CA-125 levels, although a recent trial suggested that such monitoring might result in earlier initiation of treatment for recurrence, but no difference in overall survival. Imaging studies and other blood tests are reserved for addressing specific clinical concerns. If not given on initial diagnosis, a referral for genetic counseling should be provided at initial follow-up.

KEY POINT

HVC
- Follow-up for patients who have completed treatment for ovarian cancer includes a periodic history, physical examination, and pelvic examination for 5 years after treatment; routine monitoring of CA-125 levels, other laboratory testing, and imaging studies does not improve survival and should be reserved for addressing specific clinical concerns.

Management of Recurrent Ovarian Cancer

More than 70% of women with advanced ovarian cancer will experience a relapse after first-line chemotherapy, and recurrent ovarian cancer is not curable. The goal of treatment of recurrent ovarian cancer is to improve cancer-related symptoms and extend survival. Discussion and shared decision making about goals of care and referral to a palliative care team are appropriate in the management of patients with recurrent disease.

Secondary cytoreductive surgery is best considered for patients with a progression-free interval of at least 12 months, good performance status, and a local recurrence that can potentially be rendered free of gross disease with surgery.

An elevated serum CA-125 level in a patient with a normal physical examination and CT scan and no disease symptoms constitutes the most common presentation at relapse. Patients with an isolated serum CA-125 recurrence who are not comfortable with surveillance alone can be treated with tamoxifen or an aromatase inhibitor. Initiating cytotoxic treatment confers no known benefit in this setting.

Cytotoxic chemotherapy is indicated for patients with significant disease on CT scan or physical examination or in those with disease progression–related symptoms. Treatment options include single-agent or combination chemotherapy, often involving a platinum agent if the cancer has not developed resistance, as well as anti-angiogenesis inhibitors such as bevacizumab.

Ascites can be managed with periodic paracentesis for symptomatic relief. Patients with bowel obstruction from advanced ovarian cancer are unlikely to benefit from surgery. Chemotherapy benefit in patients with bowel obstruction is often limited, and treatment should focus on comfort and palliation.

KEY POINTS

- The goal of treatment of recurrent ovarian cancer is to improve cancer-related symptoms and extend survival.
- Secondary cytoreductive surgery is best considered for patients with ovarian cancer and a progression-free interval of at least 12 months, good performance status, and a local recurrence that can potentially be rendered free of gross disease with surgery.

Cervical Cancer

Epidemiology and Risk Factors

Over 12,000 new cases of invasive cervical cancer and approximately 4000 cervical cancer–related deaths occur in the United States each year. The mean age at diagnosis is 48 years. Invasive cervical cancer incidence in the United States has decreased by more than 80% since the 1940s, largely owing to Pap smear screening. The incidence and mortality rates are higher in countries lacking screening programs.

Nearly all cases of cervical cancer are precipitated by persistent human papillomavirus (HPV) infection. HPV, most commonly subtypes 16 and 18, is detected in more than 99% of patients with cervical cancer. Both squamous cell carcinoma and adenocarcinoma are associated with HPV infection. The HPV vaccine is ideally given before sexual activity begins: if given to adolescents and young women before they develop HPV infection, it is 90% effective at preventing infection and 97% to 100% effective at preventing cervical intraepithelial neoplasia and invasive cervical cancer.

Cervical Pap smears can detect precancerous lesions that occur several years before the development of invasive disease. See MKSAP 17 General Internal Medicine for cervical cancer screening guidelines and HPV vaccine recommendations.

KEY POINTS

- Nearly all cases of cervical cancer are precipitated by human papillomavirus infection (subtypes 16 and 18).
- The human papillomavirus vaccine, given before infection develops, is 90% effective at preventing infection and 97% to 100% effective at preventing cervical intraepithelial neoplasia and invasive cervical cancer. HVC

Diagnosis, Staging, and Treatment

The most common presenting symptoms of cervical cancer are abnormal vaginal discharge, postcoital bleeding, or vaginal bleeding between menstrual cycles or after menopause. Diagnosis of cervical cancer is established by biopsy of the cervix. Colposcopy with directed biopsy is done if there is no visible lesion, with cervical conization done if colposcopy is nondiagnostic. The most common histologies are squamous cell carcinoma (69% of cervical cancers) and adenocarcinoma (25%).

