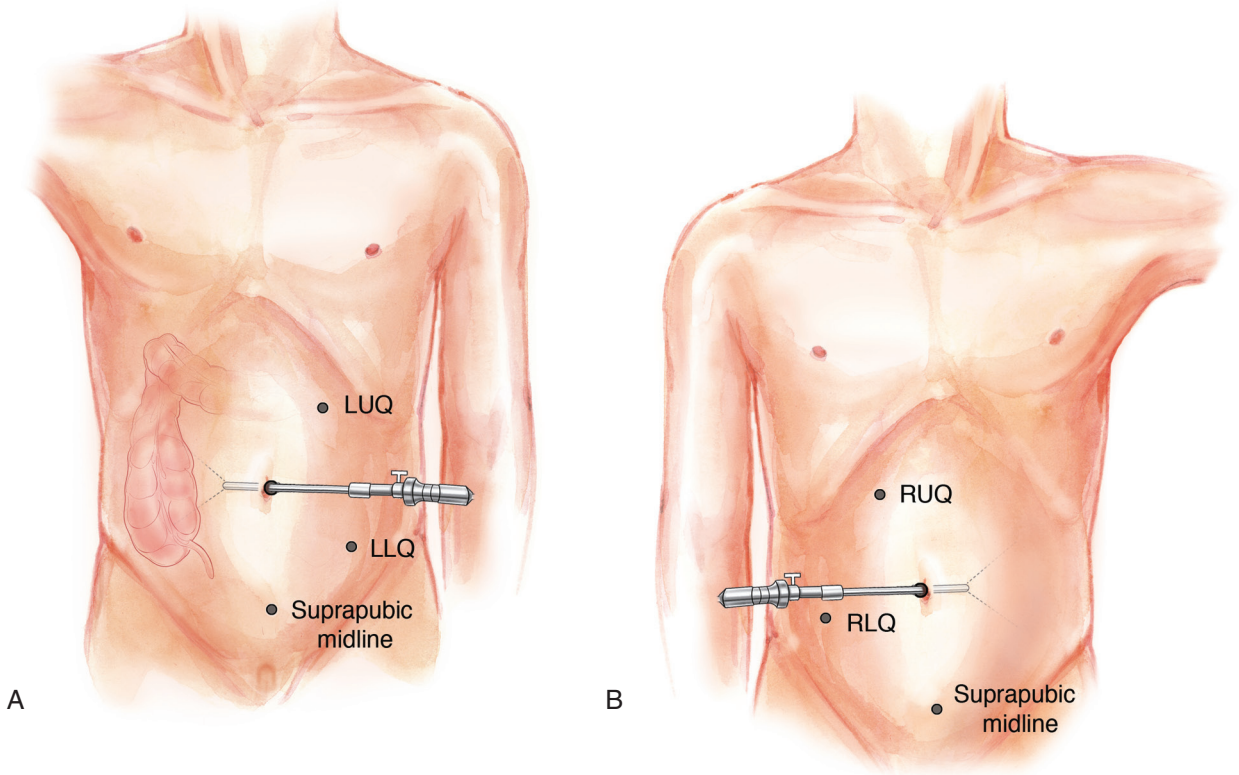

FIGURE 2 Laparoscopic port placement sites for right colectomy **(A)** and left colectomy **(B)**. *LLQ,* Left lower quadrant; *LUQ,* left upper quadrant; *RLQ,* right lower quadrant; *RUQ,* right upper quadrant. *(Illustration used with permission from Cameron JL, Sandone C:* Atlas of gastrointestinal surgery, *ed 2, vol II, 2012, Shelton, CT, PMPH-USA.)*

with delayed hepatic resection after primary tumor resection and chemotherapy.

ADJUVANT TREATMENT

Multiple options exist for systemic chemotherapy after complete resection of primary colon cancer. In contrast, postoperative radiation therapy is rarely indicated because of the risk of toxicity to the small intestine. Radiation therapy is sometimes used to irradiate the tumor bed in cases where the primary lesion invades local structures and there is an incomplete resection. Since the 1960s, 5-fluorouracil (5-FU) with leucovorin (LV) has been the cornerstone of first-line therapy for stage III colon cancer in the adjuvant setting and has been shown to decrease recurrence rates by 40%. Oxaliplatin combined with 5-FU and LV (FOLFOX) has shown even further benefit and is now standard of care for stage III disease. NCCN guidelines currently recommend 6 months of adjuvant chemotherapy. Certain stage II colon cancers are considered high risk for recurrence because of poor prognostic features like perforation, poor tumor differentiation, or histologic evidence of lymphovascular invasion. Postoperative chemotherapy should be considered in this subset of patients with stage II disease.

Increasing knowledge about the genetic diversity of colon cancers has facilitated the use of targeted adjuvant therapies in select patients. KRAS (v-Ki-ras2 Kirsten rat sarcoma viral homolog) gene molecular testing opened the era for targeted treatments. Only wild-type KRAS tumors respond to anti–epidermal growth factor receptor (EGFR) monoclonal antibodies like cetuximab. Up to 50% of colon cancers harbor a KRAS mutation, which indicates that roughly 50% of patients may benefit from this therapy. For KRAS wild-type tumors, further testing should establish BRAF (v-raf murine sarcoma viral homolog B1) gene mutation status because some data suggest that anti-EGFR agents have limited efficacy in patients with BRAF mutation.

SURVEILLANCE AND FOLLOW-UP

Intensive surveillance is important in the first 2 to 3 years after primary colon cancer resection because most patients have recurrence during this time. The goal is to identify patients with metachronous cancers or recurrent disease early so that appropriate treatment is given. Follow-up colonoscopy is recommended within 1 year of resection. If results are normal, repeat colonoscopies are generally done at 3-year intervals. Any abnormal findings mandate modification to the colonoscopy interval based on appropriate screening guidelines. A history and physical examination with a serum CEA test should be done every 4 months for the first 2 to 3 years, every 6 months for 2 years, and annually thereafter. Per NCCN guidelines, annual CT scan of the chest, abdomen, and pelvis should be considered for the first 3 years in individuals at high risk, such as patients with stage III disease or stage II disease with poor prognostic features.

SUGGESTED READINGS

American Cancer Society: *Colorectal cancer facts & figures 2011-2013*, Atlanta, 2011, American Cancer Society.

Ansaloni L, Andersson RE, Bazzoli F, et al: Guidelines in the management of obstructing cancer of the left colon: consensus conference of the world society of emergency surgery (WSES) and peritoneum and surgery (PnS) society, *World J Emerg Surg* 5(29):1–10, 2010.

Chang GJ, Kaiser AM, Mills S, et al: Practice parameters for the management of colon cancer, *Dis Colon Rectum* 55(8):831–843, 2012.

Choti MA, Sitzmann JV, Tiburi MF, et al: Trends in long-term survival following liver resection for hepatic colorectal metastases, *Ann Surg* 235(6):759–766, 2002.

Landmann RG, Weiser MR: Surgical management of locally advanced and locally recurrent colon cancer, *Clin Colon Rectal Surg* 18(3):182–189, 2005.

Levin B, Lieberman DA, McFarland B, et al: Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology, *Gastroenterology* 134(5):1570–1595, 2008.

National Comprehensive Cancer Network: *NCCN clinical practice guidelines in oncology: colon cancer,* version 3.2013, Fort Washington, PA, 2013.

Nelson H, Sargent D, Wieand HS, et al, COST Study Group: A comparison of laparoscopically assisted and open colectomy for colon cancer, *N Engl J Med* 350:2050–2059, 2004.