Staging, most often performed using the International Federation of Gynecology and Obstetrics system (**Table 57**), is done clinically and includes a pelvic examination and chest radiograph. CT, MRI, and PET/CT are often useful in planning therapy, although they are not part of the formal staging evaluation.

Primary treatment of cervical cancer based on clinical stage is outlined in Table 57. Chemotherapy given with radiation therapy improves survival in patients with intermediate-risk and high-risk cervical cancer but not in the neoadjuvant or adjuvant setting.

KEY POINTS

- The most common presenting symptoms of cervical cancer are abnormal vaginal discharge, postcoital bleeding, or vaginal bleeding between menstrual cycles or after menopause.
- Chemotherapy given with radiation therapy improves survival in patients with intermediate- and high-risk cervical cancer but not in the neoadjuvant or adjuvant setting.

Prognosis and Surveillance

The most important prognostic factor in cervical cancer is clinical stage followed by involvement of pelvic or paraaortic lymph nodes. The 5-year overall survival rate is 90% to 95% for patients with early-stage clinical disease and negative lymph nodes; the survival rate in patients with positive lymph nodes decreases to 70%. Patients with regionally advanced tumors have a 40% to 50% survival rate at 5 years.

Surveillance of patients with cervical cancer includes clinical evaluation every 3 to 6 months for 2 years, followed by evaluation every 6 months until year 5, and then annually. Surveillance evaluation should include a history, physical examination, and pelvic examination with cervicovaginal cytology. Yearly chest radiography is optional, and other imaging is done only as clinically indicated. In appropriate candidates, localized pelvic recurrence may be cured with pelvic exenteration.

KEY POINT

- In patients with cervical cancer, surveillance evaluation (a history, physical examination, and pelvic examination with cervicovaginal cytology) should occur every 3 to 6 months for 2 years, followed by evaluation every 6 months until year 5, and then annually.

TABLE 57. International Federation of Gynecology and Obstetrics Cervical Cancer Staging

Stage	Treatment
I: Carcinoma is strictly confined to the cervix	I: Radical hysterectomy or radiation; ovarian preservation can be done if fertility desired
IA: Microscopic disease only	IA: Simple hysterectomy, cone biopsy, or removal of cervix alone are options
IIA (nonbulky) and IIB (bulky): Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or lower third of the vagina	IIA: same as for stage I IIB: same as for stage III
III: The tumor extends to the pelvic wall and/or involves the lower third of the vagina and/or causes hydronephrosis or nonfunctioning kidney	III: Radiation with concurrent platinum-based chemotherapy
IV: The carcinoma extends beyond the true pelvis or involves (biopsy proven) the mucosa of the bladder or rectum	IVA: same as for stage III
IVA: spread to adjacent organs	IVB: palliative chemotherapy, with palliative radiation for local symptoms such as bleeding or pain
IVB: distant metastases	

Gastroenterological Malignancies

Colorectal Cancer

This section discusses staging through follow-up and prognosis of patients with colorectal cancer. Epidemiology, pathophysiology, risk factors, and clinical manifestations will be discussed in MKSAP 17 Gastroenterology and Hepatology. Colorectal cancer screening is discussed in MKSAP 17 General Internal Medicine.

Colorectal cancer is a common malignancy in both men and women in developed countries and is second only to lung cancer as a cause of cancer-related deaths in the United States. Symptoms and signs of bowel disease include bleeding per rectum, melena, persistent cramping or bloating, and chronic diarrhea or constipation and may indicate the presence of a

benign polyp, another nonmalignant process, or cancer. Such symptoms and signs warrant investigation regardless of age.

Colorectal cancer is a cancer of the large intestine. The most distal 12 to 15 centimeters of the large intestine, the portion below the peritoneal reflection and therefore within the pelvis, is referred to as the rectum; the rest of the organ is referred to as the colon. Metastatic disease from either the colon or the rectum is referred to as colorectal cancer. The need for a permanent colostomy is one of the most common fears in patients in whom colorectal cancer is diagnosed, and usually this fear is unfounded.

KEY POINT

- The need for a permanent colostomy is one of the most common fears in patients in whom colorectal cancer is diagnosed, and usually this fear is unfounded.

Staging

The preoperative staging workup should include a complete colonoscopy (if technically feasible) and contrast-enhanced CT scans of the chest, abdomen, and pelvis. Preoperative measurement of serum carcinoembryonic antigen (CEA) levels is also routinely done. PET scans have not been demonstrated to improve preoperative staging and should not be used routinely. Patients with local or locoregional rectal cancer require further preoperative staging with endorectal ultrasonography or a pelvic MRI to assess the depth of tumor penetration (T stage), degree of lymph node involvement (N stage), and any metastasis (M stage).

Staging using the TNM cancer staging system is the most accurate predictor of outcome in patients with colorectal cancer (**Table 58**).

KEY POINT

HVC
- PET scans have not been demonstrated to improve preoperative staging in patients with colorectal cancer and should not be routinely used.

TABLE 58: Staging of Colorectal Cancer

Stage	Description	Approximate 5-Year Disease-Free Survival
I	Tumor does not invade the full thickness of bowel wall (T1, T2); lymph nodes not involved (N0)	90%-95%
II	Tumor invades full thickness of the bowel and may invade into pericolonic or perirectal fat (T3, T4); lymph nodes not involved (N0)	70%-85%
III	One or more lymph nodes involved with cancer (N1, N2); any T stage	25%-70%
IV	Metastatic tumor spread to distant site (M1); any T stage; any N stage	0%-10%

Surgical Management

Colon Cancer

Patients with colon cancer without preoperative evidence of metastatic disease should undergo surgical resection of the primary tumor and the regional lymph nodes. Surgery of the colon should almost never result in a need for permanent colostomy, although a temporary colostomy, usually reversed after a few months, may be needed for emergent surgery due to obstruction or perforation or if the bowel is not evacuated properly before surgery. Surgery involving tumors of the upper two thirds of the rectum also should only very rarely require permanent colostomy, although temporary ostomies may be needed more frequently. Patients with colon cancer confirmed as stage I at surgery require no further treatment. In stage II colon cancer, data do not show a clear survival advantage for administration of adjuvant chemotherapy; consequently, surgery alone is acceptable standard practice for most patients. An exception is patients with stage II colon cancer with characteristics associated with a high risk for recurrence (T4 disease and inadequate lymph node sampling [<12 lymph nodes examined], lymphovascular invasion, poorly differentiated histology, or clinical perforation or obstruction). In these patients, the prognosis is similar to that of patients with stage III disease, and adjuvant chemotherapy may be appropriate.

Rectal Cancer

Patients with rectal tumors that are not full thickness and do not have lymph node involvement (stage I) on pretreatment imaging usually undergo surgery, with a total mesorectal excision being the preferred procedure. The mesorectum is a fatty sheath covering the rectum that contains the regional lymph nodes. A total mesorectal excision entails a sharp dissection of the pelvis outside of the mesorectum to allow removal of the mesorectum fully intact en bloc with the rectum. However, considerable expertise is required to avoid complications with this procedure, which should be performed only by a subspecialized surgeon. If local lymph node metastases or full-thickness tumor penetration is found after surgery in those patients thought to be stage I preoperatively, then postoperative chemotherapy and radiation therapy are indicated. Otherwise, if pathology confirms stage I cancer, no further therapy is needed. In patients with tumors that are too distal to permit an adequate margin of resection without resection of the anal sphincter muscles, an abdominal-peritoneal resection is likely to be required, which results in a permanent colostomy. Patients who have full-thickness rectal tumors (T3-T4) or clearly enlarged lymph nodes on preoperative imaging require combined-modality therapy with neoadjuvant radiation and chemotherapy and adjuvant chemotherapy alone. More recently, an accepted alternative has been chemotherapy first, followed by chemoradiotherapy, and then surgery, with no postoperative treatment ("total neoadjuvant therapy").

KEY POINTS

- Patients with colon cancer without preoperative evidence of metastatic disease should undergo surgical resection of the primary tumor and the regional lymph nodes.
- Treatment for patients with rectal tumors that are not full thickness and with no lymph node involvement (stage I) on pretreatment imaging is usually surgery alone.

Adjuvant Treatment of Colorectal Cancer

Colon Cancer

The first drug successfully used for adjuvant treatment of colorectal cancer was 5-fluorouracil (5-FU), and this agent, now in its sixth decade of clinical use, remains at the center of current treatment strategies. Newer drugs are most typically used in combination with 5-FU. 5-FU is usually given with the reduced folate leucovorin, which is inactive alone but causes 5-FU to bind more tightly to its target enzyme. Capecitabine is an oral prodrug that is converted to 5-FU in the body. Use of this agent requires a highly reliable, motivated patient who is able to adhere to a complex oral medication schedule. In patients with stage III disease, adjuvant 5-FU–based chemotherapy given for approximately 6 months after surgery has been shown to reduce the risk of cancer recurrence and death; therefore, all patients with stage III disease, regardless of age, should receive adjuvant chemotherapy barring specific medical or psychiatric contraindications. The FOLFOX (leucovorin, 5-FU, and oxaliplatin) regimen and the CAPOX (capecitabine plus oxaliplatin) regimens have been shown to be modestly but statistically significantly more effective than the same regimens without oxaliplatin in patients with stage III disease (but not in those with stage II disease); these two regimens are equally acceptable. Not all drugs that are useful for treating metastatic disease are active in the adjuvant setting. Irinotecan, bevacizumab, and cetuximab have all been shown to be ineffective in improving survival in the adjuvant setting, yet, as discussed below, all are part of standard treatment of metastatic disease. For patients with stage II disease and a high risk for recurrence, treatment with 5-FU/leucovorin or capecitabine may be appropriate. Whether the addition of oxaliplatin in patients with high-risk stage II disease is appropriate has been challenged by recent data, and patient care must be individualized based on the extent of risk factors for recurrence and the patient's overall medical condition. Although no definitive standards exist, a consensus statement from the American Society of Clinical Oncology recommends that all patients with stage II colon cancer consult with a medical oncologist to discuss the risks and benefits of adjuvant treatment.

Rectal Cancer

Radiation therapy is not routinely indicated for completely resected colon cancer. However, because of the anatomic location of rectal cancer and the difficulty in obtaining adequate tumor-free margins, local recurrence rates tend to be higher than those for completely resected colon cancer. Therefore, neoadjuvant chemoradiotherapy is indicated in patients with locally advanced (T3-T4) rectal cancer, in addition to adjuvant therapy. Clinical trials have established that 5-FU given by protracted intravenous infusion or capecitabine is an equally acceptable chemotherapeutic option to be given concurrently with radiation therapy. Data evaluating the addition of oxaliplatin during radiation have been disappointing, and this therapy is not currently recommended. The FOLFOX or CAPOX regimen is typically used after neoadjuvant chemoradiotherapy and surgery for approximately 4 months to complete a total of approximately 6 months of therapy (inclusive of pre- and postoperative treatments). More recently, use of this 4-month combination chemotherapy as an initial treatment, followed by chemoradiation and then surgery, has become an acceptable alternative.

KEY POINTS

- Adjuvant 5-fluorouracil–based chemotherapy given for approximately 6 months after surgery reduces the risk of cancer recurrence and death in patients with stage III colon cancer.
- For patients with stage II colon cancer and a high risk for recurrence, the prognosis is similar to that for patients with stage III disease, and treatment with 5-fluorouracil/leucovorin or capecitabine may be appropriate.
- Neoadjuvant and adjuvant chemotherapy is indicated in patients with stage III or IV rectal cancer.

Metastatic Disease

Most patients with stage IV colorectal cancer have treatable, but not curable, disease. A long disease-free interval, a limited number of metastases, and metastases confined to a single organ (such as liver or lung) are favorable prognostic factors. A few such patients may have disease amenable to curative surgical resection. Patients with a limited number of liver-only lesions (≤3) have been reported to have long-term disease-free survival rates of 25% to 50% in selected studies. Results are less encouraging as the number of lesions increases. Otherwise, the primary treatment modality is chemotherapy. 5-FU, often modified by the reduced folate leucovorin, is the basis of most chemotherapy regimens used in colorectal cancer. Often, the drugs oxaliplatin or irinotecan are added to these agents. The FOLFOX regimen or the 5-FU, leucovorin, and irinotecan (FOLFIRI) regimen are equally acceptable. Bevacizumab, a monoclonal antibody against vascular endothelial growth factor (VEGF), modestly improves outcome when added to chemotherapy regimens. Recent data support the use of either continued bevacizumab or ziv-aflibercept, another anti-VEGF agent, together with second-line chemotherapy.

All patients with metastatic colorectal cancer should undergo tumor genotyping to identify mutations in the K-*ras* and N-*ras* genes because the anti-epidermal growth factor receptor antibodies, cetuximab and panitumumab, are inactive in the 50% of tumors that harbor mutations. Cetuximab and panitumumab typically cause an acneiform rash, which can be uncomfortable and socially debilitating; however, for reasons that remain unclear, antitumor activity and the development of rash are tightly correlated, and patients who do not experience a substantial skin rash are extremely unlikely to benefit from these agents.

KEY POINTS

- In some patients, metastatic colorectal cancer confined to a single organ may be curable with surgical resection of the primary tumor and metastasis.
- 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin are used to treat patients with metastatic colorectal cancer.
- Bevacizumab, a monoclonal antibody against vascular endothelial growth factor, modestly improves outcome in patients with metastatic colon cancer when added to chemotherapy regimens.
- All patients with metastatic colorectal cancer should undergo tumor genotyping to identify mutations in the K-*ras* and N-*ras* genes because the anti-epidermal growth factor receptor antibodies, cetuximab and panitumumab, are inactive in the 50% of tumors that harbor mutations.

Postoperative Surveillance

The role of postoperative surveillance in patients with colorectal cancer, regardless of whether postoperative therapy has been given, is to identify surgically curable recurrence, such as oligometastatic liver disease or lung metastases, rather than to assess for more disseminated disease. Treatment of small-volume, widely metastatic, but asymptomatic, disease discovered on surveillance has not been associated with improved outcomes and may subject patients to significant treatment toxicity. CT scans of the chest, abdomen, and pelvis are recommended annually for at least the first 3 years postoperatively. PET scanning should not be used for routine surveillance but may be used to further evaluate an equivocal finding on CT scans in some patients. Colonoscopy is typically recommended 1 year after resection, 3 years later, and then every 5 years unless abnormalities are found. The main purpose of colonoscopy is to identify new polyps rather than survey for local recurrence, which is relatively rare. Serum CEA levels are measured every 3 to 6 months for the first 2 years, and then every 6 months, to complete a total of 5 years. The finding of abnormal serum CEA levels, if testing has been repeated and confirmed, warrants additional investigation, as it may indicate recurrent disease. However, therapy should not be started based on serum CEA elevation alone.

KEY POINTS

- Postoperative surveillance of patients with colorectal cancer includes CT scans of the chest, abdomen, and pelvis annually for at least the first 3 years postoperatively and colonoscopy 1 year after resection, 3 years later, and then every 5 years with the goal of identifying surgically curable recurrence.
- Treatment of small-volume, widely metastatic, but asymptomatic, disease discovered on surveillance has not been associated with improved outcomes and may subject patients to significant treatment toxicity. HVC
- PET scanning should not be used for routine surveillance of patients with colorectal cancer but may be used to further evaluate an equivocal finding on CT scans in some patients. HVC

Anal Cancer

Anal cancer is an epidermoid, or squamous cell carcinoma, in contradistinction to rectal cancer, which is an adenocarcinoma. Anal cancers are typically associated with human papillomavirus (HPV) infection and also have increased incidence in patients with HIV infection. Whereas current management of rectal cancer uniformly involves surgical resection, anal cancer is often curable with radiation therapy and concurrent chemotherapy with mitomycin plus 5-FU. This chemotherapeutic regimen was established in the 1970s, and results of studies that have explored newer, alternative agents have not demonstrated improved outcomes. Anal tumors may continue to regress for at least 6 months up to 1 year after completion of chemoradiation therapy. Therefore, treatment failure should not be declared unless unequivocal growth or metastases are documented after completion of radiation therapy. Salvage surgery is performed in patients with local tumor growth after radiation plus chemotherapy; however, this procedure necessarily removes the sphincter muscle, thus requiring a permanent colostomy.

See MKSAP 17 General Internal Medicine for discussion of HPV vaccination.

KEY POINTS

- Anal cancer is often curable with radiation therapy and concurrent chemotherapy with mitomycin plus 5-fluorouracil.
- Because anal tumors may continue to regress for 6 months to 1 year following completion of radiation therapy, treatment failure should not be declared unless unequivocal growth or metastases are documented after completion of radiation therapy.

Pancreatic Cancer

To determine the extent of disease in pancreatic cancer, clinicians use the American Joint Committee on Cancer (AJCC) TNM cancer staging system. To determine treatment approach, exocrine pancreatic cancer is typically classified based on whether it is surgically resectable, borderline resectable, or either locally advanced or metastatic unresectable disease.

Resectable tumors are confined to the pancreas or just beyond it that correspond to stage IA (tumor limited to the pancreas and ≤2 cm in diameter), IB (tumor limited to the pancreas but >2 cm in diameter), and IIA (tumor extension beyond the pancreas but without involvement of the celiac axis) without involved lymph nodes or evidence of metastatic disease.

Borderline resectable pancreatic cancer is that which extends to nearby blood vessels but that may be removed completely with surgery, such as some stage III tumors (involving the celiac axis or superior mesenteric artery with or without involved lymphadenopathy) without evidence of metastatic disease.

Unresectable cancers cannot be removed entirely by surgery and may include locally advanced disease that has not yet spread to distant organs but still cannot be completely surgically removed (stage IIB [localized tumor or with extension beyond the pancreas but with associated involved lymph nodes] and most stage III cancers).

Metastatic cancer has spread to distant organs and might involve surgery to ameliorate symptoms, but surgery cannot excise the tumor completely or cure the cancer.

Surgical resection is the only potential curative intervention for pancreatic cancer. Patients with a clinical presentation and CT or MRI scans consistent with a resectable pancreatic cancer should undergo definitive resection of the pancreatic mass. Endoscopic or percutaneous needle biopsy should not be attempted prior to definitive surgery, as these procedures have a high false-negative rate in this setting, and would therefore not change management; a suspicious pancreatic mass would require resection whether the needle biopsy showed cancer or not. Although only 15% to 20% of cases are considered resectable at presentation and the overall cure rate in patients undergoing surgical resection is low, patients without evidence of metastatic disease who appear to have resectable disease should undergo resection because it is the only potentially curative option. For patients with locally unresectable disease, neoadjuvant chemoradiation remains controversial.

Postoperative adjuvant therapy with chemotherapy, local radiation, or the combination is also controversial.

For decades, gemcitabine alone was considered an appropriate standard treatment for metastatic pancreatic cancer. More recently, a combination regimen of oxaliplatin, irinotecan, 5-FU, and leucovorin (FOLFIRINOX), has been shown to provide better outcomes; however, this regimen has substantial toxicity and is only a reasonable option in patients who are both medically well (have an excellent performance status) and who are highly motivated. A more recent trial has shown that the addition of liposomally encapsulated paclitaxel (nab-paclitaxel) to gemcitabine also improves outcome modestly, albeit with some increased toxicity.

KEY POINT

- Patients with pancreatic cancer without evidence of metastatic disease who have technically resectable disease should undergo resection because it is the only potentially curative option.

Gastroesophageal Cancer

This section discusses treatment of patients with gastroesophageal cancer. Epidemiology, risk factors, and clinical manifestations of esophageal cancer are discussed in MKSAP 17 Gastroenterology and Hepatology, Disorders of the Esophagus. The same aspects of gastric cancer are discussed in MKSAP 17 Gastroenterology and Hepatology, Disorders of the Stomach and Duodenum.

Staging of gastroesophageal cancer is based on the TNM cancer staging system. In simple terms, stage I disease is a superficial lesion that has not spread and does not penetrate the full thickness of the esophagus or stomach wall, whereas stage II disease is a full-thickness lesion. Stage III disease is defined by spread to locoregional lymph nodes, and stage IV disease is defined by the presence of distant metastatic disease. Virtually all gastric and gastroesophageal junction cancers are adenocarcinomas, as are approximately 95% of esophageal cancers. About 5% of esophageal cancers are of squamous cell histology, although currently, patients with adenocarcinomas and squamous cell carcinoma receive the same treatments.

Although only 30% to 40% of patients have potentially resectable disease at presentation, patients with local and locoregional disease (AJCC stages I, II, and III) are typically treated surgically. Unfortunately, recurrence rates are high and cure rates with surgical resection remain low. Studies have shown that administration of neoadjuvant chemotherapy improves outcome to a modest, but statistically significant, degree. The addition of preoperative radiation therapy, as well as chemotherapy, is also supported by some—although less robust—clinical data. As such, surgery alone is no longer the preferred approach, and neoadjuvant chemotherapy or chemoradiation therapy is routinely used.

Because of the low cure rates for locoregional therapy for esophageal cancer, chemotherapy has been added to many treatment regimens, and many patients are currently treated with combination chemoradiation therapy following surgery for resectable disease. However, the optimal treatment regimen and the overall effectiveness of different treatment approaches have not yet been established.

Treatment of metastatic (stage IV) gastroesophageal cancer remains unsatisfactory and palliative. Numerous agents